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E1cb Reactions: Stereochemistry And The Counterion(1)

David James Shearing

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ElcB REACTIONS : STEREOCHEMISTRY AND THE COUNTERION(1)

by
David James Shearing

Department of Chemistry

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

Faculty of Graduate Studies
The University of Western Ontario
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ABSTRACT

The stereochemistry of the alkoxide-catalyzed hydrogen-deuterium exchange and elimination components of an E1cB β-elimination reaction has been investigated as a function of cation in tert-butyl alcohol and methanol solvents. The relative rates of cis and trans exchange and cis and trans elimination for β-deuterium labelled 1-methoxyacenaphthene varied by factors of 90 and 75, respectively, when the cation was varied. Exchange and elimination stereochemistry changed from exclusively cis with lithium tert-butoxide to predominantly trans with tetramethylammonium tert-butoxide in the following order : lithium; potassium; cesium; potassium complexed with dicyclohexyl-18-crown-6 ether; tetramethylammonium. Bonding between base, substrate and cation has been proposed to account for the observed trend. Kinetic deuterium isotope effects (α,β and leaving group) have been determined for the preferential cis elimination with potassium tert-butoxide in tert-butyl alcohol.

ACKNOWLEDGEMENT

The author wishes to thank Dr. D. H. Hunter for suggesting the problem, and for his guidance throughout the course of this investigation.

The author also wishes to thank the Department of Chemistry for the facilities afforded and for financial assistance which made the completion of this study possible.

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CHAPTER 1

GENERAL REVIEW

1.1 Introduction

Even though it has been over a century since β-elimination reactions were first studied (2-4), over the last decade considerable research effort has been devoted toward elucidation of β-elimination mechanisms (5,6).

Two features receiving particular attention are stereochemistry and the ElcB mechanism. The observation of many examples of syn elimination has refocused attention on stereochemistry (7). Numerous examples of elimination reactions proceeding through carbanionic intermediates (ElcB) have also appeared (8-10).

Before beginning a detailed examination of the stereochemistry of an ElcB reaction, an attempt will be made to review the ElcB mechanism and β-elimination stereochemistry.

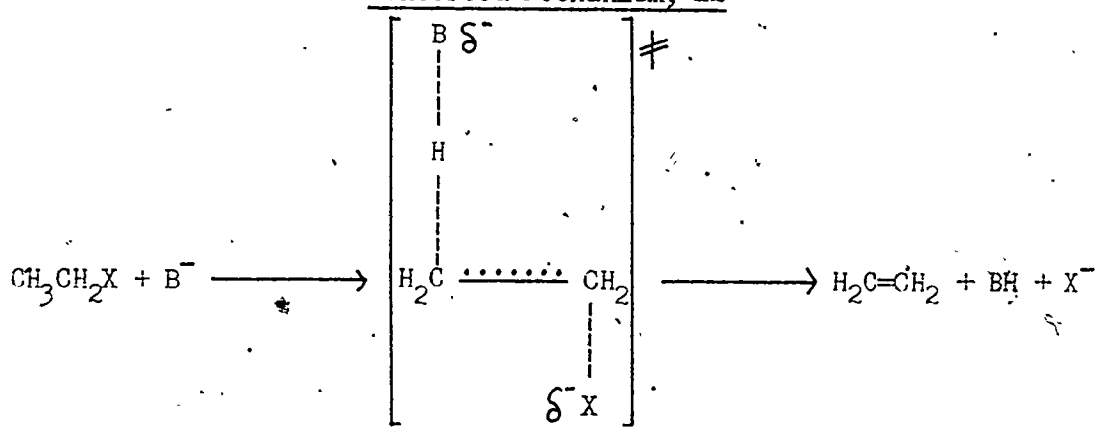
1.2 Primary Elimination Reaction Mechanisms

The basic mechanisms proposed for olefin formation via β-elimination of H-X utilizing an anionic base are illustrated in Figure 1 (11,12).

Carbonium Ion Mechanism, E1

$$CH_3CH_2X \underset{}{\overset{\text{slow}}{\rightleftharpoons}} X^- + CH_3CH_2^+ \xrightarrow{B^-,\text{fast}} H_2C{=}CH_2 + BH$$

Concerted Mechanism, E2

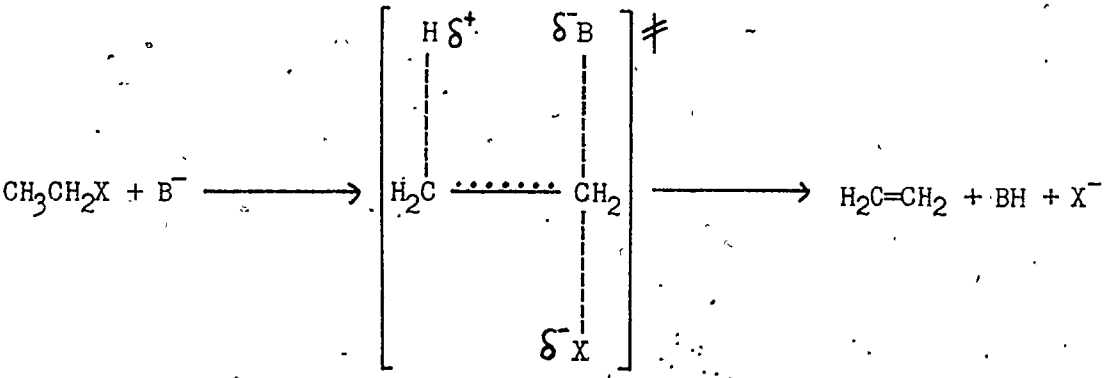


Transition State

Carbanion Mechanism, ElcB

$$CH_3CH_2X + B^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} BH + \bar{C}H_2CH_2X \xrightarrow{k_2} H_2C{=}CH_2 + X^-$$

Weak Base Mechanism, E2C



Loose Transition State

Figure 1 - Basic β-Elimination Mechanisms

The E1 and E1cB mechanisms differ from the bimolecular E2 and E2C (13-16) modes of elimination in that they are stepwise processes, involving the intermediacy of a discrete carbonium ion and carbanion respectively, whereas E2 or E2C eliminations are concerted and pass through single transition states.

For the stepwise E1cB mechanism there are three cases (see Figure 2) :

i) Where $k_1 \ll k_{-1}(BH)$ and the first step is rate determining, being essentially the bimolecular irreversible formation of the carbanion, and the second step is the more rapid ejection of the leaving group from the α-carbon atom. This is referred to as the irreversible $(E1cB)_I$ mechanism.

ii) Where $k_1 \gg k_{-1}(BH)$ and the second step is rate determining, the substrate being effectively converted entirely into the conjugate base. This is referred to as the $(E1)_{anion}$ or "E1cB of the second type" mechanism.

iii) Where $k_1 \ll k_{-1}(BH)$ and the first step is a rapidly-attained equilibrium with carbanion and the second step is the rate-limiting, unimolecular decomposition of the carbanion. The carbanion may be free or loosely solvated, or may form part of an ion pair or be tightly solvated. This is referred to as the reversible or pre-equilibrium $(E1cB)_R$ mechanism.

i) $(ElcB)_I$ MECHANISM

$k_1 << k_{-1}\,[BH] << k_2$

ii) $(El)_{anion}$ MECHANISM

$k_1 >> k_{-1}\,[BH] >> k_2$

iii) $(ElcB)_R$ MECHANISM

$k_{-1}\,[BH] >> k_1 >> k_2$

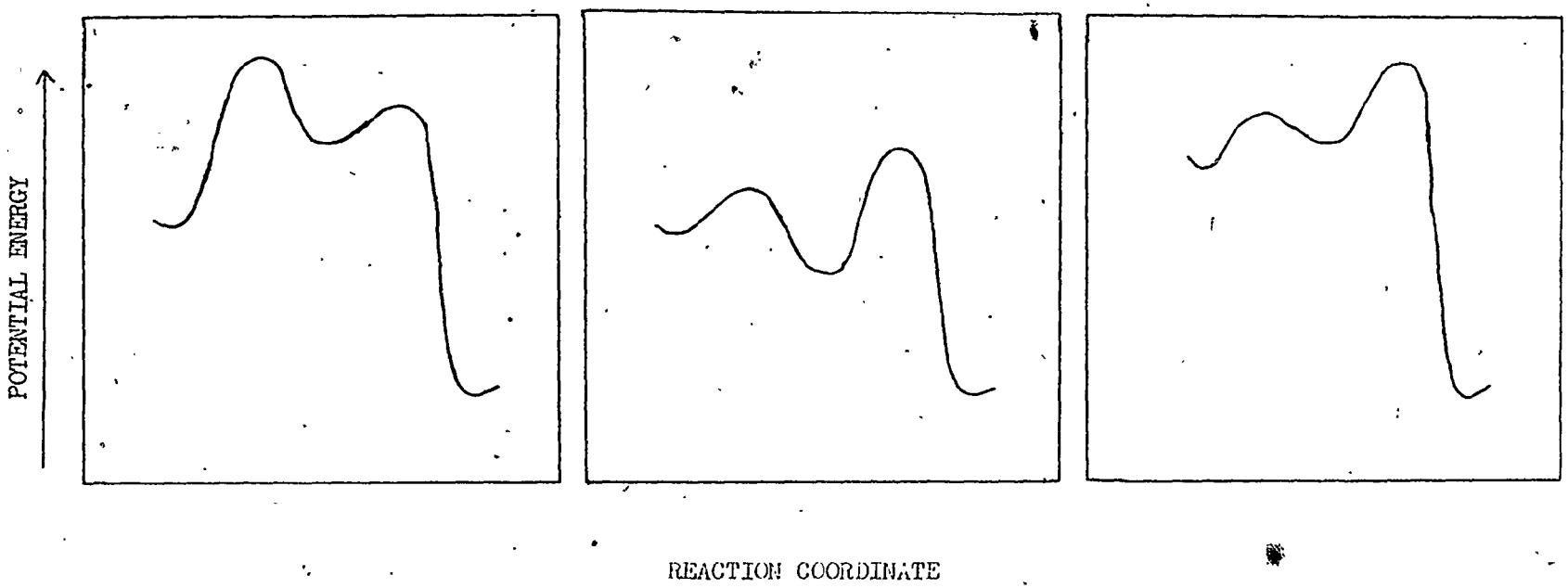


Figure 2 - Energy Diagrams for ElcB Mechanisms

Examples of possible E1cB reactions have become far more abundant since Banthorpe (17) placed them in the category of "less usual mechanisms" in 1963. Sufficiently so, that in 1972, Bordwell (9, 18) suggested that perhaps it was the concerted E2 processes that should be in the "less usual" category. However, Saunders (19) recently has reviewed the means whereby concerted E2 and nonconcerted E1cB mechanisms can be distinguished, defining a range of elimination reactions which are almost certainly concerted E2.

Current views of the E2 mechanism are based upon the "Variable Transition State Theory" of Bunnett (20). Concerted E2 reactions may occur through a spectrum of transition states ranging in structure from paenecarbanion (E1cB-like) to paenecarbonium (E1-like), (see Figure 3), depending on the relative extents to which bonds to the β-hydrogen and to the leaving group are broken. At the borderline between paenecarbanion E2 and E1cb mechanisms, More O'Ferrall (21) has proposed a structural discontinuity between the transition state and the intermediate respectively. However, recent evidence indicates that a structural similarity rather than discontinuity exists even though the structures are not identical (22).

A number of conflicting theories concerning the effect of structural changes in the reactants on the nature of the

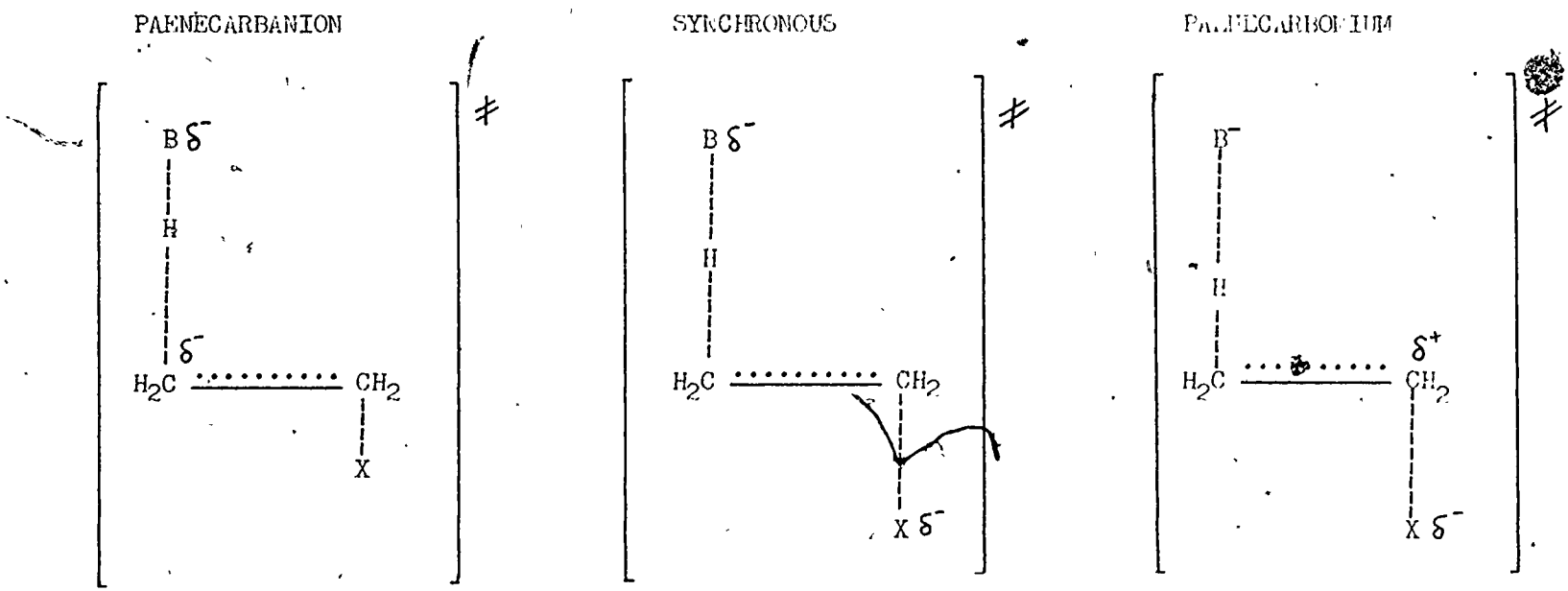


Figure 3 - Spectrum of Transition States for E2 Mechanisms

transition state of E2 elimination reactions have been put forward (20,21,23,24). Thornton (23) has proposed an alternative to the "Variable E2 Transition State Theory" of Bunnett, where substituent effects are considered as linear perturbations of the vibrational potentials for the normal coordinate motions both parallel to and perpendicular to the reaction coordinate. For ElcB-like transition states, the effects on the parallel motion are expected to dominate. This leads to the prediction that a structural change which makes the breaking of the C_β-H bond easier will cause this bond to be broken less in the transition state. The C_α -X bond will then follow along in the direction of the coordinate motion set by the former one, and be shorter as well.

Smith and Bourns (25) have studied the effect of changes in base strength on the structure and energy of the transition state for 2-arylethylammonium substrates. The β-hydrogen kinetic isotope effect indicates that increasing base strength shortens the C_β -H bond, while the nitrogen isotope effect indicates similar shortening of the C_α-X bond, making the transition state more reactant-like. Similar results are observed with changes in α and β-substituents (26 - 28) and in leaving group (29,30), thus confirming Thornton's predictions. However, with better leaving groups the perpendicular mode of

vibration dominates and the central transition state undergoes an increase in C_α-X bond length coupled with a decrease in C_β-H bond length with more electron-withdrawing substituents in the leaving group in accordance with Bunnett's theory. Thus the effect of substituents on the structure and energy of the transition state varies in degree depending upon its location in a More O'Ferrall-type potential energy diagram (30).

1.3 ElcB Mechanisms

The reversible $(ElcB)_R$ mechanism easily can be detected by β-hydrogen exchange of substrates or solvents suitably labelled with isotopic hydrogen (31), (see Figure 4). However, Breslow (32) raised the formally correct point that, depending on the relative energetics, rapid hydrogen exchange may be an irrelevant side reaction to E2 olefin formation (see Figure 5). Hine and his co-workers (33) anticipated this argument by pointing out that if carbanions are formed, they are most likely to be intermediates in the elimination, since transfer of free electron pairs should be more effective in promoting olefin formation than should transfer of a partially free electron pair in an E2 transition state.

The effect of α- and β-substituents and of leaving groups on the elimination rates of an $(ElcB)_R$ reaction has been studied (34), confirming a very high degree of carbanion character compared to similar studies with E2 reactions (see Figure 6).

