1 2

OF/DE

25411

National Library
of CanadaBibliothèque nationale
du CanadaCANADIAN THESES
ON MICROFICHETHÈSES CANADIENNES
SUR MICROFICHE

NAME OF AUTHOR/NOM DE L'AUTEUR Kevser Taymaz

TITLE OF THESIS/TITRE DE LA THÈSE Investigations on the Question of Mechanism
Multiplicity in the Cope Rearrangement

UNIVERSITY/UNIVERSITÉ Carleton University

DEGREE FOR WHICH THESIS WAS PRESENTED/
GRADE POUR LEQUEL CETTE THÈSE FUT PRÉSENTÉE Ph.D.

YEAR THIS DEGREE CONFERRED/ANNÉE D'OBTENTION DE CE DEGRÉ 1975

NAME OF SUPERVISOR/NOM DU DIRECTEUR DE THÈSE Donald C. Wigfield

Permission is hereby granted to the NATIONAL LIBRARY OF
CANADA to microfilm this thesis and to lend or sell copies
of the film.

L'autorisation est, par la présente, accordée à la BIBLIOTHÈ-
QUE NATIONALE DU CANADA de microfilmer cette thèse et
de prêter ou de vendre des exemplaires du film.

The author reserves other publication rights, and neither the
thesis nor extensive extracts from it may be printed or other-
wise reproduced without the author's written permission.

L'auteur se réserve les autres droits de publication; ni la
thèse ni de longs extraits de celle-ci ne doivent être imprimés
ou autrement reproduits sans l'autorisation écrite de l'auteur.

DATED/DATE Oct-1st-1975 SIGNED/SIGNÉ Kevser TaymazPERMANENT ADDRESS/RÉSIDENCE FIXE Kayalik ma. Bagdat sok
No:3 DENIZLI - TURKEY

INVESTIGATIONS ON THE QUESTION OF MECHANISM

MULTIPLICITY

IN THE COPE REARRANGEMENT

by

Kevser Taymaz, B. Chem. Eng., M.Sc.

A thesis submitted to the faculty of Graduate Studies in
partial fulfilment of the requirements for the degree of
Doctor of Philosophy

Department of Chemistry

Carleton University

Ottawa, Ontario

July 21, 1975

© Kevser Taymaz, 1975

The undersigned recommend to the Faculty of
Graduate Studies acceptance of the thesis
"Investigations on the Question of Mechanism
Multiplicity in the Cope Rearrangement"
submitted by Kevser Taymaz, M.Sc., in partial
fulfilment of the requirements for the degree
of Doctor of Philosophy

D.C. Wyfield
.....
Thesis Supervisor

J. H. L.
.....
Chairman, Department of Chemistry

Jerome A. Berson August 4, 1975
.....
External Examiner

Carleton University

July 21, 1975

ABSTRACT

The possible occurrence of the ionic Cope rearrangement, and other non-concerted mechanisms is discussed. The synthesis of 2-(1-ethyl-1-propenyl)-2-(3-p-methoxyphenylallyl)malononitrile (1) and its clean thermal [1,3] rearrangement to (1-ethyl-5-p-methoxyphenyl-2-methyl-4-pentenylidene)malononitrile (3) are reported. This result contrasts with the rearrangement of 2-(1,1-dideuterioallyl)-2-(1-ethyl-1-propenyl)malononitrile (7a) which isomerizes cleanly in a [3,3] rearrangement. Pyrolysis of (1) in the presence of sodium borohydride allows interception of the proposed ionic intermediates and isolation of 2-(1-ethylpropylidene)malononitrile (4) and anethole (13).

Rearrangement of 2-(1-cyclohexenyl)-2-(3-p-methoxyphenylallyl)malononitrile (20), however, leads sluggishly to [2-(p-methoxy- α -vinylbenzyl)cyclohexylidene]malononitrile (21) ([3,3] shift). This reaction, however, also gave positive results in ion trapping experiments. Rearrangement of 2-(1-isopropyl-2-methyl-1-propenyl)-2-(3-p-methoxyphenylallyl)malononitrile (24) leads, also slowly, to (1-isopropyl-5-p-methoxyphenyl-2,2-dimethyl-4-pentenylidene)malononitrile (26) ([1,3] shift). Unsuccessful attempts to synthesize further related compounds are reported.

The carbon-13 nmr spectra of (1) and (7) have been assigned and compared with those of their monosaturated analogues. The spectra are consistent with the substrates being stereochemically homogeneous and of the E configuration around the trisubstituted double bond.

Kinetic solvent effects during the rearrangement of (1) to (3)

have been measured and found to be small. The apparent incompatibility of this result with the ionic mechanism is discussed. Activation parameters for the reaction are found to be $\Delta H^\ddagger = 23.15 \pm 0.5$ kcal/mole, $\Delta S^\ddagger = -12.41 \pm 1$ e.u. and $\Delta G^\ddagger_{(87^\circ\text{C})} = 27.61 \pm 0.5$ kcal/mole, consistent with either the ionic mechanism or a concerted [1,3] shift, but not with the radical mechanism.

High temperature rearrangement of 1,5-hexadiene-1,1,6,6- d_4 was investigated and was found to proceed by a dissociation-recombination mechanism above 395° . 2-Methyl-1,5-hexadiene was found to rearrange in a concerted manner below 390° . However; at 460° , the crossover products, 1,5-hexadiene and 2,5-dimethyl-1,5-hexadiene were detected.

$\text{LiAlH}_4/\text{AlCl}_3$ Reduction of ethyl p-methoxycinnamate, p-methoxycinnamaldehyde, p-methoxycinnamyl alcohol was found to give a quantitative yield of anethole (13) and p-allylanisole (50) in a 2:1 ratio. Similar reduction of ethyl o-methoxycinnamate produced the corresponding hydrocarbons o-anethole (51) and o-allylanisole (52) in a 56/44 ratio. Reduction of ethyl p-aminocinnamate under the same conditions gave p-allylaniline and p-propenylaniline but in only 18% yield.

ACKNOWLEDGEMENTS

The author wishes to express her appreciation to Dr. D. C. Wigfield for his invaluable assistance and guidance throughout this research. The author is also thankful to ^{the} National Research Council of Canada and to ^{the} Province of Ontario for financial support.

The work reported in this thesis has been aided by collaboration for brief periods by other co-workers, Mr. S. Feiner and Mr. G. Malbacho. For the sake of completion, their contributions are included in the thesis, but specific acknowledgement of their contributions is made at each point where an experiment of theirs is mentioned.

TABLE OF CONTENTS

	<u>Page</u>
Abstract	i
Acknowledgements	iii
List of Tables	
List of Figures	
List of Schemes	
Introduction	1
Reasons for undertaking the study	9
Results and discussion	10
Section 1: Synthesis and rearrangement of 2-(1-ethyl-1-propenyl)-2-(3-p-methoxyphenylallyl)malononitrile	10
Section 2: Comparison of ^{the} apparently different rearrangement of 2-(1-ethyl-1-propenyl)-2-(3-p-methoxyphenylallyl)malononitrile <u>1</u> , and 2-(1-ethyl-1-propenyl)-2-allylmalononitrile	15
Section 3: Evidence supporting the ionic Cope rearrangement	18
Section 4: Synthesis and rearrangement of 2-(cyclohexenyl)-2-(3-p-methoxyphenylallyl)malononitrile <u>20</u> .	24
Section 5: Synthesis, rearrangement and kinetics of 2-(1-isopropyl-2-methyl-1-propenyl)-2-(3-p-methoxyphenylallyl)malononitrile	30
Section 6: Attempts to synthesize other stereochemically unambiguous compounds	34
Section 7: Stereochemical elucidation of 2-(1-ethyl-1-propenyl)-2-(3-p-methoxyphenylallyl)malononitrile	40

Stereochemical analysis	48
Section 8: Kinetics of rearrangement of 2-(1-ethyl- 1-propenyl)-2-(3-p-methoxyphenylallyl)malononitrile	49
Section 9: Conclusions on the mechanism of rearrange- ment of 1 to 3.	54
Section 10: Related work	56
a) High temperature rearrangement of 1,5-hexadiene	56
b) One step reduction of an ester to a hydrocarbon	62
Conclusions	69
Experimental part	71
References	109

LIST OF TABLES

Table 1	Rates of isomerization of compound <u>24</u> in various solvents.	P.	34
Table 2	C-13 Shieldings for compounds <u>1</u> , <u>7</u> , <u>43</u> , <u>44</u> and <u>45</u> .	P.	45
Table 3	Rates of rearrangement of compound <u>1</u> in various solvents at 75°.	P.	50
Table 4	Rates of Rearrangement of <u>1</u> in nitrobenzene at various temperatures.	P.	53
Table 5	Pyrolysis of 1,5-hexadiene and 1,5-hexadiene-1,1,6,6-d ₄ .	P.	61
Table 6	Rearrangement of compound <u>24</u> in dyglyme.	P.	88
Table 7	Kinetics of Rearrangement of <u>1</u> in ethanol-d ₆ .	P.	96
Table 8	Kinetics of rearrangement of <u>1</u> in nitrobenzene.	P.	97

LIST OF FIGURES

Figure 1	The Arrhenius Plot.	P.	98
Figure 2	Diagram of the pyrolysis apparatus	P.	102

LIST OF SCHEMES

Scheme	1	The Cope Rearrangement.	P. 1
Scheme	2	Rearrangement of <u>meso</u> -3,4-dimethyl-1,5-hexadiene <u>via</u> a four center chair-like transition state.	P. 2
Scheme	3	Cope Rearrangement <u>via</u> a boat-like transition state.	P. 3
Scheme	4	Rearrangement of <u>trans</u> -divinylcyclobutane.	P. 4
Scheme	5	Radical mechanism for the Cope rearrangement.	P. 5
Scheme	6	The pyrolysate mixture of 5,6-dimethyl- <u>trans</u> , <u>trans</u> -1,3,7,9-decatetraene.	P. 6
Scheme	7	Degenerate and high temperature rearrangement of bicyclo[5,1,0]octa-2,5-diene.	P. 7
Scheme	8	Rearrangement of <u>endo</u> - and <u>exo</u> -2-vinylbicyclo-[2,2,2]-oct-5-ene.	P. 8
Scheme	9	Ionic Cope Rearrangement.	P. 10
Scheme	10	Potential rearrangement of compound <u>1</u> .	P. 11
Scheme	11	Synthesis of compound <u>1</u> .	P. 12
Scheme	12	Product-mechanism relationship in the rearrangement of <u>1a</u> .	P. 16
Scheme	13	Synthesis of <u>1a</u> .	P. 17
Scheme	14	Ion trapping experiments.	P. 19
Scheme	15	Synthesis of compound <u>17</u> .	P. 22
Scheme	16	Nucleophilic attack of sodium borohydride on <u>17</u> .	P. 23
Scheme	17	Synthesis of compound <u>20</u> .	P. 26

Scheme 18	Potential rearrangement of compound <u>20</u>	P. 27
Scheme 19	Regioselectivity of anion <u>4a</u> and <u>23a</u> .	P. 28
Scheme 20	Rearrangement of compound <u>20</u> .	P. 29
Scheme 21	Products isolated from condensation of <u>25</u> with <u>6</u> .	P. 31
Scheme 22	Rearrangement of compound <u>24</u> .	P. 32
Scheme 23	Proposed rearrangement of compound <u>31</u> .	P. 35
Scheme 24	Proposed synthesis of <u>31</u> .	P. 35
Scheme 25	Ease of condensation of malononitriles with chloride <u>6</u> .	P. 38
Scheme 26	Proposed rearrangement of compound <u>38</u> .	P. 39
Scheme 27	Synthetic procedure.	P. 43
Scheme 28	The numbering system used for C-13 peak assignments	P. 44
Scheme 29	Proposed crossover experiment.	P. 53
Scheme 30	Synthetic scheme.	P. 60
Scheme 31	Reduction of ethyl <u>p</u> -methoxycinnamate.	P. 64
Scheme 32	The mechanism proposed by Brown and White.	P. 66
Scheme 33	The proposed mechanism for the $\text{LiAlH}_4/\text{AlCl}_3$ reduction of ethyl <u>p</u> -methoxycinnamate.	P. 68

INTRODUCTION

The thermal isomerization of 1,5-hexadienes is known as the Cope Rearrangement. Since its discovery in 1940(1), the Cope Rearrangement has been a reaction of interest to organic chemists for both synthetic and mechanistic reasons, "Scheme 1".

Scheme 1: The Cope Rearrangement

It has been stated that the rearrangement is a typical "no-mechanism" reaction(2), which is brought about solely by thermal excitation either in solution or in the vapor state. In recent years the reaction has been described as a [3,3] sigmatropic process(3).

Cope and his coworkers(4,5) studied the rearrangements of various cyanoacetic esters, malonic esters and malononitriles, and found that the reactions were first order and had negative entropies of activation. The intramolecular nature of the process was established through the absence of cross-products upon reaction of mixtures of substituted hexadienes(6). Therefore, a mechanism involving dissociation of the diene into substituted allyl radicals, followed by recombination was ruled out. Ionic or radical pathways were accepted as representing limited models of the possible transition states, in a study of high pressure kinetics(7).

A more detailed picture of the intramolecular process has been provided from the studies of Doering and Roth(8). rac-3,4-Dimethyl-1,5-hexadiene was shown to yield mainly trans,trans-2,6-octadiene, whereas the meso isomer gave predominantly cis,trans-2,6-octadiene at 225°. On the basis of these results the authors concluded that the transition state for the rearrangement involves a six membered ring, which the six carbon atoms adopt four-center chair-like conformation i.e. "the normal pathway" (Scheme 2).

Scheme 2: Rearrangement of meso-3,4-dimethyl-1,5-hexadiene via a four-center chair-like transition state.

Further work along these lines has recently been reported by Goldstein and Benzon(9,10), supplementing the previous stereochemical(8) and kinetic investigations of Doering and his coworkers(11). They reported discovery of a second degenerate rearrangement of 1,5-hexadiene; one that requires an additional 5.8 kcal/mole more in $\Delta G^\ddagger$ but 11.2 kcal/mole more in $\Delta H^\ddagger$ at 250°, and tentatively suggested the "boat" stereochemistry to this high energy transition state. The entropy of activation for this high temperature rearrangement was

found to be near zero($-3 \pm 3.6 \text{ e.u.}$).

If the steric factors present in the molecule undergoing rearrangement prevent the reaction from proceeding through the normal pathway, transformation can readily occur via the six-center boat-like conformation. Experiments by Vogel(12,13) and by Hammond and DeBoer(14) demonstrated that steric factors can indeed divert the course of the reaction from the four-center chair-like transition state to the six-center boat-like path. Thus, cis-divinylcyclopropane (13) and cis-divinylcyclobutane(14) are believed to undergo thermal rearrangement through a boat-like transition state at -40 and $150-200^\circ$ respectively (Scheme 3). In each case the "normal" processes

Scheme 3: Cope Rearrangement via ^aboat-like transition state.

would involve highly strained transition states.

On the other hand, trans-1,2-divinylcyclopropane yields 1,4-cycloheptadiene at 190° and formation of the two allyl radicals has been proposed in order to explain the stereochemistry of the product(15). Similarly, trans-divinylcyclobutane is believed to undergo rearrangement by a biradical mechanism; because the product consisted of a mixture of vinylcyclohexene, cis-divinylcyclobutane and 1,5-octadiene,

and the entropy of activation was found to be near zero, i.e. +2.9e.u.
(Scheme 4).

Scheme 4: Rearrangement of trans-divinylcyclobutane.

Therefore, Hammond and DeBoer(14) advocated that the term "Cope Rearrangement" be used to describe all processes of the following stoichiometric types irrespective of the detailed mechanisms:

A detailed examination of the literature revealed that there were at least three reports of Cope Rearrangements in which cross-over products have been obtained, and formation of diradicals has been suggested(16-18) as shown in scheme 5:

Scheme 5: Radical Mechanism for the Cope Rearrangement.

For example, Huntsman(17) was able to isolate 2-methyl-1,5-hexadiene (21%), 1,5-hexadiene(25%) and 2,5-dimethyl-1,5-hexadiene(47%) from the pyrolysis of 2-methyl-1,5-hexadiene at 460° . Recombination of allyl radicals were observed rather than the formation of propenes due to the fact that allyl radicals abstract hydrogen atoms very slowly at 400° although quite rapidly at 500° (19).

Gibson and Pettit(18) reported similar results after studying the thermal isomerization of rac- and meso-5,6-dimethyl-trans,trans-1,3,7,9-decatetraene at 375° . The products of the pyrolysis of rac- and meso- tetraenes were identical (Scheme 6). These results are in contrast to that observed by Doering and Roth(8) for the rearrangement of dimethylhexadienes at 225° . Experiments starting with the mixture of normal and deuterium labeled tetraene further demonstrated the radical nature of the rearrangement(18).

Dewar and Wade reported an intramolecular two-step biradical mechanism (119) as shown.

Starting Material 30%

Scheme 6: The pyrolysate mixture of 5,6-dimethyl-trans,trans-1,3,7,9-decatetraene.

The first example of a degenerate Cope Rearrangement^{*} was reported by Doering and Roth(20) following the examination of the temperature dependant nmr spectrum of bicyclo[5,1,0]-octa-2,5-diene. However, at higher temperature(305⁰) tetrahydropentalene was formed probably via a diradical intermediate(Scheme 7).

Scheme 7: Degenerate and high temperature rearrangement of bicyclo[5,1,0]octa-2,5-diene.

When 1,5-hexadiene-1,1d₂ was rearranged at 383°, the reaction mixture consisted of approximately 30% d₀, 50% d₂ and 20% d₄ hexadiene(11). Attempts to trap the allylic radicals with toluene were unsuccessful and the activation parameters for the rearrangement were $\Delta H^\ddagger = 33.5 \pm 0.5$ kcal/mole and $\Delta S^\ddagger = -13.8 \pm 1$ e.u. These results contrast with recent work of Goldstein and Benzon discussed in Section 10a of the results section of this thesis.

Stepwise mechanisms have been proposed for the "Oxy-Cope" rearrangements* of the vinylnorbornenols(25) and vinyl bicyclo[2,2,2]octenols(26) at 250°. This conclusion follows from the fact that the

*The term "Oxy-Cope" has been proposed for the thermal transformation of vinylallylcarbinols to the corresponding ketones(21). Analogously the rearrangement of corresponding methyl and silyl ethers have been named "methoxy-Cope" and "silyloxy-Cope" rearrangement, respectively(22,23). However, the same term has wrongly been used to describe the rearrangement of vinyl allyl ethers(24) which should be referred to as "Claisen type", the distinction lying in whether the oxygen atom is part of the hexadiene system or is merely a substituent.

rearrangement of the conformational isomers were the same and the major effect of the hydroxyl group was to weaken the central bond of the biallyl system. A similar pathway was also suggested for the corresponding methyl ethers(27,28). The allylic and α -oxygen resonance energy effects on the strengths of carbon-carbon bonds also have been investigated(29). The rearrangement of the endo-2-vinylbicyclo-[2,2,2]-oct-5-ene at 325° gave rise to cis- $\Delta^{1,6}$ -hexalin in nearly quantitative yield. Under the same conditions the exo-vinyl epimer yielded cis- $\Delta^{1,6}$ -hexalin(50-60%) and Retro Diels-Alder products (40-50%). The rate ratio of endo- to exo- was only 4.2 and $\Delta\Delta H^{\ddagger}$ of 1.8 ± 1.5 kcal/mole could best be interpreted in terms of a stepwise mechanism passing over the diradical intermediate(Scheme 8).

Scheme 8

Reasons For Undertaking the Study:

With the advent of the ideas of the conservation of orbital symmetry in 1965(30), there has been a resurgence of interest in the Cope Rearrangement, redescribed as a [3,3] sigmatropic shift in the Woodward-Hoffmann terminology, and, as a result, numerous publications have appeared on the theoretical ramifications of this reaction(31-34,9,10). It is clear, however, that these rules are applicable only if a reaction is concerted; i.e. if the 1,6 bond is constructed simultaneously with the cleavage of the 3,4 bond, although there would not appear to be any requirement for the bond cleavage and bond construction to have progressed to an equal extent in the transition state.

From the point of view of the applicability of the rules of orbital symmetry, it is thus necessary that the concerted or non-concerted nature of the rearrangement be established. Cope and co-workers have done extensive kinetic studies and cross-over experiments, concluding that the rearrangement is intramolecular, with a cyclic transition state(4-6), and this is undoubtedly the mechanism followed in the majority of Cope Rearrangements. However, in a number of cases, a radical dissociation-recombination mechanism has been proposed to account for either the detection of cross-over products(17-18) or rate independence on structure(25-29). With this evidence for at least a duality of mechanism in the Cope Rearrangement, we felt that an ionic dissociation-recombination mechanism might also be observed, given the right combination of substrates or reaction conditions. This thesis is concerned with a search for the Ionic Cope Rearrangement.

RESULTS AND DISCUSSION*

Section 1: Synthesis and Rearrangement of 2-(1-Ethyl-1-propenyl)-2-(3-p-methoxyphenylallyl)malononitrile 1:

As mentioned in the introduction, there was reason to suspect that a mechanism for the Cope Rearrangement in which the 3,4 bond would be broken heterolytically giving ionic intermediates, might well be possible, but yet had remained undetected (Scheme 9).

Scheme 9: Ionic Cope Rearrangement.

Initial work in these laboratories to uncover this mechanism focussed on the chemistry of 2-(1-ethyl-1-propenyl)-2-(3-p-methoxyphenylallyl)malononitrile 1. This molecule was selected for the following reasons:

Compound 1

* A fold-out sheet of structures is given at the end of the thesis.

