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**An Analysis of Factors Contributing to
Isotropic ^{13}C Shifts in 1,2-Dialkoxybenzene
and Cyclohexane Derivatives**

Alex B. Driega

A thesis submitted to the Faculty of
Graduate Studies in partial fulfillment
of the requirements for the degree of
Master of Science

Department of Chemistry
Carleton University

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A handwritten signature in dark ink, appearing to read "J. W. Bush", written over a horizontal line.

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ABSTRACT

The crystal structures and CPMAS powder spectra of B9C3, 4-NO₂ B9C3 and C9C3 have been obtained in order to probe the origin of aliphatic and aromatic isotropic ¹³C paramagnetic shielding. Ab initio ¹³C shifts have been calculated for B9C3 using the LORG method. The CPMAS shifts of veratrole, benzodioxepane and various other substituted cyclic and acyclic 1,2-dialkoxybenzenes have also been obtained. The aromatic shifts reflect the calculated and x-ray conformations of the alkoxy groups as well as associated ortho field interactions. An empirical method for calculating ¹³C hydrocarbon shifts is presented along with ab initio LORG calculations on ethyl methyl ether and anisole which support the hypothesis that aliphatic paramagnetic shielding arises predominantly through C-C/C-H and C-O/C-H vicinal gauche-eclipsed interactions. Based on this hypothesis the aliphatic 9C3 shifts can be accounted for.

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GLOSSARY OF TERMS

ab initio	calculations involving only fundamental constants
anisole	methoxybenzene
APT	attached proton test
ax.	axial
B9C3	benzo-9-crown-3 ether
C9C3	cis cyclohexano-9-crown-3 ether
C _{ar}	aryl carbon
catechol	2-hydroxyphenol
cos ² θ, cos ² φ	an approximate relation for predicting the amount of vicinal overlap between orbitals in a given torsional network
COSY	homonuclear correlation spectroscopy
CPMAS	cross polarization - magic angle spinning
DEPT	distortionless enhancement by polarization transfer
DMB	dimethoxybenzene
ΔE	average orbital excitation energy
Δδ	range of chemical shifts
eq.	equatorial
γ _C , γ _H	magnetogyric ratio of carbon, hydrogen nuclei
gauche	torsional networks with dihedral angle of ca. 30° → 60°
guaiacol	2-methoxyphenol
HETCOR	hetero atom correlation spectroscopy

HOMO/ LUMO	highest occupied - lowest unoccupied molecular orbitals
I	spin quantum number
J	coupling constant
LAOCOON	an iterative program for simulating NMR spectra
LORG	localized orbital - local origin
M	methyl or methylene
m_i	magnetic spin quantum number
M.O	molecular orbital
MOPAC	molecular properties package
NOESY	nuclear Overhauser enhancement spectroscopy
q_σ , q_π	σ and π electron density in charge units
RF	radio frequency
RPA	random phase approximation
σ_{11} , σ_{22} , σ_{33}	principal components of the full shielding tensor
σ^d , σ^p	diamagnetic and paramagnetic shielding tensor
σ_F , σ_R	Hammett-type substituent parameters
SCS	substituent chemical shift(s)
S/N	signal to noise ratio
STO-3G	Slater-type orbitals - 3 gaussians
TMB	trimethoxybenzene
veratrole	1,2-dimethoxybenzene
TMS	tetramethyl silane
Z	number of molecules per crystallographic unit cell

clarity and truth are complementary

N. Bohr

INTRODUCTION

A. GENERAL INTRODUCTION

The focus of this thesis is the origin of solid state ^{13}C chemical shifts in benzo and cyclohexano crown ethers,¹⁻³ veratrole,⁴⁻⁷ and cyclohomologues⁸ all of which contain the 1,2-dialkoxy moiety. The effects of hydroxyl, amino and nitro substituents on the aromatic ring are also investigated.

Using the crystallographic data as input the LORG (localized orbital-local origin) method⁹ has been used to calculate ab initio isotropic ^{13}C chemical shifts for benzo-9-crown-3 (B9C3). The Ramsey theory¹⁰ of the chemical shift tensor in molecules is the foundation of the LORG method.

From the crystal structures of B9C3 and 4-NO₂ B9C3 (Figs. 14, 15 and Tables 8, 9) the conformations of the aliphatic ether backbones are correlated with the powder ^{13}C chemical shifts (ten clearly resolved B9C3 resonances) to determine the factors important in the paramagnetic shielding σ^p and this contrasted with the LORG results. The σ^p in a given compound can vary substantially as it is dependent on the relative orientations of the nearby orbitals.^{11,12,13}

The crystal structures reveal the twisting of an O-M group (M denotes either methyl or methylene) from the aromatic ring plane which decreases its conjugation i.e., electron donating ability.¹⁴ This and other similar aspects are examined in order to understand ^{13}C chemical shifts of cyclic and acyclic 1,2-dialkoxy benzenes.

In the literature M.O. calculations on substituted benzenes^{15,16} assign π and total

(π and σ)^{17,18} electron density at each carbon which have been correlated with observed chemical shifts¹⁹⁻²¹. Assignments of aromatic powder (CPMAS) ¹³C shifts (Tables 1, 2) were facilitated by HETCOR, NOESY and ¹H iterative spectral simulation using the LAOCOON²² program.

The hydrogenation of B9C3 gives cis-cyclohexano-9-crown-3 (C9C3) and the crystal structure presented in Fig. 18, Table 12. At 210K the cyclohexyl ring inversion is slow relative to the NMR timescale^{23,24} hence the ¹³C solution spectrum shows ten clearly resolved resonances, closely resembling the powder spectrum. Utilizing low temperature spectral editing (DEPT, APT) and low temperature 2-D correlation spectroscopy (COSY and HETCOR) the dependence of ¹³C and ¹H shifts on molecular geometry is studied. A proposed method for calculating ¹³C hydrocarbon shifts (Section M) also sheds light on the nature of this dependence.

The tetradeutero d₄-B9C3 powder and d₄-C9C3²⁵ 210K solution spectra have recently been obtained (Figs. 17, 19) which unambiguously differentiate the β and γ ether carbons relative to the 6 membered ring.

B. INTRODUCTION TO ¹³C SOLUTION NMR²⁶

In 1945 Bloch and Purcell independently detected the absorption of RF radiation by a proton in an applied magnetic field. The late discovery of the NMR signal was due partly to a sensitivity problem associated with the near equal Boltzmann distribution between nuclear energy levels. With the advent of stronger and more homogeneous magnetic fields, sample spinning and deuterated solvents the

resolution and intensity of the signals were vastly improved; sample spinning helps to optimize field homogeneity in the x,y plane. Soon after the initial discovery it was evident that nuclei of a given atomic number in different parts of a molecule will resonate at energies characteristic of their chemical environment. This is called the chemical shift, the theory of which will be introduced in Section D.

Nuclei in a molecule which are close to each other are coupled either through bonds or through space which gives rise to a splitting pattern with multiplicity $\Sigma(2I+1)$ being the combination of the individual nuclear spin states. Here the magnitude is dependent on many factors, most notably the degree of overlap between vicinal bonds while the intensity is governed by the selection rule $\Delta m_I = \pm 1$ and the relaxation rate. Dipolar relaxation is an important relaxation mechanism, dependent on the rate of reorientation and magnitude of nearby (r^{-6}) nuclear or electron magnetic dipoles.

An eligible nucleus for excitation cannot possess an even and equal number of protons and neutrons, hence the proton and deuteron resonances are readily observed. In a hydrocarbon ^1H spectrum no coupling to ^{12}C is observed since the latter is ineligible. The low natural abundance of eligible ^{13}C at ca. 1% makes its NMR detection difficult. Today spectrometers use a short pulse of RF radiation to excite all ^{13}C nuclei simultaneously and then store the time dependent free induction decay waveform. After an appropriate number of pulses a Fourier transform of the stored data yields the spectrum.

It is possible to simplify a spectrum by decoupling it. For a hydrocarbon ^{13}C spectrum one may acquire data while applying strong RF radiation spanning the ^1H

chemical shift range hence the resonating proton has ground and excited levels equally populated and no coupling is detected. This decoupling results in ^{13}C absorptions at the isotropic chemical shift values with an added bonus; an increase in the intensity. This is called nuclear Overhauser enhancement and is attributed to the polarization of the nuclear spins between possible energy levels where the population of the ^{13}C ground- ^1H excited state is increased relative to other excited coupled states.

The structure of solid compounds can be investigated by NMR however there are severe difficulties due to restricted motion. The theory and instrumentation of high resolution solid state NMR will be introduced in the next section.

C. THEORY OF SOLID STATE NMR²⁷

If one were to take a ^{13}C NMR spectrum of a typical powdered organic compound as if it were in solution it would appear broad, featureless and ca. 10 times as wide due to non averaged proton dipolar fields and chemical shift anisotropy. The proton magnetic dipole moments can be effectively reduced to zero by applying a strong RF field at their resonance frequency.²⁸ This eliminates coupling directly through space and indirectly through bonding electrons which results in line narrowing.

With a powdered sample the σ , π and n electrons are not orientationally averaged with respect to the external magnetic field and the fields they produce at the ^{13}C nucleus will result in a wide resonance line. By spinning the sample at several kHz and at $\theta = \arccos(1/\sqrt{3}) = 54.73^\circ$ with respect to the external field, these induced

fields average to their isotropic value and further line narrowing results. This magic angle spinning (MAS)²⁹ also eliminates residual directly-bonded dipolar coupling with ¹H but cannot with quadrupolar nuclei such as ¹⁴N which results in asymmetric splitting.³⁰

Another difficulty in powder ¹³C NMR spectra is the low S/N ratio due to much longer relaxation times. A multiple pulse experiment termed cross polarization (CP)²⁸ is able to bring the ¹H and ¹³C spin systems into thermal contact by an on resonance RF pulse which alters the bulk magnetization vector so it is coincident with the RF field. Now the nuclei have the same Larmor frequency in the rotating frame $\gamma_C B_C = \gamma_H B_H$ (where B is the RF field and $\gamma_H = 4\gamma_C$) and the ¹H population distribution can be transferred to ¹³C spin systems resulting in an increased signal and shorter relaxation times.

One can obtain more information from a high resolution powder spectrum than a solution spectrum. In a powder intramolecular rotations and conformational averaging are usually eliminated and the isotropic shifts will reflect this;³¹ however caution must be used (Section I).^{2,32,33,34}

Even more information can be obtained from a single crystal. If a perfect crystal is successively rotated around its three Cartesian crystallographic axes and the resulting shielding tensor σ (a 3x3 matrix) for each chemically unique ¹³C nucleus diagonalized, the anisotropic chemical shifts along the x,y, and z axes can be determined. The limitation to this method is poor resolution due to large numbers of resonances from multiple or inequivalent molecules in the unit cell. Grant et al.³⁵ use

a 2-D correlative technique to combat this problem. The theory behind magnetic shielding hence the shielding tensor will be introduced in the next section.

D. THEORY OF SHIELDING IN MOLECULES - DIAMAGNETIC SHIELDING¹⁰

The interaction of the applied field and the non valence electrons of molecules is responsible for diamagnetic shielding. These s electrons experience a spherically symmetric nuclear electrical field hence their motions are constrained to a circular path even when perturbed by an applied field and nuclear spin dipolar field which are in the same direction; the perturbing nuclear orbital dipolar fields are insignificant. Note that ^{13}C nuclei have spin $\frac{1}{2}$ therefore only one excited state.

These perturbing magnetic fields induce changes in the electron spin and orbital angular momentum. The orbital motion of the inner electrons will gain a precession that results in a field at the nucleus opposing the perturbing field; the nucleus therefore will be shielded from the applied field and will precess at a lower frequency. In other words the resonant RF frequency here is lower than for an isolated nucleus. The shielding magnetic fields arising from electron spin can be omitted since they are of higher orders of smallness than the orbital contributions. This diamagnetic correction has been shown by Lamb³⁶ to be; $\sigma^d = e^2/3mc^2 \sum \langle r_i^{-1} \rangle$ (1) where r_i is the radius vector of the i^{th} electron with the shielded nucleus as the origin. This equation also arises in Ramsey's expression for the total magnetic shielding constant $\sigma = \sigma^d + \sigma^p$ the derivation of which will be discussed next.

E. PARAMAGNETIC AND DIAMAGNETIC SHIELDING REVISITED

The interaction of the applied field with the valence electrons of a molecule gives rise to paramagnetic shielding however is capable of diamagnetic shielding also. These electrons experience non spherical electric fields due to the presence of several attracting centres from massive nuclei. This paramagnetic shielding is the reason for the large range of ^{13}C chemical shifts of ca. 200 ppm while for ^1H it is ca. 10 ppm. It must be emphasized that magnetic shielding has a distinct directional dependence and is described by the chemical shielding tensor (a 3×3 matrix) but can be reduced to its isotropic value by averaging over all orientations. It is of great interest for any theory to take into account the tensorial aspect of shielding as this can be compared to experimental single crystal data.

In the early 1950's Ramsey¹⁰⁶ developed a theory of magnetic shielding in molecules, the foundations of which rested on Van Vleck's³⁷ work on electric and magnetic susceptibilities. In Ramsey's theory several essential simplifications are introduced which have stood the test of time as it is still being utilized in its original form in conjunction with supercomputers i.e., the LORG⁹ method.

The applied and nuclear dipolar fields perturb the electrons of the molecule resulting in a new energy for the electronic system. These fields $\mathbf{H}$, are conservative $\nabla \cdot \mathbf{H} = 0$ therefore have an associated vector potential $\mathbf{A}$ where $\nabla \times \mathbf{A} = \mathbf{H}$.³⁸ Van Vleck has demonstrated the absence of magneto-electric directive effects where the polarizability in molecules remains unchanged when subjected to magnetic fields and

vice versa, therefore the scalar potential $\phi = \mathbf{E} \cdot \mathbf{r}$ is omitted. A suitable potential for an electron is;

$$A = \frac{1}{2}\mathbf{H} \times \mathbf{r} + (\boldsymbol{\mu} \times \mathbf{r})/r^3 - \frac{1}{2}\mathbf{H} \times \mathbf{R} \quad (2)$$

The first and second terms are the respective potentials of the applied and dipolar fields and $\mathbf{r}$ is the position vector with the origin at the shielded nucleus. The last term arises because the the applied field does not have an origin therefore the potential ascribed to it is somewhat arbitrary; it has gauge freedom³⁸ and in calculations the gauge origin defined by $\mathbf{R}$ can be optimized. It is noted the vector dipole potential is an approximation and corresponds to the field along the dipolar axis only. If the field perpendicular to the axis was used a coefficient of $\frac{1}{2}$ would be needed.

Substituting this potential A into the electronic Hamiltonian yields;

$$\hat{H} = \frac{1}{2}m \Sigma [\dot{\mathbf{r}}^2 + e/2c(\mathbf{H} \times (\mathbf{r} - \mathbf{R}) + e/c(\boldsymbol{\mu} \times \mathbf{r})/r^3)^2] + V \quad (3)$$

After second order perturbation theory the situation is simplified by retaining only those second order energy terms linear in μH denoted as $\mu\sigma H$. This is partly justified since magnetic shielding by definition is concerned only with effects proportional to H . Implicit in Ramsey's simplification is that all other energy terms are insignificant and that perturbed electronic and nuclear energies are directly coupled. Now σ can be meaningfully interpreted as the component of the field contributed by the electrons.

The energy of the nucleus is now;

$$E = -\mu_N H + \mu\sigma H. \quad (4)$$

The shielding tensor $\sigma = \sigma^d + \sigma^p$ is made up of σ^d , a simple Lamb type diamagnetic shielding term and σ^p , a second order paramagnetic deshielding term both of comparable magnitude.

$$\sigma^d = \frac{1}{2}c^2 \langle 0 | \sum ([\epsilon_H \times (r_i - R)] \cdot [\epsilon_p \times r]) r^3 | 0 \rangle \quad (5)$$

$$\sigma^p = -1/c^2 \sum (E_q - E_0)^{-1} [\epsilon_p \cdot \langle 0 | \sum l r^3 | q \rangle] \times [\epsilon_H \cdot \langle q | \sum l' | 0 \rangle] \quad (6)$$

where ϵ_H and ϵ_p are unit vectors along the direction of the applied field and nuclear magnetic moment respectfully, $l = r \times p$ is the electronic angular momentum relative to the shielded nucleus and l' is that relative to the gauge origin at R . It is also noted that σ^d involves summations only over ground state wavefunctions while σ^p involves excited states. The σ^p term also contains the nebulous inverse energy relation $(E_q - E_0)^{-1}$ which can be thought of as an average excitation energy ΔE^{-1} .

The σ^p term has been put on a more empirical footing by Pople.¹¹

$$\sigma^p = -e^2 \hbar^2 (2m^2 c^2 \Delta E)^{-1} \langle r^{-3} \rangle_{2p} \sum Q_{AB} \quad (7)$$

The large range of ^{13}C chemical shifts for similarly bonded nuclei has its origin in the σ^p term where the mixing of excited states (ΔE) is dependent on the relative orientation of the localized M.O.'s. Atoms bonded to electronegative substituents¹⁹ experience inductive withdrawal and are deshielded due to a shrinking of the 2p orbital radius. The Q_{AB} term represents a summation of terms from the charge density bond order matrix and accounts partly for the relation between ^{13}C shifts and electron densities.

In the next section the LORG method of calculating shielding tensors is described.

F. THEORY OF THE LORG METHOD⁹

The cornerstone of the LORG (localized orbital-local origin) method is the Ramsey equation. One characteristic aspect of the LORG method consists of choosing

a local origin (instead of an arbitrary gauge origin) for the vector potential of the applied field for each localized orbital pair. This enables economy sized basis sets to be utilized in obtaining the Hartree-Fock ground state.