The irreversible $(ElcB)_I$ mechanism is more difficult to distinguish from the paenecarbanion E2 transition state which is similar

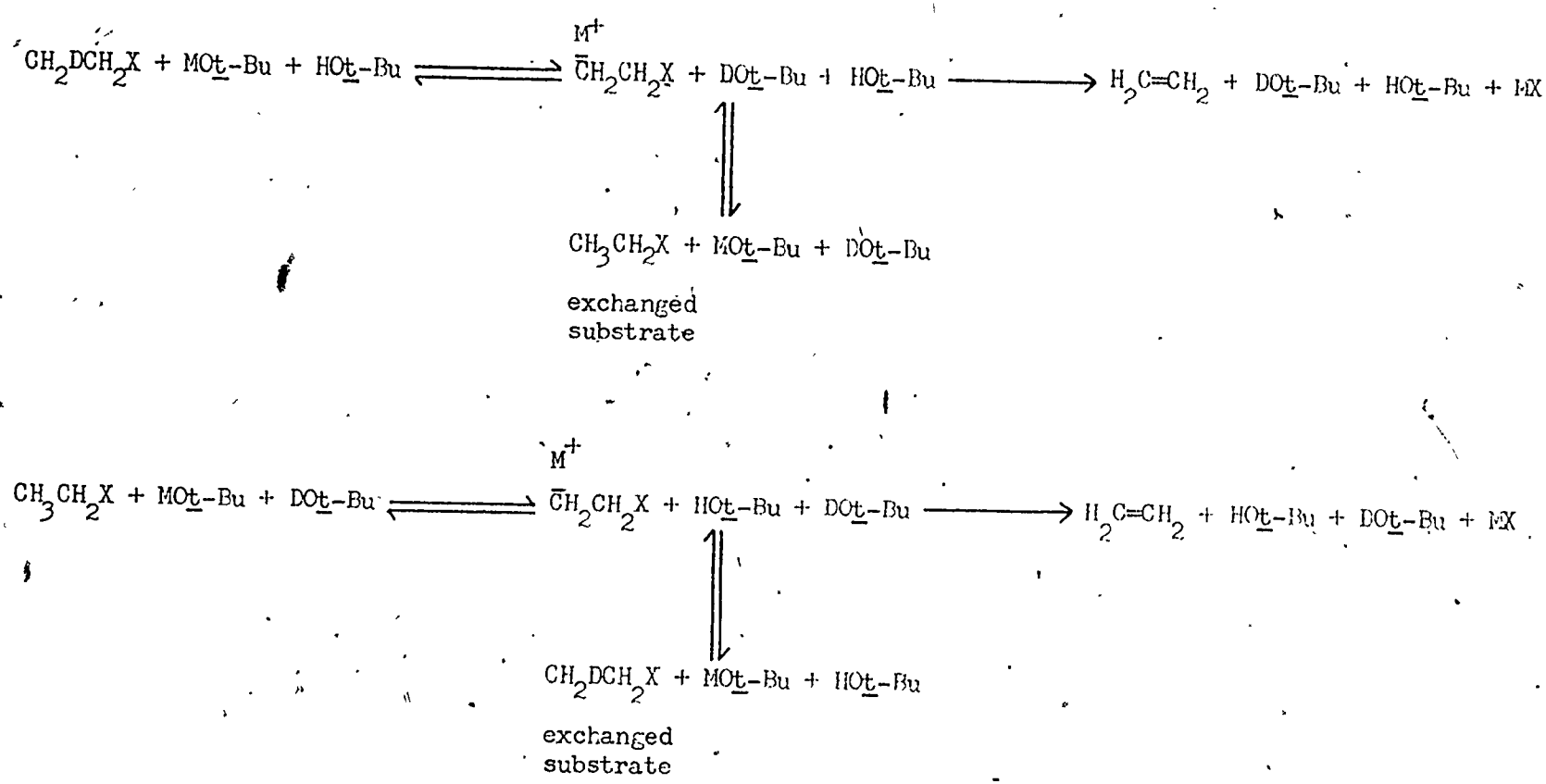


Figure 4 - Detection of $(E1cB)_R$ Mechanism by β-Exchange

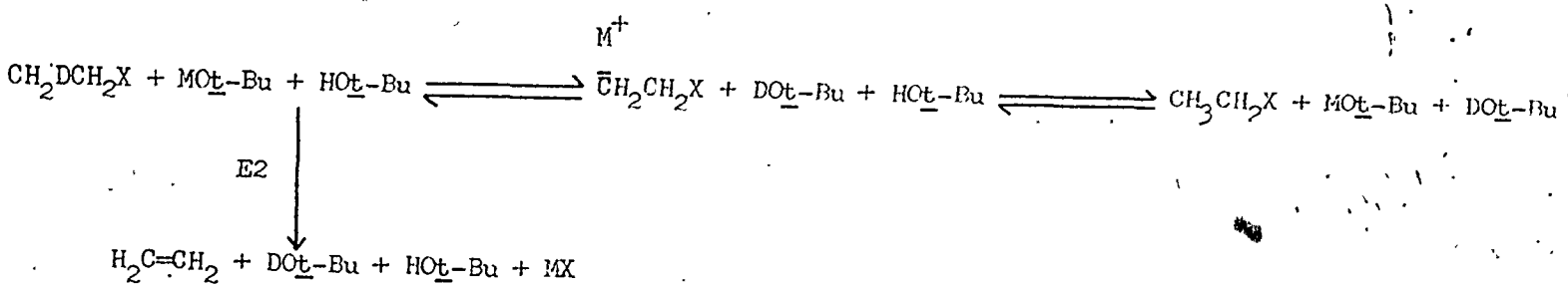
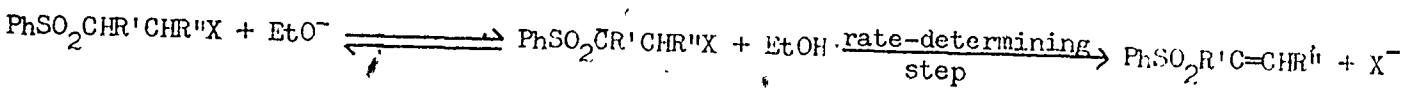


Figure 5 - β-Exchange as an Irrelevant Side Reaction to an E2 Mechanism



Where, R' = H, Me, Ph
R" = H, Me, Ph
X = OPh, SPh

Figure 6 - Substituent Effects on $(E1cB)_R$ Elimination Rates

nature. Assignment of mechanism to the $(ElcB)_I$ class has rested mainly on indirect evidence (35) since leaving group isotope effect determinations have not been carried out yet.

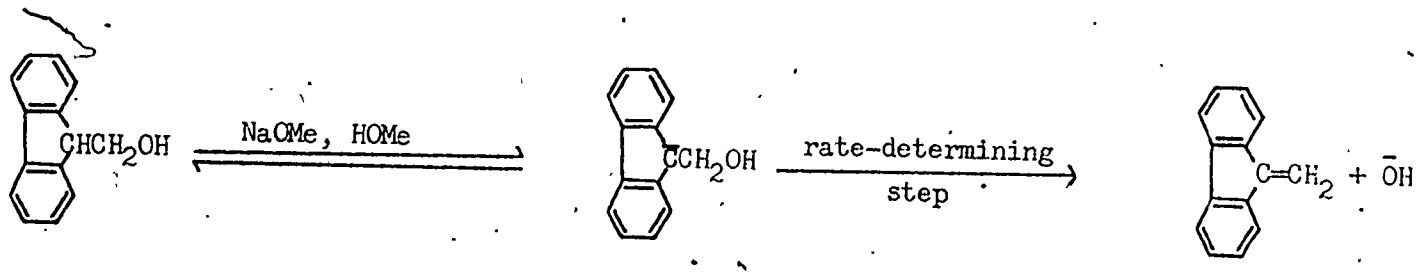
There have been a number of cases where a reversible $(ElcB)_R$ mechanism has changed to an irreversible $(ElcB)_I$ mechanism upon change of base (36), (Figure 7), or leaving group (37,38a), (Figure 8), where the latter cases involved sulphene elimination-addition reactions.

Williams and co-workers (38b) have recently proposed a variant of the concerted E2 mechanism for sulphene formation from esters of phenols with pKa<6 (Figure 9). The lifetime of the conjugate base is too short ($<10^{-13}$s) for it to exist as a discrete carbanion intermediate as in an $(ElcB)_I$ mechanism. An E2 process occurs with an unsymmetrical transition state involving no S-OAr bond cleavage and half advanced proton transfer. The transition state is intermediate between a neutral and a carbanionic species and, although the reaction coordinate does go through the carbanion structure, this does not represent a minimum on the potential energy surface.

Addition-elimination reactions also have been observed to follow the $(ElcB)_R$ mechanism (39). However, in elimination of olefins to acetylenes, competing $(ElcB)_R$ and E2 mechanisms are suggested (40), (Figure 10).

The $(El)_{anion}$ or "ElcB of the second type" mechanism has been observed for a number of reactions (41-43). Upon changing the leaving group and also the α-substituent, the $(El)_{anion}$ mechanism has been observed to change to the $(ElcB)_I$ mechanism in one case and to the E2 mechanism in the other (44), (Figure 11).

$(ElcB)_R$



$(ElcB)_I^{\cdot}$

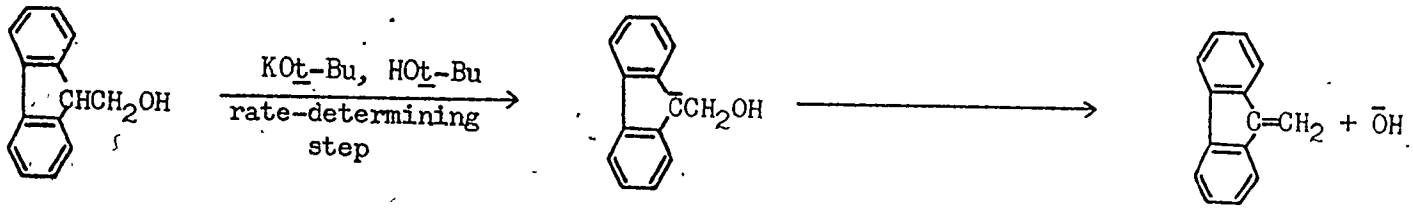


Figure 7 - Effect of Base on the ElcB Mechanism

$(ElcB)_R$

$$PhCH_2SO_2OC_6H_4\text{-}NO_2\text{-}p + Et_3N \underset{}{\overset{20\%H_2O\text{-}DME}{\rightleftharpoons}} Ph\bar{C}HSO_2OC_6H_4\text{-}NO_2\text{-}p + Et_3\overset{+}{N}H$$

$$\downarrow \text{ rate-determining step}$$

$$PhHC{=}SO_2 + \bar{O}C_6H_4\text{-}NO_2\text{-}p$$

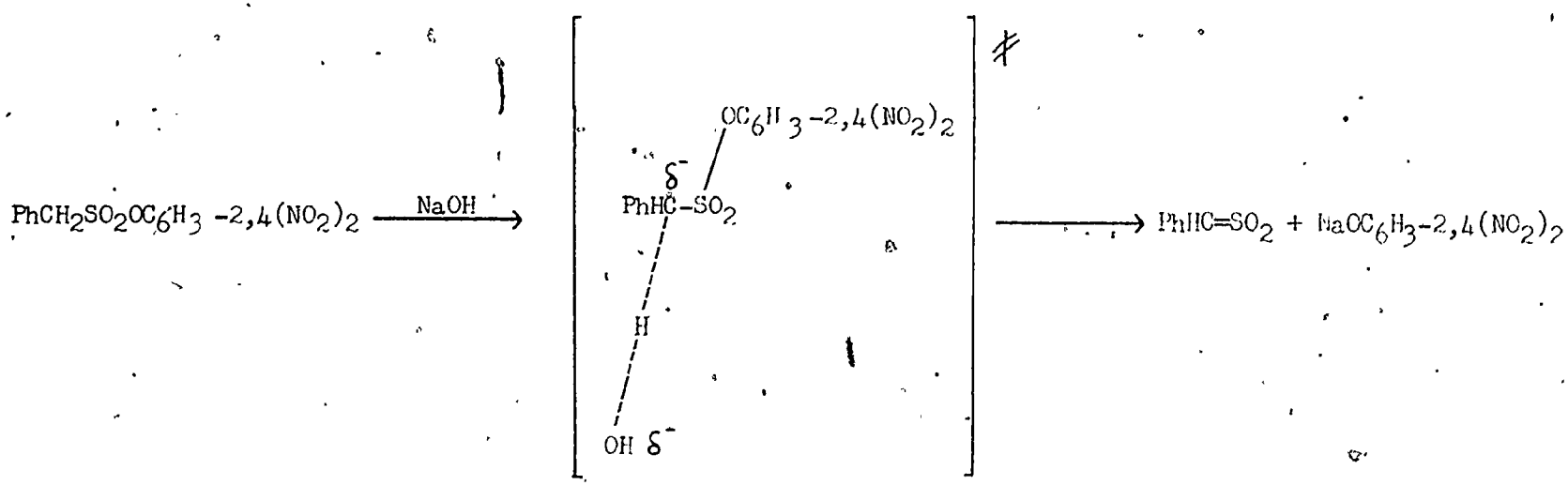
$(ElcB)_I$

$$PhCH_2SO_2OC_6H_3\text{-}2,4(NO_2)_2 + Et_3N \xrightarrow[\text{rate-determining step}]{20\%H_2O\text{-}DME} Ph\bar{C}HSO_2OC_6H_3\text{-}2,4(NO_2)_2 + Et_3\overset{+}{N}H$$

$$\downarrow$$

$$PhHC{=}SO_2 + \bar{O}C_6H_3\text{-}2,4(NO_2)_2$$

Figure 8 - Effect of Leaving Group on the ElcB Mechanism



unsymmetrical transition state

Figure 9 - Sulphene Formation through an E2 Mechanism

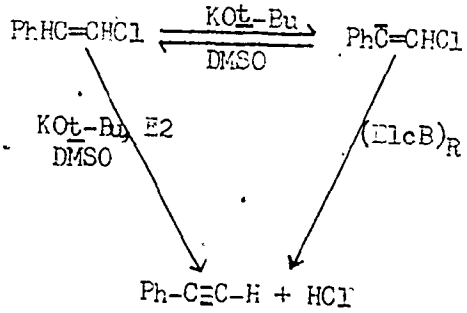


Figure 10 - Competing $(ElcB)_R$ and E2 Mechanisms

$(E1)_{anion}$

$$O_2NCH_2CH_2OPh \xrightarrow[EtOH]{NaOEt} O_2N\bar{C}HCH_2OPh \xrightarrow[step]{\text{rate-determining}} O_2NHC{=}CH_2 + \bar{O}Ph$$

E2

$$O_2NCH_2CH_2SPh \xrightarrow[EtOH]{NaOEt} O_2NHC{=}CH_2 + \bar{S}Ph$$

$(ElcB)_I$

$$O_2NCH_2CHPhSPh \xrightarrow[\text{rate-determining step}]{NaOEt, EtOH} O_2N\bar{C}HCHPhSPh \longrightarrow O_2NHC{=}CHPh + \bar{S}Ph$$

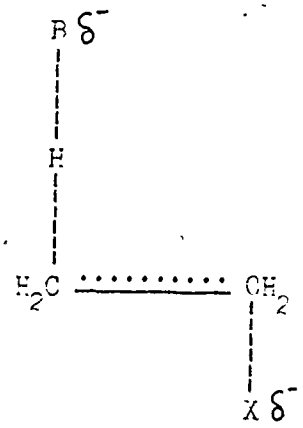
Figure 11 - Change in Mechanism with Change in Leaving Group and α-Substituent

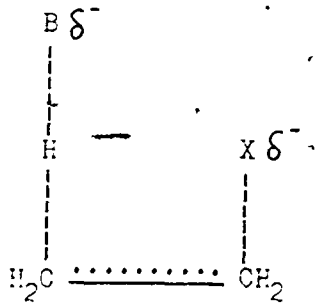
1.4 Stereochemistry of Elimination Reactions

One of the essential features in the description of the mechanism of a concerted E2 process is the dihedral angle about the $C_\alpha - C_\beta$ bond in the activated complex. In principle, this angle can possess any value between 0° and 180°. However, it is suggested by theory (e.g. the principle of maximum orbital overlap), (45), and supported by experiments on monocyclic and bicyclic ring systems that arrangements in which $C_\alpha - X$ and the $C_\beta - H$ bonds are anti periplanar (anti elimination; dihedral angle, 180°) and syn periplanar (syn elimination; dihedral angle 0°) will be greatly preferred relative to the other orientations in the transition state of an HX elimination reaction (46), (see Figure 12).

Until recently, the view has been generally accepted that, in base catalyzed bimolecular eliminations, the anti-elimination route is greatly superior to the syn route so that eliminations, in general, proceed by this mechanism (45); the only exceptions are systems in which the bonds cannot become anti periplanar, as, e.g. the norbornyl system (47,48), (see Figure 13).

The basis for preferred anti elimination has been made on the grounds of eclipsing effects and electronic effects.





	anti.	syn
DIHEDRAL ANGLE	180°	0°

Figure 12 - Preferred Dihedral Angle for the E2 Process

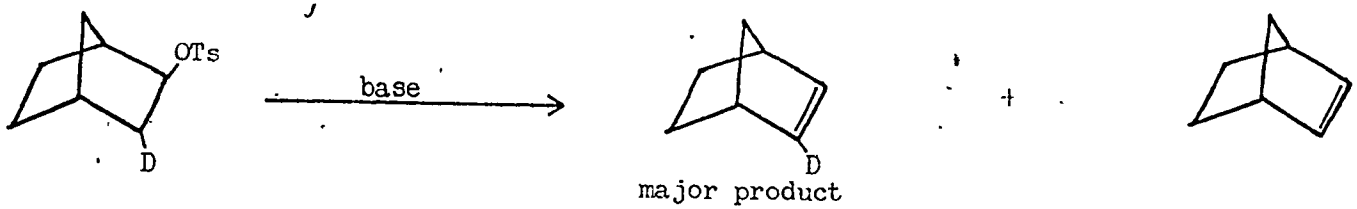
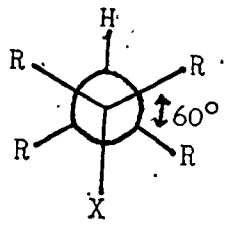


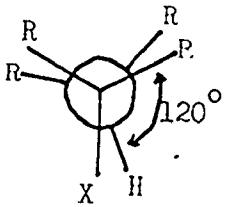
Figure 13 - syn Elimination in the Norborryl System

In syn elimination all three pairs of groups attached to C_α and C_β are eclipsed or nearly so; by contrast, the transition state for anti elimination, barring cases with highly developed double bond character, permits a staggered arrangement (see Figure 14). These conformation differences led to an estimated factor of 10^2 or 10^3 in favour of anti elimination (49). In the non-synchronous, yet concerted elimination processes (paenecarbonium ion or paenecarbanion) the advantage accruing from maximum orbital overlap is not as great as in the fully synchronous process, and, as a result, the syn-elimination transition state need not be fully eclipsed (49).