- a) Stabilization of the potential carbanion by the two nitrile groups,
- b) Stabilization of the potential carbonium ion by p-methoxyphenyl-allyl group,
- c) Consideration that the substrate might give different products according to the mechanism followed, i.e. concerted vs. fragmentation-recombination. This product-mechanism relationship is shown in Scheme 10.

Scheme 10: Potential rearrangement of compound 1.

Concerted [3,3] Cope Rearrangement of 1 can cause only the interconversion of 1 to 2, whereby conjugation with the nitrile groups is gained at the expense of loss of conjugation with the aromatic ring. If the ionic Cope Rearrangement operates, however, and the ions formed have sufficient lifetime, recombination could

give rise to compound 3, as well as 2, in which conjugation with both the nitrile groups and the aromatic ring is achieved. This compound is presumably more stable than 1. Therefore, it might be expected to be a significant product in the ionic Cope Rearrangement of 1.

The synthesis of compound 1 was achieved by the condensation of the anion of 2-(1-ethylpropylidene)malononitrile 4 with *p*-methoxycinnamyl chloride 6 as shown in Scheme 11. Dinitrile 4 was prepared from acid catalyzed condensation of malononitrile and 3-pentanone (35,36). Chloride 6 was prepared from either anisaldehyde or *p*-bromoanisole(37) by known routes.

Scheme 11: Synthesis of compound 1.

Considerable difficulty and irreproducibility was encountered in the preparation of alcohol 5 by the reaction of *p*-anisaldehyde with vinyl magnesium bromide, the reaction product being a mixture of unreacted aldehyde and the alcohol 5, with similar boiling points. This difficulty was later overcome¹ simply by doubling the amount of Grignard with respect to the aldehyde, and the desired product was obtained in 95% yield. The same compound was also synthesized either by using the *p*-bromoanisole-acrolein route(37) which gave, in our hands, a 32% yield of alcohol 5, or by using the same route, but replacing the vinyl magnesium bromide by vinyl lithium. In this case a 73% yield of alcohol was achieved. The final condensation to 1 which in principle could give rise to a complex mixture due to the potential ambivalence of both reagents gave, a 50-50 mixture of compound 1 and compound 3, presumably arising as a consequence of the ambivalence of the malononitrile anion 4a. Chromatography on alumina and preparative layer chromatography on silica gel afforded pure samples of 1.

Thermal isomerization of compound 1 was now considered. As mentioned above, it was felt that the formation of compound 3 from the rearrangement mixture of 1 and/or 2 would constitute encouraging evidence of the ionic Cope rearrangement mechanism. The pyrolysis experiment² was, therefore, extraordinarily gratifying. Mild heating (80°) of diene 1 caused rapid and quantitative conversion to the

¹This synthesis was first done in our laboratories by Mr. S. Feiner.

²The pyrolysis of 1 was first done in our laboratories by Mr. S. Feiner.

more conjugated compound 3. This reaction is precisely what one would predict if fragmentation-recombination process was involved. It is clear however, that isolation of a product does not constitute complete proof of mechanism. Only one of the two allyl units being inverted makes a concerted mechanism very improbable. It also raises the question of whether conversion of 1 to 3 is in fact a Cope rearrangement. The definition suggested by Hammond and DeBoer (14) does specifically include this type of rearrangement. The two most probable mechanisms for the rearrangement of 1 to 3 would be the fragmentation-recombination process either with ionic intermediate as shown in Scheme 12 or with radical intermediates arising from homolytic cleavage of 3,4 bond. The third possibility of concerted [1,3]-sigmatropic shift is less likely, because in the all-carbon series they are not known to take place in preference to a [3,3]-sigmatropic shift, and occur at much higher temperatures (38).

At this point two lines of advance clearly presented themselves. These were: a) to investigate how general the rearrangement might be, and b) to gather more experimental evidence to confirm or deny the ionic nature of the reaction.

the
Section 2 : Comparision of Apparently Different Rearrangement of
2-(1-Ethyl-1-propenyl)-2-(3-p-methoxyphenylallyl)malononitrile 1,
and 2-(1-Ethyl-1-propenyl)-2-allylmalononitrile 7 :

Before proceeding further to investigate the transformation of 1 to 3, we turned our attention to compound 7.

Kinetic solvent(36) and secondary deuterium isotope effects(39,40) for the rearrangement of 7 have been investigated. The magnitude of these effects have been interpreted in terms of a cyclic transition state resembling more the reactant than the product, and the possibility of a [1,3]-shift was ruled out. On the other hand the ionic mechanism has been suggested for its closely related analogue 1, by virtue of product analysis. Thus the strikingly different mechanisms suggested for the rearrangement of 1 (ionic) and 7 (concerted) had arisen by different types of evidence, the concerted suggestion for 7 from kinetics(36,39,40) and the ionic suggestion for 1 from product analysis. Therefore, we felt it was important to investigate and compare the mechanism of the rearrangement of 1 and 7 by the same method.

Product analysis to distinguish between the [1,3]- and [3,3]-shifts in rearrangement of compound 7 was tackled by consideration of its deuterated analogue 7a. Rearrangement of 7a would give rise to the products shown in the scheme, depending on the nature of the shift, the allylic deuteriums becoming scrambled in the case of the ionic rearrangement.

Scheme 12: Product-mechanism relationship in the rearrangement of 7a.

The synthesis of 7a¹ was accomplished as described by Sunko and coworkers(40), from dinitrile 4 and deuterated allyl chloride 10; see Scheme 13. Reduction of acryloyl chloride with lithium aluminum deuteride produced 9, and treatment with thionyl chloride yielded compound 10. The nmr spectrum of each product was examined and

¹The synthesis and pyrolysis were done in our laboratories in cooperation with Mr. S. Feiner.

showed over 98% labeling. The spectrum of 7a was identical with that measured previously for the non-deuterated analogue 7, with the exception of the two proton doublet at δ 2.65 ppm. The olefinic

Scheme 13: Synthesis of 7a.

the protons at Δ 5 and 6¹ positions however, have been reported to give signals at the unexpected position of τ 6.9-7.7 ppm(40). In our spectra, these proton signals are in the expected olefinic region δ 5.0-6.1 ppm, and the same values are also reported in the literature(36). The triplet at δ 1.17 ppm and the quartet at δ 2.28 ppm were due to the ethyl group, and the allylic methyl signal was at δ 1.77 ppm.

Pyrolysis of 7a in refluxing isopropanol gave quantitative conversion to the system (8a or 8b), where conjugation with the cyano groups was achieved. Careful integration of the nmr spectrum showed the formation of 8a, and the absence of any detectable 8b. This result is in agreement with previous conclusions(36) drawn following the kinetic studies. These studies unambiguously establish the [3,3]- nature

¹These positions refer to the 1,5-hexadiene portion of the molecule and similar numbering will be adopted throughout the thesis. The numbering that arises from the correct IUPAC name adds unnecessary confusion.

of the rearrangement of 7 as well as the abrupt mechanistic change between pyrolysis of compounds 1 and 7.

Section 3: Evidence Supporting the Ionic Cope Rearrangement:

Having established the overall [1,3]-nature of the rearrangement of 1 to 3, our attention was turned to gaining further evidence to support or deny the presence of the proposed ionic intermediates. One possible alternative mechanism that could be considered is the corresponding radical mechanism arising from homolytic rather than heterolytic cleavage of the 3,4 bond. In order to evaluate if there was any contribution from the radical mechanism, the reaction was followed by nmr spectroscopy to test for the presence of chemically induced dynamic nuclear polarization (CIDNP). An isopropanol solution of compound I was heated at 80° for one hour in a sealed nmr tube and its spectrum was recorded at 10 minute intervals throughout the heating. No nuclear spin polarization of the two allylic hydrogen atoms at δ 2.77 was observed. This technique has been shown to be a particularly sensitive method for the detection of short-lived free radical intermediates, although the absence of such polarization does not seem to have been utilized to rule out radical pathways(41,42). However, the absence of polarization provided no evidence for the presence of intermediate radicals, and, the ionic mechanism therefore seemed the most probable. In order to substantiate this view, it was decided to try and intercept the reaction and trap the intermediate ions.

The ion trapping experiments¹ done were those indicated in Scheme 14.

¹The trapping experiments using $I^{\ominus}$ and $C_6H_5-S^{\ominus}$ were conducted in our laboratories by Mr. S. Feiner.

Scheme 14: Ion trapping experiments

The rearrangement of 1 to 3 was firstly conducted in the presence of iodide ion. One of the products formed would be p-methoxycinnamyl iodide 11, resulting from the reaction of iodide ion, a good nucleophile, with the carbonium ion 6a. The anion 4a would presumably eventually become protonated giving rise to dinitrile 4. Following the trapping experiment using potassium iodide, an unstable compound was isolated from the reaction mixture, which showed an nmr spectrum very similar to that of chloride 6, but with the 2-proton doublet (CH_2 adjacent to halogen) appearing at $\delta 3.7$ ppm, instead of the chloride position of $\delta 4.2$ ppm. In addition a separate preparation from chloride 6 and sodium iodide gave rise to a similar unstable product, thus, strongly suggesting the formation of iodide 11, from 1. These experiments were discontinued owing to the apparent instability of the iodide.

In a second attempt the conversion was performed in the presence

of thiophenoxide as the trapping agent. Thioether 12 was prepared independently, from the chloride 6 and thiophenol, and was found to be stable. Experiments using thiophenoxide as the trapping agent were not successful in obtaining the thioether 12, from the isomerization of 1 to 3. Positive evidence for the formation of dinitrile 4, however, was obtained from glc-mass spectrometry¹ measurements on a gas chromatograph equipped with an 8-foot SE 30 on chromosorb B column, attached to an Atlas CH-4 mass spectrometer. The peak with retention time of 1.7 min. had the identical mass spectrum with that of authentic 4, the main peaks being at 134, 106, 93, 78, 54, 44 and 43 mass units. At this stage however, a serious ambiguity in the interpretation of the trapping results became apparent. Formation of dinitrile 4 could indeed result from the heterolytic cleavage of the 3,4 bond in 1, and subsequent protonation. On the other hand, it could also in principle, arise from direct nucleophilic attack on 1, by a powerful nucleophile (e.g. thiophenoxide (43)).

In order to distinguish between these two possibilities and also to be able to trap the carbonium ion, a trapping agent was required that had low nucleophilicity, but a good ability to trap carbonium ions. For these reasons, sodium borohydride² (44) seemed well suited, and the rearrangement of 1 was carried out in the presence of this compound. The product was subjected to glc-mass spectrometric analysis as previously mentioned. Formation of a small amount of

¹The glc-mass spectrometry measurements were done at National Research Council Laboratories, courtesy of Dr. R. F. Pottie.

²We are grateful to Dr. J. W. ApSimon for this suggestion.

anethole 13 was detected by its retention time (6.08 min) and from the peaks present in the mass spectrum at 148, 147, 133, 117, 105 and 77 mass units, the values identical with those of an authentic sample. These encouraging results proved that the ions could be trapped by a relatively non-nucleophilic reagent, and provided strong evidence for the presence of ions in the rearrangement of 1. The amount of anethole trapped was very small, in the presence of excess sodium borohydride. This could be that the ions formed have a very short life-time, the anion and the cation being in a common solvation shell. Tight ion-pairs have sometimes been referred to as "intimate" ion-pairs (45). As the reaction proceeds, the intimate ion pair is converted to 3 while only a small amount of the cation is being trapped. The obvious alternative interpretation for the poor yield could be that only a small amount of the rearrangement proceeds via these ions.

In order to clarify more rigidly that anethole was indeed formed from the reaction of hydride ion with the resultant carbonium ion 6a from 3,4 bond cleavage of 1, the dihydro derivative of the diene 1 was synthesized. The synthesis was achieved by two independent routes. The diimide reduction of 1 afforded the desired compound 17, which had nmr and ir spectra in agreement with its structure. It could not be purified however, to give satisfactory elemental analysis. A pure sample of 17 was later synthesized via the condensation of malononitrile 4 and 3-(p-methoxyphenyl)-1-propyl brosylate 15 (Scheme 15), the latter being prepared from the corresponding chloride 16. Compound 16 was obtained in 79% yield via reduction of ethyl p-methoxycinnamate with sodium and subsequent treatment of the alcohol 17 with thionyl chloride

Scheme 15: Synthesis of compound 17.

as shown in Scheme 15 (46). Small amounts of compound 17 were isolated, the major product being 18. A sample of 17 purified by preparative layer chromatography gave satisfactory elemental analysis by means of high resolution mass spectrometry and had similar nmr and ir spectra with those obtained from the product of diimide reduction.

Our aim was to conduct the trapping experiment with 17 in the presence of sodium borohydride, the trapping agent which enabled us to detect anethole from the rearrangement of 1. In view of the loss of conjugation with the aromatic ring, it would be anticipated that formation of the carbonium ion would be essentially completely inhibited, and thus no dihydroanethole would be formed, if the formation of anethole from 1 had occurred via the carbonium ion inter-

Scheme 16 : Nucleophilic attack of sodium borohydride on 17.

mediate, Scheme 16. If on the other hand, anethole had been formed from nucleophilic attack on 1, then dihydroanethole 19 should be able to be formed from 17 by the same means.

Before proceeding further, the structural difference between compounds 1 and 17 was considered. The displacement reaction for the two compounds would proceed at different rates, due to the absence of the conjugation with the γ -trans aromatic ring in 17. Therefore, we accounted this rate difference to be a factor of approximately 270 on the basis of the rate ratio of 40, resulting from the change of allyl group to an ethyl group(47), and the additional effect of 6.8 arising from the loss of conjugation with γ -trans aromatic ring(48). Thus, the treatment of 17 with borohydride should be conducted at 160° for 46 hours, assuming an activation energy of 19.0 kcal/mole(49). The results would then be comparable to the reaction of 1 with sodium borohydride.

The trapping experiment was, therefore, performed at 167° for 46 hours and no trace of dihydroanethole 19 was detected from glc-mass

spectral examination of the product. This result provided further evidence, that the formation of anethole from 1 was indeed from the reaction of p-methoxycinnamyl and hydride ions, but not due to direct nucleophilic attack of borohydride. The combined evidence from product analysis, CIDNP studies and trapping of the intermediate ions during the rearrangement of 1 to 3 all point to the presence of intermediate ions. Proof that this ionization can easily occur comes from the mass spectrum of compound 1, in which the molecular ion is barely detectable, and by far the largest peak occurs at M/e 147, corresponding to the ion 63.

Section 4: Synthesis and Rearrangement of 2-(1-Cyclohexenyl)-2-(3-p-methoxyphenylallyl)malononitrile 20:

The results mentioned in the previous section supported the ionic mechanism for the rearrangement of 1. In order to establish this point further, it was desirable to study the rate dependence on solvent polarity(50,51). Compound 1, however, had the distinct disadvantage of having a stereochemical ambiguity around the trisubstituted double

bond. Numbering the hexadiene system as shown in the diagram indicates that the methyl group could be cis or trans with respect to the ethyl

group attached to the adjoining vinyl carbon. If compound 1 exists as a mixture of these stereoisomers, then it would complicate the kinetics.

Stereochemical assignments around trisubstituted double bonds are frequently difficult. Assignments have been made sometimes on the basis of allylic coupling, provided that one has both the isomers available (52-60). In the case of compound 1, due to the fact that we have not detected any evidence for a mixture of isomers during our investigations, we believe it to be in configuration A. This belief however, is not certain in the absence of access to both stereoisomers A and B. The same problem presumably exists in compound 7 in which numerous kinetic investigations have been made (4,35,36,39), but for which first order kinetics are reported. It is noteworthy, however, that Cope, et al., (4) reported their best kinetic data with compound 20a, a compound devoid of this stereochemical ambiguity.

Compound 20a

In view of this stereochemical ambiguity¹, we then turned our attention to the synthesis of alternative substrates. Synthesis of the closely related compound 20 was next considered. Having necessary structural features required for the ionic rearrangement with the

¹This problem was finally solved in our laboratories, by means of C-13 nmr spectroscopy, and will be discussed in detail later in this thesis.

fixed stereochemistry around the trisubstituted double bond, it was felt that this compound would undergo an ionic Cope rearrangement. Synthesis¹ was achieved by condensation of the chloride 6, with the dinitrile 23, scheme 17. A similar route to that used for the preparation of compound 1 was followed, 3-pentanone being replaced by cyclohexanone. The final product was a white, crystalline solid.

Scheme 17 : Synthesis of compound 20.

If the rearrangement of 20 were to follow an ionic pathway, similar to that of 1, compound 21 would result as shown in scheme 18. It was found however, that compound 20 showed unusual stability relative to its analogue 1 which underwent rapid ionic conversion at 80°, and even slow rearrangement at room temperature. Pyrolysis at 140° for 36 hours caused 15% conversion to a single product which was identified as compound 22. As a result of rearrangement, conjugation with the two cyano groups has been achieved at the expense of loss of conjugation with the aromatic ring. This was the first and only rearrangement in our investigations where conjugation with the aro-

¹The synthesis and pyrolysis of 20 were performed in our laboratories by Mr. S. Malbacho.

during the rearrangement has the same substitution pattern in both compounds. Therefore, it is difficult to see why the ion formation should be any more difficult from compound 20, than from 1. It was considered that perhaps ions were indeed formed, but did not combine to give 21. Examination of models indicated that because of the ring rigidity and the planarity demanded by the delocalized system, there do seem to be interactions with ring hydrogens for alkylation on the ring in 23a. Similar interactions are not present in the ions from 1. Further support of this idea comes from the actual synthesis of compound 20. Condensation of malononitrile 4 with chloride 6 gave rise to a 50/50 mixture of 1 and 3 resulting from the attack of the carbonium ion on both ends of the ambident malononitrile anion. On the other hand, treatment of malononitrile 23 with chloride 6, under the same conditions produced only 20, none of the other isomer 22 being present. It would appear therefore, that the alkylation of the anion 23a may be considerably more regioselective than that from 4, as shown in scheme 19.

Scheme 19

These points made it easier to understand the rearrangement pathway of 20. As suggested earlier, probably the 3-4 bond cleaves to produce the ions. Once they are formed, the ions may preferentially combine back to the initial diene due to the regiochemical selectivity mentioned above. If the molecule did, in fact, ionize and then recombine to give the initial diene 20, rather than to proceed to 21, then it should still be possible to trap the intermediate carbonium ion with borohydride, as done on the rearrangement of 1, and again isolate anethole.

In order to establish this point, the trapping experiment on this "non-reaction" was performed. The reaction conditions employed were the same as for the rearrangement of 1. The pyrolysis was conducted at 80° for 16 hours in the presence of sodium borohydride. Anethole was indeed found to be formed by means of glc-mass spectrometry, from its identical retention time and mass spectrum with that of an authentic sample. This evidence suggested that the diene 20 does indeed ionize and does not have peculiar behaviour in this regard. Then the anion formed, preferentially alkylates at C-2 of the malononitrile system producing the starting material. The outline of this rearrangement is shown in scheme 20,

further investigations would be required to establish these suggestions. Since the rearrangement of 20 was not satisfactory from the point of view of our investigations, we decided to search for more suitable compounds, which would have no stereochemical ambiguity and also would undergo ionic Cope rearrangement.

Section 5: Synthesis, Rearrangement and Kinetics of 2-(1-Isopropyl-2-methyl-1-propenyl)-2-(3-p-methoxyphenylallyl)malononitrile 24:

In order to pursue the search for a stereochemically unambiguous substrate for the ionic Cope rearrangement, we next turned our attention to compound 24. This substrate also had the desired structural features to follow the rearrangement by product analysis.

Compound 24

The synthesis followed the route used for the preparation of compounds 1 and 20, using the corresponding dinitrile 25, which was prepared from diisopropyl ketone and malononitrile. The final step of the synthesis, however, gave a mixture of five compounds in addition to both unreacted starting materials. This sequence is shown in scheme 21. Each compound was purified by column and preparative layer chromatography. The structures were assigned following elemental and spectral analysis. The electronic absorption spectrum of compounds

Scheme 21: Products isolated from condensation of 25 with 6.

24, 26, 27 and 28 showed the presence of a styrene chromophore. The nitrile absorption peak in the ir spectra of 26 was intense, indicating that these were in conjugation with the double bond.

The formation of the products 27, 28 and 29 was surprising, since similar compounds have not been observed in analogous synthesis of 1 and 20. In a preparation on a 0.025 mole scale (4.05g of 25 and 4.55g of 6) 0.83, 0.17, 0.10, 0.09 and 0.98g of purified 24, 26, 27, 28 and 29 were isolated, respectively. To ensure that the formation of 28 had not occurred due to diisopropyl ketone impurity in dinitrile 25, the sample of dinitrile 25 was rechecked for purity and was shown to have no detectable diisopropyl ketone present. Thus, the formation of ketone 28 appears to arise by a retro-aldol process during the reaction.

The formation of 27 was apparently the result of hydrolysis of one of the cyano groups in 24. The isopropyl ether 29 was shown to be formed from isopropanol (the solvent) and the chloride 6, by a separate preparation in the absence of dinitrile 25.

Having obtained pure 24, we then considered its pyrolytic rearrangement. Concerted [3,3]-Cope rearrangement of 24 would give rise to 30, whereby conjugation with the nitrile groups is gained at the expense of loss of conjugation with the aromatic ring. If on the other hand, rearrangement follows the same route as 1, then compound 26 would be expected to form. In order to investigate the reaction, the diene 24 was pyrolyzed in n-butanol. Although conversion to the anticipated rearrangement product 26 did occur; the rearrangement was extremely slow. Refluxing in n-butanol (118°) for one week caused only 64% rearrangement. No detectable quantity of compound 30 was formed.

Scheme 22: Rearrangement of compound 24.

