INFORMATION TO USERS

This manuscript has been reproduced from the microfilm master. UMI films the text directly from the original or copy submitted. Thus, some thesis and dissertation copies are in typewriter face, while others may be from any type of computer printer.

The quality of this reproduction is dependent upon the quality of the copy submitted. Broken or indistinct print, colored or poor quality illustrations and photographs, print bleedthrough, substandard margins, and improper alignment can adversely affect reproduction.

In the unlikely event that the author did not send UMI a complete manuscript and there are missing pages, these will be noted. Also, if unauthorized copyright material had to be removed, a note will indicate the deletion.

Oversize materials (e.g., maps, drawings, charts) are reproduced by sectioning the original, beginning at the upper left-hand corner and continuing from left to right in equal sections with small overlaps. Each original is also photographed in one exposure and is included in reduced form at the back of the book.

Photographs included in the original manuscript have been reproduced xerographically in this copy. Higher quality 6" x 9" black and white photographic prints are available for any photographs or illustrations appearing in this copy for an additional charge. Contact UMI directly to order.

UMI

A Bell & Howell Information Company
300 North Zeeb Road, Ann Arbor MI 48106-1346 USA
313/761-4700 800/521-0600

STRUCTURE AND DYNAMICS OF T-BUTYLCALIX[4]ARENE-GUEST COMPOUNDS

by

ERIC BERTRAND BROUWER

B.Sc. (Hons.), *Queen's University at Kingston*, 1990

M.Sc., *The University of British Columbia*, 1992

A THESIS SUBMITTED in PARTIAL FULFILLMENT of the REQUIREMENTS for
the DEGREE of DOCTOR of PHILOSOPHY

in

THE FACULTY of GRADUATE STUDIES and RESEARCH

DEPARTMENT of CHEMISTRY

CARLETON UNIVERSITY

OTTAWA, CANADA

September 1996

© Copyright

Eric Bertrand Brouwer, 1996

National Library
of Canada

Acquisitions and
Bibliographic Services

395 Wellington Street
Ottawa ON K1A 0N4
Canada

Bibliothèque nationale
du Canada

Acquisitions et
services bibliographiques

395, rue Wellington
Ottawa ON K1A 0N4
Canada

Your file Votre référence

Our file Notre référence

The author has granted a non-exclusive licence allowing the National Library of Canada to reproduce, loan, distribute or sell copies of this thesis in microform, paper or electronic formats.

The author retains ownership of the copyright in this thesis. Neither the thesis nor substantial extracts from it may be printed or otherwise reproduced without the author's permission.

L'auteur a accordé une licence non exclusive permettant à la Bibliothèque nationale du Canada de reproduire, prêter, distribuer ou vendre des copies de cette thèse sous la forme de microfiche/film, de reproduction sur papier ou sur format électronique.

L'auteur conserve la propriété du droit d'auteur qui protège cette thèse. Ni la thèse ni des extraits substantiels de celle-ci ne doivent être imprimés ou autrement reproduits sans son autorisation.

0-612-22160-1

We, the undersigned, recommend to the Faculty of Graduate Studies and Research the
acceptance of the thesis

**STRUCTURE AND DYNAMICS OF T-
BUTYLCALIX[4]ARENE-GUEST COMPOUNDS**

submitted by

ERIC BERTRAND BROUWER, B.Sc., M.Sc.

in partial fulfillment of the requirements for the degree of Doctor of Philosophy

.....
Chair, Department of Chemistry

.....
Thesis Supervisor

.....
External Examiner

CARLETON UNIVERSITY

ABSTRACT

Structural and dynamic features of the solid-state *p-tert*-butylcalix[4]arene-guest inclusion compounds are examined by X-ray diffraction (XRD) and solid-state nuclear magnetic resonance (NMR) studies in a synoptic fashion. The insight into short-range order from NMR data complements the long-range order XRD data, and gives increased resolution of the structural difficulties commonly seen with calixarene-guest compounds. The nature of and the role played by host-guest interactions are discussed.

The *p-tert*-butylcalix[4]arene-toluene compound is re-examined with the synoptic approach, and several new features emerge: the host *t*-butyl positional disorder is 50:50, and results from space-averaging of two C_2 -symmetric cavity orientations at $T < 205\text{K}$ and dynamic disordering at $T > 205\text{K}$; the toluene is tilted off the calixarene symmetry axis; a small fraction of toluene sits with the methyl group out of the cavity; and the barrier to 2-fold guest rotation is $E_{\text{act}} = 34.0 (3.1) \text{ kJ mol}^{-1}$. An attractive $\text{CH}_{\text{guest}}-\pi_{\text{host}}$ interaction accounts for the methyl-inserted guest orientation in the cavity.

Most *p-tert*-butylcalix[4]arene compounds with organic guests prefer a 4-fold symmetric structure, but a guest-induced distortion of the host geometry (with no calixarene symmetry features) occurs with nitrobenzene. α -Pinene distorts the host geometry as a consequence of its chirality.

The importance of $\text{CH}_{\text{host}}-\pi_{\text{guest}}$ interactions is challenged with the *p-tert*-butylcalix[4]arene-aliphatic system. Change in guest ^{13}C chemical shift values from solution to inclusion indicates the orientation of the guest in the cavity. Long-chained *n*-alkanes adopt a 2:1 host:guest geometry. Pentane and cyclohexane guest dynamics are probed by ^2H NMR. Substitution of a small fraction of nitrobenzene guest sites by small gas molecules generates a calixarene system with two guests. The cavity environment is probed with ^{129}Xe NMR, which is sensitive to cavity geometry and symmetry. The change

in ^{13}C chemical shift for the methane compound indicates that the guest experiences significant host ring current effects. Nitrobenzene orientation and compound symmetry can be tuned by the presence of propane in the lattice. The structure and dynamics of the *p-tert*-butylcalix[4]arene compounds of benzene and pyridine are compared: while structurally similar, the guests display distinct motional behavior.

ACKNOWLEDGEMENTS

The past three years have been an extremely enjoyable period of my life. I have thoroughly enjoyed the opportunities given me over the course of my doctoral studies. Many people, in particular those at the Steacie Institute for Molecular Sciences at the National Research Council, have contributed in varied ways to this work, and I would like to take this opportunity to thank them.

First of all, I thank my thesis supervisor Dr. John Ripmeester for his encouragement, enthusiasm, guidance, freedom and perspective: I appreciate our discussion and pondering about many topics both inside and outside of science. I thank Drs. Chris Ratcliffe and Gary Enright for their contributions in NMR and single-crystal XRD respectively, as well as their careful reading of my thesis; Dr. Igor Moudrokovski for his contributions in NMR as well as his computer software acumen; Dr. Gary Lee for many discussions and fun in the lab; Drs. Keith Preston, John Tse, Dennis Klug, John Morton, and Eric Gabe for support and direction, as well as Dr. G. Buchanan at the Carleton University end of things.

Experimental work requires much technical support, and Jamie Bennett, Graham MacLaurin and Mike Vandenhoff of NRC have been more than excellent; thank you Jamie for the patience and enthusiasm to teach students such as myself. Fellow students Xu Zhu, Andrew Szabo, Luyi Ding have also made this time of learning exciting.

I thank the people of Canada for financial support in the form of a post-graduate PGS-B NSERC scholarship, as well as their past and ongoing support for the National Research Council. Thank-you also to Carleton University for various forms of financial support.

And finally, I thank those closest to me: my wife Brenda for her love, support and encouragement over the past two years; my parents Henry and Jane; and siblings Laura, Brenda, Darren and Duane. *Sola Dei Gloria.*

TABLE OF CONTENTS

Title Page	i
Acceptance Form	ii
Abstract	iii
Acknowledgements	v
Table of Contents	vi
List of Tables	xii
List of Figures	xiv
Vita	xix
 CHAPTER ONE: Calixarenes and Guest Inclusion	 1
1. Introduction: Supramolecular Chemistry	1
2. Calixarenes: History, Definition, Behavior, and Applications	2
2.1 Definition	2
2.2 History	3
2.3 Behavior	4
2.4 Applications	8
3. Calix[<i>n</i>]arene-Guest Inclusion Properties	9
3.1 Structural Studies	9
3.2 Disorder	9
3.3 Host-Guest Interactions	11
3.4 Structure and Modeling	16
3.5 Structure and Modeling: A Case Study	18
4. Thesis	21
5. References	23

CHAPTER TWO: Physical Techniques	30
1. Introduction	30
2. Single Crystal X-Ray Diffraction	32
2.1 X-rays	32
2.2 Crystals and Symmetry	33
2.3 Determination of the Crystal Structure	34
2.4 Quality of XRD Structural Data	35
3. Solid-State Nuclear Magnetic Resonance (NMR) Spectroscopy	36
3.1 Interactions in NMR Spectroscopy	39
3.2 The Zeeman Interaction	41
3.3 The Quadrupolar Interaction: ^2H NMR Spectroscopy	42
3.4 The Direct Dipolar Interaction	50
3.5 The Chemical Shielding Interaction	54
3.6 The Indirect Dipolar Interaction	61
3.7 The NMR Experiment	62
4. Summary	63
5. References	63
6. Figures	65
 CHAPTER THREE: <i>p-tert</i> -Butylcalix[4]arene-Toluene	 73
1. Introduction	73
2. Synthetic Details	75
3. Structural Studies: Solid-State ^1H and ^{13}C NMR Spectroscopy	77
3.1 ^{13}C CP-MAS NMR Spectroscopy	77
3.2 The Toluene C-1' Resonance at 230K	78
3.3 The Toluene C-1' Resonance at 115K	79
3.4 Toluene Insertion in the Calixarene Cavity	82
3.5 ^1H CRAMPS NMR Spectroscopy	82

3.6 Summary	84
4. Structural Studies: Single-Crystal X-ray Diffraction	84
4.1 Structural Features	87
4.2 Position of the Guest	90
4.3 Superlattice Peaks	93
5. Dynamic Studies: ^1H NMR Spectroscopy	95
5.1 Motion of the Guest	96
5.2 Motion of the Calixarene Host	101
5.3 Summary of Motion in C4A-Toluene	103
6. Structural Differences Induced by Isotopic Guests	105
6.1 FT-IR Spectroscopy	106
6.2 ^{13}C CP-MAS NMR Spectroscopy	108
7. CH- π Interactions in C4A-Toluene and C4A-Chlorobenzene	108
8. Summary	110
9. References	112
10. Figures	115
11. Appendix: X-Ray Diffraction Structural Data	136
 CHAPTER FOUR: Asymmetry of <i>p-tert</i> -Butylcalix[4]arene-Guest Compounds	 139
1. Introduction	139
2. Synthetic Details	141
3. Structural Studies: ^{13}C CP-MAS NMR Spectroscopy	141
3.1 Four-Fold Symmetric C4A-Guest Compounds	141
3.2 C4A-Guest Compounds with < Four-Fold Symmetry	149
3.3 Chiral-Induced Structural Differences: C4A- α -Pinene	151
4. Structural Studies: Single Crystal X-ray Diffraction	155
4.1 C4A-($\pm$)-3-methylcyclopentanone	155
4.2 C4A-(<i>R</i>)-(+)-3-methylcyclopentanone	156

4.3 <i>p-tert</i> -Butylcalix[4]arene-Nitrobenzene	158
5. Dynamic Studies	163
5.1 VT ^2H NMR Studies of C4A-NB- d_5	163
6. FT-IR Spectroscopy of C4A-Nitrobenzene	165
7. Summary	165
8. References	167
9. Figures	170
10. Appendix: X-Ray Structural Data	187
 CHAPTER FIVE: <i>p-tert</i> -Butylcalix[4]arene-Aliphatic Compounds	189
1. Introduction	189
2. Synthetic Details	192
3. Solid-State ^{13}C CP-MAS Spectroscopy	193
3.1 Guest Dynamics in the Calixarene Cavity	195
3.2 ^{13}C NMR Spectral Simulation: HYPERNMR	197
4. Single Crystal X-ray Diffraction	198
4.1 Crystallographic Evidence for C-H $\cdots\pi$ Interactions	199
4.2 <i>p-tert</i> -Butylcalix[4]arene-Cyclohexane	200
4.3 <i>p-tert</i> -Butylcalix[4]arene- <i>n</i> -Pentane	202
4.4 C4A-ClB and C4A-BrB	204
5. ^2H NMR Spectroscopy: Guest Dynamics	205
5.1 <i>p-tert</i> -Butylcalix[4]arene-Cyclohexane- d_{12}	206
5.2 <i>p-tert</i> -Butylcalix[4]arene- <i>n</i> -Pentane- d_{12}	208
6. Summary	213
7. References	214
8. Figures	217
9. Appendix: X-Ray Diffraction Structural Details	230

CHAPTER SIX: <i>p-tert</i> -Butylcalix[4]arene Gas Clathrates	231 A
1. Introduction	231
2. Synthetic Details	233
3. <i>p-tert</i> -Butylcalix[4]arene Double Guest Systems	234
3.1 <i>p-tert</i> -Butylcalix[4]arene-Nitrobenzene-Xenon	234
3.2 <i>p-tert</i> -Butylcalix[4]arene-Nitrobenzene-Methane	242
3.3 C4A-NB-Guest Compounds; Guest = CO, CO ₂ , SO ₂ , C ₂ H ₄ , C ₂ H ₆	242
3.4 Conclusion	244
4. A Tunable <i>p-tert</i> -Butylcalix[4]arene-Nitrobenzene-Propane Lattice	245
4.1 ¹³ C CP-MAS NMR Spectroscopy	246
4.2 Single Crystal X-Ray Diffraction Study of C4A-Nitrobenzene-Propane	247
4.3 ² H NMR Spectroscopy: Nitrobenzene Motion	249
4.4 Double Guests and the Host Lattice	251
5. Summary	253
6. References	254
7. Figures	256
8. Appendix: Single-Crystal X-ray Diffraction Structural Data	266
CHAPTER SEVEN: <i>p-tert</i> -Butylcalix[4]arene Compounds with Nitrogen-Containing Guests	269
1. Introduction	269
2. <i>p-tert</i> -Butylcalix[4]arene-Guest (Guest = Pyridine, Benzene)	271
2.1 ¹³ C CP-MAS NMR Spectroscopy	273
2.2 ² H NMR Spectroscopy	274
2.3 ¹⁵ N NMR Spectroscopy	282
2.4 Single Crystal X-Ray Diffraction	285
3. <i>p-tert</i> -Butylcalix[4]arene + Amines	291
3.1 <i>tert</i> -Butylamine and <i>sec</i> -Butylamine: Weakly Interacting Guests	293

3.2 Benzylamine + C4A: Distortion of the Calixarene Framework	293
3.3 Ammonia + C4A	294
3.4 1,4-Diaminobutane: a Bifunctional Amine	295
3.5 Basicity vs. Sterics	296
4. Summary	298
5. References	299
6. Figures	303
7. Appendix	321

LIST OF TABLES

CHAPTER ONE

1. XRD structural studies of cone-shaped <i>p-tert</i> -butylcalix[<i>n</i>]arene compounds.	12

CHAPTER THREE

1. Summary of C4A-Toluene ¹³ C NMR Chemical Shifts (in ppm).	81
2. ¹ H NMR chemical shifts for the guest in C4A-Toluene (in ppm).	83
3. Crystallographic data for C4A-TOL at 150 and 290K, and C4A-1-CLBZ.	86
4. Selected Bond Distances and Angles for C4A-TOL-150.	90
5. ² H NMR spectral parameters for C4A-TOL.	98
6. Toluene deuteration and ¹³ C NMR chemical shift, δ (ppm).	108

CHAPTER FOUR

1. Guest ¹³ C NMR chemical shifts (in ppm) of symmetric C4A-guest compounds.	144
2. Guest ¹³ C NMR chemical shifts (in ppm) of asymmetric C4A-guest compounds.	149
3. ¹³ C NMR Chemical shift values for α -pinene.	153
4. XRD structural parameters for C4A-guest compounds (guest = R+3MCP, 3MCP, ($\pm$)- α -pinene, (<i>I</i> R)-(+)- α -pinene).	156
5. Crystallographic data for C4A-NB.	158
6. Selected Bond Distances and Angles for C4A-NB.	163
7. ² H NMR spectral parameters for C4A-NB.	164

CHAPTER FIVE

1. Guest ¹³ C NMR chemical shifts (in ppm) of C4A-aliphatic compounds.	195
2. Crystallographic data for C4A-PT, C4A-CY, C4A-ClB and C4A-BrB.	201
3. Selected Bond Distances and Angles for C4A-CY.	202
4. Selected Bond Lengths and Angles for C4A-PT.	203
5. ² H NMR spectral parameters for C4A-CY- <i>d</i> ₁₂ .	206

6. ^2H NMR spectral parameters for C4A-PT- d_{12} .	208
--	-----

CHAPTER SIX

1. ^{129}Xe chemical shift values in various environments.	235
2. ^{129}Xe CP NMR spectral simulation parameters.	239
3. Crystallographic data for C4A-NB $_{0.83}$ -Xe $_{0.17}$ and C4A-NB $_{0.64}$ -PROP $_{0.36}$.	240
4. Selected Bond Distances and Angles for C4A- NB $_{0.83}$ -Xe $_{0.17}$.	241
5. Symmetry of C4A-Guest Structures (where guest = aliphatic or gaseous).	245
6. Selected Bond Distances and Angles for C4A- NB $_{0.64}$ -PROP $_{0.36}$.	248
7. ^2H NMR spectral parameters for β -C4A-NB.	249

CHAPTER SEVEN

1. Guest Chemical Shifts (in ppm) in C4A compounds.	273
2. ^2H Lineshape components of C4A-Bz- d_6 as a function of temperature.	275
3. The static quadrupole coupling constant (χ) and static asymmetry parameter (η) for benzene in different crystalline environments.	275
4. ^2H NMR lineshape components of C4A-Py- d_5 as a function of temperature.	279
5. The ^{15}N chemical shift (δ) and shielding (σ) anisotropy parameters (in ppm) for pure pyridine- ^{15}N (168K) and p- <i>tert</i> -butylcalix[4]arene-pyridine- ^{15}N (290K).	284
6. Crystallographic data for C4A-Benzene and C4A-Pyridine.	286
7. Selected Bond Distances for C4A-Benzene.	288
8. Selected Bond Distances and Angles for C4A-Pyridine.	290
9. Basicity of Amines.	297

LIST OF FIGURES

CHAPTER ONE

1. Conformations of <i>p-tert</i> -butylcalix[4]arene.	5
2. Functional modification of calixarenes.	6
3. Dimensions of the <i>p-tert</i> -butylcalix[4]arene cavity.	7
4. Representation of the <i>p-tert</i> -butylcalix[4]arene-toluene (C4A-TOL) structure.	10
5. The Lennard-Jones (12,6) potential.	15
6. Tetrasulfonate derivative of calix[4]resorcarene.	16
7. Relationship between structural data, modeling and the resulting insight.	17
8. XRD data for <i>p-tert</i> -butylcalix[4]arene tetraamide compounds.	19
9. The synoptic approach to structure and dynamics in solids	22

CHAPTER TWO

1. Angular momentum vectors illustrating the quantum numbers l and m .	65
2. The effects of a $(\pi/2)_x$ pulse on the magnetization vector $\mathbf{M}_0$.	65
3. Energy level diagram of a spin = l nucleus in a magnetic field.	66
4. Diagram showing the polar angles θ and ϕ made by the magnetic field vector in the principal axis system of the electric field gradient tensor.	66
5. ^2H NMR powder lineshapes as a function of the asymmetry parameter η .	67
6. Diagram showing the three rotations through the Euler angles α , β and γ .	68
7. The effects of molecular motion on ^2H NMR lineshapes.	69
8. The quadrupolar echo pulse sequence.	68
9. The ^{13}C NMR spectra of solid methanol β -quinol clathrate.	70
10. Motion of the principal components of a CSA tensor.	71
11. A diagram of the cross-polarization pulse sequence.	71

CHAPTER THREE

1. Representation of the <i>p-tert</i> -butylcalix[4]arene-toluene structure.	115
2. 50.3 MHz ^{13}C CP-MAS NMR spectra of C4A-toluene at 292 and 115K.	116
3. Expansion of the 50.3 MHz ^{13}C CP-MAS NMR spectrum of C4A-TOL at 115 K.	117
4. Two inequivalent <i>t</i> -butylphenol groups of a 2-fold symmetric C4A cavity.	118
5. <i>p-tert</i> -butylcalix[4]arene-toluene structures below the phase transition.	119
6. High field region of the 50.3 MHz ^{13}C CP-MAS NMR spectrum of C4A-TOL.	120
7. 300 MHz ^1H CRAMPS spectrum of <i>p-tert</i> -butylcalix[4]arene-toluene at 292K.	120
8. ORTEP of <i>p-tert</i> -butylcalix[4]arene-toluene at 150 K.	121
9. ORTEP of <i>p-tert</i> -butylcalix[4]arene-toluene at 150 K.	122
10. C4A chirality arising from the direction of the phenolic OH bonds.	123
11. The nature of disorder in <i>p-tert</i> -butylcalix[4]arene-toluene- d_5 .	123
12. Observed and simulated 30.7 MHz ^2H NMR spectra of C4A-TOL- d_5 .	124
13. <i>p-tert</i> -Butylcalix[4]arene-toluene- d_5 : ^2H signal intensity as a function of $\ln \kappa$. Arrhenius plot of the 2-fold guest flip in <i>p-tert</i> -butylcalix[4]arene-toluene- d_5 .	125
14. ^2H NMR lineshape components as a function of temperature for C4A-toluene- d_5 .	126
15. Observed and simulated 30.7 MHz ^2H NMR spectra of C4A-TOL- d_5 .	127
16. Arrhenius plot of the 4-fold guest flip in <i>p-tert</i> -butylcalix[4]arene-toluene- d_5 .	128
17. <i>p-tert</i> -Butylcalix[4]arene-toluene dynamics.	129
18. Observed and simulated 30.7 MHz ^2H NMR spectra of <i>t</i> -butyl- d_9 -C4A-TOL.	130
19. Orientation and motion of the deuterated <i>t</i> -butyl- d_9 group in C4A-toluene.	131
20. FT-IR spectra of C4A-toluene isotopomers.	132
21. The calix conformation affected by ring-deuteration of the guest.	131
22. 45.3 MHz ^{13}C CP-MAS NMR spectra of C4A-toluene isotopomers.	133
23. 75.2 MHz ^{13}C CP-MAS NMR spectrum of C4A-chlorobenzene at 290K.	134
24. XRD structure of C4A-chlorobenzene.	135

CHAPTER FOUR

1. 75.5 MHz ^{13}C CP-MAS NMR spectrum of C4A-2,6-lutidine at 290K.	170
2. 45.3 MHz ^{13}C CP-MAS NMR spectrum of C4A-(<i>R</i>)-(+)-3-methylcyclopentanone.	171
3. 5-Membered ring guest positions in the 4-fold symmetric calixarene cavity.	172
4. 50.3 MHz ^{13}C CP-MAS NMR spectra of C4A-racemic-3-methylcyclopentanone.	173
5. 50.3 MHz ^{13}C CP-MAS NMR spectra of C4A-($\pm$)- <i>sec</i> -phenethylalcohol.	174
6. 45.3 MHz ^{13}C CP-MAS NMR spectrum of <i>p-tert</i> -butylcalix[4]arene-nitrobenzene.	175
7. 45.3 MHz ^{13}C CP-MAS NMR spectrum of <i>p-tert</i> -butylcalix[4]arene-4-nitrotoluene.	176
8. 45.3 MHz ^{13}C CP-MAS NMR spectrum of <i>p-tert</i> -butylcalix[4]arene-3-nitrotoluene.	177
9. Enantiomers of α -pinene.	178
10. 50.3 MHz ^{13}C CP-MAS NMR spectra of <i>p-tert</i> -butylcalix[4]arene- (1 <i>R</i>)-(-)- α -pinene and <i>p-tert</i> -butylcalix[4]arene-racemic-($\pm$)- α -pinene.	179
11. 50.3 MHz ^{13}C CP-MAS NMR spectra of C4A-(1 <i>R</i>)-(-)- α -pinene and C4A-racemic-($\pm$)- α -pinene: Expansion of the guest resonances.	180
12. Consequence of chirality on <i>c</i> -axis for C4A- α -pinene.	181
13. ORTEP of C4A-NB with H atoms excluded for clarity.	182
14. Stereo view of the crystal packing in C4A-NB.	183
15. Stereo view of C4A-NB along <i>c</i> ; two layers of calixes are shown.	183
16. Observed and simulated 46.1 MHz ^2H NMR spectra of C4A-NB- <i>d</i> ₅	184
17. Arrhenius Plot of <i>p-tert</i> -butylcalix[4]arene-nitrobenzene- <i>d</i> ₅ .	185
18. FT-IR spectra of C4A-NB and C4A-NB- <i>d</i> ₅ .	186

CHAPTER FIVE

1. 75.4 MHz ^{13}C CP-MAS NMR spectrum of C4A- <i>n</i> -pentane at 290K.	217
2. 75.4 MHz ^{13}C CP-MAS NMR spectra of C4A- <i>n</i> -butane at 290K.	218
3. 75.4 MHz ^{13}C CP-MAS NMR spectrum of empty and C4A-propane at 290K.	219
4. 50.3 MHz ^{13}C CP-MAS NMR spectra of C4A-pentane at 290K and 90K.	220
5. Possible structures for C4A-aliphatic compounds.	221

6. Observed ^{13}C CP-MAS NMR and calculated ^{13}C NMR spectra for C4A-pentane.	222
7. ORTEP of <i>p-tert</i> -butylcalix[4]arene-cyclohexane.	223
8. ORTEP of <i>p-tert</i> -butylcalix[4]arene-pentane.	224
9. ORTEP of <i>p-tert</i> -butylcalix[4]arene-1-chlorobutane.	225
10. Variable temperature 46.1 MHz ^2H NMR spectra of C4A-cyclohexane- d_{12} .	226
11. Cyclohexane motion.	227
12. Variable temperature 30.7 MHz ^2H NMR spectra of C4A-pentane- d_{12} .	228
13. Plot of the C4A-pentane- d_{12} ^2H lineshape components as a function of temperature.	229
14. Scheme of end-over-end pentane motion.	230

CHAPTER SIX

1. 45.3 MHz ^{13}C CP-MAS NMR spectrum of <i>p-tert</i> -butylcalix[4]arene-nitrobenzene-Xe.	256
2. 49.8 MHz ^{129}Xe CP NMR spectrum of <i>p-tert</i> -butylcalix[4]arene-nitrobenzene-Xe.	257
3. The two C4A cavities formed by the 0.6:0.4 <i>t</i> -butyl disordering.	258
4. Single-crystal XRD Structure of <i>p-tert</i> -butylcalix[4]arene-nitrobenzene-Xe.	259
5. Illustration of the Xe position in the <i>p-tert</i> -butylcalix[4]arene cavity.	258
6. 45.3 MHz ^{13}C CP-MAS NMR spectrum of C4A-nitrobenzene- $^{13}\text{CH}_4$.	260
7. 45.3 MHz ^{13}C CP-MAS NMR spectra of C4A-NB-ethane and C4A-NB-ethene.	261
8. 45.3 MHz ^{13}C CP-MAS NMR spectrum of C4A-NB-SO ₂ .	262
9. ^{13}C CP-MAS NMR spectra of C4A-NB _{<i>x</i>} -P _{<i>1-x</i>} compounds.	263
10. ORTEP of β- <i>p-tert</i> -butylcalix[4]arene-nitrobenzene-propane.	264
11. Variable temperature 46.1 MHz ^2H NMR spectra of β-C4A-NB- d_5 -propane.	265

CHAPTER SEVEN

1. <i>p-tert</i> -Butylcalix[<i>n</i>]arene compounds with pyridine.	303
2. 45.3 MHz ^{13}C CP-MAS NMR spectra of C4A-pyridine and C4A-benzene.	304
3. 75.4 MHz ^{13}C CP-MAS NMR spectrum of C4A-2,6-dimethylpyridine.	305
4. VT 27.6 MHz ^2H NMR spectra of <i>p-tert</i> -butylcalix[4]arene-benzene- d_6 .	306

5.	109K observed and simulated ^1H NMR spectra for C4A-benzene- d_6 .	307
6.	VT 46.1 MHz ^2H NMR spectra of p- <i>tert</i> -butylcalix[4]arene-pyridine- d_5 .	308
7.	Observed and simulated FML spectra for p- <i>tert</i> -butylcalix[4]arene-pyridine- d_5 .	309
8.	30.4 MHz ^{15}N CP NMR spectra of p- <i>tert</i> -butylcalix[4]arene-pyridine- ^{15}N .	310
9.	30.4 MHz ^{15}N CP-MAS NMR spectra of p- <i>tert</i> -butylcalix[4]arene-pyridine- ^{15}N .	311
10.	Orientation of the ^{15}N CSA Tensor Components for C4A-Pyridine- ^{15}N .	312
11.	Single crystal X-ray diffraction structure of p- <i>tert</i> -butylcalix[4]arene-benzene.	313
12.	Single crystal X-ray diffraction structure of p- <i>tert</i> -butylcalix[4]arene-pyridine.	314
13.	Local host environment around the guest pyridine nitrogen.	315
14.	Proton transfer between the calixarene hydroxyl group and an amine guest.	315
15.	50.3 MHz ^{13}C CP-MAS NMR spectra of p- <i>tert</i> -butylcalix[4]arene compounds formed with <i>sec</i> -butylamine and <i>tert</i> -butylamine.	316
16.	45.3 MHz ^{13}C CP-MAS NMR spectra of p- <i>tert</i> -butylcalix[4]arene-benzylamine.	317
17.	The <i>exo</i> - and <i>endo</i> - structures of p- <i>tert</i> -butylcalix[4]arene-benzylamine.	318
18.	45.3 MHz ^{13}C CP-MAS NMR spectra of p- <i>tert</i> -butylcalix[4]arene-ammonia.	319
19.	45.3 MHz ^{13}C CP-MAS NMR spectra of C4A-1,4-diaminobutane.	320

VITA

EDUCATION

Natural Sciences Program, *Redeemer College*, Ancaster, ON (1985-1988)
B.Sc. (Honours Chemistry, First Class) *Queen's University*, Kingston, ON (1988-90)
M.Sc. (Chemistry, First Class) *University of British Columbia*, Vancouver, BC (1990-92)
Ph.D. Candidate (Chemistry) *National Research Council-Carleton University*, Ottawa, ON (1993-96)

AWARDS and SCHOLARSHIPS

Honours Scholarship, *Redeemer College*, 1985-88
NSERC Summer Research Award, *McMaster University*, 1987
Major James H. Rattray Scholarship, *Queen's University*, 1989-90
Charles A. McDowell Fellowship, *University of British Columbia*, 1990-91
UBC Graduate Fellowship Supplement, *University of British Columbia*, 1990-92
NSERC Postgraduate Scholarship, *University of British Columbia*, 1990-92
NSERC Postgraduate Scholarship, *Carleton University*, 1993-95
1st Prize (Physical Chemistry), *Ottawa-Carleton Chemistry Institute Poster Competition*, 1994
2nd Prize (Physical Chemistry), *Ottawa-Carleton Chemistry Institute Poster Competition*, 1996
NSERC Postdoctoral Fellowship 1996-1998

EXPERIENCE

1993-96	Ph.D. Thesis (J. Ripmeester) <i>Carleton University-National Research Council</i>
1993-96	Teaching Assistant (Year-I, -II Chemistry) <i>Carleton University</i>
1993	Lecturer (Year-I, -II Chemistry) <i>Redeemer College</i>
1990-92	M.Sc. Thesis (P. Legzdins) <i>University of British Columbia</i>
1990-92	Teaching Assistant (Year-I Chemistry) <i>University of British Columbia</i>
1990	Research Assistant <i>National Research Council</i> , Ottawa (J. Ripmeester, J. Tse)
1989-90	Honours Theses <i>Queen's University</i> : (i) Organometallic Chemistry (M. Baird) (ii) Physical Organic Chemistry (E. Bunce, P. Kazmaier (<i>Xerox Canada</i>))
1989	Research Assistant <i>DLR-European Space Agency</i> , Koln, Germany
1988	Research Assistant <i>Canada Centre for Inland Waters</i> , Burlington, ON
1986-87	Research Assistant <i>Dept. of Biochemistry, McMaster University</i>

WORKSHOPS

1. *NATO Advanced Research Workshop: Crystals: Supramolecular Materials*, Sestri Levante, Italy. September 1995.
2. *2nd Workshop on Neutron Powder Diffraction*, AECL Chalk River Laboratories, Chalk River, ON. May 1994.

PUBLICATIONS

1. Brouwer, E.B.; Enright, G.D.; Ripmeester, J.A. Solid-State NMR and Diffraction Studies of a Tunable p-tert-Butylcalix[4]arene-Guest Structure. *J. Am. Chem. Soc.*, manuscript in progress.
2. Brouwer, E.B.; Ripmeester, J.A.; Enright, G.D. t-Butylcalix[4]arene Host-Guest Compounds: Structure and Dynamics. *J. Incl. Phenom.*, in press.
3. Brouwer, E. B.; Enright, G. D.; Ripmeester, J. A. π -Methyl Interactions and t-Butylcalix[4]arene-Guest Stability: NMR and Crystallographic Studies of Cyclohexane and n-Pentane Inclusion Compounds. *Supramol. Chem.* **1996**, *7*, 143-145.
4. Brouwer, E. B.; Enright, G. D.; Ratcliffe, C. I.; Ripmeester, J. A. Dynamic Recognition in Solids: a Synoptic Approach to Structure Determination in t-Butylcalix[4]arene-Toluene. *Supramol. Chem.* **1996**, *7*, 79-83.
5. Brouwer, E. B.; Enright, G. D.; Ripmeester, J. A. Guest-Induced Asymmetry in the Structure of t-Butylcalix[4]arene-Nitrobenzene. *Supramol. Chem.* **1996**, *7*, 7-9.
6. Ripmeester, J.A.; Ratcliffe, C.I.; Enright, G.D.; Brouwer, E.B. Thermodynamic and Resonance Studies of Structural Changes in Crystals. *Acta Cryst.*, **1995**, *B51*, 513-522.
7. Brouwer, E. B.; Legzdins, P.; Rettig, S. J.; Ross, K. J. Facile Nitrosyl N-O Bond Cleavage upon Thermolysis of Cp*W(NO)Ph₂. *Organometallics*, **1994**, *13*, 2088-2091.
8. Brouwer, E. B.; Legzdins, P.; Rettig, S. J.; Ross, K. J. Insertions of Heterocumulenes into the M-C σ -Bonds of Cp*M(NO)(aryl)₂ (M = Mo, W) Complexes. *Organometallics*, **1993**, *12*, 4234-4240.

CHAPTER 1: Calixarenes and Guest Inclusion

1. <i>Introduction: Supramolecular Chemistry</i>	1
2. <i>Calix[n]arenes: History, Definition, Behavior, and Applications</i>	2
2.1 <i>Definition</i>	2
2.2 <i>History</i>	3
2.3 <i>Behavior</i>	4
2.4 <i>Applications</i>	8
3. <i>Calix[n]arene-Guest Inclusion Properties</i>	9
3.1 <i>Structural Studies</i>	9
3.2 <i>Disorder</i>	9
3.3 <i>Host-Guest Interactions</i>	11
3.4 <i>Structure and Modeling</i>	16
3.5 <i>Structure and Modeling: A Case Study</i>	18
4. <i>Thesis</i>	21
5. <i>References</i>	23

1. Introduction: Supramolecular Chemistry

An aspect of supramolecular chemistry is the investigation of the interactions of a substrate, or guest, by a molecular receptor, or host. Supramolecular chemistry is rooted in Emil Fischer's 1894 *Schloss-Schlüssel-Prinzip* (lock-and-key principle) with which he explained the interaction of a substrate with an enzyme. The enzyme contains a binding site that uniquely fits the shape of its substrate, and molecular recognition of the substrate by the enzyme depends on its shape and geometry.¹ The inception of supramolecular chemistry as a separate field can be traced back to Davy's discovery of clathrate hydrates in 1811^{2a} and more recently to Pedersen's discovery of metal ion complexation by crown ethers in the 1960's.^{2b}

Supramolecular species may have multiple functional features, including catalysis, transport, and recognition.³ An active area of research in this last field is based on an understanding of host-guest interactions and the factors that control the stability of these compounds. An understanding of these interactions can further knowledge of existing

receptors and hosts. The relatively simple calixarene host system is a versatile host candidate for probing molecular recognition interactions with a variety of guests. This thesis examines the difficulties in determining the dominant factors in molecular recognition.

2. Calix[*n*]arenes: Definition, History, Behavior and Applications

2.1 Definition

Calix[*n*]arenes are cyclic oligomers ($n = 4-8$) formally derived from phenol and formaldehyde. The optimized synthetic procedure involves the base-catalyzed condensation of alkylphenols and aqueous formaldehyde, as outlined in reaction (1):⁴

In addition to the major tetrameric product illustrated above, higher order macrocycles ($n = 5-8$) are also produced in small yields.

Because of the similarity between the cone-shaped cyclic tetramers and a type of Greek vase known as a *calix crater*, and the fact that the oligomers contain aromatic rings, these compounds were named calix[*n*]arenes by Gutsche.⁵ The number of repeat units *n* in the oligomer is indicated in the square brackets. The systematic calixarene nomenclature is particularly cumbersome: the formal name for the R = *t*-butyl tetramer in reaction (1) is 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrahydroxycalix[4]arene, or if

described in terms of a $[1_n]$ metacyclophane, is 5,11,17,23-tetra-*tert*-butylpentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}] octacosal-1(25),3,5,7-(28),9,11,13-(27),15,17,19(26)-21,23-dodecane-25,26,27,28-tetrol. More commonly used is a naming convention in which the aromatic phenol substituent prefixes “calix[*n*]arene” followed by the hydroxyl substituent(s), if any.

2.2 History

The history of calixarenes has been described in detail by Gutsche in several review articles.⁵⁻⁸ Of particular relevance to this dissertation is how the calixarene story unfolds in the context of synthetic developments leading those in physical characterization.

In 1872, von Baeyer reported the hard, resinous, non-crystalline product obtained upon heating aqueous aldehyde and phenol; the material was not characterized any further. In the early part of this century, Baekeland modified the von Baeyer synthesis to give a product that was a tough, resilient resin (known as a phenoplast). He marketed the product under the name “Bakelite” which generated tremendous commercial success. In the following three decades, research into phenoplasts was primarily carried out by industry, and focused on optimizing the synthetic processes and the commercial applications of these materials. Research into the curing process led Zinke in the late 1940s to isolate insoluble, high melting-point products to which a cyclic tetrameric structure was assigned. Zinke was the first to notice the ability of these materials to form molecular complexes with smaller molecules. Much of the research in the 1950s and 1960s focused on the types of products resulted from modifications of the condensation reaction. The inclusion of smaller molecules by these materials suggested a type of molecular cavity, and led Gutsche to consider these materials as enzyme mimics.^{5,9} It was not until 1979 that the single-crystal X-ray diffraction study of the toluene inclusion

compound of *p*-*tert*-butylcalix[4]arene by Andreetti¹⁰ led to the unambiguous assignment of the tetrameric structure as well as the inclusion property of the calix cavity.

Subsequently, the ease with which new, functionalization calix compounds can be synthesized, and the development of the cavity for commercial applications has driven calixarene research.

2.3 Behavior

Calixarenes are white solids that are readily prepared from a one-pot synthesis.⁴ They possess higher melting points (> 300 °C) and much lower solubilities than their acyclic phenolic counterparts.

The behavior of calixarenes in solution was explored in detail before the elucidation of the solid-state behavior. The conformational isomerism of the flexible macro-ring was first demonstrated by dynamic ¹H NMR studies.¹¹⁻¹³ Four structural isomers are possible for the calix[4]arene: the cone, partial cone, 1,2-alternate, 1,3-alternate (Figure 1). In solution, the cone interconverts by sequential inversion of each of the four phenolic subunits (Equation 2).^{14a} The cone conformation is the preferred conformation due to the cooperative hydrogen-bonded ring of OH groups at the lower rim of the calixarene.^{14b}

The free energies of activation $\Delta G^\ddagger$ for the conformational inversion of calixarenes is solvent-dependent and ranges from 57.3 to 65.7 kJ mol⁻¹.¹⁵ A low value of $\Delta G^\ddagger$ in pyridine is due to the weakening of hydrogen bonding at the base of the calix cone.

FIGURE 1. Conformations of p-*tert*-butylcalix[4]arene (clockwise from top left): cone, partial cone, 1,2-alternate, 1,3-alternate.

The transient nature of the calixarene cavity due to its flexibility limited the use of the calixarene system as a molecular receptor. By modifying the phenolic function on the lower rim of the calixarene (Figure 2), the conformation interconversion is sterically hindered, and one cavity conformation (such as the cone) may be enforced.¹⁶ Common lower-rim modifications include the following functional groups: alkyl,¹⁷ carbonate,^{18,19} acetate,^{20,20a} ester,^{20a,21} amide,²² ketone,¹⁹ bipyridyl,²³ as well as chiral alkyl groups²⁴

appended to the phenolic oxygen. Substitution at all sites is common, but partial modification is also possible.²⁵ The four conformational isomers (Figure 1) have been characterized in the solid state by single crystal X-ray diffraction.²⁶

FIGURE 2. Functional modification of calixarenes can occur on the lower (R) or upper (R') rims.

In addition to fixing the calix cavity into the cone conformation, substitution at the lower rim may also serve to incorporate additional cavities onto the calix molecular platform such as: crown ethers to give calixcrowns,^{20a,27-29} mono- and bicyclic macrocycles to give calixspherands,^{29,30} resorcin[4]arenes to give carceplexes,^{31,32} cyclodextrins,³³ as well as different-sized calixarenes.³⁴ These modifications can enhance the inclusion ability and solubility of the calixarene-based supermolecules.

One of the unique features of the calixarene system is that it possesses a cavity that is able to include a variety of guests. The cavity possesses two openings: the lower rim has a diameter of 3.8 Å whereas the upper rim is 10.1 Å wide (Figure 3). The cavity is 3.7 Å deep, and provides ample room for the inclusion of small molecules. Several X-ray diffraction structures of *p-tert*-butylcalix[4]arene show that guests occupy the calix pocket (Table 1): toluene,¹⁰ anisole,³⁵ dimethylsulphoxide,³⁶ and acetonitrile;³⁷ other guests include chloroform,⁹ benzene,⁹ and *p*-xylene.³⁸ The depth of the cavity can be extended by

placing longer alkyl groups on the upper rim.³⁹ The absence of upper-rim substituents curtails the inclusion ability of the cavity.⁴⁰

FIGURE 3. Dimensions of the 4-fold symmetric *p*-*tert*-butylcalix[4]arene cavity.

Ionic guests also are included in the calixarene cavity. Most alkali metal ions form compounds with *p*-*tert*-butylcalix[4]arene or its derivatives. Cesium sits deep in the *p*-*tert*-butylcalix[4]arene cavity along with a neutral acetonitrile solvent molecule.⁴¹ Other alkali ionic guests include sodium,^{17,21} potassium,^{22,28} rubidium,^{29,30} and calcium.⁴² The ionophoric calix cavity can be tailored to enhance the selectivity for a specific cation.^{43–45} Lanthanide and actinide metal cations also form compounds with calixarenes,^{36,46–49} as do transition^{50–58} and main group metals.^{59–61}

A variety of non-alkyl substituents may be placed on the calixarene upper rim. Hydrophilic groups such as the sulfonate group at the *para*-position impart water-solubility to the calix[4]arene, and lead to a rich and varied inclusion chemistry.^{62–65}

2.4 Applications

The structural and functional versatility of calixarenes has been developed into a wide range of applications,^{66,67} and is currently a very active area of research. Well over 600 publications have appeared in little more than three years, as indicated by a keyword search (on the word “calixarene”) of the Current Contents database. In addition, nearly 100 patents have been taken out on calixarene-based systems.⁶ What follows is a brief summary of some of the varied applications of calixarenes.

A system for the recovery of cesium from radioactive waste by *p-tert*-butylcalix[8]arene has been patented.⁶⁸ Modification of the calix by a crown-6-ether leads to a more Cs-specific ionophore.⁶⁹ Modified calixarenes can also be used as metal ion sequestering and phase-transfer agents,^{42,43,66} and can be incorporated into ion selective electrodes.⁷⁰ The separation of isomeric xylenes has been effected by *p*-alkylcalix[4]arenes: *p-iso*-propylcalix[4]arene shows a high specificity for *p*-xylene;⁶⁶ calixarenes can also be incorporated into chromatographic supports.^{66a,66b} The use of alkyl ammonium derivatives of *p*-nitrocalix[*n*]arenes (*n* = 4,6) as a catalyst for the hydrolysis of *p*-nitrophenyl dodecanoate is one of the rare examples of a calix-based catalyst system.⁷¹ The use of *p*-nitrocalix[4]arenes as molecules for second-order non-linear optics exploits the conical macro-ring geometry to align four donor-acceptor molecules.^{72,73} Functionalized calix[4]arenes have been used to transport urea through a liquid membrane.⁷⁴ Functionalized calix[4]arenes have also been used to form kinetically stable complexes with radioactive Rb⁺ with the goal of organ imaging.³⁰ In a rather different application, *p*-[(dialkylamino)-methyl]calix[*n*]arenes (*n* = 4-7) have been employed to stabilize quantum-confined CdS clusters in the solid-state.⁷⁵ Recently, two groups have investigated the water-soluble *p*-sulfonatocalix[4]arene system as a fluorescent detection system for the neurotransmitter acetylcholine.^{76,77} Finally, the 1,3-alternate-calix[4]arene

system can be linked in an extended array to generate a type of nano-tube for the transportation of metal ions.⁷⁸ This diverse list of applications indicates the wide range and versatility of calixarene based chemistry both in the solid and solution states.

3. Calix[n]arene-Guest Inclusion Properties

The majority of calixarene studies have focused on the applications of calixarenes and the synthetic versatility of this system. The techniques of solution ¹H nuclear magnetic resonance (NMR) spectroscopy and single-crystal X-ray diffraction (XRD) crystallography have been sufficient to study host:guest binding constants, and to establish the inclusion nature of the solid state. It will be argued that the current state of structural and dynamics characterization is insufficient for the type of insight necessary to develop a rigorous model of host-guest interactions in the calixarene system.

3.1 Structural Studies

The XRD study of the toluene compound of *p-tert*-butylcalix[4]arene (C4A-TOL) by Andreotti in 1979, showed toluene inserted methyl-first into the calixarene cavity with its long molecular axis aligned with the calixarene 4-fold symmetric axis (Figure 4).¹⁰ This report was a key discovery as it identified the C4A tetramer as a cone-shaped host for the toluene guest. The observation that calixarene molecules formed inclusion compounds in a manner similar to cyclodextrins⁷⁹ and other host systems laid the foundation for the extension of guest:host supramolecular chemistry concepts to the calixarene system.

3.2 Disorder

The structural model developed in this initial study was hampered by the presence of disorder and large thermal parameters, and is therefore limited in its information

FIGURE 4. Representations of the *p*-*tert*-butylcalix[4]arene-toluene (C4A-TOL) structure.

concerning the non-bonding interactions between the host and the guest. The toluene guest (with 2-fold molecular symmetry) satisfies the 4-fold symmetry requirement of the calixarene by showing a 2-fold disorder about its molecular symmetry axis. Less understood is a complex positional disorder of the *t*-butyl groups of the calixarene in which the *t*-butyl methyl groups occupy two sites in a 77:23 ratio. The 77:23 ratio is a puzzling one which is difficult to relate to specific interactions between the toluene and the calixarene. The *R*-value (which gauges the agreement of the structural model to the diffraction intensities⁸⁰) of the structure was only 0.092 ($R_w = 0.086$). Many subsequent publications acknowledge the problem of the disordered *t*-butyl groups in this and other *p*-*tert*-butylcalix[*n*]arene structures.^{7,8,31,38,41,81-88}

The presence of disordered *t*-butyl groups in *p*-*tert*-butylcalix[*n*]arene structures is widespread: disorder in the *t*-butyl group has been found in most *p*-*tert*-butylcalix[*n*]arene ($n = 4-8$) compounds for which a single crystal XRD structure has been determined. Furthermore, the guest is often disordered over several positions. Consequently, XRD

structures of *p-tert*-butyl-calix[*n*]arene compounds are characterized by large *R*-values (Table 1). In contrast, organic crystals without disorder or large thermal parameters typically refine to $R < 0.05$, and the *R*-values tabulated in Table 1 indicate a shortcoming in the modeling of calixarene-guest diffraction data. Many of the structures with low *R*-values contain heavy atoms which dominate the X-ray scattering and minimize the effects of *t*-butyl and guest disorder.

Several detailed experiments have been carried out to clarify the problem of disorder, but no conclusive results were obtained. Neutron powder diffraction studies of C4A-TOL and the 2:1 C4A-*p*-xylene compounds were carried out at 4.2 K in an attempt to freeze out any dynamic disorder, but failed to resolve the *t*-butyl disorder.^{38,83-85} Space groups and lattice parameters identical to the corresponding XRD data were determined. Variable temperature (1.8-96K) inelastic neutron scattering spectra of C4A-TOL were collected to probe the dynamics of the toluene guest motions. The authors tentatively propose that the toluene methyl group may occupy two inequivalent sites, and that the structure may differ from the room temperature structure.^{38,83-85}

3.3 Host-Guest Interactions

Lehn has made the analogy that “supermolecules are to molecules and the intermolecular bond what molecules are to atoms and the covalent bond.”³ In supramolecular chemistry, then, examination of interactions between molecules considers non-bonding interactions such as hydrogen-bonding, electrostatic interactions, and the van der Waals interactions, rather than ionic and covalent bonding interactions. While the energies of the non-bonding interactions are several orders less than those of the bonding interactions, their importance in determining structure and behavior is not insignificant. Rather, for most biological systems, it is precisely the non-bonding interactions, and the

TABLE 1. Single-crystal XRD studies of cone-shaped *p*-*tert*-butylcalix[*n*]arene compounds.

Host	Guest	<i>R</i>	Ref
t-Bucalix[4]arene	toluene	0.092	10
t-Bucalix[4]arene	anisole	0.073	35*
t-Bucalix[4]arene	DMSO	0.11	36
t-Bucalix[4]arene	MeCN	0.052	37*
[Cs][t-Bucalix[4]arene]	MeCN	0.048	41
[NEt ₄][t-Bucalix[4]arene]	MeCN, H ₂ O	0.083	88*
[NEt ₄][t-Bu(dihomooxa)calix[4]arene]	MeCN	0.067	88
t-Bu(dihomooxa)calix[4]arene	2•Et ₃ N	0.069	89
t-Bu(dihomooxa)calix[4]arene	2•THF	0.086	90
t-Bucalix[4]arene, 1,3-crown-bridged	pyridine	0.12	28
t-Bucalix[4]arene tetracarbonate	MeCN	0.075	91
t-Bucalix[4]arene, 1,3-dimethoxy	empty	0.064	92
t-Bucalix[4]arene, trimethoxy	empty	0.067	92
t-Bucalix[4]arene, tetramethoxy	empty	0.16	92
[t-Bucalix[4]arene tetramethoxy][Al]	toluene, Na ⁺	0.090	17
t-Bucalix[4]arene diquinone	Na ⁺	0.090	93
t-Bucalix[4]arene, Ti	toluene	0.067	94
t-Bucalix[4]arene, Fe	NH ₃ , hexane	0.083	94
t-Bucalix[4]arene, Co ₃	toluene, THF	0.14	94
[MoO][t-Bucalix[4]arene]t-Bucalix[4]arene	NB, H ₂ O	0.055	51
[K-t-Bucalix[4]arene][picrate]	CH ₂ Cl ₂	0.106	30
t-Bucalix[4]arene tetraMeO, <i>m</i> -terphenyl	empty	0.12	30
[Rb-1,3-diMeO-t-Bucalix[4]arene, crown-6][picrate]	empty	0.106	29
1,3-dimethoxyl-t-Bucalix[4]arene crown-5	empty	0.14	44
1,3-diethoxy-t-Bucalix[4]arene crown-5	K ⁺	0.107	44
[Li][t-Bucalix[4]areneP(H)NMe ₂]	2•THF	0.072	60*
t-Bucalix[4]arene, 2-pyridylmethoxy	ethanol	0.074	95
[ZrMe ₂][(MeO) ₂ t-Bucalix[4]arene]	empty	0.052	58
t-Bucalix[4]arene, ethylacetate	0.5•H ₂ O	0.106	43
t-Bucalix[4]arene, methylacetate	empty	0.078	43
t-Bucalix[4]arene, methylketone	acetone	0.094	43
t-Bucalix[4]arene, tetraethylacetate	water	0.106	20*
t-Bucalix[4]arene, tetra-Buacetate	empty	0.12	21*
t-Bucalix[4]arene, tetraketone	acetone	0.094	19
t-Bucalix[4]arene, tetraamide	CH ₃ OH	0.101	22
t-Bucalix[4]arene, tetraamide	KCSN, MeOH	0.113	96
t-Bucalix[4]arene, tetraamide	KI, MeOH	0.158	96
[t-Bucalix[4]arene, (bipy) ₂ (py) ₂ Cu][PF ₆]	3•toluene	0.132	23
[ZrMe ₂ (BzC ₂ H ₅)][(MeO) ₂ t-Bucalix[4]arene]	5•benzene	0.080	58
[{Ir(η ⁵ -Cp*)} ₂ (t-Bucalix[4]arene)][BF ₄] ₃	MeNO ₂ , ether	0.057	97*

TABLE 1 *continued*

Host	Guest	<i>R</i>	Ref
t-Bu(pyridylMe)oxydihydroxycalix[4]arene	ethanol	0.074	98
t-Bu(deoxy)calix[4]arene, monoMe ether	BrCH ₂ Cl	0.176	25
[W(phenato) ₂][t-Bucalix[4]arene]	self-inclusion	0.036	99
t-Bucalix[5]arene	tetralin, 2•EtOH	0.081	100
t-Bucalix[5]arene, trisferrocenoyl ester	2•EtOH, 3•H ₂ O	0.094	101
t-Bucalix[5]arene-crown-5	MeCN	0.125	102
t-Bucalix[6]arene	benzene	0.12	103
t-Bucalix[6]arene	MeCN	0.113	104
t-Bucalix[6]arene	empty	<i>high</i>	105
t-Bucalix[6]arene, ethylacetate	empty	0.078	43
[Al ₃ Me ₉][t-Bucalix[6]arene]	toluene, 2•THF	0.073	106
t-Bucalix[6]arene, Ti[Cl ₂] μ -O)TiCl ₃] ₂	4•toluene	0.094	50
[(Me ₃ N) ₂][t-Bucalix[6]arene]	MeCN, 3•H ₂ O	0.139	107
t-Bucalix[7]arene	3•pyridine	0.096	108
t-Bucalix[8]arene	pyridine	0.169	109
t-Bucalix[8]arene	8•pyridine	0.116	110
t-Bucalix[8]arene, octaacetoxy	empty	0.087	111
t-Bucalix[8]arene	C ₆₀	---	112

* no t-butyl disorder reported; bipy = bipyridine, Bu = butyl, Cp* = C₅Me₅, DMSO = dimethylsulphoxide.
Et = ethyl, Me = methyl, NB = nitrobenzene, py = pyridine.

delicate balance among them, that make life possible. The importance of the hydrogen bond in biological systems has been described in detail, and also plays a significant role in host-guest supramolecular chemistry.¹¹³

When hydrogen bonding, which involves the proton-bridged electrostatic interaction between two electronegative atoms, is absent from a host-guest system such as the calixarenes, other van der Waals interactions become significant:

1. Dipole-dipole: When two polar molecules are close together, they are attracted to each other in such a way that their dipoles are aligned head-to-tail. The interaction energy between two polar molecules in the gas or liquid phase averaged over all orientations with dipole moments μ_1 , μ_2 separated by distance R is:

$$E_{D-D} = -\left(\frac{2}{3kT}\right)\left(\frac{1}{R^6}\right)\left(\frac{\mu_1\mu_2}{4\pi\epsilon_o}\right)^2 \quad (3)$$

where ϵ_o is the vacuum permittivity. The energy of the dipole-dipole interaction goes as the inverse sixth power of the distance. At 25 °C for two molecules with $\mu = 1$ D and $R = 3$ Å, $E_{D-D} = -1.4$ kJ mol⁻¹.

2. Dipole-induced dipole: A polar molecule near a polarizable (polar or non-polar) molecule induces a dipole in the latter which causes an attractive force between the two. The energy of this interaction depends on the dipole moment of the first molecule μ_1 and the polarizability volume α_2 of the second molecule:

$$E_{D-ID} = \left(\frac{1}{R^6}\right)\left(\frac{\mu_1^2\alpha_2}{4\pi\epsilon_o}\right) \quad (4)$$

For two molecules, one with $\mu = 1$ D and the other with $\alpha = 10 \times 10^{-24}$ cm³ (like benzene) separated by $R = 3$ Å, $E_{D-ID} = -0.8$ kJ mol⁻¹.

3. Induced dipole-induced dipole (dispersion): When two non-polar molecules are near each other, an instantaneous dipole in the first may induce a distribution of electron density in the second to give an instantaneous dipole moment. The London equation is a reasonable estimation of E_{ID-ID} :

$$E_{ID-ID} = -\left(\frac{1}{R^6}\right)\left(\frac{1}{2}\alpha_1\alpha_2\left[\frac{I_1I_2}{I_1+I_2}\right]\right) \quad (5)$$

where I_1 and I_2 are the ionization energies of the two molecules.

The van der Waals interactions are taken to be pair-wise additive, and can be summed over all interacting molecules. To model the van der Waals interactions, both attractive and repulsive forces must be taken into account. A hard sphere potential assumes that the potential energy V rises abruptly to infinity once the interacting particles

come within some separation σ called the collision diameter. The (12,6) Lennard-Jones potential is widely used, and is written in the form:

$$V = 4\epsilon \left[\left(\frac{\sigma}{R} \right)^{12} - \left(\frac{\sigma}{R} \right)^6 \right] \quad (6)$$

where σ is the separation where $V = 0$, ϵ represents the depth of the potential well, and the well minimum occurs at $R_e = 2^{1/6}\sigma$ (Figure 5).¹¹⁴

FIGURE 5. The Lennard-Jones (12,6) potential.

4. C-H... π Hydrogen bonding: Knowledge of the solid-state structure of calix-guest compounds leads to insight about the guest position, as well as the relevant contacts between host and guest. Two features of the initial structures led to the development of the concept of attractive C-H... π hydrogen bonds between the methyl groups of the host and the π system of the guest:¹¹⁵ (1) the necessity of the upper-rim alkyl groups for guest inclusion, and (2) only guests with an aromatic π -system seemed to form stable calix-guest compounds.

FIGURE 6. Tetrasulfonate derivative of calix[4]resorcarene.

More recent work suggests the importance of attractive $\text{C-H}\cdots\pi$ hydrogen bonds between the π system of the host and the C-H bonds of the guest.¹¹⁶ ^1H NMR studies of hydrophilic guest molecules and calix[4]resorcarene show that complexation is promoted by electron-withdrawing substituents on the guest and electron-donating substituents in the host (Figure 6). The aromatic system of the *p-tert*-butylcalix[4]arene host contains three alkyl and one hydroxy substituents: these groups are known to be electron-donating,¹¹⁷ and make the host π -basic. Electron-withdrawing substituents on the guest increase the acidity of the guest C-H bonds, and strengthen the attractive $\text{C-H}\cdots\pi$ hydrogen bonds between the π system of the host and the C-H bonds of the guest. The upfield (deshielding) change in the guest ^1H and ^{13}C NMR chemical shift values upon calix inclusion indicates the magnitude of this interaction.^{116,118} The $\text{C-H}\cdots\pi$ hydrogen bonding interaction is described as a polarization-induced dipole interaction. The preference of the π -basic host for C-H rather than N-H or O-H bonds is rationalized in terms of the hardness/softness of acids and bases.

3.4 Structure and Modeling

The combination of the presence of *t*-butyl and guest disorder, as well as large thermal parameters gives large R -values in the above structures. Consequently, the

existence and nature of the stabilizing non-bonding interactions (which require highly accurate structural data) between the host calixarene and its various guests are poorly understood. Since modeling of host-guest interactions in calixarene compounds^{28,92,119-122} is based on the above structural information, the use of models to understand and to predict behavior in calixarene (and in general, supramolecular) chemistry by linking structure to function necessitates accurate structural data. Certainly, models based on calixarene structures have to be evaluated in terms of the quality of the structural information.

FIGURE 7. Relationship between structural data, modeling and the resulting insight.

The relationship between structural data, modeling and the resulting insight or understanding for a supramolecular system is illustrated in Figure 7. A poor structure may lead to either poor or good modeling, but since a poor structure does not allow for arbitration or estimation of the quality of modeling, both paths (*a*) and (*b*) lead to poor insight. In the case of good structural information, poor modeling will still lead to a poor understanding of the system (*c*). Ideally, good structural information plus good modeling

leads to good insight into host-guest interactions as well as structural insights (*d*). Wipff has stated: “our best knowledge rests on X-ray structures in the solid state.”¹²⁰

3.5 Structure and Modeling: A Case Study

Relationship (*b*) is illustrated in the modeling of *p-tert*-butylcalix[4]arene tetraamide compounds carried out by Wipff.¹²⁰ Three single-crystal XRD structures were used as the structural starting points for the modeling calculations: the “free” calix **A**, without an axis of symmetry, and the C_4 -symmetric calix compounds containing the potassium salts of thiocyanide (**B**) and iodide (**C**) (Figure 8).^{22,96} These hosts contain two binding sites: the methanol-occupied hydrophobic cavity and the hydrophilic cavity which is occupied by the potassium cation. All three structural refinements are characterized by large residuals ($R = 0.101 - 0.158$) which arise from a number of complications which obscure the structural features of the compound. First, the calix *t*-butyl groups are disordered over two sites; in **A** the occupancy is 0.57/0.43, whereas in **B** and **C** it is 0.50/0.50. Secondly, in all cases, the hydrophobic cavity is occupied by a disordered (oxygen-carbon) solvent molecule; its location is assumed to be on the symmetry axis in **B** and **C**, with unit occupancy. Thirdly, the amide chains are disordered about a mirror of symmetry with a 0.50/0.50 occupancy in **B**, while in **C**, the amide chains do not display this disorder. A fourth feature of the **B** and **C** structural models is the location of the anions in the interstitial sites defined by the packing of the host; in **B**, the thiocyanide anion is disordered. Finally, this intermolecular cavity also contains a non-negligible amount of solvent whose position and occupation could not be refined. In summary, each of the three structures displays severe—and often unresolved—disordering in all the structural features: the two cavities of the host, the anion, and the neutral guest.

FIGURE 8. Summary of the XRD data for p-*tert*-butylcalix[4]arene tetraamide compounds used in modeling studies.

The atomic coordinates from the above structural refinements were used as starting geometries for the modeling studies. The structures are minimized prior to calculations, which leads to different molecular geometries than observed experimentally. In the case of **A**, the minimized structure becomes C_{2v} -symmetric, and for **C**, becomes C_4 symmetric; **B** retains its C_{4v} symmetry. In order to achieve this symmetry, positions of both the *t*-butylphenol “walls” of the hydrophobic cavity and the amide chains defining the

hydrophilic cavity change. The hosts were studied both *in vacuo* and solvated with water, with both neutral guests and cations present. Modeling identifies a number of features that provide insight into this system. However, three insights or conclusions in particular do not match the solid-state structural data, or in the least, rest upon disorder-obscured structural features.

The Hydrophobic Calix Cone. A reduction in host symmetry to C_2 occurred within a few ps of molecular dynamics runs with both *in vacuo* and solvated forms. The ellipsoidal structure was found to interconvert at higher annealing temperatures, and a dynamic model of the host structure (in solution and gas phases) was developed to account for an averaged 4-fold symmetric structure. No comment was made on whether this dynamic averaging occurs in the solid-state. The amide chains at the lower rim, it is inferred, drive the hydrophobic cavity shape.

The Neutral Guest. Placing neutral guests (MeCN, MeOH, HOH) in the calix cone gives structures in which the guest hydrogen atoms are pointed as directly as possible to the cavity's aromatic walls, and as a consequence, the guests lie off the rotation symmetry axis. When dynamics runs were initiated with the guests in the inverted positions, they moved to maximize H- π contacts. It is postulated that motion of the guest may lower the kinetic barrier to C_2 -interconversion. Finally, inclusion of a guest in the calix cone leads to an amide-chain geometry which is favourable to cation binding.

The Anion. When SCN^- is placed inside the calix cone with M^+ held in the amide hydrophilic pocket, the cation moves down along the z-axis to pair with the anion. It is thought that the anion does not play a significant role since it is located far from the cation in the XRD structure.

Good modeling based on poor structural data gives structural insights that cannot be arbitrated by the experimental data, and is then by nature, speculative. The XRD structure

is severely disordered, and the disordering that gives the high C_4 symmetry for **B** and **C** has been selected. Thus, the change in symmetry seen in the dynamics run may in fact, reflect the actual disorder-obscured solid-state structure (*vide infra*). It may also be possible that the averaging dynamic picture postulated from the modeling data occurs in the solid-state. The role of the neutral guest is clearly important for the host conformation and ability to adopt the proper geometry for cation binding. The XRD structures do not show any of the methanol features observed in modeling such as the off-axis tilt, or even whether it is the -OH or the -CH₃ group that is pointed into the cavity. Finally, it would seem that severe disordering in the anion, as well as the walls of the intermolecular cavity in which it sits (the interstitial cavity contains an unknown amount of methanol) precludes any structurally-based comments on the role of the anion.

4. Thesis

It has been argued that conventional solid-state XRD structural techniques alone frequently do not provide sufficient data to unambiguously characterize host-guest interactions in the calixarene-guest system. Application of the complementary solid-state structural techniques of solid-state NMR spectroscopy and single crystal XRD to the calixarene-guest system leads to a more complete understanding of structural and dynamic features; this knowledge in turn, provides unique insight into the existence and nature of host-guest interactions in the calixarene system.

The unmodified *p-tert*-butylcalix[4]arene has been chosen because it affords a relatively simple cavity for probing host-guest interactions in the solid-state. Furthermore, it is the system from which the vast majority of derivative chemistry has developed. The calixarene is flexible, and provides a cavity geometry which has only one “pocket”.

The techniques of solid-state NMR spectroscopy and single crystal XRD are complementary: each examines a slightly different structural aspect of crystalline solids (Figure 9). Because XRD depends on lattice symmetry, information about the smallest crystalline repeat unit depends on long-range ordering, and space-averaging is inherent in this technique. Solid-state NMR spectroscopy indicates the crystallographic inequivalence of nuclei in the smallest crystalline repeat unit, and this technique is sensitive to local or short-range order. Both techniques are sensitive to molecular motion, although with different characteristic timescales.¹²³ Chapter 2 considers both components of the synoptic approach to structural determination in detail.

FIGURE 9. The synoptic approach to structural and dynamics in the solid state.

The investigation of the *p-tert*-butylcalix[4]arene-toluene compound is reported in Chapter 3. The power of the synoptic approach is demonstrated in the increased resolution in both the host *t*-butyl disordering and guest orientation in the cavity, and the role of C-H... π guest-host interactions is developed. Key themes—space-averaging of the XRD structure, dynamics of both the host and guest, and guest orientation—carried

throughout the thesis are developed. In Chapter 4, the role of the guest in distorting the *p-tert*-butylcalix[4]arene structure is examined. The next chapter explores the inclusion chemistry of *p-tert*-butylcalix[4]arene with aliphatic guests; these compounds challenge the role of attractive $C-H_{\text{host}} \cdots \pi_{\text{guest}}$ interactions. Chapter 6 reports the ability of *p-tert*-butylcalix[4]arene to form compounds with small gas molecules such as xenon and methane, as well as calix solids that contain two different types of guests. Variation in the fraction of second guest allows the host symmetry and guest orientations to be tuned. The study concludes with an investigation of *p-tert*-butylcalix[4]arene compounds formed from nitrogen-containing guests. The guest orientation and dynamics of benzene and pyridine are compared and contrasted. Preliminary studies on the host-guest proton-transfer motif are reported.

In each experimental chapter, the complementarity of the NMR and XRD techniques is emphasized, and specific examples of the increased understanding of solid-state structure are given. Suggestions for further work are included at the end of each chapter.

5. References

1. Ball, P. "The shape of things to come", *Nature*, **371**, 1994, 202-203.
- 2a. Davy, H. *Phil. Trans. Roy. Soc.* **1811**, 101, 1.
- 2b. Pedersen, C. J. *Angew. Chem. Int. Ed. Engl.* **1988**, 27, 1021-1027.
3. Lehn, J.-M. *Angew. Chem. Int. Ed. Engl.* **1990**, 29, 1304-1319.
4. Gutsche, C. D.; Iqbal, M. *Org. Synth.* **1990**, 68, 234-237.
5. Gutsche, C. D. *Acc. Chem. Res.* **1983**, 16, 161-170.
6. Gutsche, C. D. *Aldrichimica Acta* **1995**, 28, 3-9.
7. Gutsche, C. D. *Calixarenes*; RSC: Cambridge and London, 1989.
8. Vicens, J.; Bohmer, V. Eds. *Calixarenes*; Kluwer: Dordrecht, 1990.
9. Gutsche, C. D.; Dhawan, B.; No, K. H.; Muthukrishnan, R. *J. Am. Chem. Soc.* **1981**, 103, 3782-3792.
10. Andreetti, G. D.; Ungaro, R.; Pochini, A. *J. Chem. Soc., Chem. Commun.* **1979**, 1005-1007.