On the basis of electronic effects, a conceptual dissection of the process into two components has been made where a nucleophilic substitution on C_α occurs involving the C_β - H electrons with complementary substitution on the C_β atom by the C_α atom (45), (Figure 15). If C_β - H bond fission in a concerted elimination were considerably progressed in the transition state as in a paenecarbanion process, sufficient carbanion character could develop on C_β for the charge to spread on both sides of this carbon resulting in a planar transition state. The reaction could then exhibit syn stereospecificity (50).



anti



syn

Figure 14 - Staggered and Eclipsed Conformations for S2 Reaction

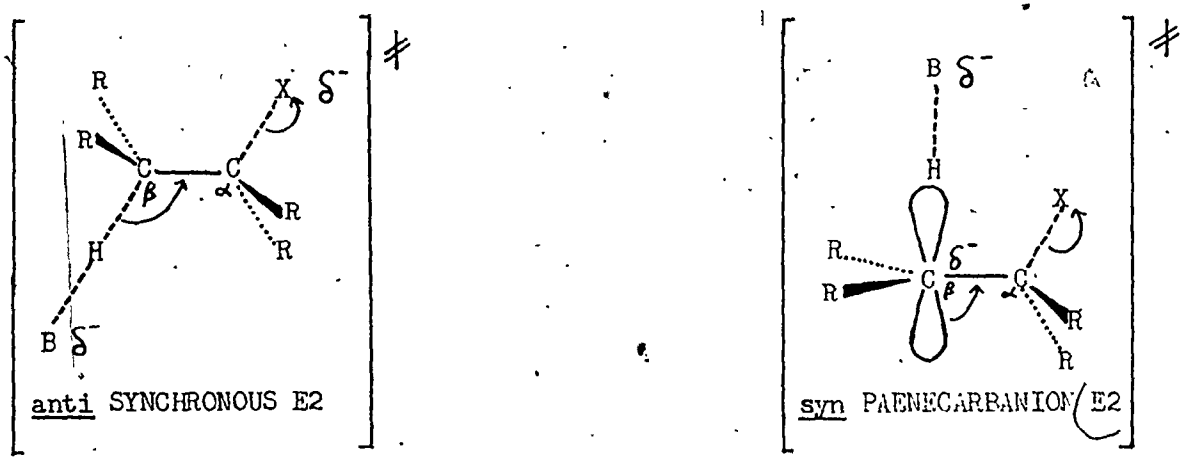
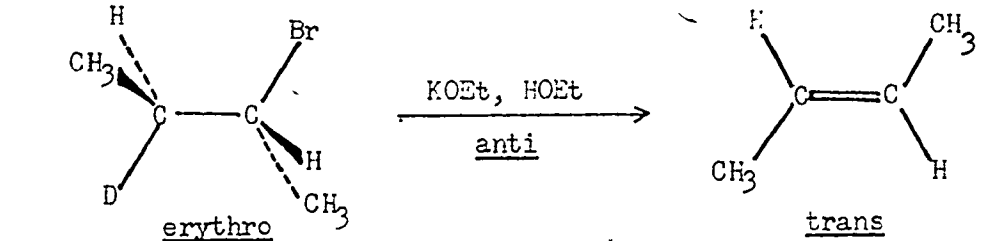


Figure 15 - Conceptual Dissection of E2 Processes

Other theoretical rationalizations for preferred anti elimination have been made both on the basis of orbital symmetry (51 - 53) and the principle of least motion (54, 55).

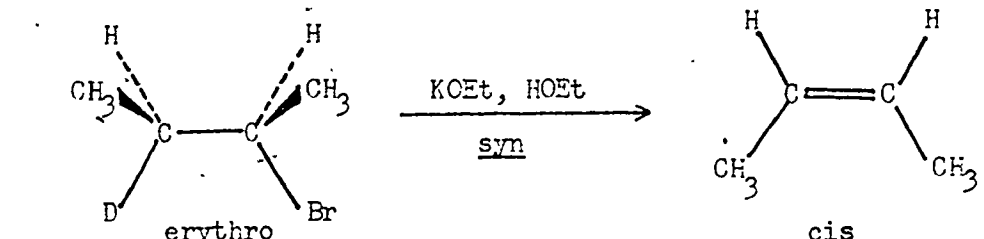
Experimental evidence for exclusive anti elimination in open-chain compounds comes from the pioneering work of Skell and co-workers (56). In their study of the elimination of hydrogen bromide from β-mono-deuterated 2-butyl bromides of known configuration with potassium ethoxide in ethanol, information about the steric course of the elimination reaction can be deduced directly from the deuterium content of the individual olefinic products. The erythro substrate yields exclusively trans undeuterated product by anti elimination whereas the threo substrate gives exclusively cis undeuterated product by anti elimination (Figure 16). Similar results were observed in the elimination of toluenesulphonic acid also using potassium ethoxide in ethanol with the corresponding 2-butyl tosylates.

Other evidence for exclusive anti elimination in open-chain compounds usually involves elimination from non-deuterated diastereoisomeric pairs. Thus the reaction of erythro -2,3-dichloropentane (57) and homologous erythro and meso-vic-dicholoroalkanes with potassium hydroxide in n-propanol gives exclusive anti elimination (see Figure 17).



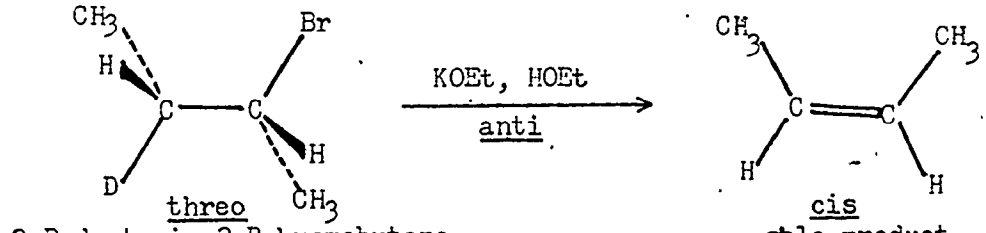
erythro
3-S-deuterio-2-R-bromobutane

trans
sole product



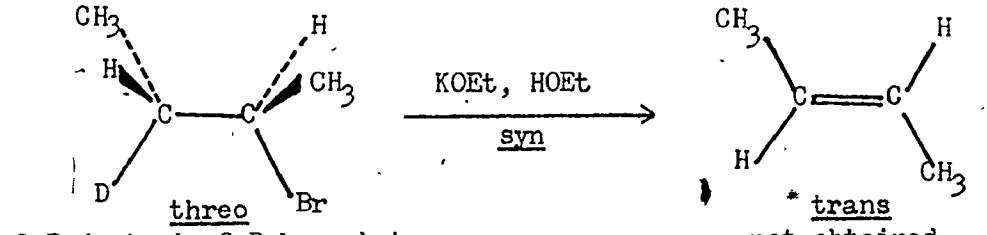
erythro
3-S-deuterio-2-R-bromobutane

cis
not obtained



threo
3-R-deuterio-2-R-bromobutane

cis
sole product



threo
3-R-deuterio-2-R-bromobutane

trans
not obtained

Figure 16 - anti Elimination from Deuterated Diasterioisomeric Pairs

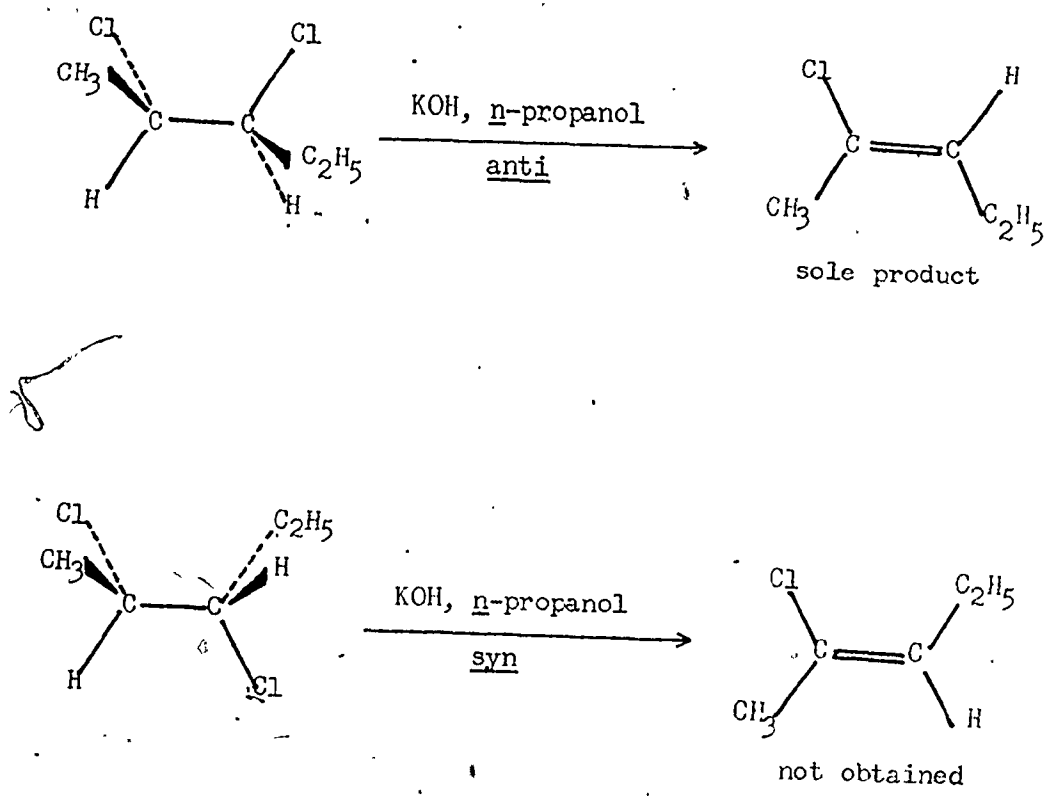


Figure 17 - anti Elimination from Non-Deuterated Diasterioisomeric Pairs

Experimental evidence for anti elimination also has been obtained from rate analysis of the elimination of alicyclic compounds (7). For cyclohexanes, it is known that the leaving group must be axial for easy anti elimination to occur (58), and preferably axial for syn elimination (59 - 62). Thus anti elimination is diaxial whereas syn elimination is axial-equatorial (see Figure 18). It can be seen that syn elimination from the trans isomer will be comparatively unfavorable because of the necessity of having two bulky groups in axial positions in the reactive conformation, which will thus be sparsely populated.

Base-catalyzed eliminations of cyclopentane derivatives to cyclopentenes also have an anti preference. In the five-membered ring a dihedral angle close to zero practically pre-exists for cis-placed groups, while for trans-placed groups a true anti-periplanar arrangement is more difficult to achieve (see Figure 19). In spite of this, on treatment with tert--butoxide in tert-butyl alcohol, the rate of anti elimination from cis-2-arylcyclopentyl p-toluenesulphonates (tosylates) was found to be higher than the rate of syn elimination from the trans isomers (46b), (Figure 20).

Bicyclic substrates also possess geometric features which are expected to be especially favorable for syn elimination.

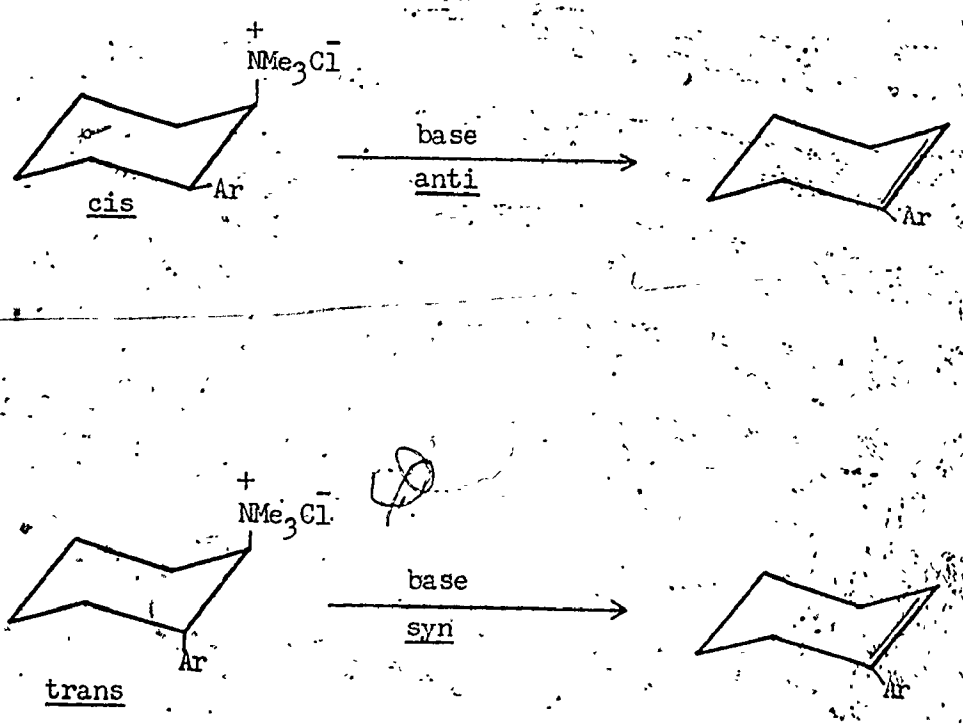


Figure 18 - Preferred anti Elimination from Cyclohexyl Derivatives

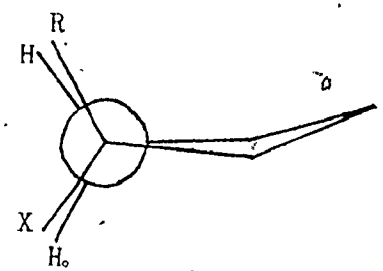
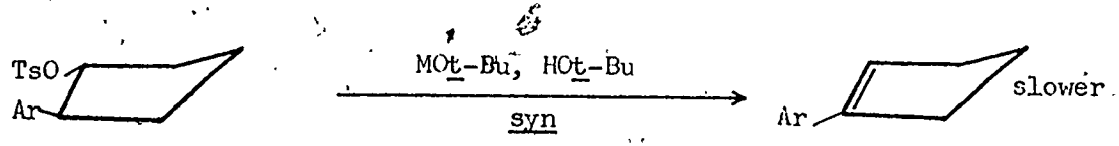
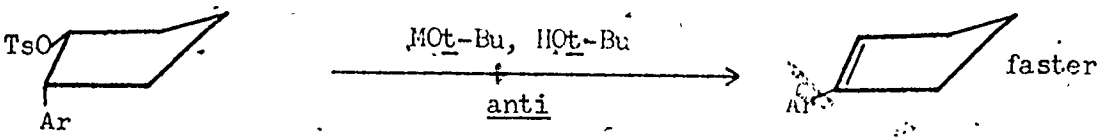


Figure 19 - Dihedral Angles for syn and anti Elimination from Cyclopentyl Derivatives



trans-2-arylcyclopentyl tosylate



cis-2-arylcyclopentyl tosylate

Figure 20.-- Relative Rates of Elimination from 2-Arylcyclopentyl Tosylates

The preferred reaction mode has been found to be syn elimination for the bicyclo [2.2.1] heptyl system provided that the leaving group occupies the exo position (48). The corresponding endo-substituted compound prefers the anti-elimination route regardless of the unfavorable dihedral angle of 120° (Figure 21).

Thus, theoretical considerations prior to 1966 largely predicted a general preference for the anti-elimination mode, although the possibility of a genuine bimolecular syn elimination also was envisioned. The available experimental evidence also appeared to be in full accord with this. However, most of the evidence for preferred anti elimination was with acyclic substrates with good leaving groups.

However, an important series of papers by the late Professor Sicher and his co-workers (63 - 67, 69, 73, 78) has forced a re-evaluation of these views. Employing initially medium-ring cycloalkyltrimethylammonium compounds, a study of the variation of rate with ring size in a homologous series of compounds for cis and trans olefin formation with potassium tert-butoxide in tert-butyl alcohol suggested a very marked difference in mechanisms (63), (Figure 22).