Conversion of 24 into 26 is an overall [1,3]-shift, as was the case for compound 1, immediately suggesting that the rearrangement had followed a similar path to that of compound 1. The sluggish rearrangement of 24, compared to 1 deserves some comment. Both compounds when rearranged gain conjugation with the two nitrile groups. Rearrangement of 1 to 3 involves conversion to a trisubstituted double bond to a tetrasubstituted double bond. Rearrangement of 24 to 26, does not change the degree of substitution around the corresponding double bond. Thus, it is possible that the driving force for rearrangement of 1 may be more connected with this aspect, rather than the drive for conjugation. It is clear however, that this rationalization between compound 1 and 24 are merely post facto suggestions, and further experimentation would be required to test them.

Since it is known that the rates of reactions involving formation of charge are accelerated by an increase in the solvent polarity (60), the rate dependence on solvent polarity was next considered. The rates of rearrangement of 24, in a number of solvents would give us more information about the mechanism. Following the reaction by means of nmr spectroscopy proved to be a convenient method. Compound 24 had two 3H singlets (integration a) at δ 1.83 and 1.97 ppm and one 6H doublet (integration b) at δ 1.28 ppm. Compound 26 had ^a12H singlet and doublet (integration b) at 1.38 ppm. The ratio of 26 to 24 at any given time was therefore equal to (b-a)/2a. Solvents of different polarity, with boiling points higher than 130° and which had no nmr signals between δ 0-3.5 ppm were chosen. These were anisole, nitro-

benzene and diglyme.

Compound 24 was dissolved in the solvent and the mixture was heated in an nmr tube at 130° using a temperature controlled oil bath. The integrated spectrum of the solution was recorded at certain time intervals. The results obtained are shown in Table 1:

Table 1: Rates of isomerization of compound 24 in various solvents*

Solvent	Rate [§] (Hour ⁻¹)	Half Life(Hours)
Nitrobenzene	2.86×10^{-2}	24:23
Diglyme	2.016×10^{-2}	34.37
Anisole	0.13×10^{-2}	533.1

* Temperature, $\approx 130^{\circ} \pm 1$

§ Average of the two first order rate constants.

It was found that the rate of isomerization was extremely slow and inconvenient for kinetics. Thus, although we had a compound with no stereochemical ambiguity, its isomerization was slow even in polar solvents. Therefore, we continued our search for better substrates.

Section 6 : Attempts to Synthesize Other Stereochemically Unambiguous Compounds:

In our search for ionic Cope rearrangement substrates synthesis of 2-(2-propenyl)-2-(3-p-methoxyphenylallyl)malononitrile 31 was next considered. This compound possessed all the required features apparently necessary for the rearrangement as shown in scheme 23. If our suggestion about the sluggish rearrangement of 24 was correct, then 31 would isomerize at a much faster rate than 24 and 1, due to the

Scheme 23 : Proposed Rearrangement of Compound 31:

fact that its rearrangement involves conversion of a disubstituted double bond to a tetrasubstituted double bond.

Efforts were made to synthesize 31 following the general route used for the preparation of 1, 20 and 24. The synthetic pathway is shown in scheme 24.

Scheme 24: Proposed synthesis of 31.

The general method used for the synthesis of dienes 1, 20 and 24 involves

condensation of the corresponding malononitrile anion with chloride 6; the anion being generated by sodium isopropoxide. In order to synthesize 31, isopropylidene malononitrile 33 was prepared according to a method described in the literature(61). The final step which was the nucleophilic attack of isopropylidene malononitrile anion 33a on chloride 6 was unsuccessful. The reaction product appeared to be mostly tars and polymers. Small amounts of *p*-(1-isopropoxyallyl)anisole 29, *p*-(3-isopropoxypropenyl)anisole 35 and an unstable compound 34 were isolated. No trace of compound 31 was detected. Compound 34 was purified with column and preparative layer chromatography. Its molecular formula was determined as $C_{19}H_{23}NO_3$ by means of high resolution mass spectroscopy. The metastable peak at 69.0 was also consistent with the formation of *m/e* 147 (*p*-methoxyphenylpropenyl) from a species with molecular weight 313. The infrared spectrum showed the presence of an unconjugated nitrile (2250 cm^{-1} weak) and a carbonyl (1735 cm^{-1} strong) group. The nmr spectrum had peaks at δ 1.23(6H, d, $J=6\text{Hz}$, $(\text{CH}_3)_2\text{-CH-O}$), 1.89(3H, s, $\text{CH}_3\text{-}$), 3.80(4H, s, $-\text{OCH}_3$ and $\text{HC-(CH}_3)_2$), 4.80-5.42(2H, m, $\text{CH}_2\text{=}$), 5.69-6.52(2H, m, $-\text{CH=CH-}$) and 6.60-7.45 ppm (4H, m, aromatic H). The structure fitting all the above information was determined as isopropyl-2-cyano-3-methyl-2-(3-*p*-methoxyphenylallyl)-3-butenate, 34.

Unsuccessful attempts to alkylate isopropylidene malononitrile 33, have also been made by Cope and Hoyle(35), and compound 33 has been found to polymerize in the presence of trace amounts of piperidine at room temperature. It was felt that although Cope and Hoyle were not able to synthesize 31, we might perhaps obtain small amounts by modifying the method and by the use of chromatographic techniques not then available. The alkylation step which involves addition of the malononitrile to a cooled solution of sodium isopropoxide in isopropanol, followed by the addition of chloride 6 failed. In a next attempt dinitrile 33 and chloride 6 were added together, hoping that some dinitrile would react with the chloride, before it dimerized. The only products obtained following the usual work up and column chromatography were the ethers 29 and 35, resulting from the reaction of the isopropoxide anion with chloride 6. The same reaction was then repeated using t-butanol and sodium, and the amount of dinitrile 33 was doubled with respect to chloride 6. It was thought that the t-butoxide anion being less nucleophilic would suppress ether formation, and thus some 31 might be formed. The only compound obtained under these conditions was p-(3-t-butoxy-2-propenyl)anisole 36, the remainder being a waxy material.

Next, it was decided to do the reaction in the presence of piperidine. Following work up the only product obtained was 2,2,6-tricyano-3,3,5-trimethylcyclohex-5-eneonimine 37, which resulted from the dimerization of isopropylidene malononitrile as shown.

Similar dimerization of alkylidene malononitriles in the presence of base has been observed previously on a number of occasions (62-64). It has been reported that the ease of dimerization depends on the availability of a base-extractable β -hydrogen in the alkylidene malononitrile. Thus, the dimers of isopropylidenemalononitrile 33, cyclohexylidenemalononitrile 23 are produced rapidly (1-2 hours) in the presence of base. 3-Pentylidenemalononitrile 4, where the intermediate carbanion will be destabilized by the adjacent methyl group, and which is also more sterically hindered, undergoes dimerization much less rapidly (65). This is consistent with compounds 1 and 3 being formed in higher yields compared to 20.

Compound 20 was formed, despite the fact that the dinitrile 23 dimerized in the presence of a base. The fact that only very small amount of condensation product 34 was formed from the reaction of dinitrile 33 with chloride 6, could be explained in terms of steric and electronic effects. Amongst the dinitriles used in our laboratory the best results were obtained in the following order:

Scheme 25: Ease of condensation of malononitriles with chloride 6

The allylic carbanions formed would be destabilized by the adjacent methyl or methylene groups, making 25 the most reactive. On the other

hand, steric hindrance of the second methyls on 25 makes its condensation with chloride 6 more difficult, thus explaining our results obtained during the synthesis of the dienes 1, 20, 24 and 34. The yield of 34 was less than 1% and no other alternative routes were tried.

Synthesis of 2-vinyl-2-(3-p-methoxyphenylallyl)malononitrile 38 was next considered. If our argument about the sluggish rearrangement of compound 24 was correct, than 38 would rearrange even at a faster rate, since the reaction involves conversion of a monosubstituted double bond to a trisubstituted double bond as shown:

Scheme 26: Proposed rearrangement of compound 38.

Preparation of 38 could be achieved following a similar pathway used for the synthesis of dienes 1, 20 and 24. It is found however, that ethylidenemalononitrile 40 dimerizes even on standing in contact with glass for one or two days(62). It has been synthesized in lab scale (62), and there have been two patented methods(66,67). In 1963 its existence in equilibrium with malononitrile and 1,1,3,3-tetracyano-2-methylpropane was demonstrated by nmr spectroscopy(68). Despite these facts, recently Krajewski and Moyer reported ethylidene malononitrile

as not being isolated and characterized(69). One other peculiar point is that condensation of malononitrile with acetaldehyde in the presence of piperidine (2 drops) has been reported to give 2,2,4,4-tetracyano-3,5-dimethylcyclohexylmalononitrile 41. It has been previously found that similar condensation in the presence of a few drops of diethylamine gives rise to 1-(2-amino-1,3,3,5,5-pentacyano-4,6-dimethyl)cyclohexene 42 (62), along with an unidentified yellow solid with no -NH or conjugated -CN group. Perhaps this unidentified compound was 41.⁸ There is no mention of this work by the later

authors. In view of these complicated dimerizations the search for better substrates was abandoned.

Section 7 : Stereochemical Elucidation of 2-(1-Ethyl-1-propenyl)-2-(3-p-methoxyphenylallyl)malononitrile 1:

Since our search for more suitable substrates which would undergo ionic Cope rearrangements had been unsuccessful, attention was now returned to compound 1. The geometrical configuration around the disubstituted double bond to which the *p*-methoxyphenyl group is attached was easily assigned as being *E*, by means of proton nmr spectroscopy ($J=15$ Hz between the vinyl hydrogens). The stereochemistry around the trisubstituted double bond however remained unknown and, in fact, has

been unknown in this type of substrate for 35 years despite the intensity of interest in the Cope rearrangement. In order to get reliable kinetic results, it was considered to be of critical importance to know the stereochemistry and purity of compounds 1 and 7.

The configuration around the trisubstituted double bond could either be E (70) or Z, or the compound could exist as a mixture of both diastereomers. Much of the fundamental kinetic work on the Cope rearrangement has been reported on such samples with unknown stereochemical homogeneity. It is interesting to note however, that Cope and his co-workers reported their most satisfactory kinetic data on compound 20a, a compound devoid of this particular ambiguity (71).

Stereochemical assignments around trisubstituted double bonds are often difficult and frequently require the comparison of both stereoisomers (52-59). We had however, no evidence of the presence of both stereoisomers and believed that compound 1 existed in the E configuration as mentioned earlier in the thesis. One method which does not require both stereoisomers, and one that has not previously been applied to these substrates, is carbon-13 nmr spectroscopy. It is reported that for olefins the α -carbons in trans- isomers are generally deshielded (by 2-5 ppm) whereas the α -carbons in cis- isomers are shielded (by 1-3 ppm) relative to their saturated analogues (72,73).

Synthesis of saturated analogues of 1 and 7 and comparison of the chemical shifts of the starred atoms with those of 1 and 7, would therefore, allow the determination of the double bond stereochemistry in these compounds.

For this reason the synthesis of compounds 43 and 44 was next considered. Condensation of the appropriate allyl chloride with 2(1-ethylpropyl)malononitrile 45 would produce the desired products. Attempts to prepare 2(1-ethylpropyl)malononitrile 45 by condensation of malononitrile with 3-bromopentane were not successful, and compound 45 was therefore prepared by reduction of 2(1-ethylpropylidene)malononitrile 4, this reduction being accomplished very conveniently by aluminum amalgam, a reagent of some antiquity (74). Condensation of compound 45 with allyl chloride and *p*-methoxyphenylallyl chloride 6 yielded compounds 43 and 44, respectively. The synthetic sequence is shown in scheme 27.

The carbon-13 spectrum of compounds 1, 7, 43, 44 and 45 were next recorded and in order to compare the chemical shifts the following numbering system was used.

Scheme 27 : Synthetic Procedure

Scheme 28 : The numbering system used for C-13 peak assignments

In order to facilitate unambiguous peak assignment, the peaks of the simplest compound, 2(1-ethylpropyl)malononitrile 45 were first

assigned. Addition of the allyl group and application of the alkane additivity shielding effects (75) yields the assignments for compound 43, which differs from compound 7 only by insertion of the double bond. Compound 43 is also instrumental in peak assignment of compound 44 the two differing only by the p-methoxyphenyl group at C-8; and insertion of the double bond gives the assignments to compound 1. Comparison of the shifts of C-2 and C-4 in both compounds 43 and 7 and in compounds 44 and 1 is the desired stereochemical analysis. Although clearly the assignment of many peaks is irrelevant to the question at hand, the complete peak assignments for all compounds have been made. These assignments are shown in Table 2.

Table 2: C-13 Shieldings for compounds 1, 7, 43, 44 and 45 (δ_C from $T_{CMS} \pm 0.1$)

Position	Compound				
	<u>45</u>	<u>43</u>	<u>7</u>	<u>44</u>	<u>1</u>
C-1	10.9	11.6	13.7	11.6	13.8
C-2	24.1	23.2	21.3	23.2	21.4
C-1'	-	-	13.7	-	13.8
C-2'	-	-	127.6	-	127.8
C-3	43.1	46.6	132.0	46.5	132.0
C-4	26.9	42.4	42.5	43.0	44.6
C-5	112.9	115.5	114.7	114.6	114.8
C-6	-	39.8	42.0	39.3	42.3
C-7	-	129.4	129.1	117.6	117.2
C-8	-	122.6	122.7	137.0	137.1

Table 2 : Continued

C-9	-	-	-	55.3	55.3
C-10	-	-	-	128.9	128.8
C-11	-	-	-	128.0	128.0
C-12	-	-	-	114.2	114.2
C-13	-	-	-	160.0	159.9

Peak assignments: (See Table 2 and Scheme 28)

Compound 45: The carbon-13 spectrum of compound 45 consists of five peaks of which the peak at 112.9 ppm is clearly due to the nitrile carbons. The other assignments made were confirmed by selective decoupling at δ 3.88 ppm (C4-H), under which conditions the peak for C-1 became a quartet, that for C-2 a triplet, and that for C-3 a doublet, while C-4 remained a singlet.

Compound 43: Peak assignments for compound 43 were made with reference to the assignments for compound 45 utilizing the alkane α - ϵ additivity factors for the additional allyl group (75). This gave the following calculated values for the peak positions of C1-4 (observed position in parentheses): C-1, 11.3 (11.6); C-2, 22.0 (23.2); C-3, 50.3 (46.6); C-4, 42.9 (42.4). Possible confusion between the assignments for C-4 and C-6 was eliminated by selective decoupling at δ 2.68 ppm (C6-H), under which conditions the peak at 39.8 remained a singlet.

Compound 7: Assignments for compound 7 were made in comparison with those for compound 43, the introduction of the double bond having little effect on carbon nuclei separated by two or more σ bonds

(72). It is noteworthy that C-1 and C-1' have almost identical chemical shifts. Rigorous distinction of the assignments for C-1' and C-2 was made by selective decoupling at δ 1.78 ppm (C1'-H). The possible ambiguity between assignments for C-4 and C-6 was also resolved, the peak at 42.0 ppm (C-6) degenerating to a triplet upon selective decoupling.

Compound 44: Assignments of the high-field peaks of compound 44 were made by comparison to those of compound 43, the introduction of the *p*-methoxyphenyl group having little effect on these shifts. Confirmation of the assignments for C1-4, C-6 and C-9 was also obtained by the appropriate multiplicity changes on selective decoupling at δ 2.77 ppm (C6-H). The aromatic carbon peaks were identified by combination of calculation (76) and comparison with the known spectrum of *p*-methoxystyrene (77). Carbons 11 and 12 are easily identified as high intensity peaks that are split into doublets upon selective decoupling at other hydrogens. The shift for C-11 of 128.0 ppm compares with the calculated (76) value of 126.7 ppm and the shift of the corresponding carbon in *p*-methoxystyrene of 126.8 ppm (77). For C-12 (114.2 ppm) the corresponding shifts are 113.4 ppm and 113.6 ppm respectively. Similar comparisons on the smaller peaks due to C-10 (calculated 129.3 ppm; comparison 130.4 ppm; observed 128.9 ppm) and C-13 (calculated 158.4 ppm; comparison 159.0; observed 160.0 ppm) allowed their assignment. These assignments leave, by difference, the peaks at 117.6 ppm and 137.0 ppm as C-7 and C-8 respectively; the assignments appear reasonable by comparison with the spectra of compounds 43 and 7, bearing in mind that an α substituent is deshielding but an α' substituent shielding (78) multiplicity changes on selective

decoupling at δ 2.77 ppm were consistent with all the above assignments.

Compound 1: With the assignments for compounds 7 and 44 in hand, the assignments of the fifteen signals of compound 1 are straightforward. Inspection of Table 2 reveals that the low-field portion of the spectrum is virtually identical with that of compound 44, with the addition of two signals due to C-2' and C-3 which have the characteristic shifts exhibited by the corresponding carbons in compound 7. As in compound 7, there is barely any distinction between carbons 1 and 1', and, as before, rigorous distinction between the shifts of C-4 and C-6 was made by selective decoupling at δ 1.73 ppm (C1'-H) and at δ 2.82 ppm (C6-H), all other multiplicity changes being consistent with assignment.

Stereochemical Analysis:

Comparison of the chemical shifts of C-2 in compounds 43 and 7, and in compounds 44 and 1 (Table 2) show that an upfield shift of 1.85 and 1.71 ppm respectively occurs upon insertion of the double bond, this shift being indicative of C-2 being cis to the methyl group in both compounds 7 and 1. Similarly the shift of the quaternary carbon C-4 is downfield in both comparisons (compounds 43 and 7, 0.12 ppm; compounds 44 and 1, 1.61 ppm), consistent with C-4 being trans to the methyl group. These shifts appear to demand the E configuration for the trisubstituted double bond of both compounds 7 and 1. One curious feature of the spectra is that the methyl group (C1, C1') in both cases undergoes a downfield shift (2.04; 2.15 ppm) upon insertion of the double bond despite the fact that the methyl clearly

must be cis to one group or the other. This may be a case, however, of electronic factors being superimposed on steric factors, the methyl becoming conjugated in a homoallylic sense with the nitrile groups on insertion of the double bond.

Section 8 : Kinetics of Rearrangement of 2-(1-Ethyl-1-propenyl)-2-(3-p-methoxyphenylallyl)malononitrile 1:

Having established the stereochemistry of compound 1, the kinetics of its rearrangement were next considered. Following the reaction by means of nmr spectroscopy proved to be a convenient method. Compound 1 has a 3H doublet at δ 1.65 ppm (allylic CH_3) and a 3H singlet at δ 3.70 ppm ($-\text{OCH}_3$). Compound 3 has no signals around δ 1.65 ppm and also has the 3H singlet at δ 3.70 ppm ($-\text{OCH}_3$). As the reaction proceeded the intensity of the doublet decreased with respect to the singlet. Therefore, disappearance of the allylic methyl doublet (intensity a) was measured with respect to the methoxy methyl singlet (intensity b). The ratio of the initial concentration of 1, to the concentration of unreacted 1 at any given time was therefore equal to b/a.

The effect of solvent polarity on reaction rate was first investigated. Solvents of different polarity with boiling points higher than 75° were chosen. These were benzene- d_6 , nitrobenzene, cyclohexane- d_{12} , ethanol- d_6 , acetic acid- d_4 and ethanol- d_6 /water- d_2 (80/20). The method used was the same as that previously described for following the rearrangement of compound 24. The samples were heated in a temperature controlled water-bath and the nmr spectrum was recorded at

appropriate time intervals. The logarithm of b/a was plotted against time.

Compound 1 was found to be insoluble in an ethanol/water mixture (80/20) at 34° , but was soluble upon heating. Therefore, in this case in order to record a spectrum, the sample cavity was heated at 75° . The results obtained are shown in Table 3.

Table 3 : Rates of Rearrangement of Compound 1 in Various Solvents at 75°

Solvent	E_T	Rate [§] (min^{-1})	Half Life (Hours)
Cyclohexane- d_{12}	-	1.189×10^{-3}	9.70
Benzene- d_6	34.5	1.439×10^{-3}	8.02
Nitrobenzene	42.0	2.101×10^{-3}	5.49
Ethanol- d_6	51.9	3.618×10^{-3}	3.19
Acetic acid- d_4	51.9	3.728×10^{-3}	3.09
Ethanol- d_6 /Water- d_2 (80/20)	53.6	4.021×10^{-3}	2.87

[§] Mean first order rate constants.

The rate of isomerization increased only by a factor of 3 on going from cyclohexane to ethanol-water mixture. Although there is an acceleration in the rate, it is not large enough to account for formation of the ionic intermediates, since rate increase for a reaction involving intermediate ions is usually considered to be 10^3 to 10^5 (79). Correctness of this rule however, demands that the transition state (as opposed to the intermediate or product) in the rate

controlling step has substantial charge development. Recently, it has been reported that the absence of a large solvent effect on the rate of a reaction does not necessarily constitute evidence of a non-ionic mechanism. A relationship between the magnitude of the solvent induced rate spread and the position of the transition state along the reaction coordinate had been suggested (51). A reaction producing ions and yet proceeding through a highly reactant-like transition state (for example (80) an exothermic ionization) will, presumably have little rate dependency on solvent and the rule of dramatic rate increase by solvent polarity being indicative of an ionic mechanism would fail. For a reaction with a very little charge development in the transition state an extremely small rate acceleration (<10) can be expected (51), even for a very wide (n-hexane-water) solvent polarity change. In this treatment, Wigfield and Lem (51) arrived at the following equation for the solvent-induced rate increase

$$\log(k_1/k_2) = \frac{1000}{2.303RT} (\Delta E_T) (\alpha_{E_T}) (T/\beta - 1)$$

where ΔE_T is the change in solvent polarity using the empirical parameter, E_T (81), β is the isokinetic temperature, and α_{E_T} a dimensionless parameter describing the position of the transition state on a scale from 0 to 1. Because the isokinetic temperature is not known for the reaction at hand, the equation may not be accurately used, however, using the rate difference between reaction in benzene and in ethanol/water (80/20) ($\Delta E_T = 19.1$), and assuming a not unreasonable value of β of 300° , the value of α_{E_T} is calculated

to be 0.23. Thus it appears that the small solvent-induced rate increase may be accommodated by quite reasonable values of β and α_{E_T} and thus, while not providing any support for the ionic mechanism, the rate-solvent polarity relationship should probably not be taken as unambiguous evidence against it although this conclusion might well have been made at first sight on inspection of the data.