11. Kammerer, H.; Happel, G.; Caeser, F. *Makromol. Chem.* **1972**, *162*, 179.
12. Happel, G.; Mathiasch, B.; Kammerer, H. *Makromol. Chem.* **1975**, *176*, 3317.
13. Gutsche, C. D.; Bauer, L. J. *Tetrahedron Lett.* **1981**, *22*, 4763-4766.
- 14a. Blixt, J.; Detellier, C. *J. Am. Chem. Soc.*, **1994**, *116*, 11957-11960.
- 14b. Groenen, L. C.; Steinwender, E.; Lutz, B. T. G.; van der Maas, J. H.; Reinhoudt, D. N. *J. Chem. Soc. Perkin Trans. 2* **1992**, 1893-1898.
15. Gutsche, C. D.; Bauer, L. J. *J. Am. Chem. Soc.*, **1985**, *107*, 6052-6059.
16. Gutsche, C. D.; Dhawan, B.; Levine, J. A.; No, K. H.; Bauer, L. J. *Tetrahedron* **1983**, *39*, 409-426.
17. Bott, S. G.; Coleman, A. W.; Atwood, J. L. *J. Am. Chem. Soc.* **1986**, *108*, 1709-1710.
18. Arduini, A.; Pochini, A.; Reverberi, S.; Ungaro, R. *J. Chem. Soc., Chem. Commun.* **1984**, 981-982.
19. Ferguson, G.; Kaitner, B.; McKervey, M. A.; Seward, E. M. *J. Chem. Soc., Chem. Commun.* **1987**, 584-585.
20. McKervey, M. A.; Seward, E. M.; Ferguson, G.; Ruhl, B.; Harris, S. J. *J. Chem. Soc., Chem. Commun.* **1985**, 388-390.
- 20a. Ungaro, R.; Pochini, A.; Andreetti, G. D. *J. Incl. Phenom.* **1984**, *2*, 199-206.
21. Arduini, A.; Pochini, A.; Reverberi, S.; Ungaro, R.; Andreetti, G.; Ugozzoli, F. *Tetrahedron* **1986**, *42*, 2089-2100.
22. Calestani, G.; Ugozzoli, F.; Arduini, A.; Ghidini, E.; Ungaro, R. *J. Chem. Soc., Chem. Commun.* **1987**, 344-346.
23. Regnouf de Vains, J.-B.; Lamartine, R.; Fenet, B.; Bavoux, C.; Thozet, A.; Perrin, M. *Helv. Chim. Acta* **1995**, *78*, 1607-1619.
24. Bohmer, V.; Kraft, D.; Tabatabai, M. *J. Incl. Phenom.* **1994**, *19*, 17-39.
25. Yoshimura, K.; Fukazawa, Y. *Tetrahed. Lett.* **1996**, *37*, 1435-1438.
26. Beer, P. D.; Drew, M. G. B.; Gale, P. A.; Leeson, P. B.; Ogden, M. I. *J. Chem. Soc., Dalton Trans.* **1994**, 3479-3485.
27. Alfieri, C.; Dradi, E.; Pochini, A.; Ungaro, R.; Andreetti, G. D. *J. Chem. Soc., Chem. Commun.* **1983**, 1076-1077.
28. Andreetti, G. D.; Ori, O.; Ugozzoli, F.; Alfieri, C.; Pochini, A.; Ungaro, R. *J. Incl. Phenom.* **1988**, *6*, 523-536.
29. Dijkstra, P. J.; Brunink, J. A. J.; Bugge, K.; Reinhoudt, D. N.; Harkema, S.; Ungaro, R.; Ugozzoli, F.; Ghidini, E. *J. Am. Chem. Soc.* **1989**, *111*, 7567-7575.

30. Bakker, W. I. I., Haas, M.; Khoo-Beattie, C.; Ostaszewski, R.; Franken, S. M.; den Hertog, H. J.; Verboom, W.; de Zeeuw, D.; Harkema, S.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1994**, *116*, 123-133.
31. Timmerman, P.; Verboom, W.; van Veggel, F. C. J. M.; van Duynhoven, J. P. M.; Reinhoudt, D. N. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2345-2348.
32. van Wageningen, A. M. A.; van Duynhoven, J. P. M.; Verboom, W.; Reinhoudt, D. N. *J. Chem. Soc., Chem. Commun.* **1995**, 1941-1942.
33. van Dienst, E.; Snellink, B. H. M.; von Piekartz, I.; Engbersen, J. F. J.; Reinhoudt, D. N. *J. Chem. Soc., Chem. Commun.* **1995**, 1151-1152.
34. Arduini, A.; Pochini, A.; Secchi, A.; Ungaro, R. *J. Chem. Soc., Chem. Commun.* **1995**, 879-880.
35. Ungaro, R.; Pochini, A.; Andreotti, G. D.; Domiano, P. *J. Chem. Soc. Perkin Trans. 2*, **1985**, 197-201.
36. Furphy, B. M.; Harrowfield, J. M.; Ogden, M. I.; Skelton, B. W.; White, A. H.; Wilner, F. R. *J. Chem. Soc. Dalton Trans.* **1989**, 2217-2221.
37. Xu, W.; Puddephatt, R. J.; Manojlovic-Muir, L.; Muir, K. W.; Frampton, C. S. *J. Incl. Phenom.* **1994**, *19*, 277-290.
38. Prager, M.; Caciuffo, R.; Amoretti, G.; Carlile, C. J.; Coddens, G.; Fillaux, F.; Francescangeli, O.; Ugozzoli, F. *Mol. Phys.* **1994**, *81*, 609-619.
39. Andreotti, G. D.; Pochini, A.; Ungaro, R. *J. Chem. Soc., Perkin Trans.* **1983**, 1773-1779.
40. Ungaro, R.; Pochini, A.; Andreotti, G. D.; Sangermano, V. *J. Chem. Soc., Perkin Trans.* **1984**, 1979-1985.
41. Harrowfield, J. M.; Ogden, M. I.; Richmond, W. R.; Skelton, B. W.; White, A. H. *J. Chem. Soc., Chem. Commun.* **1991**, 1159-1161.
42. Ogata, M.; Fujimoto, K.; Shinkai, S. *J. Am. Chem. Soc.* **1994**, *116*, 4505-4506.
43. Arnaud-Neu, F.; Collins, E. M.; Deasy, M.; Ferguson, G.; Harris, S. J.; Kaitner, B.; Lough, A. J.; McKervey, M. A.; Marques, E.; Ruhl, B. L.; Schwing-Weill, M. J.; Seward, E. M. *J. Am. Chem. Soc.* **1989**, *111*, 8681-8691.
44. Ghidini, E.; Ugozzoli, F.; Ungaro, R.; Harkema, S.; El-Fadl, A. A.; Reinholdt, D. N. *J. Am. Chem. Soc.* **1990**, *112*, 6979-6985.
45. Marsella, M. J.; Newland, R. J.; Carroll, P. J.; Swager, T. M. *J. Am. Chem. Soc.* **1995**, *117*, 9842-9848.
46. Sabbatini, N.; Guardigli, M.; Mecati, A.; Balzani, V.; Ungaro, R.; Ghidini, E.; Casnati, A.; Pochini, A. *J. Chem. Soc., Chem. Commun.* **1990**, 878-879.

47. Harrowfield, J. M.; Ogden, M. I.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1991**, 979-985.
48. Harrowfield, J. M.; Ogden, M. I.; Richmond, W. R.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1991**, 2153-2160.
49. Asfari, Z.; Harrowfield, J. M.; Ogden, M. I.; Vicens, J.; White, A. H. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 854-856.
50. Bott, S. G.; Coleman, A. W.; Atwood, J. L. *J. Chem. Soc., Chem. Commun.* **1986**, 610-611.
51. Corazza, F.; Floriani, C.; Chiesi-Villa, A.; Guastini, C. *J. Chem. Soc., Chem. Commun.* **1990**, 640-641.
52. Atwood, J. L.; Orr, G. W.; Hamada, F.; Vincent, R. L.; Bott, S. G.; Robinson, K. D. *J. Am. Chem. Soc.* **1991**, *113*, 2760-2761.
53. Steed, J. W.; Juneja, R. K.; Burkhalter, R. S.; Atwood, J. L. *J. Chem. Soc., Chem. Commun.* **1994**, 2205-2206.
54. Xu, W.; Puddephatt, R. J.; Manojlovic-Muir, L.; Muir, K. W.; Frampton, C. S. *J. Incl. Phenom.* **1994**, *19*, 277-290.
55. Parlevliet, F. J.; Olivier, A.; de Lange, W. G. J.; Kamer, P. C. J.; Kooijman, H.; Spek, A. L.; van Leeuwen, P. W. N. M. *Chem. Commun.* **1996**, 583-584.
56. Delaigue, X.; Harrowfield, J. M.; Hosseini, M. W.; De Cian, A.; Fischer, J.; Kyritsakas, N. *J. Chem. Soc., Chem. Commun.* **1994**, 1579-1580.
57. Smith, J. M.; Bott, S. G. *Chem. Commun.* **1996**, 377-378.
58. Giannini, L.; Solari, E.; Zanotti-Gerosa, A.; Floriani, C.; Chiesi-Villa, A.; Rizzola, C. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 85-87.
59. Khasnis, D. V.; Lattman, M.; Gutsche, C. D. *J. Am. Chem. Soc.* **1990**, *112*, 9422-9423.
60. Khasnis, D. V.; Burton, J. M.; Lattman, M.; Zhang, H. *J. Chem. Soc., Chem. Commun.* **1991**, 562-563.
61. Khasnis, D. V.; Burton, J. M.; McNeil, J. D.; Santini, C. J.; Zhang, H.; Lattman, M. *Inorg. Chem.* **1994**, *33*, 2657-2662.
62. Shinkai, S.; Mori, S.; Tsubaki, T.; Sone, T.; Manabe, O. *Tetrahedron Lett.* **1984**, *25*, 5315-5318.
63. Shinkai, S.; Mori, S.; Koreishi, H.; Tsubaki, T.; Manabe, O. *J. Am. Chem. Soc.* **1986**, *108*, 2409-2446.
64. Shinkai, S.; Araki, K.; Matsuda, T.; Nishiyama, N.; Ikeda, H.; Takasu, I.; Iwamoto, M. *J. Am. Chem. Soc.* **1990**, *112*, 9053-9058.

65. Coleman, A. W.; Bott, S. G.; Morley, S. D.; Means, C. M.; Robinson, K. D.; Zhang, H.; Atwood, J. L. *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1361-1362.
66. Perrin, R.; Lamartine, R.; Perrin, M. *Pure & Appl. Chem.* **1993**, *65*, 1549-1559.
- 66a. Mangia, A.; Pochini, A.; Ungaro, R.; Andreetti, G. D. *Anal. Lett.* **1983**, *16*, 1027-1036.
- 66b. Friebe, S.; Gebauer, S.; Krauss, G. J.; Goermer, G.; Krueger, J. *J. Chromat. Sci.* **1995**, *33*, 281-284.
67. Verboom, W.; Vreekamp, R.H.; Rudkevich, D.M.; Reinhoudt, D.N. in *Molecular Engineering for Advance Materials*, ed. J. Beecher and K. Schaumburg, *NATO ASI Series* **1995**, *C456*, 119-145.
68. Izatt, R. M.; Christensen, J. J.; Izatt, R. M. *U.S. Patent* 4,477,377 (1984).
69. Casnati, A.; Pochini, A.; Ungaro, R.; Ugozzoli, F.; Arnaud, F.; Fanni, S.; Schwing, M.-J.; Egberink, R. J. M.; de Jong, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1995**, *117*, 2767-2777.
70. Cadogan, A. M.; Diamond, D.; Smyth, M. R.; Deasy, M.; McKervey, M. A.; Harris, S. J. *Analyst* **1989**, *114*, 1551-1554.
71. Shinkai, S.; Shirahama, Y.; Tsubaki, T.; Manabe, O. *J. Am. Chem. Soc.* **1989**, *111*, 5477-5478.
72. Kelderman, E.; Derhaeg, L.; Heesink, G. J. T.; Verboom, W.; Engbersen, J. F. J.; van Hulst, N.F.; Persoons, A.; Reinhoudt, D. N. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1075-1077.
73. Kelderman, E.; Derhaeg, L.; Verboom, W.; Engbersen, J. F. J.; Harkema, S.; Persoons, A.; Reinhoudt, D. N. *Supramol. Chem.* **1993**, *2*, 183-190.
74. van Straaten-Nijenhuis, W. F.; van Doorn, A. R.; Reichwein, A. M.; de Jong, F.; Reinhoudt, D. N. *J. Org. Chem.* **1993**, *58*, 2265-2271.
75. Coffey, J. L.; Chandler, R. R.; Gutsche, C. D.; Alam, I.; Pinizzotto, R. F.; Yang, H. *J. Phys. Chem.* **1993**, *97*, 696-702.
76. Inouye, M.; Hashimoto, K.; Isagawa, K. *J. Am. Chem. Soc.* **1994**, *116*, 5517-5518.
77. Koh, K. N.; Araki, K.; Ikeda, A.; Otsuka, H.; Shinkai, S. *J. Am. Chem. Soc.* **1996**, *118*, 755-758.
78. Ikeda, A.; Shinkai, S. *J. Chem. Soc., Chem. Commun.* **1994**, 2375-2376.
79. Wenz, G. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 803-822.
80. Stout, G. H.; Jensen, L. H. *X-Ray Structure Determination*, 2nd ed.; Wiley: New York, **1989**, 229-230.
81. Bohmer, V. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 713-745.
82. Facey, G. A.; Dubois, R. H.; Zakrzewski, M.; Ratcliffe, C. I.; Atwood, J. L.; Ripmeester, J. A. *Supramol. Chem.* **1993**, *1*, 199-200.

83. Caciuffo, R.; Amoretti, G.; Carlile, C. J.; Fillaux, F.; Francescangeli, O.; Prager, M.; Ugozzoli, F. *Physica B* **1994**, *202*, 279-286.
84. Caciuffo, R.; Amoretti, G.; Fillaux, F.; Francescangeli, O.; Melone, S.; Prager, M.; Ugozzoli, F. *Chem. Phys. Lett.* **1993**, *204*, 427-432.
85. Caciuffo, R.; Francescangeli, O.; Melone, S.; Prager, M.; Ugozzoli, F.; Andreetti, G. D.; Amoretti, G.; Coddens, G.; Blank, H. *Physica B* **1992**, *180 & 181*, 691-693.
86. Ripmeester, J.A.; Ratcliffe, C.I.; Enright, G.D.; Brouwer, E.B. *Acta Cryst.* **1995**, *B51*, 513-522.
87. Brouwer, E.B.; Enright, G.D.; Ripmeester, J.A. *Supramol. Chem.* **1996**, *7*, 79-83.
88. Harrowfield, J. M.; Ogden, M. I.; Richmond, W. R.; Skelton, B. W.; White, A. H. *J. Chem. Soc. Perkin Trans. 2*, **1993**, 2183-2190.
89. Bavoux, C.; Perrin, M. *J. Incl. Phenom.* **1992**, *14*, 247-256.
90. Bavoux, C.; Vocanson, F.; Perrin, M.; Lamartine, R. *J. Incl. Phenom.* **1995**, *22*, 119-130.
91. McKervey, M. A.; Seward, E. M.; Ferguson, G.; Ruhl, B. L. *J. Org. Chem.* **1986**, *81*, 3581-3584.
92. Grootenhuys, P. D. J.; Kollman, P. A.; Groenen, L. C.; Reinhoudt, D. N.; van Hummel, G. J.; Ugozzoli, F.; Andreetti, G. D. *J. Am. Chem. Soc.* **1990**, *112*, 4165-4176.
93. Beer, P. D.; Chen, Z.; Drew, M. G. B.; Gale, P. A. *J. Chem. Soc., Chem. Commun.* **1994**, 2207-2208.
94. Olmstead, M. M.; Sigel, G.; Hope, H.; Xu, X.; Power, P. *J. Am. Chem. Soc.* **1985**, *107*, 8087-8091.
95. Ferguson, G.; Gallagher, J. F.; Pappalardo, S. *J. Incl. Phenom.* **1992**, *14*, 349-356.
96. Arduini, A.; Ghidini, E.; Pochini, A.; Ungaro, R.; Andreetti, G. D.; Calestani, G.; Ugozzoli, F. *J. Incl. Phenom.* **1988**, *6*, 119-134.
97. Steed, J. W.; Juneja, R. K.; Burkhalter, R. S.; Atwood, J. L. *J. Chem. Soc., Chem. Commun.* **1994**, 2205-2206.
98. Ferguson, G.; Gallagher, J.F.; Pappalardo, S. *J. Incl. Phenom.* **1992**, *14*, 349-356.
99. Zanolli-Gerosa, A.; Solari, E.; Giannini, L.; Chiesi-Villa, A.; Rizzoli, C. *Chem. Commun.* **1996**, 119-120.
100. Juneja, R. K.; Robinson, K. D.; Orr, G. W.; Dubois, R. H.; Belmore, K. A.; Atwood, J. L.; Ripmeester, J. A.; Ratcliffe, C. I. *J. Incl. Phenom.* **1992**, *13*, 93-96.
101. Beer, P. D.; Chen, Z.; Drew, M. G. B.; Gale, P. A. *J. Chem. Soc., Chem. Commun.* **1994**, 1851-1852.

102. Arnecke, R.; Bohmer, V.; Ferguson, G; Pappalardo, S. *Tetrahedron Lett.* **1996**, 37, 1497-1500.
103. Halit, M.; Oehler, D.; Perrin, M.; Thozet, A.; Perrin, R.; Vicens, J.; Bourakhouadar, M. *J. Incl. Phenom.* **1988**, 6, 613-623.
104. Thuery, P.; Keller, N.; Lance, M.; Vigner, J.-D.; Nierlich, M. *J. Incl. Phenom.* **1995**, 20, 373-379.
105. Andreetti, G. D.; Calestani, G.; Ugozzoli, F.; Arduini, A.; Ghidini, E.; Pochini, A.; Ungaro, R. *J. Incl. Phenom.* **1987**, 5, 123-126.
106. Smith, J. M.; Bott, S. G. *Chem. Commun.* **1996**, 377-378.
107. Harrowfield, J. M.; Richmond, W. R.; Sobolev, A. N. *J. Incl. Phenom.* **1994**, 19, 257-276.
108. Czugler, M.; Tisza, S.; Speier, G. *J. Incl. Phenom.* **1991**, 11, 323-331.
109. Gutsche, C. D.; Gutsche, A. E.; Karaulov, A. I. *J. Incl. Phenom.* **1985**, 3, 447-451.
110. Andreetti, G.D.; Ugozzoli, F.; Nakamoto, Y.; Ishida, S.-I. *J. Incl. Phenom.* **1991**, 10, 241-253.
111. Andreetti, G.D.; Ungaro, R.; Pochini, A. *J. Chem. Soc., Chem. Commun.* **1981**, 533-534.
112. Atwood, J. L.; Raston, C. L., Ripmeester, J. A. unpublished observations.
113. Desiraju, G. R. *Angew. Chem. Int. Ed. Engl.* **1995**, 34, 2311-2327.
114. Atkins, P. W. *Physical Chemistry*, 3rd. Ed. W. H Freeman: New York, 1986, p. 587.
115. Ungaro, R.; Arduini, A.; Casnati, A.; Ori, O.; Pochini, A.; Ugozzoli, F. in *Computational Approaches in Supramolecular Chemistry*, ed G. Wipff, *NATO ASI Series* **1994**, C426, 277-300.
116. Fujimoto, T.; Yanagihara, R.; Kobayashi, K.; Aoyama, Y. *Bull. Chem. Soc. Jpn.* **1995**, 68, 2113-2124.
117. Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry, Part A: Structure and Mechanisms*; 3rd ed.; Plenum: New York, 1990, p. 546-557.
118. Komoto, T.; Ando, I.; Nakamoto, Y.; Ishida, S. *J. Chem. Soc., Chem. Commun.* **1988**, 135-137.
119. Minn, H. H.; Chang, S.; No, K. T. *Theor. Chim. Acta.* **1989**, 75, 233-245.
120. Guilbaud, P.; Varnek, A.; Wipff, J. *Am. Chem. Soc.* **1993**, 115, 8298-8312.
121. Drew, M. G. B. in *Spectroscopic and Computational Studies of Supramolecular Systems*; Davies, J. E., Ed.; Kluwer: Dordrecht, 1992, 207-237.
122. Cohen, A.A.; Shatzmiller, S.E. *J. Comp. Chem.* **1995**, 16, 1459-1467.
123. Ripmeester, J. A.; Ratcliffe, C. I. In *Inclusion Compounds*; Atwood, J. L.; Davies, J. E. D.; MacNicol, D. D., Eds.; Oxford UP: Oxford, 1991; Vol. 5, 37-89.

CHAPTER 2: Physical Techniques

1. Introduction	30
2. Single-Crystal X-Ray Diffraction	32
2.1 X-rays	32
2.2 Crystals and Symmetry	33
2.3 Determination of the Crystal Structure	34
2.4 Quality of XRD Structural Data	35
3. Solid-State Nuclear Magnetic Resonance (NMR) Spectroscopy	36
3.1 Interactions in NMR Spectroscopy	39
3.2 The Zeeman Interaction	41
3.3 The Quadrupolar Interaction: ^2H NMR Spectroscopy	42
3.4 The Direct Dipolar Interaction	50
3.5 The Chemical Shielding Interaction	54
3.6 The Indirect Dipolar Interaction	61
3.7 The NMR Experiment	62
4. Summary	63
5. References	63
6. Figures	65

1. Introduction

Chemistry investigates the relationship between the structure of matter and the resulting physical behavior. As such, both the characterization of structure and its physical consequences are crucial for the comprehensive understanding of chemistry.

The chemistry of supramolecular compounds, and in particular that of calixarene compounds, has been characterized by an emphasis on the synthesis of new compounds.¹⁻³ It has become apparent that when questions probing the relationship between structure and behavior are considered, the physical characterization of supramolecular interactions has lagged. Unlike molecular chemistry which deals with strong interactions between atoms such as ionic and covalent bonding, supramolecular chemistry deals with much weaker interactions (such as van der Waals) between molecular entities. It must be pointed out that these weak interactions determine the structure in supramolecular

assemblies as much as the “stronger” atomic interactions do in molecular chemistry. The physical characterization techniques that have proved so powerful in examining molecular structure occasionally fall short in the structural determinations of molecular assemblies. The increase in the structural length scales provides unique characterization challenges; for example, supramolecular crystals often possess large unit cells, which make a single-crystal X-ray diffraction determination of structure a lengthy, and therefore non-routine, technique. At the other end of the length scale, the weak interactions between molecules in supramolecular compounds are difficult to identify when interatomic and intermolecular distances are poorly resolved due to motions and disorder. New physical characterization methods such as scanning microscopy have been developed consequent to these needs.⁴

This chapter outlines the fundamental aspects of two structural techniques: single crystal X-ray diffraction (XRD), and solid-state nuclear magnetic resonance (NMR) spectroscopy. The two techniques investigate different aspects of the solid-state, and thus give complementary structural information which can be combined using a synoptic approach to structural investigation. When the short-range or local symmetry environment identified by NMR spectroscopy is coupled with the long-range ordering attained from crystallography, a structural picture emerges which is greater than the sum of its parts. In particular, the following chapters illustrate how both the structural and dynamic data obtained by NMR spectroscopy have been beneficially incorporated in the structural models based on the diffraction data.

All of the single crystal XRD data collection and the majority of XRD analysis reported in this thesis has been carried out by Dr. Gary Enright of the Steacie Institute for Molecular Sciences at the National Research Council of Canada. The author's main contribution in the synoptic approach to the structural characterization of calixarene

compounds has been with NMR spectroscopy, and therefore, this technique is treated with more detail both in the current chapter and thesis.

2. Single Crystal X-Ray Diffraction

X-rays were discovered a little over a century ago by Roentgen, and for almost two decades the nature of these unknown (or “X”) rays was debated.⁵ In 1912, von Laue discovered that crystals cause X-rays to diffract, and to a certain extent, established the wave-like nature of X-rays. Shortly thereafter, W.L. Bragg treated the diffraction of X-rays by crystals as “reflections” from planes of atoms in the lattice and established the relationship:

$$2d \sin\theta = n\lambda \quad (1)$$

which can also be rearranged as

$$\sin\theta = \frac{n\lambda}{2d} \quad (2)$$

where d = the spacing between diffraction planes, θ = the incident angle of the incoming X-ray radiation to the plane, λ = the wavelength of X-ray radiation, and n = integer. In reality, a crystal is composed of a multitude of such atomic planes. In such a case, the diffraction maxima are sharp and will occur at clearly defined values of θ . Analysis of the single-crystal diffraction pattern allows for the construction of a specific arrangement of atoms in the unit cell and thus the structure of the solid-state.

2.1 X-rays

X-rays (electromagnetic radiation in the wavelength region of 0.1 - 100 Å)⁵ are produced by bombarding a metal target with fast-moving electrons. Multiple collisions with the target slow the electrons down and causes the emission of white radiation as the

kinetic energy is converted into radiation. Intense radiation is produced when the collision causes the removal of electrons from the target's innermost K shell. Filling of the now-empty orbital from higher energy levels causes nearly monochromatic X-rays to be emitted with high intensity. The structures in this thesis were determined using $K_{\alpha 1}$ radiation from a copper target.

2.2 Crystals and Symmetry

The atoms and molecules in a crystalline solid are arranged in such a fashion that the crystal contains an array of identical units repeated throughout the volume or lattice of the crystal. The smallest such regularly repeatable atomic or molecular arrangement is called the primitive cell, and the unit cell consists of the primitive cell plus symmetry elements.⁵

The arrangement of atoms and molecules in crystals has been classified into seven crystal systems which are defined by the number of independent parameters pertaining to the geometry and size of the unit cell. The seven crystal systems have been further classified by Bravais into 14 lattices in which the atomic positions are at the corners of the unit cell with one lattice point per unit cell (the seven primitive lattices) or have two or more lattice points per unit cell (the seven non-primitive lattices). The symmetry operations relating the faces of crystals (rotation, mirror, centre of symmetry, and rotation-inversion) give rise to 32 sets of operations, and are called point groups. Combination of the 14 Bravais lattices and the 32 point groups gives 230 unique arrangements of points in space; these are called space groups. The limited elements of symmetry relating the atomic positions in crystals allows for the determination of the crystal structure.

2.3 Determination of the Crystal Structure

When a suitable diffracting crystal is subjected to X-ray radiation, the diffraction pattern may be collected and analyzed to determine the electron density and hence the atomic arrangements (since one assumes electrons are primarily associated with atoms). The first step in the process is to identify the unit cell and its space group symmetry. An initial small scan of θ values is collected, and the presence and the systematic absence of diffraction peaks is analyzed to identify the smallest repeating motif as well as the unit cell symmetry. Once these are established, the positions of the remaining diffraction peaks of the unit cell are calculated and scanned. In this way, the smallest number of peaks to unambiguously characterize the unit cell are used. In cases of space group ambiguity, the lower symmetry space group is used to collect the remaining diffraction peaks. Additional data sets may be merged with the initial data set. 6-10 diffraction peaks are needed to characterize each atomic parameter.

The data set is analyzed by relating the peak intensities I to the structure amplitude or factor F_{hkl} according to:

$$|F_{hkl}| \propto \sqrt{I} \quad (3)$$

From the structure factor one can derive an electron density map of the unit cell and hence atomic positions. Whereas a unique electron density map corresponds to a specific structural factor, the reverse is not necessarily true since the phase of the structure factor cannot be experimentally determined; this limitation is known as the phase problem. Two techniques exist to treat the phase problem: the Patterson and Direct methods. Both involve an iterative model-building process. It must be pointed out that at this stage, any additional structural information can assist the structural determination and enhance accuracy.

2.4 Quality of Structural Data

The quality of the model fit to the intensity data is gauged by several parameters.

The residual index R describes the agreement between observed and calculated reflections:

$$R = \frac{\sum |\Delta F|}{\sum |F_{obs}|} = \frac{\sum \|F_{obs} - F_{calc}\|}{\sum |F_{obs}|} \quad (4)$$

where F_{obs} and F_{calc} refer to the observed and calculated structural amplitudes. Typically, well-behaved organic structures give values of $R < 0.06$. Other quality controls include whether the model makes chemical and structural sense.⁶

A common problem in single-crystal X-ray diffraction studies of supramolecular compounds is the presence of disorder in which an atom or group of atoms occupies two or more discrete positions. Improper treatment of the disorder leads to assignment of inappropriate thermal parameters of atomic positions and correspondingly poor R -values. In guest-host systems, disorder in the guest or included solvent is often observed. Molecular motion (usually in the guest) also gives rise to large thermal parameters and complicates the structural determination. Finally, it must be pointed out that single-crystal XRD is sensitive to long-range molecular ordering, and describes the regularly repeating unit cell over a nearly infinite repeating volume. In a sense, the contents of one unit cell as determined by XRD represent an average over all unit cells in the crystal, and XRD is not sensitive to small local symmetry distortions. Any local deviations in structure, if slight enough not to affect the observed symmetry, may give rise to disorder over the space-averaged structure. A key discovery in this thesis is a more accurate treatment of guest and host disorder in the *p-tert*-butylcalix[4]arene-toluene compound taking into account this limitation in the diffraction method. The structure refines to an R -value of 0.046 when local symmetry is accounted for in the treatment of the XRD data (Chapter 3).

3. Solid-State Nuclear Magnetic Resonance (NMR) Spectroscopy

The strength of NMR spectroscopy lies in its ability to uniquely identify atomic environments, and the changes that may occur with exchange. In particular, solid-state NMR informs of the local or short-range atomic environment of crystalline solids, as well as dynamic information. As such it is very much a complementary technique to single-crystal XRD which gives a static and long-range ordering structural picture. Insight from one technique can be applied to extract more detailed information from another technique; this synoptic approach to structural studies is a major theme in this thesis.

This section is meant to provide the reader with a sufficient background to the NMR concepts and techniques employed in the thesis. Certain features pertinent to the NMR studies reported herein will be highlighted, while other features commonly found in NMR textbooks and reviews are absent or only mentioned in passing. By no means is this overview exhaustive; the reader is directed to more complete and comprehensive treatments.⁷⁻¹³

Spectroscopy is invaluable to chemists who wish to ascertain molecular structure and processes. Spectroscopy can be broadly defined as the interaction between matter and electromagnetic radiation which causes energy to be absorbed or emitted according to

$$\Delta E = h\nu \quad (5)$$

where ΔE is the energy difference between the initial and final states, h is Plank's constant and ν is the frequency of the interacting electromagnetic radiation.

NMR spectroscopy is based on energy transitions between quantized or discrete nuclear spin energy levels. The nuclear spin I is characterized by its angular momentum P according to:

$$P = \hbar[I(I + 1)]^{1/2} \quad (6)$$

where $\hbar = h/2\pi$. $\mathbf{P}$ is a vector quantity so that both magnitude and direction must be defined. The component of $\mathbf{P}$ along the direction considered (usually z) is specified in terms of a quantum number m such that:

$$\mathbf{P}_z = \hbar m \quad (7)$$

Since $|m| \leq I$ and m can be either positive or negative, there are a total of $2I + 1$ possible values for m and thus $2I + 1$ non-degenerate energy levels that provide energy transitions in NMR (Figure 1).

Motion of any charged body produces a magnetic field, and at the atomic level this implies that nuclear angular momentum $\mathbf{P}$ has an associated magnetic moment μ ; μ is described in terms of a gyromagnetic ratio, γ , which is the ratio of μ to the angular momentum:

$$\mu = \gamma \mathbf{P} \quad (8)$$

The magnetic moment is also quantized according to:

$$\mu = \gamma \hbar [I(I + 1)]^{1/2} \quad (9)$$

When an isolated nucleus is placed in a magnetic field of strength $\mathbf{B}$ along z , the energy of interaction E is defined as:

$$E = -\mu \cdot \mathbf{B} = \mu_z \cdot \mathbf{B} = \gamma \hbar m \cdot \mathbf{B} \quad (10)$$

where μ_z is the component of μ along z such that:

$$\mu_z = \gamma \hbar m \quad (11)$$

Since we are dealing with changes in energy ΔE :

$$\Delta E = |\gamma \hbar \mathbf{B} \Delta m| = h\nu \quad (12)$$

and

$$\nu = |(\gamma/2\pi) \mathbf{B} \Delta m| = |(\gamma/2\pi)| \mathbf{B} \quad \text{since } \Delta m = \pm 1 \quad (13)$$

The Larmor frequency ν can also be described as follows: When a magnetic moment moves in a uniform magnetic field $\mathbf{B}_0$ at constant total energy, a torque is exerted on μ which tends to align it perpendicular to $\mathbf{B}_0$. Since torque only affects the components of the angular momentum perpendicular to μ and $\mathbf{B}$, μ never becomes perpendicular to $\mathbf{B}_0$. Instead, μ curves out a cone about $\mathbf{B}_0$ with an angular velocity:

$$\omega = -\gamma \mathbf{B}_0 \quad (14)$$

The velocity of precession is also known as the Larmor frequency, and is defined as above.

Nuclei of spin I will be distributed over $2I + 1$ precession cones (Figure 1).

Resonance is achieved when an applied radio frequency pulse induces a weak magnetic field $\mathbf{B}_1$ which in turn affects the quantized angle that μ possesses as it precesses about $\mathbf{B}_0$.

The intensity of the NMR signal is derived from transitions in many individual nuclear spins. The distribution of states obeys a Boltzmann distribution such that the difference between two states at equilibrium Δn_0 of N nuclei is:

$$\Delta n_0 = N e^{-\frac{h\nu}{kT}} \quad (15)$$

The fraction of transitions is very small (n_0/N is typically on the order of 10^{-5}) making NMR spectroscopy an inherently insensitive technique.

Relaxation is the process by which the initial state of thermodynamic equilibrium is restored after excitation. Spin-lattice relaxation (T_1) characterizes the time needed to establish longitudinal thermodynamic equilibrium magnetization after the sample has been exposed to the magnetic field or after manipulation by radio frequency pulses. Energy must be exchanged between the nuclear spins and the lattice. Transverse or spin-spin relaxation (T_2) characterizes the time taken for the amplitude of the coherent magnetic oscillation to go to zero. Decay in transverse amplitude arises from the different phases induced by exposure of the nuclei to differing local magnetic fields and subsequent loss of precession coherence. In most cases, molecular rotational and translational motions lead

to fluctuating local fields of the site of the nuclei and cause relaxation. Differences in relaxation times (in particular T_1) as a function of temperature are used to characterize molecular motion.⁹

The NMR experiment measures the precession of nuclear spins in the presence of a magnetic field. The spins may be manipulated by radio frequency pulses to probe the various interactions that dictate the behavior of the spins in a strong magnetic field. A simple NMR experiment is the application of a $\pi/2$ pulse along the x -axis of the rotating frame of reference to place the magnetization vector along the y -axis (Figure 2). Transverse relaxation effects cause the magnetization vector to spread out in a plane perpendicular to the z -axis of the magnetic field. The receiver coils detect the electrical signal induced by the fluctuating local magnetic field as a function of time; the signal is known as the Free Induction Decay (FID). If the frequency of precession is at the resonance frequency, a simple exponential decay in the FID results. However, if there is any deviation from resonance (*e.g.*, if there are many different spins, each with its own characteristic frequency), the FID will be modulated. The final NMR spectrum is a plot of the intensity as a function of frequency which is achieved by a Fourier transform of the FID signal.

3.1 Interactions in NMR Spectroscopy

The NMR spectrum of a single nucleus is the result of many interactions which are summarized below (with typical corresponding interaction frequencies in s^{-1}):

$$\mathbf{H}_{TOTAL} = \mathbf{H}_Z + \mathbf{H}_Q + \sum_{I,S} \mathbf{H}_D + \mathbf{H}_\sigma + \sum_{I,S} \mathbf{H}_J \quad (16)$$

$$10^8 \quad 10^6 \quad 5 \times 10^4 \quad 2 \times 10^4 \quad 10^3 \quad s^{-1}$$

where: $\mathbf{H}_Z$ is the Zeeman interaction which lifts the degeneracy of the spin energy levels of any non-zero spin nucleus when placed in a magnetic field,
 $\mathbf{H}_Q$ is the quadrupolar interaction of the nuclear charge with the electric field gradient at the nucleus,
 $\mathbf{H}_D$ is the dipole-dipole (or dipolar) interaction summed over all pairs of like I and unlike S spins,
 $\mathbf{H}_\sigma$ is the chemical shielding interaction resulting from the shielding of the nucleus from the static magnetic field $\mathbf{B}_0$, and
 $\mathbf{H}_J$ is the spin-spin coupling interaction which is summed over all like I and unlike S spins.

The Zeeman interaction is the fundamental interaction between a non-zero spin nucleus and a static magnetic field which makes NMR spectroscopy possible. The quadrupolar interaction is present only for those nuclei of spin $I > \frac{1}{2}$, and thus does not affect the spectra of the more common NMR nuclei such as ^1H , ^{13}C , ^{15}N , ^{29}Si and ^{31}P . The dipolar interaction generally dominates the NMR spectra of abundant nuclei of spin $I = \frac{1}{2}$, with the ^1H nucleus being the most commonly observed contributor to $\mathbf{H}_D$. The chemical shielding interaction is most easily observed for dilute spin $I = \frac{1}{2}$ nuclei where the dipolar interaction is insignificant or has been removed by high-power decoupling techniques. Heteronuclear J -coupling to protons is usually removed by high-power decoupling, and while very important for solution NMR spectroscopy, J -coupling is usually only observed with heavier nuclei in solid-state NMR spectroscopy. In the solid-state, $\mathbf{H}_J$ of the lighter nuclei are several orders of magnitude less than the other interactions.

The electronic and magnetic interactions summarized above are present in both solution and solid-state NMR spectra, but vary in importance depending on the technique.

For solution NMR, the rapid molecular tumbling motions average out many interactions and gives rise to spectra containing sharp lines at frequencies determined primarily by H_σ and H_J . For solid-state NMR, the lack of such averaging motions increases the number of interactions that contribute to the resulting lineshapes. This added complexity results in very broad NMR lines, which in principle contain far more information than observed with solution NMR spectroscopy. What follows below is an explanation of each interaction summarized in equation (16), as well as features pertinent to the types of interactions and NMR experiments carried out in this thesis work.

3.2 The Zeeman Interaction

The Hamiltonian for the Zeeman interaction of a non-zero spin nucleus in a static magnetic field B_0 is given by:

$$H_z = -\frac{\gamma\hbar}{2\pi} B_0 \cdot I, \quad (17)$$

There are $2I + 1$ eigenstates of energy, E_m :

$$E_m = -\frac{\gamma\hbar}{2\pi} m B_0 \quad (18)$$

where m is a quantum number that takes on the $2I + 1$ values from $-I$ to $+I$ in steps of $\Delta m = 1$ and B_0 is the magnitude of the magnetic field vector $\mathbf{B}_0$. Thus for a spin $I = 1/2$ nucleus such as ^1H , the Zeeman interaction gives two quantized energy levels proportional to γ and the strength of the magnetic field.

3.3 The Quadrupolar Interaction: ^2H NMR Spectroscopy

3.3.1 Theory

The nuclear quadrupole arises from the non-spherical distribution of electric charge at the site of the nucleus. The Hamiltonian for the quadrupolar interaction is given by:

$$H_Q = \frac{e^2 q Q}{4I(2I-1)} \left[3I_z^2 - I^2 + \frac{1}{2} \eta (I_+^2 + I_-^2) \right] \quad (19)$$

where eQ is the electric quadrupole moment of the nucleus, eq is the largest component of the diagonalized electric field gradient (EFG) tensor established by the electrons surrounding the nucleus, η is the asymmetry parameter of the EFG, I is the spin quantum number, I_z is the z -component of the spin operator, I , and I_+ and I_- are the raising and lowering operators respectively. Since the electric quadrupole moment couples to the EFG, the electric quadrupolar interaction is highly sensitive to the electronic structure. The EFG at the site of the nucleus is rarely spherically symmetric, and its spatial distribution may be represented by a second rank tensor (a linear vector function which relates the magnetic field and eq vectors) V_{ii} . In the principle axis system of the EFG, V_{ii} is diagonal with:

$$V_{zz} = eq \quad (20)$$

$$\eta = \frac{|V_{yy}| - |V_{xx}|}{|V_{zz}|} \quad (21)$$

$$0 \leq \eta \leq 1 \quad (22)$$

$$|V_{zz}| \geq |V_{yy}| \geq |V_{xx}| \quad (23)$$

The relative signs of V_{yy} and V_{xx} are different from V_{zz} since V_{ii} is traceless (*i.e.*, the sum of the diagonal matrix elements = 0), so that:

$$V_{xx} + V_{yy} + V_{zz} = 0 \quad (24)$$

In the absence of a magnetic field, the quadrupolar Hamiltonian for a spin $I = 1$ nucleus such as deuterium ($\eta = 0$), has three eigenstates of energy:

$$E_m = \frac{e^2 q Q}{4I(2I-1)} [3m^2 - I(I+1)] \quad (25)$$

The $m = 1$ and $m = -1$ states are degenerate. When a quadrupolar nucleus is placed in a strong magnetic field, the total Hamiltonian is as described in equation (16); however, the quadrupolar interaction is often much larger than the non-Zeeman interaction terms, and the resulting spectrum is dominated by the quadrupolar and Zeeman terms. $\mathbf{H}_{\text{TOTAL}}$ thus simplifies to:

$$\mathbf{H}_{\text{TOTAL}} = \mathbf{H}_Z + \mathbf{H}_Q \quad (26)$$

If the quadrupolar interaction is treated as a perturbation on the principal Zeeman interaction (the so-called “high-field case”) we substitute (17) and (19) into (26) and have the following energy levels for a ^2H nucleus with $\eta = 0$ (Figure 3):

$$E_{-1} = \frac{\gamma \hbar B_o}{2\pi} + \frac{e^2 q Q}{4} \quad (27)$$

$$E_0 = -\frac{e^2 q Q}{2} \quad (28)$$

$$E_{+1} = -\frac{\gamma \hbar B_o}{2\pi} + \frac{e^2 q Q}{4} \quad (29)$$

These levels give rise to two resonance lines of frequency

$$\nu = \frac{\gamma B_o}{2\pi} \pm \frac{3}{4} \left(\frac{e^2 q Q}{h} \right) \quad (30)$$

The term $e^2 q Q/h$ is known as the quadrupolar coupling constant or χ .

The resonance lines arising according to equations (27)-(29) apply to a very simplified and experimentally rare situation: the single deuterium atom fixed in a rigid molecule in a strong magnetic field where the largest component of the cylindrically

symmetric electric field gradient tensor, eq , at the site of the nucleus is parallel to the magnetic field vector. More commonly, eq is not parallel to the magnetic field, and H_Q in equation (19) must be expressed in a reference frame where the magnetic field vector is the principle axis; this introduces an angular dependence between the magnetic field vector and eq . The first order perturbations on the Zeeman energy levels (equation (25)) are then expressed as:

$$E_m^{(1)} = \frac{3e^2qQ}{8} \left(m^2 - \frac{2}{3}\right) (3\cos^2\theta - 1) \quad (31)$$

where θ is the angle between eq and B_0 . The two resonance lines are expressed as:

$$\nu = \frac{\gamma B_0}{2\pi} \pm \left[\frac{3}{8} \left(\frac{e^2qQ}{h} \right) (3\cos^2\theta - 1) \right] \quad (32)$$

with a frequency separation of:

$$\Delta\nu = \frac{3}{4} \left(\frac{e^2qQ}{h} \right) (3\cos^2\theta - 1) \quad (33)$$

For the more general case when eq does not possess cylindrical symmetry (*i.e.*, $\eta \neq 0$) then the perturbed eigenstates depend on both the polar angles θ and ϕ that describe the orientation of the magnetic field in the principal axis system of the electric field gradient tensor (see Figure 4), and are given by:

$$E_m^{(1)} = \frac{e^2qQ}{4} (3m^2 - 2) \left(\cos^2\theta - \frac{1}{2}\sin^2\theta + \frac{1}{2}\eta\sin^2\theta\cos 2\phi \right) \quad (34)$$

yielding frequency transitions:

$$\nu = \frac{\gamma B_0}{2\pi} \pm \left[\frac{3}{4} \left(\frac{e^2qQ}{h} \right) \left(\cos^2\theta - \frac{1}{2}\sin^2\theta + \frac{1}{2}\eta\sin^2\theta\cos 2\phi \right) \right] \quad (35)$$

Since eq for the deuterium nucleus is usually very close to being axially symmetric about C-D bonds in rigid organic compounds, equation (33) shows that the doublet splitting is sensitive to the orientation of the C-D bond in the magnetic field. Changes in the splitting

in the ^2H NMR spectrum can give the quadrupolar coupling constant χ and the asymmetry parameter η directly as well as the orientation of eq with respect to the crystal axes. ^2H NMR studies of single crystal compounds yield valuable structural information.⁸⁻¹³

3.3.2 The ^2H NMR Powder Pattern

Single crystals of a material are often either difficult to obtain or are inconvenient to manipulate, and it is more common to deal with powdered samples. Whereas single crystals have only a limited number of C-D bond orientations with respect to the magnetic field, powdered microcrystalline samples have all values of θ and ϕ represented (cf. equations 34-35). The resulting ^2H NMR lineshape thus consists of a weighted sum of all possible doublets and is described as:

$$F(\nu) = \iint f_A(\nu, \theta, \phi) \sin \theta d\theta d\phi + \iint f_B(\nu, \theta, \phi) \sin \theta d\theta d\phi \quad (36)$$

where the functions f_A and f_B are delta functions representing each of the lines in the doublet. When $\eta = 0$, there is no angular dependence of the lineshape on ϕ , and the lineshape resembles a Pake doublet.¹⁴ When $\eta \neq 0$, the powder spectrum is more complicated, and shows an additional discontinuity^{9,13,15} to the two seen in the axially symmetric spectrum. Since broadening effects (in particular, dipolar) affect the delta functions f_A and f_B , the powder spectrum displays rounding or broadening of the singularities.

Figure 5 shows a number of powder spectra as a function of the asymmetry parameter η . The principle components of the electric field gradient tensor, V_{ii} , and η can be read directly from the frequency separations of the pairs of singularities in the powder spectrum with:

$$|V_{xx}| \propto \Delta\nu_{xx} = \frac{1}{2} \nu_Q (1 - \eta) \quad (37)$$

$$|V_{yy}| \propto \Delta v_{yy} = \frac{1}{2} v_Q (1 + \eta) \quad (38)$$

$$|V_{xx}| \propto \Delta v_{xx} = v_Q \quad (39)$$

$$\text{where } \Delta v_{xx} \leq \Delta v_{yy} \leq \Delta v_{zz} \quad (40)$$

$$\text{and } v_Q = 3\chi/2. \quad (41)$$

$$\eta = \frac{\Delta v_{yy} - \Delta v_{xx}}{\Delta v_{zz}} \quad (42)$$

Orientational information present in the spectra of single crystals is largely lost in powdered samples.

3.3.3 Molecular Motion

The main application of ^2H NMR spectroscopy in this thesis is to characterize molecular motion. ^2H NMR spectroscopy is sensitive to dynamics because molecular motion with rates in the range of 10^3 - 10^8 Hz gives rise to a time-averaged EFG tensor which may or may not have the same orientation as the static tensor. The motional effects can be grouped into three categories based on the motional rate.

(a) **Slow Motions ($\kappa \leq 10^3$ Hz).** The motions occur on a time scale much greater than the reciprocal of the linewidth v_Q^{-1} ($\kappa \sim 10^3 \text{ s}^{-1}$) and have minimal effects on the ^2H NMR lineshape. The conventional quadrupolar echo NMR experiment used in this thesis¹⁶ is insensitive to the slow motional regime, and the spectra of slow-moving ($\kappa \leq 10^3$ Hz) molecules are indistinguishable from those of rigidly held molecules. The resulting spectrum is known as the static lineshape. There is essentially no reorientation of the EFG tensor V during the course of the quadrupolar echo measurement.

(b) **Intermediate Rate Motions ($\kappa = 10^3$ - 10^8 Hz).** These motions occur on a time scale of the same order as v_Q^{-1} ($\kappa = 10^3$ - 10^8 s^{-1}) and have a profound effect on the

observed lineshape. The lineshapes are very sensitive, both in shape and intensity, to the spacing between the pulses in the quadrupolar echo experiment as well as the rate and mechanism of the molecular motion. The intermediate rate spectra can be simulated¹⁷⁻²⁰ in order to confirm a mechanism of a particular molecular motion and to determine its rate.

(c) **Fast Molecular Motions ($\kappa > 10^8$ Hz).** These motions occur on a time scale much shorter than ν_Q^{-1} ($\kappa > 10^8$ s⁻¹) and give spectra of reduced width between the pair of features compared to static spectra. Motions that occur in this regime average the static EFG tensor and a new averaged EFG tensor V' is used to characterize the powder spectrum. Fast motion limit (FML) spectra are insensitive to changes in rates of the motion responsible for averaging the spectra. If several distinctive fast motions occur simultaneously, the spectrum reflects the overall averaged EFG tensor.

If both the static and motionally-averaged spectra are available, it is possible to obtain mechanistic information about the motion. Spectra collected as a function of temperature can be matched to those simulated as a function of motional rate and an Arrhenius plot constructed to determine the activation barrier to the motion.

In order to calculate the FML ²H NMR spectrum, the time-averaged EFG tensor V' must be determined. Once V' is determined and diagonalized (if necessary), the lineshape can be calculated in a manner exactly analogous to that of calculating the rigid spectrum. Averaged tensors are determined by describing all orientations of the rigid tensor visited over the course of the motion in a common reference frame. When the reference frame is chosen such that the motion is symmetric about the z -axis, the averaged tensors are in their principal axis systems, and the need for tensor diagonalization is eliminated. For example, in the rotation of a -CD₃ group (in *p*-*tert*-butyl-*d*₉-calix[4]arene-toluene), the principal axis of the rigid tensors along the C-D bonds must be shifted such that the principal axis of the averaged tensor V' coincides with the rotation axis of the methyl

group. When the $-\text{CD}_3$ groups rotate about the C_3' axis of the t-butyl group a second average tensor $\mathbf{V}''$ must be similarly determined. The principal axis of the averaged electric field gradient tensor $\mathbf{V}'$ and the rotation axis are related by the Euler angles²¹ α , β , γ (Figure 6):

$$\mathbf{V}'(\alpha, \beta, \gamma) = \mathbf{R}(\alpha, \beta, \gamma) \mathbf{V}_{\text{PAS}} \mathbf{R}^{-1}(\alpha, \beta, \gamma) \quad (43)$$

where $\mathbf{R}$ is the Euler angle rotation matrix describing the coordinate transformation and $\mathbf{V}_{\text{PAS}}$ is the EFG tensor in its principal axis system. $\mathbf{R}$ is defined as:

$$\mathbf{R}(\alpha, \beta, \gamma) = \mathbf{R}_z(\gamma) \cdot \mathbf{R}_y(\beta) \cdot \mathbf{R}_z(\alpha) \quad (44)$$

$$\begin{aligned} \mathbf{R}_z(\gamma) &= \begin{vmatrix} \cos \gamma & \sin \gamma & 0 \\ -\sin \gamma & \cos \gamma & 0 \\ 0 & 0 & 1 \end{vmatrix} & \mathbf{R}_y(\beta) &= \begin{vmatrix} \cos \beta & 0 & -\sin \beta \\ 0 & 1 & 0 \\ \sin \beta & 0 & \cos \beta \end{vmatrix} \\ \mathbf{R}_z(\alpha) &= \begin{vmatrix} \cos \alpha & \sin \alpha & 0 \\ -\sin \alpha & \cos \alpha & 0 \\ 0 & 0 & 1 \end{vmatrix} \end{aligned} \quad (45)$$

The EFG tensors $\mathbf{V}_i(\alpha, \beta, \gamma)$ at each of the n sites visited by the deuteron over the course of the motion are obtained from the EFG tensors of the rigid deuteron in its principal axis system. The time-averaged EFG tensor $\mathbf{V}'(\alpha, \beta, \gamma)$ for each deuteron is a simple average of those time-averaged EFG tensor sampled throughout the entire motion:

$$\mathbf{V}'(\alpha, \beta, \gamma) = \left(\frac{1}{n} \right) \sum_{i=1}^n \mathbf{V}_i(\alpha, \beta, \gamma) \quad (46)$$

This procedure must be carried out for each deuteron affected by the motion.

Figure 7 shows several ^2H NMR spectra resulting from different types of molecular motion. The appearance of the FML lineshape depends on the mechanism of the motion, and is the spectrum with which one begins to deduce a molecular motion for a set of ^2H NMR spectra. A continuous motion can sometimes be distinguished from a discrete

jumping or flipping motion. For n -fold rotations where $n \geq 3$, the fast motion limit spectrum is always axial ($\eta = 0$).

3.3.4 Arrhenius Plot: Molecular Motion Activation Barrier

When a satisfactory motional model has been developed, the rates κ at which the calculated lineshapes were matched with the spectra can be related to the temperature T at which the spectra were collected. Assuming that the process is thermally activated, the dependence of the rate κ as a function of T obeys an Arrhenius relationship:

$$\ln \kappa = -(E_a) \frac{1}{RT} + C \quad (47)$$

where C is a constant and R is the gas law constant. The barrier to activation E_a can be determined from an Arrhenius plot.

3.3.5 The Quadrupolar Echo Pulse Sequence

Since the resonance lines in ^2H NMR spectroscopy are very broad, the free induction decay (FID) decays very rapidly and a simple 90° ($\pi/2$) pulse experiment is inadequate for obtaining data. The first 20-30 μsec of the transient signal is difficult to obtain due to (i) pulse breakthrough from the very high power needed to excite the wide frequency range (500 kHz), (ii) the slow response ("dead time") of the receiver, and (iii) the ring-down time of the probe circuitry. As a result, the resultant transformed spectra are severely distorted. The distortions are circumvented by use of an echo pulse experiment.

Figure 8 depicts the $(\pi/2)_x - \tau_1 - (\pi/2)_y - \tau_2 - (\text{acquire})$ quadrupolar echo experiment.¹⁶ After the $(\pi/2)_x$ pulse, the signal is allowed to decay for a time τ_1 , where τ_1 is shorter than the transverse relaxation time T_2 . After the $(\pi/2)_y$ pulse, the signal builds

up again until it reaches a maximum after time τ_2 . At this point, the receiver is switched on, and the echo decay is collected. In principle, the two delay sequences are equal, although in practice τ_2 is slightly less than τ_1 in order to locate the peak of the echo more precisely.

The quadrupolar echo pulse sequence has the same qualitative effect on quadrupolar nuclei as the Hahn echo sequence (used to measure T_2 relaxation times) has on spin $I = 1/2$ systems in solution.²² However, unlike the Hahn echo sequence, which can be understood with vector diagrams, it requires much more elaborate analysis.²³ The quadrupolar echo experiment can provide lineshapes without distortion if the $\pi/2$ pulses are short enough and any molecular motion occurs at a rate either much faster or much slower than the time scale of the experiment.

3.4 The Direct Dipolar Interaction

The dominant NMR interaction in solids is direct dipole-dipole coupling. The dipolar interaction can be thought of classically as the direct interaction between a pair of magnetic dipoles. Consequently, the dipolar interaction is independent of the applied magnetic field and depends on the spatial arrangement of the nuclei. The strength of the dipolar interaction decreases with increasing distance, and can in principle, give interatomic distances in the solid-state.

3.4.1 Theory: Dipolar Interaction Between Like Spins

The dipolar Hamiltonian H_D for a pair of spins I_1 and I_2 is given by:

$$H_D = \left(\frac{h}{2\pi} \right) \left[\left(\frac{\mu_o}{4\pi} \right) \frac{\gamma_1 \gamma_2 h}{2\pi r_{12}^3} \right] \left(I_1 I_2 - 3 \frac{(I_1 r_{1z})(I_2 r_{2z})}{r_{12}^2} \right) \quad (48)$$

where r_{12} is the internuclear vector between the interacting spins, μ_o is permeability of free space $\mu_o = 4\pi \cdot 10^{-7} \text{ kg} \cdot \text{m} \cdot \text{s}^{-2} \text{ A}^{-2}$. The term in the square brackets is known collectively as the dipolar coupling constant, and is often given the symbol R .

If the displacement vector is expressed in polar coordinates with the z-direction parallel to the magnetic field, the dipolar Hamiltonian becomes:¹²

$$H_D = \left(\frac{h}{2\pi} \right) R (A + B + C + D + E + F) \quad (49)$$

where:

$$\begin{aligned} A &= -I_{1z} I_{2z} (3\cos^2\theta - 1) \\ B &= \frac{1}{4} [I_{1+} I_{2-} + I_{1-} I_{2+}] (3\cos^2\theta - 1) \\ C &= -3/2 [I_{1z} I_{2+} + I_{1+} I_{2z}] \sin\theta \cos\theta e^{(-i\phi)} \\ D &= -3/2 [I_{1z} I_{2-} + I_{1-} I_{2z}] \sin\theta \cos\theta e^{(i\phi)} \\ E &= -\frac{3}{4} I_{1+} I_{2+} \sin^2\theta e^{(-2i\phi)} \\ F &= -\frac{3}{4} I_{1-} I_{2-} \sin^2\theta e^{(2i\phi)} \end{aligned}$$

In the high field approximation where the dipolar interaction can be treated as a perturbation of the much stronger Zeeman interaction, only the A and B terms contribute to the spectrum of homonuclear dipolar-coupled spins. The total Hamiltonian H_{TOTAL} can thus be expressed as:

$$H_{\text{TOTAL}} = H_Z + H_D \quad (50)$$

where

$$H_Z = \frac{-\gamma h B_o}{2\pi} (I_{1z} + I_{2z})$$

$$H_D = \left(\frac{h}{2\pi} \right) R \left[\frac{(3 \cos^2 \theta - 1)}{2} \right] (I_1 I_2 - 3 I_{1z} I_{2z})$$

The unperturbed H_Z has four possible energy states: $|++\rangle$, $|+-\rangle$, $| - + \rangle$ and $|--\rangle$ where the signs represent the spin states of each of the coupled spins. It is more convenient to consider the linear combination of these states:

$$|1\rangle^T = |++\rangle \quad |0\rangle^T = \frac{1}{\sqrt{2}}(|+-\rangle + |-+\rangle) \quad (51)$$

$$|-1\rangle^T = |--\rangle \quad |0\rangle^S = \frac{1}{\sqrt{2}}(|+-\rangle - |-+\rangle) \quad (52)$$

where the superscripts T and S refer to triplet and singlet states. Since the singlet state is not coupled to any of the members of the triplet state by either Zeeman or dipolar interactions, only the triplet state needs to be considered. The three components of the triplet state are equally spaced with Zeeman energies of:

$$E_{-1} = \frac{\gamma \hbar B_o}{2\pi} \quad E_o = 0 \quad E_1 = -\frac{\gamma \hbar B_o}{2\pi} \quad (53)$$

and give rise to a single resonance line. Like the H_Q , the H_D has three eigenstates which perturb the Zeeman energies as follows:

$$E_{-1} = \frac{\gamma \hbar B_o}{2\pi} - \left(\frac{h}{2\pi} \right) \frac{R}{4} (3 \cos^2 \theta - 1) \quad (54)$$

$$E_o = \left(\frac{h}{2\pi} \right) \frac{R}{2} (3 \cos^2 \theta - 1) \quad (55)$$

$$E_1 = -\frac{\gamma \hbar B_o}{2\pi} - \left(\frac{h}{2\pi} \right) \frac{R}{4} (3 \cos^2 \theta - 1) \quad (56)$$

The corresponding transition frequencies are:

$$\nu = \frac{1}{2\pi} \left(\gamma B \pm \left(\frac{3}{4} R (3 \cos^2 \theta - 1) \right) \right) \quad (57)$$

Thus for a rigid pair of spin = $\frac{1}{2}$ nuclei, a doublet is expected with splitting:

$$\Delta\nu = \frac{1}{2\pi} \frac{\gamma}{\hbar} R(3\cos^2\theta - 1) \quad (58)$$

This expression is analogous to the doublets observed in the ^2H NMR spectra of rigid deuterons. However, in this case it is the pair of spins, rather than the nucleus, which gives rise to the spectrum. It is obvious that the doublet splitting depends on the orientation of the internuclear vector with respect to the magnetic field. Since the frequency separation of the doublets depends on the inverse cube of the internuclear distance r^{-3} , the observed spectra of isolated spin pairs can be used to determine internuclear distances in single crystals.

For polycrystalline powders, all orientations of the internuclear vector $\mathbf{r}_{12}$ with respect to the magnetic field are possible, in a situation analogous to the deuterium EFG tensor. Similarly, the powder spectrum consists of the weighted sum of all possible doublets and results in a Pake doublet pattern.¹⁴ The inner singularities are the $\pi/2$ orientations separated by $3R/4\pi$ and the outer shoulders are the 0 or π orientations separated by $3R/2\pi$. Although orientational information is lost in the powder spectrum, it is still possible to determine the internuclear distance directly from the spectrum.

3.4.2 Molecular Motion

The dipolar powder spectrum of isolated spin pairs is sensitive to molecular motion, and the internuclear vector can be treated in the same manner as the largest component of the EFG tensor in spin $I = 1$ system to calculate the averaged spectrum. For many abundant spins, the dipolar powder spectrum appears as one broad Gaussian peak. Moment or relaxation analyses can be used to study molecular motions and phase transitions.

3.4.3 Heteronuclear Dipolar Interactions

The discussion so far has only been applied to dipolar interactions between like spins. Similar interactions occur between unlike spins, and have been exploited to extract information about bond lengths and molecular motions. The heteronuclear dipolar interaction between dilute and abundant nuclei contribute significant broadening to the spectrum of the dilute nucleus, and may be removed by high-power proton decoupling in order to generate a high resolution spectrum.

3.5 The Chemical Shielding Interaction

For the spin $I = \frac{1}{2}$ nuclei studied herein, the chemical shielding interaction has a significant bearing on the resulting NMR spectra, and can be correlated to structural features of the compound studied. The observable of the NMR experiment is the frequency ν , and the chemical shielding interactions are generally given as the frequency shift relative to a reference compound. The frequency of the transition depends on the Zeeman interaction, the strength of the magnetic field B_0 , and the electronic environment around the nucleus. The mobile electrons surrounding the nucleus generated their own local magnetic fields which shield or deshield the nucleus from B_0 . Therefore the position of the resonance line in the frequency spectrum depends on the chemical environment around the nucleus. There are two shift scales, both expressed in ppm: the chemical shift denoted δ , and the chemical shielding denoted σ . The relationship between the two is:

$$\delta_{\text{obs}} = (\sigma_{\text{ref}} - \sigma_{\text{obs}})/(1 - \sigma_{\text{ref}}) \quad (59)$$

3.5.1 Theory

The chemical shielding interaction for spin $I = \frac{1}{2}$ nuclei is simpler than the dipolar interaction between spins in that it involves only one nuclear spin and thus gives only two

energy states and one transition. Like the previous interactions, the interaction of the chemical shielding with the magnetic field is described by a second-rank tensor: The electronic orbitals surrounding a nucleus are typically anisotropic (non-spherically symmetric), and the local magnetic field and applied magnetic field vectors are typically not parallel. The degree of shielding around a nucleus (and thus the position of its resonance line) depends on the orientation of the molecules with respect to the magnetic field.

The chemical shielding Hamiltonian can be represented as:

$$H_{\sigma} = \frac{\gamma \hbar}{2\pi} I_z \sigma B_o \quad (60)$$

where σ is the chemical shielding tensor. In contrast to the EFG tensor for the electric quadrupolar interaction, the chemical shielding tensor does have a trace (Σ diagonal matrix elements $\neq 0$), and is not necessarily symmetric. The chemical shielding tensor can be decomposed into an antisymmetric σ_a tensor and a symmetric σ_s tensor:

$$\sigma_s = \frac{1}{2}(\sigma + \sigma^T) \quad \text{and} \quad \sigma_a = \frac{1}{2}(\sigma - \sigma^T) \quad (61)$$

where σ^T is the transpose of σ ; to first order, σ_s determines the NMR spectra.

In the absence of dipolar and quadrupolar interactions, the total Hamiltonian for a spin = $\frac{1}{2}$ nucleus is given by:

$$H_{\text{TOTAL}} = H_Z + H_{\sigma} \quad (62)$$

$$H_{\text{TOTAL}} = -\frac{\gamma \hbar}{2\pi} I_z B_o (E - \sigma) \quad (63)$$

where E is a second rank unit matrix. The two corresponding energy levels E_m are:

$$E_{\frac{1}{2}} = -\frac{\gamma \hbar}{4\pi} B_o (1 - \sigma_{zz}) \quad \text{and} \quad E_{-\frac{1}{2}} = \frac{\gamma \hbar}{4\pi} B_o (1 - \sigma_{zz}) \quad (64)$$

where σ_{zz} is the largest principle component of the chemical shielding tensor assumed to be parallel to the magnetic field. The two levels give rise to a single resonance at:

$$\nu = \frac{\gamma}{2\pi} B_o (1 - \sigma_{zz}) \quad (65)$$

σ_{zz} is typically not parallel to the magnetic field, and thus σ must be described in an axis system where the magnetic field vector is the principal axis. Consequently, the position of the resonance line displays an orientational dependence:

$$\nu = \frac{\gamma}{2\pi} B_o \left[1 - (\sigma_{xx} \cos^2 \theta_{xx} + \sigma_{yy} \cos^2 \theta_{yy} + \sigma_{zz} \cos^2 \theta_{zz}) \right] \quad (66)$$

where σ_{ii} are the principle components of the shielding tensor and θ_{ii} are the angles between these components and the magnetic field vector. For a single crystal, this means that the resonances of each crystallographically-unique nucleus will depend on the orientation of the crystal in the magnetic field. The situation is similar to that in ^2H NMR except that in this case, there is only one—rather than two—resonance line. The principal components of σ and the orientation with respect to the crystallographic axes are determined by variation of crystal orientation with respect to the magnetic field vector.

NMR studies of single crystals are rare, and it is more common to study microcrystalline powder samples. In powders, the orientational information is lost as all values of θ_{ii} are represented and the spectrum is a superposition of all possible orientationally-dependent lines. The lineshape is identical to that of one transition (of the two) in a ^2H NMR powder spectrum (Figure 9c). The shielding parameters are read directly from the discontinuities in the spectrum.

3.5.2 Towards a Solution-Like NMR Spectrum

In solution, rapid and random molecular motion occurs and the terms $\cos^2\theta_{ii}$ take on their isotropic average value of $1/3$. A single isotropic line σ_{iso} is observed with frequency:

$$\nu = \frac{\gamma}{2\pi} B_o (1 - \sigma_{iso}) \quad (67)$$

where σ_{iso} is $1/3$ the value of the trace of σ .

The broadline spin $I = 1/2$ spectrum is rich in information concerning dipolar couplings and orientation dependence on the various interactions with the magnetic field. However, the spectra are generally broad and featureless, and it is difficult to access specific information. A variety of NMR experimental techniques are available which highlight certain features of the NMR spectrum. For spin $I = 1/2$ nuclei, information about the isotropic chemical shift is often desired and in the case of ^{13}C , two techniques, magic angle spinning and cross-polarization, are commonly employed to achieve this goal.

Figure 9a shows the broadline ^{13}C NMR spectrum of solid methanol- β -quinol clathrate. The spectrum is dominated by heteronuclear dipolar coupling of spin-abundant proton nuclei to the spin-dilute ^{13}C nuclei (the great distance between ^{13}C nuclei renders the homonuclear dipolar coupling interaction insignificant). The ^1H - ^{13}C dipolar coupling interaction can be removed by applying a high-power radio frequency pulse at the resonance frequency of the protons (Figure 9c). Other techniques to increase the resolution of the ^{13}C NMR spectrum (Figure 9d) include magic angle spinning and cross-polarization and are discussed below.

3.5.3 Magic Angle Spinning (MAS)

The anisotropic chemical shielding interaction can be removed by spinning the sample at an angle; this technique is known as magic angle spinning (MAS). When a rigid array of nuclei is spun with an angular velocity ω about an axis at an angle β to the magnetic field and at angles χ_{ii} ($i = 1, 2, 3$) to the principle components of σ (Figure 10), then the angles θ_{ii} become time-dependent. θ_{ii} can be expressed in terms of other angles in the system:

$$\cos\theta_{ii} = \cos\beta \cos\chi_{ii} + \sin\beta \sin\chi_{ii} \cos(\omega t + \Psi_{ii}) \quad (68)$$

where Ψ_{ii} are the azimuth angles of the principle components of σ at time $t = 0$. If equation (68) is substituted into equation (66) and the average over time is taken, the time-averaged resonance frequency ν becomes:

$$\nu = \frac{\gamma}{2\pi} B_o \left[1 - \left(\frac{1}{3} \sigma_{ii} \sin^2 \beta + \frac{1}{2} (3 \cos^2 \beta - 1) \sum_u \sigma_{uu} \cos^2 \chi_{uu} \right) \right] \quad (69)$$

When the angle β is set to 54.7° , the term $(3 \cos^2 \beta - 1)$ goes to zero, and equation (69) is reduced to equation (67), and a solution-like spectrum is obtained for the solid.²⁴ The angle $\beta = 54.7^\circ$ is called the “magic angle”. The time-dependent terms of $\cos\theta_{ii}$ which are periodic in ω manifest themselves as rotational echoes in the free induction decay and as sidebands in the frequency spectrum. The spinning sidebands occur about the isotropic peak with a frequency separation of $\pm n\omega$ where n is an integer, and cover a frequency range comparable to the anisotropic static signal.