By relating the "rate profile" of the process under investigation to that of a reaction of known mechanism one may

	Dihedral Angle	Relative Rate
exo leaving group	0°	100
exo leaving group	120°	3.1
endo leaving group	120°	0.21
endo leaving group	0°	0.12

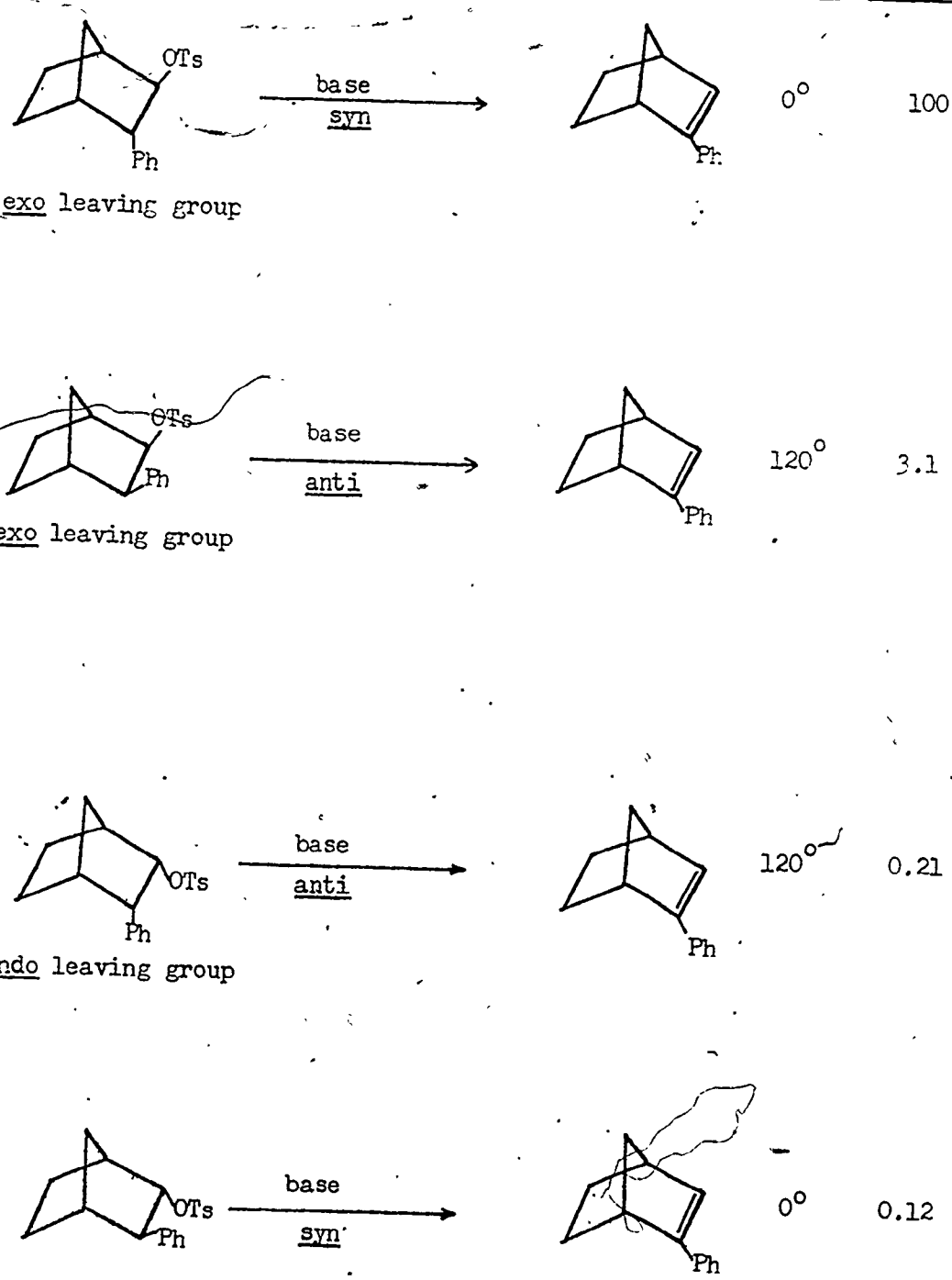


Figure 21 - endo versus exo leaving Groups in Elimination

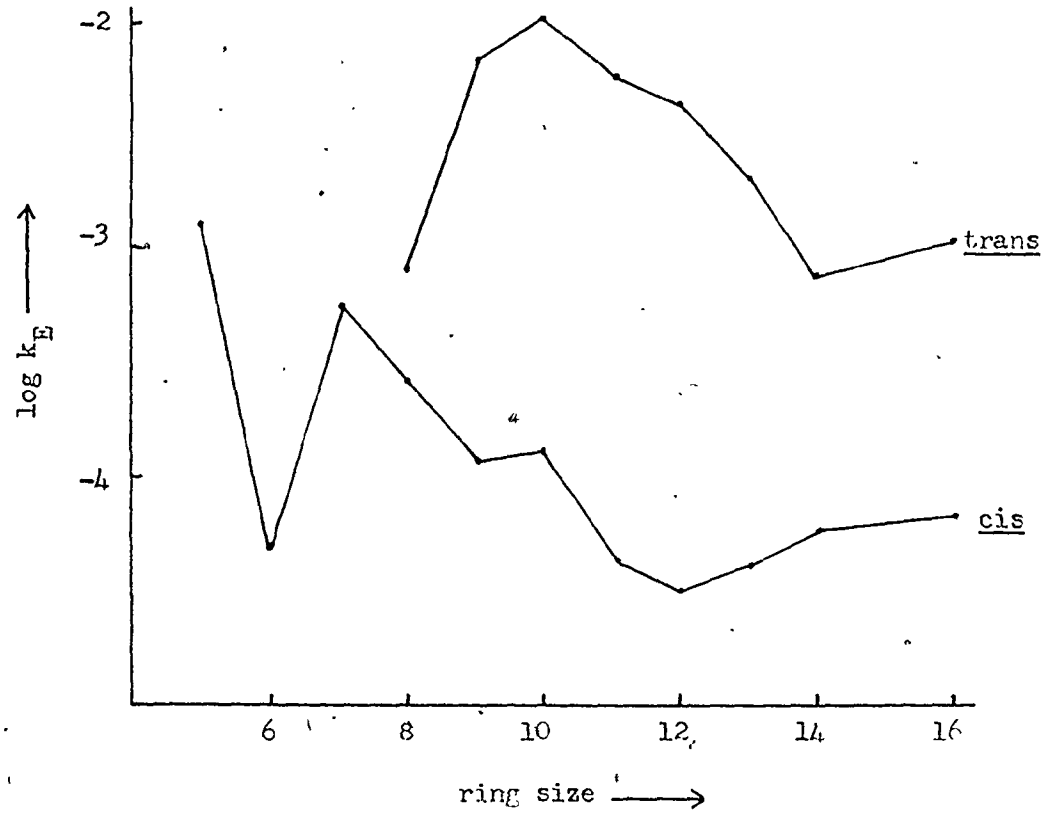


Figure 22 - "Rate Profile" for Medium-Ring Cycloalkyltrimethylammonium Derivatives

hope to obtain evidence on its course, the argument being that reactions which are similar with respect to their salient geometric features should also be similar as regards "rate profile". Conversely,"rate profiles"of different types may indicate the operation of stereochemically different mechanisms.

The preceding results together with comparison of "rate profiles" observed with that for the Cope elimination of cycloalkyldimethylamine oxides (64), (Figure 23), a known syn-elimination process, led Sicher to propose that trans-cycloalkene formation from the quaternary ammonium base elimination must arise by syn elimination. The cis-olefin formation from the quaternary ammonium base compound which had a very different "rate profile" to the Cope elimination, therefore, must not arise from syn but from anti elimination (see Figures 22 and 23).

In order to confirm these observations, cycloalkene formation from 1,1,4,4-tetramethylcyclodecyl-7-trimethylammonium chloride, and from its cis and trans-8-d labelled derivatives was investigated using potassium tert-butoxide in tert-butyl alcohol and dimethyl sulphoxide and potassium methoxide in methanol (65), (see Figures 24 and 25).

It was found that both cis and trans-1,1,4,4--tetramethylcyclodec-7-ene had retained deuterium when the cis-labelled substrate was employed (Figure 24) and that both

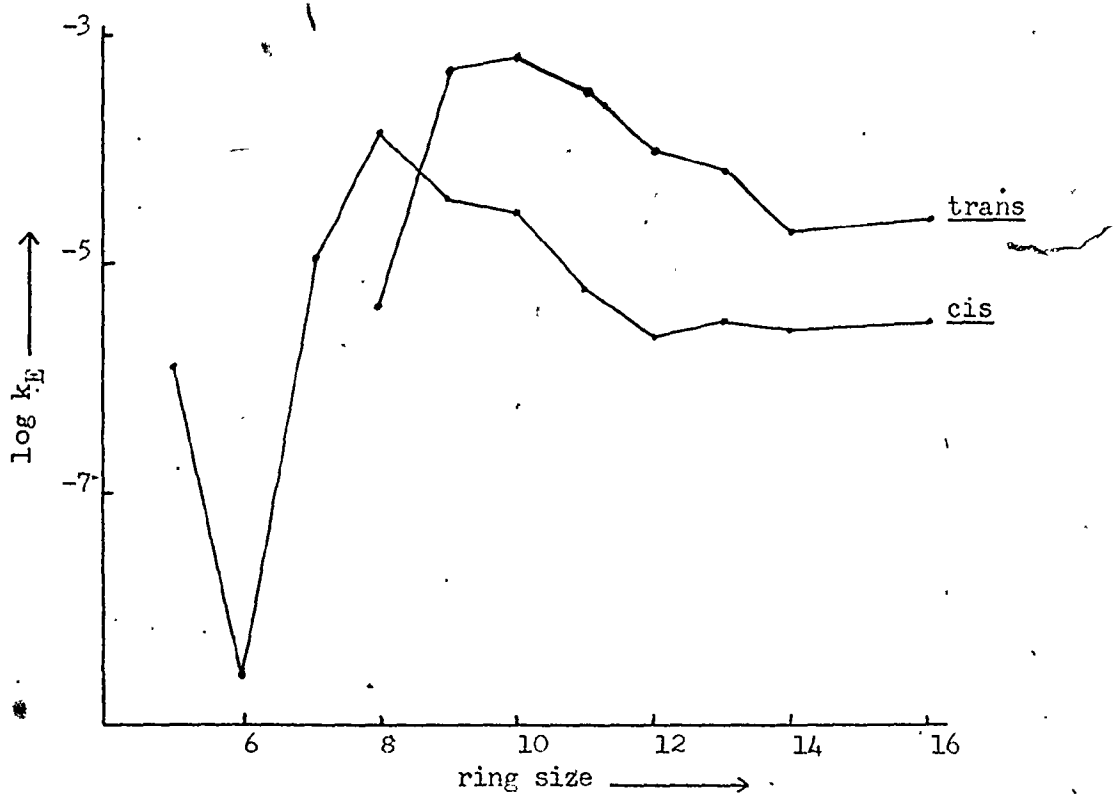
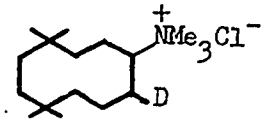


Figure 23 - "Rate Profile" for Medium-Ring Cycloalkyldimethylamine Oxides



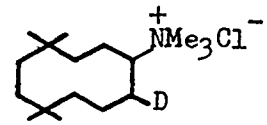
cis-8-d

KOt-Bu, HOt-Bu →

72.8% trans-1,1,4,4-tetramethyl-cyclodec-7-ene-8-d
(+ 0.2% cis olefin-d)

+ 26.8% trans-1,1,4,4-tetramethyl-cyclodec-6-ene-8-d
(+ 0.2% cis olefin-d)

Figure 24 - Elimination from cis-8-d-1,1,4,4-Tetramethylcyclodecyl-7-trimethylammonium Chloride (cis-8-d)



trans-8-d

KOt-Bu, HOt-Bu →

48.8% trans-1,1,4,4-tetramethylcyclodec-7-ene
(+ 0.15% cis olefin)

+ 50.8% trans-1,1,4,4-tetramethylcyclodec-6-ene-8-d
(+ 0.25% cis olefin-d)

Figure 25 - Elimination from trans-8-d-1,1,4,4-Tetramethylcyclodecyl-7-trimethylammonium Chloride (trans-8-d)

olefins had lost deuterium after correction for the isotope effect when the trans-labelled substrate was employed (Figure 25). Thus, cis olefins are indeed formed by anti elimination and trans olefins by syn elimination from medium-ring cycloalkyltrimethylammonium compounds with all base-solvent systems studied (see Figure 26). This phenomenon has become known as the "syn-anti bimolecular elimination dichotomy" (63b).

The syn-anti dichotomy is also observed using the "rate profile" technique in the cycloalkyl bromide series for cycloalkene formation with potassium tert-butoxide in tert-butyl alcohol or in benzene (66). However, with potassium tert-butoxide in dimethylformamide or potassium ethoxide in ethanol base-solvent systems, both cis and trans cycloalkenes arise by anti elimination.

1,1,4,4-Tetramethylcyclodec-7-ene is formed exclusively by the "syn-anti dichotomy" route from 1,1,4,4-tetramethylcyclodecyl--7 tosylate with potassium tert-butoxide in tert-butyl alcohol, dimethylformamide or benzene (67). However, with the 1,1,4,4-tetramethylcyclododecyl-8 tosylate the proportion of trans -1,1,4,4-tetramethyl-cyclododecene formed by syn elimination with potassium tert-butoxide varied from 95% in benzene, to 85% in tert-butyl alcohol and to 30% in dimethylformamide.

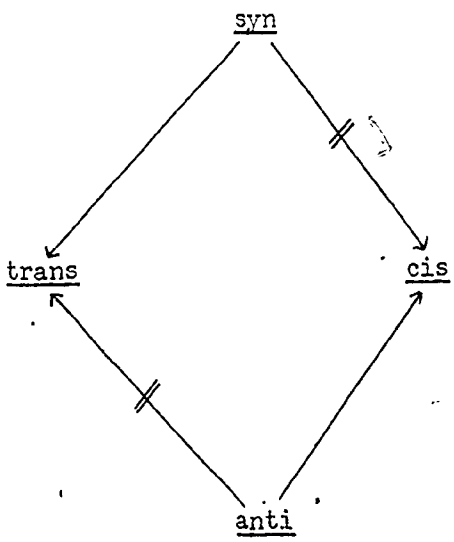


Figure 26 - syn-anti Bimolecular Elimination Dichotomy

Steryl tosylate substrates also have been observed to undergo syn elimination with sodium tert-pentoxide in benzene to varying degrees depending on stereochemistry (68). However, with dimsyl sodium in dimethyl sulphoxide these substrates yield exclusive anti elimination.

In order to show the generality of the dichotomy, Sicher studied elimination in open-chain systems. For 5-decyltrimethylammonium chloride with potassium tert-butoxide in tert-butyl alcohol (see Figure 27), benzene or dimethyl sulphoxide, the trans decenes arise by syn elimination (69). However, with potassium methoxide in methanol almost exclusive anti elimination occurs. Note, however, that for these studies, mixtures of cis-dec-4-ene and cis-dec-5-ene and also mixtures of trans-dec-4-ene and trans-dec-5-ene could not be separated and the stereochemistry of the reaction was deduced by deuterium analysis of these mixtures.

For 2,2-dimethyl-4-nonyltrimethylammonium chloride with potassium tert-butoxide in tert-butyl alcohol or dimethyl sulphoxide or potassium methoxide in methanol, the syn-anti dichotomy was observed (70), (Figure 28). While for 1-decyltrimethylammonium chloride with potassium tert-butoxide in benzene, dimethylformamide or tert-butyl alcohol, predominantly an anti-elimination pathway was followed (71), (Figure 28).

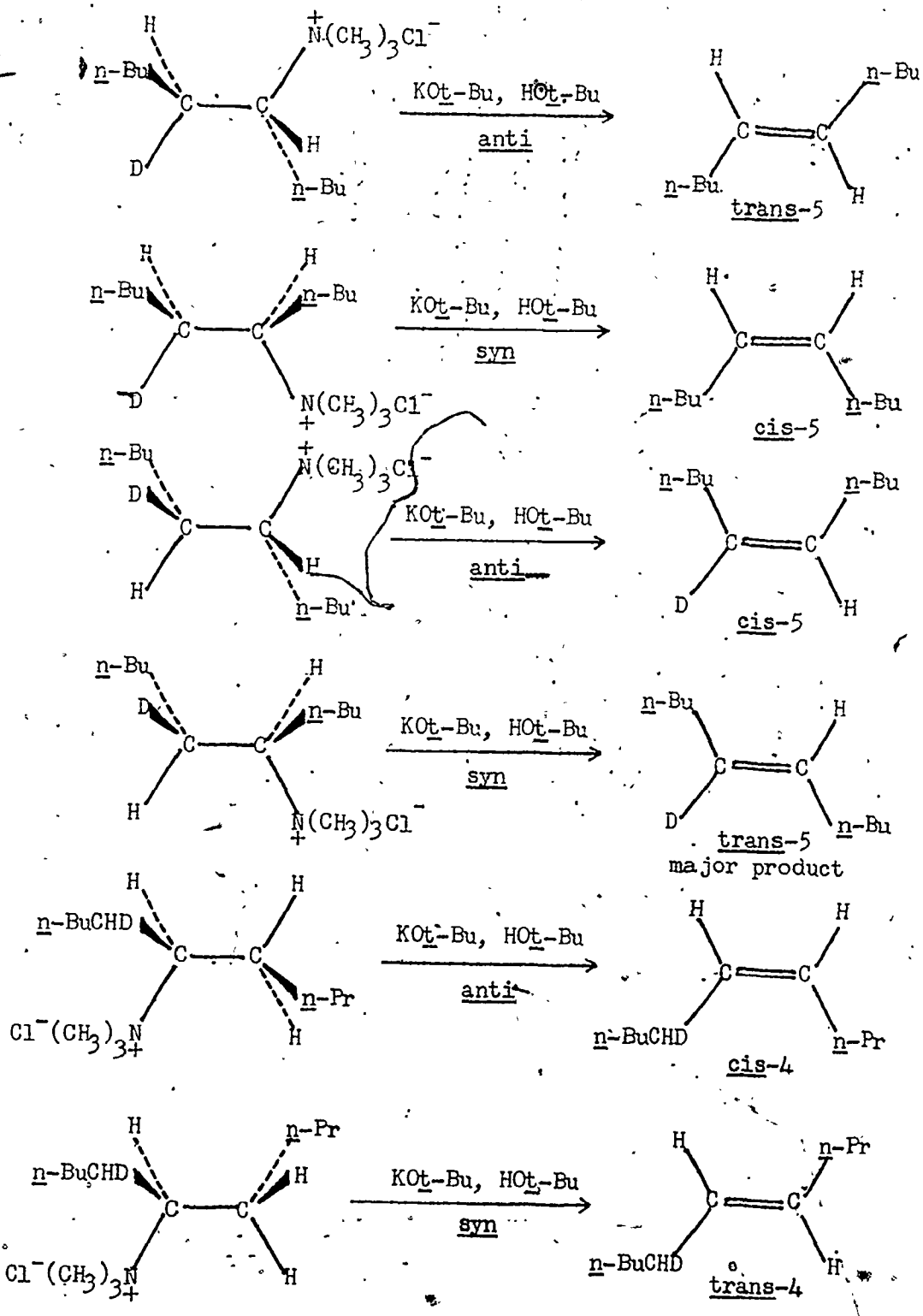
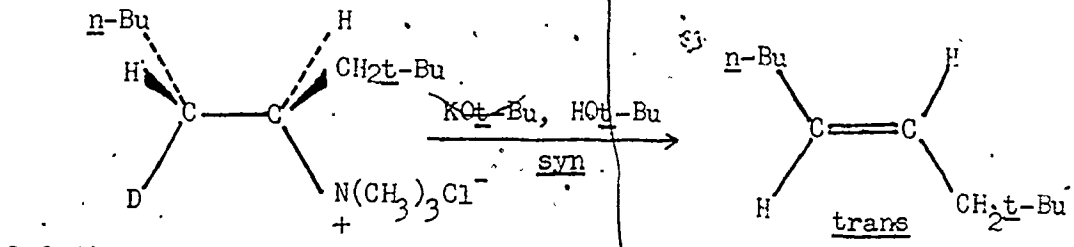
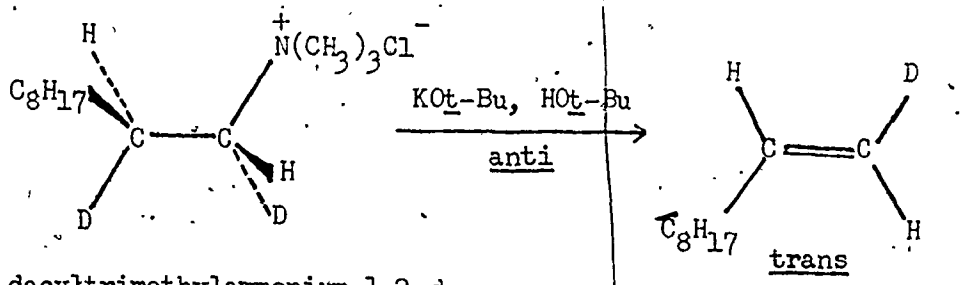