In order to gather more evidence for the mechanism of the rearrangement of 1 to 3, the activation parameters for the reaction were next determined. For these studies the nmr spectrometer was locked on methoxymethyl signal.¹ Therefore, monitoring the intensity of this signal was no longer possible. Instead the following peaks were monitored. Compound 1 had a doublet at δ 1.65 ppm (intensity a) and a triplet at δ 1.10 ppm (intensity b). Compound 3 had a multiplet at δ 1.10 ppm (intensity b). As compound 1 rearranged the intensity a decreased and the intensity b increased. The ratio of the initial concentration of 1, to the concentration of 1 at any given time was therefore equal to $(a+b)/2a$.

The rate of rearrangement in nitrobenzene² was too slow below 65° and was found to be too fast above 110°. Therefore, the reaction

¹These studies were carried out at University of Ottawa, courtesy of Dr. R. R. Fraser.

²Our aim was to do the kinetics by using pure samples. Compound 1 was however found to be very viscous to take a good nmr spectrum. Therefore, nitrobenzene was used.

was studied in the range of 65-107⁰. The reaction was first order and the rate constants were calculated by least squares analysis. The results found are shown in Table 4.

Table 4 : Rates of Rearrangement of 1 in nitrobenzene at Various
Temperatures

t ⁰ C	Rate [*] (Sec ⁻¹)	log(k/T)	1/Tx10 ³
66.8	1.6963x10 ⁻⁵	-7.3052	2.9429
75.0	3.6989x10 ⁻⁵	-6.9735	2.8735
85.0	7.6007x10 ⁻⁵	-6.6730	2.7933
93.0	1.8650x10 ⁻⁴	-6.2939	2.7248
100.0	4.2770x10 ⁻⁴	-5.9405	2.6809
107.0	7.5480x10 ⁻⁴	-5.7019	2.6315

* Mean first order rate constants.

The activation parameters were calculated by plotting log(k/T) against 1/T and the least squares programme was used¹. The parameters were found to be:

$$\Delta H^{\ddagger} = 23.15 \pm 0.5 \text{ kCal/mole,}$$

$$\Delta S^{\ddagger} = -12.41 \pm 1 \text{ e.u. and}$$

$$\Delta G^{\ddagger}_{(87^{\circ}\text{C})} = 27.61 \pm 0.5 \text{ kCal/mole.}$$

These values would certainly appear to be inconsistent with the radical mechanism. Thus, the reaction would appear to be either ionic or [1,3] concerted. The activation parameters for these pathways

¹ Corr Coeff = -.992,

are unknown, but both might be expected to have negative entropy of activation. It is noteworthy that the observed activation parameters are very similar to those for many concerted Cope rearrangements (4). This however, is presumably fortuitous since the reaction at hand is not a [3,3] shift.

Section 9 : Conclusions on the Mechanism of Rearrangement of 1 to 3

The evidence accumulated on the rearrangement of 1 to 3, discussed above, may be summarized as follows:

a) The reactant-product structural relationship defines the reaction as an overall [1,3] shift. The three most obvious mechanisms to account for the product are (i) a concerted [1,3] sigmatropic shift; (ii) ionic dissociation-recombination; (iii) radical dissociation-recombination,

b) The presence of ions was established by the ion trapping experiments. Small amounts of anethole 13 were detected when the rearrangement was carried out in the presence of sodium borohydride, and dinitrile 4 was detected when the rearrangement was performed in the presence of thiophenoxide ion. The mass spectrum of compound 1 provides additional evidence for the ready ionic cleavage of compound 1, the most intense peak of the spectrum being ^{at} m/e 147, corresponding to the p-methoxyphenylallyl ion. In contrast the molecular ion is barely visible.

c) CIDNP experiments provided no evidence for the presence of radicals during the rearrangement.

d) Kinetics as a function of solvent polarity showed little rate dependence as a function of solvent.

e) The activation parameters found were $\Delta H^\ddagger$ 23.15 ± 0.5 kcal/mole, $\Delta S^\ddagger$ -12.41 ± 1 e.u. and $\Delta G^\ddagger$ 27.61 ± 0.5 kcal/mole. The substantial negative value of $\Delta S^\ddagger$ provides further evidence against the radical mechanism.

The evidence therefore, appears to be inconsistent with a radical mechanism. It appears to be less inconsistent (but by no means convincing) with either the concerted [1,3] or an ionic mechanism. The major objection to the ionic mechanism is the small solvent effect on the rate of reaction. It has been pointed out though (*vide supra*) that the combination of $\beta=300^\circ\text{K}$ and a transition state about a quarter of the way along the reaction coordinate is apparently consistent with this magnitude of effect. One objection to the [1,3] shift is the successful trapping of ions from the reaction; however, these were trapped only in small yield (glc/mass spectroscopy detection) and may arise from a minor pathway, not related to the major mechanism of reaction. In addition, [1,3] shifts are rare. Woodward and Hoffmann (30) state, that "few thermal uncatalyzed [1,3] shifts are known. Those which formally might be considered in this category, such as the vinylcyclopropane-cyclopentene rearrangement, proceed with such high activation energies (ca. 50 kcal/mole) that the energy surface for concerted reaction cannot be far removed from that for alternative stepwise processes". Symmetry allowed suprafacial [1,3] shift, with inversion at the migrating center has been observed only at 307° (38). In this connection it should be noted that the rearrangement of 1 to 3 takes place even at room temperature and at 150° is too fast to measure the

kinetics by nmr spectroscopy.

In conclusion, it must be stated that no one mechanism clearly fits all the data. Apparently the reaction is either ionic, or is a concerted [1,3] shift that, without any great thermodynamic driving force, is so facile as to proceed at room temperature. Either possibility appears to be unprecedented.

One experiment which might distinguish between these two mechanisms would be the rearrangement of compound 1a with one deuterium stereospecifically attached to the carbon atom at the C-4¹ position of compound 1. A rearrangement proceeding through ions being expected to cause racemization. This experiment, however, remains to be done.

Section 10 : Related Work

a) High Temperature Rearrangement of 1,5-Hexadiene:

While this work was in progress the publication of Goldstein and Benzon appeared (1972) reporting the discovery of a high temperature rearrangement of 1,5-hexadiene (9). This compound was found to rearrange by two different mechanisms depending on the temperature, namely; via a four center transition state below 233° and by some other mechanism, possibly via a six-center transition state at 259-295°. The experimental distinction between the two mechanisms was the loss of stereointegrity from 1,5-hexadiene-1,3,4,6-d₄ and the entropy of activation for the new rearrangement was found to be near zero (-3±3.6 e.u.). The evidence presented, however, seemed

¹The C-4 represents allylic CH₂ in conjugation with the p-methoxy-phenylstyrene portion of the molecule.

to us not to exclude completely the possibility that the new high temperature rearrangement might be a further example of the radical dissociation-recombination mechanism, which clearly would also be consistent with the observed near zero value of $\Delta S^\ddagger$, and loss of stereointegrity. Furthermore, this near-zero entropy of activation is highly reminiscent of the radical dissociation-recombination mechanism proposed for the Cope rearrangement of trans-1,2-divinylcyclobutane (14). We found it hard to accept that a boat (cyclic) transition state would be consistent with a near-zero $\Delta S^\ddagger$, particularly since it is well established that concerted Cope rearrangements generally have substantially negative values of $\Delta S^\ddagger$ (2), such as the value for the lower energy rearrangement (chair) of 1,5-hexadiene itself, $\Delta S^\ddagger = -13.8$ e.u. (9).

Doering and Roth investigated the rearrangement of 1,1-dideuterio-hexa-1,5-diene above 300° in the presence of excess toluene in order to trap the radicals (11). Instead, bibenzyl and 4-phenyl-but-1-ene were formed and at 383° the parent compound gave 50% d_2 , 20% d_4 and 30% d_0 . No comments were made on the results found and radical mechanism was ruled out by the absence of trapped intermediates.

Goldstein and Benzon rejected the radical mechanism, because the activation parameters ($\Delta H^\ddagger = 44.7$ kcal/mole; $\Delta S^\ddagger = -3.0$ e.u.) were quite different while compared with those of formation of 1,5-hexadiene from two allyl radicals ($\Delta H = 62$ kcal/mole, $\Delta S = +35$ e.u.*).

* All thermodynamic values refer to 250° .

These values however, combine to give a value of free energy ($\Delta G^\ddagger = 46.3$ KCal/mole) similar to that calculated from the equilibrium data ($\Delta G = 44$ KCal/mole). Thus, unless there is a large barrier to radical recombination, it must be anticipated that both the observed process and the radical dissociation-recombination take place at comparable rates. Even taking into account the value of the free energy barrier to radical recombination, which can be estimated from the data of Benson and co-workers (82) as approximately 5 KCal/mole. The free energy of activation for dissociation into radicals would be $\Delta G^\ddagger = 49$ KCal/mole - a value still comparable with that observed (within the estimated experimental error) for the new high temperature rearrangement. The discrepancy between the values of the $\Delta H^\ddagger$ and $\Delta S^\ddagger$ components of the free energy barriers is reduced by consideration of the data of Benson et al (82) which shows that the rate of recombination of allyl radicals decreases with increasing temperature. Therefore, this recombination would appear to be one of those rare (83) cases of a reaction having a transition state barrier due entirely to entropy, with a negative enthalpy of activation. Using these data, the barrier appears to be composed of $\Delta H_{\text{recomb}}^\ddagger = -7$ KCal/mole, and $\Delta S_{\text{recomb}}^\ddagger = -23$ e.u. Thus the activation parameters for the dissociation reaction will differ considerably from the equilibrium values, $\Delta H_{\text{dissoc}}^\ddagger = 62 - 7 = 55$ KCal/mole, and $\Delta S^\ddagger = 35 - 23 = 12$ e.u. These values, although closer, still differ from those reported by Goldstein and Benzon for the new rearrangement by about 10 KCal/mole in $\Delta H^\ddagger$ and 15 e.u. in $\Delta S^\ddagger$.

In view of the existence of these two possible interpretations

of the mechanisms of the high temperature Cope Rearrangement of 1,5-hexadiene (concerted, possibly via the boat transition state, and non-concerted via allyl radical intermediates), we felt it desirable to devise further experimental distinction between these two processes. For this purpose, a crossover experiment seemed well suited. A mixture of deuterated 1,5-hexadiene and unlabelled 1,5-hexadiene heated at high temperature should undergo no intermolecular label redistribution via the concerted mechanism, but could do so, giving products of combination of a labelled and an unlabelled allyl radical, from the dissociation-recombination mechanism, as shown:

Scheme 29 : Proposed crossover experiment

To achieve this goal, 1,5-hexadiene-1,1,6,6-d₄ was prepared from adipic acid by the route of Sunko et al (40). Adipoyl chloride which was prepared from adipic acid and thionyl chloride was treated with N-methyl aniline to give the amide 46 which was reduced to 1,6-Bisdimethylamino-hexane-1,1,6,6-d₄ 47 in the presence of LiAlD₄. Oxidation with hydrogen peroxide followed by pyrolysis afforded the title compound 49, as shown in the Scheme 30.

Scheme 30 : Synthetic Scheme

This labelled hexadiene was mixed with an excess of unlabelled 1,5-hexadiene, and the mixture repeatedly passed through a U-tube at various temperatures in vacuo. The product mixture was then analyzed by mass spectrometry to determine whether the crossover product, 1,5-hexadiene-1,1-d₂ (M.W. 84) had been formed. It was found that no significant crossover occurred at temperatures as high as 360°. Beyond that temperature, (e.g. 395°), the presence of the m/e 84 peak becomes progressively larger. The intensity of this peak is far greater than can be accounted for by loss of a deuteron from 1,5-hexadiene-d₄ and following the correction for the contribution from 1,5-hexadiene-d₄, and assuming no isotope effect, corresponds to 12.0% of deuterated allyl groups being present as 1,5-hexadiene-d₂ at 395°. The other possible alternative origin of the m/e 84 peak of simple loss of deuterium (e.g. by exchange with the walls of the tube) appears insignificant on the basis of (a) little or no apparent formation of 1,5-hexadiene-d₃ (m/e 85) or

1,5-hexadiene- d_1 (m/e 83), and (b) nmr analysis of the product which showed an overall maximum loss of 5% of deuterium. The results obtained are shown in Table 5.

Table 5: Pyrolysis of 1,5-hexadiene and 1,5-hexadiene-1,1,6,6- d_4

Mixture of hexadienes	Mass spectral relative Intensities ^a		
	M/e 86	M/e 85	M/e 84 ^b
Unheated	1.0	2.7	2.4
Passed through tube 24 times at 3500(c)	1.0	2.9	2.0
Passed through tube 17 times at 3950(c)	1.0	2.1	12.0

^aRelative to M/e 86.

^bM/e 81, 82 very large;

^cMaterial took <1 sec. to pass through tube, but no attempt to obtain accurate contact time was made.

The above results are clearly suggestive of the formation of 1,5-hexadiene- d_2 by a dissociation-recombination mechanism at 395° although the analysis of the mass spectral fragmentation is complicated due to large M^+_{LH} and M^+_{LD} peaks.

At 395° the mixture became yellow and contained benzene as well as other unidentified side products. It was very difficult to do further experiments, due to the high volatility of hexadiene. The results support the conclusion of Goldstein et al (2,7), that the rearrangement of 1,5-hexadiene at 300° is purely concerted joined only at about 395° by the dissociation-recombination mechanism.

We next turned our attention to 2-methyl-1,5-hexadiene. It

has been reported that this compound when rearranged at 460° gives rise to crossover products (17). On the other hand 3,4-dimethyl-1,5-hexadienes had been found to rearrange in a concerted manner at 225° (8). There has been no systematic study of a single compound at various temperatures. This point seemed worth investigating, and therefore we studied the rearrangement of 2-methyl-1,5-hexadiene at 50° intervals between 250° and 460° . No crossover products were detected up to 390° , at which point small amounts of 1,5-hexadiene and 2,5-dimethyl-1,5-hexadiene were identified by means of gas-liquid chromatography. At 460° considerable crossover occurred and the mixture consisted of 1,5-hexadiene (10%), 2-methyl-1,5-hexadiene (80%) and 2,5-dimethyl-1,5-hexadiene (10%). The identity of these compounds was unambiguously established by identical glc retention times and superimposable mass spectrum with those of the authentic samples.

These results, in combination with those of Goldstein and co-workers (9,10), indicate that three distinct mechanisms for Cope Rearrangement of simple 1,5-hexadienes are experimentally demonstratable — the normal concerted mechanism at low temperatures, joined at about $259-295^{\circ}$ by the "high temperature concerted" mechanism, and joined at about 390° by the radical dissociation-recombination mechanism.

b) One-Step Reduction of an Ester to a Hydrocarbon

During the course of this investigation it was of interest to us to explore the possibility of preparing various analogues of compound 1, differing only by the substituent on the phenyl ring. Synthesis of 1 required p-methoxycinnanyl chloride 6 which was prepared from p-bromoanisole via p-methoxycinnamylbenzyl alcohol 5

in two steps, in an overall yield of 25-30%. Similarly, various cinnamyl chlorides could be synthesized from the corresponding phenyl bromides, i.e. *p*-nitro-, *p*-methyl-, *p*-amino-, etc. In order to obtain *p*-nitro- α -vinylbenzyl alcohol, *p*-nitro-benzaldehyde was reacted with vinyl lithium. Following work-up starting material was recovered. In an alternative method, the reaction of *p*-bromonitrobenzene with Mg and acrolein also did not produce any of the desired product. Further examination of the literature revealed that *p*-nitro- α -vinylbenzyl alcohol was unstable (37).

The obvious alternative route to the desired cinnamyl chlorides was from the corresponding cinnamyl alcohols. Cinnamyl alcohol has been synthesized by $\text{LiAlH}_4/\text{AlCl}_3$ reduction of ethyl cinnamate in 95% yield (84). Therefore, it was thought similar reduction of various cinnamates would produce the corresponding cinnamyl alcohols. The desired chlorides could then be obtained by displacement of hydroxide with chloride. Although conversion of allylic alcohols to their corresponding halides is accompanied by allylic rearrangement. In recent years, several successful methods have been reported (85).

For example, cinnamyl alcohol has been transformed into cinnamyl chloride in excellent yield (82%), using methanesulfonyl chloride and a mixture of lithium chloride, dimethylformamide and collidine at 0° , and any nonallylic alcohol present in the starting material was not converted to the corresponding chloride (85). It was thought that reduction of *p*-methoxyethyl cinnamate followed by displacement with chloride according to the procedures mentioned above would improve the yield of chloride 6 (over the yield from the original route, p.13), and variety of similar compounds would

also be synthesized starting with the corresponding cinnamates.

For these reasons, reduction of *p*-methoxyethyl cinnamate with $\text{LiAlH}_4/\text{AlCl}_3$ was attempted. Instead of the expected *p*-methoxycinnamyl alcohol however, a quantitative yield of the two isomers anethole 13 and *p*-allylanisole (estragole) 50 in a 2:1 ratio were isolated by means of preparative glc purification. The identity of these compounds was established by comparison of their spectral properties with those of authentic samples.

Scheme 31: Reduction of ethyl *p*-methoxycinnamate

In order to ensure that this abrupt difference in reaction was due to the methoxyl substituent and was not an artifact of the comparison of results from different laboratories, ethylcinnamate was reduced under the same conditions. No hydrocarbon formation was observed and cinnamyl alcohol was produced in 95% yield, confirming the result of Jorgenson (84). In both cases no double bond reduction was observed.

The reduction of a Group III oxidation level (1) functional group (e.g. $-\text{COOR}$) to a Group 0 functional group (e.g. $-\text{CH}_3$) is, however, a transformation for which there is no general one-step

method (86). Indeed, even the number of specific one-step transformations of this type that have been reported is rather small, the examples being apparently restricted to catalytic hydrogenation of certain substrates under vigorous conditions (87). The reaction observed is, thus a rare instance of a one-step reduction of an ester to the corresponding hydrocarbon initiated by a metal hydride reagent (88). It is by no means general, however, since the reduction of its closely related analogue ethyl cinnamate produces the primary alcohol under identical conditions.

In a search of the literature to find closely related reactions, we have found one report on the reductive rearrangement of 3-carbethoxycyclopropanes with $\text{LiAlH}_4/\text{AlCl}_3$, producing the cyclobutene. For this reaction formation of a carbonium ion, followed by ring expansion to cyclobutene has been suggested (89). Certain alcohols have also been reduced to hydrocarbons under $\text{LiAlH}_4/\text{AlCl}_3$ conditions (90,91), and in a particularly relevant paper, the reductions of *p*-amino- and *p*-methoxybenzaldehydes to the corresponding toluenes have been reported. The electron donating substituents were essential for reduction to the hydrocarbon (92). Similar reaction of benzophenones produced diphenylmethanes, and the mechanism proposed involved, Lewis acid catalyzed carbonium ion formation as shown in scheme 32.

Hydride reduction of ketones are known to show positive ρ values (93-95). The presence of AlCl_3 however, seems to change the course of the reaction, involving Lewis acid-catalyzed carbonium ion formation with a substantially negative ρ value, and consequently producing the hydrocarbon, the electron donating substituent on the

Scheme 32 : The mechanism proposed by Brown and White (92).

aromatic ring being essential for the final reduction step. These considerations make it less remarkable that ethyl cinnamate gave cinnamyl alcohol and *p*-methoxyethyl cinnamate produced the hydrocarbon.

In order to explore the limited generality of the reaction, the reductions of the corresponding aldehyde and alcohol were also studied. *p*-Methoxycinnamyl alcohol, produced by LiAlH_4 reduction of *p*-methoxyethyl cinnamate (96), also was reduced by $\text{LiAlH}_4/\text{AlCl}_3$ giving a quantitative yield of the anethole-*p*-allylanisole mixture in essentially the same proportions (64:35). *p*-Methoxycinnamaldehyde, produced by MnO_2 oxidation of *p*-methoxycinnamyl alcohol (96), was also reduced quantitatively to give the same hydrocarbon mixture (anethole-*p*-allylanisole 67:33). Reduction of ethyl *o*-methoxycinnamate also gave quantitative reduction to hydrocarbon, the proportion of double bond isomers, however, being slightly different (*o*-anethole 51-*o*-estragole 52 56:44). These compounds were isolated by means of

preparative glc purification and identified by comparison of their spectral properties with those of authentic samples.

The reduction in a system with an amino activating group rather than methoxyl was also attempted. Reduction of ethyl *p*-aminocinnamate under the same conditions gave a complex mixture of products, from which the corresponding hydrocarbons *p*-allylaniline and *p*-propenylaniline could be extracted only with tedious purification and in 18%¹ yield. The compounds were unstable and accurate elemental analysis could not be obtained. High resolution mass spectral results combined with ir and nmr spectra, however, established their structure.

$\text{LiAlH}_4/\text{AlCl}_3$ ² reduction of cinnamic esters could proceed via Lewis acid catalyzed ionization of the ester, followed by reduction, producing stabilized carbonium ion which consequently gives rise to products, a mechanism similar to that proposed by Brown and White, for the reduction of benzophenones (92), see scheme 33.