As ω approaches zero, the sideband envelope mimics the static lineshape. At slow spinning speeds, the sideband position and intensity distribution contain enough information to determine the principle components of the shielding tensor, and is useful for situations in which the signal intensity is spread out over a wide static lineshape (e.g., the ^{15}N resonance of *p-tert*-butylcalix[4]arene-pyridine- ^{15}N in chapter 7). Spinning sidebands

are often considered a nuisance as they may obscure other isotropic peaks in the spectrum, and pulse sequences that suppress spinning sidebands are available.²⁵⁻²⁷

In addition to averaging out the chemical shielding anisotropy, magic angle spinning also averages out the direct dipolar interaction to zero when $\omega_r > H_D$.

3.5.4 Cross-Polarization (CP)

Despite the advantages afforded by MAS, the NMR spectra of ^{13}C (and other spin $I = 1/2$ nuclei) are still hindered by two features: low sensitivity and long spin-lattice (T_1) relaxation times.⁷ The latter hindrance is addressed by a double resonance technique which transfers magnetization from the abundant proton spins to the dilute ^{13}C spins (Figure 11). Transverse magnetization of the protons is achieved by a $\pi/2$ pulse given in the X-channel at the resonance frequency of the protons. A contact pulse B_{1H} phase-shifted from the first by $\pi/2$ is applied to spin-lock the proton spins. Another pulse B_{1C} is applied at the ^{13}C resonance frequency such that the Hartmann-Hahn condition²⁸ is met:

$$\gamma_H B_{1H} = \gamma_C B_{1C} \quad (70)$$

In order to account for the differences in the gyromagnetic ratios, B_{1C} must be four times the power of B_{1H} . When the matching condition has been achieved, the ^1H and ^{13}C nuclei have equal energies and precess at the same rate in their respective rotating frames of reference. Magnetization is transferred from the protons to the ^{13}C nuclei via the B -term in the heteronuclear dipolar Hamiltonian in equation (49), and since the protons are much more abundant than the ^{13}C nuclei, the depletion of the proton magnetization reservoir is small. Once the ^{13}C nuclei have been magnetized, they are observed by switching off the B_{1C} pulse and switching on the receiver. The spin-locking ^1H pulse is left on during data acquisition to remove the ^1H - ^{13}C heteronuclear dipolar coupling.

What results from the CP experiment under ideal conditions is a signal enhancement of the ^{13}C resonances by a factor equal to the ratio of the gyromagnetic ratios (~ 4). Typically one transient is collected per each $B_{1\text{H}}$ pulse. The experiment is now governed by the T_1 relaxation time of the abundant proton spins which is usually smaller than for ^{13}C , and the repetition rate for the CP experiment decreases; this enhances the ^{13}C signal intensity as more transients can be collected in a given time. It should be noted that the CP experiment can also be used with other spin $I = \frac{1}{2}$ nuclei such as ^{15}N and ^{129}Xe as long as the Hartmann-Hahn matching condition is met.

In order to obtain quantitative data with the CP experiment, the duration of the contact pulse must be carefully chosen. The observed ^{13}C magnetization of different types of carbons (carbonyl, methylene) varies as the contact time. Different carbon environments give nuclei with different dipolar coupling strengths and consequently they cross-polarize with different rates. If the contact time is short, the peak intensities do not quantitatively reflect the number of carbon atoms. The contact time must be long enough to ensure that all ^{13}C nuclei reach their equilibrium magnetization, but short enough compared to the proton spin-lattice relaxation time in the rotating frame so that no intensity is lost. When the spinning sidebands are significant, quantitative interpretation must account for all the signal intensity including the sidebands.

Magic angle spinning and high power proton decoupling efficiently remove ^1H - ^{13}C dipolar couplings, but other dipolar couplings with ^{13}C do not fully remove the interactions. In particular, the dipolar couplings between ^{13}C and quadrupolar nuclei give rise to new angular terms in the dipolar Hamiltonian which are not removed by magic angle spinning. Consequently the ^{13}C CP-MAS NMR line of ^{13}C nuclei attached to quadrupolar nuclei such as ^2H , ^{14}N , ^{35}Cl , and ^{37}Cl are structured and quite broad. For some quadrupolar nuclei, rapid relaxation between the eigenstates of the quadrupolar

nuclei averages the dipolar interaction to zero and the “self-decoupling” gives sharp ^{13}C CP-MAS resonances for ^{79}Br , ^{81}Br and ^{127}I -bearing carbons.²⁹

3.5.5 The Dipolar-Dephasing Experiment: Molecular Motions

A simple modification to the CP-MAS experiment is the dipolar-dephasing (DD) experiment.^{30,31} In the CP pulse sequence, a delay of $\tau = 40\text{--}60\ \mu\text{s}$ is inserted just prior to data acquisition where the high power decoupling is switched off; the decoupling is turned on again during data collection. While the decoupler is off, the ^{13}C nuclei evolve under the influence of the heteronuclear dipolar Hamiltonian. For a rigid system, the dipolar interaction is strongest for those carbons bearing protons, and causes the signals of these carbons to decay during τ ; these carbon resonances do not appear in the spectrum. Carbons not bearing protons are not significantly influenced by dipolar interactions and the signals are only slightly attenuated. Molecular motion of proton-bearing carbons (such as methyl groups) may average the heteronuclear dipolar interaction, and the signal of dynamic carbons does not decay completely during the delay period. The DD technique is an invaluable experiment for ascertaining the presence of molecular motion of guests and hosts in supramolecular systems.

3.6 The Indirect Spin-Spin (or J -) Coupling Interaction

The last contribution to the total Hamiltonian to consider is the indirect dipolar coupling of spins through bonding electrons, the so-called scalar or J -coupling. Unlike the direct dipolar coupling, the J -coupling tensor is not traceless, and it cannot be removed by spinning. As this interaction makes a relatively insignificant contribution to H_{TOTAL} (equation (16)) in solids, its effects are usually present only when heavy nuclides

are involved. J -coupling in the solid-state does not play such an important role as it does in the NMR spectra of solutions.

3.7 The NMR Experiment

So far the theoretical background of NMR spectroscopy has been emphasized, and a few comments about the implementation of the NMR experiment are in order. Three types of Bruker spectrometers were used: the CXP-180, the MSL-200, and the AMX-300 (the numbers indicate the resonance frequency of protons in MHz at the magnetic field strength). Each spectrometer has a radio frequency transmitter, electronics to process the detected radio frequency signal, a computer processor, and a magnet. A variety of probes may be inserted into the magnet, and have the sample (50-250 mg) situated in a coil which carries both the transmitted pulse and receiver frequencies; the probe design varies with the type of experiment required. For static experiments, the sample sits in a 5- or 10-mm coil mounted horizontally. For spinning probes, the coil sits in a housing cylinder whose angle with respect to the z -direction of the magnetic field can be adjusted. The sample is spun in a non-magnetic ceramic tube (i.d. = 4-7 mm) at frequencies of 3-6 kHz. The electronic circuitry of the probe permits a very powerful (up 1 kW) pulse to be transmitted through the coil, with a rapid (within tens of μ s) detection of an extremely weak signal. When CP and high-power dipolar decoupling techniques are needed, a double resonance probe containing a second circuit tuned to the proton frequency is required. The receiver signal is amplified, and multiple FID signals are collected with a delay time $D_0 > 5T_1$. Computer algorithms may be used to process the data to present the best signal/noise Fourier-transformed spectra including line-broadening, truncation, and apodization.⁷ Optimization of the experimental collection conditions minimizes the subsequent manipulation of data, and is the preferred route to quality data.

4. Summary

Two of the most powerful structural determination techniques in chemistry have been summarized, with an emphasis on solid-state NMR spectroscopy. The CP/MAS (^1H , ^{13}C , ^{15}N , ^{129}Xe) NMR experiment identifies the number of unique nuclear chemical environments in the crystal unit cell. Good single crystal XRD establishes all atomic positions in the unit cell. The limitations of each technique are ameliorated by the strength of the other, and thus a synoptic approach in which both techniques are used in a complementary fashion provides a powerful determination of supramolecular and molecular structure. In addition, ^2H NMR spectroscopy accesses molecular motions in the solid-state, and can be used to probe local symmetry as well as provide thermodynamic data pertinent to the intermolecular interactions in supramolecular systems.

5. References

1. Gutsche, C. D. *Calixarenes*; RSC: Cambridge and London, 1989.
2. Vicens, J.; Bohmer, V. Eds. *Calixarenes*; Kluwer: Dordrecht, 1990.
3. Bohmer, V. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 713-745.
4. Frommer, J. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1298-1328.
5. Stout, G.H.; Jensen, L.H. *X-Ray Structure Determination: A Practical Guide*, 2nd ed., Wiley: New York, 1989.
6. reference 5, p. 377.
7. Stejskal, E.O.; Memory, J.D. *High Resolution NMR in the Solid State: Fundamentals of CP/MAS*. Oxford: New York, 1994.
8. Grimmer, A.-R.; Blumich, B. *Introduction to Solid-State NMR in NMR: Basic Principles and Progress*, **1993**, *30*, 1-62.
9. Fyfe, C.A. *Solid-State NMR for Chemists*. CFC Press: Guelph, Canada, 1983.
10. Harris, R.K. *Nuclear Magnetic Resonance Spectroscopy: A Physicochemical View*. Pitman: London, 1983.
11. Slichter, C.P. *Principles of Magnetic Resonance*, 3rd ed. Springer: New York, 1992.
12. Abragam, A. *The Principles of Nuclear Magnetism*. Clarendon Press: Oxford, 1961.

13. Mehring, M. *NMR Basic Principles and Progress: High Resolution NMR Spectroscopy of Solids*. Springer-Verlag: New York, 1976.
14. Pake, G. E. *J. Chem. Phys.* **1948**, *16*, 327-336.
15. Bloembergen, N.; Rowland, T. S. *Phys. Rev.* **1965**, *55*, 1679..
16. Davis, J. H.; Jeffrey, K. R.; Bloom, M.; Valic, M. I.; Higgs, T. P. *Chem. Phys. Lett.* **1976**, *42*, 390-394.
17. Wittebort, R. J.; Olejniczak, E. T.; Griffin, R. J. *J. Chem. Phys.* **1987**, *86*, 5411-5420.
18. Baram, A.; Luz, Z.; Alexander, S. *J. Chem. Phys.* **1976**, *64*, 4321-4328.
19. Spiess, H. W.; Sillescu, H. *J. Magn. Reson.* **1981**, *42*, 381-389.
20. Greenfield, M. S.; Ronemus, A. D.; Vold, R. L.; Vold, R. R.; Ellis, P. D. Raidy, T. E. *J. Magn. Reson.* **1987**, *72*, 89-107.
21. Mathews, J.; Walker, R. L. *Mathematical Methods of Physics*. W. A. Benjamin: New York. 1965, p. 374.
22. Hahn, E. L. *Phys. Rev.* **1950**, *80*, 580-594.
23. Vega, A. J.; Luz, Z. *J. Chem. Phys.* **1987**, *86*, 1803-1813.
24. Andrew, E. R. *Phil. Trans. R. Soc. Lond.* **1981**, A299, 505-520.
25. Dixon, W. T. *J. Magn. Reson.* **1981**, *44*, 220-223.
26. Dixon, W. T. *J. Chem. Phys.* **1982**, *77*, 1800-1809.
27. Dixon, W. T.; Schaeffer, J.; Sefcik, M D.; Stejskal, E. O.; McKay, R. A.; *J. Mag. Reson.* **1982**, *49*, 341-345.
28. Hartmann, S. R.; Hahn, E. L. *Phys. Rev.* **1962**, *128*, 2042-2053.
29. Spiess, H. W.; Haeberlen, U.; Zimmermann, H. *J. Magn. Reson.* **1977**, *25*, 55-66.
30. Opella, S. J.; Frey, M. H. *J. Am. Chem. Soc.* **1979**, *101*, 5854-5856.
31. Alemany, L.B.; Grant, D.M.; Alger, T.D.; Pugmire, R.J. *J. Am. Chem. Soc.* **1983**, *105*, 6697-6704.
32. Facey, G. A. *PhD Thesis*, Carleton University, Ottawa, Canada, 1992.
33. Used by permission from Ripmeester, J. A.

6. Figures

FIGURE 1. Angular momentum vectors illustrating the quantum numbers l and m : (left) the general case, (centre) for $l = 1$; (right): precession of the magnetic moment μ about an applied magnetic field B_0 .

FIGURE 2. The effects of a $(\pi/2)_x$ pulse on the magnetization vector M_0 .

FIGURE 3. Energy level diagram of a spin = 1 nucleus in a magnetic field showing the perturbation of the Zeeman levels due to the quadrupolar interaction.

FIGURE 4. Diagram showing the polar angles θ and ϕ made by the magnetic field vector in the principal axis system of the electric field gradient tensor.

FIGURE 5. ^2H NMR powder lineshapes as a function of the asymmetry parameter η . (a) $\eta = 0$, (b) $\eta = 0.2$, (c) $\eta = 0.5$, (d) $\eta = 0.8$, (e) $\eta = 1.0$.³²

FIGURE 6. Diagram showing the three rotations through the Euler angles α , β and γ .²¹

FIGURE 8. The quadrupolar echo pulse sequence.¹⁵

FIGURE 7. The effects of molecular motion on ^2H NMR lineshapes. (A) rigid C-D bond, (B) two-fold flipping of a *para*-di-substituted aromatic ring about its long axis, (C) the in-plane rotation of benzene- d_6 , (D) rotation of a deuterated methyl group about its three-fold axis.³²

FIGURE 9. The ^{13}C NMR spectra of solid methanol- β -quinol clathrate; spectra are collected under different acquisition techniques: (a) high resolution solution techniques, (b) with cross-polarization (no ^1H - ^{13}C decoupling), (c) cross-polarization and ^1H - ^{13}C decoupling, (d) cross-polarization, ^1H - ^{13}C decoupling, and magic angle spinning (CP-MAS).³³

FIGURE 10. Motion of the principal components of a chemical shift tensor as the sample is rotated macroscopically about an axis inclined at angle β to the magnetic field vector B_0 .

FIGURE 11. A diagram of the cross-polarization pulse sequence.

Carleton University
Ottawa, Canada K1S 5B6

Text complete; leaf 72 omitted in numbering.

CHAPTER 3: *p*-*tert*-Butylcalix[4]arene-Toluene*

1. Introduction	73
2. Synthetic Details	75
3. Structural Studies: Solid-State ^1H and ^{13}C NMR Spectroscopy	77
4. Structural Studies: Single-Crystal X-ray Diffraction	84
5. Dynamic Studies: ^2H NMR Spectroscopy	95
6. Structural Differences Induced by Isotopic Guests	105
7. CH- π Interactions in C4A-Toluene and C4A-Chlorobenzene	108
8. Summary	110
9. References	111
10. Figures	115
11. Appendix: X-Ray Diffraction Structural Data	136

1 Introduction

Supramolecular chemistry investigates the interactions of a substrate, or guest, with a molecular receptor, or host. The resulting supramolecular species have several functional features, including catalysis, transport, and recognition.¹ An active area of research in this last feature is to understand host-guest interactions and the factors that control stability of these compounds. An understanding of these interactions can further the knowledge of existing host-guest systems as well as direct the design of advanced molecular receptors and hosts. The relatively simple calixarene host system is a versatile candidate for probing molecular recognition interactions with a variety of guests.

Host-guest interactions in *p*-*tert*-butyl[*n*]arene-guest compounds²⁻⁵ are determined in part from solution ^1H NMR titrations.⁶⁻⁸ In many cases, *p*-*tert*-butylcalix[4]arene does not form a stable and detectable host-guest compound in solution as a result of the host flexibility. 2-Dimensional NMR studies of *p*-*tert*-butylcalix[4]arene in toluene^{8a,b} and

* Parts of this chapter have been published: Ripmeester, J.A.; Ratcliffe, C.I.; Enright, G.D.; Brouwer, E.B. *Acta Cryst.* **1995**, *B51*, 513-522; Brouwer, E.B.; Enright, G.D.; Ripmeester, J.A. *Supramol. Chem.* **1996**, *7*, 79-83; Brouwer, E.B.; Enright, G.D.; Ripmeester, J.A. *J. Incl. Phenom.* **1996**, in press.

nitrobenzene^{8c} have failed to identify any host:guest structures. Host:guest interactions may also be deduced from solid-state X-ray single-crystal diffraction structures. As described earlier, the poor quality of diffraction studies (unresolved disorder, large thermal parameters) blurs the structural features required to characterize the often subtle host-guest interactions.⁹ Consequently, when these XRD structures are used as starting geometries for computational modeling studies,^{5,10-16} features such as cavity symmetry and guest position emerge which seemingly contradict the observed XRD structures.^{10,12,16} Furthermore, the explanation of these structural features are often arbitrated solely by these poorly resolved structures.

Several attempts have been made to improve the structural resolution in *p-tert-butylcalix[4]arene*-guest compounds. Caciuffo *et al* carried out neutron powder diffraction studies of *p-tert-butylcalix[4]arene-toluene* (C4A-TOL) and C4A (2:1) *p*-xylene at 4.2 K in an attempt to freeze out dynamic disorder, but failed to resolve the *t*-butyl disorder.¹⁷⁻²⁰ Space groups and lattice parameters identical to the corresponding XRD data were determined. The dynamics of toluene in C4A-TOL were studied by variable temperature (1.8-96K) inelastic neutron scattering studies: it was proposed that the toluene methyl group may occupy two inequivalent sites, and that the compound structure may differ from the room temperature structure.¹⁷⁻²⁰

This chapter presents experimental evidence for a more complex and accurate structural model of the first structurally-characterized calixarene compound, C4A-TOL (Figure 1).²¹ A comprehensive structural picture is developed from the complementary techniques of XRD and NMR spectroscopy.²²⁻²⁶ At room temperature, XRD gives an *averaged* picture of a 4-fold symmetric calix-toluene unit that undergoes motional averaging between well-defined sites, as determined by ²H NMR. Upon cooling, the molecular motion is slowed, and the structure “frozen” in a 2-fold symmetric

conformation different from, but not unrelated to, the room temperature structure. Significantly, the previously unresolved and difficult-to-understand calix *t*-butyl disorder is clarified: the *t*-butyl groups possess a 50:50 positional disorder, related to the location of the toluene guest in the calix cavity. Unique features of each spectroscopic technique are discussed in the context of the other, resulting in additional insight. In retrospect, the C4A-TOL compound exhibits many of the “problem” features typical of calixarene compounds. It appears that the ease of synthetic access to and crystallization of this compound is inversely proportional to the ease of elucidating its structure; consequently, the results summarized in this chapter have been interpreted in light of and draw upon the structural work discussed in subsequent chapters.

Finally, the role of stabilizing π -methyl interactions between host and guest is examined with the structural elucidation of C4A-chlorobenzene. Chlorobenzene is an analogue of toluene, yet sits in the calix cavity with the ring substituent protruding, rather than inserted. An attractive interaction between the toluene CH₃ group and the host is suggested to explain the orientation of the guest.

2. Synthetic Details

Unless otherwise stated, all chemicals were purchased from Aldrich Chemical Company and used without further treatment.

C4A-TOL. C4A (0.2991 g, 0.46 mmol) was added to toluene (5 mL) in a 10 mL glass vial. Stirring for several hours at low heat (60-80 °C) led to dissolution of the white powder. Cooling to room temperature overnight led to the formation of colourless crystals of C4A-TOL (MW 741.06, 0.2659 g, 0.36 mmol, 78% yield).

C4A-TOL-*d*₅ and **C4A-TOL-*d*₈** were prepared as above from toluene-*d*₅ (C/D/N Isotopes, 99.22%) or toluene-*d*₈ (C/D/N Isotopes, 99.6%) solvent.

t-Butyl-*d*₉-phenol.²⁷ Phenol (2.8649 g, 30.44 mmol) and t-butylalcohol-*d*₉ (2.11 mL, 22.65 mmol, C/D/N Isotopes, 99%) were added to a frozen (77 K) mixture of AlCl₃ (1.68 g, 12.60 mmol) and CH₂Cl₂ (10 mL, distilled from sodium) in a Schlenk tube under a nitrogen atmosphere. The contents were allowed to warm to room temperature over 2 h. As the reaction progressed, the yellow solution developed a fine white precipitate. The reaction mixture was quenched with an aqueous saturated solution of NH₄Cl (25 mL) and the aqueous layer separated from and then extracted with CH₂Cl₂ (3 x 5 mL). The solvent was evaporated and the brown residue was extracted with small portions of hot water (20 x 1 mL). White needle-like crystals of t-butyl-*d*₉-phenol (MW 159.29, 0.3236 g, 2.03 mmol, 9%) were isolated upon cooling of the water solution.

***p*-*tert*-Butyl-*d*₉-calix[4]arene-toluene.**²⁸ t-Butyl-*d*₉-phenol (0.0223 g, 0.14 mmol) was mixed with non-deuterated t-butylphenol (0.4793 g, 3.19 mmol) in a 50 mL 2-neck round bottom flask under a nitrogen atmosphere. To this was added 37% formaldehyde (0.31 mL) and NaOH (0.0060 g, 0.15 mmol) and the solution was stirred and heated at 120 °C for 2 h. The stirring was halted and the thick yellow slurry was heated at 120 °C for 1.75 h. Removal of heat was followed by the addition of warm diphenyl ether (4 mL) and the mixture stirred overnight until the solution was clear. The solution was heated at 170 °C under a stream of nitrogen gas for 1 h, followed by refluxing at 250 °C for 2 h. The clear dark brown solution was then cooled to room temperature and precipitation was induced by the addition of ethyl acetate (8 mL). The mixture was stirred for 0.5 h and then allowed to stand for an additional 0.5 h. The beige solid was isolated by filtration and washed with ethyl acetate (3 x 0.5 mL), acetic acid (1 x 1 mL), distilled H₂O (2 x 0.5 mL) and acetone (3 x 1 mL) to yield a white solid. The white solid was dissolved in warm toluene (10 mL); colourless crystals of t-butyl-*d*₉-calix[4]arene-toluene (0.2031 g, 0.27

mmol, 33%) were isolated upon overnight cooling. Approximately 5% of the *t*-butyl methyls were deuterated.

3. Structural Studies: Solid-State ^1H and ^{13}C NMR Spectroscopy

3.1 ^{13}C CP-MAS NMR Spectroscopy

The report of the solid-state ^{13}C CP-MAS NMR spectrum of C4A-TOL in 1988 by Komoto²² established an additional technique by which to probe the structure of this prototypal calixarene complex. Subsequently Ripmeester²³ established the assignment of all guest and host lines, as well as the existence of a phase transition at 248K. Below the phase transition, the ^{13}C NMR spectrum changes dramatically indicating a lowering of symmetry of the calix compound; the asymmetric unit is thought to contain two inequivalent C4A-TOL units with either a two-fold axis or a mirror plane in each unit.

Figure 2 shows the partial ^{13}C CP-MAS NMR spectra of C4A-TOL at 292K and 115K;^{21a} the spectra agree with the previously published spectra.²²⁻²³ The 292K spectrum reveals that the structure possesses 4-fold symmetry. Each host line in the spectrum represents four equivalent carbons, confirming the equivalence of the four *t*-butylphenolic subunits. With the dipolar-dephasing (DD) NMR experiment, the resonances of carbons with attached protons that are immobile disappear.²⁹ At room temperature resonances at δ 124.7 and 125.3 ppm disappear and can be assigned to the C-3 and C-5 carbons. Furthermore, the resonance at δ 123.8 ppm also disappears, and is assigned to the *para* carbon of the guest toluene. Since the guest C-4'-H bond sits along the C_4 symmetry axis, its position is invariant under axial rotation and thus disappears with DD. The guest C-2' and C-3' are still visible under DD due to motion. ^2H NMR spectroscopy (section 5.1) confirms that the toluene guest undergoes axial rotation about its long molecular axis.²³

The spectrum at 115K shows increased complexity. In general, the host resonances are doubled, (illustrated by C-8 (δ 31.5 ppm), C-7 (δ 34.2 ppm), and C-1 (δ 144.1 ppm)) suggesting that the host symmetry has been lowered. The host C-4 resonance (δ 146.2 ppm, singlet, 292K) is split into two doublets for a total of four separate resonances at 115K; the C-8 doublet also shows signs of further doublet splitting. Overlap of the calix C-2, C-3, C-5, and C-6 resonances as well as the guest C-2', C-3', and C-4' lines in the δ 122.1-130.2 ppm region makes it difficult to discern the splitting of these resonances. The region in which these resonances lie increases from a width of 6.7 ppm at room temperature to 8.1 ppm at 115K.

3.2 The Toluene C-1' Resonance at 230 K

The toluene C-1' gives two lines of equal intensity in the 230K ^{13}C CP-MAS spectrum of C4A-TOL,²³ and this suggests that there are two crystallographically inequivalent toluene molecules. Since the ^{13}C spectrum continues to change as a function of temperature (see below), and possibly as well as time, the structure just below the phase transition is of an intermediate one. Two pieces of evidence from XRD are used to construct a structural model consistent with the observed NMR data. First, diffraction peaks of weak intensity ($\sim$ 5-10% of main diffraction peaks) occur at one-half integer positions along *h* and *k* (sharp, disappear over 6 h) and along *l* (broad, persistent). These data are evidence for aggregation of the asymmetric units into larger crystallographic repeat units, *i.e.*, doubling of the asymmetric unit along the *a*, *b* and *c* axes. Doubling along *a* and *b* fails to lift the 4-fold symmetry of the asymmetric unit whereas doubling along *c* anticipates the structure of C4A-nitrobenzene compound (Chapter 4), the second piece of XRD evidence. In this case, doubling of *c*, but not of *a* or *b*, occurs.

Unfavourable steric interactions between *t*-butyl groups of two layers of calixarene units

(i) shifts the calixarene layer along the *a* and *b* axes such that $a \neq b$ and (ii) removes a mirror plane in the *ab* plane and doubles the *c*-axis; this results in an orthorhombic space group. If an analogous distortion in C4A-TOL occurs at 230K, an intermediate orthorhombic structure would generate two crystallographically inequivalent toluenes giving two toluene C-1' NMR lines. The doubling of both the host and guest ^{13}C NMR resonances is consistent with this picture. It must be stressed, however, that the 230K ^{13}C spectrum reflects a structure intermediate to those at room temperature and at 150 (or 115) K; nevertheless, the above proposal is not unreasonable.

3.3 The Toluene C-1' Resonance at 115K

The 115K spectrum differs from the 230K spectrum in that the toluene C-1' line is split into at least seven components which vary in chemical shift and intensity (Figure 3). These spectral features, which reflect the local or short-range ordering in the solid, provide a window of the structural changes that occur far below the phase transition.

The C-1' toluene 1:1 doublet at 230K suggests there are two crystallographically inequivalent toluene molecules. The increased multiplicity at 115K implies that the number of crystallographically inequivalent toluene molecules has likewise increased. Furthermore, the long-range ordering of individual calix units appears to have been lost, and the seven lines arise from the variations in structural arrangements of neighbouring calix-toluene units.

From the XRD crystal structure, one C4A-TOL unit faces a plane of four such units with the cavity openings facing each other (Figure 4, *top left*). This arrangement, with 4-fold symmetric calixarene cavities, is represented pictorially (Figure 4, *top right*). If the toluene guest of the lower calix cavity is considered, its nearest neighbours are in the plane above it, and to a first approximation, define the local structural environment. Two

features of the low-temperature phase are salient: the calix cavities possess more than 2-fold symmetry (^2H NMR) and secondly, long-range ordering among the calix-toluene units (XRD) is absent; the latter implies a statistical distribution of calix sites. Thirty-two (2^5) structural arrangements of the five two-fold symmetric cavities are possible, of which nine are unique (Figure 4, *bottom*; the number on the upper right corresponds to the occurrence of each arrangement). The toluene guest is thus sensitive to nine different structural arrangements of its own and its four nearest neighbour hosts.

The 115K ^{13}C NMR spectrum should therefore show a 9-fold splitting pattern with a relative intensity distribution of 1:1:2:2:4:2:2:1:1 for each guest resonance. Of the toluene resonances in the 115K ^{13}C NMR spectrum, the toluene C-1' lines (δ 138.0-139.4 ppm) are most visible. Seven resonances with an intensity distribution of 3:2:1:4:3:2:1 are observed and, if two incidences of coincidental overlap of two resonances are assumed (at δ 138.0 and δ 139.0 ppm), the observed spectrum can be fitted (Figure 3).

The multiplicity of the toluene carbons ($m \leq 9$) may account for the broadened chemical shift range at 115K seen for the toluene C-2', C-3', and C-4' resonances (δ 122.1-130.2 ppm). The guest interacts with adjacent calix layers which push the toluene slightly off the host 4-fold symmetry axis; in this case, the C-4' resonance would be more informative than the C-1' resonance. Unfortunately the C-4' region is too congested and any specific features (like those seen for C-1') are obscured. Implicit in this analysis is a model in which the toluene sits in the calix cavity much like a ball and socket joint, with the "ball" being the methyl group. Displacement at the end of the toluene molecule is translated throughout the entire molecule. While C-1' might experience little off-axis displacement due to its proximity to the pivot point, the high electron density of its local chemical environment may enhance the little displacement C-1' does undergo. The toluene methyl resonance (C-5', δ 14.8 ppm) is slightly broadened at 115K, but fails to

show the resolution of the C-1' line; since it is the pivot point of the joint, it undergoes insufficient displacement to give the observed broadening.

HYPERNMR³⁰ was used to simulate the ¹³C NMR shifts of the 2-fold symmetric C4A-TOL using the geometry derived from the 150K structure (only one guest position was used). The Cartesian coordinates were transformed to the .HIN file format, read into HYPERNMR, and were used to calculate the ¹³C NMR chemical shifts without further modification (Table 1). While the trends of the calculated chemical shifts match those from the observed spectrum, there are some notable deviations. First, the calculated δ for the C4A phenolic carbons (C1) is nearly 11 ppm greater than observed. Other significant

TABLE 1. Summary of C4A-Toluene ¹³C NMR Chemical Shifts (in ppm).

<i>Molecule</i>	<i>Carbon</i>	<i>HYPERNMR^a</i>	<i>HYPERNMR^b</i>	<i>Observed (s)</i>	<i>Observed (lg)</i>
<i>Toluene</i>	1	140.5	139.0	138.6	137.8
	2	132.1	132.6	127.1	128.4
	3	133.8	130.1	128.3	129.2
	4	128.9	127.9	123.6	125.5
	5	135.1	130.3	128.3	129.2
	6	132.2	133.8	127.1	128.4
	7	19.1	21.7	15.0	21.3
<i>C4A</i>	A1		157.3	146.5	
	A2		135.4	128.6	
	A3		130.9	124.2	
	A4		149.8	144.4	
	A5		146.4	125.8	
	A6		139.8	129.3	
	A7		27.4	34.4	
	A8		29.0	32.0	
	A9		25.1	30.4	
	B1		157.0	146.5	
	B2		136.8	128.6	
	B3		143.3	125.8	
	B4		147.7	144.4	
	B5		127.0	124.2	
	B6		137.8	129.3	
	B7		29.8	34.4	
	B8		28.5	32.0	
	B9		24.3	30.4	

^atoluene only; ^bC4A-TOL.

deviations are with carbons 5A and 3B: these are also the points at which the guest interacts with the host and thus might be quite sensitive to toluene. Overall, however, the trends in calculated chemical shifts reflect the observed spectrum. In particular, the guest *ipso* carbon (C1') chemical shift is simulated well. The slight difference in chemical shifts of equivalent ring carbons may suggest a slight inequivalence arising from its off-axis tilt in a 2-fold symmetric cavity, but may also be an artifact of HYPERNMR: the calculation for toluene alone also gives different chemical shifts for equivalent ring carbons.

3.4 Toluene Inversion in the Calixarene Cavity

The suggestion from the single-crystal XRD study that a fraction of the toluene molecules in the C4A cavity are inserted upside down led to a re-examination of the 292K ^{13}C CP-MAS NMR spectrum. Figure 5 shows the high field region of the spectrum of C4A-TOL; two toluene methyl resonances are visible at δ 15.0 and 21.9 ppm. The resonance for methyls inserted deep inside the calix cavity is shifted to high field from that of the resonance due to the liquid by $\Delta\delta = 6.3$ ppm due to ring current effects¹⁸ of the neighbouring calix aromatic rings; the line at δ 15.0 ppm is therefore the inserted methyl. The other line is near the solution resonance of the toluene methyl (δ 21.3 ppm)²⁷ and corresponds to the upside-down toluene. Integrated intensities of the two lines show the inserted:inverted ratio to be approximately 95:5.

3.5 ^1H CRAMPS NMR Spectroscopy

The methyl solid-state ^{13}C NMR isotropic chemical shift of the calix-included toluene is significantly shifted from that in solution due to the aromatic ring currents of the calix. The change in the ^1H NMR complexation-induced shift (CIS) of the guest as a function of guest concentration can be used to study the complexation by calixarenes;

thermodynamic parameters for complexation can be derived.^{8,32-33} It was of interest to determine the effect of the calix ring current on the toluene methyl proton chemical shift in the solid-state. The guest hydrogens are located spatially closer to the calix aromatic groups and the ¹H NMR chemical shift is anticipated to show an even greater ring current effect than that of the methyl carbon ¹³C NMR chemical shift.

Large dipolar couplings lead to broad and featureless resonances in solid-state ¹H NMR. Use of a complicated pulse train such as the CRAMPS (Combined Rotational And Multiple Pulse Sequence) pulse sequence reduces proton dipolar couplings so that reasonably sharp ¹H NMR spectra are possible.³⁴ Figure 6 shows the 300 MHz ¹H CRAMPS spectrum of C4A-TOL. The aromatic (δ 6-8 ppm) and aliphatic (δ 0-3 ppm) regions show the calix proton lines, as well as the toluene ring hydrogen resonances. The line at δ -1.0 ppm is assigned to the guest methyl hydrogens, and like the methyl ¹³C resonance, it is shifted upfield relative to its solution value (δ 2.09 ppm). The CIS value (-3.1 ppm) is far greater than that seen in the ¹³C spectrum; this ¹H CIS value corresponds to a ¹³C CIS value of roughly -75 ppm since the ¹H chemical shift range is 10 ppm while that of ¹³C is 250 ppm. The electronic environment around the methyl group of the toluene has an enormous impact on the chemical shift of the methyl protons.

TABLE 2. ¹H NMR chemical shifts for the guest in C4A-Toluene (in ppm)

<i>Molecule</i>	<i>Proton</i>	<i>HYPERCHEM^a</i>	<i>HYPERCHEM^b</i>	<i>Observed (s)</i>	<i>Observed (lq)</i>
<i>Toluene</i>	Me	1.54	-2.57	-1.0	2.09
	2	6.60	4.75	4 - 7	7.09
	3	6.85	5.99	4 - 7	7.00
	4	6.49	5.93	4 - 7	6.98
	5	6.69	6.10	4 - 7	7.00
	6	6.52	4.75	4 - 7	7.09

^atoluene alone; ^bC4A-TOL.

HYPERNMR was used to determine the proton chemical shifts from the C4A-TOL-150 crystal structure (Table 2). The ^1H resonances shift to higher field upon enclathration, in particular that of the toluene methyl protons. The simulated chemical shift values correspond well to the experimental ones both in the calixarene and in solution.

3.6 Summary

^{13}C CP-MAS NMR spectroscopy establishes the 4-fold symmetry of C4A-TOL at room temperature. Below the 248K phase transition, the structure possesses a lower (C_2) symmetry. The DD NMR experiment identifies toluene rotation about its long molecular axis which is coincident with the calixarene C_4 symmetry axis. The chemical shift and intensity distribution of the toluene *ipso*-carbon resonances at 115K indicates that long-range ordering of C4A-toluene units in the crystalline lattice is absent and arises from the short-range order effects of a distribution of calix-toluene structures with distorted 2-fold symmetry. The room temperature ^{13}C NMR spectrum of C4A-TOL shows two high-field lines corresponding to methyl-inserted toluenes and toluenes that sit in the cavity in an inverted position. Finally, the ^1H chemical shift of the methyl deep in the calix cavity is shifted dramatically due to the close proximity of the methyl protons to the aromatic rings of the calixarene.

4. Structural Studies: Single Crystal X-Ray Diffraction

The crystal structure of C4A-TOL reported by Andreetti was obtained at room temperature.²¹ Differential scanning calorimetry revealed a thermal anomaly at 248K indicative of a phase transition.²³ Furthermore, solid-state ^{13}C and ^2H NMR spectroscopic evidence suggests strongly that the structure of this compound at low temperature differs from that at room temperature. It was surprising, then, that redetermination of the crystal

structure at 150K gave overall lattice symmetry ($P4/n$) and unit cell parameters unchanged (except for slight contraction) from the initial room temperature structure. Furthermore, initial refinement of the XRD data gave a structural model exhibiting the same t-butyl group disorder (77:23) seen for the earlier structure. The initial conclusions were therefore disheartening: there were no apparent differences between the structures above and below the phase transition.

The key breakthrough involved a more complex treatment of the t-butyl disorder. Additional structural evidence supported a lowering of the 4-fold calix cavity symmetry at temperatures below 248K. Most compelling was the ^2H NMR lineshape of the toluene- d_5 compound which is consistent with at most 2-fold symmetric cavity at $T < 179\text{K}$. When the t-butyl disorder was treated as a translation as well as a rotation of the t-butyl group, two t-butyl positions with an occupancy of 50:50 were identified. In addition, the phenol rings attached to the t-butyl groups are disordered, also with a 50:50 occupancy, and the entire t-butylphenol group pivots about the calixarene C1-C2 bond. When the two disordered positions alternate, *i.e.*, when one t-butylphenol group is “in”, one adjacent (90°) to it is “out”, the calix cavity becomes two-fold symmetric (elliptical) and matches the symmetry of the guest. The rotational component of the motion between the two disordered sites removes the possibility that the two-fold symmetry is due to a mirror plane; thus the symmetry origin of the elliptical cavity arises from C_2 and not C_{2v} symmetry.

Incorporation of the constraint that each host-guest unit has 2-fold symmetry and host-guest units are oriented perpendicular to each other gives a structural model which refines to an R -value of 0.051 for the 150 K structure. XRD data of C4A-TOL were also collected at 290K and analyzed with the structural model developed for the 150K data set

(Table 3). A similar structural picture emerges for the room temperature structure with an *R*-value (0.046) due to the increased thermal motion at the higher temperature.

TABLE 3. Crystallographic data for t-butylcalix[4]arene-TOL at 150 and 290K, and C4A-CLBZ.^a

compound	C4A•TOL-150	C4A•TOL-290	C4A•CLBZ
formula	C _{12.75} H ₁₆ O	C _{12.75} H ₁₆ O	C _{12.25} H _{15.25} OCl _{0.25}
fw	185.27	185.27	187.37
temperature, K	150	290	290
colour, habit	colourless	colourless	colourless
crystal size, mm	0.30 x 0.30 x 0.30	0.25 x 0.20 x 0.18	0.45 x 0.40 x 0.17
crystal system	tetragonal	tetragonal	tetragonal
space group	<i>P4/n</i>	<i>P4/n</i>	<i>P4/n</i>
<i>a</i> , Å	12.5540(3)	12.77259(23)	13.05500(0)
<i>b</i> , Å	12.5540(3)	12.77259(23)	13.05500(0)
<i>c</i> , Å	13.7665(17)	13.8068(5)	12.93900(0)
<i>V</i> , Å ³	2169.7(6)	2252.43(9)	2205.23 (0)
<i>Z</i>	8	8	8
ρ_{calc} , g cm ⁻³	1.124	1.089	1.129
<i>F</i> (000)	798.41	803.55	821.80
μ (Cu K α) mm ⁻¹	0.50	0.49	1.07
λ , Å	1.54056	1.54056	1.54056
scan type	$\theta/2\theta$	$\theta/2\theta$	$\theta/2\theta$
scan rate, deg min ⁻¹	2	4	4
data collected	<i>h, k, l</i>	<i>h, k, l</i>	<i>h, k, l</i>
$2\theta_{\text{max}}$, deg	139.5	139.9	139.7
total # of reflns	4963	4452	3626
# of unique reflns	2049	2157	2111
<i>R</i> _{merge}	0.013	0.014	0.033
# of reflns $I \geq 2.5\sigma(I)$	1727	1385	1579
# of variables	170	213	
<i>R</i>	0.051	0.046	0.065
<i>R</i> _w	0.077	0.063	0.152
GOF	2.73	2.24	5.68
max Δ/σ , finl cycl	0.044	0.064	0.059
resid density, e Å ⁻³	-0.22 to 0.25	-0.22 to 0.12	-0.33 to 0.71

^aConditions and collection details: Enraf-Nonius diffractometer; graphite monochromator; aperture 4.0 x 4.0 mm at a distance of 173 mm from the crystal; stationary background counts at each end of the scan (scan/background time ratio 5:1); peak and background counts determined with profile analysis procedure of Gabe *et al.*, *J. Appl. Cryst.*, **1989**, 22, 384. $\sigma(F_o)$ based on counting statistics, function minimized $\sum w(|F_o| - |F_c|)^2$, where $w = [\sigma^2(F_o) + k(F_o)^2]^{-1}$, $R = \sum ||F_o| - |F_c|| / \sum |F_o|$, $R_w = (\sum w(|F_o| - |F_c|)^2 / \sum w|F_o|^2)^{1/2}$, and $GOF = [\sum w(|F_o| - |F_c|)^2 / (m - n)]^{1/2}$. Values given for *R*, *R*_w, and GOF are based on those reflections with $I \geq 2.5\sigma(I)$.

It must be emphasized that this C_2 symmetry is a local symmetry; within the crystal lattice the elliptical calix cavities, which occupy two orientations 90° to each other, appear to the XRD technique to be superimposed. Recall that XRD is sensitive to long-range ordering and not short-range. The structural model that is developed with XRD data alone is insensitive to the 2-fold symmetry and thus leads to a 4-fold symmetric structure due to space-averaging.

The elliptical *p*-tert-butylcalix[4]arene cavity has been seen in modified calix compounds both empty^{12,35-38} and occupied^{10,39-45} as well as in modeling studies, yet this is the first observation of an elliptical cavity in an unmodified *p*-tert-butylcalix[4]arene. In the molecular dynamics studies of upper-rim tetraamide-substituted *p*-tert-butylcalix[4]arenes, Wipff *et al* used as a starting geometry a C_{4v} conical calix, which consistently evolved to a C_2 -symmetric cone within a few picoseconds at 300K.¹⁴ When the run is carried out at 800K, the two elliptical cavities interconvert, and on average, give a C_{4v} structure. The present solid-state structure of the unmodified C4A compound with toluene offers for the first time, conclusive proof for the existence of C_2 elliptical cavities in the solid-state, and occurs without the influence of additional upper- or lower-rim substituents.¹⁴

4.1 Structural Features

The ORTEP of C4A-TOL is shown in Figures 8 and 9; one of the two disordered calix-toluene units is shown with darkened atoms. The two symmetry-imposed disordered toluene orientations are visible when looking along the *c*-axis (Figure 8), and the 50:50 positional disorder of the *t*-butylphenol groups is apparent. Confusion concerning the *t*-butyl disorder in the initial structure determination likely arose from the close proximity of two sets of atom pairs: the central (C-7, C-7A) and the CT1 and CT1A methyl carbons of

the *t*-butyl group. Without the proper positional treatment, these sets of atom pairs merge and generate a disorder arising from rotation only rather than translation and rotation of the *t*-butyl group. It is interesting to note that modeling studies (*in vacuo*) have suggested that the *t*-butyl groups adopt two positions with only slight differences in energies.¹²

Despite the absence of any atomic chiral centres and the fact that C4A-TOL crystallizes in a centrosymmetric space group ($P4/n$), the C4A tetramer possesses chirality due to the directional aspects of the phenolic OH hydrogen bonds. The phenolic hydrogens of the calixarene are located in the electron density difference map. When the hydrogen bonding is considered, the four phenol groups of the macro-ring are connected with the same direction or handedness (Figure 10, *left*). In pursuing relationships between *t*-butyl group positions and various C4A-TOL structural features, it was surprising to find a significant correlation between the direction of the phenolic OH bond and the orientation of one of the C-Me bonds of the disordered *t*-butyl. Two disordered *t*-butyl positions arise from an alignment of one of the *t*-butyl C-Me bonds in either a parallel or an anti-parallel fashion relative to the direction of the phenolic OH bond which makes an angle b with the aromatic ring plane: $\beta = 32.2^\circ$; $\beta' = 30.3^\circ$ (Figure 10). The guest is aligned parallel with the *t*-butylphenol subunit in the parallel position. The parallel *t*-butyl C-Me bond lies slightly out of the aromatic ring plane, designated by the angle α ; $\alpha = 4.6^\circ$ (defined by the torsional angle: H-O-C4-C3); the anti-parallel *t*-butyl C-Me bond lies $\alpha' = 169.7^\circ$ out of the aromatic ring plane. Modeling and electron diffraction studies on *t*-butylbenzene show that the *t*-butyl group is at lowest energy when it is oriented with one C-Me bond in the plane of the benzene ring.⁴⁶ The parallel and anti-parallel positions (the starred methyl groups) are related by a rotation about the aromatic ring-C(Me)₃ bond by an angle 45.0° . The relationship between *t*-butyl orientation and phenolic O-H bond direction is present in all C4A-guest structures studied in this thesis; in the cases where the

disorder deviates from 50:50 the majority position is aligned with the OH bond and the minority position is anti-parallel.

Although the XRD data refines to a model with 50:50 positional disorder of the *t*-butylphenol groups, it is possible that each *t*-butylphenol unit is unique and gives a 25:25:25:25 positional disorder at even lower temperatures. Two pieces of data support this possibility: first, the large thermal parameters for the *t*-butyl carbons suggest that the 50:50 disordered model is at its resolution limit and may mask additional structural features. Secondly, the low temperature ^{13}C CP-MAS NMR spectrum shows four lines for each central *t*-butyl carbon (C7), and implies that there are four crystallographically inequivalent *t*-butyl groups.

The calix-toluene units form a bilayer in the *ab*-plane; these bilayers are stacked along the *c*-axis. The bilayer consists of a pair of calixarenes whose wide openings (the upper rim) face each other, but are offset along both *a* and *b*. Within the *ab* plane the calix units are assumed to be elliptical and arranged perpendicular to each other. With this ordering of calix units, the *t*-butyls are arranged like the cogs of a gear. Examination of the closest contacts between adjacent calix units (CT3-CT2A = 3.99 Å) shows that *t*-butyl group interdigitation^{47,48} may be a significant close contact. If the elliptical cones are assumed to be parallel, the closest contact between *t*-butyl groups along the major axis becomes 3.37 Å (CT3-CT3); clearly this is a “tight” fit! Based on interatomic contact distances, the interactions within the *ab*-plane are as significant as the interactions between the calix bilayers (along *c*).

The elliptical distortion of the calix cavity can be followed by examining the major and minor axes of the ellipse (Table 4). The differences at the lower rim (oxygen-oxygen) are minuscule (0.001 Å), and increase as the opening of the cone increases: 0.115 Å at C1, 0.611 Å at C4 and 0.973 Å at C7. Note that the minor axis of the ellipse shows a greater

distance at C1 than the comparable values for the major axis; this illustrates that as the upper rim of the cone expands, the lower rim contracts.

TABLE 4. Selected Bond Distances and Angles for C4A-TOL-150.

Bond	Distance (Å)	Bond	Distance (Å)
O2-C4	1.365(3)	CT-CT' (major)	10.996
C8-C5	1.523(3)	Me-H α ...C2	2.675
C4-C5	1.400(4)	Me-H β ...C1	2.704
C4-C3	1.402(4)	Me-H β ...C2	2.594
C5-C6	1.392(5)	Me-H β ...C3	2.738
C6-C1	1.354(4)	TC5-CT2	3.936
C2-C3	1.398(4)	TC5-CT1	4.50
C2-C1	1.453(4)	TC5-CT3	4.61
C7-C1	1.536(5)	TC5-CT1A	3.76/3.80
C7-Ct1	1.543(5)	TC5-CT2A	4.25
C7-Ct3	1.527(5)	TC5-CT3A	5.18
C7-Ct2	1.533(5)	TC6-CT1	3.94
C7-C7a	0.606(5)	TC6-CT2	4.01
C1-C1a	0.361(4)	TC6-CT3	4.48
O1-H...O4	1.628	TC6-CT1A	3.72/3.84
O4-H...O2	1.626	TC6-CT2A	4.19
O-O' (minor)	3.800	TC6-CT3A	5.03
C1-C1' (minor)	5.312	TC2-C4	3.47
C4-C4' (minor)	7.926	TC2-C3	3.56
C7-C7' (minor)	9.433	TC2-C5	3.61
CT-CT' (minor)	8.131	TC4-CT1	3.88
CT-CT' (minor)	10.123	TC7-CT1	3.85
O-O' (major)	3.799	TC7-C1	3.89
C1-C1' (major)	5.197	TC7-C6	3.96
C4-C4' (major)	8.537	CT3-CT2A	3.99
C7-C7' (major)	10.406	CT3-CT3	4.91
CT-CT' (major)	9.548	CT3-CT1A	5.98
Atoms	Angle (deg)	Atoms	Angle (deg)
Me-H α ...C2	151.86	O-O'-C7 (minor)	118.44
Me-H β ...C1	141.67	O-O'-C7 (major)	126.58
Me-H β ...C2	158.18	O1-H-O4	163.70
Me-H β ...C3	165.60		

4.2 Position of the Guest

The toluene methyl group is positioned deep in the calix cavity (Table 4). The methyl carbon (TC2) sits 3.54 Å above the basal plane defined by the four phenolic

oxygens. With the improved treatment of disorder and concomitant increase in resolution, additional structural features become apparent. In the first instance, the carbon bond lengths along the 4-fold axis are less than expected; this shorting is attributed to the toluene guest tilting slightly from the calix 4-fold axis. Since the 4-fold molecular calix axis is also a crystallographic symmetry axis, the XRD modeling program drives the (slightly off-axis) atomic positions to the symmetry axis and causes the observed foreshortening. When the atoms of the toluene guest are treated as a rigid body, an off-axis tilt of $\theta = 7 \pm 2^\circ$ is determined. The toluene pivots about the methyl group (the “ball” of the ball-and-socket model), and consequently the *para*-carbon is positioned furthest from the 4-fold axis. It should be noted that the inability of the XRD technique to resolve clearly the host’s four unique subunits likely restricts the determined position of the guest to an equilibrium position. While the XRD picture shows the toluene rigidly held in the cavity, the guest most likely samples the numerous sites that are generated as the host flexes.

The host atoms in close proximity to the toluene guest define the points at which the guest and host interact. The toluene interacts with not one, but with five calixarene units: that in which the toluene sits and those which “cap” the calix cavity from the above *ab*-plane. Surprisingly, it is not the toluene *para*-carbon that makes the closest contacts with the adjacent layer, but rather the two *meta*-carbons. The distances from the two toluene *meta*-carbons protruding from the calixarene cavity and to the methyl carbons of *t*-butyls from two calixarenes (α, β) in the *ab* plane above are: TC5-CT2 $_{\alpha}$ = 3.94 Å and TC5-CT1A $_{\beta}$ = 3.76, 3.81 Å; TC6-CT1 $_{\alpha}$ = 3.94 Å and TC6-CT1A $_{\beta}$ = 3.72, 3.84 Å (since the *t*-butyl groups of the capping calixarene are positionally disordered, two distances to the *meta*-carbon exist). The sum of the van der Waals’ radii of two CH bonds is 3.8 Å. The origin of the off-axis tilt appears to be related to the contact with a *t*-butyl group of a calix

in the above *ab*-plane. Molecular dynamics studies with acetonitrile and methanol in *p*-*tert*-butylcalix[4]arenetetraamide show that these guests also sit in an off-axial position.¹⁴

The closest contacts between the guest and the calixarene cavity are between the toluene methyl carbon (TC2) and the aromatic ring carbons (C3, C4, C5). C4 is the carbon to which the hydroxy group is attached (*ipso*-) and it forms the closest contact with TC2 (3.47 Å); the methyl hydrogen atoms are assumed to sit in a tetrahedral arrangement and consequently point 34° away from the TC2-C4 vector. Carbons C3 and C5 are distanced from TC2 by 3.56 and 3.61 Å respectively. The average distance that the toluene methyl carbon makes to the host aromatic carbons is 3.54 Å in the *p*-*tert*-butylcalix[4]arene-Na cation.⁴⁰

The next set of close host-guest contacts are between the two toluene *ortho*-carbons TC4 and TC7 and the host. TC4 is 3.88 Å away from the *t*-butyl CT1 while TC7 is 3.85 Å from an identical, symmetry-related *t*-butyl carbon CT1. The guest TC7 carbon also makes somewhat longer contacts with the host aromatic ring carbons C1 and C6 (3.89 and 3.96 Å). In summary, the closest contact is between the toluene methyl and the host *ipso* ring carbon (3.47 Å) followed by the guest-intercalix contacts (TC6-CT1A, 3.72 Å), the guest-intracalix contacts (TC7-CT1, 3.85 Å), and finally the intercalix *t*-butyl interactions in the *ab*-plane ($d_{\min} = 3.99$ Å). The above contacts are assumed to roughly match the significance of the stabilizing interactions in C4A-toluene.

The view along the *z*-axis (or the crystallographic *c*-axis) in Figure 8 shows that the guest aromatic ring is not positioned perpendicular to two opposite aromatic walls of the host, but rather makes an angle of 22° with the line connecting the two opposite walls of the elliptical cavity, *i.e.*, the major axis of the ellipse. The aromatic ring is positioned perpendicular to the *t*-butyl C-Me bond that forms the outer wall of the calix cavity. This arrangements affords the remaining two *t*-butyl methyls minimal contact with the aromatic

ring. Drew has superimposed three toluene-containing modified-C4A structures and noted that the guest lies along the major axis of the ellipse.¹³ In the calculation of toluene docking in a C_{4v} symmetrical cavity, the guest does not sit perpendicular to the aromatic walls of the host, but makes an angle of 21-24°; it is thought that the absence of lower-rim substituents makes the cavity more flexible and allows for a better fit of the guest.

The presence of unaccounted electron density along the 4-fold axis in the proximity of the *para*-carbon is consistent with a second toluene guest position in the cavity. The second guest sits in the cavity with the methyl group protruding from the cavity, and approximately $10 \pm 2\%$ of the toluene molecules sit in this second position for the 150K structure. (In the 290K ^{13}C NMR spectrum, only 5% of the toluenes are inverted). This intriguing structural feature suggests that more than one stable toluene orientation is possible; such information is critically important for modeling calculations. Two such studies in the gas phase have suggested that inverted toluene inclusion gives host-guest structures with energies comparable to inserted toluene inclusion.^{11,13}

Several different syntheses of C4A-TOL lead to the incorporation of varying amounts (0-10 %) of the inverted toluene. Most likely this variation arises from differences in the temperature of the saturated toluene solution and crystallization rates of C4A-TOL which have not been explored further in this work.

Both the off-axis and upside-down features of the toluene guest are corroborated by NMR techniques: the latter is confirmed by the observation of two toluene-methyl ^{13}C NMR resonances, while the former is derived from the ^2H NMR lineshape.

4.3 Superlattice Peaks

Weak reflections at one-half integer values of h , k , and l with ~5-10% of the intensity of the full integer peaks are observed when the data collection begins immediately

after cooling of the crystal to 150K. The reflections along *l* are broadened and persist over the time of collection whereas the sharper reflections along *h* and *k* disappear over the course of six hours. These observations point to dynamics as well as relaxation from non-equilibrium positions within the crystal at low temperatures. The half-integer reflection values indicate a larger crystallographic repeat unit arising from a doubling of the *a*, *b* and *c* axes.

Steric interactions between adjacent calixarene units (in the *ab*-plane perpendicular to the 4-fold axis) may induce correlated orientational jumps of the guest and account for the short-lived reflections along *h* and *k* (Figure 11). High temperature ^2H NMR lineshapes of the toluene and the calix *t*-butyl groups reveal that the 90° rotational jump of the guest is accompanied by a large change in position of the flexible host calixarene, giving a 4-fold symmetric calix and a 2-fold disordered toluene (Figure 11, *left*).¹⁴ At low temperatures, the guest still makes 90° rotational jumps, but must do so infrequently as the ^2H lineshape is not affected by this motion. As the guest pushes out one side of its host calix, its nearest neighbour in the *ab* plane is pushed in, and induces a 90° rotational jump of the toluene in the second, pushed-in calix (Figure 11, *centre*). This correlated orientational motion generates larger aggregates or repeat units in the lattice. The correlated orientational motion is short-lived, and decays once thermal equilibrium is achieved; the crystal now consists of a random arrangement of toluene-calix units oriented between two positions (Figure 11, *right*). Since these aggregates of larger crystallographic repeat units account for a small fraction of the total intensity, they must occur in isolated pockets within the crystalline lattice. This model supports the description of the calix-guest compounds as “soft” crystals (section 5.3).

The orientationally-correlated supercell retains 4-fold symmetry about *c* (Figure 11, *centre*) and causes the guests in the four calix cavities to be equal. Consequently, the toluene ^{13}C NMR resonances are insensitive to a doubling of the unit cell along *a* and *b*.

The half-integer reflections along the *c*-axis are more persistent and broader than those in the *ab* plane. Doubling along this axis occurs when two *ab*-planes slide over each other laterally; this situation is illustrated in the C4A-nitrobenzene structure (Chapter 4). In the nitrobenzene case, steric interactions between the *t*-butyl groups of two *ab*-layers of calix-guest units cause $a \neq b$ and the removal of a 4-fold axis; this results in an orthorhombic space group. Implicit in this explanation is the assumption that the interaction within the *ab* plane is stronger than between *ab* planes along the *c*-axis.

5. Dynamic Studies: ^2H NMR Spectroscopy

^2H NMR spectroscopy, sensitive to motional frequency ranging from 10^3 to 10^8 Hz, gives distinctive spectra which indicate both the type and rate of motions. ^2H NMR spectra of deuterated guest and host have been collected at various temperatures and analyzed to characterize the respective motions. Specifically, the ^2H NMR spectra reveal two important and significant features of the C4A-TOL compound: First, at low temperatures, toluene undergoes 2-fold flips about its long molecular axis and infers a 2-fold symmetric calix cavity. At higher temperatures, the toluene behaves as a 4-fold rotor, indicating a 4-fold symmetric calix cavity. Secondly, at room temperature, the calixarene is not *static*, but rather *dynamic*, as the *t*-butyl groups of the calix are rapidly alternating between two fixed positions. The motion of both guest and host is significant for host-guest interactions.

5.1 Motion of the Guest

While ^{13}C NMR spectroscopy shows that toluene undergoes axial rotation about its long molecular axis, it does not inform about the *rate* of molecular motion; this is better determined by variable temperature (VT) ^2H NMR spectroscopy. Facey *et al* first examined the guest motion in C4A-TOL- d_8 with VT ^2H NMR spectroscopy.²³ The room temperature spectra show three distinct axial lineshapes indicating three types of C-D molecular bonds. The 2-fold symmetric toluene molecule matches the 4-fold symmetric calix cavity by jumping between four positions 90° apart; toluene is thus dynamically disordered. The lineshapes arise from the methyl C-D, the *m*-, *o*-D and the *p*-D bonds in an intensity ratio of 3:4:1.

Since the barrier to methyl rotation is low it is anticipated that the methyl lineshape would not change significantly upon cooling to lower temperatures. However, the barrier to phenyl rotation is anticipated to be somewhat higher and thus toluene- d_5 was chosen as the deuterated guest for a VT ^2H NMR study. VT ^2H NMR spectra were collected over 77-337K and are divided into two sets: the 2-fold (180°) jump (129-179K, Figure 12) and the 4-fold (90°) jump (179-337K, Figure 15).

5.1.1 Two-fold Toluene Flips

The 77K spectrum indicates that toluene is immobile. The static lineshape is characterized by the effective quadrupolar coupling constant $\chi = e^2qQ/h = 178.7 \pm 1.0$ kHz and by a slight asymmetry parameter $\eta = 0.043 \pm 0.011$. Toluene remains essentially immobile (jump rate $\kappa < 3 \times 10^3$ Hz) until 135K when the lineshape begins to change. The spectrum at 179K is characteristic of an axial rotor undergoing 2-fold or 180° flips at the fast motion limit (FML).⁴⁹ The relationship between the lineshape components of the

static and FML spectra are used to determine the angle β (the angle between the rotational axis and the *ortho* and *meta* C-D bonds) according to equations 1-3.

$$a_{11}^{[179]} = \cos^2\beta v_{xx}^{[129]} + \sin^2\beta v_{zz}^{[129]} \quad (1)$$

$$a_{22}^{[179]} = v_{yy}^{[129]} \quad (2)$$

$$a_{33}^{[179]} = \sin^2\beta v_{xx}^{[129]} + \cos^2\beta v_{zz}^{[129]} \quad (3)$$

From these equations, $\beta = 59.8^\circ$, which is very close to the $\beta = 60.0^\circ$ expected. The slight difference in bond angles expected between the *ortho*- and *meta*-deuterons is not observed in the ^2H NMR spectra.

The static, FML and intermediate lineshapes are simulated using the above experimental lineshape parameters and varying the 180° jumping frequencies from 10^3 to 10^8 Hz (Figure 12).⁵⁰ Since the *para*-deuteron C-D bond lies on the rotation axis, the *para*-deuteron electric field gradient (EFG) tensor is invariant under axial motion and its lineshape does not change as the jump frequency varies. The lineshape simulation is divided into two components: the *para* deuteron, which generates a static pattern, and the remaining deuterons (*ortho*, *meta*) whose lineshape varies with jump rate. The two components are added in a 4:1 intensity ratio; the simulated spectral intensity (which also varies as a function of the jump rate) must be taken into account as well (Figure 13, *top*). The spectral intensity enters a “fade-out” region ($I_{\min} = 6 \times 10^4$ Hz $\sim 138\text{K}$) where the intensity is less than the static or FML lineshape. The loss in intensity increases the spectral noise of the 141-160K spectra.

Once the observed and simulated lineshapes are matched, the calculated jump rates κ are correlated to the temperatures at which the experimental lineshapes were collected (Figure 12, *right*). A plot of the inverse temperature ($1000/T$) against $\ln\kappa$ generates an

Arrhenius plot from which a barrier to toluene 2-fold jump of $E_{\text{act}} = 34.0 (3.1) \text{ kJ mol}^{-1}$ is obtained (Figure 13, *bottom*).

TABLE 5. ^2H NMR spectral parameters for C4A-TOL.^a

deuteron	<i>T</i> (K)	$ \Delta v_{xx} $ (kHz)	$ \Delta v_{yy} $ (kHz)	$ \Delta v_{zz} $ (kHz)	χ (kHz)	η
<i>ortho</i> -, <i>meta</i> -	77	128	140	268	178.8	0.045 ± 0.012
	179	28	140	168	112.0	0.667 ± 0.024
	337	14	14	28	18.7	0.000
<i>para</i> - ^b	77	128	140	268	178.8	0.045 ± 0.012
	179	126	134	260	173.3	0.031 ± 0.012

^a Estimated errors of ± 1.5 kHz in the measurements of the Δv_{ii} and ± 1 kHz in χ .

^b Features not observed at 337K.

5.1.2 Toluene Off-Axis Tilt

The toluene *para*-CD bond lies along the guest rotation axis, and as the toluene rotates, the lineshape of the *para*-deuteron will remain a static lineshape for a pure axial rotor. It would be anticipated, then, that the *para*-deuteron lineshapes at the static and 2-fold FML would be exactly the same. A slight narrowing is observed at the higher temperature ($\chi_{179} = 173.3 \pm 1.0$ kHz; $\chi_{129} = 178.7 \pm 1.0$ kHz) arising from toluene motion off the calix symmetry axis. An off-axis tilt of angle θ is obtained (by trial and error) from equations 4-6 which relate the averaged EFG tensor components of the *para*-deuteron of the static ($v_{xx} = -140$ kHz; $v_{yy} = -128$ kHz; $v_{zz} = +268$ kHz) and FML spectra ($a_{11} = -134$ kHz, $a_{22} = -126$ kHz; $a_{33} = +260$ kHz):

$$a_{11} = \cos^2\theta v_{xx} + \sin^2\theta v_{zz} \quad (4)$$

$$a_{22} = v_{yy} \quad (5)$$

$$a_{33} = \sin^2\theta v_{xx} + \cos^2\theta v_{zz} \quad (6)$$

Toluene lies off the axis by $\theta = 8^\circ \pm 2^\circ$ according to equations 4-6; this value compares favourably to that determined by XRD ($\theta = 7 \pm 2^\circ$).

5.1.3 Four-fold Toluene Flips

It might be expected that the transition from the toluene 2-fold to a 4-fold rotor would occur at the DSC phase transition temperature (248K). The EFG tensor components of the *ortho*- and *meta*-deuterons are plotted as a function of temperature (135-337K) in Figure 14. With most systems, the values of the EFG tensor components change at the phase transition.⁵¹ The C4A-TOL-*d*₅ EFG tensor components change gradually and continuously both below and above the phase transition temperature starting at 200K and ending at 260K. Calorimetry, which measures macroscopic events at the bulk (crystal) level, and NMR, which measures microscopic events at the molecular level, are complementary techniques. The values of the EFG tensor components in the region above and below the DSC phase transition suggest that the toluene may not be a simple 4-fold rotor and that it may exhibit a more complex dynamic behavior.

The ²H NMR spectra of C4A-TOL from 179-337K (Figure 15, *left*) show broadened features in the intermediate region that are not well simulated by a simple 4-fold flip model. This lack of agreement between simulated and observed and the continuous change of the EFG tensor component suggest that all toluene rotors may not move at a uniform rate. The lack in uniformity in rate generates a distribution of 4-fold motional frequencies which may account for the broadened ²H lineshapes. If a gaussian distribution of motions is assumed, the broadening can be accounted for, and a reasonable fit achieved (Figure 15, *right*). For a given frequency ν , seven spectra were calculated at 0, ± 0.5 , ± 1.0 , and $\pm 1.5 \sigma$, where $\sigma = 0.5\nu$, and were added with a gaussian intensity distribution (0.22, 0.36, 0.61, 1.0, 0.61, 0.26, 0.22). The motional distribution about the

central frequencies models the observed spectra better than a simple 4-fold, single-frequency simulation.

The 4-fold motional model of the C4A-TOL-*d*₅ ²H NMR spectra has two limitations: (i) the 337K spectrum is not the FML spectrum and (ii) an additional and unaccounted motion appears to further narrow the spectra at high temperatures. The first concern may not be that significant because the majority of the lineshape changes occur between the static and $\kappa = 10^5$ Hz (337K) spectra and the observed spectra correspond well to these simulated frequencies.

The 337K spectrum shows a central intensity in the experimental spectrum not matched by the simulation ($\kappa = 10^5$ Hz). In addition, the simulated spectrum is broader than the observed spectrum. While the 4-fold rotational motion successfully simulates the gross spectral features, it does not completely account for all the guest motion. Two types of additional guest motion can be reasonably considered. First, XRD has identified that 5-10% of the toluenes are inverted in the calix cavity, and an inversion motion of the guest may occur. However, exchange between the inserted and inverted guest positions will not affect the lineshape as the deuteron EFG tensor components under inversion will be identical regardless of the guest site (all C-D bonds will make the same angle with respect to the 4-fold axis). A second motion to consider is an off-axis libration motion, as seen with the 2-fold flip model (section 5.1.2); additional off-axis motion will cause further narrowing of the patterns.

A distribution of guest motions may arise from vacant calix cavities which break the correlation of the toluene motion within the crystal lattice. These vacancies or defect sites may result from loss of the guest (C4A-TOL samples lose toluene when stored at room temperature for several months). Furthermore, an inverted guest position suggests that there may be an exchange between the two guest sites. Obviously the inverted guest

experiences a different calixarene environment and it is reasonable to assume that this influences the jump rate. Finally, upon heating *p*-iso-propylcalix[4]arene-*p*-xylene, the compound transforms from a 1:1 to a 2:1 host:guest compound;⁵² a similar transition may account for some of the distribution of motions above the 2-fold FML for the C4A-TOL compound.⁵³ Any one feature (or the combination thereof) may account for the observed ²H NMR spectra.