If origin A is defined at the shielding nucleus as is done in conventional coupled Hartree-Fock (CHF) calculations, economy sized basis sets result in an error in the shielding as R^{-1} . This is attributed to inadequate balancing of paramagnetic and diamagnetic contributions from distant orbitals or bonds. If origin B is defined as the centroid of the corresponding localized orbital the error is reduced to an R^{-2} dependence. Comparisons using both types of origins resulted in a working compromise; for calculations involving directly bonded orbitals origin A is used and for calculations involving non bonded, distant orbitals origin B is used.

Another aspect of the LORG method is the utilization of the random phase approximation (RPA)³⁹ where the resulting expressions for the shielding tensor are broken down into bond contributions and bond-bond coupling contributions. The RPA has been successful in calculating molecular chiroptical properties where many of the electric and magnetic one electron integrals are the same as in magnetic shielding calculations.

G. THEORY OF ELECTRONIC STRUCTURE vs. ^{13}C NMR

Ab initio calculations of ^{13}C chemical shifts are very dependent on the size of the basis set, form of the wavefunctions and the gauge origin therefore it often escapes the mind why a certain variable works over another. In addition C-H bond lengths are important and since these are ill defined in x-ray structures further ambiguity arises.

In aromatics it has become common to correlate ^{13}C chemical shifts with empirical electronic substituent effects^{19,21} namely resonance, electric field (Coulomb and dipole) and electronegativity which are described by Hammett parameters.²¹

The resonance effect involves transfer of substituent π electronic charge and is supported by ab initio molecular orbital theory calculations of π density⁴⁰ where meta positions are minimally affected for both planar and perpendicular substituents.^{15,16} There is excellent positive correlation of para carbon substituent chemical shifts (SCS) with calculated π density for planar monosubstituted benzenes.^{4,5,19} It has also been shown that σ and π density are inversely proportional where $q_\sigma = -0.57 q_\pi$ ^{20,41} and that one π electron contributes 160 ppm⁴² in aromatic ^{13}C chemical shifts.

The para carbons are deshielded when tertiary amino,¹⁹ vinyl,^{8,43} aroxy⁴ and alkoxy^{14,44} groups are twisted from the aromatic ring plane, attributed to decreased conjugation hence decreased p-type lone pair electron donation. It has been shown that there exists a $\cos^2\theta$ dependence between the twist angle θ and para shifts for diphenyl ethers^{4,19} where $\cos^2\theta = (125.3 - \delta) \div (125.3 - 120.1)$ where 125.3, 120.1 are the ρ shifts in ppm corresponding to $\theta=90^\circ$, 0° . It must be emphasized that molecular orbital theory predicts a much greater ρ shift vs. θ dependence than is actually observed. In contrast for 2,6-dinitroanisole, where the methoxy group is very twisted ($\theta = 79^\circ$)⁴⁵ the SCS corrected shift of C-4 is less than that for anisole.¹⁴

The nature of the nitro group interaction with the benzene ring has been questioned⁴⁶ because when it is twisted M.O. calculations⁴⁷ predict shielding of the para carbon which is not observed experimentally (Section J). Electronegative substituents

induce decreased σ electron density at the directly bonded carbon only; in aromatic systems this correlates well with ipso carbon deshielding.¹⁹

The electric dipole field generated by the partial ionic character of the substituent's bonds^{44,49} can in turn polarize, hence alter the energy of a distant bond (the probe) via a through-space mechanism;

$$\Delta E_{\text{bond}} = \mu(2\cos\theta \cos\phi - \sin\theta \sin\phi)/Dr^3 \quad (8)$$

Here μ is the local dipole, r is the distance between the substituent dipole and the probe and θ , ϕ are the angles defining the orientation of μ and the probe relative to r . This equation however has limited practical use as the effective dielectric constant D is ill defined in intramolecular regions. Entire aromatic π systems are polarized by such fields.⁴⁹ The nitro group has a dipole field substituent parameter $\sigma_F = 0.65$ formulated by Taft and Topsom²¹ whereas for methoxy and amino groups $\sigma_F = 0.24$ and 0.14 respectively.

In aromatics ortho carbons are more shielded than those predicted by calculated electron densities based on two rationales; (i) γ -steric interactions i.e., repulsive electric fields, polarize C-H bond density onto the ortho carbon and (ii) the nature of the eclipsing interactions (mixing) between the p-type orbitals on the $\underline{i} \equiv$ ipso substituent atom and the $\underline{i}C-\underline{o}C$ aromatic bond.

In general there is a tendency to correlate steric crowding with ^{13}C shielding however this is not always the case. In the ^{13}C spectrum of 1,8-dimethylnaphthalene a δ cis-coplanar interaction deshields the methyl carbons relative to the monomethyl moiety.⁵⁰ Another such example is 4-tertbutylcyclohexanol where C1, C2, C3 of the

trans isomer are deshielded relative to the cis isomer^{12,51} (Table 6). Similar complexity regarding ^{13}C shifts is also apparent in methyl ethyl ether C-O-C-C and ethylene glycol O-C-C-O networks where LORG calculations predict the carbons bearing oxygen are deshielded for a dihedral angle $\theta=120^\circ$ relative to $\theta=180^\circ$ (Figs. 12, 13). It is apparent that extreme caution is needed in assigning the ^{13}C spectra of stereoisomers.

H. TWO DIMENSIONAL AND EDITING SPECTRA

The following 2-D NMR techniques have been utilized to aid in assignments (the theory i.e., pulse sequences behind such techniques are beyond the scope of this thesis). These are; (i) HETCOR (hetero-atom correlation spectroscopy) which correlates those proton and carbon chemical shifts directly bonded to one another. (ii) NOESY (nuclear Overhauser enhancement spectroscopy) which correlates the chemical shifts of non bonded protons which are close to one another in the molecule. (iii) COSY (homonuclear correlation spectroscopy) where protons directly coupled through 2 $\rightarrow$ 5 bonds are correlated. Editing techniques DEPT (distortionless enhancement by polarization transfer) and APT (attached proton test) are also utilized which distinguish quaternary and secondary carbons from tertiary carbons.

DISCUSSION

I. GENERAL DISCUSSION

Benzo crown ethers are well suited models for probing the origin of both aromatic and aliphatic ^{13}C chemical shifts. If the crystal structure is known the powder ^{13}C spectrum can be assigned utilizing the empirical dependence of isotropic shifts on the nature and geometry of the surrounding bonds. If there are few (≤ 4)³⁵ molecules per unit cell it is possible to obtain the full shielding tensors from the single crystal spectrum (Section J). In both cases the experimental data can be compared to those values calculated from an ab initio method.

It must be emphasized that for a given class of compounds i.e., crown ethers, the differences in powder shifts from one molecule to the next are due to σ^p the paramagnetic portion of the shielding tensor¹⁸ which is an excited electronic state phenomenon. The complexity of understanding this theoretically makes empirical correlations more pragmatic.

To understand the origin of the aromatic shifts in crown ethers several acyclic and cyclic homologues were prepared. The isotropic ^{13}C chemical shifts of these and of others from the literature are presented in Tables 1, 2 (note halogen, vinyl and acetylenic- type substituents are not considered).

In this thesis the crystal structures of B9C3 and 4-NO₂ B9C3 are presented along with the respective 45.3 MHz ^{13}C powder spectra and these two correlated. It is noted that the 100 MHz ^{13}C solution spectra of these two molecules remain unchanged

down to cryogenic temperatures. The *ab initio* LORG⁹ method utilizes the B9C3 crystallographic data as input to calculate the corresponding isotropic shifts for an isolated molecule in the gas phase (Table 4). The tetradeutero d_4 -B9C3 powder spectrum supports the empirical B9C3 powder assignments of the ether carbons (Table 10) which are based on the crystal structure (Fig. 14).

Hydrogenation of B9C3 yields *cis*-cyclohexano-9-crown-3 (C9C3) and the corresponding ^{13}C powder spectrum, very similar to the 210K solution spectrum, is assigned based on the crystal structure (Fig. 21) and COSY, HETCOR, DEPT obtained in the slow exchange limit at 210 K. The tetradeutero d_4 -C9C3 210K DEPT supports the empirical C9C3 powder assignments of the ether carbons (Table 13).

The replacement of a proton with a deuteron simplifies;

- (i) ^1H spectra due to the different resonance frequency of ^2H .
- (ii) ^{13}C solution spectra due to the smaller magnetic moment of ^2H which is less effective than ^1H in relaxing the bonded ^{13}C nucleus hence correspondingly weak signals ensue; the lack of nOe is also a factor.
- (iii) ^{13}C powder spectra where dephasing eliminates the signals of those ^{13}C nuclei bonded to ^1H but not to ^{12}C , ^{14}N , ^2H , etc.

Spectral assignments of the compounds in Tables 1, 2 were aided by COSY, HETCOR, NOESY and LAOCOON²² ^1H spectral simulation. Aromatic carbons bonded to nitrogen were assigned based on the wide, low intensity peaks in solution and the asymmetric splitting³⁰ in powder due to the quadrupolar nature of this atom. Care must be exercised in interpreting powder spectra as multiplicities can arise from

packing effects² and non equivalent molecules in the crystallographic unit cell.³²⁻³⁴ Other anomalies include changes in the relative positions of resonances in going from solution to solid as is observed for C2, C3 of 3-NO₂ B9C3^{32,†} (Table 2). In general though such occurrences are rare. Those compounds exhibiting large shift differences (>1 ppm) between solution and solid are deemed to reflect large conformational differences upon changing state.

ORIGIN OF AROMATIC ¹³C SHIFTS IN 1,2-DIALKOXYBENZENES

J. PARA SHIFTS

There is excellent positive correlation between π electron density from ab initio molecular orbital calculations^{16,40} and ρ ¹³C chemical shifts for planar monosubstituted benzenes (Section G).^{4,5,19} It is noted¹⁸ however that total electron density calculations correlate equally well due to the inverse linear relationship of σ and π density.^{20,41} Estimated values range from 160⁴² to 200 ppm per π electron.

OMe GROUP

Molecular orbital calculations on veratrole (1,2-dimethoxybenzene) in a variety of conformations have predicted no sharp energy minima.^{6,7,15,53,54} A literature survey of 32 crystal structures of veratrole derivatives^{53,55} reveals that the OMe groups are trans-coplanar (Fig. 2) except in two instances. The veratrole·Cr(CO)₃ complex also

† The ordering of solvent molecules by the NO₂ group is seen in the marked differences between the 3-NO₂ B9C3 ¹H spectra in CDCl₃, CD₂Cl₂ and d₆-Me₂CO (appendix).

shares this conformation.⁵⁶ Some authors have attributed this conformational preference to packing effects^{7,55} while others to the HOMO-LUMO of the ring/substituent orbitals⁵⁷ or torsional barriers.^{53,58} It has also been predicted that one OMe is perpendicular in solid veratrole.⁵⁹ Presented is the low temperature powder spectrum of veratrole (Fig. 1) which reveals an asymmetrical planar structure with one OMe slightly twisted. This will become clear to the reader as the discussion continues.

Fig. 1 272K 45.3 MHz CPMAS Spectrum of Veratrole

The ρ SCS of anisole (methoxybenzene) is -7.7 while for 2-substituted anisoles the average ρ SCS[§] is ca. -8.5 attributed to a greater degree of sterically enforced planarity.⁵ For 2,6-disubstituted anisoles the twist angle θ of the OMe group approaches 90°.⁵⁴ Meaningful correlations utilizing a $\cos^2\theta$ type dependence of

§ average SCS values are in ppm from benzene at 128.5 ppm calculated based on the isotropic solution and powder shifts presented in Tables 1, 2.

ρ shifts for mono and di-ortho substituted diphenyl ethers have been made by Buchanan et al.⁴ This type of relation holds for substituents with lone pairs such as OR, NR₂ etc. where deviation from planarity implies poorer back donation of π electron density from the p-type lone pairs into the ring. As a result 2,6-disubstituted anisoles and small cyclohomologues, where an O-M group is constrained to $135^\circ > \theta > 45^\circ$ (Fig. 2, $n=3 \rightarrow 9$) have an average solution ρ SCS of ca. -6. However for 2,6-diNO₂ anisole $\theta=79^\circ$ ⁴⁵ and 2-NO₂-6-OMe anisole the values are -8.3 and -8.4[†]; obviously factors other than the degree of oxygen lone pair overlap are responsible for the ρ shift.¹⁴ The decrease in the effective size of O1 by polarization of lone pair density into the ring serves to stabilize the system especially if both flanking substituents possess lone pairs.

A study by Grant et al.³⁵ involving the 2-D single crystal spectra and x-rays of 1,4 DMB, 1,3,5 TMB and 1,2,3 TMB* was carried out to probe the physical origins of such observations. The principal values σ_{11} , σ_{22} , σ_{33} of the chemical shift tensors of these molecules were analyzed in terms of i , ρ cis, ρ trans, m and ρ SCS parameters. Multiple regression (correlation coefficient = 0.99) confirmed additivity of these values for the planar non-ortho substituted OMe groups of 1,4 DMB and 1,3,5 TMB.

The source of the deshielded isotropic ρ SCS for O2-M2 of 1,2,3 TMB ($\theta=76^\circ$) relative to anisole was due to σ_{11} and σ_{22} . The direction of these components in aromatics is such that the π electrons are mainly responsible which supports the resonance model.

[†] powder value (Table 1, appendix)

* DMB and TMB refer to di and trimethoxybenzene.

OH and NH₂ GROUPS

The average ρ SCS for 2-substituted phenols is ca. -8.0 and for phenol is -7.3. However for intramolecularly H-bonded 2-NO₂ phenol^{60,61} the value is -9.9 while for 2-OMe-6-NO₂ phenol and 2-OH-6-NO₂ phenol it is ca. -14.8, shielded by 5 ppm over 2-NO₂ phenol. Again the system is stabilized by field induced donation of O1 p -type lone pair density into the ring.¹⁴ It is noted that 2-OH-6-NH₂ phenol is unstable.⁶²

Similarly the average ρ SCS for 2-substituted anilines is ca. -11.5 and for aniline is -9.8. Amino and hydroxyl groups are always planar however when tertiary amino groups are flanked by ortho substituents twisting is observed.¹⁹

NO₂ GROUP

The crystal structures of 2-OMe nitrobenzenes indicate preferential twisting of the NO₂, $\theta \approx 35^\circ$ whereas the OMe remains planar.^{45,63} In contrast 2-NH₂ nitrobenzene exhibits no twisting.^{61,64,65} The average ρ SCS for all 2-substituted nitrobenzenes regardless of whether intramolecular H-bonding exists is within 1 ppm of that for nitrobenzene. M.O. calculations on nitrobenzene predict substantial ρ deshielding for $\theta = 90^\circ$.⁴⁷ The absence of lone pairs[†] on the NO₂ nitrogen has led Exner et al.^{46,66} to question whether the canonical form represented by the classic resonance model exists. The Hammett type σ_F dipole field substituent parameter formulated by Taft²¹ and Topsom⁶⁷ for NO₂ is ca. 3 times that for OMe, OH and NH₂ whereas the situation is reversed for the σ_R resonance parameter. Evidently NO₂ polarization of the aromatic ring is the dominant mechanism affecting π density at the ρ carbon.