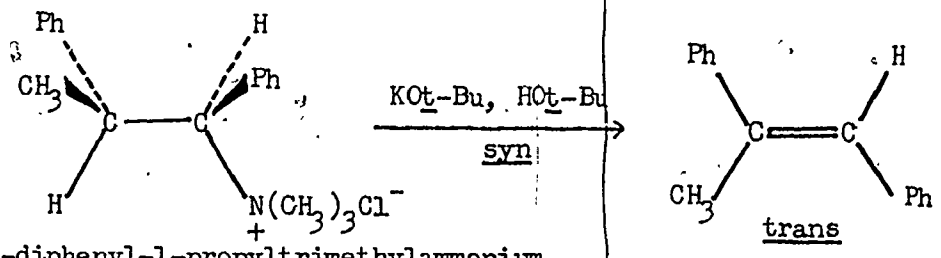
Figure 27 - Elimination from 5-Decyltrimethylammonium-6-d Chloride



2,2-dimethyl-4-nonyltrimethylammonium-5-d chloride



1-decyltrimethylammonium-1,2-d_2 chloride



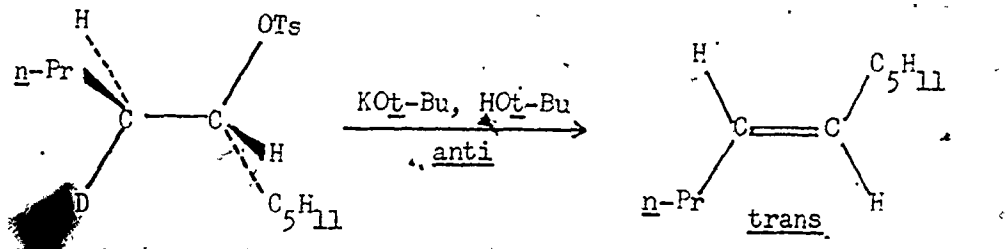
1,2-diphenyl-1-propyltrimethylammonium chloride

Figure 28 - Elimination of Branched and Long-Chain Acyclic Quaternary Ammonium Salts

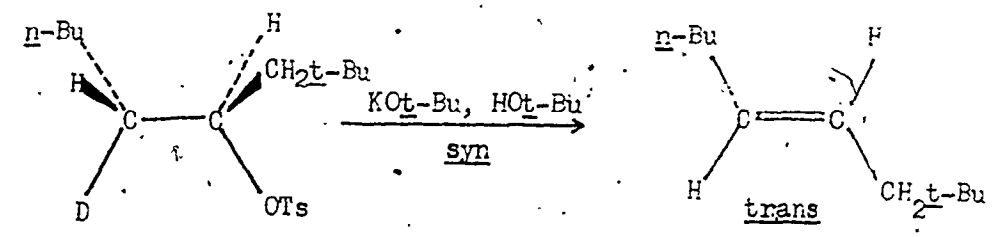
1,2-diphenyl-1-propyltrimethylammonium salts with potassium tert-butoxide in tert-butyl alcohol yield trans olefin by syn elimination (72), (Figure 28). Thus the syn-anti dichotomy is favoured for branched or long-chain acyclic quaternary ammonium salt substrates with various base-solvent systems except where 1-substituted olefins are produced.

5-decyl tosylate undergoes predominantly anti elimination for the formation of cis and trans olefins with potassium tert-butoxide in benzene, tert-butyl alcohol or dimethylformamide (73) (Figure 29). However, 2,2-dimethyl--4-nonyl tosylate with potassium tert-butoxide in tert-butyl alcohol or benzene yields trans-2,2-dimethyl-4-nonene by predominantly syn elimination (70). With potassium tert-butoxide in dimethylformamide or dimethyl sulphoxide, 2,2-dimethyl-4-nonyl tosylate yields exclusive anti elimination (70), (Figure 29). Thus the syn-anti dichotomy is observed for branched-chain acyclic tosylates.

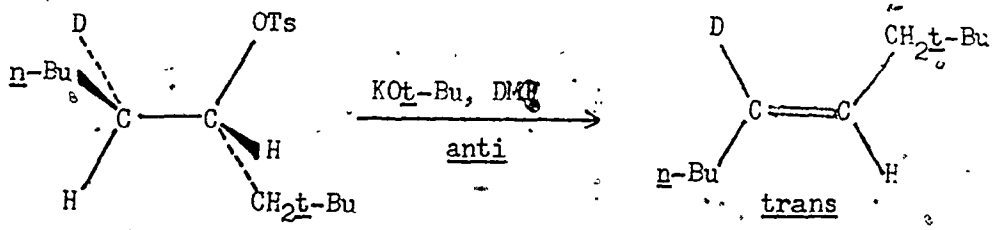
However, deuterium-labelled 2-phenylethyl tosylate yields styrene by predominantly anti elimination with potassium tert-butoxide in benzene but almost exclusive anti elimination in dimethyl sulphoxide (74), (Figure 29).



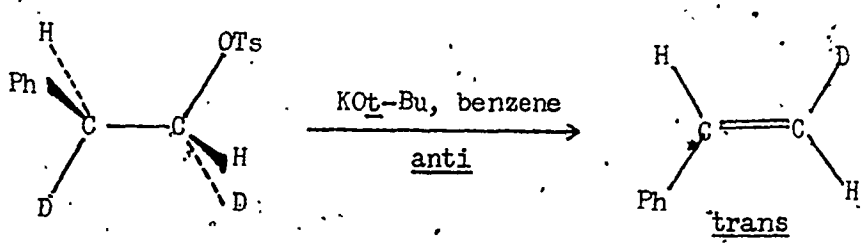
5-decyl-4-d tosylate



2,2-dimethyl-4-nonyl-5-d tosylate



2,2-dimethyl-4-nonyl-5-d tosylate



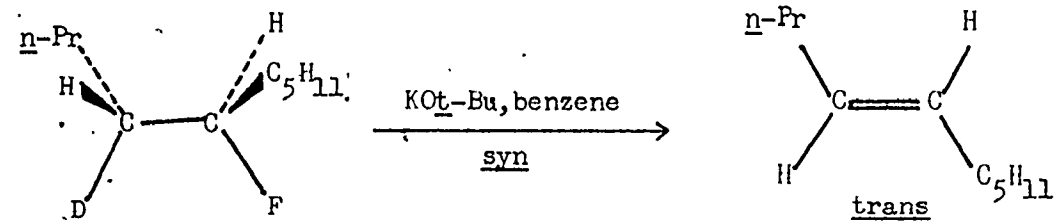
2-phenylethyl-1,2-d_2 tosylate

Figure 29. - Elimination of Branched-Chain Acyclic Tosylates

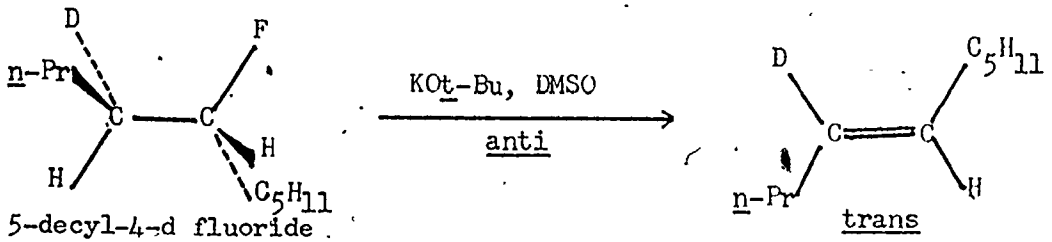
5-decyl fluoride with potassium tert-butoxide in benzene yields almost exclusively the syn-anti dichotomy whereas in dimethyl sulphoxide yields almost exclusive anti elimination (75), (Figure 30). However, 5-decyl chloride with potassium tert-butoxide in benzene followed a predominantly syn-elimination course while in dimethyl sulphoxide yields almost exclusive anti elimination (75). Thus the syn-anti dichotomy is observed with poor leaving groups that are not bulky such as fluoride.

Therefore, the syn-anti dichotomy is observed with both cyclic and acyclic derivatives. With quaternary ammonium cyclic, branched-chain acyclic and long-chain but not 1-substituted acyclic derivatives, the syn-anti dichotomy occurs almost exclusively in all base-solvent systems. However, with tosyloxy and halide cyclic and branched-chain acyclic derivatives, the syn-anti dichotomy predominates only with potassium tert-butoxide in tert-butyl alcohol or benzene (76). These results have been summarized in Tables 1 and 2.

For medium-ring cycloalkyl substrates, the syn-anti dichotomy can be rationalized on the basis of conformational analysis of the substrate (77). In 7-substituted derivatives of 1,1,4,4-tetramethylcyclodecane, the methyl groups serve as conformation holding groups. From the cis-8-d and the trans-8-d substrates in Figures 24 and 25 respectively, it



5-decyl-4-d fluoride



5-decyl-4-d fluoride

Figure 30 - Elimination of Long-Chain Acyclic Fluorides

TABLE 1

Elimination Stereochemistry of Cyclic Substrates

Substrate	Leaving Group	Base/Solvent	Elimination Stereochemistry		Ref.
			cis olefin	trans olefin	
1,1,4,4-tetramethyl--cyclodecyl-7-	trimethylammonium chloride	KOt-Bu/HOt-Bu	exclusive anti	exclusive syn	65
"	"	KOt-Bu/DMSO	"	"	65
"	"	KOMe/HOMe	"	"	65
cyclodecyl	bromides	KOt-Bu/benzene	largely anti	largely syn	66
"	"	KOt-Bu/HOt-Bu	"	"	66
"	"	KOt-Bu/DMF	exclusive anti	exclusive anti	66
"	"	KOEt/HOEt	"	"	66
1,1,4,4-tetramethyl--cyclodecyl-7-	tosylate	KOt-Bu/benzene	exclusive anti	exclusive syn	67
"	"	KOt-Bu/HOt-Bu	"	"	67
"	"	KOt-Bu/DMF	"	"	67
1,1,4,4-tetramethyl--cyclododecyl-8-	tosylate	KOt-Bu/benzene	-	95% syn	67
"	"	KOt-Bu/HOt-Bu	-	85% syn	67

TABLE 1 (contd.)

Substrate	Leaving Group	Base/Solvent	Elimination Stereochemistry cis olefin	trans olefin	Ref.
1,1,4,4-tetramethyl--cyclododecyl-8-	tosylate	KOt-Bu/DMF	-	30% syn	67
4,4-dimethyl (5α) cholestanyl-3β-	tosylate	Nat-pentoxide/ benzene	78% syn	-	68
"	"	Dimsyl sodium/ DMSO	exclusive anti	-	68
4,4-dimethyl (5α) cholestanyl-3α-	tosylate	Nat-pentoxide/ benzene	39% syn	-	68
"	"	Dimsyl sodium/ DMSO	exclusive anti	-	68

TABLE 2

Elimination Stereochemistry of Acyclic Substrates

Substrate	Leaving Group	Base/Solvent	Elimination Stereochemistry cis olefin	trans olefin	Ref.
5-decyl	trimethylammonium chloride	KOt-Bu/benzene	82% anti	92% syn	69,75
"	"	KOt-Bu/HOt-Bu	94% anti	87% syn	69
"	"	KOt-Bu/DMSO	94% anti	93% syn	69,75
"	"	KOMe/HOMe	93% anti	32% syn	69
2,2-dimethyl-4-nonyl	trimethylammonium chloride	KOt-Bu/HOt-Bu	exclusive anti	99% syn	70
"	"	KOt-Bu/DMSO	exclusive anti	99% syn	70
"	"	KOMe/HOMe	exclusive anti	89% syn	70
erythro-1-decyl	trimethylammonium chloride	KOt-Bu/benzene	-	20% syn	71
"	"	KOt-Bu/HOt-Bu	-	8% syn	71
"	"	KOt-Bu/DMF	-	14% syn	71
1,2-diphenyl-1-propyl	trimethylammonium halides	KOt-Bu/HOt-Bu	-	exclusive syn	72

TABLE 2 (contd.)

Substrate	Leaving Group	Base/Solvent	Elimination Stereochemistry cis olefin	trans olefin	Ref.
5-decyl	tosylate	KOt-Bu/benzene	93% anti	27% syn	73,75
"	"	KOt-Bu/HOt-Bu	92% anti	16% syn	73
"	"	KOt-Bu/DMF	92% anti	5% syn	73
"	"	KOt-Bu/DMSO	94% anti	4% syn	75
2,2-dimethyl-4--nonyl	tosylate	KOt-Bu/benzene	exclusive anti	about 67% syn	70
"	"	KOt-Bu/HOt-Bu	exclusive anti	about 67% syn	70
"	"	KOt-Bu/DMF	exclusive anti	exclusive anti	70
"	"	KOt-Bu/DMSO	"	"	70
2-phenylethyl	tosylate	KOt-Bu/benzene	-	19% syn	74
"	"	KOt-Bu/HOt-Bu	-	8% syn	74
"	"	KOt-Bu/HOt-Bu	-	<5% syn	74
5-decyl	fluoride	KOt-Bu/benzene	≥90% anti	≥90% syn	75
"	"	KOt-Bu/DMSO	≥80% anti	≤ 20% syn	75

TABLE 2 (contd.)

Substrate	Leaving Group	Base/Solvent	Elimination stereochemistry		Ref.
			cis olefin	trans olefin	
5-decyl	chloride	KO*t*-Bu/benzene	90% *anti*	62% *syn*	75
"	"	KO*t*-Bu/DMSO	85% *anti*	6% *syn*	75

can be demonstrated that anti elimination to trans olefin involves reaction of the intra-annular hydrogen while syn elimination to trans olefin involves reaction of the extra-annular hydrogen. In order to make the intra-annular hydrogen accessible to base approach, the molecule must twist into a less energetically favourable conformation and thereby produce cis olefin by anti or possibly syn elimination. Although these conformational features in medium ring cycloalkyl substrates can be invoked to rationalize the steric accessibility of the trans β-proton in both the syn and anti transition states, Sicher considered that such steric effects could not represent the sole cause of the syn-anti dichotomy (63c).

For the acyclic case, the syn-anti dichotomy results in preferential removal of the threo proton by base in the formation of cis olefin by anti elimination and trans olefin by syn elimination (78), (see Figure 31).