The barrier to 4-fold toluene motion can be derived from the observed temperatures and simulated jump rates, albeit with greater uncertainty than the 2-fold motion, as the motional model does not completely account for the observed spectra. The slope of the Arrhenius plot (Figure 16) gives $E_{\text{act}} = 8.0 (0.4) \text{ kJ mol}^{-1}$. For reference, the barrier to 4-fold rotation of the toluene guest in the calix cavity has been estimated by modeling calculations to be 2.5 kJ mol^{-1} .⁸ Over the temperature range of 129-337K, the toluene in the calixarene cavity undergoes first 2-fold jumps, then 4-fold jumps. The motional energy as a function of toluene position may be represented by a 4-well potential in which two of the wells (at 0 and π) are deeper than the other two below 179K (Figure 16). As the compound goes through the phase transition, the potential changes such that the four 90° sites become equally populated.

5.2 Motion of the Calixarene Host

While the calixarene framework has often been described as flexible,²⁻⁵ no experimental evidence for calixarene dynamics in the solid state has been reported. Even in the solution state, it is thought that the cone conformation of the calix is 4-fold C_{4v} symmetric. Reinhoudt *et al* first suggested that the C_{4v} structure is a saddle-point structure, and that the structure deduced from solution ¹H NMR spectra is the result of the rapid interconversion of two elliptical or pinched-cone C_{2v} structures.¹² The C_{4v}

structure was calculated to be 13.4 kJ mol^{-1} higher in energy than the C_{2v} structure. ^1H NMR spectroscopy shows evidence for the pinched-cone conformation for octyloxycalix[4]arene compounds (with various upper-rim substituents) in solution; barriers for interconversion were calculated from variable temperature studies to be 55.6 – 63.6 kJ mol^{-1} .⁵⁴

Figure 18 shows the VT ^2H NMR spectra of *t*-butyl- d_9 -C4A-toluene from 129 to 204K. The 129K spectrum indicates that the C-D bonds of the methyl groups are immobile. As temperature increases, the spectra change both in shape and width, due to motion of the methyl C-D bonds. The spectra cease changing at 204K and are invariant to 290K, indicating that the molecular motion is at the fast motion limit ($\kappa \sim 10^8 \text{ Hz}$). The relative orientation of the two different *t*-butyl sites in the calixarene may be deduced from these spectra.

5.2.1 Relative Orientation of Two *t*-Butyl Sites

The evolution of the lineshapes as a function of temperature in Figure 18 is typical of *t*-butyl methyl groups that undergo methyl group (C_3) as well as *t*-butyl group (C_3') rotation; this type of motion is called C_3, C_3' rotation⁵⁵ and is illustrated in Figure 19. The narrowing of the lineshape from 129 to 204K results from motional reorientation of the C-D bonds between specific sites. A reduction in width by one-third from the static spectrum is expected for C_3 motion, and additional C_3' motion reduces the spectral width by an additional one-third. Thus, for C_3, C_3' motion, a reduction in width of the static spectrum of one-ninth is anticipated. In this specific case, the FML axial lineshape is expected to have an effective quadrupolar coupling constant $\chi = 170 \div 9 = 18.9 \text{ kHz}$ with an asymmetry parameter (η) close to zero; however, the observed spectrum is somewhat narrower: $\chi = 17.1 \pm 1.0 \text{ kHz}$ with $\eta = 0.123 \pm 0.130$. The deviation of the observed from

the anticipated spectrum may be accounted for by a model in which there is motion between two inequivalent *t*-butyl sites separated by an angle θ . The angle θ is obtained from equations 4-6 which relate the averaged tensor components of the static $((1/9)v_{xx} = (1/9)v_{yy} = -14.2$; $(1/9)v_{zz} = +28.3$ kHz) and FML spectra ($a_{11} = -10.0$; $a_{22} = -12.8$; $a_{33} = +22.8$ kHz) for two-fold reorientation. The observed 204K spectrum is best simulated by employing an angle $\theta = 15^\circ \pm 2^\circ$ (Figure 19, *right*), which is close to the angle derived from XRD of $\theta = 10 \pm 2^\circ$.

The ^2H NMR spectra clearly show that at temperatures above 204K, the *t*-butyl groups of the calixarene are rapidly ($\kappa > 10^8$ Hz) reorienting between two inequivalent sites separated by $15^\circ \pm 2^\circ$. The 204 and 290K spectra are identical, and this implies that while the guest motion changes over this range (from 2-fold to 4-fold rotor), the rate and type of calix *t*-butyl group motion does not.

5.2.2 *t*-Butyl Motion: a Difficult Motional Model

Using the EFG tensor components of the static and FML lineshapes, the intermediate motional lineshapes may be simulated, providing the correct motional model is used. For *t*-butyl motion, three separate motions are activated between 129 and 204K: C_3 , C_3' , and the two-site reorientation, and it is impossible to identify the order in which these motions occur. An appropriate model would be complex, and would require a 3-dimensional matrix to adequately simulate this set of spectra.

5.3 Summary of Motion in C4A-Toluene

^2H NMR spectroscopy establishes three important points concerning the structure and dynamics of C4A-TOL. First, the 2-fold motion of the guest reveals the symmetry of the guest, and by extension, that of the host. Second, the calixarene host is dynamic in the

solid state. Third, both guest and host motions occur over similar temperature regimes (between 120 and 200K). The role of the guest dynamics on the host geometry has been described from molecular dynamic studies: as acetonitrile rotates about the *t*-butylcalix[4]arenetetraamide symmetry axis it “pushes out” each of the four aromatic walls and induces the oscillating C_{2v} - C_{2v} interconversion.¹⁴ The guest also lowers the kinetic barrier between C_{2v} forms. VT ^2H NMR studies provide an excellent experimental determination of dynamics parameters for comparison to molecular dynamics simulations.

While the guest and host motions are correlated, it is not clear how and to what extent, and accurate knowledge of the host *t*-butyl motional rates are needed to describe the correlation. Differences between samples (*t*-butyl deuteration, cavity occupancies, guest orientations) likely hinder acquisition of accurate data.

Raman spectroscopy or Brouillion scattering may be useful techniques to probe whether the host-guest interaction motion is a local oscillator or whether it is correlated over the crystal (a lattice mode). For the β -cyclodextrin-*t*-butanol compound, a sharp low-energy lattice mode is observed at 5 cm^{-1} which suggests correlation between the guest and host that exists throughout the crystal.⁵⁶

The role of motion in both guest and host has physical consequences for the behavior of the crystal, specifically in the gradual change in the ^2H NMR spectra in the vicinity of the phase transition. Due to the flexibility in the host architecture, C4A-TOL appears to tolerate the introduction and propagation of orientational defects. In particular, the *t*-butyl disordering is not static, and a long-range correlation of the two positions does not exist. Thus C4A-TOL—and probably all C4A-guest compounds with a propensity to introduce and propagate orientational defects or disordering—should be perceived as a “soft” crystal system. The designation “soft” indicates significant molecular motion within the constraints of the crystalline lattice.

The interaction between toluene and the calix is stronger at low temperatures than at higher temperatures. When toluene motion is reduced ($T < 129\text{K}$), the calix framework collapses around the guest and has a reduced symmetry (most likely C_2 , but possibly C_1); the host-guest interaction is then strongest. As toluene becomes mobile, the framework becomes 2-fold symmetric in response to the cavity carved out by the guest performing 2-fold flips. Finally, when toluene is a 4-fold rotor, it induces C_4 symmetry in the host and the host-guest interaction is the weakest. The extent of molecular recognition and selectivity of guests by the C4A system is thus influenced by the motion of the guest and the motion the guest induces in the host. In these cases, the shape of the guest is less important than the volume it carves out while in motion, *i.e.*, its dynamic shape. The role of guest geometry in calix recognition is discussed further in Chapter 4.

6. Structural Differences Induced by Isotopic Guests

Surprisingly, differences in both the FT-IR and ^{13}C NMR spectra of three C4A-toluene isotopomers (toluene- d_0 , toluene- d_5 and toluene- d_8) are observed. For a wide range of applications in chemistry, the substitution of ^1H by ^2H causes no apparent difference in structure or reactivity. One exception is the kinetic isotope effect⁵⁷ which probes the role of a proton in a reaction: substitution of ^1H by ^2H causes a retardation of the rate of the reaction under investigation (due to the doubled mass of the proton) related to the extent of proton involvement in the transition state. Host-guest chemistry is dominated by non-bonding interactions and thus it is striking to observe guest-induced variations in the calix structure as a function of isotopic substitution.

The non-bonding host-guest interactions are mediated by the hydrogen atoms of both the guest and host. In particular, CH- π interactions have been cited as being significant in host-guest chemistry.^{5,6,8,32,58-60} There has been some discussion in the

literature concerning the classification of the CH- π interaction; it has been described as a type of weak hydrogen bond, since it possesses specificity or directionality which sets it apart from the non-specific or van der Waals interaction. Others argue that this is just a problem of nomenclature.⁶¹⁻⁶⁵

6.1 FT-IR Spectroscopy

One physical method for probing the CH- π interaction is IR spectroscopy.

Stabilizing interactions between a C-H bond and a π -aromatic system should weaken the C-H bond, and should be observed in the IR spectrum as a high-frequency shift of $\nu_{\text{C-H}}$.³² In the case of C4A-guest compounds, the guest C-H vibrational modes are indistinguishable from those of the calix. One way to circumvent this limitation is to examine the C-D frequencies of the deuterated guest.

Figure 20 shows the FT-IR spectra of the C4A compounds of toluene- d_0 (*top*), toluene- d_5 (*middle*) and toluene- d_8 (*bottom*). The aromatic C-H stretching mode shifts to $\nu = 2274 \text{ cm}^{-1}$ from $\nu = 3026 \text{ cm}^{-1}$ upon isotopic substitution.⁶⁶ The liquid IR spectrum of per-deuterated toluene C_7D_8 shows aromatic C-D stretching frequencies in the vicinity of $\nu = 2276 \text{ cm}^{-1}$.⁶⁷ By comparison, the calix-toluene and liquid toluene IR spectra show essentially no difference in the guest C-H stretching frequencies and hence C-H bond strengths. This does not discount the presence of CH- π interactions as these type of interactions may also be present in liquid toluene. However, no features characteristic of significant CH- π interactions arise from the comparison of liquid and calix-included toluene C-H stretches.

The phenolic O-H stretch is present in all three spectra, but is shifted from $\nu = 3146 \text{ cm}^{-1}$ to 3171 cm^{-1} upon introduction of ring deuteration of the guest. The value for the

OH frequency in CHCl_3 solution is $\nu = 3160 \text{ cm}^{-1}$.⁶⁸⁻⁶⁹ Changes in $\nu_{\text{O-H}}$ frequencies may be correlated to changes in OH bond lengths as estimated by an empirical correlation of a series of hydrogen-bonded structures: $\Delta\nu/\nu_o = 3.6 \Delta r_{\text{OH}}$.⁷⁰ Accordingly, the presence of ring-deuterated guests induces a lengthening of the OH bond of the calix by 0.003 Å. Alternately, the lattice parameters (*a, b, c*) may change slightly upon deuteration and this may cause the observed changes in ν_{OH} .

The dependence of $\nu_{\text{O-H}}$ on ring deuteration of the toluene suggests a guest-induced weakening of the O-H bonding network at the base of the calix cavity. This is remarkable as the distance between the guest deuteron at the *ortho* ring position and the nearest calix oxygen is 5.18 Å! The interaction between the ring deuterons and the aromatic rings of the calixarene likely accounts for this induced OH bond weakening. Figure 21 presents a view of toluene in the calix cavity which shows OH bond lengthening arising from stronger interaction between the calix aromatic rings and the guest ring deuterons. The four phenolic repeat units of the calix are connected by methylene bridges about which the calix flexes. As the OH base increases in diameter, this is accompanied by (or results from) a decrease in the diameter of the cavity opening.

Interestingly, deuteration of the toluene methyl group does not affect the OH bond length in the calix and suggests that the dominant interactions for this feature are between the π system of the host and the ring protons of the guest. The IR data suggest a slight change in structure of the calixarene-toluene compound upon deuteration of the guest. Interactions between the π -system of the host and the aromatic CH of the toluene guest increase slightly upon deuteration, and likely results in the deuterated guest fitting inside the host cavity more tightly than the non-deuterated toluene.

6.2 ^{13}C CP-MAS NMR Spectroscopy

The ^{13}C CP-MAS NMR spectra of the three isotopomers of C4A-toluene (Figure 22) show difference in guest resonances. Of note are the differences in the *ipso*-carbon (δ 138.7-137.9 ppm) and the methyl carbon (δ 16.8-14.1 ppm); the other guest carbon resonances are not resolved due to overlap with host resonances. With both resonances there is a shift to high field upon deuteration: $\Delta\delta = 0.4$ ppm for the *ipso*-C and $\Delta\delta = 0.6$ ppm for the Me-C. The shifts correspond to chemical shift changes observed for various isotopes in CDCl_3 (Table 6) and do not suggest a change in chemical environment upon inclusion of the various deuterated toluene isotopes.

TABLE 6. Toluene deuteration and ^{13}C NMR chemical shift, δ (ppm).

Guest	Carbon	Calix ^a	Solution ^b	$\Delta\delta^c$
toluene- <i>d</i> ₀	methyl	15.1	21.3	-6.2
	<i>ipso</i>	138.7	137.7	-1.0
toluene- <i>d</i> ₅	methyl	16.8	21.5	-4.7
	<i>ipso</i>	138.3	137.6	-0.7
toluene- <i>d</i> ₈	methyl	14.1 ^d	20.7 ^d	-6.6
	<i>ipso</i>	137.7	137.7	0.0

^areferenced to hexamethylbenzene (δ 16.9 ppm).

^breferenced to CDCl_3 .

^c $\Delta\delta = \delta$ (calixarene) - δ (solution).

^dcentral transition.

7. CH- π Interactions in C4A-Toluene and C4A-Chlorobenzene

Experimental evidence with the C4A-TOL system shows little support for stabilizing $\text{CH}_{\text{guest}}-\pi_{\text{host}}$ interactions between the toluene methyl group and the aromatic system of the host. First, when C4A is dissolved in a 4:1 toluene:benzene mixture for 1 week at 80 °C, only C4A-benzene is formed. This high selectivity of the calix for a guest lacking the

methyl group suggests that the $\text{CH}_{\text{guest}}-\pi_{\text{host}}$ interactions may be insignificant in forming a thermodynamically stable C4A compound. Secondly, while the ^1H CRAMPS spectrum reveals a vastly modified electronic environment around the toluene methyl, the XRD results do not indicate any specific $\text{C-H}\cdots\pi$ interactions, based on distance as well as directional requirements. Finally, the IR spectra reveal no differences in the guest methyl ν_{CD} between C4A-TOL and the liquid guest. The role of interactions between the calix *t*-butyl groups and the aromatic system of the guest is discussed in detail in Chapter 5.

Steric and electronic effects can be studied by substituting certain groups by others that share common steric or electronic features. The chloro group is often substituted for a methyl group as both have a similar van der Waals radius. It is anticipated that in selecting chlorobenzene as a steric analogue of toluene for inclusion into the C4A cavity, the additional electron density of the chlorine will favour attractive host-guest van der Waals interactions, and the chlorine group will sit deep in the cavity. The observation that the chloro group sits outside of the calix cavity is thus surprising, and provides the strongest evidence for the role of attractive $\text{CH}_{\text{guest}}-\pi_{\text{host}}$ interactions in directing the toluene guest position in the calix cavity. Aoyama describes the calix-guest interaction as one where the host is a soft base (due to the electron-donating aromatic substituents) and the guest C-H bonds are acidic.⁷² The strength of the interaction depends on the host basicity and guest acidity; in the case of the toluene, the methyl proton acidity gives a favourable interaction with the host.

The ^{13}C CP-MAS NMR spectra of C4A-1-chlorobenzene (C4A-CLBZ; Figure 23) show the compound to possess 4-fold symmetry, and are similar to the 292K spectrum of C4A-TOL. The *ipso*-carbon of the guest is broadened due to dipolar coupling to chlorine. The guest C-2' (or C-3') resonance persists under DD conditions, and shows that the

guest is dynamic. The spectra do not reveal whether the guest ring substituent lies in or out of the calix cavity.

The XRD structure of C4A-CLBZ confirms that the chloro group points out of the calix cavity (Table 3, Figure 23). Several additional features differentiate the C4A-CLBZ structure from the C4A-TOL structure. First, the *t*-butyl groups in C4A-CLBZ do not show any positional disordering, and may be related to the symmetrical shape of the protruding chloro group. Secondly, the crystal packing along the C4A-CLBZ *c*-axis is tighter than for C4A-TOL (12.939 vs 13.807 Å), whereas packing along *a* is less tight (13.055 vs 12.7726 Å). This reflects that chlorobenzene sits deeper in the calix cavity than does toluene. Overall, C4A-CLBZ possesses a slightly higher packing coefficient than does C4A-TOL (0.6734 vs 0.6629).⁷¹ The chlorobenzene guest is tilted off the *C*₄ axis by 4° ± 2°. Residual density is observed around the aromatic ring of the guest, but cannot be fitted satisfactorily to a meaningful chemical species, and remains unaccounted for. X-ray absorption may be significant.

Distances between guest and host are as follows: the guest *para*-carbon is situated 4.08 Å above the plane defined by the four phenolic oxygens. The same carbon makes the closest contact with the C-1 (4.30 Å), C-2 (4.40 Å) and C-6 (4.31 Å) host carbons. The closest contact made by the guest with the host is the *meta*-carbon with the host C-3 carbon (4.07 Å). All these contacts are greater than the sum of the van der Waals radii (3.8 Å).

8. Summary

While the first calixarene-guest XRD crystal structure was published over 15 years ago, many structural and dynamic features of this class of supramolecular compounds have remained unresolved. Consequently, comprehensive and quantitative understanding of the

often subtle host-guest interactions has been elusive. In this chapter, a synoptic approach to *p*-*tert*-butylcalix[4]arene-guest structure and dynamics using XRD and solid-state NMR techniques has brought to light previously hidden features including:

1. resolution of *t*-butylphenol positional disorder,
2. relationship of *t*-butylphenol position and calix chirality,
3. *t*-butylcalix[4]arene flexibility in the solid state,
4. the presence of the inserted and inverted guest positions,
5. the off-axis tilt of the guest,
6. the role of adjacent calix units on the guest position,
7. the interplay of guest and host dynamics as a function of temperature, and
8. the preference for methyl rather than chloro groups to occupy the calix cavity.

These features in part have led to a more complex and accurate structural model of C4A-TOL which in turn has implications for the entire class of calix-guest compounds.

Comparison of calix inclusion of isosteric guests (toluene and chlorobenzene) offers the best experimental evidence for attractive CH- π interactions between the guest and host.

To further probe the avoidance of the chloro group by the cavity, it would be interesting to study the following guests: *p*-xylene, *p*-chlorotoluene, and 1,4-dichlorobenzene. While no XRD study has been published of C4A-*p*-xylene, there are claims that it forms a 2:1 host:guest compound in which the two methyl substituents sit in two different calix cavities;¹⁸ how will the calix-*p*-chlorotoluene compound crystallize when both ring substituents occupy two C4A cavities?

The ability of the calixarene framework to recognize and select molecular shapes is dominated by the types of motion that occur in both guest and host. The next chapter examines the role of molecular shape and motion of the guest on the geometry of the host, and builds on the structural and dynamic aspects developed in this chapter.

9. References

1. Lehn, J.-M. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1304-1319.
2. Gutsche, C. D. *Calixarenes*; RSC: Cambridge and London, 1989.
3. Vicens, J.; Bohmer, V. Eds. *Calixarenes*; Kluwer: Dordrecht, 1990.
4. Bohmer, V. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 713-745.
5. Ungaro, R.; Arduini, A.; Casnati, A.; Ori, O.; Pochini, A.; Ugozzoli, F. in *Computational Approaches in Supramolecular Chemistry*, ed G. Wipff, *NATO ASI Series* **1994**, *C426*, 277-300.
6. Fujimoto, T.; Yanagihara, R.; Kobayashi, K.; Aoyama, Y. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 2113-2124.
7. de Namor, A. F. D.; de Sueros, N. A.; McKervey, M. A.; Barrett, G.; Arnaud-Neu, F.; Schwing-weill, M. J. *J. Chem. Soc., Chem. Commun.* **1991**, 1546-1548.
8. Yoshimura, K.; Fukazawa, Y. *Tetrahedron Lett.* **1996**, *37*, 1435-1438.
- 8a. Alfieri, C.; Dradi, E.; Pochini, A.; Ungaro, R. *Gazz. Chim. Ital.* **1989**, *119*, 335-338.
- 8b. Mayzel, O.; Aleksuk, O.; Grynszpan, F.; Biali, S. E.; Cohen, Y. *J. Chem. Soc., Chem. Commun.* **1995**, 1183-1184.
- 8c. Brouwer, E. B.; Facey, G. A.; Ripmeester, J. A. unpublished observations.
9. Harrowfield, J. M.; Ogden, M. I.; Richmond, W. R.; Skelton, B. W.; White, A. H. *J. Chem. Soc. Perkin Trans 2*, **1993**, 2183-2190.
10. Andreotti, G. D.; Ori, O.; Ugozzoli, F.; Alfieri, C.; Pochini, A.; Ungaro, R. *J. Incl. Phenom.* **1988**, *6*, 523-536.
11. Minn, H. H.; Chang, S.; No, K. T. *Theor. Chim. Acta.* **1989**, *75*, 233-245.
12. Grootenhuis, P. D. J.; Kollman, P. A.; Groenen, L. C.; Reinhoudt, D. N.; van Hummel, G. J.; Ugozzoli, F.; Andreotti, G. D. *J. Am. Chem. Soc.* **1990**, *112*, 4165-4176.
13. Drew, M. G. B. in *Spectroscopic and Computational Studies of Supramolecular Systems*; Davies, J. E., Ed.; Kluwer: Dordrecht, 1992, 207-237.
14. Guilbaud, P.; Varnek, A.; Wipff, J. *Am. Chem. Soc.* **1993**, *115*, 8298-8312.
15. Ugozzoli, F.; Ori, O.; Casnati, A.; Pochini, A.; Ungaro, R.; Reinhoudt, D. N. *Supramol. Chem.* **1995**, *5*, 179-184.
16. Cohen, A.A.; Shatzmiller, S.E. *J. Comp. Chem.* **1995**, *16*, 1459-1467.
17. Caciuffo, R.; Amoretti, G.; Carlile, C. J.; Fillaux, F.; Francescangeli, O.; Prager, M.; Ugozzoli, F. *Physica B* **1994**, *202*, 279-286.
18. Prager, M.; Caciuffo, R.; Amoretti, G.; Carlile, C. J.; Coddens, G.; Fillaux, F.; Francescangeli, O.; Ugozzoli, F. *Mol. Phys.* **1994**, *81*, 609-619.

19. Caciuffo, R.; Amoretti, G.; Fillaux, F.; Francescangeli, O.; Melone, S.; Prager, M.; Ugozzoli, F. *Chem. Phys. Lett.* **1993**, *204*, 427-432.
20. Caciuffo, R.; Francescangeli, O.; Melone, S.; Prager, M.; Ugozzoli, F.; Andreetti, G. D.; Amoretti, G.; Coddens, G.; Blank, H. *Physica B* **1992**, *180 & 181*, 691-693.
21. Andreetti, G. D.; Ungaro, R.; Pochini, A. *J. Chem. Soc., Chem. Commun.* **1979**, 1005-1007.
- 21a. The probe temperature was calibrated with the ^{13}C chemical shift of samarium acetate tetrahydrate: Campbell, G. C.; Crosby, R. C.; Haw, J. F. *J. Mag. Res.* **1986**, *69*, 191-195.
22. Komoto, T.; Ando, I.; Nakamoto, Y.; Ishida, S. *J. Chem. Soc., Chem. Commun.* **1988**, 135-137.
23. Facey, G. A.; Dubois, R. H.; Zakrzewski, M.; Ratcliffe, C. I.; Atwood, J. L.; Ripmeester, J. A. *Supramol. Chem.* **1993**, *1*, 199-200.
24. Ripmeester, J.A.; Ratcliffe, C.I.; Enright, G.D.; Brouwer, E.B. *Acta Cryst.* **1995**, *B51*, 513-522.
25. Brouwer, E.B.; Enright, G.D.; Ripmeester, J.A. *Supramol. Chem.* **1996**, *7*, 79-83.
26. Brouwer, E.B.; Enright, G.D.; Ripmeester, J.A. *J. Incl. Phenom.* **1996**, in press.
27. Huston, R. C.; Hsieh, T. Y. *J. Am. Chem. Soc.* **1936**, *58*, 439-441.
28. Gutsche, C. D.; Iqbal, M. *Org. Synth.* **1990**, *68*, 234-237.
29. Alemany, L.B.; Grant, D.M.; Alger, T.D.; Pugmire, R.J. *J. Am. Chem. Soc.* **1983**, *105*, 6697-6704.
30. HYPERNMR: Hypercube, Inc., 419 Phillip St., Waterloo, Ont, Canada N2L 3X2.
31. Breitmaier, E.; Voelter, W. *^{13}C NMR Spectroscopy*; 2nd ed.; Verlag Chemie: Weinheim. **1978**, 185.
32. Nishio, M.; Hirota, M. *Tetrahedron* **1989**, *45*, 7201-7245.
33. Bauer, L.J.; Gutsche, C.D. *J. Am. Chem. Soc.* **1985**, *107*, 6063-6069.
34. Fyfe, C.A. *Solid State NMR for Chemists*; CFC Press, Guelph, Canada, 1983, 167-171.
35. Ungaro, R.; Pochini, A.; Andreetti, G. D. *J. Incl. Phenom.* **1984**, *2*, 199-206.
36. McKervey, M. A.; Seward, E. M.; Ferguson, G.; Ruhl, B.; Harris, S. J. *J. Chem. Soc., Chem. Commun.* **1985**, 388-390.
37. Arduini, A.; Pochini, A.; Reverberi, S.; Ungaro, R.; Andreetti, G.; Ugozzoli, F. *Tetrahedron* **1986**, *42*, 2089-2100.
38. Calestani, G.; Ugozzoli, F.; Arduini, A.; Ghidini, E.; Ungaro, R. *J. Chem. Soc., Chem. Commun.* **1987**, 344-346.
39. Olmstead, M. M.; Sigel, G.; Hope, H.; Xu, X.; Power, P. *J. Am. Chem. Soc.* **1985**, *107*, 8087-8091.

40. Bott, S. G.; Coleman, A. W.; Atwood, J. L. *J. Am. Chem. Soc.* **1986**, *108*, 1709-1710.
41. Arduini, A.; Ghidini, E.; Pochini, A.; Ungaro, R.; Andreetti, G. D.; Calestani, G.; Ugozzoli, F. *J. Incl. Phenom.* **1988**, *6*, 119-134.
42. Ferguson, G.; Kaitner, B.; McKervey, M. A.; Seward, E. M. *J. Chem. Soc., Chem. Commun.* **1987**, 584-585.
43. Ghidini, E.; Ugozzoli, F.; Ungaro, R.; Harkema, S.; El-Fadl, A. A.; Reinholdt, D. N. *J. Am. Chem. Soc.* **1990**, *112*, 6979-6985.
44. Ferguson, G.; Gallagher, J. F.; Pappalardo, S. *J. Incl. Phenom.* **1992**, *14*, 349-356.
45. Giannini, L.; Solari, E.; Zanotti-Gerosa, A.; Floriani, C.; Chiesi-Villa, A.; Rizzola, C. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 85-87.
46. Campanelli, A. R.; Ramondo, F.; Domenicano, A.; Hargittai, I. *J. Phys. Chem.* **1994**, *98*, 11046-11052.
47. Adams, H.; Davis, F.; Stirling, C. J. M. *J. Chem. Soc., Chem. Commun.* **1994**, 2527-2527.
48. Davis, F.; Stirling, C. J. M. *J. Am. Chem. Soc.* **1995**, *117*, 10385-10386.
49. Gall, C. M.; DiVerdi, J. A.; Opella, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 5039-5043.
50. Greenfield, M. S.; Ronemus, A. D.; Vold, R. L.; Vold, R. R.; Ellis, P. D.; Raidy, T. E. *J. Mag. Res.* **1987**, *72*, 89-107.
51. Ripmeester, J. A. *J. Chem. Phys.* **1986**, *85*, 747-750.
52. Perrin, M.; Ghamati, F.; Oehler, D.; Perrin, R.; Lecocq, S. J. *J. Incl. Phenom.* **1992**, *14*, 257-270.
53. Andreetti, G. D.; Ugozzoli, F.; *IX ICCOSS (abstract book)*, **1989**, PC42.
54. Conner, M.; Janout, V.; Regen, S. L. *J. Am. Chem. Soc.* **1991**, *113*, 9670-9671.
55. S. Nishikiori, S.; Ratcliffe, C. I.; Ripmeester, J. A. *J. Phys. Chem.* **1990**, *94*, 8098-8102.
56. Eckhardt, C. J., personal communication.
57. Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry, Part A: Structure and Mechanisms*; 3rd ed.; Plenum: New York, 1990, 216-220.
58. Kovayashi, K.; Asakawa, Y.; Kikuchi, Y.; Toi, H.; Aoyama, Y. *J. Am. Chem. Soc.* **1993**, *115*, 2648-2654.
59. Poh, B.; Tan, C. M. *Tetrahedron* **1994**, 3453-3462.
60. Amabilino, D. B.; Ashton, P. R.; Brown, C. L.; Cordova, E.; Godinez, L. A.; Goodnow, T. T.; Kaifer, A. E.; Newton, S. P.; Peitraszkiewicz, M.; Philp, D.; Raymo, F. M.; Reder, A. S.; Rutland, M. T.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *J. Am. Chem. Soc.* **1995**, *117*, 1271-1293.
61. Sennikov, P. G. *J. Phys. Chem.* **1994**, *98*, 4973-4981.

62. Hallam, H.E. *J. Mol. Struct.* **1969**, 3, 43.
63. Hobza, P.; Zahradnik, R. *Intermolecular Complexes (The Role of van der Waals Systems in Physical Chemistry and in Biodisciplines)*; Elsevier: Amsterdam, 1988.
64. Buckingham, A. D. *J. Mol. Struct.* **1991**, 250, 111.
65. Tokhadze, K. G.; Tkhorzhevskaya, N. A. *J. Mol. Struct.* **1992**, 270, 351.
66. *The Aldrich Handbook of FT-IR Spectra*, Pouchert, C.J. ed. Aldrich: Milwaukee, WI, 1985.
67. Pinchas, S.; Laulicht, I. *Infrared Spectra of Labelled Compounds*; Academic: New York, 1971, 102-103.
68. Gutsche, C.D.; Bauer, L.J. *J. Am. Chem. Soc.* **1985**, 107, 6052-6059.
69. Lutz, B.T.G.; Astarloa, G.; van der Maas, J.H.; Janssen, R.G.; Verboom, W.; Reinhoudt, D.N. *Vibrational Spectroscopy* **1995**, 10, 29-40.
70. Novak, A. in *Structure and Bonding* 18, Dunitz, J. D. ed.; Springer-Verlag: Berlin 1974, 177-216.
71. Kitaigorodsky, A. I. *Molecular Crystals and Molecules*, Academic Press: New York 1973.
72. Fujimoto, T.; Yanagihara, R.; Kobayashi, K.; Aoyama, Y. *Bull. Chem. Soc.* **1995**, 68, 2113-2124.

10. Figures

FIGURE 1. Representations of the t-butylcalix[4]arene-toluene (C4A-TOL) structure.

FIGURE 2. 50.3 MHz ^{13}C CP-MAS NMR spectra of *p*-*tert*-butylcalix[4]arene-toluene at 292 K (bottom) and 115 K (top). The guest resonances are indicated by arrows; x = spinning sidebands. Both spectra were collected on a Bruker MSL-200 spectrometer using a 7 mm spinning Chemagnetics pencil probe: 300-500 transients; recycle time: 3.5 s; $\pi/2$ pulse = 3.1 μs ; contact time = 4 ms; TD = 4K; 16K points; ν = 3.1 kHz.

δ Observed	Intensity
139.4	1
139.2	2
139.0	3
138.7	4
138.4	1
138.2	2
138.0	3

FIGURE 3. Expansion of the 50.3 MHz ^{13}C CP-MAS NMR spectrum of *p*-tert-butylcalix[4]arene-toluene at 115 K (δ 137-140.5 ppm). The toluene C-1' resonance: observed (*bottom*) and simulated (*top*).

FIGURE 4. Labeling scheme for the two inequivalent *t*-butylphenol groups of a 2-fold symmetric C4A cavity; the guest points to the *t*-butylphenol group on the left (A).

FIGURE 5. C4A-toluene structures below the phase transition. *Top:* the five circles (*right*) correspond to one calix-toluene unit capped by a layer of four calix-toluene units (*left*), all possessing 4-fold symmetric cavities. *Bottom:* nine possible structural arrangements (*a-i*) of the five calix-toluene units with 2-fold symmetric cavities; the numbers at the upper right indicate the frequency of each arrangement ($\Sigma = 32$).

FIGURE 6. High field region of the 50.3 MHz ^{13}C CP-MAS NMR spectrum of *p*-*tert*-butylcalix[4]arene-toluene at 292 K; 10,000 transients. The “upside-down” toluene methyl resonance occurs at δ 21.9 ppm with relative intensity 0.04 and the “inserted” toluene methyl resonance occurs at δ 15.0 ppm with relative intensity 0.96.

FIGURE 7. 300 MHz ^1H CRAMPS spectrum of *p*-*tert*-butylcalix[4]arene-toluene at 292K. The spectrum was collected on Bruker AMX-300 spectrometer using a 4 mm spinning probe. The sample was referenced to sodium 3-trimethyl-silylpropionate- $2,2,3,3-d_4$.

FIGURE 3.1 ORTEP of C4A-TOL at 150 K (30% thermal ellipsoids) showing the two disordered cavities; hydrogen atoms omitted for clarity.

FIGURE 9. ORTEP of C4A-TOL at 150 K (30% thermal ellipsoids); hydrogen atoms omitted for clarity. One of the two disordered elliptical cavities is shown.

FIGURE 10. C4A chirality arising from the direction of the phenolic OH bonds; the aromatic plane is represented by the thick horizontal line. The parallel ($\alpha = 4.6^\circ$; $\beta = 32.2^\circ$) and anti-parallel ($\alpha' = 169.7^\circ$; $\beta' = 30.3^\circ$) orientations of the *t*-butyl groups with respect to the direction of the phenolic OH bond. The parallel and antiparallel positions are related by a rotation about the aromatic ring-C(Me)₃ bond of $\alpha_{\text{antiparallel}} - 120 - \alpha_{\text{parallel}} = 45.0^\circ$.

FIGURE 11. Schematic representation of the nature of disorder in *p*-tert-butylcalix[4]arene-toluene-*d*₅ [in *ab* plane, *c* perpendicular]. *Left*: dynamic disorder of host-guest units with two-fold symmetry, which gives 4-fold symmetry on time average in the room temperature structure. *Middle*: lattice of host-guest units with frozen-in distortion and some correlation between orientation of neighbouring units which gives rise to superlattice reflections in the low temperature phase. *Right*: as in (*middle*), but without correlation in orientation of neighbouring units; the apparent high crystal symmetry is due to space-averaging.

FIGURE 12. Observed (*left*) and simulated (*right*) 30.7 MHz ^2H NMR spectra of *p*-*tert*-butylcalix[4]arene- $\text{toluene-}d_5$ over $T = 129\text{--}179$ K. The spectra were collected on a Bruker MSL-200 spectrometer with a 10 mm coil: 300 scans; recycle time: 10 s; $\pi/2$ pulse: 5.0 μs ; echo delay: 35 μs ; line broadening: 1 kHz; TD = 512; 1K points.

FIGURE 13. *p*-*tert*-Butylcalix[4]arene-toluene-*d*₅. ²H signal intensity as a function of ln κ (*top*). Arrhenius plot of the 2-fold guest flip in *p*-*tert*-butylcalix[4]arene-toluene-*d*₅ (*bottom*).

FIGURE 14. ^2H NMR lineshape components as a function of temperature for *p*-tert-butylcalix[4]arene-toluene- d_5 .

FIGURE 15. Observed (*left*) and simulated (*right*) 30.7 MHz ^2H NMR spectra of *p*-tert-butylcalix[4]arene-toluene- d_5 over $T = 179\text{--}337\text{ K}$. The spectra were collected on a Bruker MSL-200 spectrometer with a 10 mm coil: 300 scans; recycle time: 10 s; $\pi/2$ pulse: 5.0 μs ; echo delay: 35 μs ; line broadening: 1 kHz; TD = 512K; 1K points. The simulated lineshapes take into account a gaussian distribution of motional sites (see text).

FIGURE 16. Arrhenius plot of the 4-fold guest flip in *p*-tert-butylcalix[4]arene-toluene- d_5 .

FIGURE 17. *p-tert-Butylcalix[4]arene-Toluene Dynamics.* *Top:* Guest energy as a function of angular position in the calix cavity; the dark lines correspond to the barrier to 4-fold (90°) rotation (ΔE_2) while the combination of dark and light lines corresponds to the barrier to 2-fold (180°) rotation (ΔE_1). The lines at 0° reflect the change in guest energy potential upon change in dynamic host geometry from 2-fold to 4-fold symmetry. *Bottom:* Schematic of the toluene position in the calix cavity (view along the 4-fold z-axis of symmetry) for the elliptical ($T < 179K$) and circular ($T > 335K$) cavities.

FIGURE 18. Observed (*left*) and simulated (*right*) 30.7 MHz ^2H NMR spectra of *t*-butyl- d_9 -C4A-toluene over $T = 129$ -204 K. The spectra were collected on a Bruker MSL-200 spectrometer with a 10 mm coil: 300 scans; recycle time: 10 s; $\pi/2$ pulse: 5.0 μs ; echo delay: 35 μs ; line broadening: 1 kHz; TD = 512; 1K points.

FIGURE 19. Orientation and motion of the deuterated *t*-butyl- d_9 group in C4A-toluene; $\theta = 15^\circ$ (^2H NMR) and 10° (XRD).

FIGURE 21. Scheme of the calix conformation affected by ring-deuteration of the guest: the arrows indicate direction of calix motion upon π -CD attraction. The calix rotates about the axis defined by the methylene carbons (dashed line). The large cavity opening contracts while the small opening expands.

FIGURE 20. FT-IR spectra (KBr disk) of C4A-toluene isotopomers; toluene-d₀ (*top*), toluene-d₅ (*middle*) and toluene-d₈ (*bottom*).

FIGURE 22. 45.3 MHz ^{13}C CP-MAS NMR spectra of C4A-toluene isotopomers; toluene- d_0 (*top*), toluene- d_5 (*middle*) and toluene- d_8 (*bottom*). The spectrum was collected on a Bruker CXP-180 spectrometer using a Bruker 7 mm spinning probe and the FLIPNQS pulse sequence: 1000-2000 transients; recycle time: 3.5 s; $\pi/2$ pulse: 3.3 μs ; line broadening: 1 Hz; TD = 4K; 16K points; ν = 3.1 kHz.

FIGURE 23. 75.2 MHz ^{13}C CP-MAS NMR spectrum of *p*-*tert*-butylcalix[4]arene-chlorobenzene at 290K. The spectrum was collected on a Bruker 300-AMX spectrometer using a Bruker DAS 7 mm spinning probe and the FLIPNQS pulse sequence: 250 transients; recycle time: 3.5 s; $\pi/2$ pulse: 5.5 μs ; line broadening: 2 Hz; TD = 6K; 16K points; $\nu = 4.37 \text{ kHz}$.

FIGURE 24. XRD structure of C4A-CLBZ.

11. Appendix: X-Ray Diffraction Structural Data

A1. Final Positional and Equivalent Isotropic Parameters ($\text{\AA}^2$) for C4A-TOL-150.

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> _{iso} ^a
O2	0.31827(9)	0.38511(9)	0.45366(9)	2.60(5)
C 8	0.16537(13)	0.52404(12)	0.53908(13)	2.32(6)
C 4	0.34522(24)	0.43375(24)	0.53890(24)	2
C 5	0.27555(24)	0.50657(24)	0.58246(24)	2
C 6	0.31064(23)	0.56195(24)	0.66405(22)	1.9
C 2	0.4778 (3)	0.47531(24)	0.65808(23)	2.1
C 3	0.44747(23)	0.41615(23)	0.57658(22)	1.7
C4A	0.3498 (3)	0.4368 (3)	0.5399 (3)	2.5
C5A	0.2757 (3)	0.5063 (3)	0.5806 (3)	2.3
C6A	0.2988 (3)	0.5530 (3)	0.6694 (3)	2.7
C2A	0.46804(24)	0.4621 (3)	0.67533(24)	2.2
C3A	0.4460 (3)	0.4151 (3)	0.5869 (3)	2.6
C7	0.4505 (3)	0.6131 (3)	0.79367(25)	2.59(13)
C1	0.40788(25)	0.55148(22)	0.70549(22)	1.9
CT1	0.5012 (3)	0.5357 (3)	0.86742(24)	2.7
CT3	0.3610 (3)	0.6740 (4)	0.8441 (3)	4.08(18)
CT2	0.5357 (3)	0.6925 (3)	0.7602 (3)	3.02(15)
C7A	0.4194 (3)	0.5851 (3)	0.8156 (3)	2.59(14)
C1A	0.3987 (3)	0.52848(23)	0.7188 (3)	2.5
CT1A	0.5244 (3)	0.5456 (3)	0.8627 (3)	3.9
CT3A	0.3282 (3)	0.5642 (3)	0.8883 (3)	3.33(15)
CT2A	0.4296 (3)	0.7063 (3)	0.7980 (3)	3.57(17)
PK 1 ^b	0.2500 (0)	0.2500 (0)	1.1075 (16)	1.3 (4)
PK 2 ^b	0.2500 (0)	0.2500 (0)	0.9945 (14)	0.7 (3)
PK 3 ^b	0.2500 (0)	0.2500 (0)	0.7843 (18)	1.8 (4)
TC3	0.2456 (14)	0.2327 (6)	1.02980(17)	4.21(13)
TC5	0.2565 (10)	0.3328 (5)	0.9869 (4)	6.2 (6)
TC4	0.2597 (10)	0.3421 (5)	0.8860 (4)	4.6 (5)
TC1	0.2521 (14)	0.2513 (8)	0.82793(18)	2.88(7)
TC7	0.2413 (10)	0.1512 (6)	0.8708 (3)	3.1 (3)
TC6	0.2380 (9)	0.1419 (4)	0.9718 (4)	3.3 (3)
TC2	0.2560 (3)	0.2614 (13)	0.71868(18)	2.97(8)

^a $B_{\text{iso}} = 8/3\pi^2 \sum \sum U_{ij} a_i^* a_j^* (a_i^* a_j^*)$; B_{iso} is the mean of the principal axes of the thermal ellipsoid. ESD's refer to the last digit printed.

^b Three atoms of the inverted guest on the toluene molecular axis.

A2. Final Positional and Equivalent Isotropic Parameters ($\text{\AA}^2$) for C4A-TOL-290.

Atom	x	y	z	B_{iso}^a
O1	-0.68344 (0)	-0.61689 (0)	-0.04587(9)	5.64(4)
C1	-0.65532(12)	-0.56673(13)	0.03902(13)	4.68(7)
C2	-0.55746(13)	-0.58537(13)	0.08079(14)	4.82(8)
C3	-0.53265(14)	-0.53175(14)	0.16426(15)	5.54(9)
C5	-0.69682(14)	-0.44590(14)	0.16379(14)	5.40(9)
C6	-0.72624(13)	-0.49745(13)	0.08067(14)	4.79(8)
C8	-0.48134(14)	-0.66456(14)	0.03878(15)	5.25(8)
C7A	-0.5821 (4)	-0.4077 (4)	0.3099 (4)	8.6 (3)
C4A	-0.6006 (3)	-0.4676 (3)	0.2127 (3)	5.79(19)
CT3A	-0.5692 (4)	-0.2880 (4)	0.2802 (5)	9.8 (3)
CT2A	-0.6668 (5)	-0.4247 (5)	0.3833 (4)	9.6 (3)
CT1A	-0.4738 (5)	-0.4412 (6)	0.3500 (5)	13.3 (4)
C7B	-0.5589 (3)	-0.3958 (3)	0.2929 (3)	6.36(19)
C4B	-0.5998 (3)	-0.4556 (3)	0.2042 (3)	5.25(16)
CT3B	-0.4730 (6)	-0.3174 (5)	0.2621 (5)	11.6 (4)
CT2B	-0.6429 (6)	-0.3354 (7)	0.3417 (5)	14.9 (5)
CT1B	-0.5028 (5)	-0.4670 (4)	0.3657 (4)	8.7 (3)
PK 1 ^b	-0.7500 (0)	-0.7500 (0)	0.2900 (3)	0.6 (7)
PK 2 ^b	-0.7500 (0)	-0.7500 (0)	0.4540 (14)	13.0 (52)
PK 5 ^b	-0.7500 (0)	-0.7500 (0)	0.6100 (5)	3.1 (12)
TC1	-0.7804 (13)	-0.7576 (8)	0.53531(21)	10.8 (10)
TC2	-0.6788 (13)	-0.7589 (7)	0.4982 (3)	11.8 (9)
TC3	-0.6626 (10)	-0.7541 (5)	0.3984 (4)	9.3 (6)
TC4	-0.7480 (8)	-0.7479 (5)	0.33567(21)	5.93(9)
TC5	-0.8496 (8)	-0.7466 (5)	0.3727 (4)	8.5 (6)
TC6	-0.8658 (10)	-0.7514 (7)	0.4726 (4)	12.2 (9)
TC7	-0.7305 (11)	-0.7427 (7)	0.22763(22)	6.5 (5)

^a $B_{\text{iso}} = 8/3\pi^2 \sum \sum U_{ij} a_i^* a_j^* (a_i^* a_j^*)$; B_{iso} is the mean of the principal axes of the thermal ellipsoid. ESD's refer to the last digit printed.

^b Three atoms of the inverted guest on the toluene molecular axis.

A3. Final Positional and Equivalent Isotropic Parameters ($\text{\AA}^2$) for C4A-CLBZ.

Atom	x	y	z	B_{iso}^a
O1	0.61883	0.68805	0.05534	
C1	0.56859	0.66214	-0.03533	
C2	0.50202	0.73304	-0.07910	
C3	0.44814	0.70446	-0.16665	
C5	0.52842	0.54150	-0.16803	
C6	0.58370	0.56559	-0.07983	
C8	0.48945	0.84039	-0.03518	
C4A	0.45961	0.60912	-0.21362	
C7A	0.39635	0.58102	-0.30898	
CT1A	0.43304	0.48166	-0.35885	
CT2A	0.40478	0.66452	-0.39076	
CT3A	0.28357	0.57016	-0.27780	
G5	0.74648	0.75064	-0.49470	
G8	0.74537	0.84772	-0.44967	
G9	0.75318	0.85785	-0.34264	
G2	0.76209	0.77089	-0.28062	
G3	0.76320	0.67381	-0.32565	
G4	0.75539	0.66368	-0.43269	
G7	0.73674	0.73800	-0.62821	

^a $B_{\text{iso}} = 8/3\pi^2 \sum \sum U_{ij} a_i^* a_j^* (a_i^* a_j^*)$; B_{iso} is the mean of the principal axes of the thermal ellipsoid. ESD's refer to the last digit printed.

CHAPTER 4: Asymmetry of *p*-*tert*-Butylcalix[4]arene-Guest Compounds*

1. Introduction	139
2. Synthetic Details	141
3. Structural Studies: ^{13}C CP-MAS NMR Spectroscopy	141
4. Structural Studies: Single Crystal X-ray Diffraction	155
5. Dynamic Studies	163
6. FT-IR Spectroscopy of C4A-Nitrobenzene	165
7. Summary	165
8. References	167
9. Figures	170
10. Appendix: X-Ray Structural Data	187

1. Introduction

When considering the important factors which govern molecular recognition in *p*-*tert*-butylcalix[4]arene (C4A) and related complexes it is of interest to note that so far all evidence suggests a rather weak influence of the guest on the host geometry.¹⁻⁴ While lower-rim substituted *p*-*tert*-butylcalix[4]arene-guest compounds may adopt 2-fold (or lower) symmetries,⁵⁻¹⁵ structural¹⁶⁻²⁶ as well as modelling^{17,27-31} studies suggest that most upper-rim modified and unmodified *p*-*tert*-butylcalix[4]arenes exist in the 4-fold symmetric cone conformation in the solid state as well as in solution, regardless of the guest geometry. Observation of the chiral selectivity of *p*-sulfonatocalix[*n*]arenes towards chiral guests in solution does hint that distortion of the calixarene pocket is possible in order to incorporate specific guest shapes.³² Furthermore, the high observed symmetry for the C4A-toluene compound in the solid state results from dynamic space-averaging of a lower

* Parts of this chapter have been published: Brouwer, E.B.; Enright, G.D.; Ripmeester, J.A. *Supramol. Chem.* **1996**, 7, 7-9; Brouwer, E.B., Enright, G.D.; Ripmeester, J.A. *J. Incl. Phenom.* **1996**, in press.

symmetry cavity rather than an intrinsic property of the calixarene, as discussed in the previous chapter.^{22,23}

In order to further elucidate the role and importance of guest-host interactions in 4-fold symmetric C4A-guest compounds, over 30 new compounds were examined by solid-state ¹³C NMR spectroscopy; most of these resulted in calixarene-guest compounds that are 4-fold symmetric. The only guests for which low-symmetry conformations were indicated were nitrobenzene and several methyl-substituted nitrobenzenes. The main feature of the asymmetry-inducing guests seems to be the relatively large, asymmetric and inflexible part of the guest which protrudes from the calixarene cavity

This chapter explores the structure and dynamics of the asymmetric *p*-tert-butylcalix[4]arene-nitrobenzene (C4A-NB) compound in detail, and attempts to ascertain what makes nitrobenzene and structurally-related guests unique in their ability to distort the calixarene cavity from 4-fold symmetry. While previous structural determinations of calixarene compounds have been hampered by symmetry-related disorder (in both host and guest) and the presence of significant thermal motion,¹⁻²⁶ the asymmetry of C4A-NB and its rigidity facilitates a much more reliable structure determination. The insight gained in solving this structure has shed light on and aided the treatment of the more difficult calixarene structures such as C4A-TOL (Chapter 3).

Finally, some variations on the guest-induced asymmetry of the calix framework are explored. First, some five-membered ring systems with two similarly-shaped ring substituents occupy two sites within the calix cavity. This two-site positional disorder does not lower the overall symmetry of the calixarene-guest complex as in C4A-NB, and suggests that the guest is dynamically disordered as in the C4A-TOL compound. Secondly, ¹³C NMR evidence shows that two different C4A- α -pinene structures form depending on whether α -pinene is racemic or a single enantiomer. This chiral recognition

is the first example for the C4A system and illustrates the sensitivity of the calix framework to shape differences of the guest.

2. Synthetic Details

All chemicals were purchased from Aldrich Chemical Company and used as received unless otherwise stated.

C4A-guest. In general, C4A (0.25 - 0.30 g) was added to the liquid guest (3-5 mL) in a 10 mL glass vial. Stirring for several hours just below the boiling point of the solvent leads to the dissolution of the calixarene. Cooling to room temperature induces the formation of clear and colourless crystals of the C4A-guest compound (40-60% yield).

C4A-nitrobenzene. C4A (265 mg, 0.408 mmol) was dissolved in nitrobenzene (4 mL), stirred, and heated at 100 °C for 1 h. The clear yellow solution was cooled to room temperature which induced the formation of clear and colourless crystals of C4A-NB (189 mg, 0.245 mmol; 60% yield). **C4A-NB-*d*₅** was prepared from nitrobenzene-*d*₅ (C/D/N Isotopes, 99.71%).

C4A-4-nitrotoluene. 4-Nitrotoluene (0.0911 g, 0.6642 mmol) and C4A (0.2185 g, 0.3367 mmol) were mixed and then flame-sealed in a glass vial (o.d. 7 mm). The tube was heated at 90 °C (2 d) and then broken open and the white powder isolated.

3. Structural Studies: ¹³C CP-MAS NMR Spectroscopy

3.1 Four-Fold Symmetric C4A-Guest Compounds

Single crystal X-ray diffraction structures of C4A-guest compounds, for both neutral (guest = toluene,^{16,22} anisole,¹⁷ dimethylsulphoxide,²³ acetonitrile²⁴) and ionic (guest = toluene,¹⁰ acetonitrile^{25,26}) forms are known, and in all cases, the C4A-guest compounds possess 4-fold symmetric structures. Both XRD and ¹³C CP-MAS NMR

spectrum of the high symmetry C4A-TOL compound are known, and provide a means of correlating the complementary NMR and XRD data.^{22,33} Due to its high sample throughput relative to XRD, ¹³C CP-MAS NMR spectroscopy is more amenable to screening a large number of C4A-guest compounds for deviations from the typically observed C4A-guest 4-fold compound symmetry.

The NMR spectral features pertinent to C4A-guest structure will now be described. The ¹³C CP-MAS NMR spectrum of C4A-2,6-dimethylpyridine (Figure 1) is typical of a C4A-guest compound with a 4-fold symmetric structure (see also the discussion of C4A-TOL in Chapter 3). Each carbon of the *t*-butylphenol macro-ring shows a single line and therefore, the four *t*-butylphenols units of the calixarene are equivalent via C_4 -symmetry. Any inequivalence of the repeat units, *i.e.*, lowering of symmetry, will be manifested by an increase of the multiplicity in the ¹³C NMR resonance signals. The single guest resonances suggest that there is one guest per calix cavity, and that it achieves 4-fold symmetry to match the host by dynamic space-averaging akin to the C4A-TOL compound. The C4A-guest compounds compiled in Table 1 are 4-fold symmetric as determined by ¹³C NMR spectroscopy.

Two NMR spectral features of Table 1 are significant to the structures of C4A-guest compounds: (i) the upfield change difference in guest chemical shifts upon complexation of the liquid guest by the calix and (ii) the doubling of some guest lines (guests indicated by *).

3.1.1 Complexation-Induced Chemical Shifts

The chemical shift values of the guest in calix-guest compounds are generally lower (*i.e.*, shielded) than those of the uncomplexed guest in solution. The complex-induced shift (CIS) is seen in the ¹³C CP-MAS NMR spectrum of C4A-TOL, and has been

ascribed to the shielding effects of the host aromatic ring currents.^{18,34} Complex-induced shifts in ¹H guest resonances are also observed in solution.³⁵⁻³⁹ In C4A-TOL, the toluene methyl carbon exhibits a large CIS value (-6.3 ppm) and the XRD structure shows it to be situated deepest in the calix cavity. This correlation between the CIS value and guest methyl position suggests that the guest orientation in the calix cavity may be elucidated with some accuracy from the CIS value. As a cautionary note, |CIS| values < 3 ppm should be approached with caution on account of variation in referencing and occasional ambiguity in resonance assignment.

In addition to toluene, many guests possess large CIS values: acetone, acetylacetone, anisole, dichloroethane, dimethylformamide, ethylbenzene, (±)-α-methyl-γ-butyrolactone, methylcyclohexane, 3- and 4-nitrotoluene (Table 2), (±)-*sec*-phenethylalcohol and pyridine. For the substituted benzene guests, the CIS values suggest that the aromatic ring substituent is inserted deep in the cavity along the 4-fold axis; for C4A-anisole, this is confirmed by the single crystal X-ray diffraction structure.¹⁷ While the C4A-(±)-α-methyl-γ-butyrolactone compound has a large CIS value for the α-methyl carbon, other lactone guests in the C4A cavity fail to show large CIS values for the methyl substituents. Finally, the large CIS values of the smaller guest molecules are thought to arise from the guest's ability to fit deep into the cavity and encounter significant ring current effects.

3.1.2 Four-fold Symmetric C4A-Guest Compounds with Two-Site Guest Position

Seven guests ((±)-3-methyl-2-cyclopenten-1-one, (±)-3-methylcyclopentanone, (*R*)-(+)-3-methylcyclopentanone, (±)-α-pinene, (±)-propylene carbonate, (±)-*sec*-phenethylalcohol, and (±)-γ-valerolactone) display two lines of relatively equal intensity in

TABLE 1. Guest ^{13}C NMR chemical shifts (in ppm) of symmetric C4A-guest compounds.

Entry	Guest	Carbon	Calix ^a	Solution ^b	CIS ^c
1	acetone	Me	28.2	30.7	-2.5
		C=O	202.7	206.7	-4.0
2	acetylacetone	Me	18.3	24.9	-6.6
		-CH ₂ O	96.0	101.1	-5.1
		C=O	189.9	192.6	-2.7
3	anisole	Me	49.3	54.8	-5.5
		C-2	110.7	114.1	-3.4
		C-4	117.6	120.7	-3.1
		C-3	127.4	129.5	-2.1
4	benzaldehyde	C-1	157.9	159.9	-2.0
		C-3	128.5	129.0	-0.5
		C-2	129.4	129.7	-0.3
		C-4	132.9	134.3	-1.4
		C-1	134.9	136.7	-1.8
5	benzonitrile	C-7	191.1	192.0	-0.9
		C-1	111.4	112.8	-1.4
		CN	<i>e</i>	119.5	<i>e</i>
		C-2	129.2	132.1	-2.9
		C-3	129.2	129.2	0.0
6	benzyl alcohol	C-4	130.1	132.8	-2.7
		-CH ₂ -	61.8	64.2	-2.4
		C-2	123.9	126.6	-2.7
		C-4	<i>e</i>	127.0	<i>e</i>
		C-3	126.4	128.1	-1.7
7	benzyl mercaptan	C-1	139.0	140.6	-1.6
		-CH ₂ -	<i>e</i>	28.7	<i>e</i>
		C-4	126.0	126.8	-0.8
		C-2	127.0	127.8	-0.8
		C-3	127.5	128.4	-0.9
8	<i>t</i> -butylamine	C-1	139.0	140.9	-1.9
		Me	32.4	32.8	-0.4
9	(±)- <i>sec</i> -butylamine	C-1	45.5	47.2	-1.7
		C-3	10.3	10.8	-0.5
		C-2'	22.7	24.0	-1.3
		C-2	<i>e</i>	33.4	<i>e</i>
10	(±)-γ-caprolactone ^d	C-1	47.5	48.8	-1.3
		Me	6.1	8.1	-2.0
		C-5	24.7	26.2	-1.5
		C-2/C-3	27.9	27.2	+0.7
		C-3/C-2	30.5	27.4	+3.1
		C-4	80.0	80.8	-0.8
11	chlorobenzene	C-1	173.5	175.8	-2.3
		C-4	124.2	126.5	-2.3
		C-2	<i>e</i>	128.7	<i>e</i>
		C-3	<i>e</i>	129.5	<i>e</i>
12	1,2-dichloroethane	C-1	131.8	134.7	-2.9
		C	47.7	43.9	+3.8
13	diethylether	C-2	14.3	16.4	-2.1
		C-1	66.2	66.9	-0.7
14	<i>NN</i> -dimethylacetamide	Me	21.5	19.3	+2.2
		NMe		32.5	

15	dimethylformamide	NMe	36.6	35.6	+1.0
		C=O	166.8	167.9	-1.1
		Me	31.0	30.9	+0.1
		Me	31.8	36.0	-4.2
16	2,6-dimethylpyridine	C=O	160.9	167.9	-7.0
		Me	20.4	22.3	-1.9
		C-3	117.1	117.9	-0.8
		C-4	135.2	134.3	+0.9
17	3,5-dimethylpyridine	C-2	157.3	155.4	+1.9
		Me	12.8	16.0	-3.2
		C-3	131.1	130.4	+0.7
		C-4	132.8	134.9	-2.1
18	ethylbenzene	C-2	<i>e</i>	145.5	
		Me	10.4	15.8	-5.4
		-CH ₂ -	27.6	29.1	-1.5
		C-4	123.0	125.2	-2.2
19	(±)-3-hydroxytetrahydrofuran ^d	C-3	125.1	127.2	-2.1
		C-2	126.8	127.8	-1.0
		C-1	141.8	143.3	-1.5
		C-4	34.6	34.1	+0.5
20	(±)-3-methyl-2-cyclopenten-1-one ^{*.d}	C-3	66.2	65.5	+0.7
			70.4	70.1	+0.3
			70.6	70.1	+0.5
			74.7	74.1	+0.6
21	(±)-α-methyl-γ-butyrolactone ^d	Me	15.7	17.4	-1.7
		Me'	16.0	17.4	-1.4
		C-5	<i>e</i>	31.3	<i>e</i>
		C-4	36.9	34.1	+2.8
22	methylcyclohexane	C-3	131.9	128.6	+3.3
		C-2	179.2	177.2	+2.0
		C=O	207.3	207.2	+0.1
		C=O'	207.3	207.2	+0.1
23	(±)-3-methylcyclopentanone ^{*.d}	Me	17.3	13.8	+3.5
		C-3	29.4	29.4	0.0
		C-2	29.8	32.8	-3.0
		C-4	64.6	65.1	-0.5
24	(R)-(+)-3-methylcyclopentanone ^{*.d}	C=O	178.1	178.9	-0.8
		Me	22.0	22.8	-0.8
		C-1	25.3	33.1	-7.8
		C-2	25.3	35.8	-10.5
25	(R)-(+)-3-methylcyclopentanone ^{*.d}	C-3	<i>e</i>	26.6	<i>e</i>
		C-4	<i>e</i>	26.4	<i>e</i>
		Me	18.8	19.1	-0.3
		Me'	19.4	19.1	+0.3
26	(R)-(+)-3-methylcyclopentanone ^{*.d}	C-4/C-3	28.9	30.3	-1.4
		C-3/C-4	28.9	30.5	-1.4
		C-5	<i>e</i>	37.2	<i>e</i>
		C-2	46.2	45.4	+0.8
27	(R)-(+)-3-methylcyclopentanone ^{*.d}	C=O	215.9	217.1	-1.2
		Me	18.8	19.1	-0.3
		Me'	19.4	19.1	+0.3
		C-4/C-3	28.9	30.3	-1.4
28	(R)-(+)-3-methylcyclopentanone ^{*.d}	C-3/C-4	28.9	30.5	-1.4
		C-5	<i>e</i>	37.2	<i>e</i>
		C-2	46.2	45.4	+0.8

25	(±)- <i>sec</i> -phenethylalcohol	C=O	215.9	217.1	-1.2
		Me	21.4	24.7	-3.3
		Me'	22.1	24.7	-2.6
		-CH(OH)-	67.2	69.2	-2.0
		-C'H(OH)-	67.5	69.2	-1.7
		C-3	123.0	125.0	-2.0
		C-2	125.3	126.5	-1.2
		C-4	126.5	127.8	-1.3
		C-1	142.5	145.6	-3.1
		C-1'	142.7	145.6	-2.9
26	(±)-propylene carbonate ^{a, d}	C-4	16.1	18.0	-1.9
		C-4'	16.3	18.0	-1.7
		C-3	70.2	69.9	+0.3
		C-2	72.0	73.1	-1.1
		C=O	153.4	154.5	-1.1
		C=O'	153.7	154.5	-0.8
27	pyridine	C-3	121.0	124.2	-3.2
		C-4	133.4	136.2	-2.8
		C-2	148.1	149.6	-1.5
28	tetrahydrofuran	C-3	25.4	26.5	-1.1
		C-2	67.6	68.4	-0.8
29	toluene	Me	15.0	21.3	-6.3
		C-4	123.6	125.5	-1.9
		C-2	127.1	128.4	-1.3
		C-3	128.3	129.2	-0.9
		C-1	138.6	137.8	+0.8
30	trimethylphosphate	Me	51.9	54.2	-2.3
31	(±)-γ-valerolactone ^{a, d}	Me	20.6	19.6	+1.0
		Me'	21.6	19.6	+2.0
		C-2/C-3	25.5/26.4	27.7	-2.2/-1.3
		C2'/C-3'	25.8/27.2	27.7	-1.9/-0.5
		C-3/C-2	26.4/25.5	28.3	-1.9/-2.7
		C3'/C-2'	27.2/25.9	28.3	-1.1/-2.4
		C-4	74.4	75.9	-1.5
		C=O	174.6	175.9	-1.3
		C=O'	175.0	175.9	-0.9

^areferenced to hexamethylbenzene (δ 16.9 ppm).^bfrom reference 40, CDCl₃ solvent.^cComplexation-Induced Shift = δ (calixarene) - δ (solution).^dspectrum collected on Bruker 300 or 400 MHz MSL spectrometer, CDCl₃ solvent.^enot observed.

the ¹³C NMR spectrum for some carbons; Figure 2 shows the ¹³C CP-MAS NMR spectrum of C4A-(*R*)-(+)-3-methylcyclopentanone (R+3MCP). In contrast to the guest lines, the calix lines are not doubled, suggesting that there are two inequivalent guest orientations in a 4-fold symmetric calix cavity.

Although six of the seven guests are racemic, the enantiomer and racemate of 3-methylcyclopentanone both show doubling of the methyl resonances; thus the two-site position of the guest is unrelated to chiral resolution by the host. The molecular recognition by the host is likely too weak to discriminate between the two similarly-shaped substituents (carbonyl and methyl) of the 5-membered ring guests. However, the two local chemical environments of the ring substituents differ significantly enough to cause a splitting in the methyl and carbonyl lines of the ^{13}C NMR spectrum (Figure 2, *inset*). Figure 3 illustrates a two-site model for C4A-R+3MCP; position A has the carbonyl situated deep in the cavity whereas position B has the methyl situated deep in the cavity. The calix host is more sensitive to the dynamic shape than to the specific steric, electronic and chemical features of the guest's ring substituents and thus yields a 4-fold symmetric ^{13}C NMR spectrum. The correlation between guest orientation and host geometry is not sufficiently strong for the methyl and carbonyl substituents to induce any change from the 4-fold symmetric host architecture.

The ^{13}C CP-MAS NMR spectra of C4A-racemic-3-methylcyclopentanone (3MCP) (Figure 4) show that upon cooling to 113K the host symmetry does not lower as might be expected in light of the C4A-TOL behavior as a function of temperature (Figure 4). The guest methyl group splitting persists—and even becomes more pronounced—at 113K; there is no corresponding behavior with the guest carbonyl lines. C4A-3MCP does not undergo any symmetry-lowering structural changes as temperature decreases.

The multiplicity ($m = 2$) of the calixarene C-4 line (δ 144 ppm) in the 291K ^{13}C CP-MAS NMR spectrum of C4A-($\pm$)-*sec*-phenethylalcohol (PEA) (Figure 5, *bottom*) is intriguing: it suggests that the host is either (*i*) not 4-fold symmetric or (*ii*) there are two crystallographically-distinct 4-fold symmetric host-guest units. As the remaining host lines are singlets, the distortion (if the former scenario is correct) is very slight and occurs in the

vicinity of the C-4 host carbon. Upon cooling to 113K, the C-4 doublet feature persists as does the singlet character of the other host lines; it appears that no further distortion or change in symmetry occurs at lower temperatures.

The guest lines at 291K are resolved doublets of intensity 1:1 (Table 1). Upon cooling the sample temperature to 113K, these features sharpen (C-1' (δ 142 ppm), C-5' (δ 67 ppm), and in the case of the methyl signal, show a significant increase in the chemical shift difference between the doublet. The dipolar-dephased (DD)⁴¹ NMR 113K spectrum (Figure 5, *top*) shows the presence of guest lines and indicates that the guest is dynamic at this low temperature.

C4A compounds of both ($\pm$)-*sec*-phenethylalcohol and ($\pm$)-3-methylcyclopentanone guests show a perturbation of structure from the 4-fold symmetric C4A-guest structure in which the guest is dynamically averaged. In assessing the impact of the guest on the host architecture it is not unreasonable that in these two cases, the dynamic volume of occupation has two ambiguous sites or pockets due to the inability of the host to distinguish between similarly sized functional groups. In other words, while molecular recognition of the guest by the calix host occurs, it is not sufficient to resolve the methyl, hydroxyl, and carbonyl groups. In the former guest, -OH and -Me groups attached to the α -carbon create the ambiguity whereas in the latter, it arises from the carbonyl and methyl groups at the 1- and 3- positions. This model accounts for a 2-site guest occupation while retaining a highly symmetric host framework.

A word of caution must be added, however: the calix C-4 doublet line in C4A-PEA may arise from additional and more complex structural perturbations. Certainly there are features from the XRD data of C4A-R+3MCP which are not presently in accord with the NMR model described above. Inability to isolate single crystals of C4A-PEA limits the resolution of these structural details.

3.2 C4A-Guest Compounds with < Four-Fold Symmetry

TABLE 2. Guest ^{13}C NMR chemical shifts (in ppm) of asymmetric C4A-guest compounds.

Entry	Guest	Carbon	Calix ^a	Solution ^b	CIS ^c
1	nitrobenzene	C-2	123.4	124.2	-0.8
		C-3	126.1	129.8	-3.7
		C-4	134.7	134.7	0.0
2	4-nitrotoluene	C-1	<i>d</i>	149.1	<i>d</i>
		Me	15.0	21.4	-6.4
		C-3	123.1	123.5	-0.4
		C-2	<i>d</i>	130.0	<i>d</i>
		C-4	145.8	146.2	-0.4
3	3-nitrotoluene	C-1	149.2	146.2	+3.0
		Me	13.9	20.2	-6.3
		Me'	17.2	20.2	-3.0
		C-5	120.1	119.9	+0.2
		C-6	<i>d</i>	123.0	<i>d</i>
		C-4	<i>d</i>	128.5	<i>d</i>
		C-2	133.7	134.8	-1.1
		C-1	140.5	139.3	+1.2
		C-3	147.5	147.5	0.0
		C-3'	148.5	147.5	+1.0

^areferenced to hexamethylbenzene (δ 16.9 ppm).