It is worth noting that the attack on the double bonds of α,β -unsaturated carbonyl compounds is generally a major side reaction (98). Throughout the present work, the products consisted of only the corresponding hydrocarbons with no double bond reduction.

¹The low yield is considered to be due to decomposition of the product and does not represent the true reaction yield.

²These solutions are known to contain such intermediates as AlH_2Cl , AlHCl_2 , AlH_3 and their addition compounds with lithium chloride (97). For the sake of simplicity we assumed AlH_3 being the only reducing agent present.

Scheme 33 : The proposed mechanism for the $\text{LiAlH}_4/\text{AlCl}_3$ reduction of ethyl *p*-methoxycinnamate

CONCLUSIONS

1. A reaction (compound 1 $\rightarrow$ compound 3), which is an overall [1,3] shift, has been discovered. The reaction proceeds very readily, ~~and even~~ slowly at room temperature.
2. This reaction is not general; synthetic difficulties severely limit the range of other possible substrates, and of the two other substrates synthesized, one rearranges very sluggishly and the other not at all.
3. The rearrangement of 1 to 3 has been subjected to critical mechanistic scrutiny, yet unambiguous results have proved elusive. The data best fit either the Ionic Cope Rearrangement (but with a small solvent effect on rate) or a concerted [1,3] sigmatropic shift (but remarkably facile). The reaction does not appear to proceed via radicals.
4. The stereochemistry of the trisubstituted double bond in Cope Rearrangement substrates such as 7 has ~~remained~~ remained unknown for 35 years. Application of Carbon-13 nmr spectroscopy to substrates 7 and 1 indicate that samples are stereochemically homogeneous and of the E configuration.
5. Studies on the Cope Rearrangement of 1,5-hexadiene and 2-methyl-1,5-hexadiene indicate that 390° is the temperature at which dissociation-recombination begins to compete with the concerted process. In view of the recent work of Goldstein and coworkers, there would appear to be three distinct mechanisms for Cope Rearrangement of the parent compound 1,5-hexadiene.

6. Reduction of ethyl p-methoxycinnamate by $\text{LiAlH}_4/\text{AlCl}_3$ gives a mixture of anethole and p-allylanisole - a rare instance of a one-step reduction of an ester to the corresponding hydrocarbon.

EXPERIMENTAL PART

General

Melting points were taken on a Fischer-Johns melting point apparatus and are uncorrected. The infrared spectra were recorded on a Perkin-Elmer 237B Grating Infrared Spectrophotometer and electronic absorption spectra were measured on a Perkin-Elmer 202 Ultraviolet-Visible Spectrophotometer. The nuclear magnetic resonance spectra were obtained, except where noted otherwise, on a Varian T60 NMR spectrometer using deuteriochloroform as solvent and tetramethylsilane as internal standard. C-13 NMR spectra were recorded on a Varian XL-100 spectrometer.

Chemical shifts are expressed in the δ scale and the following abbreviations apply: s, singlet; d, doublet; t, triplet; m, multiplet.

A Hewlett Packard F and M Scientific 402 High Efficiency Gas Chromatograph was used for glc studies. High resolution molecular weight determinations were determined on an AE-MS-9 mass spectrometer at the University of British Columbia.¹

The glc-mass spectrometric analysis for trapping and crossover experiments were done at the National Research Council laboratories², on a Hewlett-Packard Model 700 gas chromatograph attached to an Atlas CH-4 mass spectrometer. Elemental analyses were performed by the Spang Microanalytical Laboratories, Ann Arbor, Michigan. Thin-layer and preparative-layer chromatography were performed on pre-

¹ Courtesy of Dr. J. P. Kutney.

² Courtesy of Dr. R. F. Pottie, N.R.C., and the R.C.M.P. Crime Detection Laboratories, Ottawa.

coated plates supplied by E. Merckag, Darmstadt, Germany. All solvents for chromatography were redistilled before use.

2-(1-ethylpropylidene)malononitrile 4

Malononitrile was condensed with 3-pentanone under the conditions of Cope and Hoyle (35) to give the title compound, b.p. 120-123° (23 mm), n_D^{25} 1.4692, $\nu_{\max}$ (film) 2240 cm^{-1} (Strong), $\lambda_{\max}$ (EtOH) 377 nm (ϵ 10200), p.m.r. δ 1.17 (6 H, t, $J = 7.6$ Hz, CH_3) and 2.60 ppm (4 H, q, $J = 7.6$ Hz, CH_2), (Lit. (35) b.p. 121-122° (20 mm), n_D^{22} 1.4694).

p-Methoxy- α -vinylbenzyl alcohol 5, Method 1

Anisaldehyde (6.8 g, 0.05 mole) was dissolved in dried, freshly distilled tetrahydrofuran (50 ml). Nitrogen was bubbled through the system for 30 minutes. The reaction flask was then placed in a CCl_4 -liquid nitrogen bath, and vinyl lithium reagent added dropwise at -15° with constant stirring, the stirring being continued for 30 minutes after completion of addition. The mixture was poured on to crushed ice, extracted with ether (3 x 50 ml), and the combined extract dried (MgSO_4) and evaporated. The residue was made into a paste with silica gel (170 gm), washed with *n*-hexane (700 ml) to remove the mineral oils, and then with a solution of chloroform (665 ml) and methanol (35 ml) to recover the product. The solution was evaporated, and then distilled (120-130°, 12 mm) over K_2CO_3 (5.0 gm) to yield the product (6.0 gm, 73%); $\nu_{\max}^{\text{neat}}$ 3400 (broad) (OH), and 1620 cm^{-1} (C = C); $\lambda_{\max}^{\text{EtOH}}$ 227 (ϵ 7600) and 277 nm (ϵ 11,000); δ 2.87 (1H, broad singlet, OH), 3.78 (3H, s, OCH_3), 4.8 - 6.4 (4H, m, olefinic and benzylic H), and 6.6 - 7.4 ppm (4H, q, aromatic H); (Lit (11) b.p. 129-130°, 12 mm).

Method 2. p-Bromoanisole (23 g; 0.12 mole) was reacted with magnesium (0.3 g; 0.12 mole) in ether, and resulting Grignard reagent reacted with acrolein (6.9 g; 0.12 mole) under the conditions of White and Fife (37). Vacuum distillation yielded the product (6.5 g; 32% yield) with physical and spectral properties as above.

Method 3. To Mg turnings (7.3 g; 0.3 mole) in freshly distilled dry THF (50 ml) was added with stirring a solution of vinyl bromide (31.9 g; 0.3 mole) at a rate sufficient to maintain reflux. The resulting dark brown solution was cooled to -10° in an ice-acetone bath and anisaldehyde (20.4 g; 0.15 mole) in THF (75 ml) was added dropwise. Stirring was continued for one hour, and the mixture was then poured into saturated NH_4Cl solution. The ether layer was separated and the aqueous layer was extracted with ether (3 x 50 ml). The combined extracts were washed with water (3 x 40 ml) dried (Na_2SO_4) and distilled from anhydrous K_2CO_3 , to obtain the desired product (23 g; 95% yield) which had same physical and spectral properties of the alcohol synthesized by the other methods described above.

p-(3-Chloropropenyl)anisole 6. (p-methoxycinnamyl chloride)

p-Methoxy- α -vinylbenzyl alcohol (5) (1.64 g, 0.01 mole) was reacted with thionyl chloride (1.19 g; 0.01 mole) in anhydrous ether as described by White and Fife (37) with the minor modification that the thionyl chloride was added dropwise to a solution of the alcohol in ether that had been cooled in an ice bath in order to control the vigorously exothermic reaction. The product was recrystallized from petroleum ether (bp $30-60^{\circ}$) yielding 1.68 g (92%), $\lambda_{\text{max}}^{\text{EtOH}}$ 270 nm

(ϵ 5700), δ 3.80 (3H, s, OCH_3), 4.22 (2H, d, $J = 6\text{ Hz}$, $\text{CH}_2 - \text{Cl}$), 5.8 - 6.6 (2H, m, olefinic), and 6.7 - 7.6 ppm (4H, q, aromatic), mp $71-72^\circ$ (Lit (11) mp $71.5-73^\circ$). Irradiation at 250 Hz (CH_2Cl), to decouple the coupling with the olefinic protons, permitted determination of the olefinic coupling constant as 15.5 Hz.

2-(1-Ethyl-1-propenyl)-2-(3-p-methoxyphenylallyl)malononitrile 1

A solution of sodium isopropoxide was prepared by dissolving sodium (0.38 g; 0.0167 mole) in isopropanol (10 ml) at 50° . When the sodium had dissolved the solution was cooled in an ice-water bath and 1-ethylpropylidene malononitrile (0.0167 mole, 2.24 g) added dropwise to give a clear orange solution of the malononitrile anion. p-Methoxycinnamyl chloride (3.0 g; 0.0165 mole) was then added as a solid in one portion and the mixture stirred at room temperature for 2 hours. Water (100 ml) was added, and the solution extracted with benzene (3 x 25 ml). The combined extracts were washed with water (2 x 25 ml), dried (Na_2SO_4) and evaporated giving a yellow-brown liquid (4.6 g). Chromatography on alumina (Woelm neutral, Activity III) yielded the product (1.4 g, 30%), eluted with 10% benzene in petroleum ether (bp $30-60^\circ$), $\nu_{\text{max}}^{\text{CHCl}_3}$ 2240 cm^{-1} (weak, CN); $\lambda_{\text{max}}^{\text{EtOH}}$ 263 nm (ϵ 28,000); δ 1.10 (3H, t, $J = 8\text{ Hz}$, $\text{CH}_2 - \text{CH}_3$), 1.65 (3H, d, $J = 6\text{ Hz}$, allylic CH_3), 2.27 (2H, q, $J = 8\text{ Hz}$, $\text{CH}_2 - \text{CH}_3$), 2.77 (2H, d, $J = 8\text{ Hz}$, $= \text{CH} - \text{CH}_2$), 3.70 (3H, s, OCH_3), 5.7 - 6.6 (3H, m, olefinic H) and 6.7 - 7.5 ppm (4H, q, aromatic H). Anal. Calc'd for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}$: C, 77.11; H, 7.19; N, 9.99. Found: 77.17; H, 7.24; N, 9.78.

2-Allyl-2-(1-ethyl-1-propenyl)malononitrile 7

Allyl chloride (1.91 g; 0.2 mole) was reacted with the sodium

anion of compound 5 (3.35 g; 0.2 mole), as described by Cope et al (4), to yield the 1,5-diene, n_D^{18} 1.4641, $\lambda_{\max}$ (film) 2250 cm^{-1} (weak), $\lambda_{\max}$ (EtOH) 246 nm (ϵ 1360), δ 1.05 (3H, t, $J = 7.5$ Hz, CH_3), 1.62 (3H, d, $J = 7$ Hz, allylic CH_3), 1.9 - 2.8 (4H, m, allylic CH_2) and 5.0 - 6.1 ppm (4H, m, olefinic protons), (lit (Cope et al) n_D^{25} 1.4639).

Allyl-1,1-d₂ alcohol 9 (bp 100-108°) was prepared in 40% yield by reduction of acryloyl chloride by LiAlD_4 as reported by Schuetz and Millard (100) (Lit. bp 98°). The nmr spectrum showed signals at δ 5.3 - 5.9 (2H, m) and 6.40 ppm (1H, m), and the absence of the finely split doublet (2H) at δ 4.1 ppm present in the spectra of nondeuterated samples. It was found that distillation of the product (100) was essential in order for the final condensation step of the synthetic sequence to proceed.

Allyl-1,1-d₂ chloride (bp 36-50°) was prepared in quantitative yield by the reaction of allyl-1,1-d₂ alcohol with thionyl chloride in the presence of di-n-butyl ether and tri-n-butylamine according to the method of Young et al (101) for preparing allyl-1-¹⁴C chloride. The nmr spectrum showed signals at δ 5.2 - 5.7 (2H, m) and 6.37 ppm (1H, m), and the absence of the finely split doublet at δ 4.1 (2H) present in the spectra of nondeuterated samples. Samples prepared for the next step of the sequence were distilled directly into a small quantity of isopropanol to minimize difficulties associated with the high volatility of allyl chloride.

2-(1,1-dideuterioallyl)-2-(1-ethyl-1-propenyl)malononitrile 7a

Allyl-1,1-d₂ chloride was reacted with the sodium anion of 2-(1-ethylpropylidene)malononitrile 4, as described by Cope et al

for the preparation of the undeuterated analogue (36,4). The nmr spectrum showed signals at δ 1.17 (3H, t, $J = 7.5$ Hz, $\text{CH}_2 - \text{CH}_3$), 1.77 (3H, d, $J = 7$ Hz, allylic CH_3), 2.28 (2H, q, $J = 7.5$ Hz, $\text{CH}_2 - \text{CH}_3$), and 5.0 - 6.1 ppm (4H, m, olefinic H), and the absence of the 2 proton doublet ($J = 6$ Hz) at δ 2.65 ppm present in spectra of non-deuterated samples.

3-p-Methoxyphenylallyl phenyl sulfide 12

p-Methoxycinnamyl chloride 6 (4.0 g) in acetone (2 ml) was added to a mixture of THAM buffer solution (102), pH 9.0 (20 ml), thiophenol (2.0 g), and sufficient isopropanol to cause solution. The solution was stirred at room temperature for 30 minutes, during which time the product precipitated from solution, and was then extracted with ether (2 x 50 ml). The combined extracts were washed with water (2 x 25 ml), dried (MgSO_4), and evaporated. The residue was recrystallized from ether-benzene giving white plates (1.4 g), mp $114-115^\circ$; $\nu_{\text{max}}^{\text{CHCl}_3}$ 1610 cm^{-1} ($\text{C} = \text{C}$), $\lambda_{\text{max}}^{\text{EtOH}}$ 271 nm (ϵ 25,000); δ 3.65 (2H, d, $J = 6$ Hz, $\text{CH}_2 - \text{S}$), 3.77 (3H, s, OCH_3), 5.7 - 6.5 (2H, m, olefinic H), and 6.7 - 7.5 ppm (9H, m, aromatic H). Anal, Calc'd for $\text{C}_{16}\text{H}_{16}\text{OS}$: C, 74.96; H, 6.29; S, 12.50. Found: C, 75.00; H, 6.25; S, 12.46.

3-(p-Methoxyphenyl)-1-propanol 14

The method of Bandhan and Mukheiji was used (46). Ethyl p-methoxycinnamate (20.6 g; 0.1 mole) and absolute ethanol (300 ml) were cooled in an ice-acetone bath and stirred. Sodium (16 g; 0.69 mole) was added in 10 portions 15 minutes apart. The contents were stirred overnight, then refluxed for 30 minutes, then cooled. Water (11 ml) was added dropwise and the mixture was refluxed again for an

hour. Following careful addition of water (100 ml), the mixture was poured into water, extracted with ether (3 x 75 ml), and dried (Na_2SO_4). Vacuum distillation gave the product (6 g; 73%) bp 86° , 0.6 mm (Lit bp (103) 107° ; 1.7 mm); $n_D^{20} = 1.5272$ (Lit (103) $n_D^{20} = 1.5275$); nmr: δ 1.76 (2H, m, $J = 7$ Hz protons on C2), 2.64 (2H, t, $J = 7$ Hz protons on C3), 2.88 (1H, broad singlet, -OH), 3.57 (2H, t, $J = 7$ Hz protons on C1), 3.76 (3H, s, $-\text{OCH}_3$), 6.62 - 7.28 ppm (4H, q, aromatic H); $\nu_{\text{max}}^{\text{film}} = 3400, 1600, 1235$ and 1120 cm^{-1} .

3-(p-Methoxyphenyl)-1-propenyl chloride 15

The procedure followed was that of Bandhan and Mukheiji's (46). 3-(p-Methoxyphenyl-1-propenol) (6 g; 0.036 mole), N,N-dimethylaniline (8.03 g; 0.066 mole) and dry CHCl_3 (8.4 ml) were cooled in an ice bath. A solution of SOCl_2 (8.4 ml; 0.117 mole) in CHCl_3 (8.4 ml) was added dropwise and the mixture was heated on a steam bath for 45 minutes. The solution was poured onto crushed ice and extracted with ether (3 x 50 ml). The extracts were combined, washed with 10% aqueous HCl (4x40ml) and dried (Na_2SO_4). Vacuum distillation gave the chloride (5.3 g; 79%); bp $102-5^\circ$, 0.9 mm (Lit (46) bp 130° , 5 mm); nmr: δ 2.5 (2H, m, $J = 7$ Hz, protons on C₂), 2.78 (2H, t, $J = 7$ Hz protons on C3), 3.52 (2H, t, $J = 7$ Hz, protons on C₁), 3.80 (3H, s, $-\text{OCH}_3$), and 6.78 - 7.34 ppm (4H, q, aromatic H); $\nu_{\text{max}}^{\text{film}} = 1615, 1510, 1245, 1175, 830$ and 810 cm^{-1} .

3-p-Methoxyphenyl-1-propyl p-Bromobenzenesulfonate 16:

3-(p-Methoxyphenyl)-1-propanol 14 (3.3 g; 0.02 mole) and p-bromobenzenesulfonyl chloride (5.1 g; 0.02 mole) were reacted in dry pyridine (50 ml) under the conditions of Winstein et al (104). The product was recrystallized from pet-ether (bp $30-60^\circ$) to give

the brosylate as white crystals (1.6 g; 59%), mp 57° (Lit (105) mp $62-64^{\circ}$).

2-(1-Ethyl-1-propenyl)-2-(3-p-methoxyphenylpropyl)-malononitrile 17

Method 1. 2-(1-Ethyl-1-propenyl)-2-(3-p-methoxyphenylallyl) malononitrile 1 was reduced by diimide, the method of Ohno and Okamoto (106) being used to produce the reducing agent in situ. The dinitrile (2.81 g; 0.01 mole) was dissolved in ethanol (50 ml) and the solution was cooled in an ice-acetone bath. Hydrazine hydrate (5 g; 0.1 mole), and a catalytic amount of CuSO_4 were added and air was bubbled through the mixture for 48 hours. The mixture was then stirred for eight hours, poured into water (100 ml) and extracted with ether (3 x 50 ml). The combined extracts were washed with 2N HCl till the aqueous layer became colorless, dried (Na_2SO_4) and evaporated. Chromatography on alumina (Woelm neutral, Activity III) using petroleum ether (bp $30-60^{\circ}$) and benzene mixture gave 0.8 g of unidentified material. Stripping the column with ether gave 0.97 g of the desired product which gave satisfactory mass, nmr and ir, spectra but could not be purified to give an acceptable elemental analysis. Therefore a second method was employed.

Method 2. A solution of sodium isopropoxide was prepared by dissolving sodium (0.058 g; 0.25×10^{-2} mole) in isopropanol (10 ml) at 50° . When the sodium had dissolved, the dinitrile 4 (0.35 g; 0.25×10^{-2} mole) was added to the cooled solution, followed by addition of the brosylate 16 (0.79 g; 0.25×10^{-2} mole) as a solid in one portion. The mixture was heated under reflux overnight. Water (50 ml) was added and the solution was extracted with benzene (3 x 25 ml). The combined extracts were washed with water (2 x

25 ml), dried (Na_2SO_4), and evaporated giving a yellow-brown liquid (0.71 g) which was purified by silica gel preparative-layer chromatography (developing solvent petroleum ether (bp 30-60°)-ether (1:1); R_f 0.69), giving a compound with the same tlc and spectral characteristics as that of Method 1, $\nu_{\text{max}}^{\text{CHCl}_3}$ 2220 (weak, CN), 1610 ($\text{C} = \text{C}$), 1030 and 825 cm^{-1} ; δ 1.2 (3H, t, $J = 6$ Hz, $\text{CH}_2 - \text{CH}_3$), 1.5 - 3.0 (11H, m, other aliphatic H), 3.86 (3H, s, OCH_3), 6.1 (1H, q, $J = 7$ Hz olefinic H), and 6.7 - 7.3 ppm (4H, q, aromatic H); Anal. Calc'd for $\text{C}_{18}\text{H}_{22}\text{N}_2\text{O}$: 282.1731. Found: 282.1726.

Cyclohexylidenemalononitrile 23

Malononitrile (3.3 g; 0.05 mole) and cyclohexanone (5.45 g; 0.05 mole) were reacted in benzene (12 ml) in the presence of ammonium acetate (0.38 g) and acetic acid (0.61 g) under the conditions described by Cope and Hoyle (35) to give cyclohexylidenemalononitrile which was distilled under vacuum yielding 6.3 g (86%). b.p. 76 - 84° (0.11 mm), n_D^{25} 1.5116 (Lit (35) n_D^{25} 1.5110), $\nu_{\text{max}}^{\text{neat}}$ 2220 (CN), 1590 cm^{-1} ($\text{C} = \text{C}$); $\lambda_{\text{max}}^{\text{EtOH}}$ 237 nm (ϵ 15,000); δ 1.4 - 2.0 (6H, m, nonallylic ring H) and 2.4 - 2.8 (4H, m, allylic H).

2-(1-Cyclohexenyl)-2-(3-p-methoxyphenylallyl)malononitrile 20

Cyclohexylidenemalononitrile (1.75 g, 0.012 mole) was added dropwise at ice-bath temperature to a solution of sodium isopropoxide (0.012 mole) in isopropanol (10 ml). The solution was warmed to room temperature and p-methoxycinnamyl chloride (2.21 g, 0.012 mole) added in one portion. The solution was stirred for 15 minutes, three volumes of saturated aqueous NaHCO_3 solution added, and extracted with benzene (4 x 20 ml). The combined benzene extracts were washed with water (4 x 10 ml), dried (MgSO_4), and evaporated.