It is not difficult to find a simple steric explanation for the almost complete absence of the syn elimination pathway to cis olefin since an eclipsed or near-to-eclipsed arrangement of two vicinal alkyl groups is required. It is less simple to give an explanation for the preference for a syn elimination pathway to trans olefin over anti elimination to both cis

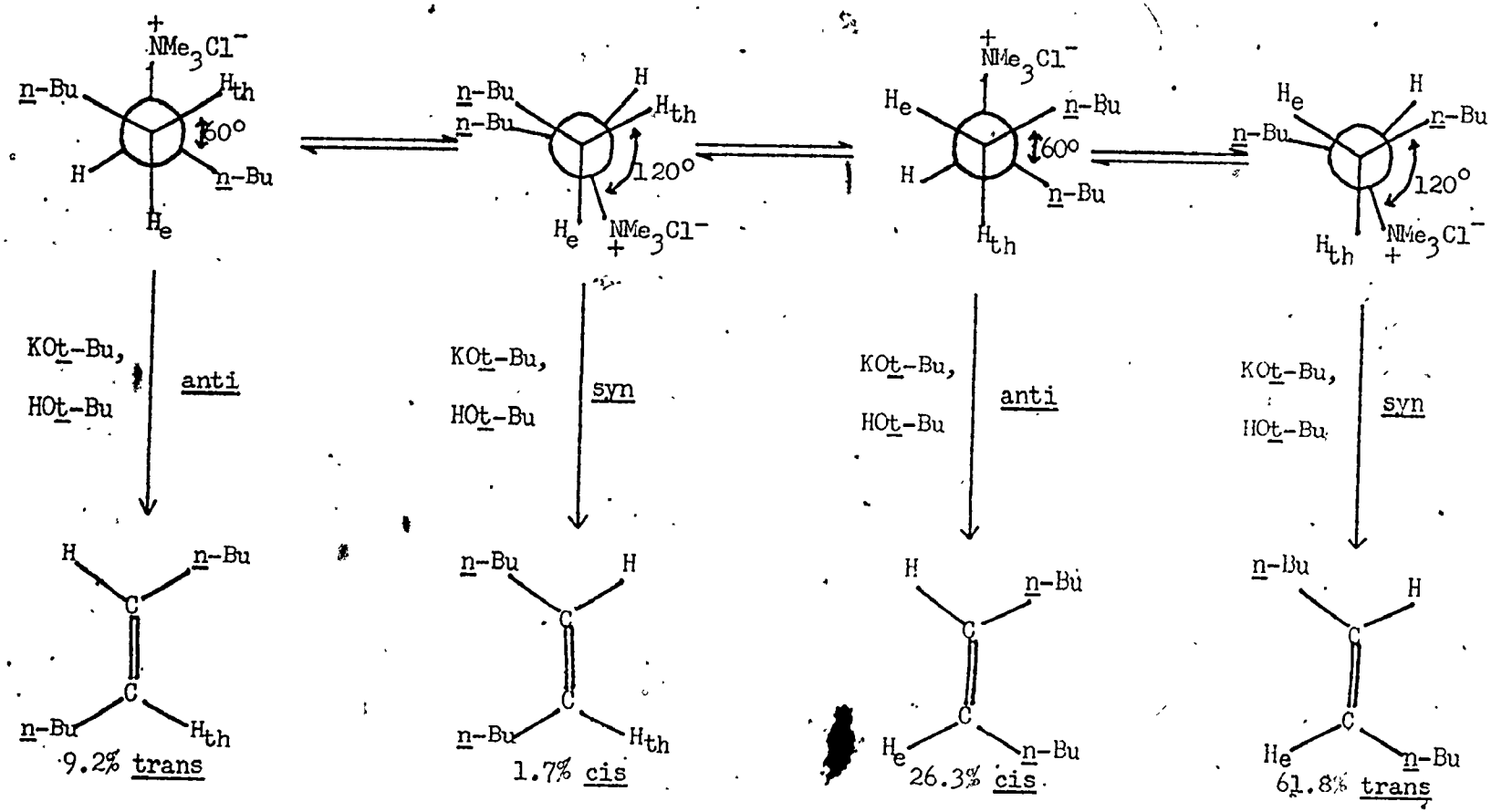


Figure 31 - syn-anti Dichotomy with 5-Decyltrimethylammonium Chloride

and trans olefins and at the same time rationalize the preferential formation of cis over trans olefin by anti elimination.

Saunders and his co-workers (79) presented a conformational explanation for the syn-anti dichotomy with acyclic substrates. They postulated that steric hindrance in trans olefin formation by anti elimination is the main cause of the dichotomy (see Figure 31). By a slowing down of the rate of the anti elimination to trans olefin, it gives the anti elimination to cis-olefin and/or the syn elimination to trans-olefin pathways the opportunity to predominate. According to the hypothesis, it is the bulk of the leaving group which is believed to enforce it, by pushing the alkyl residues into position, base approach to H_e is shielded for anti elimination leading to trans olefin. In the case of the anti elimination to cis olefin pathway, the shielding of the H_{th} is less effective because the substrate is still relatively open to attack by base from the side opposite to that on which the two alkyl groups are found.

This explanation for the syn-anti dichotomy depends upon the importance of bulky leaving groups. However, it has been shown that the dichotomy occurs for fluoride leaving groups with potassium tert-butoxide in benzene (75). Thus, in the absence of the required steric qualities, almost exclusive syn elimination leading to trans olefin occurs.

Sicher originally put forward the suggestion (76 - 78) that the syn-anti dichotomy in acyclic substrates is the result of "the operation of some effect which has so far escaped notice". It was pointed out that the protons H_{th} and H_e are diastereotopic and could, under appropriate conditions, exhibit diastereotopic reactivity (see Figure 31). Wolfe (80), in an attempt to explain this apparent difference in the reactivity of diastereotopic hydrogens has invoked the "gauche effect".

1.5 Elimination in the Acenaphthene System

The first elimination studies in an acenaphthene system were carried out by Cristol (81). Using cis and trans 1,2-dichloroacenaphthene with sodium hydroxide in 92.6% ethanol, anti elimination of the cis substrate to 1-chloroacenaphthene proceeded about 750 times faster than syn elimination of the trans substrate (see Figures 32 and 33).

These results are in general agreement with the preference for anti elimination in cyclopentane derivatives. It should be noted, however, that the relative rate ratio for anti to syn elimination is larger than normally observed for cyclopentane derivatives (82), (see Figure 33).

Dewar and co-worker (83) studied the stereochemistry of the addition of deuterium halides to acenaphthylene using

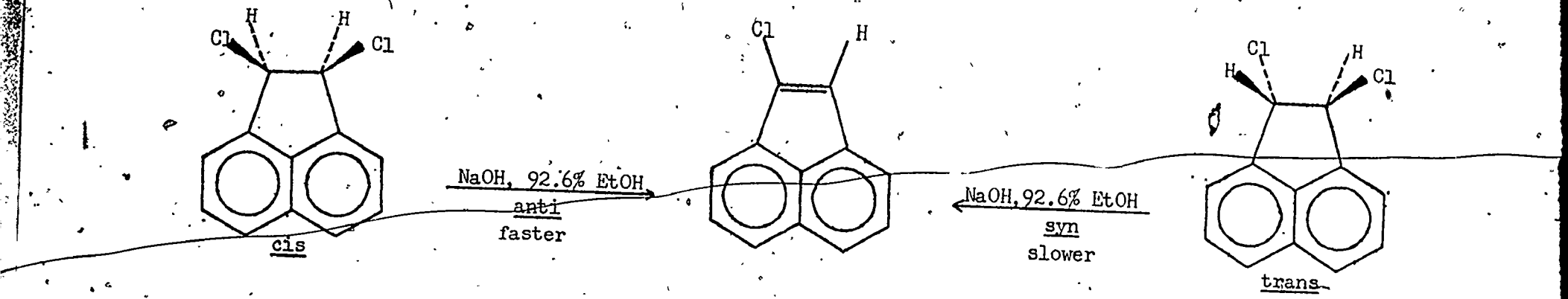
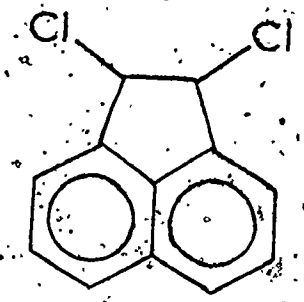
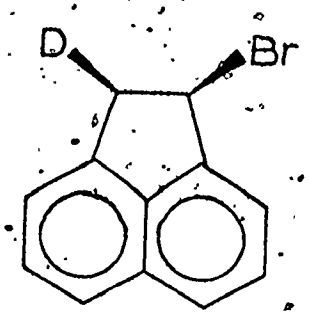


Figure 32 - Relative Rates of Elimination from cis and trans 1,2-Dichloroacenaphthene





syn/anti rate ratio 0.001 <0.05

Figure 33 - Relative Rates of Elimination (syn/anti) in Acenaphthene System

subsequent elimination of the 1-haloacenaphthene-2-d product as a means of determining the amounts of cis and trans addition (see Figures 34 and 33). Deuterium bromide addition to acenaphthylene yields predominantly cis-1-bromoacenaphthene-2-d. Upon elimination with potassium tert-butoxide in tert-butyl alcohol, the composition of the acenaphthylene-1-d produced was determined by mass spectrometric (ms) analysis.

The basic assumption, made by the authors, was that elimination is exclusively anti. In order to confirm this, nuclear magnetic resonance (nmr) spectroscopic analysis of the deuterated bromoacenaphthene addition products for cis and trans β-hydrogen was carried out. The nmr results agreed within experimental error with the elimination results, confirming that anti elimination was indeed the sole elimination pathway for 1-bromoacenaphthene substrates with potassium tert-butoxide in tert-butyl alcohol.

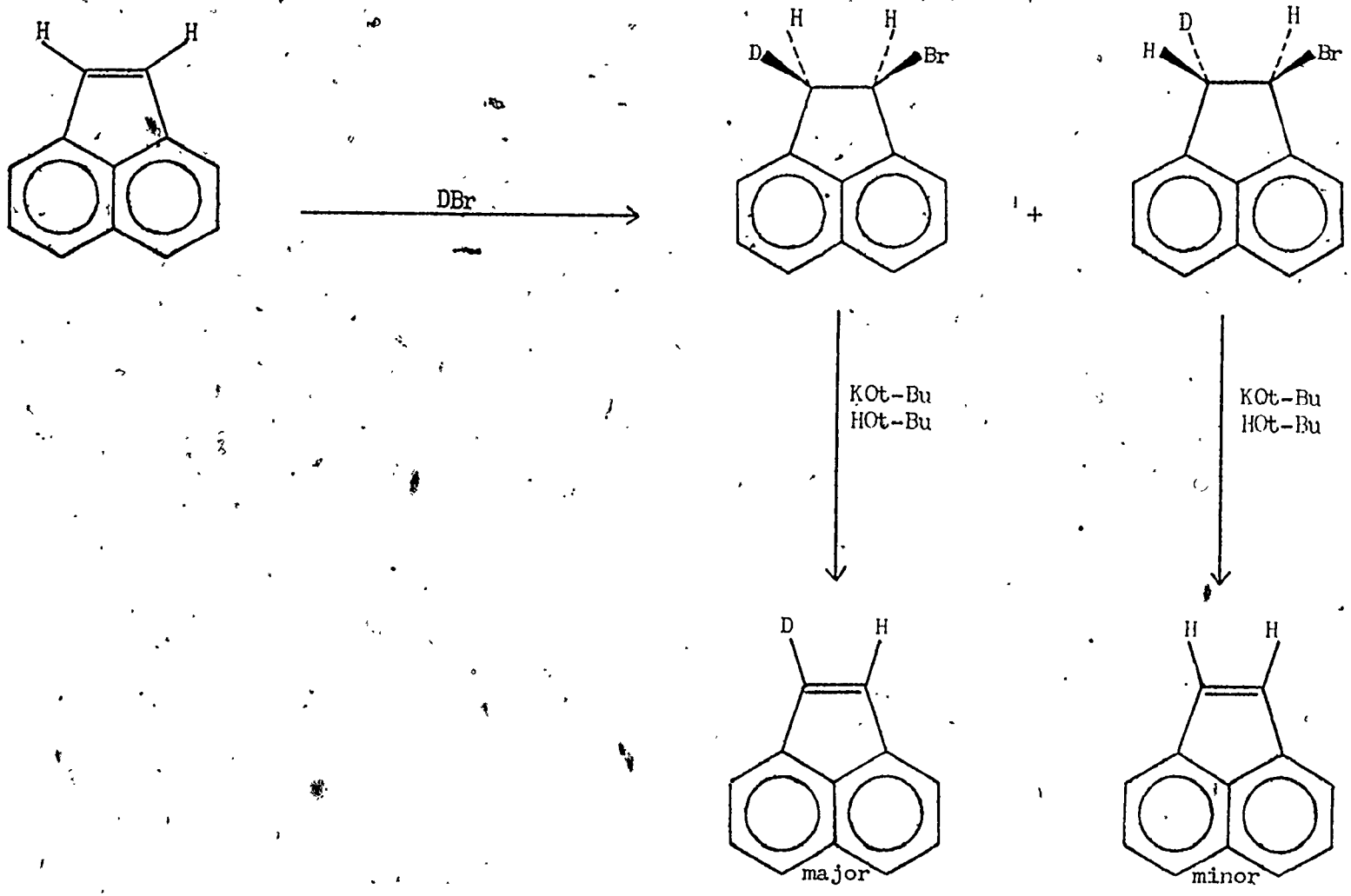


Figure 34 - Exclusive anti Elimination from 1-Bromoacephthene

CHAPTER 2

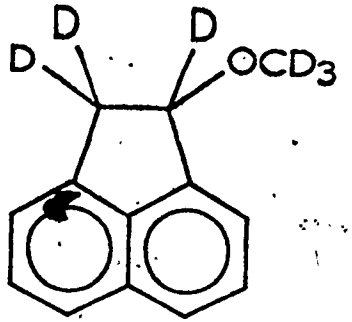
EXCHANGE STUDY

2.1 Statement of the Problem

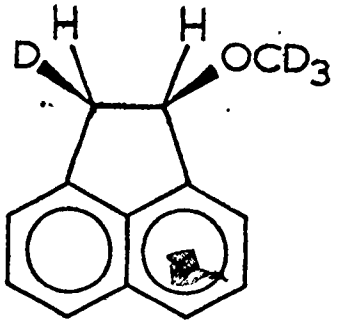
The present investigation was initiated with the object of gaining insight into the stereochemistry of elimination processes. After a preliminary screening of substrates, 1-methoxyacenaphthene, a reversible $(ElcB)_R$ system, (Figure 2), was chosen where the substrate has a fixed geometry and where there is a close competition for the carbanionic intermediate to undergo reprotonation or elimination. If the carbanionic intermediate partitions itself too preferentially to starting material, then it is likely that the stereochemical integrity of the substrate will be lost. If, on the other hand, the intermediate yields mostly elimination products, it becomes difficult to obtain even permissive evidence for prior carbanion formation. Thus the stereochemistry of the elimination process is one of the less accessible aspects of ElcB reactions.

It was proposed to synthesize cis and trans β-deuterium labelled 1-methoxyacenaphthenes and study their exchange and elimination with alkoxide-alcohol base-solvent systems (see Figure 35).

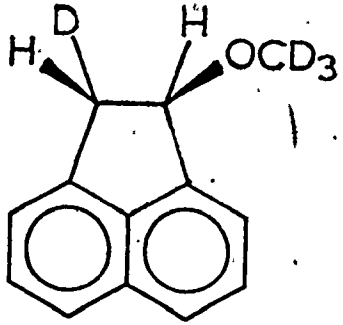
Analysis of recovered ether substrate and elimination product, acenaphthylene, for deuterium label would indicate the ratio of cis and trans exchange and elimination, respectively. The terms cis and trans (rather than syn and anti) will be used throughout to designate the geometrical relationship of the proton (or deuteron) to the methoxyl group in both exchange and elimination processes for the 1-methoxyacenaphthene system (see Figure 35).



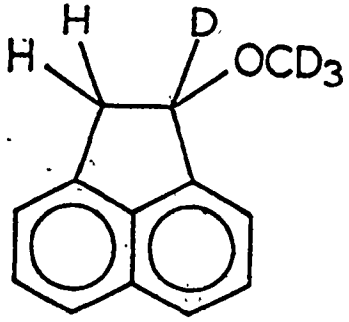
1



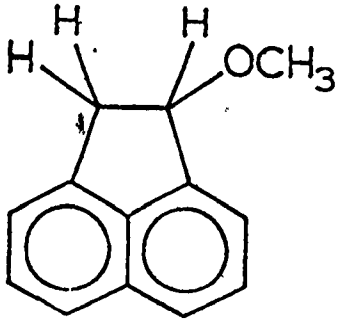
cis-2



trans-2



α-2



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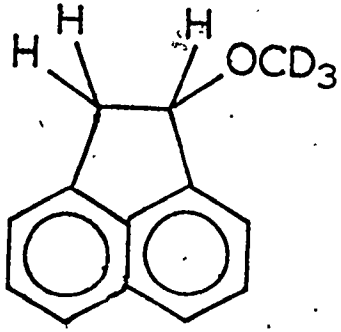

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Figure 35 - Deuterium Labelled 1-Methoxyacenaphthenes

2.2 Syntheses

As a first step towards the study of exchange and elimination processes in the 1-methoxyacenaphthene system, 1-methoxy-d_3-acenaphthene-1,2,2-d_3 (1), (Figure 35), was prepared. This was accomplished by two different routes as shown in Figure 36. The first route involved the preparation of acenaphthene-1,1,2,2-d_4, reaction with N-bromosuccinimide followed by reaction with methanol-d_4.

Acenaphthene-1,1,2,2-d_4 was successfully prepared essentially by the method of Trost (84). Naphthalic anhydride was reduced by lithium aluminum deuteride to $\alpha,\alpha,\alpha^1,\alpha^1$-$d_4$-1,8-di(hydroxymethyl)naphthalene, converted with phosphorus tribromide to the dibromo derivative, $\alpha,\alpha,\alpha^1,\alpha^1$-$d_4$-1,8-di(bromomethyl)-naphthalene and bromine eliminated by means of phenyllithium to give acenaphthene-1,1,2,2-d_4.