^bfrom ref 40, CDCl_3 solvent or spectra collected on Bruker 300MSL spectrometer, CDCl_3 solvent.

^cComplexation-Induced Shift = $\Delta\delta = \delta(\text{calixarene}) - \delta(\text{solution})$.

^dnot observed.

3.2.1 C4A-Nitrobenzene

The ^{13}C CP-MAS NMR spectrum of C4A-NB (Figure 6) indicates a significant lowering of symmetry from the 4-fold symmetric case, as some resonances such as the central carbon of the *t*-butyl group (C-7; δ 33.8-35.1 ppm) are split into as many as four components. Each of the four *t*-butylphenol monomer units of the host is unique and demonstrates clearly the guest-induced distortion of the calixarene cavity. The guest resonances C-1', C-2', C-6' are not observed and likely lie under the calix aromatic lines. The nitrobenzene C-3' and C-4' singlet resonances suggest that there is one guest per

calix cavity. The DD ^{13}C NMR experiment (not shown) shows that the nitrobenzene C-4' resonance disappears while the C-3' line remains; this result suggests large amplitude of the guest molecule with the C-4'-H bond on the symmetry axis for the motion. The ^{13}C NMR spectrum reveals the asymmetric nature of the calix framework, which has been confirmed by and further elucidated with single crystal XRD crystallography (section 3.4).

3.2.2 C4A-4-Nitrotoluene

In light of the 4-fold symmetric C4A-TOL and the asymmetric C4A-NB structures, it was of interest to see which ring substituent, methyl or nitro, would be more effective in directing the symmetry of the calix-guest compound. The ^{13}C CP-MAS NMR spectrum of C4A-4-nitrotoluene (4NT) shows a deviation from 4-fold symmetry, but not to the extent of the nitrobenzene case (Figure 7). The doublet C-7 host resonance suggests two possibilities: (i) the calix is 2-fold symmetric (like the low temperature toluene structure) or (ii) the host:guest ratio is 2:1 (as in the anisole structure) and the host is 4-fold symmetric. Although carbon intensities are not quantitative, the ratio of the host:guest lines is similar to the C4A-NB ^{13}C NMR spectrum and favours the former possibility. The guest methyl CIS value for C4A-4NT differs from that of the free guest by -6.4 ppm (Table 2). Since similar CIS values are seen for the toluene and anisole structures, the methyl group is likely inserted deep into the cavity with the nitro group protruding. The C4A-4NT structure is one in which the guest methyl group is inserted into a 2-fold symmetric calix cavity. Further structural details require XRD insight, which is limited due to the inability to grow suitable single crystals of this compound.

3.2.3 C4A-3-Nitrotoluene

The XRD structure of C4A-NB shows the nitrobenzene *meta*-hydrogen deep in an asymmetric calix cavity. If the nitrobenzene orientation is directed by the nitro group and if the methyl group prefers to be deep in a symmetric cavity, 3-nitrotoluene (3NT) should satisfy both orienting criteria. The ^{13}C CP-MAS NMR spectrum of C4A-3NT is the most complex spectrum of the three asymmetric calix-guest compounds (Figure 8). The calix lines show the absence of any symmetry elements and this suggests that each *t*-butylphenol unit is unique (see the C-7 resonance, $\delta = 33$ ppm). However, the *t*-butylmethyl signals (C-8) are less intense and show a higher multiplicity than in the spectra of the two nitro guests, and indicates a significant distortion of the *t*-butyl groups of the calix. The most striking aspect of the generally sharp guest lines is that there are two methyl group resonances (δ 17.2 ppm, broad; δ 13.9 ppm, narrow). Like the toluene and some 5-membered ring guests, there may be two orientations of the guest methyl group in the host cavity (inserted and inverted). The methyl experiencing the greatest amount of shielding (δ 13.9 ppm; CIS = -6.3 ppm) corresponds to the methyl deep in the cavity. The other methyl has a chemical shift value closer to that of the liquid (CIS = -3.0 ppm) and thus would be oriented away from the calix cavity. Attempts to obtain single crystals suitable for XRD studies failed.

3.3 Chiral-Induced Structural Differences: C4A- α -Pinene

Attempts have been made to incorporate chiral centres into the calix framework in the hope of effecting chiral recognition.^{42,43} While the C4A framework does not possess any chiral centres, the directional components of the phenolic hydrogen bonds imparts chirality. Using induced circular dichroism, Shinkai has demonstrated the chirality of *p*-sulfonato-C4A compounds formed in solution with chiral trimethylammonium guests.³²

Previously, the inability of the calix to differentiate between racemic and an enantiomer of 3-methylcyclopentanone was attributed to the small size of the dynamic guest which moves about in the spacious calix cavity without any significant shape-related host-guest interactions (section 3.2). The C4A- α -pinene compound, with a large guest, shows solid-state structural differences as a function of the guest chirality.

α -Pinene and β -pinene, both natural products, are important feedstocks for the fragrance industry.⁴⁴ α -Pinene has a bicyclic structure with 4- and 6-membered rings, and its chirality arises from the bridging carbons 4 and 6 (Figure 9). The bicyclic nature gives α -pinene a spherical molecular shape in comparison to the planar-shaped cyclopentanone molecules, and this likely forces a tighter fit of the α -pinene in the calix cavity.

The two ^{13}C CP-MAS NMR spectra of C4A- α -pinene (Figure 10) differ markedly: the calix compound with the racemic α -pinene shows very sharp lines for the host and guest carbons. Furthermore, the multiplicity ($m = 1$) of the calix lines indicates that the calix possesses 4-fold symmetry.

In contrast, the ^{13}C NMR spectrum of C4A-(*IR*)-(+)- α -pinene shows sharp guest lines, but broad host resonances which indicate a multiplicity > 1 . The asymmetric unit may possess a structure in which the calix architecture is < 4 -fold symmetric or else the asymmetric unit may contain more than one C4A-guest unit. The ^{13}C NMR spectrum of C4A-(*IS*)-(-)- α -pinene matches exactly that of its enantiomer. The guest ^{13}C NMR resonances in both racemic and enantiomeric structures are highlighted in Figure 11 and show that the α -pinene lines vary in chemical shift, intensity distribution and multiplicity (Table 3).

Surprisingly, the C4A-racemic α -pinene spectrum has several doubled guest carbon resonances (C-1', C-6', C-9', C-10') which suggests that, like the lactone guests,

the racemic α -pinene occupies two positions within the calix cavity while the cavity itself maintains 4-fold symmetry. The C4A compound of (*IR*)-(+)- α -pinene gives ^{13}C NMR lines that have a multiplicity of 1; this implies that the guest occupies only one position.

TABLE 3. ^{13}C NMR Chemical shift values for α -pinene.^a

Carbon	α -pinene (<i>lq</i>) ^b	C4A-($\pm$)- α -pinene	C4A-(<i>IR</i>)-(+)- α -pinene
1	144.1	<i>c</i>	144.9, 144.7
2	116.2	116.2	113.3
6	47.3	46.0	45.6, 45.1
4	41.5	39.2	38.4
8	38.0	37.2	38.4
3	31.5	<i>c</i>	<i>c</i>
5	31.4	<i>c</i>	<i>c</i>
9	26.5	21.2	22.4, 22.0
10	22.8	20.7	21.7, 21.5
7	20.8	19.6	19.4

^ain ppm; referenced to hexamethylbenzene (δ 16.9 ppm).

^btaken from reference 40.

^cnot observed due to overlap with calix carbon resonances.

The ^{13}C CP-MAS NMR DD NMR experiment reveals the motion of the guest; the starred peaks in Figure 11 correspond to those -CH- and -CH₂- carbons that disappear with DD—these are immobile carbons.⁴¹ For the racemic α -pinene-containing structure, no guest lines disappear with DD and thus all -CH- and -CH₂- carbons are mobile. However, the C4A compound of (*IR*)-(+)- α -pinene has -CH- and -CH₂- carbons that do disappear under DD conditions (C-2', C-4', C-6', C-8') indicating that the enantiomeric guest is held rigidly by the calixarene.

In summary, the ^{13}C NMR spectral data reveal the following about structure and dynamics of C4A-(*IR*)-(+)- α -pinene:

- the calix framework is asymmetric and has < 4-fold symmetry, or else there is more than one 4-fold symmetric calix per asymmetric unit
- there is one guest position in the calix cavity
- the guest is held tightly in that one position
- the guest C2 carbon is deepest in the host cavity due to a CIS value of -2.9 ppm
- the C4A compounds of both enantiomers are identical.

The ^{13}C NMR spectral data reveal the following about the structure and dynamics of C4A-($\pm$)- α -pinene:

- the calix framework is 4-fold symmetric
- there is one C4A-($\pm$)- α -pinene unit per asymmetric unit
- there are two guest positions in the calix cavity
- the guest is mobile in the C4A pocket.

Single crystals of C4A-($\pm$)- α -pinene and C4A-(*IR*)-(+)- α -pinene were obtained by crystallization of C4A in the guest solvent. Both compounds were examined by XRD, and show structures that are consistent with the NMR data: the enantiomer has two C4A units in the asymmetric unit as the *c*-axis is double that of the racemic structure. When considering the chiral nature of both the host and guest, these differences are not surprising. In the case of the racemic guest, the inversion symmetry generated by the glide plane ensures that throughout the crystal lattice along *c*, the two enantiomeric guests alternate about this symmetry element. In the case of the single enantiomer, no inversion symmetry can possibly relate two adjacent calix-guest units along *c* due to the handedness of the guest (and the corresponding handedness of the host). Consequently, the symmetry demands are met by doubling the repeat unit along *c* to encompass the chiral requirements of the guest enantiomer (see Figure 12).⁴⁵ Finally, the NMR results indicate the calix

binds the enantiomerically-pure guest more tightly as the *a*- and *b*- axes are smaller than in the racemic structure.

Since the position of the methyl groups of the calix *t*-butyl groups is related to the direction of the phenolic OH bonds, chiral recognition is likely communicated by the guest through the calix *t*-butyl groups. As described in Chapter 3 and will be described in the following section, the position of the *t*-butyl groups is also sensitive to the packing or “shape” of the surrounding calix-guest units. In the C4A- α -pinene case, each enantiomer is distributed evenly throughout the crystal and equally occupies the calix cavities. No long-range ordering of one handedness is possible as each guest will communicate to both enantiomers with equal probability. The calix responds to this 1:1 mixture by adopting a 4-fold symmetric cavity in which the guest can dynamically carve out an achiral volume of occupation; the NMR spectra indicate that the dynamic guests sit in two chemically distinct positions. Chiral long-range ordering occurs with the enantiomeric guest since each C4A-guest communicates with surrounding C4A-guest units with identical handedness. The guest transmits its chirality to the calix structure which in turn transmits the unit chirality to adjacent C4A-guest units. The “language” of chiral communication is molecular shape or geometry, and this explains why the guest in the C4A-enantiomerically-pure α -pinene is not mobile; its volume of occupation in the cavity is chiral and affords a better fit.

4. Structural Studies: X-Ray Crystallography

4.1 *p*-tert-Butylcalix[4]arene-($\pm$)-3-methylcyclopentanone (C4A-3MCP)

The title compound crystallizes in the *P*4/*n* space group, with lattice parameters that are similar to other *P*4/*n* C4A-guest compounds (Table 4). While the refinement of the XRD data was not completed, several structural features are notable. The host is 4-

fold symmetric, and is consistent with the ^{13}C NMR data for the host lines. The XRD data seem to indicate that the guest occupies two positions in the cavity, which is also consistent with the ^{13}C NMR data for the guest lines. The guest positions (methyl-in, methyl-out) are related throughout the crystal such that when one calix cavity has the guest situated methyl-in, the adjacent cavity is occupied by a guest situated with its methyl group out of the cavity.

TABLE 4. Summary of partial XRD structural parameters for C4A-guest compounds (guest = R+3MCP, 3MCP, ($\pm$)- α -pinene, (*IR*)-(+)- α -pinene).^a

compound	C4A-R+3MCP	C4A-3MCP	C4A-($\pm$)- α -pinene	C4A-(<i>IR</i>)-(+)- α -pinene
formula	$\text{C}_{12.5}\text{H}_{16.5}\text{O}_{1.25}$	$\text{C}_{12.5}\text{H}_{16.5}\text{O}_{1.25}$	$\text{C}_{13.5}\text{H}_{17.75}\text{O}$	$\text{C}_{13.5}\text{H}_{17.75}\text{O}$
fw	186.77	186.77	196.04	196.04
temperature, K	150	150	150	150
crystal system	tetragonal	tetragonal	tetragonal	tetragonal
space group	<i>P</i> 4	<i>P</i> 4/ <i>n</i>	<i>P</i> 4/ <i>n</i>	<i>b</i>
<i>a</i> , Å	18.0400	12.7771 (7)	13.002 (4)	12.968 (5)
<i>b</i> , Å	18.0400	12.7771 (7)	13.002 (4)	12.968 (5)
<i>c</i> , Å	13.250	13.2565 (3)	12.863 (3)	25.775 (35)
<i>V</i> , Å ³	4312.1	2164.2 (3)	2174.5 (5)	4334.6 (5)
<i>Z</i>	16	8	8	16

^a Conditions and collection details: Enraf-Nonius diffractometer; graphite monochromator; aperture 4.0 x 4.0 mm at a distance of 173 mm from the crystal; stationary background counts at each end of the scan (scan/background time ratio 5:1); peak and background counts determined with profile analysis procedure of Gabe *et al.*, *J. Appl. Cryst.*, 1989, 22, 384.

^b space group likely *P*4.

4.2 *p*-tert-Butylcalix[4]arene-(*R*)-(+)-3-methylcyclopentanone (C4A-R+3MCP)

With the collection of XRD data of C4A-TOL immediately after cooling to 150K from room temperature, superlattice peaks are observed (Chapter 3). These transitory (~6 h) peaks occur at half-integer values and suggest an intermediate crystallographic cell with doubled lattice dimensions possibly similar to C4A-R+3MCP. It was postulated that correlated motion present in the room temperature crystal may be quenched and preserved

for several hours before molecular motions break the inter-calix planar correlation and cause the crystal to adopt its final lattice parameters.

C4A-R+3MCP gives two lines of equal intensity for some guest carbon NMR resonances and was thus of interest to attempt to formulate a structural picture from XRD. Crystals of C4A-R+3MCP give superlattice lines upon cooling from room temperature to 150K, and unlike C4A-TOL, these lines persist for weeks and therefore it was feasible to collect a data set that included the superlattice lines. Although the data collection was incomplete, several structural features are worth noting.

The crystal is tetragonal *P*4 with cell parameters $a = b = 18.04 \text{ \AA}$, $c = 13.25 \text{ \AA}$, and the cell is related to the *P*4/*n* lattice by $a + b$, $a - b$, $2c$. The asymmetric unit contains two planes, A and B: Plane A consists of two 4-fold symmetric calixarenes that differ in the pattern of t-butyl group disorder. Each contains a guest that is also 4-fold disordered. Plane B contains two 2-fold disordered calix cavities that are oriented 90° with respect to each other; each also contains a 2-fold disordered guest. Plane B is the more interesting of the two in that it shows a stronger inter-calix planar correlation. That is, the interactions between adjacent calix units are sufficient to cause the 2-fold distortion to persist throughout the crystalline to a more significant extent than is found in plane A.

This structural picture is limited by the number of data that can be reasonably collected to account for the crystallographic variables, and an area detector may be needed to increase the number of observed data to adequately solve the crystal structure. Nonetheless, incorporation of the superlattice peaks generates a structural model which contributes to the understanding of the lattice dynamics in the related C4A-TOL crystal.

TABLE 5. Crystallographic data for C4A-NB.^a

compound	C4A-NB
formula	C ₄₄ H ₅₆ O ₄ , C ₆ H ₅ NO ₂
fw	771.91
temperature, K	150
colour, habit	colourless,
crystal size, mm	0.35 x 0.20 x 0.12
crystal system	orthorhombic
space group	<i>P</i> <i>c</i> 2 ₁ <i>n</i>
<i>a</i> , Å	12.4355(4)
<i>b</i> , Å	12.9346(5)
<i>c</i> , Å	26.7560(12)
<i>V</i> , Å ³	4303.7(3)
<i>Z</i>	4
ρ_{calc} , g cm ⁻³	1.191
<i>F</i> (000)	1668.42
μ (Cu K α) mm ⁻¹	0.57
λ , Å	1.54056
scan type	$\theta/2\theta$
scan rate, deg min ⁻¹	4
data collected	<i>h</i> , <i>k</i> , <i>l</i>
$2\theta_{\text{max}}$, deg	140
total no. of reflections	5465
no. of unique reflections	5377
<i>R</i> _{merge}	0.030
no. of reflectns $I \geq 2.5\sigma(I)$	5095
no. of variables	556
<i>R</i>	0.041
<i>R</i> _w	0.057
GOF	2.14
max Δ/σ (final cycle)	0.077
residual density, e Å ⁻³	-0.290 to 0.220

^aConditions and collection details: Enraf-Nonius diffractometer; graphite monochromator; aperture 4.0 x 4.0 mm at a distance of 173 mm from the crystal; stationary background counts at each end of the scan (scan/background time ratio 5:1); peak and background counts determined with profile analysis procedure of Gabe *et al.*, *J. Appl. Cryst.*, **1989**, 22, 384. $\sigma(F_o)$ based on counting statistics, function minimized $\sum w(|F_o| - |F_c|)^2$, where $w = [\sigma^2(F_o) + k(F_o)^2]^{-1}$, $R = \sum ||F_o| - |F_c|| / \sum |F_o|$, $R_w = (\sum w(|F_o| - |F_c|)^2 / \sum w|F_o|^2)^{1/2}$, and $\text{GOF} = [\sum w(|F_o| - |F_c|)^2 / (m - n)]^{1/2}$. Values given for *R*, *R*_w, and GOF are based on those reflections with $I \geq 2.5\sigma(I)$.

4.3 *p*-tert-Butylcalix[4]arene-Nitrobenzene (C4A-NB)

The C4A-NB structure was the first structure solved in this thesis research. The insights developed in solving this structure have led to a better description of the *p*-tert-

butylphenol disorder often seen with C4A-guest structures. The model of *t*-butylphenol disordering (Chapter 3) developed from this structure was applied successfully in the structure determination of the C4A-TOL compound.

The structure of C4A-NB is shown in Figure 13 (Table 5). The axis of the C4A host molecule is aligned in the *z*-direction with layers alternating head-to-head and tail-to-tail (Figure 14). Each *t*-butylphenol monomer in the calixarene unit is unique and is consistent with the ^{13}C NMR data. The *t*-butylphenol subunits (*A-D*) make dihedral angles with the horizontal plane defined by the four phenolic oxygens of the host ranging from 51.8 to 57.8°.

Two (*B, C*) of the four subunits display a positional disorder of the *t*-butylphenol groups with site occupancies of 0.57/0.43 (*B*) and 0.79/0.21 (*C*). Unlike the C4A-TOL structure, the *t*-butylphenol positional disorder does not possess an easily-understood or explainable ratio. Most likely the two *t*-butylphenol site occupancies arise from subtle interactions between the nitrobenzene in the nearest adjacent calix cavity. The packing diagram (Figure 15) shows that the *ab*-layers of calixarenes are stacked in a staggered fashion compared to the layers in C4A-TOL. The shift of the *ab*-layers is correlated to a loss of symmetry of packing which is manifested in a doubling of *c* to 26.7560 Å and a change in crystal space group to orthorhombic ($Pc2_1n$) from tetragonal ($P4/n$). Instead of one calix being capped equally by four calix cavities in the above layer, three calix macro-rings are shifted and minimize the *t*-butyl-nitrobenzene interaction while the fourth calix is shifted to a closer proximity to the nitrobenzene guest. It is the *t*-butyl group of the fourth calix that interacts strongly with the nitrobenzene (CN2-Me = 3.39 Å; Σ van der Waals (vdW) radii = 3.6 Å) and is also disordered in the ratio 0.57/0.43. The *t*-butylphenol disorder in this case arises more from the interlayer interactions with the guest than from the interactions with the resident guest.

Also of note is the absence of the disorder in two of the *t*-butylphenol units (*A*, *D*). The ordering may be related to the nitrobenzene off-axis position (and specifically the nitro group sandwiched between the two ordered *t*-butyl groups) which induces a degree of “stiffness” to the flexible C4A framework. In symmetric calix cavities, the guest, which lies on (or close to) the calix symmetry axis, is often dynamic and carves out a volume of occupation that is symmetrical as a result of fast guest motion; however, this volume is not symmetrical when the guest is immobilized. The present C4A-NB structure shows a guest restricted in its motion; the guest presents an asymmetric shape (particularly the nitro group) to the calix framework which enclathrates the guest in such a manner that locks in two of the four *t*-butyl groups.

The orientation of the disordered *t*-butyl groups is related to the orientation of the phenolic O-H bond.⁴⁶ In both cases (and in the ordered *t*-butyl groups of *A* and *D*) the majority position has the *t*-butyl C-Me bond aligned parallel with the the OH bond and the minority position is aligned anti-parallel (Chapter 3, Figure 10).

The most striking aspects of the structure are the off-axis position of the guest and the absence of guest dynamic disordering. The C_2 axis of the planar (within 0.1 Å) nitrobenzene is 68° off the *z*-axis (which is perpendicular to the plane defined by the four phenolic oxygens); as previously mentioned, all the symmetric C4A-guest structures have the calix symmetry and guest molecular axes aligned. The centre of the nitrobenzene ring is close (0.24 Å) to the axis of the host. The plane of the nitrobenzene makes an angle of 69° with the basal plane defined by the oxygens of the host.

The points where the guest and host interact are pertinent to the origin of the guest-induced calix distortion (Table 6). The interlayer interaction between the guest CN2 and the *t*-butyl methyl has been noted above. Equally important are the intramolecular interactions, *i.e.*, those between the guest and its surrounding cavity. The *D* *t*-butylphenol

unit seems to play the most important role: the nitrobenzene sits nearly perpendicular to the *t*-butylphenol aromatic ring (100°), and is very close to the geometry of T- (or edge-to-face) aromatic interactions which has been identified for stabilizing aromatic ring interactions.^{47,48} The guest CN6 makes significant contacts with the phenol C42 and C43: 3.52 and 3.62 Å ($\Sigma r_{vdW} = 3.6$ Å); this includes the hydrogen of the CN6-H bond of the guest which is directed towards the bond between C42 and C43.

The oxygen pointing towards the cavity (O6) interacts with the methyls of *t*-butylphenol groups A (T11) and D (T41), and makes contacts of 3.66 and 3.48 Å respectively ($\Sigma r_{vdW} = 3.52$ Å). The second oxygen (O5) points out of the cavity and interacts with T13 and T41 of the *t*-butyl methyls of *t*-butylphenol groups A and D: 3.69 and 3.70 Å; the shortest contact with the above *t*-butylmethyl group (T12) is comparable (3.68 Å). The two N-O bond lengths are not exactly equal: N-O6 is slightly longer (1.238 Å) than N-O5 (1.217 Å); the difference may arise from a CH...O interaction which is stronger for the longer N-O bond. These parameters quantify the origin of the compound asymmetry which arises from the steric requirements of the nitro group.

At the other end of the nitrobenzene molecule, interactions occur with the disordered *t*-butylphenol methyl groups, both with the immediate host calix and the adjacent calix. As mentioned above, the strongest interaction is that between CN2 and the methyl of the adjacent *t*-butyl group which is 3.39 Å ($\Sigma r_{vdW} = 3.8$ Å). Other contacts between the guest CH and host CH₃ group range from 3.7 Å to 4.0 Å (Σr_{vdW}). The unsubstituted end of the guest is not as tightly anchored as the nitro end and thus undergoes some motion which in turn induces motion in the two *t*-butylphenol units. The plot of the nitrobenzene structure (Figure 13) shows the equilibrium position of the nitrobenzene; the larger thermal parameters of the carbons at the unsubstituted end of the

molecule indicate small variations in guest position. The observed positional disorder in the *t*-butylphenol groups is likely related to this nitrobenzene motion.

In summary, the asymmetric C4A-NB structure determined by XRD is consistent with that proposed from ^{13}C NMR data. The nitro group is anchored between two ordered *t*-butylphenol groups and protrudes from the calix cavity. The unsubstituted end of the guest molecule interacts significantly with the adjacent layer and its motion causes the positional disorder of the remaining *t*-butylphenol groups. Compared to the C4A-TOL structure, the *ab* layers are shifted such that a doubling along *c* occurs and is the cause of the orthorhombic symmetry. The C4A-NB structure determination has been foundational in the solution of other C4A-guest structures in this thesis.

Unlike the majority of C4A-guest structures which crystallize in centrosymmetric, tetragonal space groups, C4A-NB crystallizes in a non-centrosymmetric space group. As nitrobenzene is a highly polar molecule ($\mu = 3.93$ D), its dipole is aligned in the crystal lattice such that all its dipole moments are additive. The net alignment of dipoles is a major requirement for materials that may possess non-linear optical properties.⁴⁹⁻⁵³ Non-linear optical materials show a non-linear response to light, and are used as frequency doublers and show potential for optical switching devices.^{53,54} A variety of synthetic techniques have been used to align molecular dipoles in the solid state including imbedding polar molecules in polymers^{54,55} and inclusion of polar molecules in long channels of inclusion compounds such as PHTP.^{49,56} One shortcoming of these techniques is that the molecular dipoles are diluted in the solid-state by the non-polar host by up to 100 times.

The potential of C4A-NB as an NLO material becomes quite interesting, as the fraction of molecular dipole per unit mass is high: $\text{MW}_{\text{NB}} / \text{MW}_{\text{C4A-NB}} = 124 / (124 + 648) = 0.16$. Furthermore, nitrobenzene is structurally related to the NLO “standards” 4-nitroaniline and 2-methyl-4-nitroaniline; if these compounds crystallize in a similar fashion

as C4A-NB, they could be significant candidates for NLO materials. Reinhoudt *et al* have attached nitro groups on the upper rim of calix[4]arenes and found that the cone conformation shows significant NLO activity.⁵⁷⁻⁵⁸ No work on the inclusion capabilities of these hosts were mentioned.

TABLE 6. Selected Bond Distances and Angles for C4A-NB.

Bond	Distance (Å)	Bond	Distance (Å)
O1-C11	1.386(3)	N1-CN1	1.462(4)
C11-C12	1.398(5)	CN1-CN2	1.386(4)
C11-C16	1.391(4)	CN1-CN6	1.374(4)
C12-C13	1.387(4)	CN2-CN3	1.368(5)
C12-C18	1.527(4)	CN3-CN4	1.379(5)
C13-C14	1.395(4)	CN4-CN5	1.375(6)
C14-C15	1.404(5)	CN5-CN6	1.393(6)
C14-C17	1.540(4)	CN6-C42	3.52
C15-C16	1.399(4)	CN6-C43	3.62
C16-C48	1.529(5)	O6-T11	3.66
C17-T11	1.531(4)	O6-T41	3.48
C17-T12	1.540(5)	O5-T13	3.69
C17-T13	1.537(4)	O5-T41	3.70
C18-C26	1.516(4)	O5-T12*	3.68
O5-N1	1.217(4)	CN2-T11*	3.39
O6-N1	1.238(4)		
Bond	Angle (degrees)	Bond	Angle (degrees)
O3-O1-C17	127.9	O2-O4-C47	126.5

5. Dynamic Studies

5.1 VT ²H NMR Studies of C4A-NB-*d*₅

Figure 16 shows the experimental and simulated ²H NMR spectrum of this compound from 200-290K. The 290K spectrum is typical of a 2-fold axial rotor at the fast motion limit (FML).⁵⁹ Spectra taken at lower temperatures reflect the decrease in frequency of this motion until 200K where the guest motion is frozen in. Examination of the static and FML lineshapes gives the components of the static electric field gradient

(EFG) tensor (Table 7): the effective ^2H quadrupolar coupling constant for the *para*-deuteron $\chi_{\text{para-D}} (= e^2qQ/h) = 168 \pm 1$ kHz with the asymmetry parameter $\eta_{\text{para-D}} = 0.063 \pm 0.012$. For the remaining deuterons, $\chi_{\text{ortho-, meta-D}} = 172 \pm 1$ kHz; $\eta_{\text{ortho-, meta-D}} = 0.039 \pm 0.011$. The calculated angle for the C-D bond (with respect to the long molecular axis) is 59.6° , slightly less than the expected 60° . The slight difference in bond angles expected between the *ortho*- and *meta*-deuterons is not observed with the ^2H NMR spectra.

TABLE 7. ^2H NMR spectral parameters for C4A-NB.^a

deuteron	<i>T</i> (K)	$ \Delta\nu_{xx} $ (kHz)	$ \Delta\nu_{yy} $ (kHz)	$ \Delta\nu_{zz} $ (kHz)	χ (kHz)	η
<i>ortho-, meta-</i>	77	129	138	267	178.0	0.034 ± 0.012
	200	124	134	258	172.0	0.039 ± 0.012
	290	26	132	158	105.3	0.671 ± 0.025
<i>para-</i>	77	129	138	267	178.0	0.034 ± 0.012
	200	124	134	258	172.0	0.039 ± 0.012
	290	123	133	256	170.7	0.039 ± 0.012

^a Estimated errors of ± 1.5 kHz in the measurements of the $\Delta\nu_{ii}$ and ± 1 kHz in χ .

The lineshapes were simulated using the static lineshape parameters and a model in which the nitrobenzene undergoes a two-fold jump about its long molecular axis.⁶⁰ The lineshape is a sum of the *para*-deuteron on-axis component (invariant with motion) and the *ortho*- and *meta*-deuterons (vary with motion). The frequency of motion (or the jump rate κ) is correlated to temperature by visibly matching the simulated and observed spectra. An Arrhenius plot of the inverse temperature against $\ln\kappa$ gives a barrier to 2-fold ring flips of $E_{\text{act}} = 56.6 \pm 1.3$ kJ mol⁻¹ (Figure 17).

The barrier to two-fold rotation of the nitrobenzene is nearly double that observed for the two-fold jump of the guest in C4A-TOL-*d*₅ ($E_{\text{act}} = 34 \pm 3$ kJ mol⁻¹). The difference is likely related to the inability of the nitrobenzene guest to match the host symmetry, and

is revealed in the difference in position of the two guests: the axis of motion for toluene is coincident with the 4-fold symmetric axis of the calixarene while the rotation axis of the nitrobenzene is 68° off the calix *z*-axis. The latter structure shows the aromatic ring of the guest wedged between two *t*-butylphenol units; this structural feature must raise the energy for the jumping motion compared to the toluene which occupies a more open and energetically less restricted position in the calix cavity.

6. FT-IR Spectroscopy

Whereas the FT-IR spectra of C4A-TOL showed variations in ν_{OH} as a function of toluene ring deuteration, the FT-IR spectra of C4A-NB and C4A-NB-*d*₅ do not differ (Figure 18) in either the NO or CD stretches of the guest nor the OH stretch of the guest. Furthermore, the FT-IR spectra of the calix-included guests do not significantly differ from those of the liquid guests.^{61,62} Since the toluene and nitrobenzene guests sit differently in the calix cavity, this is not surprising. Certainly in the latter case, the nitro-group seems to dictate the orientation of the guest more than $\text{CH}_{\text{guest}}-\pi_{\text{host}}$ interactions. The introduction of ring deuteration in the nitrobenzene does not induce any further distortion of the calixarene in addition to the asymmetry caused by the nitro group.

7. Summary

The objective of the work presented in this chapter was to place in the calix cavity a guest with such prominent asymmetric features that it would induce a lowering of symmetry in the resulting calix-guest compound. The objective was successful on several accounts. First, it should be noted that the cavity is resistant to distortions. Cyclic aliphatic guests with two ring substituents adopt two disordered positions in the cavity in order to maintain 4-fold symmetry. The cavity does not appear to be sensitive to the

differences between a carbonyl and a methyl group. Secondly, in the case of racemic and enantiomeric α -pinene guests, the C4A-guest structure distorts, but only to the extent that reflects the loss of inversion symmetry with the enantiomeric guest. As a result, the crystallographic *c*-axis is double that seen with the racemic guest. Interestingly, the ^{13}C NMR data suggests that the racemate and the single enantiomer guests possess different types of motions in the cavity. This difference indicates that the guests, while chemically equivalent, may be positioned in the calix pocket differently according to the symmetry differences.

Thirdly, the presence of a nitro group on the guest aromatic ring leads to the complete removal of the host C_4 symmetry axis. The structure was the first solved in this thesis work, and established the nature of the *t*-butyl group disorder prevalent in C4A-guest structures. The C4A-NB compound has been instrumental in calibrating the complicated ^{13}C NMR spectra with the lowered symmetry seen in the XRD structure. Furthermore, the consequences of a distorted host and an off-axis guest position lead to a higher barrier to guest motion than that seen with the C4A-toluene compound.

It is likely that the symmetry of the flexible calixarene host can be lowered in other ways than that seen with the C4A-NB structure. The ^{13}C NMR spectra of the 3- and 4-nitrotoluene-included calixes are different enough from the C4A-NB compound to suggest alternative structures. Of further interest is the complete structural characterization of the C4A-(*R*)-(+)-3-methylcyclopentanone structure. Preliminary work suggests that the compound crystallizes in a tetragonal $P4$ space group rather than the $P4/n$ typically seen, and that this structural arrangement may be related to the transitory structure observed with the C4A-TOL compound. Finally, the consequences of guest chirality on the guest position and dynamics in the host cavity as well as on the calix architecture itself may prove interesting if the physical properties vary widely.

8. References

1. Gutsche, C. D. *Calixarenes*, RSC, Cambridge and London, 1989.
2. Vicens, J.; Bohmer, V. (Eds.), *Calixarenes*, Kluwer, Dordrecht, 1990.
3. Ungaro, R.; Arduini, A.; Casnati, A.; Ori, O.; Pochini, A.; Ugozzoli, F. in *Computational Approaches in Supramolecular Chemistry*, Wipff, G. (Ed.); NATO ASI C426; Kluwer: Dordrecht, 1994, 277-300.
4. Bohmer, V. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 713-745.
5. Ungaro, R.; Pochini, A.; Andreetti, G. D. *J. Incl. Phenom.* **1984**, *2*, 199-206.
6. McKervery, M. A.; Seward, E. M.; Ferguson, G.; Ruhl, B.; Harris, S. J. *J. Chem. Soc., Chem. Commun.* **1985**, 388-390.
7. Arduini, A.; Pochini, A.; Reverberi, S.; Ungaro, R.; Andreetti, G.; Ugozzoli, F. *Tetrahedron* **1986**, *42*, 2089-2100.
8. Calestani, G.; Ugozzoli, F.; Arduini, A.; Ghidini, E.; Ungaro, R. *J. Chem. Soc., Chem. Commun.* **1987**, 344-346.
9. Olmstead, M. M.; Sigel, G.; Hope, H.; Xu, X.; Power, P. *J. Am. Chem. Soc.* **1985**, *107*, 8087-8091.
10. Bott, S. G.; Coleman, A. W.; Atwood, J. L. *J. Am. Chem. Soc.* **1986**, *108*, 1709-1710.
11. Arduini, A.; Ghidini, E.; Pochini, A.; Ungaro, R.; Andreetti, G. D.; Calestani, G.; Ugozzoli, F. *J. Incl. Phenom.* **1988**, *6*, 119-134.
12. Ferguson, G.; Kaitner, B.; McKervery, M. A.; Seward, E. M. *J. Chem. Soc., Chem. Commun.* **1987**, 584-585.
13. Ghidini, E.; Ugozzoli, F.; Ungaro, R.; Harkema, S.; El-Fadl, A. A.; Reinholdt, D. N. *J. Am. Chem. Soc.* **1990**, *112*, 6979-6985.
14. Ferguson, G.; Gallagher, J. F.; Pappalardo, S. *J. Incl. Phenom.* **1992**, *14*, 349-356.
15. Giannini, L.; Solari, E.; Zanotti-Gerosa, A.; Floriani, C.; Chiesi-Villa, A.; Rizzola, C. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 85-87.
16. Andreetti, G. D.; Ungaro, R.; Pochini, A. *J. Chem. Soc., Chem. Commun.*, **1979**, 1005-1007.
17. Ungaro, R.; Pochini, A.; Andreetti, G. D.; Domiano, P. *J. Chem. Soc., Perkin Trans. 2*, **1985**, 197-201.
18. Komoto, T.; Ando, I.; Nakamoto, Y.; Ishida, S. *J. Chem. Soc., Chem. Commun.*, **1988**, 135-137.
19. McKervery, M. A.; Seward, E. M.; Ferguson, G.; Ruhl, B. L. *J. Org. Chem.* **1986**, *81*, 3581-3584.

20. Corazza, F.; Floriani, C.; Chiesi-Villa, A.; Guastini, C. *J. Chem. Soc., Chem. Commun.*, **1990**, 640-641.
21. Atwood, J. L.; Orr, G. W.; Hamada, F.; Vincent, R. L.; Bott, S. G.; Robinson, K. D. *J. Am. Chem. Soc.* **1991**, *113*, 2760-2761.
22. Brouwer, E.B.; Enright, G.D.; Ripmeester, J.A. *Supramol. Chem.* **1996**, *7*, 79-83.
23. Furphy, B. M.; Harrowfield, J. M.; Ogden, M. I.; Skelton, B. W.; White, A. H.; Wilner, F. R. *J. Chem. Soc. Dalton Trans.* **1989**, 2217-2221.
24. Xu, W.; Puddephatt, R. J.; Manojlovic-Muir, L.; Muir, K. W.; Frampton, C. S. *J. Incl. Phenom.* **1994**, *19*, 277-290.
25. Harrowfield, J. M.; Ogden, M. I.; Richmond, W. R.; Skelton, B. W.; White, A. H. *J. Chem. Soc., Chem. Commun.* **1991**, 1159-1161.
26. Harrowfield, J. M.; Ogden, M. I.; Richmond, W. R.; Skelton, B. W.; White, A. H. *J. Chem. Soc. Perkin Trans. 2*, **1993**, 2183-2190.
27. Minn, H. H.; Chang, S.; No, K. T. *Theor. Chim. Acta*, **1989**, *75*, 233-245.
28. Grootenhuis, P. D. G.; Kollman, P. A.; Groenen, L. C.; Reinhoudt, D. N.; van Hummel, G. J.; Ugozzoli, F.; Andreotti, G. D. *J. Am. Chem. Soc.* **1990**, *112*, 4165-4176.
29. Drew, M. G. B. in *Spectroscopic and Computational Studies of Supramolecular Systems*, Davies, J. E. D. (Ed.) Kluwer, Dordrecht, 1992.
30. Guilbaud, P.; Varnek, A.; Wipff, G. *J. Am. Chem. Soc.* **1993**, *115*, 8298-8312.
31. Cohen, A.A.; Shatzmiller, S.E. *J. Comp. Chem.* **1995**, *16*, 1459-1467.
32. Morozumi, T.; Shinkai, S. *J. Chem. Soc., Chem. Commun.*, **1994**, 1219-1220.
33. Facey, G. A.; Dubois, R. H.; Zakrzewski, M.; Ratcliffe, C. I.; Atwood, J. L.; Ripmeester, J. A. *Supramol. Chem.*, **1993**, *1*, 199-200.
34. Minkin, V. I.; Glukhovtsev, M. N.; Simkin, B. Y. *Aromaticity and Antiaromaticity: Electronic and Structural Aspects*. Wiley: New York, 1994, 71-74.
35. Gutsche, C. D.; Bauer, L. J. *J. Am. Chem. Soc.* **1985**, *107*, 6063-6069.
36. Gutsche, C. D.; Iqbal, M.; Alam, I. *J. Am. Chem. Soc.* **1987**, *109*, 4314-4320.
37. Gutsche, C. D.; Iqbal, M.; Nam, K. S.; See, K.; Alam, I. *Pure & Appl. Chem.* **1988**, *60*, 483-488.
38. Ahn, S.; Chang, S.-K.; Kim, T.; Lee, J. W. *Chem. Lett.* **1995**, 297-298.
39. Jung, Y. E.; Song, B. M.; Change, S.-K. *J. Chem. Soc. Perkin Trans. 2* **1995**, 2031-2034.
40. Breitmaier, E.; Voelter, W. *¹³C NMR Spectroscopy*; 2nd ed.; Verlag Chemie: Weinheim, 1978.

41. Alemany, L.B.; Grant, D.M.; Alger, T.D.; Pugmire, R.J. *J. Am. Chem. Soc.* **1983**, *105*, 6697-6704.
42. Bohmer, V.; Kraft, D.; Tabatabai, M. *J. Incl. Phenom.* **1994**, *19*, 17-39.
43. Arnecke, R.; Bohmer, V.; Ferguson, G.; Pappalardo, S. *Tetrahedron. Lett.* **1996**, *37*, 1497-1500.
44. Crombie, L. *Nature*, **1994**, *370*, 428.
45. Regnouf de Vains, J.-B.; Lamartine, R.; Fenet, B.; Bavoux, C.; Thozet, A.; Perrin, M. *Helv. Chim. Acta* **1995**, *78*, 1607-1619.
46. as discussed in Chapter 3, section 4.1.
47. Hunter, C. A. *Chem. Rev.* **1994**, 101-109.
48. Paliwal, S.; Geib, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1994**, *116*, 4497-4498.
49. Eaton, D. F.; Anderson, A. G.; Tam, W.; Wang, Y. *J. Am. Chem. Soc.* **1987**, *109*, 1886-1888.
50. Eaton, D. F. *Science*, **1991**, *253*, 281-287.
51. Cox, S. D.; Gier, T. E.; Stucky, G. D.; Bierlein, J. *J. Am. Chem. Soc.* **1988**, *110*, 2986-2987.
52. Ashwell, G. J.; Jackson, P. D.; Crossland, W. A. *Nature* **1994**, *368*, 438-440.
53. Mark, T. J.; Ratner, M. A. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 155-173.
54. Service, R. F. *Science* **1995**, *267*, 1918-1922.
55. Beecher, J. E.; Frechet, J. M. J.; Willand, C. S.; Robello, D. R.; Williams, D. J. *J. Am. Chem. Soc.* **1993**, *115*, 12216-12217.
56. Konig, O.; Hoss, R.; Hulliger, J. *Adv. Mater.* **1995**, *7*, 719-721.
57. Kelderman, E.; Derhaeg, L.; Heesink, G. J. T.; Verboom, W.; Engbersen, J. F. J.; van Hulst, N.F.; Persoons, A.; Reinhoudt, D. N. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1075-1077.
58. Kelderman, E.; Derhaeg, L.; Verboom, W.; Engbersen, J. F. J.; Harkema, S.; Persoons, A.; Reinhoudt, D. N. *Supramol. Chem.* **1993**, *2*, 183-190.
59. Gall, C. M.; DiVerdi, J. A.; Opella, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 5039-5043.
60. Greenfield, M. S.; Ronemus, A. D.; Vold, R. L.; Vold, R. R.; Ellis, P. D.; Raidy, T. E. *J. Mag. Res.* **1987**, *72*, 89.
61. Kross, R. D.; Fassel, V. A. *J. Am. Chem. Soc.* **1956**, *78*, 4225-4229.
62. *The Aldrich Handbook of FT-IR Spectra*, Pouchert, C.J. ed. Aldrich: Milwaukee, WI, 1985.

9. Figures

FIGURE 1. 75.5 MHz ^{13}C CP-MAS NMR spectrum of *p*-*tert*-butylcalix[4]arene-2,6-lutidine at 290K. The spectrum was collected on a Bruker AMX-300 spectrometer using a Doty DAS 7 mm spinning probe: 200 transients; recycle time: 3.5 s; $\pi/2$ pulse = 6 μs ; contact time = 3 ms; TD = 6K; 8K points; ν = 4.5 kHz; ss = spinning sidebands.

FIGURE 2. 45.3 MHz ^{13}C CP-MAS NMR spectrum of *p*-*tert*-butylcalix[4]arene-(*R*)-(+)-3-methylcyclopentanone; *inset*: δ 28 - 8 ppm region. The spectrum was collected on a Bruker MSL-180 spectrometer using a 7 mm spinning Bruker probe: 750 transients; recycle time: 3.5 s; $\pi/2$ pulse = 2.8 μs ; contact time = 3.5 ms; TD = 4K; 16K points; ν = 4.65 kHz; ss = spinning sidebands.

FIGURE 3. 5-Membered ring guest positions in the 4-fold symmetric calixarene cavity.

FIGURE 4. 50.3 MHz ^{13}C CP-MAS NMR spectra of *p*-*tert*-butylcalix[4]arene-racemic-3-methylcyclopentanone at 291 K (*bottom*) and 113 K (*top*). The spectra were collected on a Bruker MSL-200 spectrometer using a 7 mm spinning Chemagnetics pencil probe: 150-600 transients; recycle time: 3.6-6.0 s; $\pi/2$ pulse = 3.7 μs ; contact time = 3.5 ms; TD = 4K; 16K points; ν = 3 kHz; ss = spinning sidebands; uncertainty in T : $\pm 4\text{K}$.

FIGURE 5. 50.3 MHz ^{13}C CP-MAS NMR spectra of *p*-*tert*-butylcalix[4]arene-(±)-sec-phenethylalcohol at 291K (*bottom*), 113K (*middle*), and 113K, dipolar-dephased (*top*). Note the splitting of the guest resonances at low temperature. The spectra were collected on a Bruker MSL-200 spectrometer using a 7 mm spinning Chemagnetics pencil probe: 150-320 transients; recycle time: 3.6-6.0 s; $\pi/2$ pulse = 3.8 μs ; contact time = 3.5 ms; TD = 4K; 16K points; ν = 3 kHz; ss = spinning sidebands; uncertainty in T : $\pm 4\text{K}$.

FIGURE 6. 45.3 MHz ¹³C CP-MAS NMR spectrum of *p*-*tert*-butylcalix[4]arene-nitrobenzene. The spectrum was collected on a Bruker MSL-180 spectrometer using a Bruker 7 mm spinning probe: 1500 transients; recycle time: 3.5 s; $\pi/2$ pulse = 2.8 μ s; contact time = 3.5 ms; TD = 4K; 16K points; ν = 2.86 kHz; ss = spinning sidebands.

FIGURE 7. 45.3 MHz ¹³C CP-MAS NMR spectrum of *p*-*tert*-butylcalix[4]arene-4-nitrotoluene. The spectrum was collected on a Bruker MSL-180 spectrometer using a 7 mm spinning Bruker probe: 700 transients; recycle time: 3.5 s; $\pi/2$ pulse = 2.8 μ s; contact time = 3.5 ms; TD = 4K; 16K points; ν = 3.05 kHz.

FIGURE 8. 45.3 MHz ¹³C CP-MAS NMR spectrum of *p*-*tert*-butylcalix[4]arene-3-nitrotoluene. The spectrum was collected on a Bruker MSL-180 spectrometer using a 7 mm spinning Bruker probe: 800 transients; recycle time: 3.5 s; $\pi/2$ pulse = 2.8 μ s; contact time = 3.5 ms; TD = 4K; 16K points; ν = 3.14 kHz.

FIGURE 9. Enantiomers of α -pinene; chirality arises from C4 and C6.

FIGURE 10. 50.3 MHz ^{13}C CP-MAS NMR spectra of *p*-*tert*-butylcalix[4]arene-(1*R*)-(-)- α -pinene (*top*); *p*-*tert*-butylcalix[4]arene-racemic-($\pm$)- α -pinene (*bottom*). Guest lines (where visible) are indicated by arrows. The spectra were collected on a Bruker MSL-200 spectrometer using a 7 mm spinning Chemagnetics pencil probe: 500 transients; recycle time: 3.5 s; $\pi/2$ pulse = 3.8 μs ; contact time = 3.5 ms; TD = 4K; 16K points; ν = 3 kHz; ss = spinning sidebands.

FIGURE 11. 50.3 MHz ^{13}C CP-MAS NMR spectra of *p*-*tert*-butylcalix[4]arene-(1*R*)-(-)- α -pinene (top); *p*-*tert*-butylcalix[4]arene-racemic($\pm$)- α -pinene (bottom): Expansion of the guest resonances: δ = 150-140, δ = 120-110, δ = 50-38, δ = 24-16 ppm. Chemical shift (δ) values for α -pinene in CDCl_3 are given in brackets (from ref 40); * signal disappears under the dipolar-dephasing experiment.

FIGURE 12. C₄A- α -pinene chirality, shown with a simple chiral guest. *Left:* racemic guests are related by an inversion centre and the repeat along $c = c$. *Right:* the enantiomers cannot be related by inversion symmetry and thus the repeat along $c = 2c$.

FIGURE 13. ORTEP of C4A-NB with H atoms excluded for clarity. The thermal ellipsoids are drawn at the 30% probability level.

FIGURE 14. Stereo view of the crystal packing in C4A-NB

FIGURE 15. Stereo view of C4A-NB along *c*; two layers of calixes are shown.

FIGURE 16. Observed (*left*) and simulated (*right*) 46.1 MHz ^2H NMR spectra of *p*-*tert*-butylcalix[4]arene-nitrobenzene- d_5 over $T = 200$ – 290 K. The spectra were collected on a Bruker AMX-300 spectrometer with a 5 mm coil: 400 scans; recycle time: 5 s; $\pi/2$ pulse: 2.5 μs ; echo delay: 35 μs ; line broadening: 0.5 kHz; TD = 512; 1K points.

FIGURE 17. Arrhenius Plot of *p*-tert-butylcalix[4]arene-nitrobenzene- d_5 .

FIGURE 18. FT-IR spectra (KBr) of *p*-tert-butylcalix[4]arene-nitrobenzene and *p*-tert-butylcalix[4]arene-nitrobenzene-*d*₅.

10. Appendix: X-ray Structural Data

A1. Final Positional and Equivalent Isotropic Thermal Parameters ($\text{\AA}^3$) for C4A-NB.

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> _{iso} ^a
O 1	0.76876(14)	0.98149	0.22971(6)	1.91(7)
C11	0.81668(19)	1.0125 (3)	0.27404(10)	1.49(9)
C12	0.79542(20)	1.11092(25)	0.29322(10)	1.61(9)
C13	0.85038(20)	1.1420 (3)	0.33574(10)	1.61(10)
C14	0.92558(19)	1.0791 (3)	0.35966(10)	1.62(9)
C15	0.94181(20)	0.9797 (3)	0.34000(9)	1.57(9)
C16	0.88737(19)	0.94472(25)	0.29750(10)	1.47(9)
C17	0.98821(21)	1.1230 (3)	0.40454(10)	1.74(10)
C18	0.71386(21)	1.1837 (3)	0.26910(10)	1.72(9)
O 2	0.56331(14)	1.04462(22)	0.22662(7)	2.01(7)
C21	0.53081(20)	1.0968 (3)	0.26916(9)	1.59(9)
C22	0.42852(20)	1.08026(25)	0.28963(10)	1.59(9)
C23	0.39866(20)	1.1392 (3)	0.33095(10)	1.67(9)
C25	0.56769(21)	1.2249 (3)	0.33144(10)	1.89(10)
C26	0.60153(20)	1.1687 (3)	0.28987(10)	1.69(9)
C28	0.35236(20)	0.9988 (3)	0.26905(10)	1.59(9)
O 3	0.49369(14)	0.85015(20)	0.22533(7)	1.85(7)
C31	0.44428(19)	0.8224 (3)	0.27003(9)	1.42(9)
C32	0.46552(20)	0.7261 (3)	0.29179(9)	1.52(9)
C33	0.41195(21)	0.7011 (3)	0.33553(10)	1.84(10)
C35	0.32057(20)	0.8631 (3)	0.33560(10)	1.77(10)
C36	0.37255(19)	0.89233(25)	0.29155(10)	1.49(9)
C38	0.54636(21)	0.6504 (3)	0.27012(10)	1.71(10)
O 4	0.69978(14)	0.78990(21)	0.23161(7)	1.92(7)
C41	0.73002(21)	0.7369 (3)	0.27389(9)	1.52(9)
C42	0.83057(20)	0.7534 (3)	0.29613(9)	1.47(9)
C43	0.85850(20)	0.6912 (3)	0.33673(10)	1.57(9)
C44	0.79066(20)	0.6161 (3)	0.35617(10)	1.58(9)
C45	0.68921(19)	0.60554(25)	0.33379(10)	1.56(9)
C46	0.65807(19)	0.6640 (3)	0.29291(10)	1.58(9)
C47	0.81998(21)	0.5460 (3)	0.40054(10)	1.91(10)
C48	0.90828(20)	0.8361 (3)	0.27714(10)	1.58(10)
T11	1.07096(22)	1.0466 (3)	0.42534(11)	2.37(11)
T12	1.04917(22)	1.2204 (3)	0.38745(10)	2.21(10)
T13	0.91041(24)	1.1527 (3)	0.44678(11)	2.32(11)
T41	0.93650(23)	0.5611 (3)	0.41762(12)	2.78(12)
T42	0.74421(24)	0.5688 (3)	0.44433(11)	2.79(12)
T43	0.80719(24)	0.4324 (3)	0.38491(12)	2.58(12)
O 5	0.86224(20)	0.9026 (3)	0.51497(10)	4.28(11)
O 6	0.89929(20)	0.8211 (3)	0.44647(13)	5.06(14)
N 1	0.83913(21)	0.8741 (3)	0.47299(11)	3.01(12)
CN1	0.73554(23)	0.9052 (3)	0.45202(11)	2.16(10)
CN2	0.6674 (3)	0.9649 (3)	0.48111(11)	2.71(12)
CN3	0.5702 (3)	0.9940 (3)	0.46173(13)	3.57(14)
CN4	0.5408 (3)	0.9654 (3)	0.41399(14)	3.63(14)
CN5	0.6096 (3)	0.9066 (3)	0.38547(13)	3.98(16)
CN6	0.7085 (3)	0.8748 (3)	0.40444(13)	3.47(14)

Table A1 *continued*

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> _{iso} ^a
C37	0.28288(18)	0.7303 (3)	0.40709(8)	2.37(18)
C34	0.3370 (3)	0.7678 (4)	0.35872(10)	1.84(13)
TA 1	0.36941(25)	0.7067 (3)	0.44648(12)	3.36(18)
TA 2	0.21772(25)	0.6319 (3)	0.39625(13)	3.04(16)
TA 4	0.2074 (3)	0.8150 (3)	0.42688(14)	4.12(21)
C37A	0.2726 (8)	0.7513 (9)	0.4052 (3)	2.7 (7)
C34A	0.3422 (12)	0.7716 (14)	0.3588 (4)	1.9 (5)
TA1A	0.3027 (15)	0.6461 (10)	0.4280 (6)	6.2 (12)
TA2A	0.1533 (8)	0.7505 (15)	0.3902 (6)	4.9 (10)
TA4A	0.2920 (13)	0.8371 (11)	0.4439 (5)	4.2 (8)
C27	0.4208 (3)	1.2786 (3)	0.39837(17)	1.80(25)
C24	0.4634 (6)	1.2129 (6)	0.3548 (3)	1.73(18)
TB 2	0.3397 (4)	1.3582 (4)	0.37844(18)	2.98(24)
TB 3	0.5150 (4)	1.3351 (6)	0.42359(24)	4.8 (4)
TB 1	0.3650 (6)	1.2081 (5)	0.4367 (3)	3.0 (3)
C27A	0.4427 (6)	1.2788 (5)	0.3964 (3)	2.1 (3)
C24A	0.4714 (10)	1.2105 (8)	0.3513 (4)	1.92(19)
TB 4	0.4247 (9)	1.3905 (6)	0.3787 (3)	5.2 (5)
TC 3	0.5353 (7)	1.2761 (7)	0.4344 (3)	3.8 (4)
TC 2	0.3395 (7)	1.2380 (9)	0.4211 (5)	6.0 (7)

$$^a B_{\text{iso}} = 8/3\pi^2 \sum \sum U_{ij} a_i^* a_j^* (a_i \cdot a_j).$$

CHAPTER 5: *p*-*tert*-Butylcalix[4]arene-Aliphatic Compounds*

1. Introduction	189
2. Synthetic Details	192
3. Solid-State ^{13}C CP-MAS Spectroscopy	193
4. Single Crystal X-ray Diffraction	198
5. ^2H NMR Spectroscopy: Guest Dynamics	205
6. Summary	213
7. References	214
8. Figures	217
9. Appendix: X-Ray Diffraction Structural Details	230

1. Introduction

The nature and strength of guest-host interactions are important for molecular recognition processes in nature as well as in supramolecular materials such as the calixarenes. The interaction between the host *t*-butyl groups and the aromatic ring of the guest is often invoked to explain the stability of calixarene host-guest compounds.¹⁻⁴ Early work on calixarenes showed that aromatic guests and *p*-*tert*-butylcalix[4]arenes (C4A) form stable (with respect to guest loss) inclusion compounds. Crystallographic results on several compounds formed the basis for the conjecture that the structures are stabilized by the interaction of the aromatic rings with the *t*-butyl methyl groups.^{4,6} The *t*-butyl groups are significant for guest inclusion as the related calix[4]arene (without *t*-butyl groups) is a poor host for similar small guest molecules.⁷ In an often-cited 1988 paper, molecular mechanics calculations of the host-guest interactions in a 1:1 crown-bridged-C4A-pyridine compound were carried out.⁴ The compound's potential energy due to van der Waals, electrostatic, and hydrogen bonding ($\text{N-H}\cdots\text{N}$) forces was calculated as a function of

* Parts of this chapter have been published: Brouwer, E.B.; Enright, G.D.; Ripmeester, J.A. *Supramol. Chem.* **1996**, 7, 143-145.

guest position as it was rotated in the calix cavity. The guest potential as a function of angle failed to match the observed XRD structure so an additional stabilizing $\pi_{\text{guest}}\text{-Me}_{\text{host}}$ interaction was introduced. In subsequent structural work on calixarene compounds, the stability of calixarene compounds is attributed to $\pi_{\text{guest}}\text{-Me}_{\text{host}}$ interactions,⁴⁻⁹ including the recently reported calix-fullerene compounds.¹⁰ Understanding the role of this interaction has been hindered by (a) the unresolved disorder ubiquitous in diffraction studies on C4A compounds which has led to structural models with large residuals¹⁻⁹ (see also Chapters 3 and 4), (b) large atomic thermal parameters due to motion and in part to the unresolved disorder; both often obscure subtle host-guest interactions, and finally (c) the perception that non-aromatic guests are unable to form stable C4A compounds.

Several structures of modified C4A compounds with non-aromatic compounds are known. As early as 1981, Gutsche reported the synthesis of C4A-chloroform, but did not report a single-crystal XRD structural study.¹¹ The tetraethylcarbonate C4A calix forms a crystalline inclusion compound with acetonitrile in which the guest lies along the 4-fold axis.¹² Acetonitrile is also included in the tetraacetamide-C4A compounds with alkali cations KI and KSCN.¹³ Harrowfield reported the incorporation of acetonitrile in the C4A-Cs compound; cesium sits in the calix cavity and the solvent molecule “caps” the ion.¹⁴ C4A and a related calix host, the di(homooxa) analogue of C4A, include acetonitrile in the cavity when binding tetraalkylammonium cations.¹⁵ In these structures, the acetonitrile guest generally lies along the calix symmetry axis. An asymmetric *R*-calix[4]arene (with *R* = isopropyl, methyl in the *tert*-position) crystallizes with acetone in the cavity.¹⁶ Metallation of the outer face of C4A with transition metals results in calixarene cavities occupied with diethylether and nitromethane.¹⁷ Di(homooxa)-C4A forms a 1:2 structure with triethylamine in which one amine is in the cavity and the other is in the interhost space.¹⁸ The same host can also incorporate both dimethylsulphoxide and

acetone when complexed with Eu^{III} .¹⁹ The C4A-related calixarenes C5A and C6A form inclusion compounds with tetralin²⁰ and acetonitrile,²¹ respectively. In the former, the aromatic rather than the aliphatic ring is included in the calix cavity. Acetone is a guest within the cavity of an anionic calix[4]arenesulfonate cavity; note that this calix has no *t*-butyl groups.²²

In most post-1988 papers, $\pi_{\text{guest}}\text{-Me}_{\text{host}}$ interactions are discussed as potential stabilizing forces, but the authors often report the inability to identify specific C-H bonds that interact with the calix π system.^{15-17, 21} In the above survey, the guests are polar and most show double-bond character—features which may provide alternative host-guest interactions. Furthermore, all calix compounds described above are modified by ring size, by incorporation of metals, or by modification on the upper or lower rim; these modifications increase the complexity of host:guest interactions. In summary, there is a paucity of structures of strictly C4A compounds with aliphatic hydrocarbon guests—guests that would provide the best test of the necessity of $\pi_{\text{guest}}\text{-Me}_{\text{host}}$ interactions in stable host:guest compounds.

This chapter extends the work of Chapter 3 in which the calix cavity was shown to preferentially accommodate the methyl group over the chloro group due to an attractive $\pi_{\text{host}}\text{-Me}_{\text{guest}}$ interaction. Herein, the exigency of $\pi_{\text{guest}}\text{-Me}_{\text{host}}$ interactions in the formation of stable calix-guest compounds is addressed with the investigation of the structural and dynamic properties of C4A-aliphatic compounds. Aliphatic guests do not have the potential for attractive $\pi_{\text{guest}}\text{-Me}_{\text{host}}$ interactions and the stability of C4A-aliphatic compounds questions the importance of $\pi_{\text{host}}\text{-Me}_{\text{guest}}$ interactions. It will be demonstrated that the calix cavity prefers to host the methyl rather than the halogen (Cl, Br) group in the pocket due to an attractive $\pi_{\text{host}}\text{-Me}_{\text{guest}}$ interaction. *t*-Butyl methyl groups are integral to

the stability of C4A-guest compounds by extending the cavity to a useful inclusion depth, but their role is significant more in directing crystal packing than in π -methyl interactions.

2. Synthetic Details

C4A is insoluble in aliphatic solvents.⁴ C4A-aliphatic compounds may be prepared by either vapour diffusion of the aliphatic guest into a saturated nitrobenzene or 3-nitrotoluene solution of C4A or by physical mixing of C4A with the liquid guest. This synthesis provides a new class of guests that form inclusion compounds with C4A.

The synthesis of C4A-cyclohexane (CY) is typical of a C4A-aliphatic compound:

Vapour Diffusion: C4A (238 mg, 0.366 mmol) was dissolved in 3-nitrotoluene or nitrobenzene (3 mL) in a small vial which was placed inside a larger, capped vial containing cyclohexane (3 mL) at room temperature. After 2 d, the crystal-containing solution in the inner vial was filtered yielding colourless crystals of C4A-CY (179 mg, 0.244 mmol, 67 % yield). In the case of propane and ethane diffusing into a saturated solution of C4A in nitrobenzene, the solvent molecule also crystallizes.

Physical Mixing: Microcrystalline powders of C4A-aliphatic compounds may also be prepared by mixing C4A with the appropriate hydrocarbon at low heat for 1 h, followed by filtration. In the case of C4A-butane, the reaction was carried out at -2 °C in a saline solution bath for 1 h, and then the butane boiled off (b.p. 0.5 °C). The preparation of C4A-propane was similar. Propane (4 mL) was condensed from the gas in a vial submerged in an ethanol/CO₂ cold bath (-65 °C) containing a stirbar and approximately 300 mg of C4A. The mixture was stirred for 1 h before the vial was removed from the bath to boil off the propane (b.p. -42 °C). The white solid was immediately placed in a dewar containing dry ice for storage. When C4A-propane is kept at room temperature, it out-gasses over a period of several hours. Attempts to prepare C4A-ethane and C4A-

methane ($\text{bp}_{\text{ethane}} = -88\text{ }^{\circ}\text{C}$, $\text{bp}_{\text{methane}} = -161\text{ }^{\circ}\text{C}$) in this manner failed to yield a compound stable enough to characterize by ^{13}C NMR spectroscopy at room temperature.

Both techniques yield C4A-aliphatic compounds that are stable (with respect to loss of guest) for several weeks at room temperature for the longer-chained aliphatics and several hours for propane. To minimize guest loss, the compounds were stored at $-40\text{ }^{\circ}\text{C}$.

3. Solid-State ^{13}C CP-MAS NMR Spectroscopy

^{13}C CP-MAS NMR spectroscopy is a powerful, versatile and relatively easy-to-apply technique to probe the solid-state structure and symmetry of C4A-guest compounds. In the 4-fold symmetric C4A-aliphatic compounds, the guest is dynamically averaged about the calix 4-fold symmetry axis. Figure 1 shows the room temperature ^{13}C CP-MAS NMR spectrum of a typical C4A-aliphatic compound, C4A-*n*-pentane (PT). Each carbon of the *t*-butylphenol subunit gives rise to a characteristic resonance; since the multiplicity of each line = 1, the four subunits are equivalent and thus the calix has a conical, 4-fold symmetric structure. The dipolar-dephasing (DD) NMR experiments²³ indicate that in all aliphatic guests, each proton-bearing guest carbon is dynamic.

Two of the three *n*-pentane carbon resonances are observed (the third, C-3, lies under the calix methyl signal ($\delta = 32.6\text{ ppm}$). Since the five potentially inequivalent carbons fail to give rise to five single carbon resonances, dynamic averaging of the pentane (and other aliphatic guests) position in the calix cavity is likely.

The chemical shifts (δ) of the aliphatic guests in the calixarene and in neat solution are collected in Table 1. The first four entries show insignificant differences in δ between the calix and solution (the complexation-induced shift, CIS), which suggests that the guests possess motions that are fast (on the NMR timescale) and average out the differences between the two ends of the aliphatic chain or ring. For propane, *n*-butane and

n-pentane, the end-over-end motion is in addition to the dynamic disorder along the calix 4-fold axis. Since the CIS values are not large, the methyl groups must jump between a site deep in the cavity (with a large CIS value) and one quite removed from the cavity (with a more solution-like value of δ_{Me}). Averaging between the two different sites leads to an intermediate CIS value for the methyl ^{13}C resonance.

Two synthetic routes to the C4A-aliphatic compounds exist: one by vapour diffusion into a C4A-saturated nitrobenzene (or 3-nitrotoluene) solution, and the other by physical mixing of the aliphatic guest and the empty C4A. Figure 2 illustrates the ^{13}C CP-MAS NMR spectra of C4A-*n*-butane prepared by both techniques and confirms that the two compounds are identical.

The boiling point of the aliphatic guest materials appears to limit the scope of the physical mixing technique: neither C4A-methane nor C4A-ethane compounds were prepared in this fashion. The guest may not be large enough to form a stable guest-host compound and induce a change in the calix architecture upon enclathration; if it does, the rate of out-gassing (and hence collapse of the host lattice) is high. By the time the ^{13}C NMR spectra were collected, there was no detectable C4A-guest species. Figure 3 shows the ^{13}C CP-MAS NMR spectra of a 4-fold symmetric C4A-propane prepared by condensation of propane on C4A at -65 °C, as well as the spectrum of C4A without any guest. The C4A-propane spectrum shows the presence of lines corresponding to those of the empty calix. Propane appears to be the smallest aliphatic guest prepared by the physical mixing technique. The ^{13}C CP-MAS NMR spectrum of C4A containing no guest (Figure 3) reveals a structure in which the calix has no elements of symmetry. Strong evidence for this is found in the quadruplet resonance of C-4 (δ 142-146 ppm), C-8 (δ 34-36 ppm) and C-9 (δ 29.5-34 ppm) corresponding to four distinct *t*-butylphenol subunits. This spectrum is in contrast to the spectra of 4-fold symmetric C4A-guest compounds.

TABLE 1. Guest ^{13}C NMR chemical shifts (in ppm) of C4A-aliphatic compounds.

Entry	Guest	Carbon	Calix ^a	Solution ^b	CIS ^c
1	propane	Me	14.5	15.4	-0.9
		C-2	15.9	15.9	0
2	<i>n</i> -butane	Me	11.6	13.1	-1.5
		C-2	24.5	24.9	-0.4
3	<i>n</i> -pentane	Me	12.3	13.7	-1.4
		C-2	23.5	22.6	+0.9
		C-3	<i>d</i>	34.6	<i>d</i>
4	cyclohexane	C	26.4	27.6	-1.2
5	1-bromobutane	Me	9.0	13.0	-4.0
		C-3	22.3	21.2	+1.1
		C-2	<i>d</i>	33.0	<i>d</i>
6	1-chlorobutane	C-1	36.0	34.7	+1.3
		Me	8.7	13.0	-4.3
		C-3	20.5	20.0	+0.5
		C-2	35.6	34.7	+0.9
		C-1	45.0	44.3	+0.7
7	<i>n</i> -hexane	Me	8.4	13.7	-5.8
		C-2	19.9	22.8	-2.9
		C-3	26.0	31.9	-5.9
8	<i>n</i> -heptane	Me	8.7	13.8	-5.1
		C-2	22.8	22.8	0.0
		C-3	30.0	29.3	+0.7
		C-4	32.3	32.2	+0.1
9	<i>n</i> -dodecane	Me	12.1	14.8	-2.7
		C-2	23.0	23.3	-0.3
		C-6	30.2	30.5	-0.3
		C-5	31.2	30.5	0.7
		C-4	31.7	30.5	1.2
		C-3	33.8	32.8	1.0

^a referenced to hexamethylbenzene (δ 16.9 ppm).^b from reference 24, CDCl_3 solvent or spectra collected on Bruker 300MSL spectrometer, CDCl_3 solvent.^c CIS = complexation-induced shift = $\Delta\delta = \delta(\text{calixarene}) - \delta(\text{solution})$.^d not observed.