The residue (3.41 g) was chromatographed on alumina (Woelm, Activity III; 150 g), the product was eluted with benzene, and recrystallized from petroleum ether (bp 30-60°) giving the product (1.53 g, 44%), mp 69-70°; $\nu_{\text{max}}^{\text{CHCl}_3}$ 2240 (weak, CN) and 1600 cm^{-1} (strong C = C); $\lambda_{\text{max}}^{\text{EtOH}}$ 266 nm (ϵ 24,000); δ 1.72 (4H, m, non-allylic ring H), 2.2 (4H, m, allylic ring H), 2.86 (2H, d, J = 7 Hz, allylic CH_2), 3.77 (3H, s, OCH_3), 5.7 - 6.6 (3H, m, olefinic H) and 6.7 - 7.3 ppm (4H, q, aromatic H). Anal. Calc'd for $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}$: C, 78.05; H, 6.90; N, 9.58. Found: C, 78.12; H, 6.78; N, 9.48.

(1-Isopropyl-2-methylpropylidene)malononitrile 25

Malononitrile (19.0 g, 0.29 mole) and diisopropyl ketone (32.54 g, 0.29 mole) were condensed as described by Hart and Kim (107), to give the product (40.3 g, 87%) bp 84-92° (0.5 mm); n_D^{23} 1.4708; $\nu_{\text{max}}^{\text{film}}$ 2220 (strong, CN), 1580 cm^{-1} (C = C); $\lambda_{\text{max}}^{\text{EtOH}}$ 238, (ϵ 14,000); δ 1.22 (12H, d, J = 7 Hz, CH_3) and 3.10 ppm (2H, m, methine). (Lit. n_D^{20} 1.4714, bp 97-98° (4 mm), $\lambda_{\text{max}}^{\text{EtOH}}$ 237.5 (log ϵ 4.15) (106).

Reaction of chloride 6 with dinitrile 25

preparation of 2-(1-isopropyl-2-methyl-1-propenyl)-2-(3-p-methoxyphenyl-allyl)malononitrile (24); (1-isopropyl-5-p-methoxyphenyl-2,2-dimethyl-4-pentenylidene)malononitrile (26); 2-cyano-3-isopropyl-2-(3-p-methoxyphenylallyl)-4-methyl-3-pentenamide (27); 7-p-methoxyphenyl-2,4,4-trimethylhept-6-en-3-one (28); and p-(1-isopropoxyallyl)anisole (29)

A solution of sodium isopropoxide was prepared by dissolving sodium (0.575 g; 0.025 mole) in isopropanol (75 ml) at 50°. When the sodium had dissolved, the dinitrile 25 (4.05 g; 0.025 mole) was added, followed by the addition of p-methoxycinnamyl chloride (4.55 g; 0.025 mole). The mixture was stirred at room temperature for one hour.

Water (150 ml) was added, and the solution extracted with benzene (3 x 100 ml). The combined extracts were washed with water (3 x 300 ml), dried (MgSO_4) and evaporated to give a residue (7.9 g) which was chromatographed on alumina (Woelm, Activity III, 250 g), 50 ml fractions being taken. Fractions 1 - 46 (petroleum ether bp 30-60 $^{\circ}$) gave 980 mg of ether 29. Fractions 47 - 52 (2% benzene in petroleum ether) and 53 - 57 (5% benzene) gave a further 670 and 390 mg respectively of 29 contaminated by dinitrile and chloride starting reagents. Fractions 58 - 64 (10% benzene in petroleum ether) gave 745 mg of desired dinitrile 24 with some impurity of dinitrile 26. Fractions 65 - 69 (10% benzene) yielded 240 mg of 26 with some impurity of 24. Fractions 70 - 83 (25% benzene) gave 450 mg of 28 again with some impurity of 24. Fractions 84 - 90 (50% benzene) and 91 - 107 (100% benzene) gave 15 and 105 mg respectively of unidentified materials. Stripping the column with methanol gave 420 mg of a mixture containing amide 27. Further purification was achieved by preparative layer chromatography on silica gel using 10% ether in petroleum ether (bp 30-60 $^{\circ}$) as the developing solvent. In this way pure samples of compound 29 (980 mg; R_f 0.83), compound 24 (825 mg; R_f 0.50), 28 (85 mg; R_f 0.76) and 26 (165 mg; R_f 0.42) were obtained. Compound 27 was purified by preparative layer chromatography on alumina using ether as solvent (R_f 0.65) giving 100 mg.

Spectral and analytical details:

Compound 29. $\nu_{\text{max}}^{\text{CHCl}_3}$ 1600 cm^{-1} (C = C); $\lambda_{\text{max}}^{\text{EtOH}}$ 228 (ϵ 17,500); δ 1.20 (6H, 2 doublets, $J = 7$ Hz, $(\text{CH}_3)_2\text{CH}$), 3.65 (1H, m, $(\text{CH}_3)_2\text{CH-O}$), 4.7-6.6 (4H, m, olefinic H and Ar-CH-O), and 6.7-7.4 ppm (4H, q, aromatic H); m/e 206 (M^+), 164, 163 (base), 148, 147, 137, 135, 121.

Anal. Calc'd for $C_{13}H_{18}O_2$: C, 75.67; H, 8.79. Found: C, 75.59; H, 8.72.

Compound 24. $\nu_{\max}^{CHCl_3}$ 2240 (weak, CN); $\lambda_{\max}^{EtOH}$ 265 nm (ϵ 23,500); δ 1.28 (6H, d, $J = 6$ Hz, $CH(CH_3)_2$), 1.83 and 1.97 (3H, s, each, allylic CH_3), 2.93 (2H, d, $J = 7$ Hz, allylic CH_2), 2.8-3.2 (1H, m, allylic CH), 3.78 (3H, s, OCH_3), 5.9-6.7 (2H, m, olefinic H), and 7.1 ppm (4H, q, aromatic H); m/e 308 (M^+), 260, 147 (base), 121, 85, 83.

Anal. Calc'd for $C_{20}H_{24}N_2O$: C, 77.87; H, 7.82; N, 9.08. Found: C, 77.78; H, 7.93; N, 8.85.

Compound 28. $\nu_{\max}^{CHCl_3}$ 1695 cm^{-1} (strong, $C = O$); $\lambda_{\max}^{EtOH}$ 263 nm (ϵ 21,000); δ 1.03 (6H, d, $J = 6$ Hz, $(CH_3)_2CH$), 1.20 (6H, s, $(CH_3)_2C=$), 2.40 (2H, d, $J = 6$ Hz, allylic CH_2), 3.20 (1H, m, allylic CH), 3.80 (3H, s, OCH_3), 5.7-6.6 (2H, m, olefinic H) and 7.1 ppm (4H, q, aromatic H); m/e 260 (M^+), 147 (base), 136, 135, 121, 77.

Anal. Calc'd for $C_{17}H_{24}O_2$: C, 78.45; H, 9.23. Found: C, 78.23; H, 8.95.

Compound 26. $\nu_{\max}^{CHCl_3}$ 2210 (strong, CN); $\nu_{\max}^{EtOH}$ 258 nm (ϵ 20,000); δ 1.38 (6H, s, and 6H, d, $J = 7$ Hz, methyls), 2.56 (2H, d, $J = 6$ Hz, allylic CH_2), 3.40 (1H, m, allylic CH), 3.82 (3H, s, OCH_3), 5.4 - 6.6 (2H, m, olefinic H) and 7.1 ppm (4H, q, aromatic H); m/e 308 (M^+), 148, 147 (base), 115, 91.

Anal. Calc'd for $C_{20}H_{24}N_2O$: C, 77.87; H, 7.82; N, 9.08. Found: C, 77.73; H, 7.67; N, 8.82.

Compound 27. $\nu_{\max}^{CHCl_3}$ 3450 (NH_2) and 1700 cm^{-1} ($C = O$); $\lambda_{\max}^{EtOH}$ 263 nm (ϵ 20,500); δ 1.24 (6H, d, $J = 7$ Hz, $(CH_3)_2CH$), 1.77 and 1.23 (3H, s, each, allylic CH_3), 3.0 (3H, m, allylic CH_2 and CH), 3.60 (3H,

s, OCH_3), 5.8-6.6 (4H, m, olefinic H and NH_2), 7.1 ppm (4H, q, aromatic H); m/e 147, 118, 87, 85, 83 (base), 82. No molecular ion (326) visible.

Anal. Calc'd for $\text{C}_{20}\text{H}_{26}\text{N}_2\text{O}_2$: C, 73.60; H, 8.03; N, 8.58. Found: C, 73.41; H, 8.14; N, 8.60.

Pyrolysis of Compound 1

Dinitrile 1 was distilled at 110° (0.7 mm) to give a quantitative yield of (1-ethyl-5-p-methoxyphenyl-2-methyl-4-pentenylidene) malononitrile 3, ν_{max} 2220 cm^{-1} (strong, CN); $\lambda_{\text{max}}^{\text{EtOH}}$ 263 nm (ϵ 26,000); δ 1.22 (3H, d, $J = 7\text{ Hz}$, $\text{CH}-\text{CH}_3$), 1.23 (3H, t, $J = 7.5\text{ Hz}$, CH_2-CH_3) 2.2-3.6 (5H, m, allylic H), 3.78 (3H, s, OCH_3), 5.5-6.6 (2H, m, olefinic H), and 6.7-7.5 ppm (4H, q, aromatic H).

Anal. Calc'd for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}$: C, 77.11; H, 7.19; N, 9.99. M.W. 280.1575. Found: C, 77.02; H, 7.25; N, 10.04. M.W. 280.1588.

Acryloyl chloride (bp $100-108^\circ$); δ 6.0-6.8 ppm (m) was prepared in 70% yield from acrylic acid by the method of Stempel et al (116). (Lit. bp $72-74^\circ$ (740 mm) (116)).

Pyrolysis of Compound 20

Dinitrile 20 (726 mg) was heated at 140° for 36 hours under nitrogen. The brown residue was chromatographed on silica gel and recrystallized from petroleum ether (bp 30-60°) to give 2-(p-methoxy- α -vinylbenzyl)cyclohexylidene malononitrile 19 as white crystals (105 mg), mp 71-72°; $\nu_{\text{max}}^{\text{CHCl}_3}$ 2225 (strong, CN), 1600 cm^{-1} (C = C); $\lambda_{\text{max}}^{\text{EtOH}}$ 231 nm (ϵ 13,800); δ 1.0-1.9 (6H, m, non-allylic ring H), 1.9-3.2 (3H, m, allylic H), 3.2-3.7 (1H, m, benzylic H), 3.80 (3H, s, OCH₃), 4.8-5.4 (2H, m, CH₂ =), 5.4-6.6 (1H, m, CH =), and 6.7 to 7.5 ppm (4H, q, aromatic H).

Anal. Calc'd for C₁₉H₂₀N₂O: C, 78.03; H, 6.90; N, 9.58.

Found: C, 77.97; H, 6.99; N, 9.48.

Pyrolysis of Compound 24

Dinitrile 24 was heated under reflux in n-butanol (bp 118°) for 7 days. The resulting mixture, purified as described above in the preparation of 24, was shown to consist of 64% compound 26 and 36% unchanged 24, identical in all respects with samples encountered in the preparation of 24.

Pyrolysis of compound 7a

Deuterated dinitrile 7a (90 mg) was heated under reflux in isopropanol (15 ml) for 7 hours. Water (50 ml) was added and the solution extracted with ether (2 x 20 ml) and chloroform (1 x 20 ml). The combined extracts were washed with water (2 x 20 ml), dried (MgSO₄), and evaporated giving a residue (61 mg) which was chromatographed on alumina (Woelm, Activity III, 12 g), the product being eluted with 15% benzene in petroleum ether (bp 30-60°). The nmr spectrum of the product was identical with that of nondeuterated

samples of (1-ethyl-2-methyl-4-pentenylidene)malononitrile 3 (36) with the exception of the olefinic region which integrated for only 1.0 proton (δ 5.68 ppm, t, $J = 8$ Hz).

Pyrolysis of compound 1 in presence of sodium borohydride

A solution of 1 (56 mg, 2×10^{-4} mole), NaBH_4 (58.4 mg, 16×10^{-4} mole), and sodium hydroxide (16 mg, 4×10^{-4} mole) in diglyme (0.5 ml) and water (0.2 ml) (44) was heated at 88° for 16 hours. Water (1 ml) was added and the mixture extracted with petroleum ether (bp $30-60^\circ$) (3×5 ml). The combined extracts were washed with water (2×5 ml), dried (CaCl_2), and evaporated to give a residue which was subjected to glc-mass spectrometric analysis on Hewlett-Packard Model 700 gas chromatograph equipped with an 8-foot SE30 on chromosorb B column (130°) attached to an Atlas CH-4 mass spectrometer. Anethole 13, retention time 6.08 minutes; m/e 148 (M^+ , base), 147, 133, 117, 105, 77) and dinitrile 4 (retention time 1.7 minutes: m/e 134 (M^+), 106, 93, 78, 58, 44, 43 (base)) were identified by identity of retention time and fragmentation pattern with those of authentic samples.

Pyrolysis of compound 17 in presence of sodium borohydride

A solution of dinitrile 17 (0.97 g, 3.4×10^{-3} mole), NaBH_4 (1.05 g, 27.5×10^{-3} mole) and sodium hydroxide (285 mg, 6.9×10^{-3} mole) in diglyme (5 ml) and water (1 ml) was heated at 167° for 46 hours. Work-up and analysis as described above in the pyrolysis of compound 1 showed no detectable trace of dihydroanethole 19.

Pyrolysis of compound 20 in presence of sodium borohydride

A solution of dinitrile 20 (58.4 mg, 2×10^{-4} mole), NaBH_4 (58.4 mg, 16×10^{-4} mole) and sodium hydroxide (16 mg, 4×10^{-4} mole)

2 2

OF/DE

in diglyme (0.5 ml) and water (0.2 ml) was heated at 88° for 16 hours. Water (1 ml) was added and the mixture extracted with petroleum ether (bp $30-60^{\circ}$) (3 x 5 ml). The combined extracts were washed with water (2 x 5 ml), dried (CaCl_2), and evaporated. Glc-mass spectrometric analysis of the residue as described above demonstrated the presence of anethole.

Kinetics of Rearrangement of 24

Isomerizations of compound 24 were performed by heating approximately 100 mg of sample in 500 mg of the solvent¹ in an nmr tube. The solutions were heated at 130° in an oil bath and the tube was taken out at appropriate time intervals (30 or 60 minutes), and the nmr spectrum immediately recorded on a Varian T-60 spectrometer. The total intensity (a) of the two singlets at 1.83 and 1.97 ppm (allylic methyls in compound 24) were measured in comparison with the intensity (b) of the singlet and doublet at 1.38 ppm (all non-allylic methyls in both compounds 24 and 26) in the particular solvent of interest. The ratio of the initial concentration of 24, to the concentration of unreacted 24 at any given time was equal to $(b + a)/2a$. Readings were taken for two half-life periods. The logarithm of $(b + a)/2a$ was plotted against time. The first-order rate constants from these linear relationships were obtained via a least-squares programme on an Olivetti-Underwood Programma 101 Desk Computer. Each rate constant

¹ Solvents with boiling points above 130° and which do not exhibit any nmr signals at δ 0-3.5 ppm were selected. All solvents used were spectroscopic grade and freshly distilled before use.

was measured at least in duplicate to ensure reproducibility.

Representative data are shown on Table 5, the rate constant found for this particular experiment being 1.93×10^{-2} (Corr. Coeff. = 0.996)

Isopropylidene malononitrile 33

The method of Prout was used (61). A mixture of malononitrile (14.8 g; 0.224 mole), acetone (17.6 g; 0.303 mole), β -alanine (0.16 g) and acetic acid (3.3 ml) were heated under reflux with a Dean-Stork water trap attached. The reaction was continued until no more water separated (5.8 ml of water was collected after three hours). The mixture was then washed with water (4 x 25 ml) and with saturated salt (25 ml) solution, dried (MgSO_4) and distilled to give the desired dinitrile (14 g; 60%), bp $90-92^\circ$, 10 mm (Lit (35) bp $107-108^\circ$, 23 mm), $n_D = 1.4658$ (lit (35) $n_D = 1.4662$).

$\nu_{\text{max}}^{\text{film}}$ 2970, 2210, 1580 and 1420 cm^{-1} , δ 2.29 ppm.

Attempts to synthesize 2-isopropenyl-2-(3-p-methoxyphenylallyl)

malononitrile 32: Reaction of chloride 6 with dinitrile 33:

Preparation of isopropyl-2-cyano-3-methyl-2-(3-p-methoxyphenylallyl)

-3-butenolate 34; p-(3-isopropoxypropenyl)anisole 35; p-(1-isopropoxy-

allyl)anisole 29; p-(3-t-butoxypropenyl)anisole 36; and 2,2,6-

tricyano-3,3,5-trimethylcyclohex-5-eneimine 37:

A solution of i-PrONa was prepared by dissolving Na (0.23 g; 0.01 mole) in i-PrOH (25 ml) at 50° . When the Na had dissolved, the solution was cooled in an ice-bath and the dinitrile 33 (1.07 g; 0.01 mole) was added, followed by the addition of p-methoxycinnamyl chloride (1.82 g; 0.01 mole). The mixture was then stirred at room temperature for one hour. Water (50 ml) was added, and the mixture

Table 6: Rearrangement of compound 24 in dyglyme*

Time(Hours)	a [†]	b [§]	- Log[(a+b)/2a]
0	32	32	0
1	32	33	0.00673
2	31.7	35.3	0.0240
3	33.7	33.3	0.0287
4	30.25	36.75	0.0443
5	36	49	0.0721
6.08	46	63.7	0.0764
7	35	48.2	0.0750
8.13	35.6	50	0.0799
9	29	45	0.1058
11.25	25.3	44.3	0.1385
13.25	32	56.7	0.1417
14.75	30	53.0	0.1410
16	25.7	50.3	0.1698
17.5	35	73	0.1883
19.78	25.3	53.7	0.1935
21.5	22.7	53.3	0.2238
23	21.7	51.3	0.2258
26	20	48.3	0.2324
27.5	23	63	0.2717
29	23.3	64	0.2726
31	24.3	64.7	0.2627
32.25	10	38.3	0.2689
34	26	79	0.3052

Table 6 Continued

36.25	19	62	0.3287
38.5	16.7	55.3	0.3336
40.5	18	60.7	0.3397
42.6	15	59.3	0.3939
45.0	14.7	57-	0.3872
47.8	16.3	66	0.4022
49.	16.7	78.3	0.4539
51	11	48.7	0.4336

*Temperature 130 ± 1

[†]Total intensity of the two singlets at 1.83 and 1.97 ppm.

[§]Total intensity of the singlet and the doublet at 1.38 ppm.

extracted with benzene (3 x 25 ml). The combined extracts were washed with water (3 x 25 ml), dried (MgSO_4) and evaporated to give a residue (4.7 g), which was chromatographed on alumina (Woelm, Activity III, 100 g), 200 ml fractions being taken. Fractions 1-7 (98% petroleum ether (bp 30-60 $^\circ$), 12% benzene) gave 280 mg of 29. Fractions 8-10 (95% petroleum ether (bp 30-60 $^\circ$); 5% benzene) gave 78 mg of 35 and fractions 11-20 (90% petroleum ether (bp 30-60 $^\circ$); 10% benzene) gave 250 mg of 34. Compound 34 was further purified by means of preparative layer chromatography on silica gel using 15% ether in benzene. In this way pure sample of compound 34 was isolated (R_f 0.43) which decomposed slowly.

Spectral and analytical details:

Compound 34. $\nu_{\text{max}}^{\text{film}}$ 2250 weak, 1735 strong, 1260 and 950 cm^{-1} , δ 1.23 (6H, d, $J=6$ Hz, $(\text{CH}_3)_2\text{-CH-O}$), 1.89 (3H, s, $\text{CH}_3\text{-}$), 3.80 (4H, s, -OCH_3 and $\text{HC-(CH}_3)_2\text{-}$), 4.80-5.42 (2H, m, $\text{CH}_2\text{=}$), 5.69-6.52 (2H, m, -CH=CH-) and 6.60-7.45 ppm (4H, m, aromatic H). Molecular weight (high resolution mass spectrometry) calculated for $\text{C}_{19}\text{H}_{23}\text{NO}_3$: 313.1678. Found: 313.1684.

Compound 35. $\nu_{\text{max}}^{\text{film}}$ 1600 and 950 cm^{-1} ($\text{C}=\text{C}$); δ 1.21 (6H, D, $J=6$ Hz, $(\text{CH}_3)_2\text{-CH}$), 3.45-3.90 (1H, m, $J=6$ Hz, $\text{CH-(CH}_3)_2$), 3.81 (3H, s, OCH_3), 4.13 (2H, d, $J=6$ Hz, allylic H), 5.86-6.44 (2H, m, olefinic H) and 6.62-7.43 ppm (4H, m, aromatic H).

Anal. Calc'd for $\text{C}_{13}\text{H}_{18}\text{O}_2$: C, 75.67; H, 8.79. Found: C, 75.42; H, 8.68.

p-(3-t-Butoxypropenyl)anisole 36

A solution of t-BuONa was prepared with Na (0.23 g; 0.01 mole) and t-BuOH (25 ml). Immediately following the dropwise addition of the dinitrile 33 (2.14 g; 0.02 mole), chloride 6 (1.82 g; 0.01

mole) was added in one portion. The mixture was stirred at 40° for one hour. After the usual work-up a waxy looking residue (3.1 g) was chromatographed on alumina (Woelm, Activity III, 100 g), 200 ml fractions being taken. Fractions 1 (petroleum ether, bp $30-60^{\circ}$), 2-5 (2% benzene in light petroleum), and 10-12 (10% benzene in light petroleum) did not contain any material. Fractions 13-16 (25% benzene in light petroleum) gave compound 36 (56 mg), no other pure material being detected from the rest of the fractions. Compound 36 had the following spectral and analytical details; m.p. = $49-50^{\circ}$, $\nu_{\text{max}}^{\text{mull}}$ 1600, 1370, 1250 and 975 cm^{-1} . δ 1.21 (9H, s, $(\text{CH}_3)_3\text{-C}$), 3.74 (3H, s, $-\text{OCH}_3$), 4.01 (2H, d, $J = 5\text{ Hz}$, allylic H), 6.0-6.61 (2H, m, olefinic H and 6.68-7.50 ppm (4H, m, aromatic H).
 Anal. Calc'd for $\text{C}_{14}\text{H}_{20}\text{O}_2$: C, 76.26; H, 9.09. Found: C, 76.09; H, 8.94.