The second route to 1 involved the preparation of acenaphthene-1-one-2,2-d_2, reduction with lithium aluminum deuteride to 1-acenaphthenol-1,2,2-d_3 and reaction with methyl iodide-d_3 (85). The deuterated ketone was prepared by Friedel-Crafts acylation of 1-naphthylacetyl chloride to acenaphthene-1-one followed by basic -exchange using deuterium oxide. Acenaphthene-1-one was also prepared from acenaphthylene by peroxide oxidation to 1,2-epoxyacenaphthene (86), followed

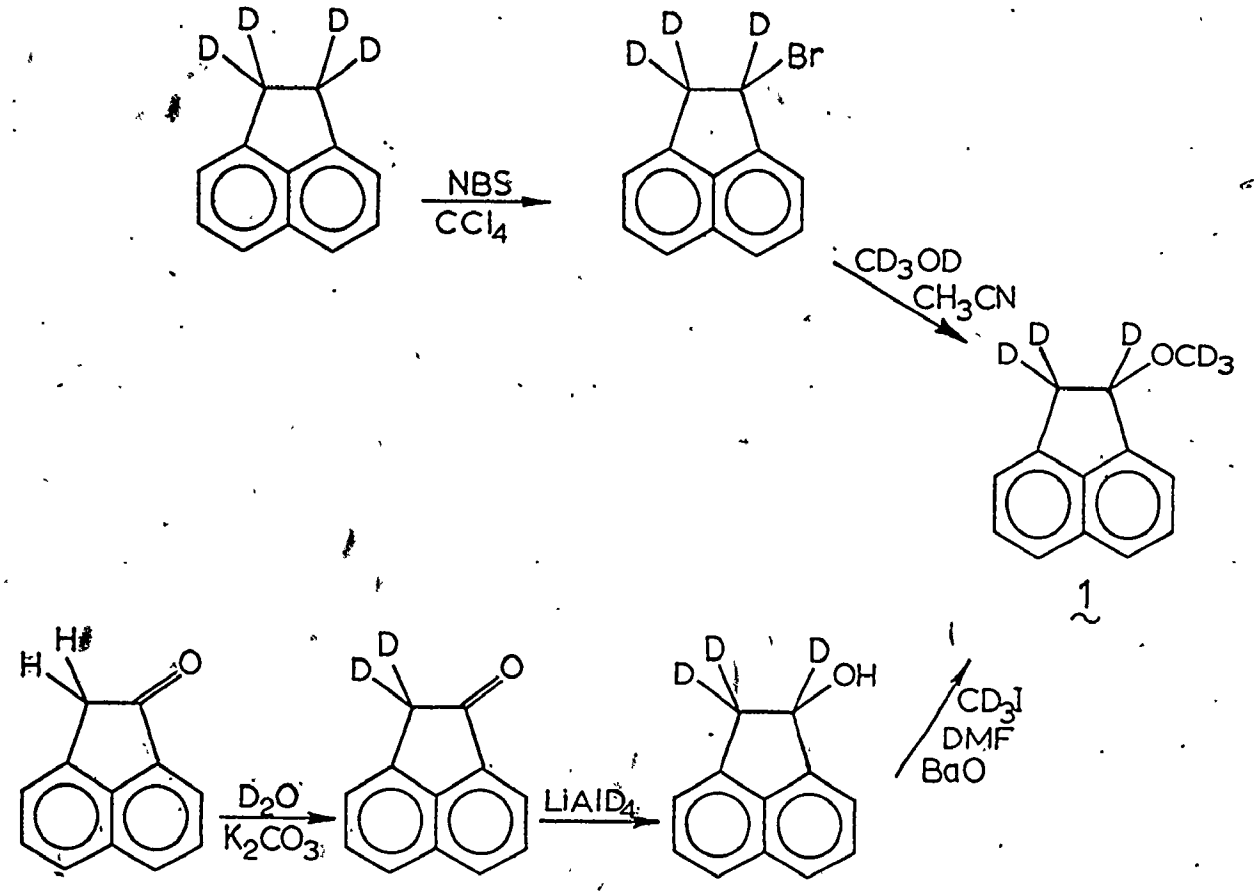


Figure 36 - Synthetic Routes to 1-Methoxy-d_3-acenaphthene-1,2,2-d_3 (1)

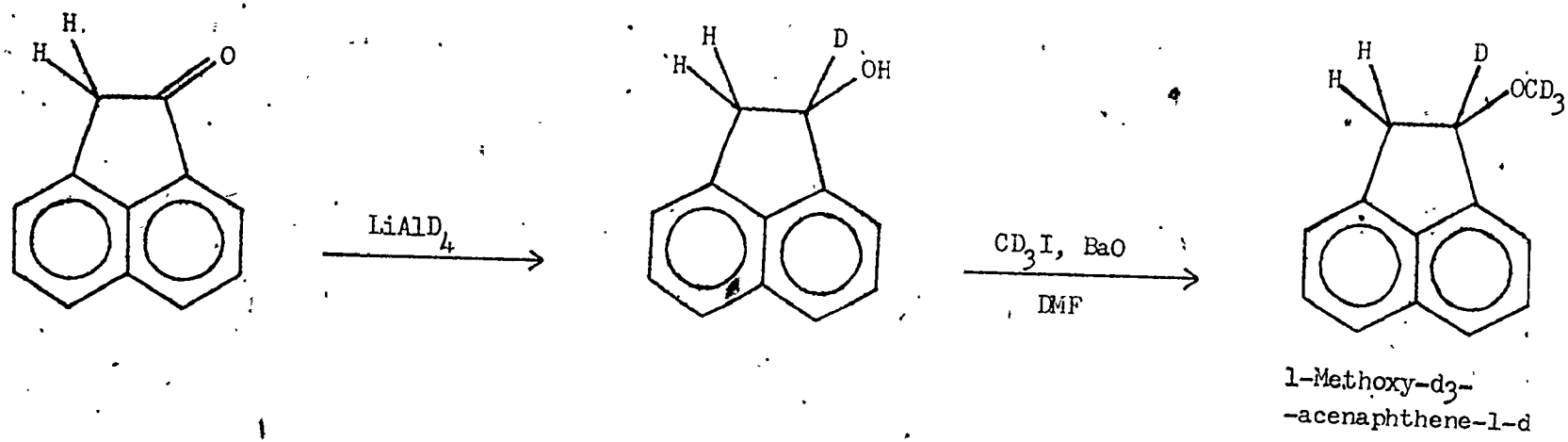
by isomerization to the ketone on silica gel.

1-Methoxy-d_3-acenaphthene-1-d (α-2), (see Figure 35), was prepared by lithium aluminum deuteride reduction of acenaphthene-1-one to 1-acenaphthenol-1-d followed by reaction with methyl iodide-d_3 (see Figure 37).

In an attempt to prepare pure cis-1-acenaphthenol-2-d from acenaphthylene by deuterioboration with trimethylamine--borane-d_3 (87) at 127°, significant deuterium incorporation at all positions occurred including aromatic ring deuteration as described in the Experimental 4.11. Pure cis-1-acenaphthenol--2-d was prepared successfully from acenaphthylene by deuterioboration at 35° using lithium aluminum deuteride and boron trifluoride etherate followed by oxidation with basic hydrogen peroxide (88), (Figure 38).

cis-1-Methoxy-d_3-acenaphthene-2-d (cis-2), (see Figure 35), was prepared from cis-1-acenaphthenol-2-d by reaction with methyl iodide-d_3. trans-1-Methoxy-d_3-acenaphthene-2-d (trans-2), (see Figure 35), was prepared from 1,2-epoxyacenaphthene (86) by reduction with lithium aluminum deuteride followed by reaction with methyl iodide-d_3 (Figure 38).

1-Methoxyacenaphthene (3) and 1-methoxy-d_3-acenaphthene (4) were prepared by reaction of 1-acenaphthenol with methyl iodide



1-Methoxy-d_3-
-acenaphthene-1-d

Figure 37 - Synthetic Route to ∝-2

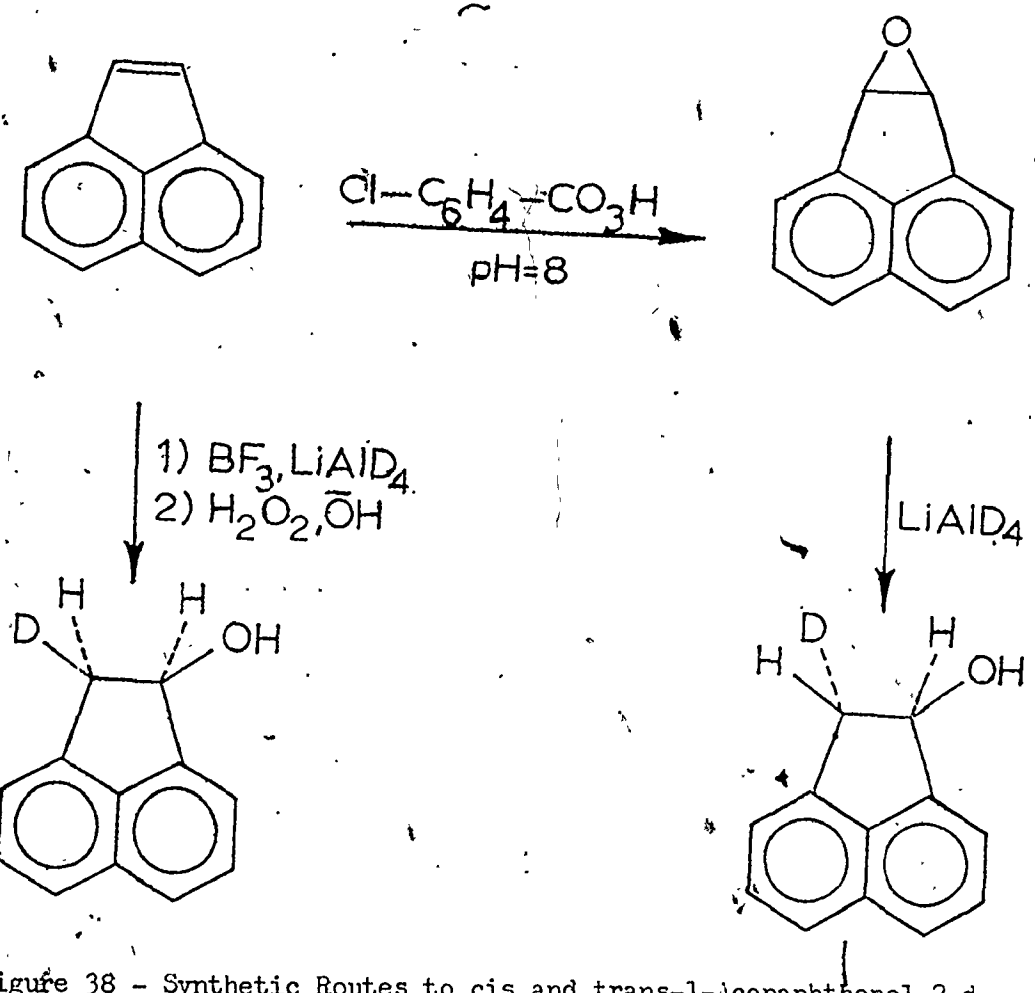


Figure 38 - Synthetic Routes to cis and trans-1-Acenaphthenol-2-d

and methyl iodide-d_3 respectively (see Figure 35).

2.3 Nmr Proton Assignments

The hydrogen-deuterium exchange reaction of 1-methoxy-d_3-acenaphthene-1,2,2-d_3 (1) in protic solvents was monitored by the rate of appearance of broadened singlets due to cis and trans β-protons by nmr spectroscopy (1a). This method is much simpler than following the changes in complex patterns using 4 and deuterated solvent especially when small percentages of isotopic exchange have occurred.

The three protons at the α and β positions in 3 were assigned using three consistent pieces of evidence. The first assignment was on the basis of coupling constants and relative chemical shifts (89) obtained by an ABX analysis of the proton nmr spectrum of 4 ($\delta_{cis-\beta}$=3.14 ppm; $\delta_{trans-\beta}$=3.36 ppm; δ_{α}=5.14 ppm; $J_{cis-\beta, trans-\beta}$=-17.7 Hz; $J_{\alpha, cis-\beta}$=2.6 Hz; $J_{\alpha, trans-\beta}$=7.1 Hz) obtained with decoupling of the appropriate ring protons. The methoxyl-d_3 group proved essential throughout this study because of the unfortunate overlapping of the methoxyl signal and the signal of the β-protons.

The second assignment involved the stereoselective synthesis of cis-2 as shown in Figure 38 (see Experimental 4.11). Analogously the third assignment consisted in the stereoselective synthesis of trans-2 (Figure 38), (see Experimental 4.12).

2.4 Exchange Results

In an attempt to assess the stereoselectivity of exchange under basic conditions of the deuterons β to the methoxyl-d_3 group, the substrate 1 was treated with selected base-solvent pairs. With the chemical shifts of the bridge protons assigned, recovered substrate could be analyzed for the ratio of cis and trans β-protons by nmr integration and for α-protons, which were always near zero. Low voltage mass spectrometry then allowed more complete analysis of recovered ethers into 1, 1-methoxy-d_3--acenaphthene-cis-1,2-d_2 (cis-5) and 1-methoxy-d_3-acenaphthene--trans-1,2-d_2 (trans-5), (see Figure 39).

Formation of the elimination product, acenaphthylene, occurred concurrently with exchange and the percentage was estimated by gas chromatographic (glpc) analysis. Its deuterium content also was analyzable by mass spectrometry. Figure 39 summarizes the species involved and the likely interconversions that are occurring.

Two solvents were chosen for study, tert-butyl alcohol and methanol. The corresponding alkoxides were used as bases and in the case of tert-butyl alcohol, the counterion was varied: lithium, potassium, cesium, potassium complexed with dicyclohexyl--18-crown-6 ether (crown ether) (90 - 96) and tetramethylammonium.

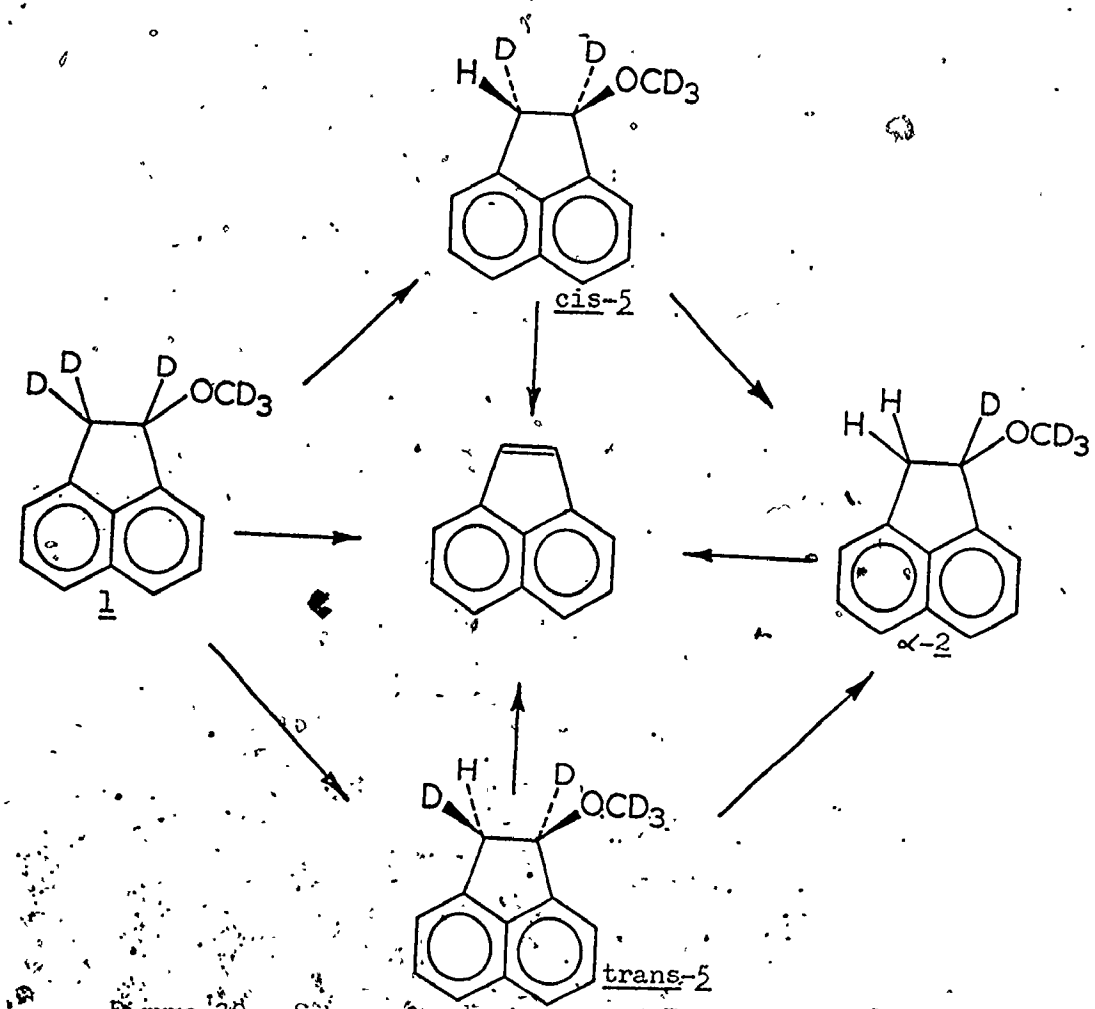


Figure 39 - Scheme for Exchange and Elimination of 1

Table 3 contains the calculated percentages of 1, cis-2 and trans-2 present in the reaction mixture. To facilitate comparison, the results for each run have been further organized by listing also in Table 3 the relative rate of exchange and elimination (Ex./Elim.) which is defined as :

$$\frac{\text{Exchange}}{\text{Elimination}} = \frac{\text{fraction ether exchanged}}{\text{fraction olefin produced}}$$

$$= \frac{\dfrac{\%\text{cis-2} + \%\text{trans-2} + 2\%\alpha\text{-2}}{2(\%\text{ total ether})} \times 100}{\%\text{ olefin}}$$

$$= \frac{\%\text{cis-2} + \%\text{trans-2} + 2(\%\alpha\text{-2})}{(\%\text{ olefin})\ 2(\%\text{ total ether})} \times 100$$

The relative rate of cis and trans exchange in the recovered ether are also summarized under the heading k_{cis}/k_{trans} which is defined as :

$$k_{cis}/k_{trans} = \frac{\log\left(1 - \dfrac{\%\text{cis-2} + \%\alpha\text{-2}}{\%\text{ total ether}}\right)}{\log\left(1 - \dfrac{\%\text{trans-2} + \%\alpha\text{-2}}{\%\text{ total ether}}\right)}$$

This was derived assuming pseudo first-order kinetics as follows:

$$k = \frac{1}{t} \ln \frac{(a)}{(a-x)}$$

$$k_{\underline{cis}} = \frac{1}{t} \ln \frac{(1)}{(1\text{-fraction of } \underline{cis} \text{ protons})}$$

$$k_{\underline{trans}} = \frac{1}{t} \ln \frac{(1)}{(1\text{-fraction of } \underline{trans} \text{ protons})}$$

$$k_{\underline{cis}}/k_{\underline{trans}} = \frac{\log (1\text{-fraction of } \underline{cis} \text{ protons})}{\log (1\text{-fraction of } \underline{trans} \text{ protons})}$$

2.5 Effect of Cation on the Reaction Rate

As can be seen in Table 3, the change of cation for tert-butoxide in tert-butyl alcohol from lithium to tetramethylammonium (runs 10 and 19) required a temperature increase of 115° which corresponds to an increase in rate of elimination of about 10^4. Since ion pairing (97 - 99) is common in tert-butyl alcohol, the variation in elimination rate with cation indicates that lithium, potassium and cesium tert-butoxide must exist primarily as ion pairs or aggregates in tert-butyl alcohol.