3.1 Guest Dynamics in the Calixarene Cavity

Harris has studied the structure and dynamics of the 1:1 *n*-pentane- C_{60} inclusion compound with variable temperature ^{13}C CP-MAS NMR spectroscopy.²⁵ Pentane undergoes three types of motion: (i) rotation about its main molecular axis, (ii) flipping of this axis between two sites related by a crystallographic mirror plane and (iii) end-over-

end motion. The third motion is rapid (on the NMR timescale) at 303K and thus gives rise to a single ^{13}C resonance line at δ 16.9 ppm. At 163K, this motion is frozen and two methyl resonance lines indicate distinct methyl groups (δ 15.0, 17.6 ppm). Figure 4 shows two ^{13}C CP-MAS NMR spectra of C4A-PT prepared by physical mixing: one at 90K and the other at 290K.²⁶ The 90K spectrum shows single resonances for the terminal methyl and α -methylene groups which is similar to the 290K spectrum. Unlike the pentane- C_{60} inclusion compound, the two methyl groups of *n*-pentane in C4A are dynamically averaged at 90K. Furthermore, the calixarene *t*-butyl lines are sharp at 90K which indicates the calix C_4 symmetry persists at this temperature. That the C4A architecture fails to collapse to a lower symmetry form indicates that the motion of the guest is significant in carving out a symmetrical occupational space.

It is anticipated that the end-over-end hydrocarbon motion would be retarded upon substitution of a terminal methyl group with a heavier halogen atom. The larger electron cloud of the halogen atom favours stronger van der Waals interactions with the host, and consequently the halogen atom is expected to sit deep in the cavity and “anchor” the aliphatic chain. The ^{13}C spectra of the 1-*X*-butanes (*X* = Br, Cl) differ from *n*-pentane in exhibiting a significant difference in methyl resonance shifts in the calix from those in solution: CIS = -4.0, -4.3 ppm for 1-bromo- and 1-chlorobutane respectively, compared to the CIS value of -1.4 ppm for the *n*-pentane methyl. The further the methyl is inserted into the calix cavity, the greater the CIS value: the shift in δ_{Me} suggests that the halogenated hydrocarbons may indeed be “anchored” in the cavity, but instead of the halogen lying deep in the pocket as would be expected according to van der Waals interactions, the methyl group is inserted deep in the calix cavity. Indeed, single crystal XRD work confirms this structural assignment.

If the relationship between methyl CIS values and methyl position holds, then the longer chain ($n > 5$) aliphatic guests have both methyl groups in the calixarene cavity since the methyl CIS values are large. An averaging motion between two methyl sites may still occur (as in propane, *n*-butane and *n*-pentane), but the two sites must be similarly deep in the calixarene cavity. This may occur in two ways (Figure 5): First the long chain may kink and the two methyl groups occupy one calix cavity. Alternatively, each end of the chain occupies its own calixarene cavity and a 2:1 host:guest stoichiometry is achieved.⁶ The 2:1 host:guest structure has been observed for the C4A-*n*-hexane structure: *tetragonal P4/n*, $a = b = 12.8 \text{ \AA}$, $c = 25.5 \text{ \AA}$, and confirms a model in which each methyl group of the *n*-alkane is deep in a separate calixarene cavity.

3.2 ¹³C NMR Spectral Simulation: HYPERNMR

The HYPERNMR spectral simulation computer software package²⁷ was used to simulate the ¹³C CP-MAS NMR spectrum of C4A-PT. Because the structure of C4A-PT (*vide infra*) shows no positional disorder in the host *t*-butyl groups and is 4-fold symmetric, it is an attractive candidate to study by spectral simulation. C4A-PT is a relatively easy and simple supramolecular system with which to evaluate HYPERNMR's ability to simulate solid-state supramolecular systems. Furthermore, it was of interest to see whether the multiplicity and position of the pentane resonances determined experimentally (which indicate dynamic exchange of the two ends of the guest) could be generated with this package.

The 290K observed and simulated ¹³C NMR spectra of C4A-PT are shown in Figure 6. The simulated spectra are divided into the host and guest contributions for clarity of presentation. Overall, the host ¹³C lines are not well simulated by HYPERNMR, as some chemical shift values between the observed and simulated differ by as much as 10 ppm.

Even the pattern and multiplicity of the simulated spectrum do not correspond in a consistent fashion with the observed spectrum. While the appearance of the host C-1 and C-4 lines are in agreement, those of the host C-7, C-8, and C-9 are not.

The presence of only one ^{13}C methyl guest line when the XRD structure clearly indicates two different methyl environments suggests that dynamic averaging over two methyl group orientations occurs. The guest position taken from the XRD structure was used to calculate the ^{13}C NMR spectrum and as expected, the two methyl (as well as the two methylene) carbons give rise to distinctive lines. Indirectly, this simulation supports a model in which the pentane is dynamically-averaged. Of additional interest is the difference in the chemical shift values of the two terminal methyl carbons: C-5 is inserted deepest in the calix pocket and its resonance lies upfield (δ 14 ppm) relative to the C-1 carbon which protrudes from the cavity (δ 19 ppm). The trend mirrors the experimental feature of upfield shifts for atoms occupying positions deep in the cavity. A dynamic inversion process (fast on the NMR timescale) would cause the averaged resonance to appear between these two chemical shift values. However, the methyl signal in the calculated spectrum is over-estimated by 5 ppm.

HYPERNMR is not accurate enough in the chemical shift values nor the ^{13}C resonance to give the insight required to interpret solid-state ^{13}C NMR spectra of supramolecular systems. However, HYPERNMR simulations of the guest ^{13}C NMR resonances based on the 150K XRD structure suggest that the observed guest spectral features reflect dynamic averaging of the guest in the calix cavity.

4. Single Crystal X-ray Diffraction

In order to elucidate the structural differences between the C4A-aliphatic compounds and to probe the role of π -CH₃ interactions, four compounds were selected

for study by single-crystal X-ray diffraction. As with the previous structures in this thesis, the interactions between calix layers are significant for host-guest stability. Interestingly, the calix *t*-butyl groups show little (C4A-CY) or no (C4A-guest; guest = *n*-pentane, 1-chlorobutane, 1-bromobutane) positional disorder. This is perhaps due to a more cylindrical shape of the dynamically-averaged guest which minimize interactions between the guest and host *t*-butyl groups. Finally, substitution of a terminal methyl group of *n*-pentane by chlorine or bromine changes the aliphatic orientation in the corresponding C4A-guest structures. The calix cavity is occupied not by the halogen, which would maximize the host-guest van der Waals interactions, but by the terminal methyl. Furthermore, the halogen end of the chain is kinked, as opposed to the straight, all-*trans* *n*-pentane.

4.1 Crystallographic Evidence for C-H... π Interactions.

Recently, Steiner has examined weak hydrogen bonding in short C-H... π contacts by crystallographic, spectroscopic and quantum mechanical studies.²⁸ A survey of the Cambridge Structural Database yielded 141 terminal alkynes-containing residues in 113 structures; of these, 8 form a C-H... π interaction with an arene. The acidic alkyne hydrogen is the electron acceptor and the π -system the donor. From this work, structural, spectroscopic and energetic guidelines for C-H... π interactions are developed. First, the H... π distance ranges from 2.51-2.79 Å and that of C... π ranges from 3.58-3.82 Å. Secondly, the C-H... π angle has a value of between 147 and 171° in the 8 structures examined. Thirdly, the alkynyl IR ν_{CH} band in the crystal structure shifts to lower frequency by 7-38 cm⁻¹ compared to the alkyne in an apolar solvent. As the acidic C-H bond accepts electron density from the π system, the C-H bond weakens. Finally, *ab*

initio quantum mechanical studies indicate that the bond energy of a C-H... π interaction is as large as -9.2 kJ mol^{-1} (corresponding to the ν_{CH} shift of -38 cm^{-1}). Of course, comparison of the alkynyl system to aliphatic C-H... π interactions changes as the aliphatic C-H hydrogen is far less acidic than the alkynyl hydrogen ($\text{p}K_{\text{a}}$ toluene methyl-H: 41, $\text{p}K_{\text{a}}$ phenylacetylene: 26.5);²⁹ the alkynyl C-H bond perhaps represents the “best-case scenario” for C-H... π interaction. Nevertheless, the above parameters may serve as a rough guide for identifying C-H... π interactions in calix-aliphatic guest compounds.

4.2 *p*-tert-Butylcalix[4]arene-Cyclohexane (C4A-CY)

Representation of the C4A-CY structure is shown in Figure 7 and selected distances summarized in Table 3. Cyclohexane was modeled as a rigid group (C-C bond length = $1.535 \text{ \AA}$) in the chair conformation. Each calix *t*-butyl group is disordered (88:12) over two positions separated by an angle of 10° . The ratio of the disordering can also be interpreted as a local structure in which only one of the four *t*-butyl groups positionally disordered in a 50:50 ratio; space-averaging of the local structure over the crystal lattice leads to the observed disordering ratio. The *t*-butyl disorder may arise from the off-axis cyclohexane “pushing” out against one side of the calix cavity. The guest is motionally averaged about the 4-fold symmetry axis. The guest carbon atom (CH5) deepest inside the calix cavity is close to the axis of the calixarene, and the line between CH5 and the cyclohexane carbon atom directly across the ring (CH2) is 13.1° off the calix C_4 axis. The CH5 atom is $4.15 \text{ \AA}$ above the plane defined by the four phenolic oxygens and is located $3.54 \text{ \AA}$ from the plane of the nearest phenyl ring, approximately equidistant ($3.80 \text{ \AA}$) from the lower three phenyl ring carbons. Steric interaction between the CH6 (labeled sequentially around the cyclohexane ring) atom and the adjacent phenyl carbons (CH6-C distances of 3.40 , 3.49 and $3.52 \text{ \AA}$) prevents deeper penetration of the cyclohexane. Other

TABLE 2. Crystallographic data for C4A-PT, C4A-CY, C4A-CIB and C4A-BrB.^{a,b}

compound	C4A-PT	C4A-CY	C4A-C ₄ H ₉ Cl	C4A-C ₄ H ₉ Br
formula	C _{12.25} H ₁₇ O	C _{12.5} H ₁₇ O	C ₁₂ H _{16.25} Cl _{0.25} O	C ₁₂ H _{16.25} Br _{0.25} O
fw	180.27	183.27	185.37	216.45
temperature, K	150	150	150	150
colour, habit				
crystal size, mm	0.10 x 0.16 x 0.30	0.16 x 0.25 x 0.30	0.10 x 0.20 x 0.20	
crystal system	tetragonal	tetragonal	tetragonal	tetragonal
space group	<i>P</i> 4/ <i>n</i>	<i>P</i> 4/ <i>n</i>	<i>P</i> 4/ <i>n</i>	<i>P</i> 4/ <i>n</i>
<i>a</i> , Å	13.0230(19)	12.9446 (4)	13.0571(15)	13.0560 (37)
<i>b</i> , Å	13.0230(19)	12.9446 (4)	13.0571(15)	13.0560 (37)
<i>c</i> , Å	12.6190(12)	12.8156(25)	12.5986(15)	12.5611 (64)
<i>V</i> , Å ³	2140.2	2147.4(4)	2144.4(4)	2141.2
<i>Z</i>	8	8	8	8
ρ_{calc} , g cm ⁻³	1.119	1.134	1.148	
<i>F</i> (000)	790.04	802.08	806.73	
μ (Cu K α) mm ⁻¹	0.50	0.51	1.09	
λ , Å	1.54056	1.54056	1.54056	1.54056
scan type	$\theta/2\theta$	$\theta/2\theta$	$\theta/2\theta$	$\theta/2\theta$
data collected	<i>h, k, l</i>	<i>h, k, l</i>	<i>h, k, l</i>	<i>h, k, l</i>
$2\theta_{\text{max}}$, deg	139.9	140.1	140	
total # refls	2154	4655	4084	
# of unique reflns	2045	2052	2046	
<i>R</i> _{merge}	0.017	0.017	0.052	
# reflns $I \geq 2.5\sigma(I)$	1641	1697	1549	
# of variables	145	185	140	
<i>R</i>	0.048	0.051	0.090	
<i>R</i> _w	0.070	0.079	0.131	
GOF	2.58	3.18	4.79	
max Δ/σ , finl cycl	0.030	0.182	0.180	
resid density, e Å ⁻³	-0.200 to 0.190	-0.250 to 0.360	-0.84 to 1.37	

^aConditions and collection details: Enraf-Nonius diffractometer; graphite monochromator; aperture 4.0 x 4.0 mm at a distance of 173 mm from the crystal; stationary background counts at each end of the scan (scan/background time ratio 5:1); peak and background counts determined with profile analysis procedure of Gabe *et al.*, *J. Appl. Cryst.*, **1989**, 22, 384. $\sigma(F_o)$ based on counting statistics, function minimized $\sum w(|F_o| - |F_c|)^2$, where $w = [\sigma^2(F_o) + k(F_o)^2]^{-1}$, $R = \sum ||F_o| - |F_c|| / \sum |F_o|$, $R_w = (\sum w(|F_o| - |F_c|)^2 / \sum w|F_o|^2)^{1/2}$, and $\text{GOF} = [\sum w(|F_o| - |F_c|)^2 / (m - n)]^{1/2}$. Values given for *R*, *R*_w, and GOF are based on those reflections with $I \geq 2.5\sigma(I)$.

^bStructure for C4A-1-Bromobutane not completely determined.

short contacts occur between the cyclohexane carbon atoms CH1, CH3 and the *t*-butyl carbons in the next layer (CH1, CH3-methyl distances are 3.58, 3.77 Å). Of significance

to the question of attractive $\pi_{\text{host}}\text{-CH}_{\text{guest}}$ interactions, the cyclohexane CH5 hydrogens are not oriented towards the phenyl ring but rather point to the space in between two adjacent phenyl rings.

TABLE 3. Selected Bond Distances C4A-CY.

Bond	Distance (Å)	Bond	Distance (Å)
O1-C1	1.3840(18)	C7-CT1	1.518(3)
C1-C2	1.3956(21)	C7-CT2	1.538(4)
C1-C6	1.3956(20)	C7-CT3	1.527(3)
C2-C3	1.3889(22)	C7-C7A	0.239(8)
C2-C8	1.5272(20)	C7-C4A	1.532(9)
C3-C4	1.3881(23)	C7-CT4	1.748(13)
C3-C4A	1.411(10)	C7-CT5	1.544(12)
C5-C6	1.3863(22)	C7-CT6	1.366(14)
C5-C4	1.3965(24)	C4-C7A	1.561(7)
C5-C4A	1.405(10)	C4-C4A	0.159(10)
C6-C8A	1.5202(21)	CT1-C7A	1.735(8)
C8-C6B	1.5202(20)	CT1-CT6	1.289(14)
C7-C4	1.545(3)	CT2-C7A	1.512(8)

4.3 *p*-tert-Butylcalix[4]arene-*n*-Pentane (C4A-PT)

Representation of the C4A-PT structure is shown in Figure 8 and selected distances and bond angles summarized in Table 4. Unlike the majority of C4A-guest structures (Chapter One), the *t*-butyl groups in C4A-PT show no positional disorder. *n*-Pentane was modeled as a rigid group (C-C bond length = 1.535 Å) in the all-*trans* conformation. The long axis (CP1-CP5) of the *n*-pentane molecule is within 2° of the calix 4-fold axis. The methyl group deepest inside the cavity is 4.05 Å above the plane defined by four phenolic oxygens and 3.52 Å from the plane of the nearest phenyl ring, approximately equidistant (3.70 Å) from the bottom three phenyl carbon atoms of the phenyl ring. The α -hydrogen of CP5 is the deepest guest atom inserted in the cavity; it lies 3.58 Å from O1 and cannot be considered important for H-bonding to the phenolic oxygen. The closest approach to the calix by a guest hydrogen occurs with the CP5 β -hydrogens which approach the calix

C3 carbon with a distance of 2.86 Å. Significantly short contacts occur between the protruding two pentane carbon atoms and the *t*-butyl methyls of the next layer ($d_{\text{CP2-C}} = 3.37$ Å; $d_{\text{CP1-C}} = 3.67, 3.75, 3.98$ Å).

TABLE 4. Selected Bond Lengths and Angles for C4A-PT

Bond	Distance (Å)	Bond	Distance (Å)
O1-C1	1.3848(19)	O1-O1'	3.7914
C1-C2	1.3985(21)	C1-C1'	5.2589
C1-C6	1.3954(21)	C8-C8'	7.2069
C2-C3	1.3875(23)	C4-C4'	8.3549
C2-C8	1.5225(21)	C7-C7'	10.1037
C3-C4	1.4000(22)	H01-O1'	1.7377
C4-C5	1.3953(22)	HCP5A-O1	3.5819
C4-C7	1.5329(24)	HCP5B-C3	2.8555
C5-C6	1.3914(22)	CP5-C2	3.6744
C6-C8	1.5182(21)	CP5-C3	3.7592
C7-CT1	1.530(3)	CP5-C4	3.9193
C7-CT2	1.535(3)	CP5-C6	3.8504
C7-CT3	1.538(3)		
Bond	Angle (degree)	Bond	Angle (degree)
C6-C8-C2'	112.07	C7-C4-C1	178.00
HO1-O1-O1'	153.49	HO1-O1-C7-CT1	14.85
C4-O1-O1'	122.99		

Distances between opposite and equivalent atoms define the cavity. The distance between opposite phenolic oxygen atoms is 3.79 Å, and as the cone increases, so does the distance between opposite atoms: $d_{\text{C1-C1}'} = 5.26$ Å, $d_{\text{C8-C8}'} = 7.21$ Å, $d_{\text{C4-C4}'} = 8.35$ Å, $d_{\text{C7-C7}'} = 10.10$ Å. The cone expands by 123° along an angle defined by two basal plane oxygens (O1, O1') and the phenol *para*-carbon. The methylene (C8) linking adjacent phenols through C6 and C2 makes an angle of 112.1°. The cavity collapses slightly at the *t*-butyl group, which forms an angle of 178° with the C1-C4 backbone. The four phenolic oxygens are hydrogen-bonded with a directionality which imparts chirality to the calix. The OH...O distances at 1.74 Å, and the hydrogens are out of the oxygen basal plane and below the cavity by 26.5°. One final geometric feature is the relationship between the

relative orientation of the *t*-butyl C-Me bond and the OH bond. The two bonds are oriented with a *cis* geometry and make a torsional angle of 14.8°; for C4A compounds that display disordering in the *t*-butylphenol moieties, this is the major position (Chapter 3).

4.4 C4A-1-Chlorobutane (C4A-ClB) and C4A-1-Bromobutane (C4A-BrB)

The structure of C4A-ClB (Figure 9) shows the guest situated in a C_4 symmetric calix cavity with its methyl group inside and the chloro group outside of the cavity. As in the C4A-PT structure, the host *t*-butyl groups do not display any positional disorder. The guest displays 4-fold disordering about the host symmetry axis; only one of four positions is shown. The structural refinement of C4A-BrB was not completed, but shows that the bromobutane guest occupies an orientation in the cavity identical to chlorobutane.

The 1-halobutane guests are oriented in the cavity differently than the pentane guest. Whereas the pentane adopts an all-*trans* geometry, the 1-halobutanes exhibit a *gauche* conformation at the C2-C3 bond, with the halogen, C1, and C4 atoms sitting on the compound symmetry axis. The line defined by the guest atoms chlorine and C4 is tilted off the calix symmetry axis by 4°. Carbon C4 is situated deepest in the cavity, and sits 5.13 Å above the basal plane defined by the four phenolic oxygen atoms.

What, then, are the stabilizing interactions between guest and host? Clearly, for the four C4A-aliphatic compounds studied by XRD and the additional five C4A-aliphatic compounds studied by solid-state ^{13}C NMR spectroscopy, no $\pi_{\text{guest-methyl}_{\text{calix}}}$ interactions are possible, yet this absence does not hinder their formation and stability. The host *t*-butyl groups may be important in extending the cavity depth than participating in attractive $\text{CH}_{\text{host-guest}}$ interactions.

Certainly there is a preference of the calix cavity for terminal methyl groups over terminal halogen groups, as demonstrated elegantly by the C4A-guest structures. Each halogen group is similar to the methyl group in electronegativity (C: 2.55; Br: 2.96; Cl: 3.16) and van der Waals radius (CH₃: 2.0; Br: 2.0; Cl: 1.8 Å).³⁰ Based on non-bonded van der Waals interactions between host and guest, it is anticipated that 1-halobutane would prefer to occupy the cavity with the halogen deepest in the pocket; the fact that the reverse occurs lends experimental support to the attractive π_{calix} -methyl_{guest} interaction.^{3,12} These observations concur with those of Chapter 3 in which the methyl-substituted benzene guest is inserted into the cavity while the chloro-substituted benzene guest occupies a position with the substituent pointing out of the cavity. However, in all XRD structures studied here, there are no significantly close host-guest contacts deep in the cavity; the minimum distance between the most deeply-inserted carbon and the calix aromatic ring is 3.52 Å. What may be more significant is the distance from the penultimate terminal guest carbon to the host aromatic ring $d_{\text{min}} = 2.86$ Å. In addition the adjacent layer of C4A t-butyl groups that “cap” the cavity come into close contact with the protruding guest carbons: $d_{\text{min}} = 3.37$ Å. A final note: one must be careful to consider the *direction* of the C-H bonds in the interacting guest-host carbon pair; as the guest hydrogen atom positions were not refined, the directional requirement of the interaction may be compromised due to uncertainty in the hydrogen atom position.

5. ²H NMR Spectroscopy

To further understand the dynamics of the aliphatic guests in the calix cavity, ²H NMR studies of C4A-PT-*d*₁₂ and C4A-CY-*d*₁₂ were undertaken. The ²H NMR data are used interactively with diffraction data to refine structural models of the two C4A-aliphatic compounds.

5.1 *p*-tert-Butylcalix[4]arene-Cyclohexane- d_{12} (C4A-CY- d_{12})

The VT ^2H NMR spectra of C4A-CY- d_{12} (Figure 10) are consistent with three types of guest motion: The first is rotation of the cyclohexane (in the chair conformation) about its C_3 molecular axis, which narrows the pattern from that of the static guest by one-third. Secondly, the cyclohexane rotates about the calix C_4 axis. Finally, at higher temperatures, the axial and equatorial positions become equivalent with cyclohexane inversion. These motions are illustrated in Figure 11 and the ^2H NMR spectral parameters are summarized in Table 5. Inversion and reorientation about the cyclohexane C_3 molecular axis as well as other motions that produce further averaging have been observed in channel inclusion compounds of cyclophosphazene³¹ and thiourea,³² as well as in the (*N*-methyl-1,3-diaminopropane)Cd(II) tetracyanonickelate(II)-CY- d_{12} 2:1 clathrate.³³

TABLE 5. ^2H NMR spectral parameters for C4A-CY- d_{12} .^a

deuteron	<i>T</i> (K)	$ \Delta\nu_{xx} $ (kHz)	$ \Delta\nu_{yy} $ (kHz)	$ \Delta\nu_{zz} $ (kHz)	χ (kHz)	η
<i>axial</i>	77	127.5	127.5	255	170.0	0.00
	146	127.5	127.5	255	170.0	0.00
	243	34.5	34.5	69	46.0	0.00
<i>equatorial</i>	77 ^b	-	-	-	-	-
	146	42	42	84	56.0	0.00
	243	11.5	11.5	23	15.3	0.00
<i>c</i>	345	12	12	25.5	17.0	0.00

^a Estimated uncertainties of ± 1.5 kHz in the measurements of the $\Delta\nu_{ii}$ and ± 1 kHz in χ .

^b Lineshape reflects intermediate motional regime.

^c Inversion motion causes the axial and equatorial deuterons to be equivalent.

C_3 Rotation. C_3 Molecular rotation reaches the fast motion limit (FML; $\kappa > 10^8$ Hz) at 146K. The 77K spectrum suggests that this motion is already present at the low temperature detection limit. Since only the equatorial deuterons reorient, the FML spectrum shows two axial lineshapes in a 1:1 ratio: the outer lineshape ($\chi_{ax} = 170$ kHz)

arises from the axial deuterons and is the lineshape of the static spectrum. Since the C-D_{ax} bonds are aligned with the C_3 axis, the electric field gradient (EFG) tensor components are invariant with C_3 motion. The inner lineshape ($\chi_{eq} = 56$ kHz) is reduced by a factor of 3 and results from the equatorial deuterons.

4-Fold Rotation. The second motion, rotation of cyclohexane about the calix 4-fold axis, occurs over the range 146-243 K. The lineshapes in this region are broadened as in the C4A-TOL- d_5 case, and this suggests a distribution of motions throughout the crystalline array. The two lineshapes retain their C_3 FML shape, but are narrower at 243K than at 146K: $\chi_{ax} = 46$ kHz; $\chi_{eq} = 15$ kHz. The extent of narrowing reflects the angular tilt ϕ of the cyclohexane C_3 axis off the calix C_4 axis, and can be calculated as follows:

$$\pm v_{zz}' = v_{zz}(\frac{1}{2})(3\cos^2\phi - 1) \quad \text{where } v_{zz}' = 243\text{K}; v_{zz} = 146\text{K} \quad (1)$$

$$\pm 23.0 \text{ kHz} = 84.0 \text{ kHz}(\frac{1}{2})(3\cos^2\phi - 1) \quad (2)$$

$$\phi^+ = 44.1^\circ; \phi^- = 67.1^\circ \pm 3.7^\circ \quad (3)$$

There are two solutions for the value of ϕ due to uncertainty in the sign of v_{zz}' ; it is ϕ^- that makes more physical sense. ϕ describes the angle between the calix C_4 axis and the cyclohexane C_3 axis (Figure 11). The angle θ between the calix C_4 axis and the cyclohexane C1-C4 molecular axis is then $\theta = 11^\circ \pm 4^\circ$, which agrees well with the angle determined by XRD of $\theta = 13^\circ \pm 2^\circ$ and furthermore illustrates the complementarity of the two techniques.

Inversion. The spectra in the region 243-345K narrow as temperature increases, becoming an axial pattern at 345K ($\chi_D = 17.0$ kHz); the central isotropic intensity arises from liquid cyclohexane outside the cavity. The single sharp line at 292K arises from the orientations of the crystal in which the two parallel tensors are oriented at 54.1° (the magic

angle) with respect to the external magnetic field. This set of spectra is consistent with cyclohexane inversion motion in which the equatorial and axial deuterons are equivalent.

The ^2H NMR lineshape simulation for cyclohexane inversion requires an exchange rate matrix which accounts for the C_3 , C_4 and inversion motions—this demands a rather daunting 24×24 rate matrix! Of course, the C_3 and C_4 motions are in the fast motion limit, but these motions do not have coincidental axes, and the simple 2-site exchange proposed in the (*N*-methyl-1,3-diaminopropane) Cd^{II} tetracyanonickelate $^{\text{II}}$ -CY- d_{12} 2:1 clathrate is not feasible. The cyclohexane lineshapes were not simulated due to the computational complexity and the existence of cyclohexane inversion data in the literature. Cyclohexane inversion is well-known, and occurs with an activation energy of $44.7 \pm 1 \text{ kJ mol}^{-1}$ in the (*N*-methyl-1,3-diaminopropane) Cd^{II} tetracyanonickelate $^{\text{II}}$ -CY- d_{12} 2:1 clathrate,³³ 48.1 and 43.1 kJ mol^{-1} in solution,^{34,35} and 50.6 kJ mol^{-1} in the gas phase.³⁶

5.2 *p*-tert-Butylcalix[4]arene-*n*-Pentane- d_{12} (C4A-PT- d_{12})

TABLE 6. ^2H NMR spectral parameters for C4A-PT- d_{12} .^a

deuteron	<i>T</i> (K)	$ \Delta\nu_{xx} $ (kHz)	$ \Delta\nu_{yy} $ (kHz)	$ \Delta\nu_{zz} $ (kHz)	χ (kHz)	η
-CD ₂ -	static ^b	119	119	236	157.3	0.00
	77	59	59	118	78.7	0.00
	151	56	56	112	74.7	0.00
	240	53	53	106	70.7	0.00
-CD ₃	77 ^c	-	-	-	-	-
	151	13	13	26	17.3	0.00
	240	17.7	17.7	35.4	23.6	0.00

^a Estimated uncertainties of $\pm 1.5 \text{ kHz}$ in the measurements of the $\Delta\nu_{ii}$ and $\pm 1 \text{ kHz}$ in χ .

^b reference 37

^c Lineshape reflects intermediate motional regime.

The 90K ^{13}C CP-MAS NMR spectrum of C4A-PT suggests that the two *n*-pentane methyls are equivalent, suggesting that the guest undergoes end-over-end motion at 90K. To further examine the dynamics of *n*-pentane in C4A, VT ^2H NMR spectra were collected from 77 to 290K (Figure 12; the ^2H NMR spectral parameters are summarized in Table 6).

5.2.1 The Static and FML Lineshapes

The broad component of the 77K lineshape ($\chi_{77}(\text{CD}_2) = 78.7 \text{ kHz}$) is consistent with *n*-pentane rotating about its molecular axis; methylene in-plane motion causes the lineshape to narrow by a factor of two from the static spectrum.³⁸ End-over-end motion is invisible to ^2H NMR as the EFG tensor components are invariant with this motion. The lack of sharpness in the lineshape suggests a distribution of methylene motions like that seen for C4A-TOL and C4A-CY-*d*₁₂, and may arise from defects in the crystal lattice. The central intensity is attributable to the methyl deuterons which are in an intermediate C_3 rotation motional regime; this lineshape sharpens as the motion reaches its FML at 117K.

The lineshape continues to evolve until 240K, at which point it becomes invariant with temperature (290K). The high temperature lineshape consists of two axially symmetric patterns with equal intensities. The inner pattern is due to the methyl deuterons ($\chi_{240}(\text{CD}_3) = 23.6 \text{ kHz}$) and the outer pattern is from the methylene deuterons ($\chi_{240}(\text{CD}_2) = 70.7 \text{ kHz}$). Unlike the low temperature lineshapes, these are sharp and show no distribution of motions. It is known from the XRD structure that *n*-pentane is close to the calix symmetry axis and is in the all trans conformation. The methyl group motions include: (a) C_3 rotation, which reduces the linewidth by 3, (b) rotation about the molecular axis, which reduces the linewidth by 2, and (c) C_4 rotation about the calix symmetry axis,

which reduces the linewidth by a factor dependent on the coincidence of the calix symmetry and guest rotational axes.

Motions (*a*) and (*b*) are expected to reduce $\chi_{\text{static}}(\text{CD}_3)$ by a factor of six from 157.3 kHz to $\chi_{240}(\text{CD}_3) = 26.2$ kHz. The additional narrowing to $\chi = 23.6$ kHz can be attributed to a third, librational motion or the presence of fraction of gauche *n*-pentane conformers.³³⁻³⁵ Both possibilities will be considered below:

The C4A-PT librational narrowing is akin to the C4A-CY-*d*₁₂ case, and equation (1) is restated below for the methyl deuterons:

$$\chi_{240}' = \chi_{240}(\frac{1}{2})(3\cos^2\theta - 1) \quad \text{where } \chi_{240}' = \text{observed; } \chi_{240} = \text{expected} \quad (4)$$

$$23.60 = 26.22(\frac{1}{2})(3\cos^2\theta - 1)$$

Solving for θ leads to a tilt angle between the calix symmetry axis and the *n*-pentane rotational axis of $\theta = 15^\circ \pm 2^\circ$ which is larger than that calculated from XRD ($\theta = 2^\circ$).

n-Alkanes included in the channels of urea rotate rapidly and adopt an extended, all-trans geometry.^{38,39} However, 25-35% of the alkanes are thought to be in gauche conformations near the ends of the hydrocarbon chains. In addition to measurements of the ¹³C CP-MAS NMR spectra⁴⁰ and C-H dipolar splittings,⁴¹ ²H NMR spectra of deuterated alkanes support the existence of gauche conformations at the C₂-C₃ alkane bond, and extra reduction in ²H linewidth is used to estimate the amount of gauche conformers.^{38,39}

Vibrational deformations may play a role in lineshape reduction,³⁹⁻⁴⁶ but would lead to reduction in all the splittings—this contrasts what is observed for C4A-PT-*d*₁₂. Three lineshape splittings (Δ) are observed for *n*-alkanes: Δ_1 (-CD₃), Δ_2 (α -CD₂-), and Δ_3 (β -CD₂-); Δ_3 increases with increasing chain length *n*, Δ_2 is independent of *n*, and Δ_1 decreases with *n*.⁴⁶ For C4A-PT-*d*₁₂, Δ_2 and Δ_3 overlap and are indistinguishable in all

spectra except $T = 217\text{K}$ where the inner intensity of the outer pattern corresponds to Δ_2 . The following assumptions allow for the correlation of the linewidth Δ with the fraction of trans conformations, p_t , for *n*-pentane in C4A: (a) ideal tetrahedral geometry, (b) all static χ 's are equal, (c) end-over-end rotation and the rotations about the cavity axis, $\text{C}_1\text{-C}_2$ bond, and trans-gauche isomerizations are all fast compared to Δ , and (d) gauche conformations happen only at the $\text{C}_2\text{-C}_3$ bond. Thus,

$$\Delta_1 = -(1/6)(3/4)\chi_{\text{STATIC}}(2p_t - 1) \quad (5)$$

$$\Delta_2 = -(1/4)(3/4)\chi_{\text{STATIC}}(2p_t) \quad (6)$$

where χ_{STATIC} = the static quadrupolar coupling constant (157.3 kHz) and p_t is the $\text{C}_2\text{-C}_3$ trans population. From (5) where $\Delta_1 = 17.7\text{ kHz}$ we derive a value for $p_t = 0.95 \pm 0.08$; from (6) where $\Delta_2 = 52.0\text{ kHz}$, we obtain $p_t = 0.88 \pm 0.03$. Thus according to this model, 5-12% ($\pm 8\%$) gauche conformers accounts for the observed reductions in ^2H linewidths.

It is likely that both the presence of a minor fraction of gauche conformations at the $\text{C}_2\text{-C}_3$ bond and an *n*-pentane molecular tilt off the calix C_4 axis accounts for the observed lineshapes. Certainly XRD suggests the presence of the latter feature, but the XRD tilt angle (2°) is smaller than the tilt angle (15°) calculated from the ^2H NMR spectra.

5.2.2 Intermediate Lineshapes

A plot of the lineshape components as a function of temperature is given in Figure 13. The values between 77 and 240K can be divided into the 77-151K region and the 151-240K region. The spectra between 77 and 151K change tremendously, and are characterized by broadened lineshapes, specifically the outer $-\text{CD}_2-$ pattern, arising from a distribution of motional regimes in the crystal. The CD_2 linewidth reduces from $\chi_{77} = 78.7\text{ kHz}$ to $\chi_{151} = 74.7\text{ kHz}$; this may be due to off-axis libration or the presence of gauche

conformations. Pentane rotates about its molecular axis, but in this temperature range does not undergo 4-fold jumps. The CD₃ lineshape becomes sharp and narrow ($\chi_{151} = 17.3$ kHz) at 151K as methyl rotation reaches the FML. Surprisingly, $\chi_{151}(\text{CD}_3) < \chi_{240}(\text{CD}_3)$: the methyl groups appear to be further off-axis at lower temperatures than at 240K! Alternately, the % gauche conformations may be higher at 151K than at higher temperatures, but this model may not apply at lower temperatures due to the breakdown in assumption (c).

What pentane geometry could cause both methyls to be significantly off-axis at low temperature? The all-trans pentane rotation axis cannot be significantly tilted off the host C₄ axis due to the constraints of the cavity geometry. The C4A-1-X-butane (X = Cl, Br) guest positions from single-crystal XRD provide a clue: If pentane adopts a gauche conformation and begins to “curl up” in the cavity, the inserted methyl will be axial and the opposite methyl groups form the tetrahedral angle with the symmetry (and rotation) axis. The corresponding reductions in χ from χ_{STATIC} are then 1/3 and 1/9. As the two methyls are equivalent by end-over-end motion, the effective reduction in $\chi_{151}(\text{CD}_3)$ is $(1/3 + 1/9)/2 = 1/4.5$. This model thus predicts the 151K quadrupolar coupling constant to be $\chi = (1/4.5)(1/2)(157.33) = 17.5$ kHz which compares well with $\chi_{\text{observed}} = 17.3$ kHz.

The gauche model does not fit the XRD picture of an all-trans pentane at 150K. Some reconciliation may be possible when considering that the XRD model is generated from an average of all possible guest positions. Pentane is still mobile at 150K and since it is disordered over four positions, the precision of the fit is not high enough to exclude the presence of non-trans geometries. However, the end-over-end guest motion requires an intermediate structure which supports the gauche model. To cause the two methyl to be equivalent, pentane must reorient in the cavity. As the calix geometry forbids simple 180°

rotation of the trans *n*-pentane, the guest must first curl up, rotate, and then re-extend (Figure 14). The C4A-CY structure illustrates that the cavity is big enough to host a curled-up *n*-pentane. Furthermore, this motion forces the methylene deuterons to undergo non-planar motion as pentane rotates; this may account for the observed narrowing in χ_{151} (CD_2).

The 151-240K spectra show that the methyl patterns go through broadened (motionally-distributed) intermediate lineshapes. It is difficult to assign a motional model to these spectra. By analogy to C4A-CY, 90° molecular jumps between the host-imposed symmetry sites likely occur in this regime.

The VT ^2H NMR spectra of C4A-PT- d_{12} are complex and not easily interpreted. The model developed here is by no means an exclusive one, but is reasonable and consistent with the available data. A more complete understanding of pentane dynamics may be possible with the VT ^2H NMR spectra of C4A-PT-3,3- d_2 and C4A-1-bromobutane- d_9 . The former indicates the motion of the C-3 deuterons; the spectra may be difficult to obtain due to the small amount of label, and the interpretation may be hindered by motional distribution which broadens the spectra. The latter guest should give lineshapes consistent with an aliphatic guest in the gauche conformation.

6. Summary

A wide range of C4A compounds with *n*-alkanes have been prepared, and demonstrates that while the guests do not possess an aromatic π system to facilitate stabilizing $\text{CH}_{\text{host}}-\pi_{\text{guest}}$ interactions, these guests still form isoluble and stable compounds with the C4A host. What has emerged from this work is evidence for the role of $\pi_{\text{host}}-\text{CH}_{\text{guest}}$ interactions: the structure of C4A-chlorobutane shows the cavity prefers the

methyl to the chloro group. Evidence for stabilizing $\pi_{\text{host}}\text{-CH}_{\text{guest}}$ interactions is also found with the C4A structures with toluene and chlorobenzene (Chapter 3).

The methyl group affinity results from molecular recognition by the cavity. It would be of interest to probe this further by examining 5-membered-chain guests with two different ends such as 1-butanol, 1-butanethiol, and *n*-butylamine to define the strength of the attractive $\pi_{\text{host}}\text{-CH}_{\text{guest}}$ interaction. Of further interest would be the ability of the cavity to discriminate between proton and deuteron in pentane-1- d_3 .

The dynamics of the cyclohexane and pentane guests in C4A have been studied with ^2H NMR spectroscopy. While the cyclohexane behavior has been established, the mechanism of the pentane motion remains to be unambiguously identified. The pentane-3- d_2 guest may be used to further elucidate the guest motion.

Finally, ^{13}C CP-MAS NMR spectroscopy with C4A-aliphatic compounds has been correlated with the structural motifs, *i.e.*, whether the compound is in a 1:1 or 2:1 host:guest ratio. This relationship establishes the complexation-induced shift of the ^{13}C NMR resonance as an important indicator of C4A-guest structure.

7. References

1. Andreetti, G. D.; Ugozzoli, F. in *Calixarenes*, Vicens, J. and Bohmer, V. (Eds.), Kluwer, Dordrecht, **1990**, p. 87.
2. Gutsche, C. D. *Calixarenes*, RSC, Cambridge and London, **1989**.
3. Bohmer, V. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 713-745.
4. Andreetti, G. D.; Ori, O.; Ugozzoli, F.; Alfieri, C.; Pochini, A.; Ungaro, R. *J. Incl. Phenom.* **1988**, *6*, 523-536.
5. Andreetti, G. D.; Ungaro, R.; Pochini, A. *J. Chem. Soc., Chem. Commun.* **1979**, 1005-1007.
6. Ungaro, R.; Pochini, A.; Andreetti, G. D.; Domiano, P. *J. Chem. Soc., Perkin Trans. 2*, **1985**, 197-202.
7. Ungaro, R.; Pochini, A.; Andreetti, G. D.; Sangermano, V. *J. Chem. Soc., Perkin Trans. 2*, **1984**, 1979-1985.

8. Perrin, M.; Oehler, D. in *Calixarenes*, Vicens, J. and Bohmer, V. (Eds.), Kluwer, Dordrecht, **1990**, p. 65.
9. Ungaro, R.; Arduini, A.; Casnati, A.; Ori, O.; Pochini, A.; Ugozzoli, F. in *Computational Approaches in Supramolecular Chemistry, NATO ASI Series C426* Wipff, G. (Ed.), Kluwer, Dordrecht, **1994**, p. 277.
10. Constable, E. C. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2269-2271.
11. Gutsche, C. D.; Dhawan, B.; No, K. H.; Muthukrishnan, R. *J. Am. Chem. Soc.* **1981**, *103*, 3782-3792.
12. McKervery, M. A.; Seward, E. M.; Ferguson, G.; Ruhl, B. L. *J. Org. Chem.* **1986**, *51*, 3581-3584.
13. Arduini, A.; Ghidini, E.; Pochini, A.; Ungaro, R.; Andreetti, G. D.; Calestani, G.; Ugozzoli, F. *J. Incl. Phenom.* **1988**, *6*, 119-134.
14. Harrowfield, J. M.; Ogden, M. I.; Richmond, W. R.; White, A. H. *J. Chem. Soc., Chem. Commun.* **1991**, 1159-1161.
15. Harrowfield, J. M.; Ogden, M. I.; Richmond, W. R.; Skelton, B. W.; White, A. H. *J. Chem. Soc. Perkin Trans 2* **1993**, 2183-2190.
16. Ueda, Y.; Fujiwara, T.; Tomita, K.-I.; Asfari, A.; Vicens, J. *J. Incl. Phenom.* **1993**, *15*, 341-349.
17. Steed, J. W.; Juneja, R. K.; Burkhalter, R. S.; Atwood, J. L. *J. Chem. Soc., Chem. Commun.* **1994**, 2205-2206.
18. Bavoux, C.; Perrin, M. *J. Incl. Phenom. Mol. Recog. Chem.* **1992**, *14*, 247-256.
19. Asfari, Z.; Harrowfield, J. M.; Ogden, M. I.; Vicens, J.; White, A. H. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 854-856.
20. Juneja, R. K.; Robinson, K.D.; Orr, G. W.; Dubois, R. H.; Belmore, K. A.; Atwood, J. L.; Ripmeester, J. A.; Ratcliffe, C. I. *J. Incl. Phenom.* **1992**, *14*, 93-96.
21. Thuery, P.; Keller, N.; Lance, M.; Vigner, J.-D.; Nierlich, M. *J. Incl. Phenom.* **1995**, *20*, 373-379.
22. Coleman, A. W.; Bott, S. G.; Morley, S. D.; Means, C. M.; Robinson, K. D.; Zhang, H.; Atwood, J. L. *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1361-1362.
23. Alemany, L.B.; Grant, D.M.; Alger, T.D.; Pugmire, R.J. *J. Am. Chem. Soc.* **1983**, *105*, 6697-6704.
24. Breitmaier, E.; Voelter, W. *¹³C NMR Spectroscopy*; 2nd ed. Verlag Chemie: New York 1978.
25. Aliev, A. E.; Harris, K. D. M.; Tegze, M.; Pekker, S. *J. Mat. Chem.* **1993**, *3*, 1091-1094.

26. The probe temperature was calibrated with the ^{13}C chemical shift of samarium acetate tetrahydrate: Campbell, G. C.; Crosby, R. C.; Haw, J. F. *J. Mag. Res.* **1986**, 69, 191-195.
27. HYPERNMR: Hypercube, Inc., 419 Phillip St., Waterloo, Ont, Canada N2L 3X2.
28. Steiner, T.; Starikov, E. B.; Amado, A. N.; Teixeira-Dias, J. J. C. *J. Chem. Soc. Perkin Trans. 2*, **1995**, 1321-1326.
29. Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry, Part A: Structure and Mechanisms*, 3rd ed. Plenum: New York 1991, p 401-403.
30. Atkins, P. W. *Physical Chemistry*, 3rd. Ed. W. H Freeman: New York, 1986, T4.10(a), T23.2.
31. Meirovitch, E.; Belsky, I. *J. Phys. Chem.* **1984**, 88, 4308-4315.
32. Meirovitch, E.; Krant, T.; Vega, S. *J. Phys. Chem.* **1983**, 87, 1390-1396.
33. Nishikori, S.; Ratcliffe, C. I.; Ripmeester, J. A. *J. Phys. Chem.* **1990**, 94, 8098-8102.
34. Hofner, D.; Lesko, S. A.; Binsch, G. *Org. Mag. Reson.* **1978**, 11, 179-196.
35. Poupko, R.; Luz, Z. *J. Am. Phys.* **1981**, 75, 1675.
36. Ross, B. D.; True, N. S. *J. Am. Chem. Soc.* **1983**, 105, 1382-1383.
37. Cannarozzi, G. M.; Meresi, G. H.; Vold, R. L.; Vold, R. R. *J. Phys. Chem.* **1991**, 95, 1525-1527.
38. static ^3H lineshape for pentane- d_{12}
39. El Baghdadi, A.; Dufourc, E.J.; Guillaume, F. *J. Phys. Chem.* **1996**, 100, 1746-1752.
40. Imashiro, F.; Maeda, T.; Nakai, T.; Saika, A.; Terao, R. *J. Phys. Chem.* **1986**, 90, 5498-5500.
41. Imashiro, F.; Kuwahara, D.; Nikai, T.; Terao, T. *J. Chem. Phys.* **1989**, 90, 3356-3362.
42. Casal, H. L.; Cameron, D. G.; Kelushky, E. *J. Chem. Phys.* **1984**, 80, 1407-1410.
43. Gilson, D. F. R.; McDowell, C. A. *Mol. Phys.* **1961**, 4, 125.
44. Greenfield, M. S.; Vold, R. R.; Vold, R. L. *Mol. Phys.* **1988**, 66, 269.
45. Henry, E. R.; Szabo, A. *J. Chem. Phys.* **1985**, 82, 4753-4761
46. Vold, R. L.; Vold, R. R.; Heaton, N. J. *Adv. Magn. Res.* **1989**, 13, 17-42.

8. Figures

FIGURE 1. 75.4 MHz ^{13}C CP-MAS NMR spectrum of *p*-*tert*-butylcalix[4]arene-*n*-pentane at 290K. Guest values are indicated in brackets, solution values in { }; ss = spinning sideband. The spectrum was collected on a Bruker AMX-300 spectrometer using a Doty DAS 7 mm spinning probe: 700 transients; recycle time: 5 s; $\pi/2$ pulse = 5.5 μs ; contact time = 4 ms; TD = 6K; 16K points; ν = 4.1 kHz.

FIGURE 2. 75.4 MHz ^{13}C CP-MAS NMR spectra of *p*-*tert*-butylcalix[4]arene-*n*-butane at 290K, prepared by physical mixing (*top*) and vapour diffusion (*bottom*). The guest assignments are indicated. The spectra were collected on a Bruker AMX-300 spectrometer using a Doty DAS 7 mm spinning probe: 700 transients; recycle time: 5 s; $\pi/2$ pulse = 5.5 μs ; contact time = 4 ms; TD = 6K; 16K points; ν = 4.1 kHz.

FIGURE 3. 75.4 MHz ^{13}C CP-MAS NMR spectrum of empty (*top*) and *p*-*tert*-butylcalix[4]arene-propane (*bottom*) at 290K. The guest assignments are indicated; x = empty *p*-*tert*-butylcalix[4]arene. The spectra were collected on a Bruker AMX-300 spectrometer using a Doty DAS 7 mm spinning probe: 700 transients; recycle time: 5 s; $\pi/2$ pulse = 5.5 μs ; contact time = 4 ms; TD = 6K; 16K points; ν = 4.1 kHz.

FIGURE 4. 50.3 MHz ^{13}C CP-MAS NMR spectra of *p*-*tert*-butylcalix[4]arene-pentane; 290K (bottom), 90K (top). The guest resonances are indicated by arrows; x = spinning sidebands. The spectra were collected on a Bruker MSL-200 spectrometer using a 7 mm spinning Chemagnetics pencil probe and the FLIPNQS pulse sequence: 120 transients; recycle time: 3.6 s; $\pi/2$ pulse = 3.5 μs ; contact time = 3.5 ms; TD = 4K; 16K points; ν = 3.1 kHz.

FIGURE 5. Possible structures for C4A-aliphatic compounds; entry numbers correspond to those in Table 1.

FIGURE 6. Observed ^{13}C CP-MAS NMR (*bottom*) and calculated ^{13}C NMR spectra (*middle*: host, *top*: guest) for *p*-tert-butylcalix[4]arene-pentane.

FIGURE 7. ORTEP of *p*-tert-butylcalix[4]arene-cyclohexane; 30% thermal ellipsoids. Hydrogen atoms are omitted for clarity.

FIGURE 8. ORTEP of *p*-tert-butylcalix[4]arene-pentane; 30% thermal ellipsoids. Hydrogen atoms are omitted for clarity.

FIGURE 9. ORTEP of *p*-*tert*-butylcalix[4]arene-1-chlorobutane; 30% thermal ellipsoids. Hydrogen atoms are omitted for clarity.

FIGURE 10. Variable temperature 46.1 MHz ^2H NMR spectra of *p*-*tert*-butylcalix[4]arene-cyclohexane- d_{12} . The spectra were collected on a Bruker AMX-300 spectrometer with a Bruker static probe with a 5 mm coil and a quadrupolar echo pulse sequence: 40-100 transients; recycle time: 5 s; $\pi/2$ pulse: 2.6 μs ; sweep width: 500 kHz; echo delay: 35 μs ; 0.5 kHz line broadening; TD = 2K; 1K points. The spike in the centre of the high temperature spectra is due to trace amounts of uncomplexed guest.

FIGURE 11. Cyclohexane motion: rotation about C_3 molecular axis, molecular rotation about calix C_4 axis, off-axis tilt of 11° .

FIGURE 12. Variable temperature 30.7 MHz ^2H NMR spectra of *p*-*tert*-butylcalix[4]arene-pentane- d_{12} . The spectra were collected on a Bruker MSL-200 spectrometer with a Bruker static probe with a 5 mm coil and a quadrupolar echo pulse sequence: 80-145 transients; recycle time: 8-10 s; $\pi/2$ pulse: 2.9 μs ; echo delay: 35 μs ; 1 kHz line broadening; TD = 1K; 1K points. The spike in the centre of the high temperature spectra is due to trace amounts of uncomplexed guest.

FIGURE 13. Plot of the *p*-*tert*-butylcalix[4]arene-pentane- d_{12} ^2H lineshape components as a function of temperature.

FIGURE 14. Scheme of end-over-end pentane motion.

9. Appendix: X-Ray Diffraction Structural Details

A.1 Final Positional and Equivalent Isotropic Parameters ($\text{\AA}^3$) for C4A-CY.

Name	<i>x</i>	<i>y</i>	<i>z</i>	B_{iso}^a
O1	0.61919(8)	0.68808(7)	0.05074(8)	3.04(4)
C1	0.56769(0)	0.66023(11)	-0.03962(11)	2.65(5)
C2	0.58296(10)	0.56285(10)	-0.08374(11)	2.69(5)
C3	0.52498(11)	0.53665(11)	-0.17100(13)	3.07(6)
C5	0.44218(11)	0.70049(11)	-0.16947(12)	3.07(6)
C6	0.49855(10)	0.73104(10)	-0.08282(11)	2.69(6)
C8	0.66052(11)	0.48568(11)	-0.03916(12)	2.87(6)
C7	0.38549(18)	0.57504(15)	-0.31029(17)	4.48(9)
C4	0.45425(13)	0.60374(13)	-0.21611(15)	3.25(7)
CT1	0.39602(21)	0.65502(21)	-0.39627(19)	5.58(12)
CT2	0.27219(18)	0.57231(19)	-0.27430(22)	5.47(11)
CT3	0.41495(25)	0.46938(21)	-0.35421(24)	7.30(14)
CH1	0.64741(44)	0.78261(72)	-0.41211(50)	7.0(5)
CH2	0.72784(49)	0.75659(60)	-0.49611(37)	14.8(11)
CH3	0.83621(45)	0.78320(65)	-0.45558(43)	6.9(5)
CH4	0.85871(41)	0.72012(64)	-0.35674(43)	6.0(4)
CH5	0.77829(55)	0.74613(78)	-0.27274(34)	10.9(10)
CH6	0.66992(45)	0.71953(88)	-0.31326(56)	9.3(7)
C7A	0.38436(55)	0.55774(63)	-0.30385(50)	2.9(4)
C4A	0.44460(75)	0.59953(77)	-0.20971(64)	3.2(10)
CT4	0.32108(95)	0.46306(97)	-0.27046(92)	5.9(9)
CT5	0.46041(89)	0.52658(110)	-0.39019(74)	5.7(8)
CT6	0.31134(107)	0.64181(101)	-0.34505(99)	8.1(11)

^a $B_{\text{iso}} = 8/3\pi^2 \sum \sum U_{ij} a_i^* a_j^* (a_i \cdot a_j)$; B_{iso} is the mean of the principal axes of the thermal ellipsoid. ESD's refer to the last digit printed.

A.2 Final Positional and Equivalent Isotropic Parameters ($\text{\AA}^2$) for C4A-PT.

Atom	x	y	z	B_{iso}^a
O1	0.68937(8)	0.61767(8)	0.06250(8)	2.31(4)
C1	0.66242(11)	0.56808(11)	-0.03052(12)	1.83(5)
C2	0.73402(11)	0.50115(11)	-0.07581(12)	1.89(5)
C3	0.70623(11)	0.44817(11)	-0.16679(12)	2.08(6)
C4	0.61066(11)	0.46106(11)	-0.21583(12)	2.05(5)
C5	0.54246(11)	0.52984(11)	-0.16859(12)	2.04(5)
C6	0.56622(11)	0.58358(11)	-0.07650(12)	1.87(5)
C7	0.58427(13)	0.39926(13)	-0.31556(13)	2.60(7)
C8	0.84157(11)	0.48890(11)	-0.03023(13)	2.04(6)
CT1	0.66835(17)	0.41162(18)	-0.39923(16)	4.00(9)
CT2	0.48172(17)	0.43368(18)	-0.36393(17)	4.20(9)
CT3	0.57555(16)	0.28496(14)	-0.28638(16)	3.60(8)
CP5	0.72429(96)	0.73629(146)	-0.25872(34)	6.0 (7)
CP4	0.78503(88)	0.77375(134)	-0.35502(38)	8.3 (10)
CP3	0.72925(56)	0.74193(100)	-0.45655(34)	7.5 (8)
CP2	0.78998(71)	0.77939(92)	-0.55286(39)	5.5 (6)
CP1	0.73420(62)	0.74757(160)	-0.65438(35)	4.1 (6)

$^a B_{\text{iso}} = 8/3\pi^2 \sum \sum U_{ij} a_i^* a_j^* (a_i^* a_j^*)$; B_{iso} is the mean of the principal axes of the thermal ellipsoid. ESD's refer to the last digit printed.

A.3 Final Positional and Equivalent Isotropic Parameters ($\text{\AA}^2$) for C4A-1-Chlorobutane.

Atom	x	y	z	B_{iso}^a
O1	0.61790 (18)	0.68967 (17)	0.06288 (17)	2.90 (9)
C1	0.56827 (24)	0.66299 (23)	-0.03093 (24)	2.45 (11)
C2	0.58339 (23)	0.56648 (24)	-0.0776 (3)	2.53 (11)
C3	0.5291 (3)	0.54277 (24)	-0.1691 (3)	2.74 (13)
C4	0.4600 (3)	0.6114 (3)	-0.2163 (3)	2.98 (13)
C5	0.4484 (3)	0.70639 (25)	-0.1674 (3)	2.86 (13)
C6	0.50164 (24)	0.73450 (24)	-0.0765 (3)	2.58 (12)
C7	0.3976 (3)	0.5845 (3)	-0.3157 (3)	3.92 (17)
C8	0.65792 (25)	0.48943 (24)	-0.0311 (3)	2.67 (13)
CT1	0.4088 (4)	0.6682 (4)	-0.3992 (4)	6.0 (3)
CT2	0.2851 (3)	0.5755 (4)	-0.2849 (4)	4.94 (20)
CT3	0.4341 (5)	0.4826 (4)	-0.3654 (4)	6.44 (25)
Cl	0.7444 (18)	0.7504 (25)	0.3302 (4)	12.17 (14)
CB1	0.7696 (11)	0.7698 (14)	0.4687 (6)	10.6 (14)
CB2	0.7502 (21)	0.6698 (13)	0.5295 (11)	12.4 (23)
CB3	0.7719 (23)	0.6865 (23)	0.6482 (9)	41.0 (97)
CB4	0.7492 (21)	0.798 (3)	0.6775 (9)	21.3 (34)

$^a B_{\text{iso}} = 8/3\pi^2 \sum \sum U_{ij} a_i^* a_j^* (a_i^* a_j^*)$; B_{iso} is the mean of the principal axes of the thermal ellipsoid. ESD's refer to the last digit printed.

CHAPTER 6: *p*-*tert*-Butylcalix[4]arene Gas Clathrates

1. Introduction	231
2. Synthetic Details	233
3. <i>p</i> - <i>tert</i> -Butylcalix[4]arene Double Guest Systems	234
4. A Tunable <i>p</i> - <i>tert</i> -Butylcalix[4]arene-Nitrobenzene-Propane Lattice	245
5. Summary	253
6. References	254
7. Figures	256
8. Appendix: Single-Crystal X-ray Diffraction Structural Data	266

1. Introduction

Numerous inclusion compounds simultaneously incorporate more than one guest molecule in the crystalline lattice. In particular, help guests such as xenon and H₂S in smaller cavities are often necessary for the formation of clathrate hydrates with guests occupying larger cavities.^{1,2} These additional guests may occupy different host cavities, or may share one cavity and exhibit partial occupancy. This chapter describes the preparation and the structural and dynamic properties of *p*-*tert*-butylcalix[4]arene (C4A) compounds containing two guests: one guest is nitrobenzene, and the other may be one of a number of small gas molecules.

The inclusion of small (often gaseous) molecules by a host system is common: in addition to clathrate hydrates,^{1,2} the related clathrasils provide a framework system which includes small guests.¹⁻⁶ The porous zeolite system offers cavities and channels accessible to gasses. Small molecules may function as probes (¹²⁹Xe NMR⁷ or nitrogen and argon porosimetry⁸) as well as reagents for unique reactions that occur due to the geometrical-constraining host environment.^{9,10} Organic hosts that include small gas molecules encompass those that offer pre-existing cavities such as cyclodextrins,¹¹ as well as those that form cavities and channels upon assembling in the solid-state such as Dianin's

compound,¹² β -quinol¹³ and β -phenol.¹ Rebek has reported the formation of a gas-trapping cavity that self-assembles and persists in solution.¹⁴ To date, calixarene compounds that include gas molecules have not been reported.

The C4A-nitrobenzene-xenon (C4A-NB-Xe) compound illustrates that the second guest can partially displace the nitrobenzene guest from the calix cavity without affecting the host structure or compound symmetry. This compound is examined both by single crystal XRD and solid-state ^{129}Xe and ^{13}C NMR spectroscopy, and gives an opportunity to calibrate NMR spectral features to the shape, symmetry and size of the calix pocket. The cavity features probed by ^{129}Xe NMR techniques and those established by the XRD structure show a high correlation. Ripmeester has reported on the relationship between the mean free radius presented by the host cavity and the ^{129}Xe chemical shift;³ C4A-NB-Xe provides the largest Xe-occupied cavity and lowest ^{129}Xe chemical shift value reported to date for a xenon clathrate.

The second guest molecule may act as a probe of guest-host interactions. In particular, the role of attractive $\text{CH}_{\text{guest}}-\pi_{\text{host}}$ interactions may be investigated with the C4A-NB-methane compound. The CH_4 guest show the largest change in ^{13}C NMR chemical shift upon complexation of all guests formed with C4A.

Reinhoudt has recently reported a calixarene-based carceplex host system in which guests are permanently incarcerated due to the covalent bonds between the two calix units forming the cavity.¹⁵⁻¹⁸ Since the two calix components forming the carceplex differ, a guest such as dimethylformamide may adopt two orientations, and thus give a molecular switching device providing the two guest orientations do not interconvert at room temperature.¹⁷ Sherman has also reported similar types of carceplex compounds containing incarcerated guests.^{18,19}

The compound symmetry, host structure and nitrobenzene guest orientation in the C4A-NB-propane compound vary with the propane content, and this compound offers potential as a molecular switching device. Propane occupancy allows the lattice structure and guest orientation (axial vs non-axial) to be tuned. Alignment of the nitrobenzene dipoles in the C4A-NB was explored as a potential non-linear optical (NLO) system in Chapter 4; change in the guest orientation would influence the system's NLO properties, and thus provide a physical observable with which to read the changes in guest orientation. Finally, the nitrobenzene motion in the axial and non-axial position is compared and contrasted using ^2H NMR spectroscopy.

2. Synthetic Details

C4A compounds containing nitrobenzene and a second gaseous guest were prepared by the vapour diffusion method. The preparation of the Xe-containing compound is typical.

C4A-NB-Xe: C4A (0.4415 g, 0.680 mmol) was dissolved in nitrobenzene (4 mL) with heating (100 °C) in a 10 mL sample vial. The vial was placed in a pressure vessel (i.d. = 40 mm, length: 200 mm) that was warmed to 95 °C in a sand bath, flushed twice with Xe, and pressurized with 55 psig Xe gas (Matheson). The temperature of the bath was lowered to 50 °C over 14 h, then allowed to return to ambient temperatures. Once the apparatus was cooled, the Xe pressure was released, and colourless crystals were isolated from the inner vial by filtration ($\text{C}_{44}\text{H}_{56}\text{O}_4 \cdot \text{C}_{4.98}\text{H}_{4.15}\text{N}_{0.83}\text{O}_{5.66} \cdot \text{Xe}_{0.17}$, 0.4315 g, 0.557 mmol, 82%). **C4A-NB_x-PROP_{1-x}** was prepared in a similar fashion with propane pressures of 15, 20, 100, and 175 psig.

C4A-NB- $^{13}\text{CH}_4$: C4A (0.2345 g, 0.361 mmol) was placed in a glass sample tube (o.d. 10 mL) containing a constriction 1.5 cm from the bottom. To this was added

nitrobenzene (0.8 mL). The tube was placed on a vacuum line and mixture degassed (freeze-pump-thaw) twice. Methane- ^{13}C (0.044 atm, Cambridge Isotopes Laboratory, 99.9%) was condensed on to the mixture (the partial pressure of methane at 77K is 0.0138 atm), and the sample tube flame-sealed at the constriction. The sample was allowed to warm to room temperature; the methane pressure was about 10 atm. The tube was then placed in an oven (100 °C) for 2 months in order to dissolve the calixarene in the nitrobenzene. The sample was then cooled to room temperature to induce crystal formation, the tube cracked open, and clear, colourless crystals isolated by filtration (0.1196 g). Less than 5% of the calix cavities were estimated (from the ^{13}C NMR spectrum) to be occupied with methane. The sample was stored at -40 °C.

3. *p*-tert-Butylcalix[4]arene Double Guest Systems

The incorporation of a gaseous guest by the calixarene dissolved in nitrobenzene solution leads to the formation of a solid containing both the liquid and gaseous guest. The structural motif adopted by the double-guest compound is identical to C4A-NB. Several gasses were used to form double-guest inclusion compounds with C4A, and the preliminary results suggest inclusion of a wide range of gases by the calix is possible.

3.1 *p*-tert-Butylcalix[4]arene-Nitrobenzene-Xenon

3.1.1 ^{13}C CP-MAS NMR Spectroscopy

The ^{13}C CP-MAS NMR spectrum of C4A-NB-Xe (Figure 1) is identical to that of C4A-NB (Chapter 4, Figure 7). In this structure, the host has no symmetry elements, and the nitrobenzene guest lies off the *z*-axis axis by 68°.

TABLE 1. ^{129}Xe chemical shift values in various environments.^a

		δ_{av} (ppm)	$\Delta\delta$ (ppm) ^b	cavity size (Å) ^c
Xenon	<i>gas, 0 density</i>	0		
	<i>gas, density 100 amagat</i>	53		
	<i>liquid, 244K</i>	161		
	<i>liquid, 161K</i>	229		
	<i>solid, 161K</i>	274		
Structure I Hydrate	<i>small cage</i>	242	0	5.0
	<i>large cage</i>	152	-32	5.9
Structure II Hydrate	<i>small cage</i>	229	-18	5.0
	<i>large cage</i>	80	0	6.6
Structure H Hydrate	<i>small cage</i>	232	-5	5.0
	<i>large cage I</i>	215	-40	
	<i>large cage II</i>			
Clathrasil D3C	<i>small cage</i>	253	-45	4.9
	<i>large cage</i>	81	0	6.7
β -Quinol		210	160	4.8
β -Phenol	<i>small cage</i>	229	171	
	<i>large cage I</i>	248	105	
	<i>large cage II</i>	279	53	
α -Cyclodextrin	<i>fully hydrated</i>	192	-23	5.3
Dianin's Compound	<i>site I</i>	133	85	6.3
	<i>site II</i>	152	55	6.3
<i>t</i> -Butylcalix[4]arene	<i>site I</i>	59	27	10.4
	<i>site II</i>	64	19	10.4

^a compiled from data in ref 1 and 3.^b $\Delta\delta$ = chemical shift anisotropy.^c cavity diameter.

3.1.2 ^{129}Xe CP (MAS and Static) NMR Spectroscopy

Since the second guest is undetected by ^{13}C NMR spectroscopy, the compound was examined by ^{129}Xe CP NMR spectroscopy using both magic angle spinning (MAS) and static techniques. The MAS spectrum (Figure 2a) shows two isotropic Xe lines (α : δ 59.4 ppm ($I_\alpha = 0.58$); β : δ 64.2 ppm ($I_\beta = 0.42$)) with the indicated intensities. The NMR data correlate well with the structural features determined by single crystal XRD (*vide infra*).

A significant area of research in ^{129}Xe NMR spectroscopy has been the use of xenon ($d_{\text{VDW}} = 4.4 \text{ \AA}$) as a probe gas of microporous materials such as zeolites,^{7,20} clathrasils,¹⁻⁶ cyclodextrins,^{21,22} and clathrate hydrates.¹⁻⁴ The ^{129}Xe isotropic chemical shift (δ_{iso}) has been correlated empirically to the size of cavity it occupies: the larger the pore, the lower the δ_{iso} value relative to the chemical shift value of the infinitely dilute gas ($\delta \text{Xe}_{\text{free gas}} = 0.0 \text{ ppm}$). Table 1 summarizes the ^{129}Xe NMR studies of Xe in organic host-guest systems. The XRD structure and ^{129}Xe NMR spectra of a xenon-containing Dianin's compound have been reported: the guest sits in an hour-glass shaped cage with two wide sections of $6.3 \text{ \AA}$ joined by a narrow neck, and has ^{129}Xe NMR δ_{iso} values of 134 and 152 ppm for the singly- and doubly-occupied hour-glass cavity.¹² The isotropic chemical shift in ^{129}Xe NMR spectrum of xenon in α -cyclodextrin ($d = 5.3 \text{ \AA}$) occurs at δ 192 ppm.^{21,22} The β -quinol cavity ($d = 4.8 \text{ \AA}$) shows a ^{129}Xe NMR δ_{iso} value of 210 ppm.¹³ By comparison, the calix cavity ($d = 10.4 \text{ \AA}$ at the centre of gravity of the guest) provides a looser fit for the guest, and the δ_{iso} values for the two guests are shifted upfield, in keeping with the conventional δ_{iso} value-pore size trend.³ The significant upfield ^1H and ^{13}C NMR δ values for the guests in the calix has been attributed to the influence of the host aromatic ring currents,²⁴ and the same interaction between the host and xenon may influence the ^{129}Xe NMR δ_{iso} value. Ripmeester and Ratcliffe have argued that Xe as a probe gas interacts with micropore surfaces in an anisotropic fashion since the Xe electron charge distribution is easily polarized.^{25,26} The C4A-NB-Xe compound, with its aromatic-walled cavity, may demonstrate a more significant type of guest-host interaction than that seen in typical microporous systems, and may be useful as a model of the gas-surface interactions thought to account for the chemical shift.