[†] It is noted that vinyl groups behave similarly to lone pair type substituents in this respect.⁴³

Table 1. ^{13}C Shifts of Substituted Benzenes

R1	R2	R3	R4	C1	C2	C3	C4	C5	C6	M1	M2	M3	ref
OMe				159.2	113.8	128.9	120.1	128.9	113.8	55.1			4
OMe	Me			157.5	126.4	130.4	120.1	126.5	109.6	54.9			54
OMe	IPt			156.7	137.0	126.3	120.5	125.9	110.6				4
OMe	OMe			148.5	148.5	110.8	120.2	120.2	110.8	55.0	55.0		
			*	148.6	148.6	111.2	120.3	121.9	109.6	54.1	56.0		
OMe	OH			146.4	145.4	114.4	119.9	121.1	110.7	55.4			
OMe	NH ₂			146.9	136.3	114.6	121.0	117.7	110.3	55.4			68
OMe	NO ₂			153.0	139.9	125.8	120.9	134.5	114.3	57.4			4
OH				154.4	114.8	129.9	121.2	129.9	114.8				
OH	OH			143.4	143.4	115.5	121.3	121.3	115.5				69
OH	NH ₂			145.8	137.8	116.3	121.4	118.7	116.5				70
OH	NO ₂			152.6	136.6	125.2	119.5	135.6	119.4				60
NH ₂				147.3	115.3	129.5	118.1	129.5	115.3				69
NH ₂	NH ₂			135.0	135.0	116.4	120.0	120.0	116.4				70
NO ₂				147.8	122.9	129.1	134.3	129.1	122.9				69
OMe		Me		159.5	114.7	139.4	121.4	129.1	110.7				71
OMe	OMe			160.8	100.4	160.8	106.1	129.8	106.1				71
OMe	NH ₂			160.6	101.0	147.7	107.8	130.0	103.9				71
OMe	NO ₂			160.0	108.1	149.2	115.6	129.8	121.2				71
OMe		OMe		153.8	114.6	114.6	153.8	114.6	114.6				35
			*	153.8	118.6	112.6	153.8	118.6	112.6				35
OMe		OH		-	115.3	116.5	-	116.5	115.3				32
			*	-	119.4	117.1	-	118.0	112.1				32
OMe		NH ₂		152.8	114.8	116.3	139.9	116.3	114.8	55.7			75
			*	150.7	115.8	116.9	141.9	116.9	111.2	55.9			75
OMe		NO ₂		165.0	115.1	126.5	142.3	126.5	115.1	56.6			32
			*	165.5	117.8	125.5	141.5	125.5	109.9	56.6			32
OMe		CO ₂ H		-	115.7 (131.6)	-	-	130.8 (130.8)	110.0				34

Table 1 (continued)

R1	R2	R3	R4	C1	C2	C3	C4	C5	C6	M1	M2	M3	ref
OH			CO ₂ H	*	-	117.1	-	-	-	114.9			75
OH			CH ₂ OH	*	-	115.3	-	-	-	115.3			75
				*	155.4	116.7	130.7	130.7	130.7	114.5			75
OP			CO ₂ H		156.1	117.3	128.2	121.6	128.2	117.3			4
Et				*	-	129	131.5	128	131.5	129			34
				*	-	126.5	131.5	126.5	131.5	(131.5)			34
Me	OMe	Me			129.3	156.2	129.3	127.6	122.6	127.6	57.9		4
Me	OP	Me			131.0	150.5	131.0	129.0	124.5	129.0			4
tBu	OMe	tBu			142.6	158.9	142.6	125.9	122.7	125.9	63.7		4
NO ₂	OMe	NO ₂			141.4	154.7	141.4	123.9	123.3	123.9	61.6		14
OMe	OMe	Me			152.0	146.8	131.1	122.1	123.0	109.5	54.9	59.2	54
OMe	OMe	OMe			153.1	137.8	153.1	105.0	123.2	105.0	55.7	60.4	35
			*		154	138	153	105	124	105	54	60	55
OMe	OMe	NH ₂			153.1	136.0	140.7	108.8	124.2	102.3	56.0	60.0	
OMe	OMe	NO ₂			154.3	142.9	145.0	116.0	123.8	116.1	56.4	62.0	
			*		155.0	142.6	144	115.9	122.0	115.9	58.0	61.3	
OH	OH	NO ₂			146.5	142.9	133.8	119.9	115.9	121.7			
OMe	OH	NO ₂			150.0	146.3	133.9	118.9	116.0	117.6	56.6		
OMe	OMe	NH ₂			141.9	149.7	100.5	143.4	106.2	112.9	(56.4)(55.5)		
OMe	OMe	NO ₂			154.2	148.5	106.0	141.0	117.4	109.5	56.1	55.9	
			*		154	148	106	141	118	110	56	54	

^a δ_c from TMS $\pm$ 0.1 ppm; powder values; brackets refer to possible interchange of values

Table 2. ^{13}C Shifts of Substituted Cyclic 1,2 Dialkoxybenzenes^a

compound	n	R3	R4	C1	C2	C3	C4	C5	C6	M1	M2	M3	M4	ref
benzodioxole	1			148.0	148.0	109.2	122.1	122.1	109.2					79
	1		NH ₂	153.1	148.2	98.0	141.4	106.8	108.5					79
	1		NO ₂	153.1	148.3	104.5	142.7	119.8	107.6					79
benzodioxane	2			143.5	143.5	117.1	121.2	121.2	117.1	64.0	64.0			
	2		NO ₂	149.3	143.1	113.2	141.6	117.1	117.4	64.6	64.0			
			*	151.4	143.1	113.0	139	117.0	117.3	66.5	66.4			
benzodioxepane	3			151.2	151.2	121.5	123.3	123.3	121.5	70.4	70.4	31.7		
			*	152.8	151.9	122.9	122.9	124.5	122.9	72.0	72.0	33.5		
	3		NO ₂	153.0	144.7	144.0	118.4	122.5	125.4	70.8	71.5	31.0		
	3		NO ₂	156.6	150.3	117.5	142.7	118.9	121.2	70.4	70.2	30.4		
			*	156.8	149.7	115.4	141.6	118.1	120.3	70.5	70.5	29.2		
benzodioxenane	5			151.6	151.6	122.7	123.7	123.7	122.7	74.5	74.5			
	5		NO ₂	157.5	150.5	119.5	142.7	119.8	122.0	77.0	73.4			
B9C3	5			151.4	151.4	122.9	123.9	123.9	122.9	72.3	72.3	74.0	74.0	
			*	151.0	148.7	124.6	121.8	127.2	119.0	68.2	76.1	72.6	70.4	
	5		NH ₂	152.0	138.4	140.9	(110.4)	124.0	(111.9)	(73.2)	74.2	(72.2)	(71.8)	
	5		NO ₂	153.8	145.2	144.8	119.2	123.3	127.1	74.4	75.8	72.3	71.5	
			*	152.5	141.9	146.9	115.9	124	124.9	69.7	81.0	69.7	69.7	
	5		NH ₂	143.4	152.0	108.5	143.3	110.2	123.9	(75.3)	(73.0)	(72.5)	(72.0)	
	5		NO ₂	157.3	150.6	120.1	142.6	120.3	122.1	75.4	72.0	71.7	72.8	
			*	158.1	148.1	120	140	121	121	69	77.4	70	73.5	
DB9C3	5			152.0	151.4	123.2	(124.7)	(123.2)	122.2	75.3	-	-	75.3	
DB12C4	8			150.8	150.8	119.2	123.2	123.2	119.2	71.0	71.0	71.0	71.0	84
			*	151.6	150.6	122.8	121.3	126.7	114.0	72.2	75.0	-	-	84
DB13C4	9			146.0	143.0	115.2	120.0	120.0	111.0	67.9	67.9	28.0	28.0	99
DB14C4	10			149.5	149.5	115.6	121.7	121.7	115.6	67.3	67.3	29.3	29.3	98
			*	149.3	148.0	111.8	118.0	120.0	110.5	67.0	67.0	(26.6)	(29.3)	98
B15C5	11			149.2	149.2	114.2	121.4	121.4	114.2	-	-	-	-	80
			*	150.4	149.4	111.2	120.0	119.0	111.2	-	-	-	-	80
DB30C10	26			149.1	149.1	114.5	121.5	121.5	114.5	69.2	69.2	69.9	69.9	72
			*	149.5	149.5	113.8	119.2	120.	114.8	(68.3)	(69.5)	(72.4)	(73.7)	72

^a δ_{C} from TMS ± 0.1 ppm; * powder shifts; brackets denote possible interchange of values

K. ORTHO SHIFTS

The origin of $\underline{o}$ shifts is somewhat nebulous as they do not correlate with calculated π electron densities^{19,54,73} due to γ steric shielding of the $\underline{o}$ carbon and other electronic effects. For anisole, phenol, aniline and nitrobenzene the $\underline{o}$ carbons are shielded relative to benzene.

OMe GROUP

2-D single crystal spectra of methoxybenzenes³⁵ yield an $\underline{o}$ cis and $\underline{o}$ trans SCS of -16.3 and -10.4 respectively (solution value is -14.4). The origin of the $\underline{o}$ trans SCS is due to σ_{11} and σ_{22} which supports a resonance model (Section J). The extra 5.9 ppm $\underline{o}$ cis shielding originates in σ_{33} and the direction of this principal element in aromatics is such that σ electrons in the ortho C-H bond are responsible. Therefore a steric interaction is assumed where electric fields (Coulombic and dipolar) polarize C-H σ density onto the ortho carbon thereby shielding it.^{73,74}

The powder spectra of some 4-substituted phenols^{32,75} show an OH $\underline{o}$ cis and $\underline{o}$ trans SCS of -13.7 and -11.5 respectfully (solution value is -12.7). There are negligible differences between anisole and phenol re: the STO-3G[†] π electron density maps which assign a slight excess of $0.0165 \pi e^- \times 180 = 3$ ppm (Section G) on the $\underline{o}$ cis carbons. Therefore if the extra 2.5 ppm experimental $\underline{o}$ cis shielding of anisole relative to phenol is strictly a steric effect then a similar trend should be present for planar ethylbenzene.

† STO-3G; molecular orbital theory using Slater Type Orbitals with 3 primitive Gaussians.¹⁶

A literature survey revealed few powder studies on such molecules. Saito et al.⁷⁵ present the powder spectrum of 4-ethylbenzoic acid where two large peaks at ca. 126.5 ppm and 131.5 ppm are assigned to C1,C3,C5 and C2,C6 respectively based solely on the STO-3G equivalence of the ortho positions in planar ethylbenzene. However based on the powder spectrum of meso-hexestrol (3,4-di-4-hydroxyphenyl hexane) in the same paper one could assign them to C1,C3 and C2,C5,C6 instead. Even though ethyl groups prefer the planar conformation, without the crystal structures the analysis of such spectra are somewhat ambiguous however the latter assignment supports an σ steric effect. The powder spectrum of 4-OH benzyl alcohol⁷⁵ shows a single peak for C2,C6. A crystal structure of this compound would be illuminating.

For 2-substituted anisoles the average σ cis SCS is -19 hence ca. 3 ppm of shielding is attributed to steric interactions due to a greater degree of enforced eclipsing in the torsional network around C1-O1.^{5,54,76} This is supported by the negligible changes in the σ cis SCS of phenols and anilines when 2-substituted.

In contrast the σ cis SCS for 2-NO₂ anisole is -15 hence ca. 1.3 ppm deshielding could be the result of greater mobility around C1-O1 due to the twist $\theta \approx 35^\circ$ of the NO₂ group.⁷⁷ For 2,6-disubstituted anisoles (OMe $\theta = 75^\circ$) the σ SCS cannot be quantified. Surely decreased resonance would result in deshielding but how the O1-M1 field⁷⁸ anisotropically affects the R2, R6 $\perp$ SCS is unknown (Section L).

NO₂ GROUP

Based on calculated π densities and the absence of any strong steric

interactions the σ carbons of nitrobenzene are expected to be deshielded, however the σ SCS is -4.8. For intramolecularly hydrogen bonded 2-OH nitrobenzenes the average σ SCS (C6) is ca. -1.2. Evidently subtle changes in the bond order hence dipole field of the cis N-O bond are responsible for this trend.

CYCLIC 1,2-DIALKOXYBENZENES

Representative σ SCS (C3,C6) and ρ SCS (C4,C5) values for some cyclohomologues are presented in Table 3 and the preferred solid state conformations in Fig. 2.

Table 3. SCS for Cyclic 1,2-Dialkoxybenzenes^{a, b}

compound	n	σ		ρ		λ_{max} [nm]	ϵ	relative rate of bromination ^e
		C3	C6	C4	C5			
benzodioxole ^c	1	-20.3		-7.4		284, 3122		2
benzodioxane	2	-12.4		-8.3		278, 2340		2
benzodioxepane	3	-8.0		-6.2		275, 1360		1
		-6.6	-6.6	-6.6	-5.8			
benzodioxenane	5	-5.8		-4.8		275, 1322		178
B9C3	5	-6.6		-5.6				
		-4.9	-10.5	-7.7	-2.3			
B15C5 ^d	11	-15.3		-8.1				
		-18.3	-18.3	-10.5	-10.5			
veratrole	*	-18.7		-9.3		277, 2336		44
		-18.3	-19.9	-9.5	-7.5			

^a * powder values

^b SCS from benzene at 128.5 ppm

^c ref. 79

^d ref. 80

^e ref. 81

Fig. 2 Experimental and Theoretical Solid State Conformations of Cyclic 1,2-Dialkoxybenzenes

	compound	n	θ_1	θ_2
benzodioxole	1	0	0
	benzodioxane ^a	2	20	20
benzodioxepane ^b	3	64	64
B9C3	5	10	80
	4-NO ₂ B9C3	5	1	74
DB12C4 ^c	8	24	62
	B13C4 ^d	9	3	69
B15C5 ^e	11	13	14
	veratrole ^f	-	0	15

^a based on Drieding models ref. 82,83

^b based on Drieding models ref. 82 and CPMAS Fig. 3

^c x-ray ref. 84 ^d x-ray ref. 85 ^e x-ray ref. 86

^f based on CPMAS Fig. 1

For benzodioxole ($n=1$)^{20,41,82,87} and benzodioxane ($n=2$)^{82,83} both oxygens are constrained to be well conjugated with the ring which is reflected in the large ortho shielding of C3,C4 (recall the planar OMe σ trans SCS is -10.4). The degree of oxygen lone pair overlap with the aromatic p orbitals can be approximated by $\cos^2(\theta-30^\circ)$ for $0^\circ \leq \theta \leq 90^\circ$.⁴ It is noted for $\theta=0^\circ$ each lone pair (overlap of 0.75) has substantial p-type symmetry.

The anomalously large σ shielding for benzodioxole is also present in indole where the σ SCS is -17.5 (relative to the carbon bearing theazole nitrogen).⁸⁴ The angle strain in the pseudoaromatic C-O-C dioxole and C-NH-Cazole bonds alters the lone pair interaction with the ring. This is a through-space field effect since the difference between the ρ SCS for $n=1$ and $n=2$ is less than 1 ppm.

The low temperature powder spectrum of benzodioxepane ($n=3$) is presented in Fig. 3 which reveals substantial twisting around both C1-O1 and C2-O2 as the σ and ρ SCS are -6.6 and ca. -5.8 respectively. This is supported by Archer et al.⁸² where $\theta_1=\theta_2 \approx 49^\circ \rightarrow 64^\circ$ has been calculated.

Fig. 3 272K 45.3 MHz CPMAS Spectrum of Benzodioxepane

An interesting trend pointed out by Baddelley et al.⁸¹ are the unexpectedly high nitration/ bromination rates of benzodioxenane (n=5) over veratrole, benzodioxole, benzodioxane and benzodioxepane⁸⁷ (Table 3). This trend is supported by experimental observations in this thesis. It was concluded that the relative orientation of oxygen lone pairs for n=5 could stabilize an oxonium ion transition state (Fig. 4) more effectively⁸¹ whereas the O1 and O2 lone pairs for n=3 are constrained to move in a synchronous fashion either together or apart.

The ORTEP diagrams of B9C3, 4-NO₂ B9C3 (benzodioxenane homologues) are presented in Figs. 14, 15. These reveal a twist angle about C1-O1 of $\theta = 10^\circ, 1^\circ$ with an sp² C1-O1-M1 bond angle of $124.4^\circ, 123.3^\circ$. In contrast the twist angle around C2-O2 is $\theta = 80^\circ, 74^\circ$ with an sp³ C2-O2-M2 bond angle of 115.4° for both. The respective degree of oxygen lone pair overlap with the aromatic p orbitals, approximated by $\cos^2(\theta - 30^\circ)$ for O1 = 0.88, 0.76 and for O2 = 0.41, 0.52

Fig. 4 Major Canonical Form of B9C3

Literature surveys of various alkoxybenzenes^{2,14,53} and crown ethers^{1,2,85,86,89,90} reveal an average C_{ar}-O-M bond angle of 117° for planar alkoxy (for diphenyl ether it is 124°). For non-planar alkoxy $\theta > 70^\circ$ the average value is 115° which is close to

that of dimethyl ether. It is also noted that the C1-O1 bond lengths for B9C3 and 4-NO₂ B9C3 are 0.04 Å shorter than the corresponding average value.⁵³

As a result the canonical form depicted in Fig. 4 is favoured which shields C4 by 5.4 ppm over C5. The 45.3 MHz CPMAS powder spectrum of B9C3 (Fig. 5) is assigned along with the LORG results in Table 4. It is noted that the LORG method does not take into account any ring current effects, only the flat "pancake" nature of the π bonds. There is some ambiguity in the LORG calculations for C3 and C5, separated by only 1.1 ppm. In 1,2-dialkoxy benzenes the ortho carbons can be assigned by NOESY (Section H) however in the absence of steric interactions the ortho position is still shielded relative to the para i.e., benzodioxane. Therefore the B9C3 assignment of C5 at 127.2 ppm (O2-M2 p SCS of -2.3) and C3 to 124.6 ppm, contrary to LORG, is partly justified. Furthermore O2-M2 has only one ortho substituent, with the O1 lone pairs facing away therefore field polarization of O2 lone pair density into the ring¹⁴ is expected to be minimal. The resulting C5 shift truthfully mirrors the lack of conjugation around C2-O2. Single crystal NMR, x-ray and LORG analysis of B9C3*, B13C4⁶⁶ and veratrole (Fig. 2) would be helpful to verify this assumption.

L. IPSO C-SHIFTS

The origin of δ shifts is attributed to the electronegativity and conjugative ability of the bonded substituent which affect the σ and π electron densities respectively. There is good correlation between electronegativity and the δ shift.¹⁹ The δ shift is expected to reflect changes in θ especially if the substituent possesses

* A collaborative project with the University of Utah is now in progress involving 2-D single crystal ¹³C NMR of B9C3.

Fig. 5 45.3 MHz CPMAS Spectrum of B9C3

Table 4. Observed and Calculated B9C3 ^{13}C Chemical Shifts^a
Aromatic Region

	C1	C2	C3	C4	C5	C6
solution	151.4	151.4	122.9	123.9	123.9	122.9
powder	151.0	148.7	(124.6) ^b	121.8	(127.2)	119.0
LORG ^c	152.9	150.0	137.9	134.4	136.8	126.9

^a δ_c from TMS $\pm$ 0.1 ppm^b assignments may be interchanged^c ab initio for an isolated molecule

lone pairs. Elucidation of this dependency should begin with low temperature single crystal NMR and x-ray work on veratrole to verify whether there are any field interactions between C1-O1 and C2-O2 reflected by deviations in the σ_{11} , σ_{22} and σ_{33} SCS for C1 and C2 relative to anisole.³⁵

It is noted the isotropic $\underline{j}$ SCS for O1-M1 and O2-M2 of veratrole is that of anisole assuming an $\underline{o}$ trans SCS of -10.4. On this basis one might dismiss the existence of field interactions between the trans coplanar methoxyl groups (Fig. 2). A similar analysis on 1,2,3 TMB gives the same $\underline{j}$ SCS for O2-M2 $\theta=76^\circ$ which implies no dependence on twist angle. Obviously caution is needed when attributing physical origins to these ortho compounds based solely on isotropic shifts.