2,2,6-Tricyano-3,3,5-trimethylcyclohex-5-ene-onimine 37

Isopropylidene malononitrile 33 (2.12 g; 0.02 mole) was added into a solution of piperidine (1.7 g; 0.02 mole) in benzene (25 ml) and the mixture was cooled in an ice-acetone bath, followed by immediate addition of chloride 6 (1.82 g; 0.01 mole) in one portion. The mixture was stirred for two hours in an ice-bath, then overnight at room temperature. Water (25 ml) was added, and the solution extracted with ether (3 x 30 ml). The combined extracts were washed with water (3 x 30 ml), then with 10% HCl (3 x 30 ml), dried (Na_2SO_4), and evaporated giving a yellowish-brown solid (3.1 g) which was purified by column chromatography on alumina (Woelm, Activity III, 250 g), 100 ml fractions being taken. Fractions 1-21 (petroleum ether and benzene mixtures) did not contain any of the desired compound. Stripping the column with MeOH gave a light yellow solid

(1.2 g) which was crystallized twice from ethanol yielding pure 37 (0.8 g), m.p. 168° (Lit m.p. $168-170^{\circ}$ (63)

Chem., 28, 1054 (1963)). $\nu_{\text{max}}^{\text{mull}}$ 3450, 3340, 3230, 2210, 1650, 1480 and 1385 cm^{-1} . δ 1.28 (6H, broad singlet, $(\text{CH}_3)_2\text{-C}$), 1.92 (3H, broad singlet, $\text{CH}_3\text{-C}$), and 5.20-5.52 ppm (3H, two broad singlets, NH and CH_2).

2-(1-Ethylpropyl)malononitrile 45

Aluminum amalgam¹ (15 g) was added to a solution of dinitrile 4 (13.4 g; 0.1 mole) in ether (200 ml), and water (200 ml) was added. The mixture was refluxed until all the dinitrile had reacted. Completion of the reaction was checked by recording nmr spectra of the ether layer. At the end of three days all the aluminum had reacted and freshly prepared amalgam (10 g) and water (100 ml) were added. At the end of one week the quartet due to the starting material at δ 2.6 ppm had disappeared. The ether layer was then separated and the aqueous layer was hydrolyzed with ice cold hydrochloric acid (100 ml), extracted with ether (3 x 100 ml). The combined extracts were dried (Na_2SO_4), evaporated and distilled to give title compound (9.2 g; 67%), bp 8° , 0.14 mm, n_D^{20} 1.4431, $\nu_{\text{max}}^{\text{film}}$ 2986, 2950, 2251, 2214 and 1463 cm^{-1} ; nmr δ 0.99 (6H, t, $J = 5 \text{ Hz}$, $\text{CH}_3\text{-CH}_2$), 1.37-2.20 (5H, m, protons on secondary and tertiary carbons), and 3.9 ppm (1H, d, $J = 5 \text{ Hz}$ -HC-(CN)_2).

Anal. Calc'd for $\text{C}_8\text{H}_{12}\text{N}_2$: C, 70.56; H, 8.87; N, 20.57. Found: C, 70.61; H, 9.00; N, 20.64.

¹ The amalgam was prepared according to a method described by Fieser and Fieser (108).

2-Allyl-2-(1-ethylpropyl)malononitrile 43

A solution of sodium isopropoxide was prepared by dissolving sodium (0.23 g; 0.01 mole) in isopropanol (25 ml) at 50°. The solution was then cooled in an ice-water bath and 2-(1-ethylpropyl)malononitrile 45 (1.36 g; 0.01 mole) added dropwise to give a clear yellow solution of the malononitrile anion. Allyl chloride (0.76 g; 0.01 mole) was added in one portion and the mixture stirred at room temperature for one day, then refluxed for one hour. Water (100 ml) was added, and the solution extracted with benzene (3 x 30 ml). The extracts were combined, washed with water (2 x 25 ml), dried (Na_2SO_4) and evaporated giving a yellow liquid (1.7 g). Preparative layer chromatography on silica gel using 25% ether in benzene gave the pure compound (0.8 g; 45%), $R_f = 0.86$, $n_D^{20} = 1.4512$, $\nu_{\text{max}}^{\text{film}} 3000, 2970, 2255, 1470, 975 \text{ and } 910 \text{ cm}^{-1}$; pmr δ 1.06 (6H, t, $J = 5 \text{ Hz } -\text{CH}_3$), 1.64 (5H, m, $-\text{CH}-(\text{CH}_2)_2-$), 2.65 (2H, d, $J = 6 \text{ Hz}$, allylic H), and 5.06-6.32 ppm (3H, m, olefinic H).

Anal. Calc'd for $\text{C}_{11}\text{H}_{16}\text{N}_2$: C, 74.95; H, 9.16; N, 15.83. Found: C, 74.89; H, 9.20; N, 15.07. Molecular weight (High Resolution mass spectrometry). Found: 176.1313. Calc'd: 176.13134.

2-(1-Ethylpropyl)-2-(3-p-methoxyphenylallyl)malononitrile 44

2-(1-Ethylpropyl)malononitrile 45 (1.36 g; 0.01 mole) was added dropwise at ice-bath temperature to a solution of sodium isopropoxide (0.01 mole) in isopropanol (25 ml). p-Methoxycinnamyl chloride (1.82 g; 0.01 mole) was added in one portion and the mixture was stirred at room temperature for one day, then refluxed for one hour. Water (100 ml) was added, and the solution extracted with benzene (3 x 30 ml). The extracts were combined, washed with water

(2 x 25 ml), dried (Na_2SO_4) and evaporated giving a dark yellow viscous liquid (2.8 g). Preparative layer chromatography on silica gel using 90-10 ether/petroleum ether gave the pure compound (0.9 g; R_f 0.80) in 32% yield. Further purification by the same technique using 50 ether-50 pet-ether as developer, gave the pure product (0.6 g; 21.3%). R_f 0.64, $n_D^{20} = 1.5982$; $\nu_{\text{max}}^{\text{film}} = 3000, 2230, 1610, 1510, 1255$ and 1040 cm^{-1} ; pmr δ 1.10 (6H, t, $J = 5 \text{ Hz}$ $-\text{CH}_3$), 1.66 (5H, m, $-\text{CH}-(\text{CH}_2)_2-$), 2.77 (2H, d, $J = 7 \text{ Hz}$, allylic H), 3.72 (3H, s, $-\text{OCH}_3$), 5.88-6.50 (2H, m, olefinic H), and 6.68-7.46 ppm (4H, m, aromatic H).
 Anal. Calc'd for $\text{C}_{18}\text{H}_{22}\text{N}_2\text{O}$: C, 76.59; H, 7.85; N, 9.92. Found: C, 76.61; H, 7.86; N, 9.25. Molecular Weight (High Resolution mass spectrometry). Found: 282.1734. Calc'd: 282.1732.

Kinetics of Rearrangement of 1

Isomerizations of compound 1 were performed in cyclohexene- d_{12} , benzene- d_6 , nitrobenzene, ethanol- d_6 and ethanol- d_6 (80%) - water- d_2 (20%). The solutions were prepared by dissolving approximately 100 mg of sample in 500 mg of solvent in an nmr tube. These samples were then heated in a Haake-E52 Temperature regulator; these were taken out at appropriate intervals (30 or 60 minutes), and the nmr spectrum was immediately recorded on a Varian T-60 spectrometer¹.

The intensity (a) of the doublet at 1.65 ppm (allylic methyl) and the intensity (b) of the singlet at 3.70 ppm (methoxymethyl) were measured. Readings were taken for two half-life periods, and each rate constant was measured at least in duplicate to ensure reproducibility.

¹ A Varian HA-100 spectrometer was used in the case of ethanol-water being the solvent, and the instrument was heated at 75° due to the fact that compound 1 was insoluble in the solvent below 60° .

Logarithms of the ratio of b/a were plotted against time. Data were treated in the same manner as those of compound 24. The rate constants were calculated by a LFIT.TSL least-squares programme on a Perex Sigma 7 computer. Representative data are shown in Table 7, the rate constant found for this particular experiment being 3.0737×10^{-3} (Corr. Coef. .996).

The mean values of the rate constants are reported in Table 3.

Determination of the activation parameters were done using nitrobenzene as solvent; the solutions were heated at 66.8, 75, 85, 93, 100 and 107° in a temperature controlled oil-bath. The solutions were prepared as before and the nmr spectrum was recorded at appropriate time intervals. A Varian HA-100 spectrometer¹ was used and the instrument was locked on the methoxymethyl signal (δ 3.70 ppm). The intensity of the doublet at δ 1.65 ppm (a) (3H of compound 1) and the multiplet at δ 1.10 ppm (b) (3H of compound 1 and 6H of compound 3) were monitored at certain time intervals. The ratio of the initial concentration of 1, to the concentration of unreacted 1 at any given time was equal to $(a + b)/2a$. The logarithm of $(a + b)/2a$ against time was plotted. The first order rate constants were calculated using a LFIT.TSL least squares programme. The representative data are shown on Table 8, the rate constant found for this particular run being $8.888 \times 10^{-4} \text{ min}^{-1}$ (Corr. Coef. .995).

The Arrhenius plot ($\log k/T$ vs $1/T$) was constructed (Figure 1) and the activation parameters were calculated by LFIT.TSL least squares programme. The data are shown in Table 4.

¹ Courtesy of Dr. R. F. Fraser, Ottawa University.

Table 7 : Kinetics of Rearrangement of 1 in Ethanol-d₆^{*}

Time(Minutes)	a ¹	b ²	Log(b/a)
0	41	39	0.02172
21	46	38	0.08297
46	44	34.5	0.1056
61	43	32	0.1283
88	42	31	0.1319
114	42	27.5	0.1839
143	44.5	25	0.2504
169	45	24	0.2730
199	42	20	0.3222
236	42	19	0.3445
276	42	16	0.4191
319	45	16	0.4491
364	38	11	0.5384

^{*} Temperature = 75°C

¹ The intensity of the methoxymethyl peak at δ 3.70 ppm.

² The intensity of the allylic methyl doublet at δ 1.65 ppm.

Table 8 : Kinetics of Rearrangement of 1 in nitrobenzene*

Time(minutes)	a ⁻	b [§]	Log[(a+b)/2a]
0	52	70	0.0693
74	44	70	0.1124
134	39	65	0.1249
245	39	76	0.1686
357	34	82	0.2319
419	35	91	0.2552
541	33	100	0.3043
661	28	102	0.3657
766	29	116	0.3979
846	27	110	0.4043
951	29	134	0.4487
1196	21	118	0.5198

* Temperature = 66.8°C

† The intensity of the doublet at δ 1.65 ppm.§ The intensity of the multiplet at δ 1.20 ppm.

Figure 1 : The Arrhenius Plot ($\log k/T$ vs $1/T$)

Adipoyl Chloride

Adipic acid (36.6 g; 0.2 mole) and thionyl chloride were warmed at 45-50° for four days under the conditions of Raha (109). The distilled yield was 35 g; 97%, bp 82°, 1.6 mm (Lit bp, 130-132°, 18 mm (110) nmr: δ 1.9 (4H, m, protons on carbons 3 and 4), 3.0 (4H, m, protons on carbons 2 and 5).

Adipic Acid Bis(N,N-dimethyl)amide 46

The method of Sunko et al was used (40). A 25% aqueous solution of dimethylamine (100 ml) was cooled and stirred in an ice-bath and adipoyl chloride (18.3 g; 0.1 mole) was added dropwise. The mixture was stirred overnight at room temperature. Removal of water under vacuum gave a yellowish-white residue which was crystallized from ether giving 10 g (52% yield) of the diamide as white platelets¹; m.p. 82-83° (Lit m.p. 82° (40)), $\nu_{\text{max}}^{\text{mull}}$ 2900, 1675, 1600, 1410 and 1290 cm⁻¹, nmr: δ 1.68 (4H, m, protons in carbons 3 and 4), 2.32 (4H, m, protons on carbons 2 and 5) and 2.9 ppm (12H, d (restricted rotation due to resonance around the C-N bond gives rise to two singlets for the methyl groups), J = 4.5 Hz, -N(CH₃)₂).

1,6-Bisdimethylaminohexane-1,1,6,6-d₄

The method of Micovic and Mihailovic was used (111) LiAlD₄ (6 g; 0.143 mole) was suspended with ether (300 ml) in a 500 ml flask which was attached to a Soxhlet extractor. Adipic acid bis(N,N-dimethyl) amide (18 g; 0.09 mole) was wrapped with filter paper, and extracted

¹ This compound was synthesized several times. Once the crystals obtained were colorless needles with identical spectra, and the melting point was 34°. When the crystals with high melting point were dissolved in acetone and left at room temperature, the crystals obtained melted at 34°. Thus, it was concluded that these two compounds were different crystalline forms of one compound. It was outside the scope of our work to investigate further in this area.

for 60 hours. The mixture was hydrolyzed by the careful addition of water (24 ml) and 15% NaOH (6 ml). The ether layer was separated and the aqueous layer was extracted with ether (3 x 50 ml). The combined extracts were dried over anhydrous Na_2SO_4 and ether was evaporated. The oily residue was dissolved in 10% hydrochloric acid and was washed with ether (3 x 75 ml). The solution then was made basic with 10% sodium hydroxide and the organic layer was extracted with ether (3 x 50 ml), dried over anhydrous Na_2SO_4 , and ether was removed. The amine (6.8 g; 42% yield) was used without further purification. $\nu_{\text{max}}^{\text{film}}$: 3380, 2920, 2875, 2815, 2790, 1470 and 760 cm^{-1} , τ_{max} : δ 1.4 (8H, broad singlet, methylene protons), and 2.29 (12H, s, $-\text{N}-(\text{CH}_3)_3$) ppm.

1,6-Bisdimethylaminohexane oxide-1,1,6,6- d_4

The method of Vogel et al was used (112). 1,6-Bisdimethylaminohexane-1,1,6,6- d_4 (6.8 g; 0.0386 mole) was placed in a flask which was cooled with ice. Thirty percent hydrogen peroxide (40 ml) was added dropwise and the mixture was stirred at room temperature. The end of the reaction was detected by negative phenolphthaleine test. Excess peroxide was destroyed by a catalytic amount of lead oxide. Removal of water gave a white solid residue which was pyrolyzed without purification.

1,5-Hexadiene-1,1,6,6- d_4

The method of Sunko et al was followed (40). 1,6-Bisdimethylaminohexane oxide-1,1,6,6- d_4 was pyrolyzed under vacuum in an oil bath at 170°C . The products were collected in two U-shaped tubes cooled with liquid nitrogen. The organic layer was separated from

water, washed with 5% hydrochloric acid and saturated sodium carbonate solution. Great difficulty was experienced in handling the diene, due to its high volatility. Therefore a sufficient amount was dissolved in CDCl_3 for nmr studies and the rest was kept in ether for further studies. The nmr spectrum had no signals at δ 4.2-4.6, which would be due to four protons at positions 1 and 6; nmr: δ 1.4-1.7 (4H, m, allylic H) and 5-5.5 (2H, m, vinylic H) ppm; m/e 86 (M^+).

Crossover Experiment of 1,5-hexadiene with 1,5-hexadiene-1,1,6,6- d_4

To an ethereal solution of hexadiene-1,1,6,6- d_4 , unlabeled hexadiene was added approximately 10 times in excess. The mixture was kept in a flask cooled with liquid nitrogen. The flask was connected to a U tube which was heated at 347° and filled with glass beads. The other end of the tube was joined to another flask, then to a vacuum line. The system was evacuated and the mixture was transferred to the other flask, simply by removing the liquid nitrogen and placing it around the empty flask. This way the solution passed through the heated tube, and the procedure was repeated 24 times. Mass spectral analysis of 1,5-hexadiene, 1,5-hexadiene-1,1,6,6- d_4 , and the mixture before and after heating were performed.

Pyrolysis of 2-methyl-1,5-hexadiene

2-Methyl-1,5-hexadiene was heated in the same apparatus as in the case of 1,5-hexadiene. The experiments were done at 250, 300, 350, 400, 460° . The final product at the end of each experiment was subjected to glc separation and the mass spectral analysis were performed.

Figure 2 : Diagram of the pyrolysis apparatus

Ethylcinnamate

A mixture of cinnamic acid (14.8 g; 0.1 mole) and H_2SO_4 (25 ml) in ethanol (250 ml) was refluxed overnight. The mixture was then poured into water (150 ml) and extracted with ether (3 x 50 ml). The combined extracts were washed with 10% Na_2CO_3 solution (3 x 50 ml), dried (Na_2SO_4), and evaporated. The residue was distilled at $90-95^\circ$, 0.5 mm (110) bp $158.5-159^\circ$, (24 mm) to yield the ester (14.9 g; 85%). The nmr spectrum showed signals at δ 1.34 (3H, t, $J = 7.5$ Hz, CH_2-CH_3), 4.22 (2H, q, $J = 7.5$ Hz, CH_2-CH_3), 6.28 (1H, s, olefinic H), 6.53 (1H, s, olefinic H) and 7.32-7.85 ppm (5H, m, aromatic H), $\nu_{\text{max}}^{\text{film}} = 3000\text{w}, 1710\text{s}, 1640\text{s}, 1310\text{s}, 1205\text{s}, 1175\text{s}, 985\text{m}, 772\text{s cm}^{-1}$.

Methyl p-methoxycinnamate

p-Methoxycinnamic acid (17.82 g; 0.1 mole) and H_2SO_4 (25 ml) were reacted in methanol (250 ml) as described above. The product was crystallized from hot water to give the ester (15.1 g; 78%), mp. 90.5° (Lit mp 90° (110)); δ 3.80 (3H, s, ester CH_3), 3.83 (3H, s, $\text{Ph}-\text{OCH}_3$), 6.18 (1H, s, olefinic H), 6.50 (1H, s, olefinic H) 6.50-7.74 (4H, m, aromatic H).

Ethyl p-methoxycinnamate

p-Methoxycinnamic acid (17.8 g; 0.1 mole) and H_2SO_4 (25 ml) were treated as described above. The product was crystallized from ethanol to give the ester (16 g; 82%) m.p. 50° (Lit m.p. $49-50^\circ$ (110)), δ 1.34 (3H, t, $J = 7.5$ Hz $-\text{O}-\text{CH}_2-\text{CH}_3$), 3.83 (3H, s, $\text{Ar}-\text{O}-\text{CH}_3$), 4.22 (2H, q, $J = 7.5$ Hz $-\text{O}-\text{CH}_2-\text{CH}_3$), 6.21 (1H, s, olefinic H), 6.50 (1H, s, olefinic H), and 6.51-7.74 (4H, m, aromatic H) ppm, $\nu_{\text{max}}^{\text{film}} = 3000, 1700, 1250, 980$ and 825 cm^{-1} .

Ethyl *o*-Methoxycinnamate

o-Methoxycinnamic acid (1.78 g; 0.01 mole) was treated with H_2SO_4 (2.5 ml) in ethanol (50 ml) as described above. The mixture was distilled at 102-105°, 0.7 mm (Lit bp 150°, 8 mm)(110). The ester (1.6 g, 79%) gave the following nmr spectrum: δ 1.34 (3H, t, $J = 7.5$ Hz -O-CH₂-CH₃), 3.83 (3H, s, Ph-O-CH₃), 4.22 (2H, q, $J = 7.5$ Hz -O-CH₂-CH₃), 6.31 (1H, s, olefinic H), 6.55 (1H, s, olefinic H), 6.72-7.59 (4H, m, aromatic H).

Ethyl *p*-Aminocinnamate

p-Aminocinnamic acid hydrochloride (1.99 g; 0.01 mole) and H_2SO_4 (2.5 ml) was refluxed overnight in ethanol (50 ml). The solution was made basic with 10% NaOH and extracted with ether (3 x 50 ml). The extracts were combined, dried (Na_2SO_4), and evaporated. The residue was crystallized from EtOH to give the ester (1.4 g, 73% yield) m.p. 68 (Lit m.p. (110) 68-69°). δ 1.34 (3H, t, $J = 7.5$ Hz -O-CH₂-CH₃), 3.80 (2H, s, -NH₂), 4.22 (2H, q, $J = 7.5$ Hz -O-CH₂-CH₃), 6.08 (1H, s, olefinic H), 6.42 (1H, s, olefinic H) and 6.50-7.48 ppm (4H, m, aromatic H). $\nu_{\text{max}}^{\text{mull}}$ 3395w, 3310w, 2890s, 1685s, 975s, 822s and 715m cm^{-1} .

p-Methoxycinnamyl alcohol¹

Methyl *p*-methoxycinnamate (8 g; 0.0417 mole) and LiAlH_4 (1.2 g; 0.0316 mole) were heated under reflux in ether (50 ml) for one hour. The mixture was hydrolyzed with water (10 ml) and 10% aqueous tartaric acid solution (50 ml) was added. The organic layer was separated and the aqueous layer was extracted with ether (3 x 50 ml). The combined ethereal extracts were dried (Na_2SO_4) and evaporated. The solid residue was crystallized from an EtOH-H₂O mixture and the

alcohol (5.7 g) was obtained in 83% yield, m.p. 78° (Lit m.p. $76-79^{\circ}$ (96)); δ 3.80 (3H, s, $-\text{OCH}_3$), 4.25 (2H, d, $J = 5$ Hz, allylic CH_2), 5.98-6.58 (2H, d, olefinic H), 6.7-7.5 (4H, m, aromatic H), $\nu_{\text{max}}^{\text{film}}$ 3240, 2900, 2820, 1600, 1020 and 960 cm^{-1} .