Two Calixarene Cavities: XRD. The two lines in the ^{129}Xe CP-MAS NMR spectrum indicate that there are two crystallographically-inequivalent xenon sites with

slightly different occupancies and void space volumes. The single-crystal XRD structure (discussed below) shows two of the four *t*-butylphenol units of the host are disordered in a ratio of 0.57:0.43 (*B*) and 0.66:0.34 (*C*): this gives a potential of four unique cavities of slightly different geometries. The ^{129}Xe NMR spectra indicate that the gas occupies two rather than four sites, and in a ratio that matches the occupancy ratio of the first *t*-butylphenol (*B*) unit disordering. The cavity dimensions are described by the distances between the central *t*-butyl carbons of the four *p*-tert-butylphenol units of the calix macroring. The disordered positions of *t*-butyl group *C* do not cause an appreciable change in cavity dimension as the distance to the opposite *t*-butyl central carbon (*A*) varies by only 0.006 Å over the two disordered positions. The second disordered *t*-butyl group (*B*) gives a cross-distance difference to that of the *D* *t*-butyl carbon of 0.13 Å, and to a first approximation, there are only two cavities that differ slightly in volume. Figure 3 indicates the cavity dimensions at the central carbon of the *t*-butyl groups and close to the location of the xenon atom; disordering in one *t*-butylphenol unit (*B*) gives rise to the two slightly different cavities ($d_1 = 10.65$ Å, $d_2 = 10.52$ Å).

The sites occupied by Xe have so far been described by dimensions in the *xy*-plane, and a proper treatment must consider any differences along the *z*-axis. Disordering of the *t*-butyl groups in the *z*-direction also defines a second variable for the cavity volume. Only one *t*-butyl group (*B*) in an above calixarene caps the calix cavity along the *z*-axis. The average position of the three methyl carbons only varies by 0.03 Å over the two disordered sites, and since this value is less than the difference in the *xy*-plane of 0.13 Å, the calix cavity assumed to be invariant along the *z*-direction.

Although two of the four *t*-butyl groups are disordered in the calix macroring, only the *B* *t*-butyl disordering in the *xy*-plane causes distortion of the calix cavity. The disordering leads to two slightly different calix cavities (α, β) in the crystal. Occupation of

these two cavities by Xe leads to two Xe environments which are indicated by the two lines in the ^{129}Xe NMR spectrum.

Two Calixarene Cavities: ^{129}Xe CSA Tensors. The components of the chemical shift anisotropy (CSA) tensors can be obtained for the two sites from the static ^{129}Xe CP NMR spectrum (Figure 2b), and reflect both the chemical environment and symmetry of the α and β cavity sites. The spectrum was fitted with the Bruker WIN-FIT software package using a two-site model employing the ^{129}Xe NMR δ_{iso} values from the spinning spectrum (Figure 2c); the fit parameters are summarized in Table 2. The signal intensities of the two sites determined by both NMR techniques agree with the t-butyl disordering from the XRD data.

Both powder patterns are characterized by nearly axially symmetric CSA tensors ($\eta = 0.3$), and reflect the relatively high symmetry of the xenon sampling the two different calix cavities in the *xy*-plane. The largest component of both pattern ($\delta_{33} = \delta_{\parallel}$) is assumed to be along the *z*-axis; since $\delta_{\parallel}^{\alpha} = \delta_{\parallel}^{\beta}$, the two cavities share similar dimensions along the *z*-axis. Since $\delta_{\parallel}$ shows the least amount of shielding, the CSA tensor has positive anisotropy indicative of an oblate spheroidal CSA tensor.³ The δ_{11} and δ_{22} values of the two patterns indicate that for each cavity Xe samples different dimensions along the *x*- and *y*-axes. Site β , occupied by the minor fraction of xenon, is slightly more symmetric ($\delta_{22}^{\beta} - \delta_{11}^{\beta} = 4$ ppm) than the majority site ($\delta_{22}^{\alpha} - \delta_{11}^{\alpha} = 5$ ppm). The XRD data show this cavity to possess *xy*-dimensions of 10.15 x 10.52 Å at the host central t-butyl carbons. The values for Xe in site α shows that the difference between the *x*- and *y*-dimensions to be slightly greater than in site β , and is confirmed by the XRD data: 10.15 x 10.65 Å. In conclusion, there is a high correlation between the cavity mapped out by the Xe guest as monitored by ^{129}Xe NMR spectroscopy and the cavity dimensions characterized by XRD.

TABLE 2. ^{129}Xe CP NMR spectral simulation parameters.^a

Site	occupancy	δ_{iso} (ppm)	$\Delta\delta$ (ppm)	δ_{11} (ppm)	δ_{22} (ppm)	δ_{33} (ppm)
α	0.6	59	27	49	54	76
β	0.4	64	19	56	60	75

^a $\Delta\delta = \delta_{33} - \delta_{11}$; $\delta_{\text{iso}} = (\delta_{11} + \delta_{22} + \delta_{33})/3$; $\eta = |\delta_{22} - \delta_{11}|/|\delta_{33} - \delta_{\text{iso}}| = 0.3$; uncertainties: ± 2 ppm.

3.1.3 Single Crystal X-Ray Diffraction

The XRD structure of C4A-NB-Xe is shown with the minority guest ($r_{\text{VDW}} = 2.2 \text{ \AA}$) in Figure 4; the nitrobenzene guest is arranged as in the C4A-NB structure (Chapter 4). The C4A-NB-Xe structure results from substitution of nitrobenzene by Xe in 17% of the cavities without significant changes in the gross features of the C4A-NB structure.

The off-axis orientation of the nitrobenzene guest is similar in the two structures; the two structures show slightly different unit cell values: C4A-NB-Xe is slightly larger along *a*, but shorter along *b* and *c* than C4A-NB; the unit cell volume is essentially identical. Substitution of nitrobenzene by Xe does not change the pattern of host t-butyl disordering (2 of the 4 groups disordered), but it does change the ratio of disordering in t-butyl group C to 0.66:0.34. The change in disordering reflects the guest's ability to perturb the host structure, and also indicates which part of the host is most sensitive to the guest.

The positional disordering in the two t-butyl groups affects the cavity differently: the diameter of the cavity at the central t-butyl carbon remains constant over the two sites of the one disordered t-butyl group (C), while the other disordering pattern (B) leads to a

TABLE 3. Crystallographic data for C4A-nitrobenzene-Xe and C4A-nitrobenzene-propane.^a

compound	C4A•NB _{0.83} •Xe _{0.17}	C4A•NB•C ₃ H ₈
formula	C _{48.98} H _{60.15} O _{5.66} N _{0.83} Xe _{0.17}	C _{12.23} H _{15.52} N _{0.16} O _{1.33}
fw	773.43	185.90
temperature, K	150	150
colour, habit	colourless	colourless
crystal size, mm	0.33 x 0.30 x 0.18	0.20 x 0.20 x 0.20
crystal system	orthorhombic	tetragonal
space group	<i>Pc</i> 2 ₁ <i>n</i>	<i>P</i> 4/ <i>n</i>
<i>a</i> , Å	12.4872(7)	12.946(11)
<i>b</i> , Å	12.8909(8)	12.946(11)
<i>c</i> , Å	26.6893(17)	12.568(10)
<i>V</i> , Å ³	4296.2(5)	2106.3
<i>Z</i>	4	8
ρ_{calc} , g cm ⁻³	1.199	1.172
<i>F</i> (000)	1666.75	877.89
μ (Cu K α) mm ⁻¹	1.63	0.62
λ , Å	1.54056	1.54056
scan type	$\theta/2\theta$	$\theta/2\theta$
data collected	<i>h</i> , <i>k</i> , <i>l</i>	<i>h</i> , <i>k</i> , <i>l</i>
$2\theta_{\text{max}}$, deg	140.0	140
total # refls	5416	4113
# of unique reflns	5304	2008
<i>R</i> _{merge}	0.009	0.039
# reflns <i>I</i> $\geq$ 2.5 σ (<i>I</i>)	4258	1313
<i>R</i>	0.048	0.125
<i>R</i> _w	0.062	0.167
GOF	1.92	5.83
max $\Delta\sigma$, finl cycl	0.048	0.049
resid density, e Å ⁻³	-0.290 to 0.210	-0.36 to 0.39

^aConditions and collection details: Enraf-Nonius diffractometer; graphite monochromator; aperture 4.0 x 4.0 mm at a distance of 173 mm from the crystal; stationary background counts at each end of the scan (scan/background time ratio 5:1); peak and background counts determined with profile analysis procedure of Gabe *et al.*, *J. Appl. Cryst.*, **1989**, 22, 384. $\sigma(F_o)$ based on counting statistics, function minimized $\sum w(|F_o| - |F_c|)^2$, where $w = [\sigma^2(F_o) + k(F_o)^2]^{-1}$, $R = \sum ||F_o| - |F_c|| / \sum |F_o|$, $R_w = (\sum w(|F_o| - |F_c|)^2 / \sum w|F_o|^2)^{1/2}$, and $GOF = [\sum w(|F_o| - |F_c|)^2 / (m - n)]^{1/2}$. Values given for *R*, *R*_w, and GOF are based on those reflections with *I* $\geq$ 2.5 σ (*I*).

significant change in the cavity size. With the disordering in *B*, cavity dimensions of 10.52 and 10.65 Å by 10.15 Å are obtained. Closer C-Xe contacts are made with some of the *t*-butyl methyl groups that are pointing into the cavity: the *d*_{C-Xe} values range from 4.47 to 5.06 Å. The host methyl groups are an integral part of the host cavity, and also define the

cavity dimensions. The disordering in *C* leads to a difference in cross-cavity distances of $9.45-9.37 = 0.08$ Å, but the disordering in *B* defines a more significant cross-cavity difference of $10.00-9.76 = 0.24$ Å. The ^{129}Xe NMR spectra indicate that the minority guest sits in two slightly different cavities, and corroborates the observation of two cavities in the XRD structure.

TABLE 4. Selected Bond Distances and Angles for C4A-NB-Xe.^a

Bond	Distance (Å)	Bond	Distance (Å)
O1-C11	1.392 (5)	C17-CT12	1.571 (8)
C11-C22	1.387 (7)	C17-CT13	1.525 (7)
C11-C16	1.388 (6)	C24-C24A	0.126 (16)
C12-C13	1.392 (6)	C27-C27A	0.270 (10)
C12-C18	1.517 (6)	C34-C34A	0.068 (14)
C13-C14	1.394 (6)	C37-C37A	0.262 (11)
C14-C15	1.405 (7)	O5-N1	1.230 (7)
C15-C16	1.398 (6)	O6-N1	1.204 (7)
C16-C48	1.535 (7)	N1-CN1	1.450 (5)
C17-CT11	1.515 (6)		
Bond	Angle (deg)	Bond	Angle (deg)
O2-O4-C47	129.2	O3-O1-C17	125.9

^a for host-Xe distances, see Figure 5.

Xe sits at the centre of the cavity, and lies in the plane defined by the central carbon of the host *t*-butyl groups. Xe is 4.33 Å from the basal plane defined by the four phenolic oxygens. Xe does not show any protrusion from the cavity and is in fact, located deep in the cavity relative to other guests. The closest contacts to the host are to the lower three carbons of each *p*-tert-butylphenol unit (C1,C2,C6), with an average distance of 4.13 Å from these carbons to xenon; the sum of the van der Waal's radii is 3.9-4.0 Å. The XRD structure fails to resolve the two Xe sites observed by NMR spectroscopy; the low occupation (17%) of the cavity makes it difficult to resolve the two sites.

3.2 *p*-tert-Butylcalix[4]arene-Nitrobenzene-Methane

A natural convergence of the C4A-aliphatic structures (Chapter 5) and the C4A-NB-Xe system is a double guest system containing the smallest aliphatic guest: methane. It is anticipated that methane will penetrate deep into the calix cavity, and will exhibit a significant upfield shift in its ^{13}C NMR δ in the compound relative to its gas phase value.

Initial synthetic attempts to incorporate methane into the C4A-NB lattice were hampered by the low quantity of methane in the calix cavities, as evidenced by the lack of any methane signal in the ^{13}C CP-MAS NMR spectrum. The synthesis with ^{13}C -labeled methane gave a guest signal in the ^{13}C CP-MAS NMR spectrum of C4A-NB-Me (Figure 6). It is estimated that no more than 5% of the cavities are occupied by methane; the majority are occupied by nitrobenzene.

The host ^{13}C resonances are the same as those in C4A-NB and C4A-NB-Xe (Figure 1), and indicate that the C4A-NB-Me structure is identical to these structures. The single guest ^{13}C resonance indicates that, unlike Xe, methane occupies only one type of cavity (on the NMR timescale). Methane shows the largest ^{13}C resonance complexation-induced shift (CIS) (-9.5 ppm)²⁷ of any calix guest. The CIS value suggests that the methane guest experiences significant ring-current effects,²⁴ and is included deep in the calix cavity.

Preparation of single crystals for single-crystal XRD was not attempted. However, it would be of interest to determine the position of the methane guest (if possible), which would give valuable structural data to investigate the role of attractive CH- π interactions between the guest and the host.

3.3 C4A-NB-Guest Compounds where Guest = CO, CO₂, SO₂, CH₂CH₂, CH₃CH₃.

The ability of C4A to incorporate a gaseous guest appears to be a general phenomenon, and the synthesis of C4A-NB-Xe and C4A-NB-CH₄ has been extended to

other small guests. The C4A-NB-guest compounds were characterized by solid-state ^{13}C CP-MAS NMR spectroscopy, and show that the host includes both nitrobenzene and a second guest.

The ethylene guest ^{13}C NMR resonance in solution occurs at $\delta = 123$ ppm, which is in the same region as the aromatic carbon resonances of nitrobenzene and the calixarene. A very small amount of ethylene is incorporated in C4A-NB- C_2H_4 (Figure 7), as indicated by the weak resonances at $\delta = 118.6$ and 118.9 ppm. The complexation-induced shift (CIS) in the chemical shift values is large (-4.1 , -4.4 ppm) and suggests that the small amount of ethylene included in the cavity experiences significant ring-current effects.²⁴ The nitrobenzene and calixarene ^{13}C lines are identical to those of C4A-NB.

The ethane guest resonance occurs at $\delta = 4.8$ ppm (Figure 7) and displays a CIS value of -0.9 ppm; the δ value is consistent with guest dynamic averaging in the host cavity between methyl-in and methyl-out positions. The nitrobenzene lines are similar to those seen in C4A-NB. However, the broadened and low multiplicity of the host resonances is in contrast with the sharp and high multiplicity host resonances seen in C4A-NB. This suggests that the local compound symmetry may be greater than in C4A-NB: the singlet *t*-butyl lines indicate that the host may adopt a C_4 symmetry, similar to that seen with the preparation of C4A-NB-propane (Figure 9c, 9d).

The ^{13}C CP-MAS NMR spectra of the CO_2 and CO compounds of C4A-NB-guest compounds do not unambiguously prove the incorporation of the second guest. Both C4A-NB-guest compounds gives ^{13}C CP-MAS NMR spectra identical to that of C4A-NB. The carbon resonance of CO_2 gas occurs at $\delta = 132$ ppm; this region in the C4A-NB- CO_2 spectrum contains aromatic carbon resonances from both the host and the nitrobenzene guest. The carbon resonance of CO gas occurs at $\delta = 181$ ppm; this region in the C4A-NB-CO spectrum shows no peaks corresponding to carbon monoxide. It is possible that

in both cases, the amount of gas incorporated is very low, and ^{13}C -labelled guests would give ^{13}C NMR spectra that indicate the presence of the second guest.

The ^{13}C CP-MAS NMR spectrum of C4A-NB-SO₂ (Figure 8) cannot obviously indicate the presence of SO₂ in a direct fashion. There is indirect evidence to suggest that SO₂ has been incorporated into a fraction of the calix cavities. The host carbon lines (sharp singlets) indicate that the symmetry of the host is greater than the C_2 symmetry seen with C4A-NB. SO₂ may cause the nitrobenzene guest to align along the calix C_4 cavity like in C4A-NB-ethane. Further characterization techniques are necessary to confirm the presence of SO₂ in the calix cavity.

3.4 Conclusion

A second guest (in addition to nitrobenzene) may be incorporated into the calix cavity. The C4A-NB-Xe compound illustrates that the second guest replaces nitrobenzene in a minor fraction of cavities. The incorporation of gases such as methane, ethane, and ethylene into the calix to give C4A-NB-guest compounds has been confirmed by ^{13}C CP-MAS NMR spectroscopy. Methane and ethylene are present in very small amounts. The synthesis of CO₂-, CO-, and SO₂-containing C4A-NB-guest compounds have also been attempted, with no direct confirmation of second guest incorporation.

This work is of a preliminary nature. Extension of this chemistry to other gas molecules may well indicate the scope of gas inclusion by the calix system. Knowledge of the guest position in the calix cavity may provide insight to the inclusion of guests in other host systems. Finally, selectivity of the calix cavity system to differently-sized gases (such as natural gas or hydrocarbon mixtures) should be investigated in the context of separation technologies.

4. A Tunable *p*-tert-Butylcalix[4]arene-Nitrobenzene-Propane Lattice

The nitrobenzene orientation in the calix cavity can be tuned by incorporation of propane as a second guest. As the propane pressure, P_P , increases during the preparation of C4A-NB, propane is incorporated in increasing amounts. Consequently, the nitrobenzene orientation switches to an on-axis from an off-axis position relative to the calix *z*-axis.

The synthesis of C4A-aliphatic compounds developed from the discovery that C4A-PT, and not C4A-3-nitrotoluene, crystallizes from vapour diffusion of *n*-pentane into a saturated solution of C4A in 3-nitrotoluene. The subsequent chemistry of C4A-guest compounds branches out in two directions: one in which an aromatic, nitro-containing solvent is not required for C4A-guest compound formation (Chapter 5), and one in which C4A-guest compounds require the presence of an additional “help” guest such as nitrobenzene or 3-nitrotoluene.

TABLE 5. Symmetry of C4A-Guest Structures (where guest = aliphatic or gaseous).^a

	1	2	3	4	5	6
Guest-1 [position]	NB ^b [off-axis]	xenon ^b methane ethylene ethane propane butane [axial]	propane ^b [axial]	NB [axial]	propane <i>n</i> -butane <i>n</i> -pentane ^b C ₄ H ₉ Cl ^b C ₄ H ₉ Br ^b cyclohexane ^b [axial]	<i>n</i> -dodecane <i>n</i> -hexane <i>n</i> -heptane [axial]
Guest-2 [position]	none	NB [off-axis]	NB [axial]	none	none	none
symmetry	C _s	C _s	C ₂ ^c	C ₄	C ₄	C ₄
host:guest	1:1	1:1	1:1	1:1	1:1	2:1

^a all compounds characterized by solid-state ¹³C CP-MAS NMR spectroscopy.

^b characterized by single-crystal XRD.

^c C₂ local symmetry indicated by ¹³C NMR; XRD indicates C₄ symmetry (space averaging).

The symmetries of C4A-guest compounds (guest = aliphatic or gaseous) range from C_s (C4A-NB: host has some *t*-butyl disordering, guest is non-axial) to C_4 (C4A-PT: no *t*-butyl group disorder, guest axially positioned on the host C_4 axis), and are related to the position of the guest in the cavity. The progression of structure symmetry reflects the differing strengths and nature of calix:guest interactions (Table 5).

4.1 ^{13}C CP-MAS NMR Spectroscopy

^{13}C CP-MAS NMR spectra of C4A-NB $_x$ -PROP $_{1-x}$ (where x is the fraction of the nitrobenzene guest: $0 \leq x \leq 1$) monitor the transition in structures from asymmetric to C_2 -symmetric, and finally to C_4 -symmetric (Figure 9). In the first transition, the nitrobenzene orientation changes from a non-axial position to an axial one in which the nitrobenzene molecular axis is coincident with the calix symmetry axis. The off-axis α -C4A-NB structure persists when synthesized under $P_{\text{PROP}} = 15$ psi (Figure 9A), and the ^{13}C NMR spectrum is identical to that of C4A-NB (Chapter 4, Figure 8) and C4A-NB-Xe (Figure 1). Preparation under $P_{\text{PROP}} = 20$ psi (Figure 9B) gives a compound that incorporates a small amount of the second guest ($\delta = 14, 16$ ppm), and shows two nitrobenzene orientations as identified by the nitrobenzene C-3' resonances at $\delta = 123.4$ and 121.9 ppm. The former line arises from the nitrobenzene in the non-axial position, while the latter corresponds to the axial guest. With $20 \text{ psi} < P_{\text{PROP}} < 100$ psi, the product (Figure 9C) is solely the β -C4A-NB $_x$ -P $_{1-x}$ compound with incorporation of propane and nitrobenzene in the axial orientation, as determined by the XRD structure (below). Finally, under higher propane pressures (175 psi), no propane is incorporated in the solid product which shows a ^{13}C NMR spectrum of a C_4 -symmetric compound (Figure 9D).

The ^{13}C CP-MAS NMR spectra indicate the structural changes as P_{PROP} increases. The nitrobenzene C-3' resonance is the guest signal most sensitive to the guest

orientation; the other guest carbon resonances are invariant (C-4', $\delta = 134.7$ ppm) or are partially (C-1', $\delta = 147.2$ ppm) or fully obscured (C-2') by the calixarene aromatic carbon resonances. The upfield shift in the δ C-3' indicates that this carbon moves closer to the aromatic walls of the calix cavity as the guest adopts the axial position.

The calix ^{13}C lines become sharper as P_{PROP} increases, and indicate that the calix cavity symmetry increases as the nitrobenzene becomes axial. In particular, the t-butyl carbons (δ 35, 33 ppm) are sharp 1:1 doublets (at $P_{\text{PROP}} = 100$ psi) which suggest that the cavity possesses local two-fold symmetry. The NMR data is at odds with the XRD structure which shows a 4-fold symmetric compound which may result from space-averaging as in C4A-toluene.^{28,29} At higher P_{PROP} , propane is (surprisingly) absent from the β -C4A-NB lattice to give an axial nitrobenzene and a C_4 -symmetric compound. The absence of propane may be due to rapid decompression of the propane as the synthetic cell is disassembled; the migration of propane is related to the nitrobenzene cavity position and the compound symmetry. Finally, the downfield shift of the host aliphatic δ values with increasing P_{PROP} may result from the proximity of the guest nitro group to the host t-butyl groups.

4.2 Single Crystal X-Ray Diffraction Study of C4A-Nitrobenzene-Propane

Single crystals of C4A-PROP-NB were prepared by the vapour diffusion method. The XRD structure (Figure 10) shows the majority guest which sits on the C_4 symmetry axis of the 4-fold symmetric cavity; only one of the two orientations (related by a 90° rotation along the z-axis) is shown. The nitro group protrudes out of the cavity along the 4-fold axis. The minority guest which is not shown, is also positioned along the 4-fold symmetry axis. Of note is the absence of t-butyl disordering.

The structural refinement for this structure is not as good as that achieved with C4A-NB-Xe, but unambiguously identifies that the nitrobenzene position is different than in the C4A-NB structure. The terminal carbons of the propane guest overlap with the *ipso*- and *para*- carbons of the nitrobenzene and make it difficult to refine the two guest occupancies and the minor guest position. The loose fit of the propane in the cavity likely causes the propane carbons to have large thermal parameters. The large residuals preclude comments about the secondary structural features of the guest such as an off-axis tilt and inversion.

The view along the symmetry axis shows the aromatic ring to be rotated 23° from the line connecting two opposite *t*-butyl groups. Like the toluene guest, the aromatic ring sits perpendicular to the *t*-butyl C-C bond that forms the outside wall of the cavity, and illustrates the relationship between the guest orientation and *t*-butyl group orientation.

TABLE 6. Selected Bond Distances and Angles for C4A-NB-PROP.

Bond	Distance (Å)	Bond	Distance (Å)
O1-C1	1.414 (6)	C7-CT3	1.521 (10)
C1-C2	1.389 (7)	NNB-ONB1	1.23 (3)
C2-C8	1.496 (8)	NNB-ONB2	1.23 (3)
C2-C3	1.403 (7)	NNB-CNB1	1.462 (16)
C6-C5	1.416 (7)	CNB3...CT2	3.62
C6-C1	1.361 (8)	CNB2...C5	3.74
C6-C8A	1.524 (8)	CNB6...C3	3.89
C5-C4	1.360 (8)	CNB4...C1	4.30
C4-C3	1.380 (8)	CNB4...C2	4.26
C7-CT1	1.527 (11)	CNB4...C6	4.39
C7-CT2	1.523 (10)		
Bond	Angle (deg)	Bond	Angle (deg)
O1-O3-C34	123.6		

Nitrobenzene sits 4.49 Å above the basal plane defined by the four phenolic oxygens. Contacts at or less than the sum of the van der Waals radii (3.8 Å) between guest and host include: CNB3...*t*-BuMe (3.62 Å), CNB2...C5 (3.74 Å), CNB6...C3

(3.89 Å). The guest CNB4 approaches the host C1, C2, and C6 with distances of 4.30, 4.26, and 4.39 Å.

4.3 ^2H NMR Spectroscopy: Nitrobenzene Motion

Comparison of the guest dynamics in the axial and non-axial guest position in the calix cavity show key differences in the *type* of motion as well as the energetic barrier to the respective motions. The reader is referred to the VT ^2H NMR spectra of the low symmetry α -C4A-NB- d_5 in which the nitrobenzene occupies a non-axial position (Chapter 7, Figure 17) and the discussion therein.

TABLE 7. ^2H NMR spectral parameters for β -C4A-NB.^a

deuteron	<i>T</i> (K)	$ \Delta\nu_{xx} $ (kHz)	$ \Delta\nu_{yy} $ (kHz)	$ \Delta\nu_{zz} $ (kHz)	χ (kHz)	η
<i>ortho-, meta-</i>	77	129	138	267	178.0	0.034 ± 0.012
	136	32	130	162	108.0	0.617 ± 0.030
	319	12	12	23.3	15.5	0.000 ± 0.05
<i>para-</i>	77	129	138	267	178.0	0.034 ± 0.012
	136	130	138	267	178.0	0.034 ± 0.012
	319	130	138	267	178.0	0.034 ± 0.012

^a Estimated uncertainties of ± 1.5 kHz in the measurements of the $\Delta\nu_{ii}$ and ± 1 kHz in χ ; those for the 319K spectra are twice as high.

Figure 11 depicts the 136-319K ^2H NMR spectra of the high symmetry β -C4A-NB- d_5 -PROP in which the nitrobenzene occupies an axial position; the spectral features are collected in Table 7. The 136K spectrum has the distinctive 2-fold FML lineshape ($\chi_{136} = 108$ kHz; $\eta = 0.62$). In contrast to the α -C4A-NB- d_5 compound, in which the nitrobenzene is non-axial, the axial nitrobenzene is already undergoing 2-fold flips below the temperature the non-axial nitrobenzene even begins to be dynamic (jump rate $< 10^3$ Hz; static line at 200K). The axial guest thus experiences a significantly lower barrier to

rotation. If a static lineshape at 77K is assumed, the minimum barrier to the axial nitrobenzene 2-fold flip is $E_{\text{act}} = 14 \text{ kJ mol}^{-1}$ compared to the non-axial 2-fold flip barrier of $E_{\text{act}} = 57 \pm 2 \text{ kJ mol}^{-1}$.

An axial rotor like the nitrobenzene- d_5 guest has its *para*-C-D bond along the molecular rotation axis. The *para*-deuteron EFG tensor components will be invariant with axial motion, while the EFG tensor components of the remaining deuterons will vary. As a result, the ^2H NMR spectra of 2-fold and 4-fold axial motion consist of two patterns in a ratio of 4:1, and the minor lineshape retains its static features. If there is any component of the guest motion that lies off the rotation axis (such as libration), the *para*-deuteron linewidth should narrow. The ^2H NMR spectral parameters for α -C4A-NB- d_5 are $\chi_{\text{static}} = 178 \pm 1 \text{ kHz}$, $\eta = 0.03$ (Chapter 4, Table 6); the values for both the 136 and 319K *para*-deuteron spectra of β -C4A-NB- d_5 -PROP are $\chi = 179 \pm 1 \text{ kHz}$, $\eta = 0.03$. This suggests there is no component of the guest motion that lies off the motional axis, and that the guest and host symmetry axes are coincident.

Like most of the 4-fold dynamically averaged guests in the calix cavity studied in this thesis, the axial nitrobenzene- d_5 lineshapes narrow further at higher temperatures, and show the gross features expected for 90° jumps about the C_4 symmetry axis. However, two factors also seen with C4A-TOL- d_5 hinder the simulation of the ^2H NMR data: First, the FML for the motional narrowing is not reached by the maximum observed temperature of 319K; the FML lineshape is crucial for selecting a motional model. Secondly, the broadened features suggest the presence of a distribution of motions, which complicate the lineshape intensity distribution with the simulated lineshapes.

If a Gaussian distribution of motions (as suggested for the 4-fold motion in C4A-TOL- d_5) is assumed, the 319K β -C4A-NB- d_5 -PROP spectrum can be compared to one of the simulated lineshapes for C4A-TOL- d_5 , and a rate of motion of $\kappa = 4 \times 10^4 \text{ Hz}$

estimated. From this match, the barrier to the 90° flip of the axial nitrobenzene can be roughly determined: $E_{\text{act}} = 7 \text{ kJ mol}^{-1}$. Since the FML spectrum was not attained in this temperature regime, and not all the spectra were matched with a jump rate, it must be stressed that this value is only approximate. The low barrier to 4-fold rotation arises from the fact that 4-fold motion is activated over a wide temperature regime. For comparison, $E_{\text{act}} = 8 \text{ kJ mol}^{-1}$ for the 4-fold motion of the toluene rotor in C4A.

In conclusion, the mixed-guest C4A system in which the nitrobenzene sits in an axial position shows a marked departure in the ^2H NMR lineshapes from those observed with the non-axial C4A-nitrobenzene. As the lineshapes were not simulated, only a qualitative comparison can be made between the two structural isomers. Nonetheless, it appears that the axial nitrobenzene undergoes a different set of motions and experiences a significantly lower barrier to 2-fold rotation than does the non-axial nitrobenzene.

4.4 Double Guests and the Host Lattice

Several structural motifs occur with the compounds of C4A with nitrobenzene and small gas molecules as the major and minor guests, respectively. The α -C4A-NB and the β -C4A-NB structures differ in the major guest orientation as well as the symmetry of the host. The quantity rather than the exact nature of the minor guest appears to be crucial in directing which structure the resulting compound will adopt. That the C4A structure is very sensitive to the presence of the second guest indicates the importance of the relationship between guest and host.

Translational ordering of C4A-guest compounds arises from a repeatable orientation of the guest in a calix cavity: each guest must sit in an identical position in a calix cavity that has a shape that persists throughout the lattice. Since the guest environment is defined by several calixarenes, the long-range ordering is propagated (in part) by the guest

orientation. Defect sites arise when the long-range ordering is broken when either one guest adopts an alternative orientation, or a cavity is occupied by a second guest. The C4A-NB structure is invariant to the presence of a small fraction of a second guest. As the number of defect sites increases, the off-axis nitrobenzene orientation and the host symmetry are no longer propagated through the lattice, and an axial nitrobenzene orientation and C_4 host symmetry are adopted.

The NMR and XRD studies of the C4A-NB_x-PROP_{1-x} compound serve to bridge solid-state and solution studies. As the number of defects increases in the C4A-NB_x-PROP_{1-x} lattice, a molecular interpretation becomes appropriate, and is analogous to a description of the solution state. However, as the number of defects in the C4A-NB_x-PROP_{1-x} lattice decreases, a lattice interpretation is more suitable.

It is surprising that the 4-fold symmetric β -C4A-NB structure (Figure 9D) contains no propane, despite its preparation under a high pressure of propane (175 psi). It is likely that the propane guest initially occupies a large enough fraction of defect sites to cause the nitrobenzene guest to become axial and the host to have C_4 symmetry. The high symmetry β -structure must not bind the second guest as tightly as the α -structure, and subsequent to the formation of β -C4A-NB-PROP, the propane migrates out of the lattice. It is anticipated that the β -C4A-NB lattice contains a large number of empty calix cavities. Departure of propane from the lattice is not unexpected in light of the penetration of the empty solid C4A lattice by liquid propane (Chapter Five, Figure 3) to give a C_4 -symmetric structure. The mostly empty β -C4A-NB lattice might actually be microporous, and possess structural characteristics of a pillared material.

In light of the propane behavior, it appears that the symmetry of the C4A-NB-guest compound influences the cavity-to-cavity migration of the second guest. The interstitial volumes may differ between the $P4/n$ and the $Pc2_1n$ structures. Furthermore, the

nitrobenzene guest may act as a gate to propane site-to-site migration: when it is in the off-axis position (the α -structure), the interstitial channels are closed, but when the nitrobenzene is in the on-axis position (the β -structure), the interstitial channels are opened.

The process of crystal nucleation and propagation must be considered to understand fully the relationship between the two guests and the host in the crystalline lattice. Fundamental questions arising from this initial work will need to be addressed. In particular, what species is initially nucleated—C4A-NB or C4A-gas? The synthesis of C4A-pentane by the vapour diffusion method shows that in some cases, C4A-NB does not crystallize at all, whereas with smaller guests such as methane, the vast majority of calix cavities are occupied by nitrobenzene. The species that nucleates first may do so as a function of C4A solubility: the calix has a much lower solubility in aliphatic hydrocarbons than it does in nitrobenzene. The second feature to consider is crystal growth. Once nucleation has occurred, is one guest preferentially incorporated into the growing lattice? Does guest migration take place? Is the rate of crystal growth more significant than the thermodynamic stability of the product under the synthesis conditions? Many questions need to be addressed to fully understand the structure and behavior of this system.

5. Summary

Incorporation of a variety of small molecules as second guests (in addition to nitrobenzene) by C4A demonstrates the versatility of the host, and opens up new dimensions in the host:guest chemistry of the calixarene system. Two systems have been studied in detail: C4A-NB compounds with Xe and propane as second, minority guests. Xe is a very sensitive NMR probe of the calix cavity, and the ^{129}Xe NMR data show a remarkable consistency with the XRD data, which shows that Xe occupies two slightly

different calix cavities defined by the disordering of one of the host's four *t*-butylphenol entities. The major guest nitrobenzene occupies an off-axial position in the cavity, and the compound adopts the same structural motif as α -C4A-NB.

Propane as a second guest shows a more pronounced influence on the compound structure. By varying the propane fraction in the lattice, the orientation of the majority guest as well as the compound symmetry may be tuned. As the nitrobenzene guest moves to an on-axis position, the host structure becomes 4-fold symmetric. The role of the second guest in the introduction of lattice defects has been discussed.

Preliminary work was carried out to discover if additional gaseous guests are incorporated in fashion similar to Xe and propane. Methane is incorporated, and the C4A-NB-methane compound shows a very pronounced complexation-induced ^{13}C NMR shift of -9.5 ppm. Other guests examined included ethane, ethylene, carbon dioxide, carbon monoxide, and sulphur dioxide. The potential use of the calixarene to effect gas separation makes further research in this area attractive.

6. References

1. Davidson, D. W.; Ripmeester, J. A. In *Inclusion Compounds*; Atwood, J. L.; MacNicol, D. D.; Davies, J. E. D., Eds.; Academic Press: London, 1984; Vol. 3, 69-128.
2. Ripmeester, J. A.; Ratcliffe, C. I. In *Inclusion Compounds*; Atwood, J. L.; Davies, J. E. D.; MacNicol, D. D., Eds.; Oxford UP: Oxford, 1991; Vol. 5, 37-89.
3. Ripmeester, J.A.; Ratcliffe, C.I.; Tse, J.S. *J. Chem. Soc., Faraday Trans. 1*, **1988**, 84, 3731-3745.
4. Ripmeester, J. A. *J. Chem. Soc., Chem. Commun.* **1988**, 608-610.
5. Tse, J. S.; Desando, M.; Ripmeester, J. A.; Handa, Y. P. *J. Am. Chem. Soc.* **1993**, 115, 281-284.
6. Wiebcke, M.; Emmer, J.; Felsche, J. *J. Chem. Soc., Chem. Commun.* **1993**, 1604-1606.
7. Ripmeester, J. A. *J. Am. Chem. Soc.* **1982**, 104, 209-210.
8. Saito, A.; Foley, H. C. *Microporous Mat.* **1993**, 3, 543-556.

9. Davis, M. E. *Acc. Chem. Res.* **1993**, 26, 111-115.
10. Wu, C.-G.; Bein, T. *Science*, **1994**, 264, 1757-1759.
11. Wenz, G. *Angew. Chem. Int. Ed. Engl.* **1994**, 33, 803-822.
12. Lee, F.; Gabe, E.; Tse, J. S.; Ripmeester, J. A. *J. Am. Chem. Soc.* **1988**, 110, 6014-6019.
13. Mak, T. C. W.; Tse, J. S.; Tse, C.; Lee, K.; Chong, Y. *J. Chem. Soc., Perkin Trans. 2*, **1976**, 1169-1172.
14. Branda, N.; Wyler, R.; Rebek, J. *Science* **1994**, 263, 1267-1268.
15. Timmerman, P.; Verboom, W.; van Veggel, F. C. J. M.; van Hoon, W. P.; Reinhoudt, D. N. *Angew. Chem. Int. Ed. Engl.* **1994**, 33, 1292-1295.
16. Timmerman, P.; Verboom, W.; van Veggel, F. C. J. M.; van Duynhoven, J. P. M.; Reinhoudt, D. N. *Angew. Chem. Int. Ed. Engl.* **1994**, 33, 2345-2348.
17. van Wageningen, A. M. A.; van Duynhoven, J. P. M.; Verboom, W.; Reinhoudt, D. N. *J. Chem. Soc., Chem. Commun.* **1995**, 1941-1942.
18. Huisman, B.-H.; Rudkevich, D. M.; van Veggel, F. C. J. M.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1996**, 118, 3523-3524.
19. Chapman, R. G.; Chopra, N.; Cochien, E. D.; Sherman, J. C. *J. Am. Chem. Soc.* **1994**, 116, 369-370.
20. Ripmeester, J. A.; Ratcliffe, C. I. *J. Phys. Chem.* **1995**, 99, 619-622.
21. Ripmeester, J. A.; Ratcliffe, C. I. *Proceedings of the 5th International Symposium on Cyclodextrins*, **1990**, 107-113.
22. Ripmeester, J.A.; Ratcliffe, C.I.; Enright, G.D.; Brouwer, E.B. *Acta Cryst.* **1995**, B51, 513-522.
23. Fraser, J. R.; Borecka, B.; Trotter, J.; Sherman, J. C. *J. Org. Chem.* **1995**, 60, 1207-1213.
24. Komoto, T.; Ando, I.; Nakamoto, Y.; Ishida, S. *J. Chem. Soc., Chem. Commun.* **1988**, 135-137.
25. Ripmeester, J. A.; Ratcliffe, C. I. *Anal. Chim. Acta* **1993**, 283, 1103-1112.
26. Ripmeester, J. A.; Ratcliffe, C. I. *J. Phys. Chem.* **1995**, 99, 619-622.
27. Breitmaier, E.; Voelter, W. *¹³C NMR Spectroscopy*; 2nd ed. Verlag Chemie: New York 1978.
28. Ripmeester, J.A.; Ratcliffe, C.I.; Enright, G.D.; Brouwer, E.B. *Acta Cryst.* **1995**, B51, 513-522.
29. Brouwer, E.B.; Enright, G.D.; Ripmeester, J.A. *Supramol. Chem.* **1996**, 7, 79-83.

7. Figures

FIGURE 1. 45.3 MHz ^{13}C -CP-MAS NMR spectrum of *p*-*tert*-butylcalix[4]arene-nitrobenzene-Xe. The spectrum was collected on a Bruker CXP-180 NMR spectrometer with a Bruker 7 mm spinning probe: 400 transients; recycle time: 4 s; $\pi/2$ pulse = 3.5 μs ; contact time = 3.5 ms; TD = 4K; 16K points; SW = 20 kHz; ν = 3.01 kHz.

FIGURE 2. 49.8 MHz ^{129}Xe CP NMR spectrum of *p*-tert-butylcalix[4]arene-nitrobenzene-Xe. (a): with MAS, 1219 transients; recycle time: 2 s; TD = 512; 20 Hz linebroadening; $\nu = 2.65$ kHz; (b): Static (with simulation), 2080 transients; recycle time: 3 s; TD = 256; (c): Fitted spectra. Both experimental spectra were collected on a Bruker CXP-180 NMR spectrometer with a Bruker 7 mm spinning probe: $\pi/2$ pulse = 3.5 μs ; contact time = 3.5 ms; 16K points; SW = 20 kHz.

FIGURE 3. The two *p*-*tert*-butylcalix[4]arene cavities formed by the 0.6:0.4 disordering in one of the calix *p*-*tert*-butylphenol units: cross-section in the *xy*-plane.

FIGURE 5. The Xe position in the *p*-*tert*-butylcalix[4]arene cavity. The smaller numbers indicate the distance (in Å) to Xe, and the larger numbers indicate the cavity dimensions at the level of the Xe; two values reflect disordering in the carbon. The starred letters indicate that the *p*-*tert*-butylphenol units are disordered in the C4A-NB structure: *B*: 57:43; *C*: 66:34.

FIGURE 4. Single-crystal XRD Structure of *p*-tert-butylcalix[4]arene-nitrobenzene-Xe.

FIGURE 6. 45.3 MHz $^{13}\text{CP-MAS}$ NMR spectrum of *p*-*tert*-butylcalix[4]arene-nitrobenzene- $^{13}\text{CH}_4$; x = spinning sidebands. The spectrum was collected on a Bruker CXP-180 NMR spectrometer with a Bruker 7 mm spinning probe: 2000 transients; recycle time: 4 s; $\pi/2$ pulse = 3.5 μs ; contact time = 3.5 ms; TD = 4K; 16K points; SW = 20 kHz; ν = 3.47 kHz.

Figure 7. 45.3 MHz ^{13}C CP-MAS NMR spectra of C4A-NB-ethane (*bottom*) and C4A-NB-ethylene (*top*); *inset*: C4A-NB-ethane $\delta = 110$ -124 ppm; ss = spinning sidebands. The spectra were collected on a Bruker CXP-180 NMR spectrometer with a Bruker 7 mm spinning probe: 1500 transients; recycle time: 4 s; $\pi/2$ pulse = 3.5 μs ; contact time = 3.5 ms; TD = 4K; 16K points; SW = 20 kHz; ν = 3.5 kHz; line broadening = 1 Hz.

FIGURE 8. 45.3 MHz ^{13}C CP-MAS NMR spectrum of C4A-NB-SO₂ (*bottom*); with dipolar-dephasing (*top*). The spectra were collected on a Bruker CXP-180 NMR spectrometer with a Bruker 7 mm spinning probe: 400 transients; recycle time: 4 s; $\pi/2$ pulse = 3.5 μs ; contact time = 3.5 ms; TD = 4K; 16K points; SW = 20 kHz; ν = 3.145 kHz.

Figure 9. ^{13}C CP-MAS NMR spectra of $\text{C}_4\text{A-NB}_x\text{-P}_{1-x}$ compounds prepared with an over pressure of propane: (A) 15 psi, $x = 1$ (B) 20 psi, (C) 100 psi, (D) 175 psi, $x = 0$; X = spinning sideband. Spectra (A) - (C) were collected on a Bruker CXP-180 NMR Spectrometer at 45.3 MHz with a Bruker 7 mm spinning probe: 800-3500 transients; recycle time: 4 s; $\pi/2$ pulse = 3.5 μs ; contact time = 3.5 ms; TD = 3K; 8K points; SW = 20 kHz; $\nu = 2.9\text{-}3.2$ kHz. Spectrum (D) was collected on a Bruker AMX-300 NMR Spectrometer at 75.5 MHz with a Bruker 5 mm spinning probe: 750 transients; recycle time: 3 s; $\pi/2$ pulse = 3.9 μs ; contact time = 3.0 ms; TD = 6K; 16K points; SW = 30 kHz; $\nu = 4.62$ kHz.

Figure 10. The β -*p*-tert-butylcalix[4]arene-nitrobenzene_{0.64}-propane_{0.36} structure showing only the majority guest.

FIGURE 11. Variable temperature 46.1 MHz ^2H NMR spectra of β -*p*-*tert*-butylcalix[4]arene-nitrobenzene- d_5 -propane. The spectra were collected on a Bruker AMX-300 spectrometer with a Bruker static probe with a 5 mm coil and a quadrupolar echo pulse sequence: 200 transients; recycle time: 8-15 s; $\pi/2$ pulse: 2.6 μs ; sweep width: 1.25 MHz; echo delay: 35 μs ; 0.2 kHz line broadening; TD = 2K; 1K points.

8. Appendix: X-Ray Structural Data

A1. Final Positional and Equivalent Isotropic Parameters ($\text{\AA}^2$) for C4A-NB_{0.83}-Xe_{0.17}.

Atom	x	y	z	B_{iso}^a
O1	0.23471 (23)	0.40873	0.22872 (9)	2.76 (11)
C11	0.1863 (3)	0.4395 (4)	0.27328 (15)	2.30 (15)
C12	0.2066 (3)	0.5375 (4)	0.29243 (15)	2.45 (16)
C13	0.1518 (3)	0.5684 (4)	0.33532 (15)	2.51 (17)
C14	0.0771 (3)	0.5050 (4)	0.35915 (15)	2.45 (15)
C15	0.0618 (3)	0.4053 (4)	0.33918 (15)	2.45 (16)
C16	0.1161 (3)	0.3711 (4)	0.29646 (15)	2.25 (15)
C17	0.0158 (3)	0.5470 (4)	0.40439 (15)	2.84 (16)
C18	0.2874 (3)	0.6109 (4)	0.26903 (15)	2.74 (17)
CT11	0.0910 (4)	0.5789 (5)	0.44616 (15)	3.83 (20)
CT12	-0.0471 (4)	0.6466 (5)	0.38764 (15)	3.71 (20)
CT13	-0.0691 (4)	0.4726 (5)	0.42427 (15)	3.80 (20)
O4	0.30297 (23)	0.2155 (3)	0.23079 (10)	2.73 (11)
C41	0.2731 (3)	0.1622 (4)	0.27343 (14)	2.21 (14)
C42	0.1728 (3)	0.1803 (4)	0.29544 (14)	2.16 (14)
C43	0.1439 (3)	0.1185 (4)	0.33615 (16)	2.31 (16)
C44	0.2130 (3)	0.0441 (4)	0.35629 (15)	2.35 (16)
C45	0.3140 (3)	0.0333 (4)	0.33425 (15)	2.41 (16)
C46	0.3445 (3)	0.0909 (4)	0.29312 (15)	2.28 (15)
C47	0.1831 (3)	-0.0256 (4)	0.40115 (16)	30.1 (17)
C48	0.0948 (3)	0.2619 (4)	0.27577 (15)	2.39 (16)
CT41	0.0667 (4)	-0.0114 (5)	0.41814 (20)	4.43 (23)
CT42	0.1950 (4)	-0.1398 (5)	0.38621 (19)	4.01 (21)
CT13	0.2599 (4)	-0.0031 (5)	0.44469 (17)	4.10 (23)
O3	0.50782 (22)	0.2770 (3)	0.22549 (10)	2.69 (11)
C31	0.5576 (3)	0.2496 (4)	0.27060 (14)	2.16 (14)
C32	0.5368 (3)	0.1534 (4)	0.29227 (15)	2.21 (15)
C33	0.5914 (3)	0.1288 (4)	0.33599 (16)	2.60 (17)
C35	0.6816 (3)	0.2902 (4)	0.33559 (15)	2.42 (16)
C36	0.6292 (3)	0.3196 (4)	0.29170 (15)	2.20 (15)
C38	0.4564 (3)	0.0764 (4)	0.27050 (16)	2.57 (17)
C37	0.7190 (3)	0.1574 (4)	0.40688 (14)	3.3 (3)
C34	0.6652 (5)	0.1948 (5)	0.35843 (18)	2.19 (22)
CT31	0.7956 (5)	0.2416 (5)	0.42619 (24)	5.6 (4)
CT32	0.7823 (4)	0.0577 (5)	0.39628 (23)	4.0 (3)
CT33	0.6331 (4)	0.1355 (6)	0.44661 (22)	4.5 (4)
C37A	0.7282 (7)	0.1756 (8)	0.4079 (3)	3.7 (91)
C34A	0.6627 (12)	0.1971 (13)	0.3604 (4)	3.5 (22)
CT34	0.8478 (8)	0.1727 (11)	0.3948 (5)	5.0 (7)
CT35	0.6946 (12)	0.0707 (9)	0.4302 (6)	6.6 (10)
CT36	0.7077 (10)	0.2618 (10)	0.4464 (4)	4.0 (7)

Table A.1 *continued*

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> _{iso} ^a
O2	0.43829 (23)	0.4727 (3)	0.22582 (10)	2.88 (12)
C21	0.4710 (3)	0.5243 (4)	0.26915 (15)	2.44 (16)
C22	0.5722 (3)	0.5076 (4)	0.28991 (15)	2.47 (15)
C23	0.6010 (3)	0.5651 (4)	0.33140 (16)	2.59 (16)
C25	0.4317 (3)	0.6513 (4)	0.33176 (16)	2.76 (17)
C26	0.3995 (3)	0.5958 (4)	0.29002 (16)	2.50 (16)
C28	0.6486 (3)	0.4258 (4)	0.26920 (15)	2.45 (16)
C27	0.5783 (4)	0.7055 (5)	0.39953 (22)	2.8 (3)
C24	0.5360 (7)	0.6416 (7)	0.3552 (3)	2.1 (3)
CT21	0.6306 (8)	0.6327 (7)	0.4379 (3)	5.0 (6)
CT22	0.4851 (5)	0.7637 (8)	0.4243 (4)	6.5 (7)
CT23	0.6616 (7)	0.7839 (6)	0.3806 (3)	5.0 (5)
C27A	0.5572 (7)	0.7045 (7)	0.3974 (3)	3.7 (4)
C24A	0.5323 (12)	0.6353 (10)	0.3520 (5)	3.7 (8)
CT24	0.6634 (9)	0.6703 (11)	0.4211 (6)	6.3 (9)
CT25	0.4668 (10)	0.6946 (10)	0.4361 (5)	5.1 (7)
CT26	0.5662 (10)	0.8179 (8)	0.3803 (4)	5.0 (6)
O5	0.1014 (3)	0.2484 (4)	0.44679 (19)	6.6 (3)
O6	0.1395 (3)	0.3290 (4)	0.51527 (17)	5.56 (21)
N1	0.1608 (3)	0.3010 (3)	0.47340 (20)	3.15 (22)
CN1	0.3900 (4)	0.3334 (4)	0.38417 (11)	3.1 (3)
CN2	0.4602 (3)	0.3927 (3)	0.41306 (14)	4.7 (3)
CN3	0.43197 (24)	0.4212 (3)	0.46172 (13)	4.9 (3)
CN4	0.3335 (3)	0.3905 (3)	0.48148 (9)	3.43 (19)
CN5	0.26337 (21)	0.33122 (25)	0.45260 (12)	2.89 (17)
CN6	0.2916 (3)	0.3027 (3)	0.40394 (12)	4.56 (25)
Xe	0.3758 (3)	0.3447 (3)	0.38914 (13)	5.98 (17)

^a $B_{\text{iso}} = 8/3\pi^2 \sum \sum U_{ij} a_i^* a_j^* (a_i^* a_j^*)$; B_{iso} is the mean of the principal axes of the thermal ellipsoid. ESD's refer to the last digit printed.

A2. Final Positional and Equivalent Isotropic Parameters ($\text{\AA}^2$) for C4A-NB_{0.64}-PROP_{0.36}.

Atom	x	y	z	B_{iso}^a
O1	0.6893 (3)	0.6174 (3)	0.06123 (23)	4.38 (17)
C2	0.7336 (4)	0.5018 (4)	-0.0777 (4)	3.93 (23)
C6	0.5651 (4)	0.5837 (4)	-0.0777 (3)	3.91 (23)
C5	0.5398 (4)	0.5277 (4)	-0.1709 (4)	4.3 (4)
C4	0.6073 (4)	0.4598 (4)	-0.2154 (4)	4.5 (3)
C1	0.6601 (4)	0.5678 (4)	-0.0344 (4)	3.80 (23)
C8	0.8398 (4)	0.4866 (4)	-0.0335 (4)	4.22 (24)
C3	0.7031 (4)	0.4473 (4)	-0.1689 (4)	4.15 (24)
C7	0.5801 (5)	0.3947 (6)	-0.3156 (5)	6.3 (3)
CT1	0.6627 (6)	0.4106 (7)	-0.4001 (6)	8.2 (5)
CT2	0.5725 (6)	0.2808 (6)	-0.2849 (6)	7.2 (4)
CT3	0.4774 (7)	0.4284 (8)	-0.3634 (5)	10.0 (5)
NNB	0.749 (3)	0.7658 (14)	-0.6294 (8)	6.9 (20)
ONB1	0.746 (4)	0.6821 (18)	-0.6752 (9)	9.5 (21)
ONB2	0.754 (3)	0.8491 (18)	-0.6757 (15)	18.0 (34)
CNB1	0.7453 (19)	0.7663 (9)	-0.5132 (8)	3.7 (27)
CNB2	0.739 (3)	0.6734 (11)	-0.4597 (10)	7.3 (22)
CNB3	0.736 (3)	0.6739 (19)	-0.3499 (10)	23.3 (**)
CNB4	0.739 (3)	0.7672 (24)	-0.2953 (8)	4.4 (33)
CNB5	0.745 (3)	0.8601 (19)	-0.3505 (15)	16.5 (58)
CNB6	0.7484 (21)	0.8596 (11)	-0.4602 (15)	7.2 (23)
CP1	0.755 (12)	0.713 (3)	-0.258 (3)	4.5 (13)
CP2	0.767 (13)	0.677 (4)	-0.373 (4)	12.0 (37)
CP3	0.787 (4)	0.771 (6)	-0.445 (3)	3.4 (11)

^a $B_{\text{iso}} = 8/3\pi^2 \sum \sum U_{ij} a_i^* a_j^* (a_i^* a_j^*)$; B_{iso} is the mean of the principal axes of the thermal ellipsoid. ESD's refer to the last digit printed.

CHAPTER 7: *p*-*tert*-Butylcalix[4]arene Compounds with Nitrogen-Containing Guests

1. Introduction	269
2. <i>p</i> - <i>tert</i> -Butylcalix[4]arene-Guest (Guest = Pyridine, Benzene)	271
2.1. ^{13}C CP-MAS NMR Spectroscopy	273
2.2. ^2H NMR Spectroscopy	274
2.3. ^{15}N NMR Spectroscopy	282
2.4. Single Crystal X-Ray Diffraction	285
3. <i>p</i> - <i>tert</i> -Butylcalix[4]arene + Amines	291
4. Summary	298
5. References	299
6. Figures	303
7. Appendix	321

1. Introduction

Chemists have traditionally viewed the molecular structure of a molecule as embodying all of its chemical and physical properties.¹⁻⁴ However, structural and characteristic properties of assemblies of molecules are distinct from those expected from individual molecules—this distinction forms the basis for supramolecular chemistry. Lehn has made the analogy that “supramolecules are to molecules and the intermolecular bond what molecules are to atoms and the covalent bond.”^{5,6} The formation of a crystalline compound represents in a sense the perfect supramolecule where non-bonding interactions such as hydrogen bonds, van der Waals, and electrostatic interactions direct molecular recognition and self-assembly of millions of structural units. Crystal formation via these interactions is to the supramolecular chemist what covalent bond formation is to the traditional synthetic chemist.

This analogy between molecular and supramolecular may remain somewhat esoteric if not for the enormous potential for producing complex molecular assemblies from

relatively simple building blocks. Successful synthesis of nano-, meso-, and macro-pore structures is predicated on highly specific molecular recognition between the template (often an alkyl ammonium organic molecule) and the inorganic skeletal framework.⁷⁻¹⁰ To this end, a tremendous range of structures and devices can be prepared including nanoscale sensors, motors, and electronics. The recent ability to mimic marine shell structures involves the judicious choice of supramolecular building blocks and synthetic conditions.¹¹⁻¹⁴

Solid-state or crystal engineering seeks to identify and categorize the range of non-bonding interactions possible in supramolecular chemistry, and employ the resulting “tool box” of interaction motifs of synthons⁴ to rationally design new supramolecular architectures. Desiraju summarized over 35 supramolecular synthons, including aromatic interactions (herringbone and stacking) and hydrogen-bonding (NH•••O, OH•••O, NH•••N, CH•••O).

Crystal engineering and template-based syntheses rely on molecular recognition of two or more components, and is key to the success of these endeavours. The calixarene system provides a relatively simple and flexible cavity which includes and enclathrates guest molecules with varying degrees of selectivity. Probing the interactions present in these simple guest-host system furthers the understanding of molecular recognition.

This chapter focuses on the supramolecular chemistry of calixarenes and nitrogen-containing guests. *p*-*tert*-Butylcalix[4]arene (C4A) forms 1:1 compounds with both pyridine and benzene in which the guests occupy very similar orientations in the two crystal structures, but possess significantly different guest dynamics. These two compounds allow for an elegant probe of nitrogen-based guest interactions. The interactions of alkylamines in solution was first described by Gutsche in 1985.¹⁵⁻¹⁷ Proton transfer from the phenolic hydroxyl hydrogen to the amine acceptor nitrogen (sitting *exo*

to the cavity), followed by inversion of the cavity gives a complex in which the cationic guest sits inside the anionic host. Since then, several crystal structures have suggested the existence of proton transfer in the solid-state. This chapter continues with solid-state NMR spectroscopic and X-ray diffraction studies of C4A with amines. Interestingly, amines behave in one of two ways: (1) as a classic inclusion compound guest in which the amine is inside (*endo*) a 4-fold symmetric cavity, and (2) as a proton-transfer acceptor in which the amine may be inside or outside (*exo*) the cavity. These behavioral patterns arise from a competition between the amine's function dictated by its geometry (steric) or its basicity (electronic).

2. *p*-*tert*-Butylcalix[4]arene-Guest (Guest = Pyridine (C4A-Py), Benzene (C4A-Bz))

^1H NMR studies of C4A show that the host conical structure inverts in solution. The inversion process is detected by the coalescence of the host methylene ^1H NMR resonances upon heating; the barrier to inversion is solvent-dependent.¹⁵ C4A inversion in pyridine occurs with $\Delta G^\ddagger = 57.3 \text{ kJ mol}^{-1}$ whereas in benzene the barrier to inversion is $\Delta G^\ddagger = 61.9 \text{ kJ mol}^{-1}$. The lower inversion barrier in pyridine arises from disruption of the ring hydrogen-bonding network by the solvent, and illustrates some different behavior between these similarly-shaped molecules.

Pyridine is a common solvent for calix[*n*]arenes, and crystallizes both inside (*endo*) and outside (*exo*) the calix cavity. *p*-*tert*-Butylcalix[7]arene, when crystallized from pyridine, shows a structure ($R = 0.096$) in which two pyridine molecules sit in the crystal lattice while a third pyridine guest hydrogen-bonds to one of the phenolic OH groups at a distance $d_{\text{O}\cdots\text{N}} = 2.63 \text{ \AA}$ and angle $\angle\text{OH}\cdots\text{N} = 159^\circ$ (Figure 1b).¹⁸ Four of the seven host *t*-butyl groups are disordered. Attractive $\text{Me}_{\text{host}}\cdots\pi_{\text{guest}}$ interactions between the *t*-butylmethyl (E) and a clathrated pyridine (I) is inferred from the separation $d_{\text{C}\cdots\text{C}} = 3.83$

Å; due to the disordering of the pyridine nitrogen over the six guest atomic positions, it is unclear whether this is a CH₃-π or a CH...N interaction.

The first *p*-tert-butylcalix[8]arene (C8A) XRD study was of C8A crystallized from pyridine, although no pyridine was incorporated.¹⁹ Attempts to obtain a C8A compound with Cu(pyridine)_x, led to the isolation of C8A-Py₈ (Figure 1c; *R* = 0.096).²⁰ Eight pyridine molecules are associated with each octamer which displays a conformation analogous to two C4A units in the partial cone configuration. Two of the eight guest shows a OH...N hydrogen-bond interaction $d_{O...N} = 2.71$ Å which breaks the phenolic OH hydrogen bonding network; the remaining guests sit in interstitial sites. Disorder is present in both the host *t*-butyl groups and the interstitial pyridine guests.

A pyridine guest may play two roles in large calixarene cavities: (1) as an interstitial or clathrate guest, and (2) as an acceptor for a phenolic OH...N bond. The smaller conical C4A cavity differs from the above two cavities in that it presents a smaller void space. Furthermore, guests typically occupy the C4A cavity in the *endo* arrangement.

1,3-Crown-5-bridged C4A crystallizes from pyridine with one solvent molecule in the calix cavity (Figure 1a).²¹ The pyridine nitrogen atom was unambiguously determined, and the structure refines to *R* = 0.12. The crown ether, attached to the calix via two phenolic oxygens opposite in the calix cone, causes an elliptical deformation of the calix cavity; the pyridine plane lies along the major axis of the ellipse defined by the unconnected *t*-butylphenol units. The pyridine nitrogen sits in a pocket defined by two methyl groups: one from a *t*-butyl group of the calix and the other from a *t*-butyl group of an adjacent calix. The distance from the nitrogen to the methyl hydrogen $d_{H...N} = 2.58$ Å suggests a hydrogen-bond type of interaction; no angular information for this interaction is given. The energy of this H-bond interaction was estimated to be 8.2 kJ mol⁻¹. Calculation of the total potential energy as a function of pyridine rotation angle about its *C*₂ axis led to

the introduction of an attractive $\text{Me}_{\text{host}}-\pi_{\text{guest}}$ interaction between the methyl groups of the host and the aromatic guest.

2.1 ^{13}C CP-MAS NMR Spectroscopy

Pyridine (Py) and benzene (Bz) both form 1:1 compounds with C4A. The ^{13}C CP-MAS NMR spectra of C4A-Py and C4A-Bz (Figure 2) show that both possess 4-fold symmetry with one guest per C4A cavity. The dipolar-dephasing (DD) NMR experiment²² establishes that both guests are mobile. The change in chemical shift from liquid to enclathrated guest (the complexation-induced shift, CIS) is not dramatic for the benzene carbons and fails to inform on the orientation of the guest inside the host cavity. With C4A-PY, CIS values are significant for guest carbons C-3 and C-2, and suggest that these carbons sit deep in the calix cavity. The ^{13}C CP-MAS NMR spectra of the two calix compounds are similar to that of the majority of 4-fold symmetric C4A-guest structures.

TABLE 1. Guest Chemical Shifts (in ppm) in C4A-Guest compounds.

Guest	Carbon	Calix ^a	Solution ^b	CIS ^c
Benzene	aromatic	126.5 ^d	128.4	-1.9 ^d
Pyridine	C-3	121.0	124.2	-3.2
	C-4	133.4	136.2	-2.8
	C-2	148.1	149.6	-1.5
3,5-dimethylpyridine	Me	12.8	16.0	-3.2
	C-3	131.1	130.4	+0.7
	C-4	132.8	134.9	-2.1
	C-2	<i>d</i>	145.5	<i>d</i>
2,6-dimethylpyridine	Me	20.4	22.3	-1.9
	C-3	117.1	117.9	-0.8
	C-4	135.2	134.3	+0.9
	C-2	157.3	155.4	+1.9

^a referenced to hexamethylbenzene (δ 16.9 ppm)

^b from reference 23. CDCl_3 or collected on Bruker MSL300 in CDCl_3

^c CIS = complexation induced shift = δ (calixarene) - δ (solution)

^d carbon resonance lies under calix aromatic lines.

The ^{13}C CP-MAS NMR spectra of two C4A compounds with dimethyl-substituted pyridine guests (Figure 3) show that both compounds are 4-fold symmetric. The change in guest methyl CIS values provides the best data for interpretation of the guest position in the cavity: the methyl CIS value for 3,5-dimethylpyridine is greater than the comparable value for the 2,6-dimethyl isomer and suggests that the former occupies a site similar to that of pyridine. The steric bulk of the methyl groups close to the nitrogen of 2,6-dimethylpyridine may lead to a different positioning of the guest in the cavity. The DD ^{13}C NMR spectra suggest that both guests are dynamic.

2.2 Variable Temperature ^2H NMR Spectroscopy

Guest motions ($\kappa = 10^3$ - 10^8 Hz) in host cavities may be characterized by ^2H NMR spectroscopy. Molecular reorientation of benzene in the solid state is a historical landmark in the development of solid-state NMR spectroscopy. In 1950, Andrew showed using the method of second moments (^1H NMR) that benzene reorients within its plane about a 6-fold axis.²⁴⁻²⁵ Benzene clathrates are well known²⁶⁻³¹ and the guest typically shows planar reorientation about the 6-fold axis.

2.2.1 C4A-Benzene- d_6

The variable temperature (VT) ^2H NMR spectra of C4A-Bz- d_6 are shown in Figure 4 and the lineshape components are tabulated in Table 2. The 77K lineshape is distorted by molecular reorientation in the intermediate motional regime ($\kappa = 10^4$ - 10^7 Hz). The guest motion reaches a fast motion limit (FML; $\kappa = 10^8$ Hz) by 109K, after which the spectra narrow slightly but retain the axial pattern to 291K. The static lineshape of pure benzene- d_6 is known, as well as the static lineshapes of benzene- d_6 in a variety of crystalline environments (Table 3). The FML lineshape (109K) is axially symmetric, with

the quadrupolar coupling constant $\chi = e^2qQ/h = 42.3$ kHz; the splitting is just slightly less than a four-fold reduction from the static line ($\chi^{77} = 183 \div 4 = 45.8$ kHz).

TABLE 2. ^2H Lineshape components of C4A-Bz- d_6 as a function of temperature; values in kHz.^a

T (K)	$ v_{xx} $	$ v_{yy} $	$ v_{zz} $	χ	η
77	31.2	32.2	63.4	42.3	0.016
98	31.3	32.2	63.4	42.3	0.014
109	31.4	32.0	63.4	42.3	0.009
118	31.4	32.0	63.4	42.3	0.009
138	31.4	32.0	63.4	42.3	0.009
156	31.1	32.2	63.4	42.3	0.026
173	31.3	32.1	63.4	42.3	0.019
195	31.2	32.2	63.4	42.3	0.016
291	30.2	31.2	61.2	40.8	0.016

^aUncertainties: $v_{ii} = \pm 0.5$ kHz; $\chi = \pm 0.7$ kHz; $\eta = \pm 0.007$.

TABLE 3. The static quadrupole coupling constant (χ) and static asymmetry parameter (η) for benzene in different crystalline environments.

system	χ (kHz)	η	ref.
C_6D_6	180.7 ± 1.5	0.041 ± 0.007	33
C_6D_6	183	0.04	26
$(\eta^6\text{-C}_6\text{D}_6)\text{Cr}(\text{CO})_3$	183	0.05	28
$\text{C}_6\text{D}_6 \cdot 1,3\text{-cyclohexanedione}$	181	0.04	26
$2 \text{ C}_6\text{D}_6 \cdot \text{Cd}(\text{NH}_3)_2\text{Ni}(\text{CN})_4$	181.6	0.036	27
$2 \text{ C}_6\text{D}_6 \cdot \text{Cd}(\text{NH}_2\text{C}_2\text{H}_4\text{NH}_2)\text{Ni}(\text{CN})_4$	184.4	0.047	27

To explain both the 4-fold reduction in χ as well as the axial symmetry, several guest motions are considered. First, benzene in-plane rotation about its 6-fold symmetry axis is likely.^{26-31,33} Rapid in-plane rotation averages the electric field gradient (EFG) tensor components along the x - and z -axes ($V_{xx} = -132$; $V_{zz} = +274$ kHz) to a value of $V_{xx}' = V_{zz}' = 71$ kHz whereas the component along the y -axis ($V_{yy} = V_{yy}' = -142$ kHz) is invariant; this reduces the static pattern by a factor of two.

Benzene rotation about the calix 4-fold symmetry axis may be possible, as guest rotation about the calix 4-fold axis is often observed for guests in the symmetric C4A cavity. Four-fold rotation perpendicular to the hexad rotation axis causes a further reduction in the linewidth by a factor of two, and the pattern remains axial. The 6-fold motionally-averaged EFG tensor component along the *z*-axis ($V_{zz}' = 71$ kHz) is invariant under 4-fold rotation while the components along the *x*- and *y*-axes will average such that $V_{xx}'' = V_{yy}'' = -35.5$ kHz and $\chi = 47.3$ kHz.

These two motional models account for the FML axial lineshape and for most of the reduction of the FML χ from the static χ . Additional reduction in the effective quadrupole coupling constant at 109K is accounted for by guest motion that occurs off the host 4-fold axis, according to:

$$\chi_{obs} = \left(\chi_{|6+4|}\right)^{\frac{1}{2}}(3\cos^2\theta - 1) \quad (1)$$

where $\chi_{obs} = \chi$ at 109K. The non-axial component of the motion will introduce a slight asymmetry η ($\eta = |\Delta v_{yy} - \Delta v_{xx}| / \Delta v_{zz}$) and the motionally-averaged χ will be proportional to the angle $\perp$ to the benzene 6-fold motion and the host symmetry axis (Figure 5).