The crystal structures of B9C3, 4-NO₂ B9C3 (Figs. 14, 15) reveal a torsional angle about C1-O1 of $\theta=80^\circ$, 74° and C2-O2 of $\theta=10^\circ$, 1° . This unusual geometry with an alkoxy group cis to a carbon bearing a twisted alkoxy group (Fig. 2) makes the differentiation of the $\underline{j}$ SCS for O1-M1 from the $\underline{o}$ SCS for O2-M2 highly speculative. A similar situation exists with other small cyclohomologues $n=1 \rightarrow 8$ (Table 2, Fig. 2).

In conclusion, for cyclic and acyclic 1,2-dialkoxy derivatives one cannot meaningfully separate $\underline{o}$ and $\underline{j}$ contributions to the C1 and C2 isotropic shifts since they are dependent on the relative orientation and subsequent stability of the two alkoxy groups. More single crystal work is needed to understand this phenomenon. As will be discussed in the next section, the stability of the C_{ar}-O bond plays a key role since $\sigma^p \propto \Delta E^{-1}$.^{11,91}

ORIGIN OF ALIPHATIC ^{13}C SHIFTS IN CROWN ETHERS

M. GENERAL INTRODUCTION - HYDROCARBON SHIFTS

There is a well known empirical equation for calculating solution ^{13}C chemical shifts for non cyclic hydrocarbons.⁹²

$$\delta = -2.6 + 9.1n_{\alpha} + 9.4n_{\beta} - 2.5n_{\gamma} + 0.3n_{\delta} \quad (9)$$

This involves the summation of incremental values based on the number n of α , β , γ and δ carbons relative to the shielded nucleus. This equation has little practical use since it breaks down for branched molecules.

Presented is an alternative method a) $\rightarrow$ d) which can be used to calculate ^{13}C shifts of linear and highly branched hydrocarbons both to a high level of accuracy (Table 5).

$$\text{a) } \delta_{\alpha} = 31.0n_{\alpha}^0 + 24.7n_{\alpha}^1 + 17.7n_{\alpha}^2 + 7.1n_{\alpha}^3 - 3.0n_{\gamma} \quad (10)$$

The superscripts refer to the number of protons on a given α carbon. This equation is applicable for all except three types of carbons;

$$\text{b) } \text{HC}^*\text{R}_3 \quad \delta_b = \delta_{\alpha} - 4n_{\beta} \quad (n > 1)$$

$$\text{c) } \text{H}_3\text{C}^*\text{-CR}_3 \quad \delta_c = 31 - 2n_{\gamma}$$

$$\text{d) } \text{C}^*\text{R}_4 \quad \delta_d = 29 + 2n_{\beta}$$

The overall range $\Delta\delta$ in experimental hydrocarbon shifts⁹³ is due primarily to σ^p , the paramagnetic portion of the isotropic shielding tensor. As discussed previously σ^p is a result of an external magnetic field perturbing the electrons such that excited orbitals become occupied.

Table 5. Observed and Calculated ^{13}C Hydrocarbon Shifts^a

Compound		C1	C2	C3	C4	C5	C6	C7	C8
2-Me propane	obs.	24.5	24.5						
	calc.	24.7	21.3						
2,2-diMe propane		31.6	28.0						
		31.0	29.0						
n-butane		13.2	25.1						
		14.7	24.8						
2-Me butane		21.9	29.9	31.6	11.5				
		21.7	31.9	31.6	11.7				
2,2-diMe butane		28.7	30.3	36.5	8.5				
		29.0	31.0	35.1	8.7				
2,3-diMe butane		19.2	34.0						
		18.7	34.9						
2,2,3-triMe butane		27.0	32.7	37.9	17.7				
		27.0	33.0	37.2	15.7				
2,2,4,4-tetraMe butane		25.6	35.0						
		25.0	35.0						
n-pentane		13.5	22.2	34.1					
		14.7	21.8	35.4					
3-Me pentane		11.4	29.4	36.8	18.7				
		11.7	28.8	38.5	18.7				
2,3-diMe pentane		18.8 ^a	31.9	40.6	26.8	11.6	14.5		
		18.7	31.9	41.5	25.8	11.2	15.7		
2,4-diMe pentane		22.7	25.7	49.0					
		21.7	25.9	49.4					
3,3-diMe pentane		7.7	33.4	32.3	25.6				
		8.7	35.1	33.0	26.0				
2-Me-3-Et pentane		19.0	29.1	47.6	22.6	11.8			
		18.7	28.9	48.1	22.8	11.7			
3,3-diEt pentane		7.1	27.1	37.1					
		8.7	29.1	37.0					
2,2,3-triMe pentane		27.1	33.0	45.4	24.4	13.0	13.3		
		27.0	33.0	43.8	22.8	11.7	12.7		

2,3,3-triMe pentane	17.1	35.1	34.9	32.6	7.9	23.3	
	15.7	34.2	35.0	32.1	8.7	25.0	
2,2,3,3-tetraMe pentane	25.6	36.0	37.3	28.8	9.0	20.6	
	25.0	35.0	37.0	29.1	8.7	20.5	
2,2,3,4-tetraMe pentane	28.2	34.0	47.9	27.4	24.5	11.6	
	27.0	33.0	46.8	25.9	25.9	9.7	
n-hexane	13.7	22.7	31.7				
	14.7	21.8	32.4				
3-Me hexane	10.9	29.5	34.3	39.0	20.2	13.9	18.8
	11.7	28.8	35.5	39.4	18.8	14.7	18.7
2,4-diMe hexane	22.7 ^a	25.4	46.6	32.1	29.9	11.0	19.0
	21.7	25.9	46.4	32.5	28.8	11.7	18.7
3,3-diMe hexane	8.1	34.3	32.8	44.3	17.3	14.8	26.5
	8.7	35.1	33.0	45.7	15.8	14.7	27.0
3,4-diMe hexane	11.8	26.7 ^a	39.0 ^a	14.8 ^a			
	11.7	25.8	38.5	15.7			
2,3,3-triMe hexane	17.1	35.0	35.5	43.1	17.0	14.8	23.8
	15.7	34.2	35.0	42.7	15.8	14.7	25.0
2,2,5-triMe hexane	29.3	30.1	42.0	33.9	28.9	22.5	
	29.0	31.0	42.7	33.4	28.9	21.7	
n-heptane	13.7	22.6	32.0	29.0			
	14.7	21.8	32.4	29.4			
3-Me heptane	11.3	29.7	34.7	36.5	29.7	23.3	14.1
	11.7	28.8	35.5	36.4	29.4	21.8	14.7
3-Et heptane	10.6	25.6	40.7	32.7	29.2	23.1	13.7
	11.7	25.8	40.6	33.4	29.4	21.8	14.7
2,2-diMe heptane	29.2	30.2	44.4	24.4	33.0	22.8	13.8
	29.0	31.0	45.7	23.4	32.4	21.8	14.7
2,3-diMe heptane	19.0 ^a	32.2	38.8	34.0	30.0	23.1	13.8
	18.7	31.9	38.5	33.4	29.4	21.8	14.7
4,4-diMe heptane	14.9	17.3	44.8	32.8	27.0		
	14.7	15.8	45.7	33.0	27.0		
3,5-diMe heptane	11.0 ^a	30.0 ^a	32.0 ^a	44.4 ^a	19.2 ^a		
	11.7	28.8	32.5	43.4	19.7		

^a observed values from refs. 93, 94

^b the symmetry related backbone carbons of the parent hydrocarbon are numbered first.⁹³ (* average diastereotropic shift value).

In a freely rotating molecule the number and nature of eclipsing conformations in a X-C1-C2-Y torsional network should be reflected in σ^p for C1, C2 based on the following hypothesis. Mixing between the C1-X and C2-Y orbitals (excited/excited and ground/excited couples) occurs if the proper symmetry is present. Excited orbitals are oriented away from the internuclear axes hence mixing is favoured for eclipsed and to a lesser extent gauche conformations. The lower the excitation energies ΔE of these orbitals, the more π type hyperconjugative electron density is expected between C1 and C2 hence these nuclei are deshielded (recall $\sigma^p \propto \Delta E^{-1}$).^{11,91}

For molecules with γ substituents repulsive Coulombic forces result in preferred conformations with C-C/C-H gauche-eclipsed. Similar preference is seen in the 2.3 ppm diastereotropic inequivalence (temperature dependent) of the geminal CH₃ carbons of 2,4-diMe hexane whereas for 2-Me-4-tBu hexane it is 7.2 ppm.¹³

Inspection of the proposed empirical method a) $\rightarrow$ d) reveals that σ^p indeed arises through C-H/C-C gauche-eclipsing interactions since the magnitudes of the incremental values for δ_a are roughly $n_a^k \approx (4-k) n_a^3$. It is noted that the chemical shift range for the carbons relevant to c), d) is $\Delta\delta = 9.3, 6.7$ ppm whereas for all other types $\Delta\delta = \text{ca. } 26\text{--}40$ ppm.⁹³

This method also reveals that the small, shielding γ -shifts apply only to non-quaternary carbons since δ_a has no γ dependence. It is noted these carbons are in the interior of torsional networks R-R₂C_d-C-C_b hence $\Delta\sigma^p \equiv \Delta\delta \propto n_b$. Large torsional (rotational) barriers between conformations due to γ -steric interactions keep C-H/C-C orbitals in "fixed" orientations long enough on average so that the effects of

excited state orbital mixing (σ^p) can be detected.

An examination of equatorial substituted cyclohexanes reveal that all carbons in the locked $C_\gamma-C_\beta-C_\alpha-R$ torsional networks ($R = CH_3, OH, OMe, NH_2$) are deshielded by ca. 3-4 ppm relative to the axial stereoisomer (Table 6).^{51,95} The Newman projections for methylcyclohexane (Fig. 6) reveal more C-H/C-C gauche networks in the equatorial isomer. For comparison, the corresponding SCS of a hypothetical acyclic $R-(H_2C)_n-H_2C_\gamma-H_2C_\beta-HC_\alpha(H_3C)-(H_2C)_n-R$ fragment $n \geq 3$ were calculated utilizing the proposed method a) $\rightarrow$ d) and are presented in Table 6.

Fig. 6 Newman Projections for Eq. and Ax. Methylcyclohexane

Table 6. SCS for Cyclohexanes^a

		C_α	C_β	C_γ	C_δ
CH ₃	ax	1.4	5.4	-6.4	0.0
	eq	5.0	9.0	0.0	-0.2
	acyclic ^b	5.4	9.3	0.7	-
OMe ^c	ax	47.0	1.8	-7.2	-1.4
	eq	51.8	4.5	-2.8	-1.8
OH	ax	37.8	5.5	-6.8	-0.7
	eq	42.6	8.0	-2.7	-2.1
NH ₂	eq	23.8	9.9	-1.6	-1.0

^a ref. 51; in ppm from cyclohexane δ_c 27.1

^b calculated using proposed method a) $\rightarrow$ d)

^c ref. 95; at 180K

On this basis the data reveals that acyclic compounds favour those conformations with maximum C-H/C-C gauche networks and also casts doubt on the steric origin of γ shifts.

It is also noted from table 6 that C1 of methoxycyclohexane is substantially deshielded ca. 9 ppm relative to cyclohexanol. In contrast C2 of cyclohexanol is deshielded ca. 3 ppm relative to methoxycyclohexane. These observations are consistent with the proposed hypothesis because C1 of the methoxy moiety is involved in two deshielding M-H/C1-O, C1-H/M-O networks and C2 of the hydroxyl moiety is only involved in O-H/C1-C2. Evidently C-H (C-C) and O-H (C-O) bonds are similar with respect to σ^p paramagnetic shielding (Section O).

The similar C3 shifts in the axial isomers of cyclohexanol and methoxycyclohexane suggest a preferred orientation about C1-O where the oxygen lone pairs face inward, minimizing 1,3-diaxial steric interactions. This is not certain since theoretical⁹⁶ LORG data (Section O) and experimental⁹⁷ observations (table 6) question the overall significance of the H-H steric contribution to γ -shifts.

N. ASSIGNMENT OF THE CYCLOHEXYL CARBONS IN THE C9C3 POWDER SPECTRUM

The 45.3 MHz CPMAS powder spectrum of C9C3 is presented in Fig. 7. Unambiguous assignments of the six cyclohexyl carbons has been achieved. At 210K the C9C3 chair-chair interconversion is slow relative to the NMR timescale and all six cyclohexyl resonances are separated (Fig. 8)^{23,24} due to the differing torsional

Fig. 7 45.3 MHz CPMAS Spectrum of C₉C₃ Fig. 8 210 → 300K 100 MHz ¹³C Spectra and 210K DEPT of C₉C₃

environments around C1-C6 and C2-C3 (Fig. 6). The four ether resonances are also well separated at this temperature in contrast to B9C3. The similarity between the the 210K solution spectrum and the powder spectrum is unmistakable hence the latter is assigned based on this and the complementary crystal structure (Fig. 18).

The 210K DEPT spectrum unambiguously assigns the α carbons to 75.7 ppm and 82.2 ppm which correlate respectively to H1_{ax} at 3.10 ppm and H2_{eq} at 4.15 ppm via 210K HETCOR (Fig. 9). The doublet centered at 3.10 ppm (vicinal coupling $^3J=10.8$ Hz) is indicative of the $\theta=178.1^\circ$ H1_{ax}-C1-C6-H6_{ax} dihedral angle.

Fig. 9 210K HETCOR of C9C3

The origin of the 1.1 ppm deshielding of H2 relative to H1 will be discussed in detail in Section R. The 210K COSY spectrum (Fig. 10) reveals H2 has a crosspeak to an H3 doublet (12.8 Hz) centered at 1.76 ppm; from HETCOR C3 is assigned to 30.1 ppm and the second H3 to the broad peak at 1.12 ppm. Similarly H1 has COSY crosspeaks to both H6"; the singlet at 1.53 ppm and the doublet (11.6 Hz) at 1.45 ppm; from HETCOR C6 is assigned to 27.9 ppm.

Fig. 10 210K COSY of C9C3

COSY reveals no correlation between the H6 resonances and the tall peak at 1.26 ppm hence this is attributed to the H4"; from HETCOR C4 is assigned to 19.4 ppm. By elimination C5 is at 24.8 ppm which has two H5 HETCOR crosspeaks; a doublet (12.0 Hz) at 1.60 ppm and the broad peak at 1.12 ppm. The cyclohexyl ¹³C assignments are summarized in Table 7 (the ¹H data will be discussed in Section R).

Table 7. Observed C9C3 ^{13}C Chemical Shifts^a
Cyclohexyl Region

		C1	C2	C3	C4	C5	C6
solution	300K	79.0	79.0	29.0	22.1	22.1	29.0
solution	210K	82.2	75.7	30.1	19.4	24.8	27.9
powder		83	77	29	20	26	29

^a δ_c from TMS $\pm$ 0.1 ppm

It is noted that previous assignments of the carbons in locked cis-1,2-dimethoxycyclohexanes and cis-cyclohexano crown ethers were based on the assumption that substituent parameters for ax. and eq. methoxycyclohexanes (Table 6)⁹⁵ were additive. There is some ambiguity using this method for the β carbons in cis-1,2-dimethoxycyclohexane due to the large ax. OMe γ SCS which results in C6 shielded by only 1.6 ppm relative to C3. The unambiguous assignment of C3 and C6 in Table 7 confirm β substituent additivity for this class of molecules.

O. ETHER CARBON SHIFTS

In crown ethers C-O-C-C and O-C-C-O aliphatic torsional networks are present. Buchanan et al. have correlated crystal structures with solid phase^{1,98-100} and low temperature solution²⁴ spectra and verified a large chemical shift dependence on θ for the carbons bearing oxygen in these networks. Ab initio LORG⁹ analysis of the CH_3 shift of anisole versus θ (fully optimized MOPAC¹⁰¹ geometry for each θ) is presented in Fig. 11.

Fig. 11 LORG θ vs. M1 Shift of Anisole

In a study by Grant et al.³⁵ of the CH_3 principal tensor elements of 1,2,3 TMB $\theta=76^\circ$ (single crystal) and anisole $\theta=90^\circ$ (LORG, Fig. 11) the ca. 5 ppm isotropic CH_3 deshielding^{5,54,102} relative to $\theta=0^\circ$ is attributed to two factors; (i) a destabilized $\text{C}_\alpha\text{-O}$ bond due to decreased resonance. This results in a lower ΔE where more $\text{C}_\alpha\text{-O}$ antibonding density is available to mix with a methyl C-H bond of suitable symmetry and (ii) decreased steric interactions between the CH_3 group and the $\underline{o}$ C-H bond.

Similar LORG data for methyl ethyl ether (MOPAC geometry for $\theta=0^\circ$ only) is presented in Fig. 12 and for ethylene glycol in Fig. 13[†]. The common feature for these two is that deshielding occurs for carbons in eclipsing C-H/C-O networks hence the similar shapes of the C1 and C3 curves for methyl ethyl ether. This is in keeping with the previous hypothesis where a similar situation exists for C-H/C-C gauche eclipsing in hydrocarbons.⁹⁶ It is noted that this effect is diminished for C4 (Fig. 12)

[†] unpublished observations by G.W. Buchanan

Fig. 12 LORG θ vs. C1, C3, C4 Shifts of EtOMe Fig. 13 θ vs. ^{13}C Shift of Ethylene Glycol

* absolute scale (CH_4 221 ppm); TMS appears at ca. 119 ppm

attributed to lone pair/C-C eclipsing instead.¹⁰³ For methyl ethyl ether $\theta=0^\circ$ the LORG σ^p shielding for C1, C4 (γ cis-coplanar) and C3 is expected to be quite dependent on the relative orientation of the methyl C-H bonds^{74,104} as pointed out by Garber et al.⁹⁶ and Whitesell et al.⁹⁷ both of whom question the steric factor in γ shifts. Recall in the ^{13}C spectrum of 1,8-dimethylnaphthalene the CH_3 groups (δ cis-coplanar) are deshielded relative to methylnaphthalene.⁵⁰ It has been shown that for $\theta>60^\circ$ the shielding is greatly attenuated;¹⁰⁵ in light of this and the LORG data, C1 and C2 in crown ether C1-O-C2-C networks ($\theta>60^\circ$) are expected to be equally dependent on θ .