Active Manganese Dioxide

The oxide was prepared according to the method of Sondheimer (113,114). A 10% solution of MnSO_4 (500 ml) was heated to 90° and stirred. A concentrated aqueous solution of KMnO_4 was added slowly until a slight excess was present. The mixture was further stirred at 90° for 15 minutes and filtered. The solid was washed with hot water (50 ml), MeOH (50 ml) and ether (50 ml), and dried at $120-130^{\circ}$ to constant weight.

p-Methoxycinnamaldehyde

p-Methoxycinnamyl alcohol (2 g; 0.012 mole) was treated with freshly prepared active manganese dioxide (16 g) in tetrachloroethylene (200 ml) according to the method of Marshall and Whiting (96). The product was crystallized from petroleum ether (bp $30-60^{\circ}$) to give the aldehyde (0.95 g; 49%), m.p. $58-59^{\circ}$ (Lit m.p. 59° (96)); δ 3.82 (3H, s, $-\text{OCH}_3$), 6.27-6.70 (2H, m, olefinic H), 6.8-7.5 (4H, m, aromatic H), 9.72 (1H, d, $J = 7.5$ Hz $-\text{C}=\text{O}$).

Cinnamyl alcohol or reduction of ethylcinnamate with $\text{AlCl}_3/\text{LiAlH}_4$

LiAlH_4 (2.28 g; 0.06 mole) was mixed with anhydrous ether (100 ml) in a three-neck round bottom flask and cooled in an ice-bath. AlCl_3 (2.67 g; 0.02 mole) dissolved in ether (100 ml) was mixed with stirring. When the slurry became white (due to LiCl), a solution of ethylcinnamate (2.52 g, 0.02 mole) in ether (75 ml) was added dropwise and the mixture was further stirred for 30 minutes

at room temperature. The mixture was hydrolyzed with 20% H_2SO_4 (20 ml) and was extracted with ether (3 x 50 ml). The combined extracts were dried over anhydrous Na_2SO_4 and evaporated. The product was distilled at 256-257° (Lit bp 257°) to yield cinnamyl alcohol (1.9 g; 72%).

Reduction of Ethyl p-methoxycinnamate with $\text{LiAlH}_4/\text{AlCl}_3$

LiAlH_4 (2.28 g; 0.06 mole), AlCl_3 (2.67 g; 0.02 mole) and ethyl p-methoxycinnamate (4.12 g; 0.02 mole) were reacted as described above. The nmr spectrum of the product (2.95 g) showed the presence of anethole and p-allyl anisole, and the mixture could not be separated by means of column and thin-layer chromatography. Therefore preparative glc purification using 5% QF-1 on chromosorb G was performed at 130°. A quantitative yield of the two compounds, anethole (retention time 4.5 minutes) and p-allyl anisole (retention time 2.9 minutes) was obtained in a 2:1 ratio. The identity of the

two compounds was established by comparison of spectral properties with those of authentic samples (anethole: $\nu_{\text{max}}^{\text{film}}$ 1605, 1500, 1220 and 968 cm^{-1} ; $\lambda_{\text{max}}^{\text{EtOH}}$ 259 nm (log ϵ 4.29) (lit. $\lambda_{\text{max}}^{\text{EtOH}}$ 258 nm (log ϵ 4.31)(117), and $\lambda_{\text{max}}^{\text{EtOH}}$ 260 nm (log ϵ 4.26)(118); δ 1.78 (3H, d, $J=5\text{Hz}$, CH_3), 3.67 (3H, s, OCH_3), 5.7-6.3 (2H, m, vinyl H), 6.6-7.4 ppm (4H, q, aromatic H); p-allylanisole: $\nu_{\text{max}}^{\text{film}}$ 1605, 1500, 1220 and 915 cm^{-1} ; $\lambda_{\text{max}}^{\text{EtOH}}$ 229 (log ϵ 4.26), 281 (log ϵ 3.60) and 287 nm (log ϵ 3.52)(Lit λ_{max} 279 nm (log ϵ 3.60)⁶); δ 3.25 (2H, d, $J = 6\text{ Hz}$, Ar-CH_2), 3.67 (3H, s, OCH_3), 4.7-5.2 (2H, m) and 5.6-6.2 (1H, m) (vinyl H), and 6.6-7.2 ppm (4H, q, aromatic H)).

Reduction of p-methoxycinnamyl alcohol

The alcohol (0.82 g; 0.005 mole), LiAlH_4 (0.57 g; 0.015 mole) and AlCl_3 (0.67 g; 0.005 mole) were treated as described above.

Glc analysis of the product (0.75 g) showed the presence of anethole (64%) and p-allyl anisole (36%), and the reaction was quantitative.

Reduction of p-methoxycinnamaldehyde

The aldehyde (0.81 g; 0.005 mole), LiAlH_4 (0.57 g; 0.015 mole) and AlCl_3 (0.67 g; 0.005 mole) were treated as described above to give anethole (67%) and p-allyl anisole (33%).

Reduction of Ethyl o-methoxycinnamate

Ethyl o-methoxycinnamate (10.3 g; 0.05 mole) was treated with LiAlH_4 (5.7 g; 0.15 mole), and AlCl_3 (6.7 g; 0.05 mole) in anhydrous ether (250 ml). The product obtained following the usual work up, was separated by glc at 130° and contained 56% o-anethole (retention time 3.2 minutes) and 46% o-estragole (retention time 6.5 minutes).

They had the following spectral data: (o-anethole: $\lambda_{\text{max}}^{\text{EtOH}}$ 250 nm (log ϵ 4.03) (Lit $\lambda_{\text{max}}^{\text{EtOH}}$ 248 nm (log ϵ 4.03)⁶; δ 1.90 (3H, d, J =

6 Hz, CH_3), 3.42 (3H, s, OCH_3), 6.0-6.5 (2H, m, vinyl H), and

6.6-7.5 ppm (4H, m, aromatic H), 56%. o-Estragole: $\lambda_{\text{max}}^{\text{EtOH}}$ 272 nm (log ϵ 3.36) (Lit $\lambda_{\text{max}}^{\text{EtOH}}$ 273 nm (log ϵ 3.38)⁶; δ 3.38 (2H, d, J =

7 Hz, Ar-CH_2), 3.80 (3H, s, OCH_3), 4.8-5.2 (2H, m) and 5.6-6.3

(1H, m) (vinyl H), and 6.8-7.3 ppm (4H, m, aromatic H) 44%).

Reduction of Ethyl p-aminocinnamate

Ethyl p-aminocinnamate (4.7 g; 0.025 mole), LiAlH_4 (2.85 g; 0.075 mole) and AlCl_3 (3.4 g; 0.025 mole) were treated in ether (125 ml) in the same manner as before. Following the hydrolysis the mixture was made basic with 20% NaOH solution and extracted with ether (3 x 50 ml). The combined extracts were dried (Na_2SO_4) and evaporated, and the waxy looking product (2.24 g) was purified by preparative layer chromatography on silica gel using benzene as the developing solvent. The MeOH extraction of one of the bands

($R_f = 0.39$) gave a yellow oil (0.6 g; 18%) which was separated by means of preparative glc using a QF-1 column at 130° . The mixture consisted of 24% *p*-allylaniline (retention time 8 minutes) and 76% *p*-propenylaniline (retention time 17 minutes). These compounds had the following data: *p*-allylaniline: n_D^{20} 1.5567 (Lit (115) $n_D^{20} = 1.5668$), δ 3.12 (2H, d, $J = 6$ Hz, benzylic and allylic CH_2), 4.38 (2H, broad s, -NH_2), 4.75-5.21 (3H, m, olefinic H) and 6.40-7.28 (4H, m, aromatic H). *p*-Propenylaniline δ 1.80 (3H, d, $J = 6$ Hz, allylic CH_3), 4.59 (2H, broad s, -NH_2), 6.00-6.35 (2H, m, olefinic H) and 6.48-7.32 (4H, m, aromatic H); m/e 133 (M^+). Molecular weight calc'd for $\text{C}_9\text{H}_{11}\text{N}$, 133.0890. Found, 133.0884.

REFERENCES

1. A. C. Cope and E. M. Hardy, J. Amer. Chem. Soc., 62, 441 (1940).
2. S. J. Rhoads, Molecular Rearrangements, P. de Mayo, Editor, Interscience Publishers Inc., New York, 1963, p. 684-696.
3. R. B. Woodward and R. Hoffmann, J. Amer. Chem. Soc., 87, 2511 (1965).
4. A. C. Cope, K. E. Hoyle and D. Heyl, J. Amer. Chem. Soc., 63, 1843 (1941).
5. E. G. Foster, A. C. Cope and F. Daniels, J. Amer. Chem. Soc., 69, 1893 (1947).
6. A. C. Cope, C. M. Hoffmann and E. M. Hardy, J. Amer. Chem. Soc., 63, 1852 (1941).
7. C. Walling and M. Naiman, J. Amer. Chem. Soc., 84, 2628 (1962).
8. W. von E. Doering and W. R. Roth, Tetrahedron, 18, 67 (1962).
9. M. J. Goldstein and M. S. Benzon, J. Amer. Chem. Soc., 94, 7147 (1972).
10. M. J. Goldstein and M. S. Benzon, J. Amer. Chem. Soc., 94, 7149 (1972).
11. W. von E. Doering, V. G. Toscano and G. H. Beasley, Tetrahedron, 27, 5299 (1971).
12. E. Vogel, Justus Liebigs Ann. Chem., 615, 1 (1958).
13. E. Vogel, Angew. Chem., Int. Ed. Engl. 2, 1 (1963).
14. G. S. Hammond and C. D. DeBoer, J. Amer. Chem. Soc., 86, 899 (1964).
15. W. von E. Doering and W. R. Roth, Angew. Chem, Int. Ed. Engl. 2, 115 (1963).
16. H. P. Koch, J. Chem. Soc., 1111 (1948).

17. W. D. Huntsman, J. Amer. Chem. Soc., 82, 6389 (1960).
18. H. Gibson and R. Pettit, J. Amer. Chem. Soc., 87, 2620 (1965).
19. J. R. McNesby and A. S. Gordon, J. Amer. Chem. Soc., 79, 4593 (1957).
20. W. von E. Doering and W. R. Roth, Tetrahedron 19, 715 (1963).
21. E. Brown, P. Leriverend and J. M. Conia, Tetrahedron Letters, 6115 (1966).
22. J. A. Berson and E. J. Walsh, J. Amer. Chem. Soc., 90, 4732 (1968).
23. R. W. Thies, J. Amer. Chem. Soc., 94, 7074 (1972).
24. N. Anand, J. S. Bindra and S. Ranganathan, Art In Organic Synthesis, Holden-Day, Inc., San Francisco, (1970) p. 377.
25. J. A. Berson and M. Jones, J. Amer. Chem. Soc., 86, 5019 (1964).
26. ~~J. A. Berson and M. Jones, J. Amer. Chem. Soc., 86, 5017 (1964).~~
27. J. A. Berson and E. J. Walsh J. Amer. Chem. Soc., 90, 4729 (1968).
28. J. A. Berson and E. J. Walsh, J. Amer. Chem. Soc., 90, 4732 (1968).
29. J. A. Berson and E. J. Walsh, J. Amer. Chem. Soc., 90, 4730 (1968).
30. R. B. Woodward and R. H. Hoffmann, The Conservation of Orbital Symmetry, Academic Press (1971) p. 120.
31. J. A. Berson, P. B. Dervan, J. Amer. Chem. Soc., 94, 7597 (1972).
32. J. A. Berson, P. B. Dervan and J. A. Jenkins, J. Amer. Chem. Soc., 94, 7598 (1972).
33. J. A. Berson and L. Salem, J. Amer. Chem. Soc., 94, 8917 (1972).
34. J. A. Berson and P. B. Dervan, J. Amer. Chem. Soc., 95, 267 (1973).

35. A. C. Cope, and K. E. Hoyle, J. Amer. Chem. Soc., 63, 733 (1941).
36. D. C. Wigfield and S. Feiner Canad. J. Chem., 48, 855 (1970).
37. W. H. White and W. K. Fife, J. Amer. Chem. Soc., 83, 3846 (1961).
38. J. A. Berson and G. L. Nelson, J. Amer. Chem. Soc., 89, 5503 (1967).
39. K. Humski, T. Strelkov, S. Borcic, and D. E. Sunko, Chem. Commun. 693 (1969).
40. K. Humski, R. Malojcic, S. Borcic, and D. E. Sunko, J. Amer. Chem. Soc., 92, 6534 (1970).
41. H. R. Ward, R. G. Lawler and H. Y. Loken, J. Amer. Chem. Soc., 90, 7359 (1968).
42. H. R. Ward, R. G. Lawler and R. A. Cooper, J. Amer. Chem. Soc., 91, 746 (1969).
43. P. B. D. de la Mare and C. A. Vernon, J. Chem. Soc., 3331 (1952).
44. H. C. Brown and H. M. Bell, J. Org. Chem. 27, 1928 (1962).
45. E. S. Gould, Mechanism and Structure in Organic Chemistry, Holt, Reinhart and Winston, Inc., New York, p.580.
46. J. C. Bardhan and D. N. Mukherji, J. Chem. Soc., 4629 (1956).
47. A. Streitweiser, Jr., Chem. Revs. 56, 571 (1956).
48. R. H. DeWolfe and W. G. Young, Chem. Revs. 56, 765 (1956).
49. J. Hine, Physical Organic Chemistry (2nd Edition) p. 175, McGraw-Hill, New York (1962).
50. D. A. Brown and R. F. Hudson, J. Chem. Soc., 3352 (1953).
51. D. C. Wigfield and B. Lem, Tetrahedron, 31, 9 (1975).
52. R. B. Bates and D. M. Gale J. Amer. Chem. Soc., 82, 5749 (1960).
53. K. H. Dahm, B. M. Trost, and H. Roller, J. Amer. Chem. Soc., 89, 5292 (1967).

54. S. F. Brady, H. A. Ilton, and W. S. Johnson, J. Amer. Chem. Soc., 90, 2882 (1968).
55. A. F. Thomas, Chem. Commun, 1657 (1968).
56. W. S. Johnson, T. Li, D. J. Faulkner, and S. F. Campbell, J. Amer. Chem. Soc., 90, 6225 (1968).
57. R. Zurfluh, E. N. Wall, J. B. Siddall, and J. A. Edwards, J. Amer. Chem. Soc., 90, 6224 (1968).
58. E. J. Corey, J. A. Katzenellenbogen, J. Amer. Chem. Soc., 91, 1851 (1969).
59. W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T. Li, D. J. Faulkner, and M. R. Petersen, J. Amer. Chem. Soc., 92, 741 (1970).
60. F. D. Hughes and C. K. Ingold, J. Chem. Soc., 244, (1935).
61. F. S. Prout, J. Org. Chem., 18, 928 (1953).
62. R. S. Wair and J. B. Hyne, Canad. J. Chem., 43, 772 (1965).
63. J. K. Williams, J. Org. Chem., 28, 1054 (1963).
64. J. W. ApSimon, J. W. Hooper and B. A. Laishes, Canad. J. Chem., 48, 3064 (1970).
65. M. R. S. Wair and J. B. Hyne, Canad. J. Chem., 42, 1440 (1964).
66. Farbenfabriken Bayer Akt. Ges. Brit. Patent, No. 812,240 (April 22nd, 1959).
67. G. Kolb (to Akfa Akt. Ges.), U. S. Patent, No. 2,971,977 Feb. 14th, 1961.
68. H. Hart and F. Freeman, Chem. Ind, (London), 333 (1963).
69. J. J. Krajewski and J. W. Moyer, Canad. J. Chem., 52, 3626 (1974).
70. J. E. Blackwood, C. L. Gladys, K. L. Loering, A. E. Petrarca, and J. E. Rush, J. Amer. Chem. Soc., 90, 509 (1968).

71. See reference 4, Footnote 6.
72. J. B. Stothers, Carbon-13 NMR Spectroscopy, Academic Press Inc., New York. p. 80-82 1972.
73. D. E. Dorman, M. Jautelat and J. D. Roberts, J. Org. Chem., 36, 2757 (1971).
74. H. Wislicenus and L. Kaufmann, Chem. Ber., 28, 1323 (1895).
75. See reference 72, p.58.
76. See Reference 72, p. 197
77. K. S. Dharmi and J. B. Stothers, Canad. J. Chem., 43, 510 (1965).
78. See Reference 72, p. 72.
79. R. Huisgen and P. Otto, J. Amer. Chem. Soc., 94, 3907 (1972).
80. J. E. Leffler and E. Grunwald, Rates and Equilibria of Organic Reactions, Wiley New York, 1963, p.156-159 and 238-241.
81. C. Reichardt, Angew. Chem., Int. ed. Eng. 29 (1965).
82. D. M. Golden, N. A. Gac and S. W. Benson, J. Amer. Chem. Soc., 91, 2136 (1969).
83. K. J. Laidler, Theories of Chemical Reactions Rates, McGraw-Hill Book Company, New York 1969, p. 76-79.
84. M. J. Jorgenson, Tetrahedron Letters, 559 (1962).
85. E. W. Collington and A. I. Meyers, J. Org. Chem., 36, 3044 (1971).
86. J. B. Hendrickson, D. J. Cram and G. S. Hammon, Organic Chemistry McGraw-Hill Book Company Inc., New York, 3rd Edition , 1970, p. 74.
87. P. N. Rylander, Catalytic Hydrogenation Over Platinum Metals, Academic Press, New York, 1967, p.230, 320, 476.
88. For Another Example, see H. O. House, Modern Synthetic Reactions,

- W.A. Benjamin, Inc., Menlo Park, California, 1972, p. 84.
89. W. J. Gensler, J. J. Langone, and M. B. Floyd, J. Amer. Chem. Soc., 93, 3823 (1971).
 90. J. H. Brewster, S. F. Osman, H. O. Bayer, and H. B. Hopps, J. Org. Chem., 29, 121 (1964).
 91. S. B. Nerali and K. K. Chakravarti, Tetrahedron Letters, 2447 (1967).
 92. B. R. Brown and A. M. S. White, J. Chem. Soc., 3755 (1957).
 93. J. A. Parry and K. D. Warren, J. Chem. Soc., 4049 (1965).
 94. K. Bowden and M. Hardy, Tetrahedron, 22, 1169 (1966).
 95. A. F. Cockerill and M. Rackham, J. Chem. Soc., Perkin II, 2076 (1972).
 96. D. Marshall and M. C. Whiting, J. Chem. Soc., 4082 (1956).
 97. U. E. Diner, H. A. Davis, and R. K. Brown, Canad. J. Chem., 45, 207 (1967).
 98. R. L. Augustine, Reduction Techniques and Applications in Organic Chemistry, Marcel Dekker, Inc., New York 1968, p. 58.
 99. M. J. S. Dewar and L. E. Wade, J. Amer. Chem. Soc., 95, 290 (1973).
 100. R. D. Schuetz and F. W. Millard, J. Org. Chem., 24, 297 (1959).
 101. S. H. Sharman, F. F. Caserio, R. F. Nystrom, J. C. Leak, and W. G. Young, J. Amer. Chem. Soc., 80, 5965 (1958).
 102. G. Gomori, Methods in Enzymology Vol. 1, pp. 138-144. Academic Press, New York (1955).
 103. E. N. Marvell, D. Sturmer and C. Rowell, Tetrahedron, 22, 861 (1966).
 104. S. Winstein, E. Grunwald and L. L. Ingraham, J. Amer. Chem. Soc., 70, 821 (1948).

105. R. Heck and S. Winstein, J. Amer. Chem. Soc., 79, 3105 (1957).
106. M. Ohno and M. Okamoto, Tetrahedron Letters, 2423 (1964).
107. H. Hart and Y. C. Kim, J. Org. Chem., 31, 2784 (1966).
108. L. F. Fieser and M. Fieser, Reagents for Organic Synthesis,
Vol. 1, John Wiley and Sons Inc., New York (1967).
109. C. Raha, Organic Synthesis, Coll. Vol. IV P. 263.
110. Heilbrun, Dictionary of Organic Compounds.
New York, Oxford University Press (1953).
111. V. M. Micovic and M. L. Mihailovic, J. Org. Chem., 18, 1190
(1953).
112. E. Vogel, K. H. Ott, and K. Gajek, Justus Liebigs Ann. Chem.,
644, 172 (1961).
113. O. Mancera, G. Rosenkranz and F. Sondheimer, J. Chem. Soc.,
2189 (1953).
114. F. Sondheimer, O. Mancera, M. Urquiza and G. Rosenkranz, J. Amer.
Chem. Soc., 77, 4145 (1955).
115. C. D. Hund and W. W. Jenkins, J. Org. Chem., 22, 1418 (1957).
116. G. H. Stempel Jr., R. P. Cross, and R. P. Mariella, J. Amer. Chem.
Soc., 72, 2299 (1950).
117. J. W. Campbell, S. Linden, S. Godshalk, and W. G. Young, J. Amer.
Chem. Soc., 69, 880 (1947).
118. E. A. Braude, J. Chem. Soc., 1902 (1949).
119. M.J.S. Dewar and L.E. Wade, J. Amer. Chem. Soc., 95, 290 (1973).

TABLE OF STRUCTURES

35

36

37

38

39

40

41

42

43

44

45

46

47

48

49

50

51

52

END

270776

FIN