According to equation (1), θ is calculated to be $15^\circ \pm 3^\circ$; the angle θ determined by XRD is $\theta = 12^\circ$, and illustrates nicely the complementarity of the NMR spectroscopic and diffraction techniques. The lineshape narrows slightly as the temperature increases to 291K ($\chi = 40.8 \pm 0.7$ kHz; $\eta = 0.016 \pm 0.008$) and indicates that the benzene libration angle increases to $\theta = 18^\circ \pm 3^\circ$.

Figure 5 illustrates the motional model, and shows the simulated and 109K observed spectra. Benzene sits tilted off the host C_4 axis by an angle of $\theta = 15^\circ$. To simulate the spectrum at 109K, the averaged EFG tensor components of the in-plane FML were

calculated and subjected to 4-fold rotation at $\kappa = 10^8$ Hz (where the in-plane guest and C_4 -host rotational axes are perpendicular).

In conclusion, the motion of the benzene in the C4A cavity consists of in-plane 6-fold reorientation plus 4-fold rotation about the calix symmetry axis. These motions are present at 77K and reach the FML by 109K.

2.2.2 C4A-Pyridine- d_5

Two papers examining the dynamics of pyridine in a tri-*ortho*-thymotide (TOT) host have been published recently.^{32,35} Pyridine undergoes restricted in-plane rotation at lower temperatures followed by an additional 2-fold rotation about the molecular axis of the guest. The second study also reports the in-plane rotation of benzene in the TOT host.³⁵

The ^2H NMR spectra of C4A-Py- d_5 from 77-296K (Figure 6) differ from the C4A-Bz- d_6 spectra as well as from the spectra for both pyridine and benzene in TOT. Three types of motion have been considered in the analysis of the ^2H NMR spectra. The static spectrum of pure pyridine- d_5 is a Pake doublet with $\chi = 182.5 \pm 1$ kHz; $\eta = 0.039$.³² The 77K spectrum of C4A-Py- d_5 is not static however, but is indicative of 2-fold motion (180° flip) at—or just above—the fast motion limit: $\chi = 96.9 \pm 1.4$ kHz; $\eta = 0.75 \pm 0.01$; this motion will be designated motion I. As temperature increases above 77K, the lineshape changes and the linewidth decreases until the fast motion limit of the second motion (II) occurs at 166K. Further narrowing of the inner feature occurs as the temperature increases without any change in the shape of the pattern; this is motion III.

The spectra above 166K (motion III) are characterized by two component lines: an axially symmetric outer set of features (line A) and a central intensity of axial symmetry which narrows as temperature increases to 296K (line B). The spectral intensities of the two lines (A:B) integrate in a 4:1 ratio over these temperatures, and suggests that one C-

D bond is unique under these motions, while the four remaining C-D bonds undergo a motion which causes them to be equivalent. Two motions may account for these lines:

- (1) two crystallographically inequivalent pyridine guests (as in the larger calixarene-pyridine compounds) *or*
- (2) only one pyridine guest oriented in the cavity such that molecular motion causes four deuterons to be equivalent and the fifth to be unique.

From the ^{13}C CP-MAS NMR spectrum of C4A-Py (Figure 2), it is clear that there is only one crystallographically unique pyridine, and this evidence favours the latter scenario.

Motion I: 2-Fold Molecular Reorientation of Pyridine. The lineshape at 77K is typical of 2-fold reorientation about the pyridine 2-fold molecular axis. For the *ortho*- and *meta*- deuterons, this motion causes the reorientation of the V_{xx} and V_{zz} components of the EFG tensor which lie in the same plane as the C_2 symmetry axis, but no reorientation of the V_{yy} component of the EFG which is perpendicular to the plane (Figure 7, *top left*). For C4A-Py- d_5 , the frequency of V_{yy} , $\Delta\nu_{yy}$, at the 2-fold fast motion limit is expected to be the same as $\Delta\nu_{yy}$ of the pure pyridine- d_5 static spectrum; comparison of the two values show that C4A-Py- d_5 $\Delta\nu_{yy}$ at 77K is smaller than that of the static lineshape of pure pyridine- d_5 (128 kHz vs. 142 kHz). It is likely that the pattern is reduced in width by librational motion about the 2-fold flip axis, and a librational angle of $\phi = 15 \pm 2^\circ$ is calculated according to:

$$\chi_{obs} = (\chi_{static})^{\frac{1}{2}} (3 \cos^2 \phi - 1) \quad (2)$$

A π reorientation of pyridine- d_5 about its C_2 molecular axis should have no effect on the spectrum of the *para*-deuteron, and it will retain its static pattern. The 77K spectrum shows a doublet of very weak intensity with $\Delta\nu_{zz} = 252 \pm 3$ kHz which is narrowed from the static $\Delta\nu_{zz}$ of the pure pyridine- d_5 ($\Delta\nu_{zz} = 273.6 \pm 1$ kHz). Use of equation (2) gives an

angle of $\phi = 13 \pm 2^\circ$ for libration that the *para*-deuteron undergoes with the 2-fold molecular reorientation.

TABLE 4. ^2H NMR lineshape components of C4A-Py- d_5 as a function of temperature (values in kHz): second major column: *meta*-, *ortho*-deuterons; third major column: *para*-deuteron.^a The angle between the (2-fold motionally-averaged) *para*-C-D bond and the 4-fold C4A axis ($\pi/2$ motional axis) is β .^b

T /K	$ \Delta v_{xx} $	$ \Delta v_{yy} $	$ \Delta v_{zz} $	χ	η	$ \Delta v_{xx} $	$ \Delta v_{yy} $	$ \Delta v_{zz} $	χ	η	β
77	19.0	127.6	145.4	96.9	0.75	126	126	252 $\pm$ 3	168	0.0	-
166	39.8	43.0	83.8	55.9	0.04	9.2	9.3	18.6	12.4	0.0	51.8
188	40.5	43.5	85.0	56.7	0.04	7.5	7.5	14.9	9.9	0.0	52.4
194	41.0	44.0	85.0	56.7	0.04	6.6	6.6	13.3	8.9	0.0	52.6
210	41.0	44.8	85.4	56.9	0.04	5.6	5.6	11.4	7.6	0.0	52.9
232	40.5	44.7	84.9	56.6	0.05	4.9	4.9	9.0	6.0	0.0	53.3
296	38.6	41.5	80.1	53.4	0.04	4.4	4.4	8.8	5.9	0.0	53.3

^aUncertainties: $\Delta v_{ii} = \pm 1.0$ kHz; $\chi = \pm 1.4$ kHz; $\eta = \pm 0.01$; $\beta = \pm 0.5^\circ$.

^b β is calculated with the effective $\chi_{x\text{-flip}} = 168$ kHz; $\eta = 0.0$ according to equations (3-5), and is illustrated in Figure 7.

The 77K spectrum is simulated by employing a 2-fold molecular reorientation at the FML and adding the *ortho*-, *meta*-deuteron spectrum and the *para*-deuteron spectrum in an intensity ratio of 4:1 using a line-broadening component of 3 kHz (Figure 7). The gross features of the 2-fold FML simulated spectra match those of the 77K observed spectrum, but some differences exist: First, the outer features (the shoulders) of the simulated spectrum are more pronounced and have greater intensity than in the observed spectrum, and may arise from the introduction of the calix 4-fold rotational motion in addition to the molecular 2-fold reorientation at the FML. Secondly, the presence of the central intensity in the 77K spectrum may arise from the *para*-deuteron undergoing 4-fold rotation at some intermediate rate. In addition, the model assumes that the *ortho*- and *meta*- C-D bonds make an angle of 60° with the pyridine 2-fold rotation axis and are thus equivalent. Deviations from this model (due to the presence of the nitrogen in the ring)

may result in the loss of intensity and sharpness of the outer shoulders. Finally, the width of the 77K spectral shoulders is narrower than in the simulated spectrum, which employs the parameters of the pure pyridine-*d*₅ static lineshape as its initial values. The reduction of the 77K linewidth is due to a non-axial motional component, as discussed above.

It is interesting to compare the 2-fold molecular reorientation of pyridine-*d*₅ in the TOT cage and the C4A cavity. In the latter, the 180° reorientation develops *after* the guest has reached the fast motion limit for a restricted in-plane motion. This sequence of motions is not observed for pyridine in the C4A cavity (which has only the *C*₂ reorientation), and is reflected in differences in the 180°-flip FML spectra: C4A-Py-*d*₅ χ = 97 kHz, η = 0.75; TOT-Py-*d*₅ χ = 80 kHz, η = 0.78.³² The C4A-Py-*d*₅ 77K spectrum arises only from 2-fold flips with a slight off-axis wobble, and not from any other type of motion.

Motion II: Pyridine 4-Fold Reorientation About the C4A Symmetry Axis. As the temperature increases from the 2-fold fast motion limit at 77K, the spectra develop two axial features: line A which is wide, and line B which is narrow. Motion II reaches the FML at 166K. From the intensity ratio of A:B = 4:1, line B is due to the *para*-deuteron while line A arises from the remaining guest deuterons. The inner lineshape (line B) changes the most drastically from the 2-fold flip FML at 77K: it remains axial, but is narrowed significantly to χ = 12.4 kHz from the effective quadrupolar coupling constant of the π -flip of the *para*-deuteron (χ = 168 kHz). The axial characteristic of both lines is consistent with a 4-fold reorientation of the guest in the 4-fold symmetric cavity. The uniqueness of the *para*-deuteron eliminates the possibility of an in-plane rotational model—regardless of whether restricted or unrestricted.³²

To account for the narrowing feature of the *para*-deuteron spectrum, a motional model which orients the pyridine in the cavity so that the *para*-deuteron is near the magic

angle $\theta = 54.7^\circ$ (the angle θ which causes $3\cos^2\theta - 1 = 0$) was selected. A 4-fold reorientation of pyridine about the calix symmetry axis at this angle causes the spectrum of the *para*-deuteron to be both axial and nearly isotropic.

The reduction in the *para*-deuteron component of the ^2H NMR spectrum scales as a function of the angle θ as in equations (3-5):

$$V_{xx}'' = \frac{1}{2}[(\cos^2 \theta)V_{xx}' + V_{yy}' + (\sin^2 \theta)V_{zz}'] \quad (3)$$

$$V_{yy}'' = \frac{1}{2}[(\cos^2 \theta)V_{xx}' + V_{yy}' + (\sin^2 \theta)V_{zz}'] \quad (4)$$

$$V_{zz}'' = (\sin^2 \theta)V_{xx}' + (\cos^2 \theta)V_{zz}' \quad (5)$$

where θ is the angle between the guest 2-fold and the compound 4-fold axes; V_{ii}' are the 2-fold FML EFG tensor components in kHz and V_{ii}'' are the observed values in kHz. At $T = 166\text{K}$, $V_{xx}'' = V_{yy}'' = -9.3\text{ kHz}$; $V_{zz}'' = 18.6\text{ kHz}$ and $\theta = 51.8^\circ \pm 0.5^\circ$. The angle θ establishes the pyridine orientation in the calixarene cavity (Figure 4); since there is no pyridine in-plane rotation, this also establishes a unique pyridine nitrogen atom position, which for the XRD analysis, eliminates the common problem of pyridine nitrogen disordering over the six aromatic atomic positions. In the single-crystal XRD structural determination of TOT-pyridine, inability to locate the pyridine nitrogen unambiguously was problematic.^{32,35} As the temperature increases from 166 to 296K, the *para*-deuteron lineshape narrows (Table 4, Figure 7) and corresponds to a tilting of pyridine further off the calix C_4 axis (motion III). The angle θ calculated at 296K is $53.3^\circ \pm 0.5^\circ$.

Four-fold motion of the pyridine *ortho*- and *meta*-deuterons about the calix symmetry axis in addition to rapid 2-fold flips about the guest molecular axis gives rise to the axial lineshape of line A. To calculate the *o*-, *m*-deuteron lineshape at the 4-fold FML, it is necessary to use the EFG tensor components as they are averaged under the FML 2-

fold pyridine reorientation (because the guest 2-fold the host 4-fold axes do not coincide) using equations (3-5). Figure 7 (*top right*) shows the averaged V_{zz} component of the *ortho*-deuterons (which are equivalent under fast 2-fold reorientation): V_{zz} lies in the plane, and makes an angle ψ with the 4-fold axis of $\psi = 90 - 51.8 = 38.2^\circ$. The determination of ψ incorporates the angle of orientation θ calculated from the *para*-deuteron lineshape above ($\theta = 51.8^\circ$). The angular information is combined with the observed quadrupolar coupling constant χ and asymmetry factor η of the 77K spectrum, and an exchange rate of $\kappa = 10^8$ Hz in order to calculate the *o*-, *m*-deuteron component of the FML lineshape.³⁶ The 166K spectrum is simulated by adding the calculated lineshape of the *o*-, *m*-deuteron to the lineshape of the *para*-deuteron in a 4:1 intensity ratio (Figure 7). The agreement between the 166K observed and simulated spectra is good, and confirms a motional model in which pyridine first undergoes rapid 2-fold reorientation about its molecular axis followed by molecular reorientation of the guest about the host 4-fold axis. The guest and host symmetry axes make an angle $\theta = 51.8^\circ$ and allows for an unambiguous identification of the guest nitrogen position.

2.3 ^{15}N CP-MAS NMR Spectroscopy

^{15}N NMR spectroscopy ($^{15}\text{N} = \text{spin } 1/2$) of C4A-pyridine- ^{15}N probes the chemical environment around the pyridine nitrogen. Pyridine- ^{15}N (20% enrichment) was used to prepare C4A-Py- ^{15}N which was characterized by ^{13}C and ^{15}N CP-MAS NMR spectroscopy (Figure 8D). The single resonance indicates that there is only one crystallographically unique nitrogen, and the chemical shift value of δ -64.4 ppm is similar to solution values (δ -63.9 ppm).^{37,38} Pyridine- ^{15}N chemical shift values in a variety of solvents have been correlated to the proton-donating ability of the solvent; pyridine δ ^{15}N

values are shifted towards the pyridinium ion (δ -179.6 ppm) as the proton-donating ability of the solvent increases.³⁸ The δ value of pyridine-¹⁵N in C4A shows no evidence for proton-donation from the calix to the pyridine, as was suggested from the crown-bridged C4A-pyridine structure.^{39,40}

The components of the nitrogen chemical shift anisotropy (CSA) tensor indicate the type of averaging motions experienced by the nucleus. No signal with adequate signal/noise was detected from the static ¹⁵N CP NMR spectrum since the signal intensity is distributed over a wide range of chemical shift values. To access the CSA tensor, a series of ¹⁵N CP-MAS NMR spectra were collected at different spinning rates and the spinning sideband intensities analyzed. Four spectra (at ν = 3654, 2184, 1959 and 1743 $\pm$ 3 Hz) were fitted using the Bruker WINFIT program.⁴¹ Figure 9 shows the observed and modeled spectra for the different spinning rates and the averaged (from each spectral fit) CSA tensor components are reported in Table 5.

Table 5 also collects the ¹⁵N CSA tensor components of pure pyridine at 168K and C4A-PY at 290K. The reduction in the chemical shift anisotropy ($\Delta\delta$) and its change of sign of the C4A-Py ¹⁵N lineshape relative to the static pyridine-¹⁵N lineshape⁴² arises from a motional-averaging process also characterized by ¹³C CP-MAS DD and VT static ²H NMR spectra. From the analysis of the change in lineshape components, the orientation of the ¹⁵N CSA tensor (and thus the pyridine molecule) in the calix cavity can be determined, providing the proper motional model is used. From the ²H NMR data, it is known that the pyridine undergoes 2-fold flips about its long molecular axis followed by 4-fold reorientation of the guest molecule about the calix C₄ axis such that the two axes make an angle $\theta = 51.8^\circ$. This motional model is used in the analysis of the pyridine ¹⁵N spectrum.

TABLE 5. The observed ^{15}N chemical shift anisotropy (δ_{ii}) parameters (in ppm) for pure pyridine- ^{15}N (168K)⁴² and *p*-tert-butylcalix[4]arene-pyridine- ^{15}N (290K); errors ± 10 ppm. $\delta_{iso} = (\delta_{11} + \delta_{22} + \delta_{33})/3$; static asymmetry parameter $\eta = |\delta_{22} - \delta_{11}| / |\delta_{33} - \delta_{iso}|$; chemical shift anisotropy $\Delta\delta = -\delta_{33} + (\delta_{22} + \delta_{11})/2$. Values are also given such that $\delta_{iso} = 0$. To relate δ and σ , use the equation $\delta = -135.8 - \sigma$ so that $\delta(\text{MeNO}_2) = 0.0$ ppm.

sample	δ_{iso}	δ_{xx}	δ_{yy}	δ_{zz}	$\Delta\delta$	η
pyridine- ^{15}N (static)	-64	51	-512	270	672	0.49
C4A-Py- ^{15}N	-65	-177	-140	122	-280	0.24
pyridine- ^{15}N (static)	0	115	-448	334	672	0.49
C4A-Py- ^{15}N	0	-112	-75	187	-280	0.24

Pyridine- ^{15}N : Static. The 168K ^{15}N spectrum of pyridine (Figure 8A) shows an anisotropy $\Delta\delta = 672$ ppm with a large asymmetry parameter of $\eta = 0.49$.⁴²⁻⁴³ In order to compare the ^{15}N NMR data with the C4A-Py- d_5 ^2H NMR data, the ^{15}N CSA tensor components must be in the same coordinate system as the ^2H EFG tensor components (Figure 10). Thus the CSA component perpendicular to the pyridine plane ($\delta_z = -448$ ppm) is assigned to δ_{yy} . The assignments of the in-plane components δ_{xx} and δ_{zz} are not readily apparent; the subsequent calculation of the 4-fold averaged CSA tensor (equations 6-8) gives only one satisfactory solution: $\delta_{xx} = 115$, $\delta_{zz} = 334$ ppm.

Pyridine 2-Fold Flip + Molecular Rotation about the Calix C_4 Axis. The treatment of the ^{15}N CSA follows closely that of the *para*-deuteron EFG tensor (*vide supra*). 2-fold molecular reorientation about the pyridine symmetry axis does not average the static CSA tensor since one of the CSA tensor components (δ_{zz}) lies on the rotation axis; thus the static lineshape persists under 2-fold rotation. However, averaging of the CSA components will occur under motion about the compound 4-fold symmetry axis according to equations (6-8), which are just a re-statement of equations (3-5):

$$\delta'_{xx} = \frac{1}{2} \left[(\cos^2 \theta) \delta_{xx} + \delta_{yy} + (\sin^2 \theta) \delta_{zz} \right] \quad (6)$$

$$\delta'_{yy} = \frac{1}{2} \left[(\cos^2 \theta) \delta_{xx} + \delta_{yy} + (\sin^2 \theta) \delta_{zz} \right] \quad (7)$$

$$\delta'_{zz} = (\sin^2 \theta) \delta_{xx} + (\cos^2 \theta) \delta_{zz} \quad (8)$$

where δ_{ii} are the static CSA tensor values and δ'_{ii} are the observed RT ^{15}N CSA tensor values; the pyridine 2-fold molecular axis makes an angle θ to the C4A 4-fold rotation axis. From equations (6-8) the angle between the pyridine 2-fold molecular axis and the calix 4-fold rotation axis is calculated to be $\theta = 55^\circ \pm 3^\circ$.

The C4A-PY motional model developed from the ^{15}N NMR CSA is consistent with the model developed from the ^2H NMR data, as well as with the single-crystal XRD study (*vide infra*). The ^{15}N data suggest that the pyridine is oriented in the cavity with its 2-fold molecular axis oriented 55° to the calix 4-fold symmetry axis.

2.4 Single Crystal X-Ray Diffraction Studies of C4A-Bz and C4A-Py

The XRD structures of C4A-Bz and C4A-Py are similar, but show slight differences. Both are tetragonal $P4/n$, and show a 7:1 positional disordering in the *t*-butyl groups. The most remarkable feature of the structures is that both guests occupy essentially the same position in the calix cavity despite having very different dynamic features. The substitution of CH by N at one position of the ring gives a significant difference in guest dynamics, and the XRD structure gives a picture of the calix environment around the guest's substitution point. The benzene guest sits slightly deeper in the cavity than does the pyridine, and this difference is due to a steric rather than an electronic interaction between host and guest.

TABLE 6. Crystallographic data for C4A-Benzene and C4A-Pyridine.^a

compound	C4A-benzene	C4A-pyridine
formula	C _{12.5} H _{15.5} O	C _{12.25} H _{12.25} N _{0.25} O
fw	181.75	182.01
temperature, K	150	150
colour, habit	colourless	colourless
crystal size, mm	0.10 x 0.16 x 0.30	0.16 x 0.25 x 0.30
crystal system	tetragonal	tetragonal
space group	<i>P</i> 4/ <i>n</i>	<i>P</i> 4/ <i>n</i>
<i>a</i> , Å	13.0230(19)	12.9446 (4)
<i>b</i> , Å	13.0230(19)	12.9446 (4)
<i>c</i> , Å	12.6190(12)	12.8156(25)
<i>V</i> , Å ³	2140.2	2147.4(4)
<i>Z</i>	8	8
ρ_{calc} , g cm ⁻³	1.119	1.134
<i>F</i> (000)	790.04	802.08
μ (Cu K α) mm ⁻¹	0.50	0.51
λ , Å	1.54056	1.54056
scan type	$\theta/2\theta$	$\theta/2\theta$
data collected	<i>h</i> , <i>k</i> , <i>l</i>	<i>h</i> , <i>k</i> , <i>l</i>
$2\theta_{\text{max}}$, deg	139.9	140.1
total # refls	2154	4655
# of unique reflns	2045	2052
<i>R</i> _{merge}	0.017	0.017
# reflns <i>I</i> $\geq 2.5\sigma(I)$	1641	1697
# of variables	145	185
<i>R</i>	0.048	0.051
<i>R</i> _w	0.070	0.079
GOF	2.58	3.18
max Δ/σ , finl cycl	0.030	0.182
resid density, e Å ⁻³	-0.200 to 0.190	-0.250 to 0.360

^aConditions and collection details: Enraf-Nonius diffractometer; graphite monochromator; aperture 4.0 x 4.0 mm at a distance of 173 mm from the crystal; stationary background counts at each end of the scan (scan/background time ratio 5:1); peak and background counts determined with profile analysis procedure of Gabe *et al*, *J. Appl. Cryst.*, **1989**, 22, 384. $\sigma(F_o)$ based on counting statistics, function minimized $\sum w(|F_o| - |F_c|)^2$, where $w = [\sigma^2(F_o) + k(F_o)^2]^{-1}$, $R = \sum ||F_o| - |F_c|| / \sum |F_o|$, $R_w = (\sum w(|F_o| - |F_c|)^2 / \sum w|F_o|^2)^{1/2}$, and $GOF = [\sum w(|F_o| - |F_c|)^2 / (m - n)]^{1/2}$. Values given for *R*, *R*_w, and GOF are based on those reflections with *I* $\geq 2.5\sigma(I)$.

2.4.1 The XRD Structure of *p*-tert-butylcalix[4]arene-benzene

The structure of C4A-BZ shows a C_4 -symmetric calix cavity which is occupied by the guest (Figure 11). The guest is disordered about the 4-fold axis, and the plot in Figure 11 shows only one of the four symmetry-related guest positions. The *t*-butyl group shows a 1:7 disordering which may be interpreted in the context of the local environment as one of the four *t*-butyl groups of the macro-ring possessing a 1:1 disordering over two positions while the remaining three *t*-butyl groups are not disordered.

The view along the *z*-axis shows the guest in a position that minimizes contact with the four *t*-butylphenol walls that compose the calix cavity. In fact, the plane of the benzene lies almost exactly on the plane connecting two of the four bridging methylene carbons and lying on the *z*-axis. In particular, the benzene plane is oriented with respect to the *t*-butyl methyl groups in such a fashion that appears to minimize—rather than maximize—contact. This questions the role of $\text{Me}_{\text{host}}-\pi_{\text{guest}}$ interactions in stabilizing the host:guest compound that have been invoked in other C4A-guest compounds such as the 1,3-crown-5-calix.^{21,37c}

The distances between C4A and the benzene guest are summarized in Table 7. No contact distance is at or less than the sum of the van der Waals radii ($\Sigma r_{\text{VDW}} = 3.6 \text{ \AA}$) save one: one of the *t*-butyl methyl carbons (CT1a) is situated $3.54 \text{ \AA}$ from the benzene CB2 carbon. There do not appear to be any specific points of contact between the host and the guest. The plane of the guest is slightly tilted off the host symmetry axis by 12° along both the *x*- and the *y*-axes. The aromatic guest tilting as well as the positioning with respect to the host *t*-butyl groups is consistent with what is observed with the C4A-toluene and C4A-anisole structures.

TABLE 7. Selected Bond Distances for C4A-BZ.

Bond	Distance (Å)	Bond	Distance (Å)
O1-C1	1.3955 (22)	C7a-C4a	1.535 (3)
C2-C8	1.523 (3)	C7a-CT1a	1.535 (3)
C2-C1	1.396 (3)	C7a-CT2a	1.535 (3)
C2-C3	1.390 (3)	C7a-CT3a	1.535 (3)
C6-C8a	1.525 (3)	C4a-C4b	0.169 (15)
C6-C1	1.397 (3)	C7a-C7b	0.174 (10)
C6-C5	1.396 (3)	CB4...C2	3.86 (1)
C3-C4a	1.423 (3)	CB4...C3	3.77 (1)
C3-C4b	1.333 (16)	CB4...C4a	3.97 (1)
C5-C4a	1.391 (3)	CB4...C4b	4.10 (1)
C5-C4b	1.435 (16)	CB2...CT1a	3.54 (1)

2.4.2 The XRD Structure of *p*-tert-butylcalix[4]arene-pyridine

Figure 12 shows the calixarene tetramer, the pyridine guest, and four *t*-butyl groups of the next layer along the *c*-axis. As in other C4A-guest compounds, the next layer along the *c*-axis is important in visualizing what “caps” the calix cavity and completes the incarceration of the guest.

Initial refinement of the XRD data was hampered by the inability to unambiguously define the guest nitrogen position. In other host:guest structures, the pyridine nitrogen is often undefined since nitrogen and carbon do not differ in the number of electrons. Furthermore, in-plane motion may cause the nitrogen to be disordered over the six aromatic atomic positions.¹⁸ The TOT-pyridine crystal structure typifies the problems often encountered with a pyridine guest. The highest peak in the electron diffraction map of the pyridine ring was attributed to the nitrogen atom,³⁵ but subsequent NMR work showed pyridine to undergo restricted in-plane motion which would cause a positional disordering in the nitrogen atom.³² In the present case, the disordering of the pyridine guest over 4 symmetry-related positions in the calix cavity caused further complications. The pyridine motional model developed from the ²H NMR data suggested a unique

position for the *para*-deuteron, and thus the nitrogen. When the nitrogen position determined from the ^2H NMR study was entered into the refinement, the *R*-value dropped significantly; in order to confirm the unique nitrogen position, a nitrogen atom placed at other guest ring positions caused the *R*-value to increase. This example illustrates the importance and power of a complementary approach to structure determination.

The host calixarene is 4-fold symmetric along the *z*-axis, and shows a 1:7 disordering in the *t*-butyl group. As for the C4A-benzene structure, this disordering pattern may be interpreted locally as one of the four *t*-butyl groups being disordered in a 1:1 ratio; the remaining three *t*-butyl groups are not disordered. This local disordering is space-averaged over the entire crystal, and thus gives the 1:7 ratio.

Pyridine occupies essentially the same orientation in the calix cavity as the benzene. The pyridine plane is tilted off the compound's symmetry axis by an angle of $16^\circ \pm 4^\circ$, and the *para*-C-D bond makes an angle of $49^\circ \pm 4^\circ$ with the symmetry axis. The pyridine position in the cavity is such that $\text{Me}_{\text{host}}-\pi_{\text{guest}}$ interactions are minimized. This is in contrast to the 1,3-crown-5-C4A-pyridine compound (Figure 1a) in which the pyridine plane sits along the major axis of the 2-fold symmetric cavity and appears to maximize $\text{Me}_{\text{host}}-\pi_{\text{guest}}$ interactions. The pyridine guest sits 0.2 Å higher in the calix cavity than does the benzene, and suggests that the packing of the calix layers may not push pyridine down as far into the cavity as benzene due to the absence of a C-H bond at the nitrogen position.

Consideration of the host layer along the *c*-axis allows for a complete description of the host environment surrounding the pyridine nitrogen. Two *t*-butylmethyl...N contacts are significant: one with the calix cavity ($d = 3.62$ Å), and one with the above layer ($d = 3.57$ Å). With both contacts, the C-H bond points directly at the nitrogen (angles of 158° and 159°); the two C-H bonds are oriented 90° to each other, and sandwich the pyridine such that the nitrogen is in a tetrahedral environment with the two covalent and the two

non-bonding interactions (Figure 13). In context of the earlier calix-pyridine work which suggested a C-H...N hydrogen bond,²¹ the evidence for such a bonding interaction must be considered. The angular requirement for H-bonding ($\angle > 140^\circ$) is met, but the C...N distance is of the same order as the sum of the van der Waals radii of CH and an aromatic N (3.6 Å). Since the ¹⁵N NMR chemical shift of C4A-pyridine-¹⁵N is unchanged from pyridine-¹⁵N in solution, it is unlikely that H-bonding occurs. Other guest-host distances (Table 8) are larger than the sum of the van der Waals radii (3.6 Å). The shortest distances are distributed over different contact points, and thus there does not appear to be any further specific points at which the guest and host interact. Finally, the interlayer (along *c*) *t*-butyl methyl groups get no closer than 4.15 Å to each other.

TABLE 8. Selected Bond Distances and Angles for C4A-PY.

Bond	Distance (Å)	Bond	Distance (Å)
O1-C11	1.386 (2)	CP5...C11	3.78 (1)
C12-C18	1.519 (2)	CP5...C12	3.86 (1)
C12-C11	1.395 (2)	CP5...C16	4.10 (1)
C12-C13	1.388 (2)	CP5...C21	3.94 (1)
C16-C15	1.393 (2)	CP6...C15	3.70 (1)
C16-C28	1.521 (2)	CP6...C24	3.85 (1)
C16-C11	1.401 (2)	CP6...C23	3.66 (1)
C15-C14a	1.386 (2)	CP4...C43	3.54 (1)
C15-C14b	1.498 (18)	CP4...C44	3.65 (1)
C13-C14a	1.424 (2)	NP1...CT11a	3.62 (1)
C13-C14b	1.254 (18)	NP1...CT21a	4.38 (1)
C14a-C17a	1.535 (2)	NP1...CT33a*	3.57 (1)
C14a-C14b	0.230 (17)	NP1...CT22a*	3.87 (1)
C17a-C17b	0.160 (11)	CP3...CT32a	3.61 (1)
C17a-CT11a	1.535 (18)	CP3...CT12a*	3.79 (1)
C17a-CT12a	1.535 (18)	CP2...CT12a*	3.83 (1)
C17a-CT13a	1.535 (18)		
Atoms	Angle (deg)	Atoms	Angle (deg)
O3-O1-C4	123.8		

* indicates from the layer above

3. *p*-*tert*-Butylcalix[4]arene Compounds with Amines

The solution chemistry of calixarenes in alkyl amines has been studied,¹⁵⁻¹⁷ and a two-step process postulated in which the amine interacts with the calix: proton-transfer (PT) from the calix to the amine located outside the cavity (*exo*) forms the amine cation, followed by inversion of the calix, and finally association of the cation (now inside the cavity (*endo*)) to form a complex (Figure 14). Solution ^1H T_1 measurements for amine protons are invariant with amine basicity, and suggest that complexation of the amine is not determined by this guest feature. For *tert*-butylamine and *neo*-pentyl amine, amines of comparable basicity, the latter is less effective in inhibiting calixarene inversion. In all cases, it is thought that the amine guest sits inside the cavity, *i.e.*, the *endo* position.

In solution, complexation of ethylammonium cations by ester derivatives of *p*-*tert*-butylcalix[6]arenes has been examined by ^1H NMR spectroscopy, and the EtH_3N^+ cation is thought to be held tightly inside the calix cavity.⁴⁵ The large upfield shifts of the methyl proton signals suggest that the methyl group of the cation sits deep in the conical calix cavity. Interactions between cyclic amines and *p*-*tert*-butylcalix[*n*]arene (*n* = 4, 8) in acetonitrile have been characterized by UV-VIS spectroscopy.⁴⁶ Unlike acyclic amines which form *endo* complexes, cyclic amines are postulated to form *exo* complexes. Cyclic guests with only one amine functionality form 1:1 host:guest complexes while diamine guests form 1:2 complexes.

XRD structures of calixarenes and calixarene derivatives with amine, ammonium, and amide⁴⁷⁻⁴⁸ guests show that amine guests act in two manners: they can be included into the calix cavity as neutral, unprotonated guests, or can participate in the formation of an ionic guest-calix system via abstraction of a calix phenolic hydrogen. Ammonium guests occupy sites that provide minimal and maximal guest-host ionic interactions. Several

calix-guest structures have been published and illustrate the dual nature of amine and ammonium guests.⁴⁹⁻⁵³

PT plays an important role in biochemistry, as illustrated by the catalytic hydrolysis of amides and esters by serine proteases (below).⁵⁴ The active site of the enzyme is thought to be composed of three amino acid residues: asparagine, histidine, and serine which are arranged in such a fashion to make the serine sufficiently nucleophilic to attack the carbonyl of the amide substrate. The initial step is thought to involve PT from the serine alcohol to the imidazole nitrogen. PT between calixarenes and amines may provide further insight into this biochemical process.

PT in the solid-state has been previously reported for a host:guest system.⁵⁵ The oxygen of the 1,1-di(2,4-dimethylphenyl)but-2-yn-1-ol host participates in intermolecular proton transfer with nitrogen atoms of the pyrazole guests, and a rate constant of 75 s^{-1} was estimated from ^{15}N CP-MAS NMR spectroscopy. The XRD structure shows the hydrogen atom involved in PT disordered over two sites in a 0.6:0.4 ratio.

Two types of structural motifs exist in C4A-amine compounds: one in which the amine behaves as a classic inclusion guest and sits exclusively in the *endo* position, and

another in which the amine interacts more strongly with the host. The former is distinguished by relatively simple ^{13}C NMR spectra that indicate a 4-fold symmetric compound, whereas the latter structures are characterized by more complicated ^{13}C NMR spectra and show a lowering of calix symmetry and/or an increase in size and complexity of the crystallographic asymmetric repeat unit.

3.1 *tert*-Butylamine and *sec*-Butylamine: Weakly Interacting Guests

In the ^{13}C CP-MAS NMR spectra of C4A-(*tert*-, *sec*-)butylamine compounds (Figure 15), the calixarene carbon resonances are typical of a 4-fold symmetric compound, and are consistent with one guest occupying the calix cavity. The DD NMR experiments indicate that both guests are motionally-averaged about the C_4 axis of the compound. The changes in chemical shift values from neat to included guest are insignificant.

In solution, the amine abstracts a proton from the acidic ($pK_1 \sim 3$)⁵⁶ phenolic hydroxyl group; if PT persists in the solid state, a structural distortion in the calix host is expected. The solid-state ^{13}C NMR spectra suggest that on the NMR timescale, the ring of hydrogen-bonding among the four phenolic hydroxyl groups is not perturbed by the presence of the base sitting inside the cavity.

3.2 Benzylamine + C4A: Distortion of the Calixarene Framework

A striking feature of the ^{13}C CP-MAS NMR spectrum of C4A-benzylamine is the abundance of host aromatic lines (Figure 16). In addition, the calix *t*-butyl resonances display a significant multiplicity ($m > 3$). Both features suggest a guest-induced distortion of the host from its typical 4-fold symmetry as in C4A-NB (Chapter 4). The aromatic guest lines are not readily apparent with the exception of the *ipso*-carbon at δ 134.7 ppm, and the benzyl methylene line lies under the host aliphatic resonances. The host lines in

the δ 137-155 ppm region are assigned to calix carbons C-1 and C-4 as in high-symmetry calixarene compounds: it is expected that the eight resonances in this region can be similarly assigned to a host without any symmetry elements. The spectrum then indicates the presence of two crystallographically inequivalent calixarene units (without any symmetry axes).

Without a single crystal XRD structure, it is difficult to assign unambiguously the origin of this distortion: does the guest occupy a position like nitrobenzene or has proton-transfer occurred between the amine and the host? The former possibility is unlikely in light of the ^{13}C CP-MAS NMR spectra of benzylalcohol, benzylthiol and ethylbenzene, guests with geometry similar to benzylamine: these spectra indicate that the hosts possess higher symmetry. With PT, two structural arrangements can be envisioned (Figure 17): one in which the PT occurs between the host and an *endo* amine guest and one in which PT occurs between the calix and an *exo* amine guest in an adjacent cavity.

The methylene carbon of benzylamine is prochiral, and substitution of one proton by a methyl group gives the chiral methylbenzylamine. Solutions of C4A in methylbenzylamine fail to crystallize under an inert atmosphere. Despite the failure to obtain an insoluble calix compound with a chiral amine, the use of chiral benzylamines as guests to form potentially interesting chiral compounds remains an attractive goal.

3.3 Ammonia + C4A

When ammonia gas is condensed onto solid C4A and the slurry stirred for 1 hour, followed by warming to room temperature, a white solid forms.⁵⁷ Two ^{13}C CP-MAS NMR features characterize this compound (Figure 18): the calix C-1 and C-4 resonances in the δ 138-170 ppm region show a distribution and multiplicity typical of calix-amine compounds in which the amine participates in PT. The multiplicity indicates a lowering of

calix symmetry. The remaining calix aromatic carbons (2,3,5,6) occur in the δ 120-133 ppm region and are broad, in contrast to the sharp lines typically observed with high symmetry calixarenes. The second feature is the multiplicity of the sharp aliphatic lines at δ 30-36 ppm which suggests that *t*-butyl groups are not as perturbed by the amine as seen in the other proton-transfer calix-amine compounds. The sharpness contrasts with the broadness of the aromatic resonances; the latter feature may be due to the decomposition or outgassing of ammonia over the course of the NMR experiment; the smell of ammonia was detectable in the handling of the sample both before and after loading of the spinner.

The position of the ammonia is impossible to ascertain from this experiment. The pattern of the calix aromatic resonances suggest that proton-transfer has occurred, but whether this is with an *endo* or *exo* ammonium remains undefined.

3.4 1,4-Diaminobutane: a Bifunctional Amine

Diamines and calixarenes form 1:2 host:guest complexes in acetonitrile solution.⁴⁶ The ^{13}C CP-MAS NMR spectrum of the compound formed between C4A and 1,4-diaminobutane (1,4-DAB) suggests that a host-distorting host:guest interaction occurs (Figure 19). Like the ^{13}C NMR spectrum of C4A-benzylamine, the spectrum of C4A-1,4-DAB shows a large multiplicity for all the host carbon lines. In particular, the host C-1 and C-4 resonances are spread over the δ = 140-160 ppm region whereas in the high symmetry case these carbons give two lines at δ = 142-148 ppm. The remaining host carbon lines lie in the δ = 127-130 ppm (C-3, C-5) and δ = 131-136 ppm (C-2, C-6) regions; the line multiplicity is larger than that typically observed with the high symmetry case. Likewise the aliphatic region (δ 33-39 ppm): at least nine lines are resolved whereas in the high symmetry case, only two host *t*-butyl lines typically appear (the methylene

carbons appear as a broad feature at δ 31 ppm). Both the aromatic and aliphatic regions suggest that there are at least two crystallographically inequivalent C4A macro-rings.

Of the two sets of aromatic host lines, the δ 140-160 ppm region is better resolved, and at least sixteen individual lines can be found. Since each C4A macro-ring contains eight crystallographically inequivalent carbons (both *ipso* and *para*), this suggests many C4A-1,4-DAB structural options, among them being the following:

- 2 C4A units in the asymmetric unit; both C4A macro-rings show no symmetry,
- 3 C4A units in the asymmetric unit; one macro-ring is 2-fold symmetric and the remaining two possess no symmetry elements,
- 4 C4A units in the asymmetric unit, with both macro-rings possessing 2-fold symmetry, and
- 8 distinct C4A units in the asymmetric unit, each possessing high, 4-fold symmetry.

The ^{13}C CP-MAS NMR spectral evidence alone does not lead to an unambiguous assignment.

A 300 MHz ^1H solution NMR spectrum (not shown) of the compound dissolved in CDCl_3 indicates that the solid-state compound does not persist in solution. The signal intensities integrate to give a host:guest ratio of 1:1, and implies that for each of the four above solid-state structural scenarios, there is a corresponding number of amine molecules in the crystallographic repeat unit.

3.5 Basicity vs. Sterics

The interaction of C4A with amines has not been unambiguously structurally characterized by either previous XRD studies or by the current work. The solid-state ^{13}C NMR spectra of the C4A compounds formed with interacting amines differ significantly from the spectra of C4A compounds formed with non-interacting, guest amines.

Amine basicity and the type or extent of amine-calix interaction in solution do not appear to be related.^{15,16} Table 9 below summarizes the base strength of various amines; those footnoted have been studied herein. The symmetric C4A structures of aniline ($pK_a = 4.63$) and *t*-butylamine ($pK_a = 10.83$) indicate that amine basicity is not a determining factor in the C4A-amine structure. Rather, with benzylamine ($pK_a = 9.33$) and *t*-butylamine, the final structure may be influenced more by geometry, and possibly the preference for the calix cavity to prefer an aliphatic rather than an aromatic amine. Ammonia, despite its small volume of occupation, prefers to interact with the calix in an ionic fashion. PT may take place from an *endo* rather than an *exo* guest position, as the small volume may allow the guest closer access to the calix hydroxyl groups from within the cavity; the same may be said of the benzylamine and 1,4-diaminobutane guests. In fact, the specific geometrical constraint may arise from the steric volume about the carbon attached to the nitrogen: if that carbon's substituents are bulky, approach of the amine to the calix hydroxyl hydrogens from within the cavity (*endo*) is hindered. Furthermore, one could define an amine cone-angle in a fashion similarly used to describe phosphine ligands in inorganic chemistry. The steric explanation accounts for the structural behavior of the aniline, *t*-butylamine, *sec*-butylamine, and pyridine guests.

TABLE 9. Basicity of Amines

amine	pK_a	amine	pK_a
aniline ^a	4.63	morpholine	8.33
benzylamine ^b	9.33	piperazine	9.83, 5.56
<i>t</i> -butylamine ^a	10.83	piperidine	11.12
diethylamine	10.49	pyridine ^a	5.25
dimethylamine	10.73	4-picoline	6.02
ethylamine	10.81	ammonia ^b	9.25
2-aminoethanol ^b	9.50	1,4-diaminobutane ^b	11.15, 9.71

^aforms a high symmetry, C_4 calix-amine structure.

^bforms a low symmetry, calix-amine structure with possible proton-transfer.

The model developed so far assumes that the amine in both cases occupies the calix cavity *i.e.*, the *endo* position. In the absence of single crystal XRD structural data, the *exo*-position cannot be ruled out. The location of the amine in the *exo*-position certainly has precedent with larger calixarenes. Finally, no higher order (2°, 3°) amines were studied; the C4A compounds formed with these amines may serve to clarify the factors interactions between amines and calixarenes.

4. Summary

The C4A compounds with N-containing guests studied in this chapter indicate a rich and previously undiscovered variety of structural and dynamic features. The C4A compounds of pyridine and benzene have been characterized by both XRD and solid-state NMR spectroscopy, and illustrate the importance of applying a complementary approach to structure determination. Local ordering and guest motional data from ^2H , ^{13}C , and ^{15}N NMR spectroscopy allow for the unambiguous resolution of the pyridine nitrogen position. Comparison of the C4A-Py and C4A-Bz structures shows the guest position and orientation in the C4A cavity to be almost identical. It is significant that pyridine, unlike pyridine guests other host cavities and benzene in the C4A cavity, does not show (pseudo) 6-fold in-plane motion. The observed dynamics result from a slightly different host environment that is sensitive to the presence of a ring substituent (hydrogen) at the nitrogen position.

Comparison of the C4A-Py and C4A-Bz structures challenges two conclusions based on an earlier C4A-Py structure: First, there is no evidence (XRD or ^{15}N NMR) that the pyridine nitrogen is involved in C-H...N hydrogen bonding. Secondly—and perhaps more importantly since the concept of an attractive $\text{Me}_{\text{host}}-\pi_{\text{guest}}$ is widely held—the pyridine aromatic plane is oriented to minimize interactions with the host *t*-butyl methyl

groups. The pyridine position is in contrast to that seen in the earlier structure, and suggests that the crown-5 modification of the C4A host may be the directing feature of the pyridine position in that guest cavity.

C4A compounds with alkylamine guests have been also studied, though in a more preliminary fashion. The ^{13}C NMR spectra indicate clearly whether the amine behaves as a classic inclusion guest, or whether a host-distorting interaction like proton-transfer occurs. Several N-containing compounds show great promise as calixarene spacers in the construction of extended calix-based supramolecular structures. In particular, the C4A-1,4-diaminobutane compound warrants further XRD structural study.

5. References

1. Lehn, J.-M. *Supramolecular Chemistry*, VCH: Weinheim, 1995.
2. Vögtle, F. *Supramolecular Chemistry: An Introduction*, Wiley: Chichester, 1991.
3. Whitesides, G. M.; Mathias, J. P.; Seto, C. T. *Science* **1991**, *254*, 1312-1319.
4. Desiraju, G. R. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2311-2327.
5. Lehn, J.-M. *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 89-112.
6. Lehn, J.-M. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1304-1319.
7. Ozin, G. A. *Adv. Mat.* **1992**, *4*, 612-649.
8. Monnier, A.; Schuth, F.; Huo, Q.; Kumar, D.; Margolese, D.; Maxwell, R. S.; Stucky, G. D.; Krishnamurty, M.; Petroff, P.; Firouzi, A.; Janicke, M.; Chmelka, B. F. *Science* **1993**, *261*, 1299-1303.
9. Huo, Q.; Margolese, D. I.; Ciesla, U.; Feng, P.; Gier, T. E.; Slegler, P.; Leon, R.; Petroff, P. M.; Schuth, F.; Stucky, G. D. *Nature* **1994**, *368*, 317-321.
10. Yang, H.; Kuperman, A.; Coombs, N.; Mamiche-Afara, S.; Ozin, G. A. *Nature* **1996**, *379*, 703-705.
11. Ozin, G. A.; Oliver, S. *Adv. Mat.* **1995**, *7*, 943-947.
12. Oliver, S.; Kuperman, A.; Coombs, N.; Lough, A.; Ozin, G. A. *Nature* **1995**, *378*, 47-50.
13. Walsh, D.; Mann, S. *Nature* **1995**, *377*, 320-323.
14. Fritz, M.; Belcher, A. M.; Radmacher, M.; Walters, D. A.; Hansma, P. K.; Stucky, G. D.; Morse, D. E.; Mann, S. *Nature* **1994**, *371*, 49-51.

15. Gutsche, C. D.; Bauer, L. J. *J. Am. Chem. Soc.* **1985**, *107*, 6063-6069.
16. Gutsche, C. D.; Iqbal, M.; Alam, I. *J. Am. Chem. Soc.* **1987**, *109*, 4314-4320.
17. Gutsche, C. D.; Iqbal, M.; Nam, K. S.; See, K.; Alam, I. *Pure & Appl. Chem.* **1988**, *60*, 483-488.
18. Andreetti, G. D.; Ugozzoli, F.; Nakamoto, Y.; Ishida, S. *J. Incl. Phenom.* **1991**, *11*, 241-253.
19. Gutsche, C. D.; Gutsche, A. E.; Karaulov, A. I. *J. Incl. Phenom.* **1985**, *3*, 447-451.
20. Czugler, M.; Tisza, S.; Speier, G. *J. Incl. Phenom.* **1991**, *11*, 323-331.
21. Andreetti, G. D.; Ori, O.; Ugozzoli, F.; Alfieri, C.; Pochini, A.; Ungaro, R. *J. Incl. Phenom.* **1988**, *6*, 523-536.
22. Alemany, L. B.; Grant, D. M.; Alger, T. D.; Pugmire, R. J. *J. Am. Chem. Soc.* **1983**, *105*, 6697-6704.
23. Breitmaier, E.; Voelter, W. *¹³C NMR Spectroscopy*; 2nd ed. Verlag Chemie: New York 1978.
24. Andrew, E. R. *J. Phys. Chem.* **1950**, *18*, 607-618.
25. Andrew, E. R.; Eades, R. G. *Proc. Roy. Soc. Lond.* **1953**, *A218*, 537-552.
26. Ok, J. H.; Vold, R. R.; Vold, R. L. *J. Phys. Chem.* **1989**, *93*, 7618-7624.
27. Nishikiori, S.; Ratcliffe, C. I.; Ripmeester, J. A. *J. Phys. Chem.* **1991**, *95*, 1589-1596.
28. Aliev, A. E.; Harris, K. D. M.; Guillaume, F. *J. Phys. Chem.* **1995**, *99*, 1156-1165.
29. Hall, L. D.; Lim, T. K. *J. Am. Chem. Soc.* **1986**, *108*, 2503-2510.
30. Meirovitch, E.; Belsky, I.; Vega, S. *J. Phys. Chem.* **1984**, *88*, 1522-1526.
31. Chopra, N.; Chapman, R. G.; Chuang, Y.-F.; Sherman, J. C.; Burnell, E. E.; Polson, J. M. *J. Chem. Soc.; Faraday Trans.* **1995**, *91*, 4127-4131.
32. Facey, G. A.; Ratcliffe, C. I.; Ripmeester, J. A. *J. Phys. Chem.* **1995**, *99*, 12249-12256.
33. Barnes, R. G.; Bloom, J. W. *J. Chem. Phys.* **1972**, *57*, 3082-3086.
34. Aliev, A. E.; Harris, K. D. M.; Mahdyarfar, A. *J. Chem. Soc. Faraday Trans.* **1995**, *91*, 2017-2026.
35. Brunie, S.; Navaza, A.; Tsoucaris, G.; Declercq, J. P.; Germain, G. *Acta Cryst.* **1977**, *B33*, 2645-2647.
36. The following is an MXET1 input file for generating the *o*-, *m*-deuteron C4A-PY-*d*₅ 2-fold flip spectrum without any 4-fold motion (exchange rate = 10³ Hz):
do matrix test? -> N
spectra to be calculated -> 1
output file (no ext.) -> pyr2fld
of axes -> 1
parameters for axis 1:
of exchange sites -> 4


```

site 1: theta -> 38.0000 phi -> 0.0000 rho -> 0.0000
site 2: theta -> 38.0000 phi -> 90.0000 rho -> 0.0000
site 3: theta -> 38.0000 phi -> 180.0000 rho -> 0.0000
site 4: theta -> 38.0000 phi -> 270.0000 rho -> 0.0000
model: all sites exchange=1, nearest neighbor=2, other=3 -> 1
exchange rate (1/sec) -> 1.00000E+03
equal a priori probabilities? -> Y
site symmetry (cn), n-> 4
90 degree pulse length (μs) -> 2.5000
composite pulse? -> N
pulse spacing (μs) -> 35.0000
spectral width (kHz) -> 400.0000
# powder increments -> 120
# points of fid calculated -> 512
# real points in spectrum -> 512
qcc (khz) -> 96.90 96.90 96.90 96.90
static asymmetry parameter -> 0.750 0.750 0.750 0.750
lorentzian broadening (kHz) -> 0.0000
gaussian broadening (kHz) -> 3.0000
calculate virtual fid? -> n
46.052 Larmor frequency [MHz]
3.600 inversion pulse width [μsec]
1.000 inversion efficiency of 1st pulse

```

37. Jameson, A. K.; Moyer, J.; Jameson, C. J. *J. Chem. Phys.* **1978**, *68*, 2873-2877.
38. Witanowski, M.; Stefaniak, L.; Webb, G. A. Nitrogen NMR Spectroscopy in *Ann. Reports NMR Spectroscopy*, ed. Webb, G.A. **1993**, *25*, 2-480.
39. Duthaler, R. O.; Roberts, J. D. *J. Am. Chem. Soc.* **1978**, *100*, 4969-4973.
40. Denisov, G. S.; Gindin, V. A.; Golubev, N. S.; Ligay, S. S.; Shchepkin, D. N.; Smirnov, S. N. *J. Mol. Liquids* **1995**, *67*, 217-234.
41. The spectra were processed to maximize signal to noise (TD = 3K, SI = 4K; line broadening = 50 Hz) and the spectra corrected to give a flat baseline. The isotropic line was identified and fitted for linewidth, chemical shift position and intensity. Next, the spinning sidebands were identified, and then fitted for intensity using the Herzfeld-Berger method. Finally the spinning speed was optimized to match the experiment sideband positions with the model. The fitting proceeds iteratively, and after the final iteration, each peak was examined visually to ensure that the fit was acceptable. The chemical shift anisotropy parameters were determined from a least-squares fit of the modeled spectra.
42. Schweitzer, D.; Spiess, H. W. *J. Mag. Res.* **1974**, *15*, 529-539.
43. At this temperature, pyridine is static; any in-plane motion would cause the in-plane tensor components to average to an axially-symmetrical lineshape. Furthermore, the ^2H NMR spectra of pyridine- d_5 shows it to be static from 77K to its melting point at 231K.

44. Ungaro, R.; Arduini, A.; Casnati, A.; Ori, O.; Pochini, A.; Ugozzoli, F. in *Computational Approaches in Supramolecular Chemistry*, Wipff, G. (Ed.); NATO ASI C426; Kluwer: Dordrecht, 1994, 277-300.
45. Ahn, S.; Chang, S.-K.; Kim, T.; Lee, J. W. *Chem. Lett.* **1995**, 297-298.
46. Görner, G.; Seiffarth, K. *J. Prakt. Chemie* **1991**, 333, 475-479.
47. Furphy, B. M.; Harrowfield, J. M.; Ogden, M. I.; Skelton, B. W.; White, A. H.; Wilner, F. R. *J. Chem. Soc. Dalton Trans.* **1989**, 2217-2221.
48. Harrowfield, J. M.; Ogden, M. I.; Richmond, W. R.; White, A. H. *J. Chem. Soc. Dalton Trans.* **1991**, 2153-2160.
49. Thuery, P.; Keller, N.; Lance, M.; Vigner, J.; Nierlich, M. *J. Incl. Phenom.* **1995**, 20, 89-96.
50. Bavoux, C.; Perrin, M. *J. Incl. Phenom.* **1992**, 14, 247-256.
51. Harrowfield, J. M.; Ogden, M. I.; White, A. H. *J. Chem. Soc. Dalton Trans.* **1991**, 979-985.
52. Harrowfield, J. M.; Ogden, M. I.; Richmond, W. R.; Skelton, B. W.; White, A. H. *J. Chem. Soc. Perkin Trans. 2* **1993**, 2183-2190.
53. Harrowfield, J. M.; Richmond, W. R.; Sobolev, A. N. *J. Incl. Phenom.* **1994**, 19, 257-276.
54. Daggett, V.; Schroder, S.; Kollman, P. *J. Am. Chem. Soc.* **1991**, 113, 8926-8935.
55. Toda, F.; Tanaka, K.; Foces-Foces, C.; Llamas-Saiz, A. L.; Limbach, H.; Aguilar-Parrilla, F.; Claramunt, R. M.; Lopez, C.; Elguero, J. *J. Chem. Soc., Chem. Commun.* **1993**, 1139-1142.
56. Gutsche, C. D. *Aldrichimica Acta* **1995**, 28, 3-9.
57. C4A (0.2274 g, 0.350 mmol) was placed in a 10 mL vial containing a stir bar. Ammonia (bp -33 °C, 4 mL) was condensed from the gas into the vial which was placed in a liquid nitrogen bath. The vial was transferred to an acetonitrile/CO₂ bath (-43 °C) and the ammonia allowed to melt. The sample was stirred for 1h at this temperature after which the vial was warmed briefly to room temperature to boil off excess NH₃. The white powder was stored at -40 °C.

6. Figures

FIGURE 1. *p*-*tert*-Butylcalix[*n*]arene compounds with pyridine. Clockwise from upper left-hand corner: (a) 1,3-crown-5-bridged *p*-*tert*-butylcalix[4]arene-pyridine, (b) *p*-*tert*-butylcalix[7]arene-3•pyridine, (c) *p*-*tert*-butylcalix[8]arene-8•pyridine.

FIGURE 2. 45.3 MHz ^{13}C CP-MAS NMR spectra of *p*-*tert*-butylcalix[4]arene-pyridine (*top*) and *p*-*tert*-butylcalix[4]arene-benzene (*bottom*). The guest resonances are indicated by the arrows, and the starred peaks are those that disappear under dipolar-dephasing conditions. The spectra were collected on a Bruker CXP-180 spectrometer with a Bruker 7 mm spinning probe using the FLIPNQS pulse sequence: 160-800 transients; recycle time: 2 s; $\pi/2$ pulse: 3 μs ; contact pulse 3.0 ms; TD = 4K; 16K points; $\nu = 2.9$ kHz.

FIGURE 3. 75.4 MHz ^{13}C CP-MAS NMR spectrum of *p*-*tert*-butylcalix[4]arene-2,6-dimethylpyridine. The guest resonances are indicated by the arrows, and the starred peaks are those that disappear under dipolar-dephasing conditions. The spectrum was collected on a Bruker AMX-300 spectrometer with a Doty Scientific 5 mm spinning probe using the CP-MAS pulse sequence:

FIGURE 4. VT 27.6 MHz ¹H NMR spectra of *p*-tert-butylcalix[4]arene-*benzene-d*₆. The spectra were collected on a Bruker CXP-180 spectrometer with a Bruker static probe with a 10 mm coil and a quadrupolar echo pulse sequence: 150-600 transients; recycle time: 2 s; $\pi/2$ pulse: 4.3 μ s; echo delay: 33 - 35 μ s; line broadening: 100 Hz; TD = 1K; 4K points. The spike in the centre of the high temperature spectra is due to trace uncomplexed benzene. The spectra were collected by Glenn Facey.

FIGURE 5. 109K observed (*bottom*) and simulated (*top*) ^2H NMR spectra for C4A-benzene- d_6 . The simulated spectrum is based on a motional model in which the benzene undergoes rapid in-plane rotation as well as rapid 4-fold reorientation in the calix cavity about the host symmetry axis. A tilt of the benzene plane off the host 4-fold axis of $\theta = 15^\circ$ is incorporated to account for the 109K linewidth.

FIGURE 6. VT 46.1 MHz ^2H NMR spectra of *p*-*tert*-butylcalix[4]arene-pyridine- d_5 . The spectra were collected on a Bruker AMX-300 spectrometer with a Bruker static probe with a 5 mm coil and a quadrupolar echo pulse sequence: 50-200 transients; recycle time: 3.5 s; $\pi/2$ pulse: 2.6 μs ; echo delay: 35 μs ; 1 kHz line broadening; TD = 512; 1K points. The 77K spectrum was collected on a Bruker MSL-200 spectrometer (30.7 MHz) with a 10 mm coil: 300 scans; recycle time: 5 s; $\pi/2$ pulse: 5.0 μs ; echo delay: 35 μs ; line broadening: 300 Hz; TD = 512; 2K points. The spike in the centre of the high temperature spectra is due to trace amounts of uncomplexed pyridine.

FIGURE 7. Observed (*solid*) and simulated (*dashed*) FML spectra for *p*-tert-butylcalix[4]arene-pyridine-*d*₅; *bottom*: 77K, motion I; *middle*: 166K, motion II. *Top left*: guest rotation about its 2-fold molecular axis *Top centre*: Libration about 2-fold axis; $\phi = 14^\circ$. *Top right*: 2-fold rotation of pyridine + motion about calix 4-fold axis; the guest is oriented so that the angle between the two motional axes is 52° . Note also the orientation of the averaged V_{ii} components of the EFG tensor.

FIGURE 8. 30.4 MHz ^{15}N CP NMR spectra of *p*-tert-butylcalix[4]arene-pyridine- ^{15}N (25% enriched). (D): with MAS at 5.4 kHz; spinning sidebands are started. The spectrum was collected on a Bruker AMX-300 spectrometer with a Doty Scientific 5 mm spinning probe using the CPMAS pulse sequence: 1000 transients; recycle time: 2 s; $\pi/2$ pulse: 3 μs ; contact pulse: 10 ms; 20 Hz line broadening; TD = 2K; 4K points. (A) the static spectrum at 168K (ref 37). (B) the simulated static spectrum resulting from rapid 2-fold rotation about the pyridine molecular axis. (C) the static spectrum determined from the 4 MAS spectra in Figure 9. The chemical shift is referenced to nitromethane $\delta = 0$ ppm using the nitrate line of NH_4NO_3 $\delta = -5.0$ ppm.

FIGURE 9. 30.4 MHz ^{15}N CP-MAS NMR spectra of *p*-tert-butylcalix[4]arene-pyridine- ^{15}N (25% enriched) at indicated spinning rates. The spectra were collected on a Bruker AMX-300 spectrometer with a Doty Scientific 5 mm spinning probe using the CPMAS pulse sequence: 1000 transients; recycle time: 2 s; $\pi/2$ pulse: 3 μs ; contact pulse: 10 ms; 20 Hz line broadening; TD = 2K; 4K points. Above each spectrum is the WINFIT fit from which the chemical shift anisotropy parameters are calculated. The chemical shift is referenced to nitromethane $\delta = 0$ ppm using the nitrate line of NH_4NO_3 $\delta = -5.0$ ppm.

FIGURE 10. Orientation of the ^{15}N CSA Tensor Components for C4A-Pyridine- ^{15}N .

FIGURE 11. Single crystal X-ray diffraction structure of *p*-*tert*-butylcalix[4]arene-benzene.

FIGURE 12. Single crystal X-ray diffraction structure of *p*-tert-butylcalix[4]arene-pyridine.

FIGURE 13. Local host environment around the guest pyridine nitrogen.

FIGURE 14. Proton transfer between the calixarene hydroxyl group and an amine guest.

FIGURE 15. 50.3 MHz ^{13}C CP-MAS NMR spectra of *p*-*tert*-butylcalix[4]arene compounds formed with *sec*-butylamine (*top*) and *tert*-butylamine (*bottom*). The guest resonances are indicated by arrows and the spinning sidebands by an X. Both spectra were collected on a Bruker MSL-200 spectrometer using a 7 mm spinning Chemagnetics pencil probe: 300-500 transients; recycle time: 3.5 s; $\pi/2$ pulse = 3.1 μs ; contact time = 4 ms; TD = 4K; 16K points; ν = 3.1 kHz.

FIGURE 16. 45.3 MHz ^{13}C CP-MAS NMR spectra of p-*tert*-butylcalix[4]arene-benzylamine. The guest resonances are indicated by arrows and the spinning sidebands by an X. The spectrum was collected on a Bruker CXP-180 spectrometer using a Bruker 7 mm spinning probe and the FLIPNQS pulse sequence: 2000 transients; recycle time: 5 s; $\pi/2$ pulse: 3.3 μs ; line broadening: 2 Hz; TD = 4K; 16K points; $\nu = 3.1$ kHz.

FIGURE 17. The *exo*- and *endo*- structures of *p*-tert-butylcalix[4]arene-benzylamine.

FIGURE 18. 45.3 MHz ^{13}C CP-MAS NMR spectra of *p*-*tert*-butylcalix[4]arene-ammonia. The spectrum was collected on a Bruker CXP-180 spectrometer using a Bruker 7 mm spinning probe and the FLIPNQS pulse sequence: 1000 transients; recycle time: 3.5 s; $\pi/2$ pulse: 3.1 μs ; line broadening: 0.5 Hz; TD = 4K; 16K points; $\nu = 2.9$ kHz.

FIGURE 19. 45.3 MHz ^{13}C CP-MAS NMR spectra of *p*-*tert*-butylcalix[4]arene-1,4-diaminobutane. The guest $-\text{CH}_2\text{N}-$ resonances are indicated by arrows and the spinning sidebands by an X. The spectrum was collected on a Bruker CXP-180 spectrometer using a Bruker 7 mm spinning probe and the FLIPNQS pulse sequence: 1600 transients; recycle time: 2 s; $\pi/2$ pulse: 3.0 μs ; line broadening: 2 Hz; TD = 4K; 16K points; $\nu = 3.12$ kHz.

7. Appendix: X-Ray Diffraction Structural Data

A1. Final Positional and Equivalent Isotropic Parameters ($\text{\AA}^2$) for C4A-BZ.

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> _{iso} ^a
O1	0.68630	0.61819	0.05203(10)	2.47(3)
C2	0.72979(14)	0.49749(14)	-0.08231(15)	2.12(7)
C6	0.56058(14)	0.58321(14)	-0.08261(15)	2.10(7)
C8	0.83870(15)	0.48332(14)	-0.03799(15)	2.27(8)
C1	0.65848(14)	0.56664(14)	-0.03855(14)	2.04(7)
C3	0.70005(15)	0.44313(15)	-0.17013(15)	2.40(7)
C5	0.53467(15)	0.52699(15)	-0.17102(15)	2.40(8)
HO1	0.6459 (11)	0.6856 (12)	0.0614 (13)	3.2 (4)
C7A	0.57456(13)	0.38983(13)	-0.31295(13)	3.59(12)
C4A	0.60162(22)	0.45681(19)	-0.21869(17)	2.56(10)
CT1A	0.65738(18)	0.40573(22)	-0.39680(17)	4.96(16)
CT2A	0.46754(16)	0.42213(23)	-0.35484(22)	6.79(20)
CT3A	0.57172(22)	0.27464(14)	-0.28146(20)	5.02(15)
C7B	0.5639 (7)	0.3908 (7)	-0.3048 (7)	3.9
C4B	0.6041 (13)	0.4483 (13)	-0.2091 (11)	2.5
CT1B	0.6513 (9)	0.3230 (11)	-0.3497 (12)	4.8 (4)
CT2B	0.5286 (11)	0.4704 (10)	-0.3859 (11)	4.1 (3)
CT3B	0.4715 (9)	0.3214 (10)	-0.2746 (10)	3.6 (3)
CB1	0.7282 (5)	0.7201 (6)	-0.4843 (3)	3.8 (5)
CB2	0.8295 (5)	0.7516 (6)	-0.4611 (3)	5.3 (5)
CB3	0.8557 (4)	0.7788 (7)	-0.3603 (4)	6.4 (6)
CB4	0.7807 (5)	0.7746 (6)	-0.2827 (3)	3.3 (4)
CB5	0.6794 (4)	0.7431 (7)	-0.3059 (4)	5.2 (5)
CB6	0.6531 (4)	0.7158 (7)	-0.4066 (4)	5.9 (5)

^a $B_{\text{iso}} = 8/3\pi^2 \sum \sum U_{ij} a_i^* a_j^* (a_i^* a_j)$; B_{iso} is the mean of the principal axes of the thermal ellipsoid. ESD's refer to the last digit printed.

A2. Final Positional and Equivalent Isotropic Parameters ($\text{\AA}^2$) for C4A-PY.

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> _{iso} ^a
O1	0.61737(8)	0.68666(8)	0.05303(7)	2.34(4)
C2	0.49728(11)	0.73002(10)	-0.08246(11)	1.97(5)
C6	0.58312(10)	0.56053(10)	-0.08307(11)	1.95(5)
C5	0.52679(11)	0.53440(11)	-0.17228(12)	2.21(5)
C8	0.48330(11)	0.83895(11)	-0.03813(11)	2.12(5)
C1	0.56665(10)	0.65883(10)	-0.03842(11)	1.93(5)
C3	0.44284(11)	0.70006(11)	-0.17118(11)	2.22(5)
HO1	0.680	0.648	0.063	3.2
C7A	0.38861(9)	0.57425(9)	-0.31493(9)	3.04(7)
C4A	0.45618(13)	0.60108(15)	-0.21974(11)	2.20(7)
CT2A	0.41939(15)	0.46642(10)	-0.35667(14)	5.07(11)
CT1A	0.40552(14)	0.65630(12)	-0.40050(12)	3.94(9)
CT3A	0.27336(9)	0.57321(14)	-0.28282(14)	3.99(9)
C7B	0.3922 (8)	0.5658 (9)	-0.3064 (8)	3.2 (4)
C4B	0.4453 (14)	0.6097 (14)	-0.2085 (12)	2.40(24)
CT2B	0.4752 (12)	0.5388 (15)	-0.3884 (13)	7.7 (6)
CT1B	0.3172 (13)	0.6476 (11)	-0.3513 (14)	7.1 (5)
CT3B	0.3310 (12)	0.4671 (10)	-0.2776 (13)	5.7 (4)
NP1	0.6635 (6)	0.7573 (9)	-0.4565 (5)	5.8 (5)
CP2	0.7600 (7)	0.7272 (11)	-0.4826 (4)	5.1 (7)
CP3	0.8420 (6)	0.7179 (11)	-0.4117 (5)	4.7 (6)
CP4	0.8229 (6)	0.7414 (10)	-0.3070 (5)	5.4 (7)
CP5	0.7229 (6)	0.7730 (8)	-0.2783 (4)	4.1 (6)
CP6	0.6467 (5)	0.7796 (7)	-0.3556 (5)	4.9 (6)

^a $B_{\text{iso}} = 8/3\pi^2 \sum \sum U_{ij} a_i^* a_j^* (a_i^* a_j^*)$; B_{iso} is the mean of the principal axes of the thermal ellipsoid. ESD's refer to the last digit printed.