P. ASSIGNMENT OF THE ETHER CARBONS IN THE B9C3 AND 4-NO₂ B9C3

POWDER SPECTRA

The crystallographic data and ORTEP diagrams for B9C3, 4-NO₂ B9C3 are presented in Tables 8, 9 and Figs. 14, 15. The LORG calculations for EtOMe indicate that one cannot make any assumptions on the relative positions of M3 and M4 based solely on θ for the M2-M3-O3-M4 and M1-M4-O3-M3 networks for $\theta>60^\circ$. Similarly one cannot assign M2 and M3 based on O2-M2-M3-O3 etc., each network is complimentary. For M-M-O-M $\theta<60^\circ$ shielding of ca. 3 ppm is expected for the terminal γ methylene carbons. The 45.3 MHz CPMAS powder spectra (aliphatic regions) for B9C3 and 4-NO₂ B9C3 are presented in Fig. 16 with the assignments and B9C3 LORG calculations in Table 10.

Fig. 14 ORTEP Diagram of B9C3

Fig. 15 ORTEP Diagram of 4-NO₂ B9C3

Table 8a B9C3 Crystallographic Data

formula	C ₁₀ H ₁₂ O ₃
FW	180.20
crystal system	orthorhombic
space group	P cab
a, Å	8.5351(18)
b, Å	25.005(5)
c, Å	8.2679(16)
V, Å ³	1764.5(6)
Z (molecules/cell)	8
D _c , g/cm ³	1.357
cryst dimensions, mm ³	0.20 x 0.20 x 0.20
radiation (λ, Å)	MoKα (0.70930)
octants measured	h, k, l, -h, -k, -l
max 2θ	47.0
temperature	20°C
no. of unique reflections	1312
no. of observed reflections	667
(Iσ(I) ratio)	0.008
R _f	0.080
R _w	0.040
Goodness of Fit	3.21

Table 8b B9C3 Atomic Parameters x, y, z and Biso^a

	x	y	z	Biso
O2	0.1561(8)	0.65243(21)	0.2289(6)	4.1(3)
O1	-0.0707(7)	0.57272(21)	0.3402(8)	5.8(4)
O3	0.2696(8)	0.55548(22)	0.3649(7)	5.0(3)
C2	0.0406(10)	0.6616 (4)	0.3436(10)	3.6(5)
C1	-0.0656(11)	0.6233 (4)	0.3881(11)	4.0(5)
C6	-0.1851(11)	0.6354 (4)	0.4974(12)	4.8(5)
C5	-0.1963(11)	0.6839 (4)	0.5614(10)	4.9(5)
C4	-0.0925(13)	0.7237 (3)	0.5166(11)	4.7(5)
C3	0.0240(11)	0.7113 (3)	0.4061(11)	4.1(5)
M1	0.0214(11)	0.5511 (3)	0.2116(11)	4.5(5)
M4	0.1617(12)	0.5234 (3)	0.2798(11)	4.6(5)
M3	0.3640(10)	0.5897 (4)	0.2673(10)	4.5(5)
M2	0.3123(11)	0.6454 (4)	0.2921(11)	4.6(5)
H6	-0.272	0.605	0.542	5.4
H5	-0.284	0.697	0.649	5.9
H4	-0.096	0.766	0.567	5.2
H3	0.110	0.742	0.370	5.2
H1A	0.068	0.581	0.128	5.4
H1B	-0.045	0.522	0.138	5.4
H4A	0.225	0.501	0.181	6.0
H4B	0.117	0.491	0.361	6.0
H3A	0.487	0.582	0.290	5.2
H3B	0.346	0.578	0.135	5.2
H2A	0.397	0.672	0.234	5.4
H2B	0.318	0.652	0.422	5.4

* Biso is the Mean of the Principal Axes of the Thermal Ellipsoid.

E.S.Ds. refer to the last digit printed.

Table 8c B9C3 Bond Distances in Angstroms

O2-C2	1.387(11)	M4-H4B	1.124(8)
O2-M2	1.443(12)	M3-M2	1.475(13)
O1-C1	1.326(11)	M3-H3A	1.084(9)
O1-M1	1.429(11)	M3-H3B	1.140(9)
O3-M4	1.409(11)	C6-C5	1.326(14)
O3-M3	1.425(11)	C6-H6	1.124(8)
C2-C1	1.369(13)	C4-H5	1.384(15)
C2-C3	1.354(13)	C4-H4	1.147(8)
C1-C6	1.396(14)	M1-H1A	1.084(8)
C3-C4	1.385(14)	M1-H1B	1.112(8)
C3-H3	1.110(8)	M2-H2A	1.093(8)
M4-M1	1.494(13)	M2-H2B	1.091(9)
M4-H4A	1.128(9)	C5-H5	1.097(9)

Table 8d B9C3 Bond Angles in Degrees

C2-O2-M2	115.4(6)	H3A-M3-H3B	104.9(7)
C1-O1-M1	124.4(7)	C1-C6-C5	120.6(8)
M4-O3-M3	115.3(7)	C1-C6-H6	123.3(9)
O2-C2-C1	122.6(8)	C5-C6-H6	116.0(9)
O2-C2-C3	119.2(8)	C3-C4-C5	118.3(8)
C1-C2-C3	118.0(8)	C3-C4-H4	118.1(9)
O1-C1-C2	127.5(9)	C5-C4-H4	123.6(9)
O1-C1-C6	112.1(8)	O1-M1-M4	109.6(7)
C2-C1-C6	120.4(8)	O1-M1-H1A	114.7(7)
C2-C3-C4	122.2(8)	O1-M1-H1B	112.3(7)
C2-C3-H3	118.1(9)	M4-M1-H1A	105.1(7)
C4-C3-H3	119.6(8)	M4-M1-H1B	107.8(7)
O3-M4-M1	116.6(6)	H1A-M1-H1B	106.8(7)
O3-M4-H4A	109.6(8)	O2-M2-M3	110.0(7)
O3-M4-H4B	109.7(8)	O2-M2-H2A	112.4(8)
M1-M4-H4A	109.9(8)	O2-M2-H2B	112.3(7)
M1-M4-H4B	107.1(8)	M3-M2-H2A	108.3(8)
H4A-M4-H4B	103.1(6)	M3-M2-H2B	105.9(8)
O3-M3-M2	108.6(7)	H2A-M2-H2B	107.7(8)
O3-M3-H3A	110.2(7)	C6-C5-C4	120.3(8)
O3-M3-H3B	108.3(7)	C6-C5-H5	126.5(10)
M2-M3-H3A	115.3(8)	C4-C5-H5	113.2(9)
M2-M3-H3B	109.3(7)		

Table 8e B9C3 Torsion Angles

M2-O2-C2-C1	-105.0(9)	M2-O2-C2-C3	79.9(8)
C2-O2-M2-M3	111.9(9)	M1-O1-C1-C2	-10.5(5)
M1-O1-C1-C6	170.3(10)	C1-O1-M1-M4	98.4(8)
M3-O3-M4-M1	-73.4(7)	M4-O3-M3-M2	108.7(9)
O2-C2-C1-O1	4.4(4)	O2-C2-C1-C6	-176.4(11)
C3-C2-C1-O1	179.5(12)	C3-C2-C1-C6	-1.3(5)
O2-C2-C3-C4	177.6(11)	C1-C2-C3-C4	2.3(5)
O1-C1-C6-C5	178.4(12)	C2-C1-C6-C5	-0.9(5)
C1-C6-C5-C4	2.1(5)	C6-C5-C4-C3	-1.1(5)
C5-C4-C3-C2	-1.2(5)	O1-M1-M4-O3	-63.3(6)
O3-M3-M2-O2	-66.7(6)		

Table 9a 4-NO₂ B9C3 Crystallographic Data

formula	C ₁₀ H ₁₁ NO ₅
FW	225.20
crystal system	monoclinic
space group	P 2 ₁ /c
a, Å	4.3393(14)
b, Å	12.562(5)
c, Å	18.321(4)
V, Å ³	994.5(5)
Z (molecules/cell)	4
D _c , g/cm ³	1.504
cryst dimensions, mm ³	0.10 x 0.10 x 0.30
radiation (λ, Å)	MoKα (0.70930)
octants measured	h, k, l, -h, -k, -l
max 2θ	50.00
temperature	-90°C
no. of unique reflections	1460
no. of observed reflections	1227
(Iσ(I) ratio)	0.055
R _f	0.052
R _w	0.070
Goodness of Fit	5.67

Table 9b 4-NO₂ B9C3 Atomic Parameters x, y, z and Biso^a

	x	y	z	Biso
O1	0.6609(6)	0.77547(20)	0.20823(13)	2.75(13)
O2	0.5696(6)	0.60959(20)	0.09095(13)	2.57(11)
O3	0.8710(6)	0.55039(20)	0.22997(13)	2.69(13)
O4	1.3688(8)	0.90156(25)	-0.05923(16)	4.25(16)
O5	1.2101(8)	0.74678(24)	-0.09618(15)	4.55(17)
N1	1.2249(8)	0.8196 (3)	-0.05086(17)	2.99(16)
C1	0.7796(9)	0.7769 (3)	0.14194(19)	2.08(15)
C2	0.7488(9)	0.6991 (3)	0.08637(19)	2.05(15)
C3	0.8956(9)	0.7154 (3)	0.02392(20)	2.34(17)
C4	1.0671(9)	0.8065 (3)	0.01530(19)	2.28(16)
C5	1.0948(10)	0.8845 (3)	0.06865(21)	2.43(18)
C6	0.9496(9)	0.8691 (3)	0.13131(21)	2.41(18)
M2	0.7380(12)	0.5110 (3)	0.10282(23)	2.92(21)
M3	0.7220(12)	0.4747 (3)	0.18058(22)	2.94(21)
M4	0.6664(11)	0.6069 (4)	0.27307(24)	3.03(20)
M1	0.4715(10)	0.6893 (3)	0.23200(23)	2.74(19)
H3	0.885 (8)	0.654 (3)	-0.0159 (19)	2.7 (8)
H5	1.209 (9)	0.940 (3)	0.0631 (19)	2.7 (9)
H6	0.958 (9)	0.924 (3)	0.1710 (19)	2.8 (8)
H2A	0.642 (9)	0.462 (3)	0.0683 (20)	2.6 (8)
H2B	0.957 (9)	0.524 (3)	0.0874 (18)	2.3 (8)
H3A	0.496 (10)	0.465 (3)	0.1880 (19)	3.0 (9)
H3B	0.835 (9)	0.405 (3)	0.1851 (20)	3.1 (9)
H4A	0.526 (10)	0.557 (3)	0.2894 (22)	3.9 (10)
H4B	0.804 (9)	0.648 (3)	0.3115 (20)	3.1 (9)
H1A	0.329 (8)	0.657 (3)	0.1848 (20)	2.9 (8)
H1B	0.349 (10)	0.725 (3)	0.2647 (22)	3.7 (10)

^a Biso is the Mean of the Principal Axes of the Thermal Ellipsoid.

E.S.D.'s refer to the last digit printed.

Table 9c 4-NO₂ B9C3 Bond Distances (Å)

O1-C1	1.362(4)	C4-C5	1.381(6)
O1-M1	1.450(5)	C5-C6	1.373(6)
O2-C2	1.374(4)	C5-H5	0.87(4)
O2-M2	1.444(5)	C6-H6	1.00(4)
O3-M3	1.427(5)	M2-M3	1.504(6)
O3-M4	1.430(5)	M2-H2A	0.95(4)
O4-N1	1.221(5)	M2-H2B	1.03(4)
O5-N1	1.233(5)	M3-H3A	1.01(4)
N1-C4	1.455(5)	M3-H3B	1.00(4)
C1-C2	1.409(5)	M4-M1	1.496(6)
C1-C6	1.397(5)	M4-H4A	0.94(4)
C2-C3	1.375(5)	M4-H4B	1.02(4)
C3-C4	1.382(6)	M1-H1A	1.09(4)
C-H3	1.06(4)	M1-H1B	0.95(4)

Table 9d 4-NO₂ B9C3 Atomic Bond Angles in Degrees

C1-O1-M1	123.3(3)	O2-M2-M3	109.7(4)
C2-O2-M2	115.4(3)	O2-M2-H2A	105.8(22)
M3-O3-M4	114.4(3)	O2-M2-H2B	107.1(19)
O4-N1-O5	122.5(3)	M3-M2-H2A	112.0(21)
O4-N1-C4	119.0(3)	M3-M2-H2B	115.5(19)
O5-N1-C4	118.6(3)	H2A-M2-H2B	106(3)
O1-C1-C2	128.1(3)	O3-M3-M2	109.9(3)
O1-C1-C6	112.5(3)	O3-M3-H3A	112.4(21)
C2-C1-C6	119.4(3)	O3-M3-H3B	109.7(23)
O2-C2-C1	122.7(3)	M2-M3-H3A	107.1(20)
O2-C2-C3	118.8(3)	M2-M3-H3B	106.1(21)
C1-C2-C3	118.5(3)	H3A-M3-H3B	111(3)
C2-C3-C4	121.0(4)	O3-M4-M1	114.6(3)
C2-C3-H3	117.7(19)	O3-M4-H4A	107.4(25)
C4-C3-H3	121.2(19)	O3-M4-H4B	106.1(21)
N1-C4-C3	119.2(3)	M1-M4-H4A	105(3)
N1-C4-C5	119.5(4)	M1-M4-H4B	105.5(21)
C3-C4-C5	121.3(4)	H4A-H4-H4B	118(3)
C4-C5-C6	118.4(4)	O1-M1-M4	111.0(4)
C4-C5-H5	120.1(24)	O1-M1-H1A	109.5(18)
C6-C5-H5	121.4(24)	O1-M1-H1B	101.5(24)
C1-C6-C5	121.5(4)	M4-M1-H1A	113.3(19)
C1-C6-H6	117.0(21)	M4-M1-H1B	109.6(24)
C5-C6-H6	121.5(21)	H1A-M1-H1B	111(3)

Table 9e

4-NO₂ B9C3 Torsion Angles

M1-O1-C1-C2	-0.9(2)	M1-O1-C1-C6	179.0(4)
C1-O1-M1-M4	91.4(4)	C1-O1-M1-H1A	-34.4(19)
C1-O1-M1-H1B	-152.2(24)	M2-O2-C2-C1	-108.5(4)
M2-O2-C2-C3	73.9(3)	C2-O2-M2-M3	106.2(4)
C2-O2-M2-H2A	-132.8(22)	C2-O2-M2-H2B	-19.9(19)
M4-O3-M3-M2	111.7(4)	M4-O3-M3-H3A	-7.5(21)
M4-O3-M3-H3B	-132.0(22)	M3-O3-M4-M1	-73.7(3)
M3-O3-M4-H4A	43.1(25)	M3-O3-M4-H4B	170.4(21)
O4-N1-C4-C3	177.9(5)	O4-N1-C4-C5	-3.0(2)
O5-N1-C4-C3	-2.7(2)	O5-N1-C4-C5	176.5(5)
O1-C1-C2-O2	4.0(1)	O1-C1-C2-C3	-178.3(5)
C6-C1-C2-O2	-175.9(4)	C6-C1-C2-C3	1.8(2)
O1-C1-C6-C5	178.3(5)	O1-C1-C6-H6	-2.7(20)
C2-C1-C6-C5	-1.8(2)	C2-C1-C6-H6	177.2(21)
O2-C2-C3-C4	177.1(5)	O2-C2-C3-H3	-6.7(19)
C1-C2-C3-C4	-0.6(2)	C1-C2-C3-H3	175.5(19)
C2-C3-C4-N1	178.5(5)	C2-C3-C4-C5	-0.6(2)
H3-C3-C4-N1	2.5(19)	H3-C3-C4-C5	-176.6(19)
N1-C4-C5-C6	-178.5(5)	N1-C4-C5-H5	-1.4(25)
C3-C4-C5-C6	0.6(2)	C3-C4-C5-H5	177.6(25)
C4-C5-C6-C1	0.6(2)	C4-C5-C6-H6	-178.4(21)
H5-C5-C6-C1	-176.4(25)	H5-C5-C6-H6	4.6(32)
O2-M2-M3-O3	-63.3(3)	O2-M2-M3-H3A	59.1(21)
O2-M2-M3-H3B	178.1(23)	H2A-M2-M3-O3	179.5(22)
H2A-M2-M3-H3A	-58.1(30)	H2A-M2-M3-H3B	60.9(31)
H2B-M2-M3-O3	57.8(20)	H2B-M2-M3-H3A	-179.8(30)
H2B-M2-M3-H3B	-60.7(29)	O3-M4-M1-O1	-66.2(3)
O3-M4-M1-H1A	57.5(19)	O3-M4-M1-H1B	-177.5(25)
H4A-M4-M1-O1	175.9(25)	H4A-M4-M1-H1A	-60.5(31)
H4A-M4-M1-H1B	64.5(35)	H4B-M4-M1-O1	50.1(21)
H4B-M4-M1-H1A	173.7(28)	H4B-M4-M1-H1B	-61.3(32)

Inspection of the important torsional networks (Table 10) reveals only one $\theta < 60^\circ$, network (I). The crystal structures of B9C3, 4-NO₂ B9C3 reveal a strong δ cis-coplanar steric interaction between M1 and O2. The relative orientation of the the M1-H bond and O2 lone pair^{14,74} is such that steric repulsion is expected to polarize bond density onto M1 thereby shielding it. LONG calculations on veratrole using the θ (I) and θ (VIII) values but varying θ (II) would be needed to validate this.

Table 10. Important Torsional Networks^a

	network	B	N	C	network	B	N	C
		θ	θ	θ		θ	$\cos^2\theta$	$\cos^2\theta$
I	O2 C1-O1-O1-M1 O2	10.5	0.9	161.1 76.8	H1a1-C1-O1-M1	-	-	40.1 0.58
II	O1-O1-M1-M4	95.4	91.4	120.3	H1-M1-O1-O1	22	0.86	34.4 0.88 5.5 0.99
III	O1-M1-M4-O3	63.3	66.2	67.4	H1-M1-M4-O3	57	0.30	57.0 0.30 55.5 0.31
					H4-M4-M1-O1	57	0.31	50.1 0.41 56.0 0.31
IV	M1-M4-O3-M3	73.4	73.7	96.1	H4-M4-O3-M3	47	0.46	43.2 0.53 38.2 0.78
V	M3-M3-O3-M4	108.7	111.7	127.7	H3-M3-O3-M4	11	0.98	7.5 0.98 2.6 1.00
					H2-M2-M3-O3	53	0.36	57.8 0.28 43.8 0.50
VI	O2-M3-M3-O3	66.7	63.3	78.0	H3-M3-M2-O2	53	0.36	59.1 0.28 43.2 0.53
VII	O2-O2-M3-M3	111.9	106.2	78.0	H2-M2-O2-O2	8	0.98	19.9 0.88 49.2 0.43
VIII	O3 C2-O2-O2-M2 O1	79.9	73.9	117.1 122.1	H2a2-O2-O2-M2	-	-	2.8 1.00

^a B, N, C refer to B9C3, 4-NO₂ B9C3, C9C3

For B9C3 the angle ϕ between M-H and M-O bonds in an "ether-backbone" torsional network can be approximated by $\phi = |120^\circ - \theta|$, only $\phi \leq 60^\circ$ considered, where large $\cos^2\phi$ overlap implies large σ^p . The experimental ϕ values for 4-NO₂ B9C3 and C9C3 were available for verification of this approximation (Table 10). Ab initio LORG data (Figs. 12, 13) suggest all oxygen-bearing methylene carbons in a given network have a similar σ^p vs. ϕ dependence. It is noted that each carbon in O-M-M-O networks has two associated ϕ values; with poor overlap negligible difference is expected however for $\cos^2\phi > 0.5$ σ^p is amplified relative to M-O-M-M networks. LORG analysis on ethylene glycol would be helpful.

For B9C3, 4-NO₂, B9C3 there is excellent M-H/M-O $\cos^2\phi$ overlap in network (V)=0.96, 0.98 which results in a large σ^p for M3 and M4. There is also excellent M-H/C_{ar}-O overlap involving M2 (VII)=0.98, 0.88 and to a lesser extent M1 (II)=0.86, 0.68 (all other networks have $\cos^2\phi < 0.5$ hence no significant σ^p contribution).

As discussed on pg. 42 factor (i), the low ΔE of the destabilized C2_{ar}-O2 bond θ (VIII)=79.9°, 73.9° results in a large σ^p for M2. Also the δ cis-coplanar M1-O1-C1-C2-O2 network is expected to shield M1. Therefore M1 and M2 are expected to be separated by at least 6 ppm (Fig. 11) and are assigned to the respective flanking upfield (68.2, 69.6 ppm) and downfield (76.1, 77.4 ppm) powder resonances (Fig. 16). The B9C3 LORG data (Table 11) supports this interpretation as does the recently obtained 45.3 MHz dephased CPMAS spectrum of d₄-B9C3 (Fig. 17) which unambiguously assigns M1, M2 to the flanking resonances.

Inspection of Table 10 suggests the source of the 2.5 ppm separation of M3,

M4 is due to differences between (IV), (V) which leads one to conclude that for a given torsional network, interior carbons have a somewhat greater σ^p vs. ϕ dependence than terminal carbons. This trend is not reflected in the LORG analysis of EtOMe (Fig. 12). Therefore for B9C3, 4-NO₂ B9C3 M3 is assigned to 72.9, 71.7 ppm and M4 to 70.4, 70 ppm.

Fig. 16 45.3 MHz CPMAS Spectra of B9C3, 4-NO₂ B9C3 Aliphatic Region

In Section K it was concluded that the constraint imposed by ring size on the relative orientations of the O1, O2 lone pairs has a profound effect on the rate of aromatic electrophilic substitution. This is reflected in $\Delta\delta = \underline{o}\delta - \underline{p}\delta$ for the powder spectra of benzodioxepane (Fig 2) and B9C3 (Fig. 5). In the solution spectra of 4-NO₂ benzodioxepane and 4-NO₂ benzodioxene (appendix) $M1\delta - M2\delta = 0.2$ and 3.6 ppm respectively. Evidently such concerted through-space field effects between O1 and O2 may be another operative factor in the large separation of M1 and M2 in the B9C3, 4-NO₂ B9C3 powder spectra.[†]

† The CPMAS M2 resonance of 3-NO₂ B9C3 (appendix) is assigned to 81 ppm, deshielded by 11 ppm relative to M1, M3, M4.

Table 11. Aliphatic ^{13}C Chemical Shifts^a

	B9C3				4-NO ₂ B9C3			
	M1	M2	M3	M4	M1	M2	M3	M4
solution ^b	74.0	74.0	72.3	72.3	75.4	72.0	71.7	72.8
powder	68.2	76.1	72.9	70.4	69	73.5	71.7	70
LORG ^c	61.9	69.6	69.7	70.1	-	-	-	-

^a δ_{C} from TMS $\pm$ 0.1^b assignments consistent with d₄-B9C3 (appendix)^c ab initio for an isolated gas molecule Fig. 17 45.3 MHz CPMAS Routine and Dephased Spectra of d₄-B9C3

Q. ASSIGNMENT OF THE C9C3 POWDER SPECTRUM - ETHER REGION

The crystallographic data and ORTEP diagram for C9C3 are presented in Table 12, Fig. 18. The 45.3 MHz CPMAS spectrum for C9C3 and the assignments thereof are presented in Fig. 7, Table 13. Note the similarity with the 210K solution spectrum (Figs. 8, 22).

Inspection of Table 10 reveals no $\theta < 60^\circ$ networks hence no steric interactions. The high degree of planarity in the cisoid H4A-M4-O3-M3-H3A system $\cos^2\phi$ (IV)=0.78, (V)=1.00 results in a large σ^p for M3, M4 relative to M1, M2. For the benzo moieties it was concluded that interior carbons show a larger σ^p vs. ϕ dependence hence M3 is assigned to 78.6 ppm and M4 to 74.3 ppm. The recently

Fig. 18 ORTEP Diagram of C9C3

Table 12a C9C3 Crystallographic Data

formula	C ₁₀ H ₁₈ O ₃
FW	186.25
crystal system	monoclinic
space group	P 2 ₁ /a
a, Å	8.6768(13)
b, Å	7.3553(20)
c, Å	15.6677(20)
V, Å ³	986.3(3)
Z (molecules/cell)	4
D _c , g/cm ³	1.254
cryst dimensions, mm ³	0.20 x 0.20 x 0.20
radiation (λ, Å)	MoKα (0.70932)
octants measured	h, k, l, -h, -k, -l
max 2θ	49.9
temperature	-130°C
no. of unique reflections	1741
no. of observed reflections	1871
(Iσ(I) ratio)	0.177
R _f	0.051
R _w	0.039
Goodness of Fit	10.29

Table 12b C9C3 Atomic Parameters x, y, z and Biso*

	x	y	z	Biso
O2	0.17241(19)	0.59535(23)	0.21880(10)	1.97(8)
O1	0.22742(19)	0.22035(23)	0.26015(10)	1.81(8)
O3	0.05931(20)	0.29485(23)	0.08329(10)	2.04(8)
C2	0.0663 (3)	0.4938 (4)	0.26153(17)	1.60(11)
C1	0.1550 (3)	0.3408 (4)	0.31308(16)	1.55(11)
C6	0.2832 (3)	0.4172 (4)	0.38248(17)	1.80(12)
C5	0.2114 (4)	0.5430 (4)	0.44281(18)	2.06(14)
C4	0.1168 (3)	0.6952 (4)	0.39396(18)	2.00(12)
C3	-0.0061 (3)	0.6188 (4)	0.32106(17)	1.89(12)
M1	0.1207 (3)	0.0949 (4)	0.21044(17)	2.01(13)
M4	0.1231 (4)	0.1224 (4)	0.11371(17)	2.16(13)
M3	0.1698 (4)	0.4361 (4)	0.08002(18)	2.37(14)
M2	0.1318 (4)	0.6055 (4)	0.12637(17)	2.27(13)
H2eq	-0.014 (3)	0.443 (3)	0.2211 (14)	1.9 (6)
H1ax	0.0740 (25)	0.272 (3)	0.3400 (12)	1.4 (5)
H3ax	0.365 (3)	0.482 (3)	0.3545 (14)	2.7 (6)
H3eq	0.3440 (22)	0.308 (3)	0.4155 (11)	0.5 (5)
H4ax	0.143 (3)	0.467 (3)	0.4653 (15)	2.0 (6)
H4eq	0.296 (3)	0.595 (3)	0.4779 (16)	3.8 (7)
H5ax	0.186 (3)	0.783 (3)	0.3697 (13)	2.1 (6)
H5eq	0.0636 (24)	0.777 (3)	0.4314 (12)	1.1 (5)
H6ax	-0.080 (3)	0.546 (3)	0.3412 (15)	2.5 (7)
H6eq	-0.060 (3)	0.731 (3)	0.2859 (13)	2.4 (6)
H1A	0.155 (3)	-0.050 (3)	0.2287 (13)	2.4 (6)
H1B	0.016 (3)	0.109 (3)	0.2271 (13)	1.4 (5)
H4A	0.234 (3)	0.109 (3)	0.1000 (13)	1.7 (5)
H4B	0.055 (3)	0.008 (3)	0.0814 (14)	2.1 (5)
H3A	0.270 (3)	0.386 (3)	0.1025 (15)	2.4 (6)
H3B	0.173 (3)	0.469 (4)	0.0174 (18)	4.8 (8)
H2A	0.196 (3)	0.714 (3)	0.1117 (13)	2.6 (6)
H2B	0.003 (3)	0.648 (3)	0.1136 (15)	3.7 (7)

* Biso is the Mean of the Principal Axes of the Thermal Ellipsoid.

E.S.D.'s refer to the last digit printed.

Table 12c C9C3 Atomic Bond Distances (Å)

O2-C2	1.435(3)	C4-C3	1.536(4)
O2-M2	1.435(3)	C4-H4ax	0.999(24)
O1-C1	1.428(3)	C4-H4eq	1.003(24)
O1-M1	1.442(3)	C3-H3ax	0.93(3)
O3-M4	1.434(3)	C3-H3eq	1.057(24)
O3-M3	1.421(3)	M1-M4	1.533(4)
C2-C1	1.518(4)	M1-H4A	1.129(22)
C2-C3	1.517(4)	M1-H1B	0.994(23)
C2-H2eq	0.937(23)	M4-H4A	1.024(23)
C1-C6	1.529(4)	M4-H4B	1.102(23)
C1-H1ax	1.014(22)	M3-M2	1.506(4)
C6-C5	1.527(4)	M3-H3A	0.96(3)
C6-H6ax	1.010(25)	M3-H3B	1.02(3)
C6-H6eq	1.051(20)	M2-H2A	1.03(3)
C5-H4	1.519(4)	M2-H2B	1.15(3)
C5-H5ax	0.93(3)		
C5-H5eq	0.93(3)		

Table 12d C9C3 Atomic Bond Angles in Degrees

C2-O2-M2	115.34(20)	C2-C3-C4	111.84(23)
C1-O1-M1	113.94(19)	C2-C3-H3ax	103.9(14)
M4-O3-M3	115.66(21)	C2-C3-H3eq	110.2(12)
O2-C2-C1	109.02(21)	C4-C3-H3ax	113.2(14)
O2-C2-C3	109.51(21)	C4-C3-H3eq	107.2(12)
O2-C2-H2eq	110.7(14)	H3ax-C3-H3eq	110.5(19)
C1-C2-C3	110.30(21)	O1-M1-M4	109.71(22)
C1-C2-H2eq	108.6(14)	O1-M1-H1A	110.2(11)
C3-C2-H2eq	108.7(14)	O1-M1-H1B	109.2(12)
O1-C1-C2	112.57(20)	M4-M1-H1A	109.2(11)
O1-C1-C6	107.63(20)	M4-M1-H1B	114.2(12)
O1-C1-H1ax	109.4(12)	H1A-M1-H1B	104.3(17)
C2-C1-C6	110.60(22)	O2-M4-M1	112.20(22)
C2-C1-H1ax	105.5(12)	O2-M4-H4A	109.9(13)
C6-C1-H1ax	111.2(11)	O2-M4-H4B	111.8(11)
C1-C6-C5	109.85(22)	M1-M4-H4A	111.2(12)
C1-C6-H6ax	110.1(13)	M1-M4-H4B	105.0(11)
C1-C6-H6eq	108.5(10)	H4A-M4-H4B	106.5(17)
C5-C6-H6ax	111.7(13)	O3-M3-M2	112.63(24)
C5-C6-H6eq	112.4(10)	O3-M3-H3A	106.6(15)
H6ax-C6-H6eq	104.1(16)	O3-M3-H3B	109.7(15)
C6-C5-C4	112.12(23)	M2-M3-H3A	113.4(14)
C6-C5-H5ax	102.9(14)	M2-M3-H3B	108.2(15)
C6-C5-H5eq	104.6(16)	H3A-M3-H3B	106.0(20)
C4-C5-H5ax	107.9(14)	O2-M2-M3	114.00(23)
C4-C5-H5eq	107.8(16)	O2-M2-H2A	102.4(12)
H5ax-C5-H5eq	121.5(20)	O2-M2-H2B	105.1(12)
C5-C4-C3	110.87(23)	M3-M2-H2A	111.5(13)
C5-C4-H4ax	111.0(13)	M3-M2-H2B	115.3(12)
C5-C4-H4eq	114.2(11)	H2A-M2-H2B	107.5(18)
C3-C4-H4ax	110.0(12)		
C3-C4-H4eq	108.9(11)		
H4ax-C4-H4eq	101.6(17)		

Table 12e C9C3 Torsion Angles

M2-O2-C2-C1	122.1(2)	M2-O2-C2-C3	-117.1(2)
M2-O2-C2-H2eq	2.8(13)	C2-O2-M2-M3	-78.0(2)
C2-O2-M2-H2A	161.4(13)	C2-O2-M2-H2B	49.2(12)
M1-O1-C1-C2	-76.8(2)	M1-O1-C1-C6	161.1(3)
M1-O1-C1-H1ax	40.2(11)	C1-O1-M1-M4	120.3(3)
C1-O1-M1-H7A	-119.5(11)	C1-O1-M1-H1B	-5.5(12)
M3-O3-M4-M1	96.1(2)	M3-O3-M4-H4A	-28.2(12)
M3-O3-M4-H4B	-146.3(11)	M4-O3-M3-M2	-127.7(3)
M4-O3-M3-H3A	-2.6(14)	M4-O3-M3-H3B	111.8(15)
O2-C2-C1-O1	-58.9(2)	O2-C2-C1-C6	61.5(2)
O2-C2-C1-H1ax	-178.1(12)	C3-C2-C1-O1	-179.2(3)
C3-C2-C1-C6	-58.8(2)	C3-C2-C1-H1ax	61.6(11)
H2eq-C2-C1-O1	61.8(13)	H2eq-C2-C1-C6	-177.8(13)
H2eq-C2-C1-H1ax	-57.4(17)	O2-C2-C3-C4	-63.6(2)
O2-C2-C3-H3ax	174.0(14)	O2-C2-C3-H3eq	55.5(12)
C1-C2-C3-C4	56.3(2)	C1-C2-C3-H3ax	-66.1(14)
C1-C2-C3-H3eq	175.5(12)	H2eq-C2-C3-C4	175.3(13)
H2eq-C2-C3-H3ax	52.9(19)	H2eq-C2-C3-H3eq	-65.6(18)
O1-C1-C6-C5	-178.3(3)	O1-C1-C6-H6ax	58.3(12)
O1-C1-C6-H6eq	-55.0(10)	C2-C1-C6-C5	58.4(2)
C2-C1-C6-H6ax	-65.0(13)	C2-C1-C6-H6eq	-178.4(10)
H1ax-C1-C6-C5	-58.5(11)	H1ax-C1-C6-H6ax	178.1(17)
H1ax-C1-C6-H6eq	64.7(15)	C1-C6-C5-C4	-56.2(2)
C1-C6-C5-H5ax	59.5(14)	C1-C6-C5-H5eq	-172.7(16)
H6ax-C6-C5-C4	66.2(13)	H6ax-C6-C5-H5ax	-178.1(19)
H6ax-C6-C5-H5eq	-50.3(20)	H6eq-C6-C5-C4	-177.1(10)
H6eq-C6-C5-H5ax	-61.4(17)	H6eq-C6-C5-H5eq	66.4(18)
C6-C5-C4-C3	53.7(2)	C6-C5-C4-H4ax	-68.8(12)
C6-C5-C4-H4eq	177.2(12)	H5ax-C5-C4-C3	-58.9(14)
H5ax-C5-C4-H4ax	178.6(19)	H5ax-C5-C4-H4eq	64.6(18)
H5eq-C5-C4-C3	168.3(16)	H5eq-C5-C4-C4ax	45.8(20)
H5eq-C5-C4-H4eq	-68.2(19)	C5-C4-C3-C2	-53.7(2)
C5-C4-C3-H3ax	63.3(14)	C5-C4-C3-H3eq	-174.6(12)
H4ax-C4-C3-C2	69.4(12)	H4ax-C4-C3-H3ax	-173.6(19)
H4ax-C4-C3-H3eq	-51.5(17)	H4eq-C4-C3-C2	179.9(12)
H4eq-C4-C3-H3ax	-63.2(18)	H4eq-C4-C3-H3eq	59.0(16)
O1-M1-M4-O3	-67.4(2)	O1-M1-M4-H4A	6.2(12)
O1-M1-M4-H4B	171.0(11)	M1A-M1-M4-O3	171.8(11)
H1A-M1-M4-H4A	-64.6(16)	H1A-M1-M4-H4B	50.2(15)
H1B-M1-M4-O3	55.5(12)	H1B-M1-M4-H4A	179.1(17)
H1B-M1-M4-H4B	-66.1(16)	O3-M3-M2-O2	78.0(2)
O3-M3-M2-M2A	-166.7(13)	O3-M3-M2-H2B	-43.8(12)
H3A-M3-M2-O2	-43.2(14)	H3A-M3-M2-H2A	72.1(19)
H3A-M3-M2-H2B	-165.0(18)	H3B-M3-M2-O2	-160.6(15)
H3B-M3-M2-H2A	-45.3(19)	H3B-M3-M2-H2B	77.6(19)

obtained 210K DEPT spectrum of d_4 -C9C3 (Fig. 19) unambiguously assigns M3,M4 as deshielded relative to M1,M2 which supports these assignments. Similar reasoning enables one to assign M1 to 71.6 ppm and M2 to 70.8 ppm.

Fig. 19 210K DEPT Spectra of C9C3 and d_4 -C9C3

Table 13. C9C3 ^{13}C Chemical Shifts^a
Ether Region

		M1	M2	M3	M4
solution ^b	300K	70.1	70.8	75.7	75.7
solution	210K	71.6	70.8	78.6	74.3
powder		72	72	79	76

^a δ_c from TMS ± 0.1 ppm

^b consistent with d_4 -C9C3 (appendix)

R. ORIGIN OF ^1H SHIFTS IN THE 210K SOLUTION SPECTRUM OF C9C3

The 210K HETCOR and COSY for C9C3 (Figs. 10, 11) assign H2_{eq} as deshielded 1.1 ppm relative to H1_{ax} . One may conjecture that protons involved in C-C or C-O eclipsing networks, like carbons, are also deshielded since the $\cos^2\phi$ overlap (VIII)=1.0 whereas for (I)=0.58 (Table 11).

The C9C3 protons involved in gauche-eclipsed $\phi < 60^\circ$ M-H/M-O networks are H1B , H2B , H3A , H4A (Tables 10, 12). The ORTEP diagram (Fig. 18) reveal these protons are "axial" to the heterocyclic ring.

The 210K HETCOR of d_4 -C9C3 (Fig. 20) shows that M3 at 78.6 ppm is correlated to the pair of doublets H3A (3.97 ppm) and H3B (3.51 ppm) with geminal coupling $^2J=12.4$ Hz. Similarly M4 at 74.3 ppm correlates to the pair H4A (3.75 ppm) and H4B (3.45 ppm) where $^2J=13.4$ Hz. The 210K COSY (Fig. 20) verifies that each pair reside on the same carbon.

Fig. 20 210K HETCOR and COSY of d_4 -C9C3

Inspection of the M-H/M-O torsional networks (Table 10) reveal that H3A has an associated $\cos^2\phi$ (V)=1.0 whereas for H4A (IV)=0.78 . This provides a rationale for the 0.22 ppm difference between these two.

The 210K ^1H solution spectra of C9C3 and d_4 -C9C3 are presented in Fig. 21. The doublet on the downfield shoulder of H4A can now be assigned to H1B at 3.81 ppm since it has an associated $\cos^2\phi$ overlap (II)=0.99 whereas for H2B (VI)=0.52 .

Fig. 21 210K 400 MHz ^1H Spectra of C9C3 and d_4 -C9C3

Table 14 C9C3 ¹H Chemical Shifts*

		H1	H2	H3	H4	H5	H6
Cyclohexyl	ax	3.10	-	1.76	1.26	1.60	1.53
	eq	-	4.15	1.12	1.26	1.12	1.45
Ether	A	-	-	3.97	3.75		
	B	3.81	-	3.51	3.45		

* δ_c from TMS $\pm$ 0.1 ppm

If a similar trend is operative in the cyclohexyl region then the downfield resonances at 1.76, 1.60, 1.53 ppm can tentatively be assigned to axial H3, H5, H6 however this would be difficult to substantiate due to the similar C-O/C-H torsional environments for both eq. and ax. H3, H6. In general these observations support the well known fact that ¹H shifts are more dependent on bulk anisotropic effects than ¹³C shifts.

CONCLUSION

Non 3-substituted acyclic and large cyclic 1,2-dialkoxybenzenes adopt the trans-coplanar conformation and as a result have similar solution and powder isotropic ^{13}C aromatic shifts. This conformation minimizes steric interactions between the O-M groups in exchange for a smaller interaction with the ring, while maintaining optimal lone pair/ aromatic p-orbital overlap.

When 1,2-dialkoxybenzenes are 3-substituted and/ or constrained by small ring size, the isotropic powder σ and ρ SCS for a given O-M can be interpreted by taking the following factors into account; (i) degree of lone pair/ aromatic p-orbital overlap, determined crystallographically or theoretically (ii) effective size of the 3-substituent (iii) ring strain.

The 2-D single crystal NMR work currently in progress on B9C3 will hopefully yield all principal components of the anisotropic shifts however complications may arise due to the large number of molecules ($Z=8$) per crystallographic unit cell. If successful, the differentiation of C3 and C5 for B9C3 should be possible since σ_{33} of the latter is expected to be close to that for 1,2,3 TMB. The breakdown of the anisotropic C1 and C2 shifts into ρ and σ SCS is expected to be fraught with uncertainty since the corresponding values for veratrole are unknown. It is noted that single crystal NMR/ x-ray work on veratrole (mp=15 $^{\circ}$) would be difficult.

The hypothesis that aliphatic torsional networks with greater C-H/C-C and C-H/C-O overlap have a greater associated σ^{p} successfully accounts for the observed 9C3 ether-carbon powder shifts

For methylcyclohexane one may wonder why the β carbons are deshielded while the γ carbons are shielded relative to cyclohexane. The origin of this trend can be understood by considering the total number of vicinal $C^*-H/C-C$ and $C-H/C^*-C$ relations for a given C^* in a linear hydrocarbon; this is accomplished by summing the number of protons on C^* and all α , β carbons. For propane both C1 and C2 (ca. 16 ppm) have 8 such relations. However for butane C1 (13.2 ppm) has 7 while C2 (25.1 ppm) has 10; for pentane C3 (34.1 ppm) has 12. It is of interest to note that γ shielding is semi-qualitatively accounted for here without relying on the H-H steric mechanism. Instead steric repulsion is manifest in the relatively large σ^p for crowded sites where a higher population of conformations with large C-H/C-C overlap exist i.e., C3 (49.4 ppm) of 2,4-diMe pentane.

This work also illustrates that satisfactory agreement between ab initio LORG calculated ^{13}C calculated shifts at a double zeta basis set level and solid phase shifts is possible for medium molecular weight materials, provided that x-ray data for the solids are available. The utility of combining state of the art experimental techniques with the most recent computational methods is demonstrated. With more powerful computing capabilities becoming available, one can anticipate extension of studies of this nature to molecules of increasing complexity.

EXPERIMENTAL

Fig. 22 Synthetic Scheme

The asterisks denote the following starting compounds (top to bottom): catechol, guaiacol, bis-2-hydroxyphenyl ether and 3,4-dihydroxybenzaldehyde all purchased from Aldrich. The letters denote the general manner in which a compound is prepared; C cyclization, H, h Hydrogenation and N nitration.

1C benzo-9-crown-3	5 2-(3-OH propoxy) phenol	10 3-NO ₂ guaiacol
1N 4-NO ₂ B9C3	5C ethylene glycol di-2-(3-OH propoxy) phenyl ether	11 veratrole
1H 4-NH ₂ B9C3	6N 3-NO ₂ catechol	11N 4-NO ₂ veratrole
2C benzodioxane	7C 3-NO ₂ B9C3	11H 4-NH ₂ veratrole
2N 4-NO ₂ benzodioxane	7H 3-NH ₂ B9C3	12C DB9C3
3C benzodioxepane	8C 3-NO ₂ benzodioxepane	13C 4-COH B9C3
3N 4-NO ₂ benzodioxepane	9 3-NO ₂ veratrole	
4C benzodioxenane	9H 3-NH ₂ veratrole	
4N 4-NO ₂ benzodioxenane		

GENERAL EXPERIMENTAL

C Cyclizations involve initially a 30 min reflux with 1 × mol of the catechol derivative, 2 × mols LiOH·H₂O and 12 × litres H₂O. Then 1 × mol of the aliphatic dihalo derivative (Aldrich) is added and the reflux continued for 72 hr. The solution was then neutralized, filtered and extracted with CH₂Cl₂. Successive washings with 2% NaOH, drying over Na₂SO₄ and rotaryevaporation yielded the crude product. Purification procedures are described below.*

N Nitration of catechol and 1,2-dialkoxybenzenes involved a variety of conditions owing to the marked differences in reactivities of these starting compounds (Table 3).

H Hydrogenation of the aromatic nitro compounds to the aniline derivatives involved 10:1 (w/w)= reactant: Rh on alumina at 600 psi H₂ in 25 mL absolute EtOH for 2 hr (ibid. for the B9C3 Hydrogenation 1h except 4 hr). The solution was then filtered and rotaryevaporated; the purification procedures are described below.

1C B9C3 The cyclization (bis-2-chloroethoxy ether/ catechol) residue was then refluxed in hexane with stirring and the supernatant repeatedly decanted while hot. After rotaryevaporation of the hexane recrystallization from Me₂CO gave B9C3. mp 64-66° (lit. mp 67-69°)¹⁰⁶ yield 25%

1h C9C3 The hydrogenation residue was recrystallized from cold MeOH to give C9C3 mp 38-39° yield 85%

1N 4-NO₂ B9C3 To a solution of B9C3 (4.00 g, 0.022 mol), Ac₂O (0.57 g, 0.006 mol) and 1 drop 96% H₂SO₄ was added anhydrous CH₂Cl₂ until dissolution. To this solution was added 70% HNO₃ (1.39 g, 0.022 mol) in Ac₂O (1.74 g, 0.017 mol) dropwise keeping the temperature below 40°. After refluxing for 2 hr ice was added followed by dilute KOH at 0-5°. The solution was then extracted with CH₂Cl₂, backwashed with sat. NaHCO₃ and H₂O, dried over Na₂SO₄ and rotaryevaporated. Silica column chromatography with hexane: Et₂O: CH₂Cl₂ = 3:1:1 followed by recrystallization from CH₂Cl₂/hexane gave 4-NO₂ B9C3 (3.2 g, 0.01 mol). mp 95-97° yield 64%

1H 4-NH₂ B9C3 The hydrogenation residue was purified by flash silica column chromatography with Et₂O to give 4-NH₂ B9C3, an oil. yield 64%

2C Benzodioxane The cyclization (1,2-dibromoethane/ catechol) residue was purified by flash silica column chromatography with CH₂Cl₂: hexane = 2:7 to give benzodioxane, an oil. (lit. bp 82-83° 6 mm)^{81b} yield 66%

2N 4-NO₂ Benzodioxane The room temperature nitration procedure^{10r} employed for veratrole 11N gave no reaction however upon heating to 75°C for another 2 hr the reaction was complete; the workup procedure was the same. Recrystallization from hexane/Me₂CO gave 4-NO₂ benzodioxane. mp 122-124° (lit. mp 118.2-119.4°)^{10k} yield 74%

3C Benzodioxepane The cyclization (1,3 dibromopropane/ catechol) residue was purified by silica column chromatography with EtOAc: hexane = 1:10 to give benzodioxepane, an oil, solid at 0° (lit. bp 107-108° 15 mm, lit. bp 110-114° 18 mm, lit. mp 14-15°)^{81b 10w} yield 50%

3N 4-NO₂ Benzodioxepane The nitration procedure employed for benzodioxane 2N gave no reaction however upon adding 1 drop 96% H₂SO₄ and heating for 12 hr the reaction was complete; the workup procedure was the same. Recrystallization from hexane/Me₂CO gives 4-NO₂ benzodioxepane. mp 110-112° (lit. mp 106-107°)¹⁰⁹ yield 83%

4C Benzodioxenane The cyclization (1,5 dibromopentane/ catechol) oil was pure by ¹³C solution NMR spectral analysis (lit. bp 119-120° 9 mm)^{81b} yield 61%

4N 4-NO₂ Benzodioxenane The veratrole room temperature nitration¹⁰¹-workup procedure 11N was satisfactory. Purification by flash silica chromatography with EtOAc: hexane = 1:4 gives the product, an oil. yield 70%

5 2-(3-OH Propoxy) Phenol After a 30 min reflux with catechol (10.0 g, 0.09 mol), LiOH·H₂O (7.6 g, 0.045 mol) and 500 mL H₂O, was added 3-chloropropanol (8.6 g, 0.09 mol) and the reflux continued for 24 hr. The reaction mixture was then neutralized and extracted with CH₂Cl₂ (3 × 50 mL). The combined organic extracts were then washed repeatedly with 2% NaOH until the aqueous layer was clear. After neutralization, extraction with CH₂Cl₂ (3 × 25 mL), rotaryevaporation and drying over Na₂SO₄ there was 6.1 g of 2-(3-OH propoxy) phenol, pure by ¹³C NMR. yield 40% This material solidifies after standing 24 hr. From the organic layer was obtained 1,2-di-(3-OH propoxy) phenol. mp 61-62°

5C Ethylene Glycol Di-2-(3-OH Propoxy) Phenyl Ether The intended B10C3 cyclization was unsuccessful; the above mentioned material was the major product. In a flame dried apparatus under Ar was combined 2-(3-OH propoxy) phenol (5.0 g,

0.03 mol) and 500 mL dry THF. Then NaH (0.82 g, 0.034 mol) was added and the mixture stirred for 30 min after which 1,2-dibromoethane (5.6 g, 0.03 mol) was added and the reflux continued for 48 hr. The reaction mixture was then quenched with 50 mL MeOH, neutralized, filtered and rotaryevaporated. The residue was taken up in 50 mL CH₂Cl₂, washed with 2% NaOH (3 × 25 mL) then H₂O (1 × 25 mL), dried over Na₂SO₄ and rotaryevaporated. Purification by silica column chromatography with CH₂Cl₂: EtOAc = 1:4 gave ethylene glycol di-2-(3-OH propoxy) phenyl ether (1.6 g, 0.004 mol). mp 98-99.5°

6N 3-NO₂ Catechol⁶² To catechol (50.0 g, 0.45 mol) in 1L anhydrous Et₂O under Ar was slowly added fuming HNO₃ (20 ml). After stirring for 12 hr the mixture was filtered and rotaryevaporated. To the resulting black residue was added 20 ml 30/60 pet ether, refluxed with stirring for 10 min after which the pet ether was decanted. This was repeated 7 times and the combined washings rotaryevaporated and recrystallized from hexane/Me₂CO to give 3-NO₂ catechol (14.0 g, 0.09 mol). mp 84-86° (lit. mp 84°)⁶² yield 20%

7C 3-NO₂ B9C3 The cyclization (bis-2-chloroethoxy ether/ 3-NO₂ catechol) residue was purified by silica column chromatography with Et₂O: hexane = 3:1 and recrystallized from Et₂O/hexane. mp 54-56° yield 13%

7H 3-NH₂ B9C3 The hydrogenation residue was purified by column chromatography with Et₂O: hexane = 3:2 to give the product. mp 89-91° yield 42%

8C 3-NO₂ Benzodioxepane The cyclization (1,3-dibromopropane/ 3-NO₂ catechol) residue was purified by flash silica column chromatography with CH₂Cl₂ to give the product, an oil. yield 28%

9 3-NO₂ Veratrole To a solution of KOH (4.0 g, 0.07 mol), 3-NO₂ catechol (5.5 g, 0.035 mol) in absolute MeOH (60 ml) was slowly added MeI (15.0 g, 0.10 mol) and then refluxed under Ar for 16 hr. The mixture was then neutralized, rotaryevaporated and the residue taken up in CH₂Cl₂. This was then backwashed with 2% Na₂S₂O₃, 2% NaOH then H₂O, dried over Na₂SO₄ and rotaryevaporated. Recrystallization from Et₂O/hexane gives 3-NO₂ veratrole (1.8 g, 0.01 mol). mp 63-64° (lit. mp 64-65°)¹¹⁰ yield 24%

9H 3-NH₂ Veratrole The hydrogenation residue was purified by silica column chromatography with Et₂O: hexane = 1:1 giving the product, an oil. (lit. bp 136-138° 15 mm)¹¹¹ yield 38%

10 2-OMe-6-NO₂ Phenol To a solution of KOH (0.24 g, 4.4 mmol), 3-NO₂ catechol (1.40 g, 8.9 mmol) in 20 mL H₂O was slowly added (MeO)₂SO₂ (0.55 g, 4.4 mmol) and the mixture stirred 16 hr. Then it was boiled for 30 min to destroy excess sulfate, made slightly acidic and extracted with CH₂Cl₂, dried over Na₂SO₄ and rotaryevaporated. Silica column chromatography with Et₂O: hexane = 1:4 and recrystallization from cold MeOH gave 2-OMe-6-NO₂ phenol (0.73 g, 4.3 mmol). mp 58-61° (lit. mp 62°)¹¹² yield 49%

11 Veratrole To guaiacol (15.0 g, 0.12 mol) in NaOH (5.0 g, 0.13 mol) and 75 mL H₂O was added (MeO)₂SO₂ (15.1 g, 0.12 mol). The mixture was vigorously stirred for 15 min then boiled for 30 min to destroy excess sulfate. The oil was extracted with Et₂O (4 x 15 mL) and dried over Na₂SO₄ and rotaryevaporated. The residue was distilled and collected at 91-94° 14 mm to give veratrole (11.1 g, 0.08 mol), an oil solid at 0° (lit. bp 88-90° 10 mm, lit. mp 15°)¹¹³ yield 67%

11N 4-NO₂ Veratrole¹⁰⁷ To a cooled solution of 70% HNO₃ (7.6 mL) in 7.6 mL H₂O was slowly added veratrole (8.0 g, 0.07 mol) and stirred for 2hr. The yellow solid was carefully taken up in CH₂Cl₂ and 2% NaOH. The organic layer was then backwashed with sat. NaHCO₃ and H₂O, dried over Na₂SO₄ and rotaryevaporated. Recrystallization from Et₂O/CH₂Cl₂ gives 4-NO₂ veratrole (9.2 g, 0.05 mol). mp 97-99° (lit. mp 96°)¹¹⁴ yield 73%

11H 4-NH₂ Veratrole The hydrogenation residue was purified by silica column chromatography with Et₂O: hexane = 1:1 to give the product (0.77 g, 0.005 mol). mp 86-88° (lit. mp 86°)¹¹⁴ yield 92%

12C DB9C3 The cyclization (1,2-dibromoethane/ bis-2-hydroxyphenyl ether) residue was purified by sublimation onto the bulb of a water cooled condenser by gentle heating to give DB9C3 (dibenzo-9-crown-3). mp 103-105° yield 41%

13C 4-COH B9C3 The cyclization (bis-2-chloroethoxy ether/ 3,4-dihydroxy benzaldehyde) residue was recrystallized from hot THF to give the product. mp 50-52° yield 13% This compound is extremely insoluble in CDCl₃, d₆-Me₂CO and d₆-DMSO.

SPECTRA

The ^{13}C solution spectra were obtained using VARIAN XL-200 and Bruker AMX 400 spectrometers. Sample concentrations were approximately 0.2 M CDCl_3 or CD_2Cl_2 solutions contained in 5 mm o.d. tubes. Routinely spectra were recorded with complete ^1H noise decoupling. Normal operating conditions were as follows; sweep width = 5 kHz with 16K data points; pulse width = 6 μs (45°) and a repetition rate of 1.0 s. The number of accumulations for the low temperature spectra was typically 1000-2000. Temperatures were calibrated using a copper-constantan thermocouple in a dummy NMR tube.

The ^{13}C CPMAS spectra were recorded at 45.3 MHz on a Bruker CXP-180 spectrometer. CP times were typically 3 ms, with the RF field amplitude 60 kHz. Satisfactory S/N ratios were obtained after a maximum of 400 spectral accumulations. The sweep width was 20 kHz with a recycle time of 4-8 s. Normally 2K data points were collected with zero filling to 8K before Fourier transformation. MAS rates of ca. 3 kHz were obtained with the use Kel-F spinners of the Andrew-Beams type. Chemical shifts were measured relative to external solid hexamethylbenzene (HMB) and converted to the TMS scale via the factor of 16.9 ppm, which is the chemical shift for the CH_3 group of HMB.

CRYSTALLOGRAPHIC MEASUREMENTS AND REFINEMENTS

Single crystals of B9C3, 4- NO_2 B9C3 and C9C3 were hand-picked, mounted on a glass capillary and measured on a Rigaku diffractometer. Accurate cell parameters and intensity data for these three compounds were respectively obtained at

20°, -90° and -130° using graphite monochromated MoK α radiation. Crystal data are provided in Tables 8, 9, 12 and were corrected in the usual fashion for Lorentz and polarization effects.¹¹⁵ The structures were solved using direct methods and all atoms refined anisotropically except hydrogens, which were calculated. Weights based on counting statistics were used and all calculations were performed using the NRCVAX crystallographic software package.¹¹⁶

COMPUTATIONS

Calculations were done at SIUE using the experimental geometry obtained by x-ray analysis. A Silicon Graphics 4D/310S computer was employed for all calculations with shielding constants calculated using the RPAC molecular properties program.¹⁰¹ Molecular wavefunctions used in the RPAC program were calculated using the Gaussian 90 set of programs.¹¹⁷

Computed shift values for B9C3 were obtained by calculating shielding constants for the atoms and finding the difference between these and the carbon of TMS (198.62 ppm from the bare nucleus). The D95V basis set was used to calculate the molecular wavefunction of B9C3 and the D95V coefficients and exponents were used to represent the carbon and hydrogen atoms in the TMS calculation. The silicon atom of TMS however was represented with D95 coefficients and exponents since the D95V basis set does not represent the silicon atom.

For anisole, the shielding constants were obtained from D95V basis set utilization with geometries obtained from the MOPAC¹⁰¹ geometry optimization routine. Bond lengths and bond angles were optimized at each dihedral angle for

which shielding constants were calculated.

Shielding constants for ethyl methyl ether were calculated using the 6-31G* basis set with the geometry optimized via MOPAC¹⁰¹ at the 0° torsional angle. Bond lengths and angles for the other eight torsional angles for which shielding constants were calculated were left unoptimized and geometries were obtained by rotation about the central C-O bond. The NOSORT localization scheme was used in the RPAC¹⁰¹ program for the calculation of shielding constants in B9C3, anisole and TMS while a block localization scheme was employed for ethyl methyl ether.

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APPENDIX

Each of the compounds presented herein have an associated code which pertains to the route (Synthetic Scheme, Fig. 22) and manner (General Experimental) in which they were synthesized. The tables and spectra are coded as follows;

- a** table of ^{13}C (solution, * powder) and ^1H chemical shifts in ppm
- b** mass spectrum in electron impact mode
- c** CPMAS ^{13}C spectrum
- d** solution ^{13}C spectrum
- e** ^1H spectrum - aromatic region
- f** simulated ^1H spectrum - aromatic region
- g** HETCOR
- h** COSY

The H-H coupling constants given are in Hz and were measured directly from the experimental spectra or were those used in the simulation. The aliphatic and aromatic protons in O-C-C-O fragments and non-substituted 1,2-dialkoxybenzenes are part of AA'BB' H-H spin systems hence the associated coupling constants are not given as this would necessitate iterative spectral simulation; only for B9C3 was this carried out. Those cyclic and acyclic compounds with O-C-C-C-O fragments had similar corresponding ^1H spectra, close to that of propylene glycol (note t $\equiv$ triplet and p $\equiv$ quintet).

2C Benzodioxane

a

	1	2	3	4	5	6	M1	M2
C	143.5	143.5	117.1	121.2	121.2	117.1	64.0	64.0
H	-	-	-	-	-	-	4.14	4.14

3C Benzodioxepane

	1	2	3	4	5	6	M1	M2	M3
C	151.2	151.2	121.5	123.3	123.3	121.5	70.4	70.4	31.7
C*	152.8	151.9	122.9	122.9	124.5	122.9	72.0	72.0	33.5
H	-	-	-	-	-	-	4.20 t	4.20 t	2.17 p

a

$$^3J_{\text{aliphatic}} = 5.62$$

c

4C Benzodioxene

a

	1	2	3	4	5	6	M1	M2	M3	M4
C	151.6	151.6	122.7	123.7	123.7	122.7	74.5	74.5	29.3	24.9
H	-	-	-	-	-	-	6.96	6.96	4.24	1.82

b **d**

1C B9C3 and d₄-B9C3

a

	1	2	3	4	5	6	M1	M2	M3	M4
C	151.4	151.6	122.9	123.9	123.9	122.9	74.0	74.0	72.3	72.3
C*	151.0	148.7	124.6	121.8	127.2	119.0	68.2	76.1	72.9	70.4
H	-	-	7.02	6.98	6.98	7.02	4.33	4.33	3.89	3.89

$$^3J_{5,6} = ^3J_{3,4} = 9.00 \quad ^3J_{4,5} = 8.60 \quad ^4J_{3,5} = ^4J_{4,6} = 2.00 \quad ^5J_{3,6} = 0.50$$

$$^3J_{\text{aliphatic}} = 6.17, 2.69 \quad ^2J_{\text{aliphatic}} = 10.91, 11.01$$

Simulated

5, 5C B10C3 adducts

a

		1	2	3	4	5	6	M1	M2	M3	M4	ϕOH	ROH
phenol	C	146.0	146.1	115.1	120.0	121.8	113.2	-	67.0	31.3	59.9	-	-
	H	-	-	-	-	-	-	-	4.07	1.95	3.78	7.07	3.68
monobenzo	C	148.2	148.2	112.8	121.1	121.1	112.8	-	67.2	31.6	60.4	-	-
	H	-	-	-	-	-	-	-	4.11	2.02	3.81	-	-3.8
dibenzo	C	148.6	148.8	114.1	121.5	121.8	114.3	68.2	67.5	31.7	60.9	-	-
	H	-	-	-	-	-	-	4.37	4.17	2.02	3.64	-	5.21

Aliphatic Coupling Constants for the Propoxy Protons

$$^3J_{\text{phenol}} = 5.85 \quad ^3J_{\text{monobenzo}} = 5.70 \quad ^3J_{\text{dibenzo}} = 5.35$$

12C DB9C3 and related adduct

	DB9C3		d.OMe adduct	
	C	H	C	H
1	152.0	-	150.4	-
2	151.4	-	145.8	-
3	123.2	-	118.6	-
4	124.8	-	120.7	-
5	125.2	-	123.7	-
6	122.2	-	112.3	-
MI	75.3	4.33	55.7	3.83

a

11N 4-NO₂ Veratrole **a**

	1	2	3	4	5	6	M1	M2
C	154.2	148.5	105.9	141.0	117.4	109.5	56.1	55.9
C [*]	154	148	106	141	118	110	56	54
H	-	-	7.71	-	7.58	6.93	4.00	3.97

$$^3J_{5,6} = ^3J_{6,5} = 8.96 \quad ^4J_{3,5} = 2.61 \quad ^5J_{3,6} = 0.0$$

c **d**

2N 4-NO₂ Benzodioxane

a

	1	2	3	4	5	6	M1	M2
C	149.3	143.1	113.3	141.6	117.4	117.1	64.6	64.0
C'	151.4	143.1	113.0	139	117.0	117.3	66.5	66.4
H	-	-	7.79	-	7.78	6.94	4.36	4.32

$$^3J_{5,6} = ^3J_{6,5} = 9.07 \quad ^4J_{3,5} = 2.24 \quad ^5J_{3,6} = 0.51$$

3N 4-NO₂ Benzodioxepane

	1	2	3	4	5	6	M1	M2	M3
C	156.6	150.3	117.5	142.7	118.9	121.2	70.4	70.2	70.4
C'	156.8	149.7	115.4	141.6	118.1	120.3	70.5	70.5	70.4
H	-	-	7.84	-	7.81	7.01	4.38 t	4.33 t	2.28 p

a

$$^3J_{5,6} = ^3J_{6,5} = 8.75 \quad ^4J_{3,5} = 2.72 \quad ^5J_{3,6} = 0.0 \quad ^3J_{\text{aliphatic}} = 5.88$$

4N 4-NO₂ Benzodioxene

a

	C	H
1	157.5	-
2	150.5	-
3	119.5	7.69
4	142.7	-
5	119.8	7.64
6	122.0	7.03
M1	77.0	4.52
M2	73.4	4.24
M3	29.0	1.86
M4	24.5	
M5	29.8

$$^3J_{5,6} = ^3J_{6,5} = 9.36$$

$$^4J_{3,5} = 1.40$$

$$^5J_{3,6} = 0.0$$

1N 4-NO₂ B9C3

	1	2	3	4	5	6	M1	M2	M3	M4
C	157.3	150.6	120.1	142.6	120.3	122.1	75.4	72.0	72.8	71.7
C*	158.1	148.1	120	140	121	121	69	77.4	70	73.5
H	-	-	7.90	-	7.85	7.01	4.31	4.65	3.90	3.93

a

$$^3J_{5,6} = ^3J_{6,5} = 8.80 \quad ^4J_{3,5} = 2.80 \quad ^5J_{3,6} = 0.0$$

^{11}H 4- NH_2 Veratrole
a

	C	H
1	140.6	-
2	149.7	-
3	149.5	6.29
4	141.9	-
5	149.2	6.01
6	143.2	6.12
NH1	51.4	3.53
NH2	55.5	3.79

$$^3J_{5,6} = ^3J_{6,5} = 8.44$$

$$^4J_{3,5} = 2.47$$

$$^5J_{1,5} = 0.06$$

^1H 4-NH₂ B9C3

	1	2	3	4	5	6	M1	M2	M3	M4
C	143.3	152.0	108.5	143.3	110.2	123.9	75.3	73.0	72.5	72.0
H	-	-	6.93	-	6.25	6.93	4.40	3.13	3.38	3.35

a
 ^{13}C 4-COH B9C3

6N 3-NO₂ Catechol

	C	H
1	146.5	-
2	142.9	-
3	133.8	-
4	119.9	7.64
5	115.9	6.90
6	121.7	7.24
OH1	-	5.93
OH2	-	10.62

$$^3J_{4,5} \approx ^3J_{5,6} = 8.03$$

$$^4J_{4,6} = 1.50$$

$$^4J_{6,OH1} = 0.78$$

10 3-NO₂ Guaiacol (2-OMe-6-NO₂ Phenol)

	C	H
1	150.0	-
2	146.3	-
3	133.9	-
4	118.9	7.67
5	116.0	6.89
6	117.6	7.12
M1	56.6	3.93
OH	-	10.75

a

$$^3J_{4,5} \approx ^3J_{5,6} = 8.67$$

$$^4J_{4,6} = 1.42$$

9 3-NO₂ Veratrole

	1	2	3	4	5	6	M1	M2
C	154.3	142.9	145.0	116.0	123.8	116.1	56.4	62.0
C'	155.0	142.6	144	115.9	122.0	115.9	58.0	61.3
H'	-	-	-	7.32	7.12	7.11	3.93	3.98

a **c** **d**

8C 3-NO₂ Benzodioxepane. **a**

	1	2	3	4	5	6	M1	M2	M3
C	153.0	144.7	144.1	118.4	122.5	125.4	70.8	71.5	31.0
H	-	-	-	7.37	6.99	7.18	4.28 t	4.33 t	2.27 p

$$^3J_{4,5} = ^3J_{5,6} = 8.07 \quad ^4J_{4,6} = 1.78$$

7C 3-NO₂ B9C3

a

	1	2	3	4	5	6	M1	M2	M3	M4
C CDCl ₃	153.8	145.2	144.8	119.2	123.3	127.1	74.4	75.8	72.3	71.5
C CD ₂ Cl ₂	154.3	145.5	145.0	119.3	123.4	127.4	75.1	75.7	72.7	71.8
C Me ₂ CO	154.7	145.3	-	-	-	-	75.4	75.7	73.0	71.8
C*	152.5	141.9	146.9	115.9	124	124.9	69.7	81.0	69.7	69.7
H CDCl ₃	-	-	-	7.47	7.06	7.24	4.41	4.45	3.99	3.95
H CD ₂ Cl ₂	-	-	-	-	-	-	4.27	4.35	3.82	3.86
H Me ₂ CO	-	-	-	-	-	-	4.36	4.48	3.90	3.93

$$^3J_{5,6} \approx ^3J_{4,5} = 8.15 \quad ^4J_{4,6} = 1.68$$

9H 3-NH₂ Veratrole **a**

	1	2	3	4	5	6	M1	M2	M3
C	153.1	136.0	140.7	108.8	124.2	102.3	55.7	59.9	-
H	-	-	-	6.34	6.85	6.39	3.83	3.84	-

$$^3J_{4,5} = ^3J_{5,6} = 8.15 \quad ^4J_{4,6} = 1.28$$

7H 3-NH₂ B9C3 **a**

	1	2	3	4	5	6	M1	M2	M3	M4
C	152.2	138.4	140.9	(110.4)	124.0	(111.9)	73.2	74.2	72.2	71.8
H	-	-	-	6.41	6.78	6.45	4.35	4.27	3.97	3.92

$$^3J_{4,5} \approx ^3J_{5,6} = 8.03 \quad ^4J_{4,6} = 1.51$$

b **e** **d**

1h C9C3 and d₄-C9C3

	1	2	3	4	5	6	M1	M2	M3	M4
C	78.9	78.9	28.9	21.9	21.9	28.9	70.8	70.8	75.7	75.7
C'	83	77	29	20	26	29	72	72	79	76
H	3.69	3.69	1.42	1.28	1.28	1.42	3.55	3.55	3.55	3.55
			1.74	1.57	1.57	1.74	3.83	3.83	3.91	3.91

a

See Discussion. Sections N, Q, R for low temperature spectra.

END

1 6 - 1 2 - 9 3

FIN