TABLE 3

Effect of Counterion on Relative Exchange and Elimination Rate of 1

Run	Temp. (°C)	Base Conc.(M)	Time (min.)	Mole% Olefin	Ether Mole%	%1	%trans-5	%cis-5	%2	Ex./Elim.	k_{cis}/k_{trans} Exchange
i) Potassium tert-butoxide in tert-butyl alcohol											
1	85.0 ± 0.1	0.43 ± 0.01	90 ± 1	10 ± 1	90 ± 1	71 ± 1	6 ± 1	13 ± 1	0 ± 2	1.1 ± 0.3	2.1 ± 0.4
2	85.0	0.43	188	23	77	44	10	19	4	1.0 ± 0.2	1.8 ± 0.2
3	85.0	0.43	500	57	43	11	4	18	10	0.8 ± 0.2	2.6 ± 0.2
4	85.0	0.43[a]	135	17	83	-	-	-	-	1.3 ± 0.2	2.1 ± 0.2
5	85.6	0.022 ± 0.001	1830	8	92	67	6	16	3	1.9 ± 0.6	2.3 ± 0.3
6	65.0	0.37 ± 0.01	700	4	96	64	8	19	5	4.8 ± 1.9	1.9 ± 0.3
7	65.0	0.37	1600	10	90	57	7	20	6	2.2 ± 0.6	2.2 ± 0.3
8	60.0	0.021[b] ± 0.001	107	8	92	65	15	6	6	2.2 ± 0.6	0.56 ± 0.07

TABLE 3 (contd.)

Run	Temp. (°C)	Base Conc. (M)	Time (min.)	Mole% Olefin	Ether Mole%	Ether %1	Ether %trans-5	Ether %cis-5	Ether %2	Ex./Elim.	k_{cis}/k_{trans} Exchange
9	45.0	0.021[b]	1818	4	96	73	13	8	2	3.2 ± 1.4	0.62 ± 0.10
ii) Lithium tert-butoxide in tert-butyl alcohol											
10	160 ± 1	0.14 ± 0.01	1010	34[c]	66	50	0.3	15.5	0	0.35 ± 0.1	45 ± 23
11	160	0.14	1900	51[c]	49	30	1.0	18.0	0	0.38 ± 0.1	22 ± 6
12	160	0.14	4023	76[c]	24	7	0.0	15.0	2	0.52 ± 0.2	22 ± 4
iii) Cesium tert-butoxide in tert-butyl alcohol											
13	85.6 ± 0.1	0.20	37	11	89	54	15	14	6	2.1 ± 0.5	0.92 ± 0.1
14	85.6	0.20	124	30	70	22	16	16	15	1.5 ± 0.2	1.00 ± 0.1
15	85.6	0.20	241	54	46	6	11	8	20	1.2 ± 0.1	0.95 ± 0.1

TABLE 3 (contd.)

Run	Temp. (°C)	Base Conc.(M)	Time (min.)	Mole% Olefin	Ether Mole%	%1	%trans-5	%cis-5	%α-2	Ex./Elim.	k_{cis}/k_{trans} Exchange
iv) Tetramethylammonium tert-butoxide in tert-butyl alcohol											
16	44.8	0.11	100	6	94	67	21	6	0	2.4 ± 0.8	0.26 ± 0.04
17	44.8	0.11	500	9	91	55	25	9	2	2.3 ± 0.6	0.37 ± 0.05
18	44.8	0.11	4842	8	92	54	26	10	2	2.7 ± 0.7	0.40 ± 0.05
19	44.9	0.11	319	24	76	21	36	8	11	1.8 ± 0.2	0.34 ± 0.03
v) Potassium methoxide in methanol											
20	150.3	0.40	200	8[c]	92	-	-	-	-	3.0 ± 0.7	1.00 ± 0.1
21	150.3	0.40	810	30[c]	70	-	-	-	-	1.7 ± 0.1	1.00 ± 0.1

a) 0.06 M in potassium acetate
b) Added equivalent of dicyclohexyl-18-crown-6 ether
c) Extensive loss of product due to side reactions

Ion pairing also is suggested by conductance experiments (100, 101); sodium tert-butoxide changes the conductivity of tert--butyl alcohol only slightly whereas benzyltrimethylammonium salts appear significantly dissociated. Addition of crown ether to potassium tert-butoxide in tert-butyl alcohol also increases the conductivity considerably (102).

Kinetics of some hydrogen-deuterium exchange reactions are consistent with aggregation (103); kinetic order in added potassium tert-butoxide is found to be greater than one (~1.5). Kinetics of dehydrohalogenation of vic-dihaloalkanes and vic-dihalocycloalkanes with potassium tert-butoxide in low polarity solvents also indicate aggregation of the base (104).

The effect of ion pairing on kinetic basicity is also illustrated by the effect of added crown ether on the reaction catalyzed by potassium tert-butoxide in tert-butyl alcohol (runs 5 and 8 of Table 3). The rate of elimination was increased by a factor of about 300 as was the rate of exchange when an equivalent of crown ether was added. The catalytic effect of crown ether because of ion pairing in tert-butyl alcohol has been reported for other systems (26c, 105 - 108). In contrast to results in tert-butyl alcohol, added crown ether had no significant effect on the rates of the reactions run in methanol implying that potassium methoxide is predominantly dissociated in methanol (85).

The reaction in methanol and with lithium tert-butoxide in

tert-butyl alcohol was complicated by side reactions. At these temperatures (150°-160°), the acenaphthylene formed reacts competitively to form products of yet unknown composition, (see Experimental 4.15).

The instability of the tetramethylammonium tert--butoxide solutions in tert-butyl alcohol, (see Experimental 4.14) made rate constant measurements impossible but comparison within a run should be valid (e.g. k_{cis}/k_{trans} exchange; or Exchange/Elimination).

2.6 Effect of Cation on the Exchange Stereochemistry

In order to determine the relative rates of exchange and elimination and the relative rates of cis and trans exchange with greater precision, in several cases the individual values in Table 3 were extrapolated to zero percentage reaction and extrapolated values are shown in Table 4. Of the two ratios, the k_{cis}/k_{trans} exchange ratio did not change very significantly with percentage of reaction and thus extrapolated values are not very different from the observed values. However, it is expected that, as a result of the definition in which deuterium isotope effects are neglected, the ratio Exchange/Elimination would be sensitive to extent of reaction and thus extrapolated values are not highly significant. These are used merely as an indication of the competition between the exchange and elimination processes.

TABLE 4

Relative Exchange and Elimination Rates[a] for 1

Runs	Base[b]	T (°C)	Ex./Elim.	Exchange k_{cis}/k_{trans}
10 - 12	Li Ot-Bu	160	0.3 ± 0.1	31 ± 6
1 - 3	KOt-Bu	85	1.2 ± 0.3	1.6 ± 0.2
6, 7	KOt-Bu	65	7 ± 2	1.6 ± 0.3
13 - 15	Cs Ot-Bu	86	2.0 ± 0.5	1.0 ± 0.1
16 - 19	$(CH_3)_4$ NOt-Bu	45	2.8 ± 0.8	0.30 ± 0.05
8	KOt-Bu[c]	60	2.2 ± 0.6	0.56 ± 0.1
9	KOt-Bu[c]	45	3.2 ± 1.4	0.62 ± 0.1
20, 21	$KOCH_3$	150	3.4 ± 0.7	1.0 ± 0.1

a) Extrapolated to zero time when more than one run involved
b) The solvent is the alcohol corresponding to the base
c) With added equivalent of dicyclohexyl-18-crown-6 ether.

As the results summarized in Table 4 indicate, the stereochemistry of the hydrogen-deuterium exchange reaction is also markedly affected by the nature of the cation. The stereochemical selectivity changes from exclusive cis exchange with lithium to preferential trans with either tetramethylammonium or potassium-crown ether counterions. The rate of cis exchange has changed by a factor of at least 90 relative to trans exchange.

Since the large reactivity differences upon changing the cation necessitated a change of temperature, the effect of temperature change on the exchange stereochemistry was also investigated. With both potassium tert-butoxide at 85°and 65° and potassium tert-butoxide-crown ether at 60° and 45°, no discernable change in the relative rates of cis and trans exchange was noted. Thus, the change in stereoselectivity of the exchange process seems primarily related to the cation present in solution.

Both potassium tert-butoxide and cesium tert-butoxide show stereoselectivity intermediate between lithium and tetramethyl--ammonium tert-butoxides. The possibility that this intermediate stereoselectivity represented a competition between two or more active base species (109, 110), one reacting with highly selective cis exchange (e.g. associated base) and one with preferential trans exchange (e.g. dissociated base), was investigated in two ways

using potassium tert-butoxide in tert-butyl alcohol. In one experiment the base concentration was changed by a factor of 20 (run 1-3 and 5 in Table 3) and in the other (run 4 in Table 3) potassium acetate (0.06M) was added resulting in no observable change in the k_{cis}/k_{trans} exchange rate ratio. Since either dilution or added common ion would be expected to alter the proportions of two species having different extents of association, it would appear that the intermediate stereoselectivities are characteristic of one reactive base species in solution.

Potassium methoxide in methanol showed no preference for cis exchange over trans exchange and added crown ether produced no change in the exchange rates (85). Thus, it would appear that dissociated methoxide ion is the active base in methanol and shows little selectivity between the diastereotopic deuterons at the β-position of 1.

2.7 Model for the Exchange Reaction

The sensitivity of the rates of the exchange and elimination reactions to the cation in solution requires that the tert-butoxide salts of lithium, potassium and cesium exist in solution as ion pairs or aggregates. The sensitivity of the k_{cis}/k_{trans} ratio to cation requires that these cations also be present in the intermediates responsible for hydrogen-deuterium exchange. Thus, the salts of

lithium, potassium and cesium would appear to exist and also react as ion pairs or aggregates.

It is tempting to postulate a specific role for the cations since the changes in preference for cis exchange parallels the expected solvation energies (111, 112) of these cations in tert-butyl alcohol. In the postulated intermediate for cis exchange (Figure 40) the cation is bonded to the ether oxygen of 1, while in the intermediate for trans exchange, this bonding interaction is absent. Bonding between substrate and the cation present in the base ion pair would serve to lower the activation energy for cis deuteron removal and for reprotonation on the cis side. As this bonding interaction becomes stronger ($Li^+ > K^+ > Cs^+$) the preference for cis reaction increases.

The observation of preferential trans exchange with crown ether-potassium tert-butoxide seems consistent with this type of interpretation as does the result using tetramethylammonium cation. For both these cations bonding to substrate should be greatly reduced although the active base may still be ion pairs. Ion pairing is suggested since potassium-crown ether and tetramethyl--ammonium ions do show somewhat different exchange preferences.

The stereochemistry of the exclusive cis isotopic exchange reaction with lithium tert-butoxide can be deduced from the relative

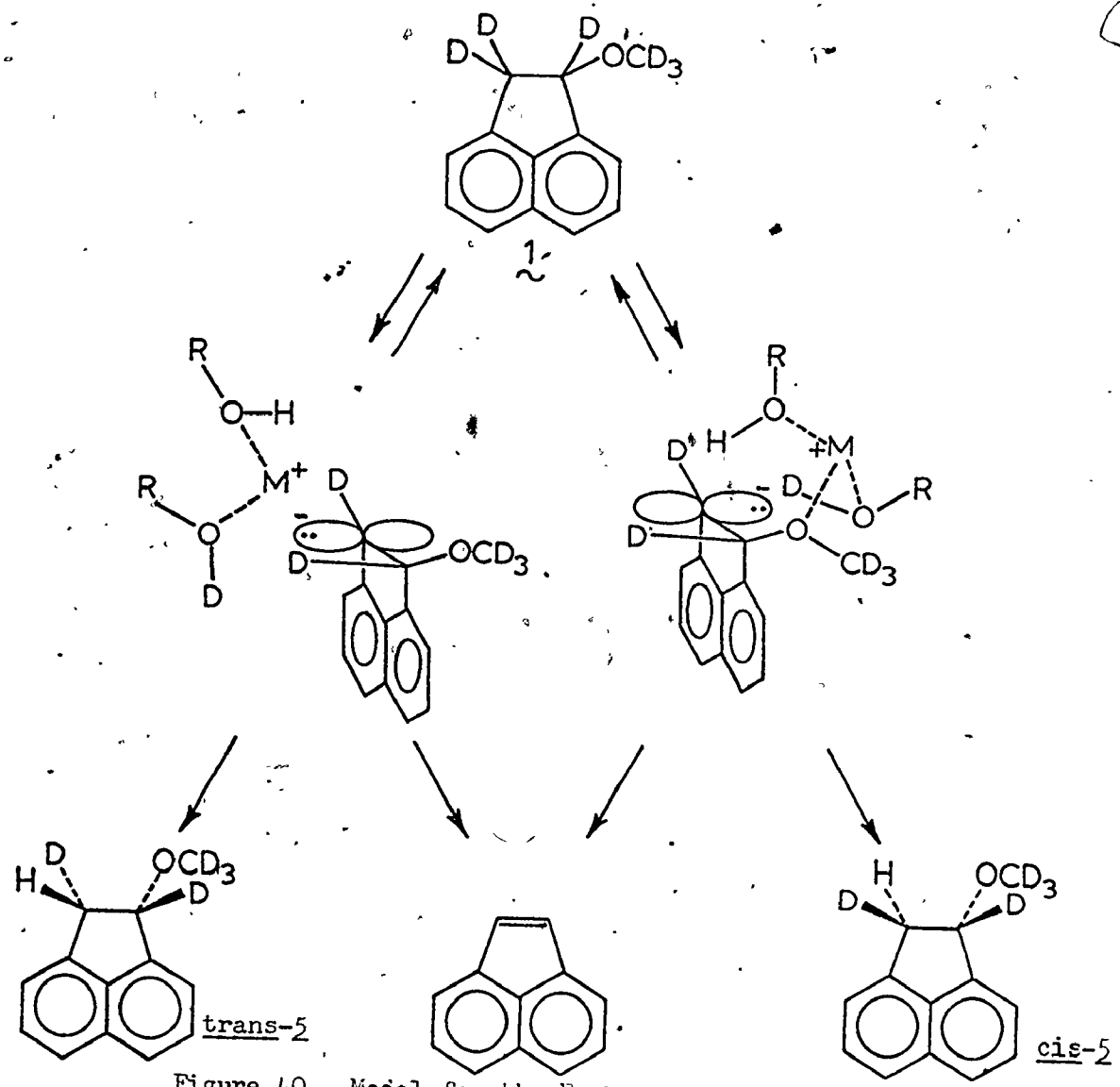


Figure 40 - Model for the Exchange Reaction of 1

rates at which cis-5 and α-2 are produced (Figure 39). Exchange of the cis deuteron with retention would yield cis-5 as the only product; α-2 would arise only through removal of trans deuterons or by involvement of an inversion component. Exchange of the cis deuteron with inversion would require selective removal from the backside of 1 and selective protonation of the front side to form cis-5. However, this would lead to further exchange of cis-5 and the rapid production of α-2. As can be seen in runs 10 - 12 in Table 3, α-2 is being produced at a rate much slower than cis-5. This is consistent only with a retention mechanism. The results with the other cations are not as readily interpretable in terms of retention and inversion components.

The stereoselectivity of these exchange reactions has been interpreted as primarily due to asymmetry induced by the substrate on its environment rather than reflecting the preferential stability of the ion pairs themselves. Even with potassium methoxide in methanol, where it seems methoxide itself is the active base, it is not clear that the relative rates of exchange ($k_{cis}/k_{trans}=1$) reflect "pure" carbanion stabilities. Exchange of diastereotopic protons α to a sulphoxide grouping provides other examples of this phenomenon. While it is possible to interpret relative rates of exchange in terms of preferred carbanion stability (80), again there are now several examples of marked changes in the relative reactivity of diastereotopic protons (113, 114). Thus, it would appear that assignment of carbanion stabilities should be made with caution.

CHAPTER 3

ELIMINATION STUDY

3.1. Elimination Results

Compound 1 was not an appropriate substrate for the elimination study since usually four differently labelled ethers were present in varying amounts during the reaction course. This made interpretation of the deuterium composition of the recovered acenaphthylene nearly impossible. Thus cis-2 and trans-2 were chosen as substrates (see Figure 35).

Since exchange accompanies elimination, the isotopic composition of ether substrate can change significantly during the course of the elimination reaction. The change in isotopic labelling can be minimized by appropriate choice of either cis-2 or trans-2 as substrate. Thus, for a medium where cis exchange dominates, trans-deuterated material, trans-2, was used (and vice-versa for trans).

In an attempt to assess the stereochemistry of the elimination processes, the appropriate ether, cis-2 or trans-2, was treated in alcohol-alkoxide media chosen to complement the exchange study of 1. As illustrated in Figure 41, if prior exchange of cis-2 or trans-2 is not extensive, the stereochemistry of the elimination process can be determined from the isotopic composition of isolated acenaphthylene. To minimize errors due to exchange,

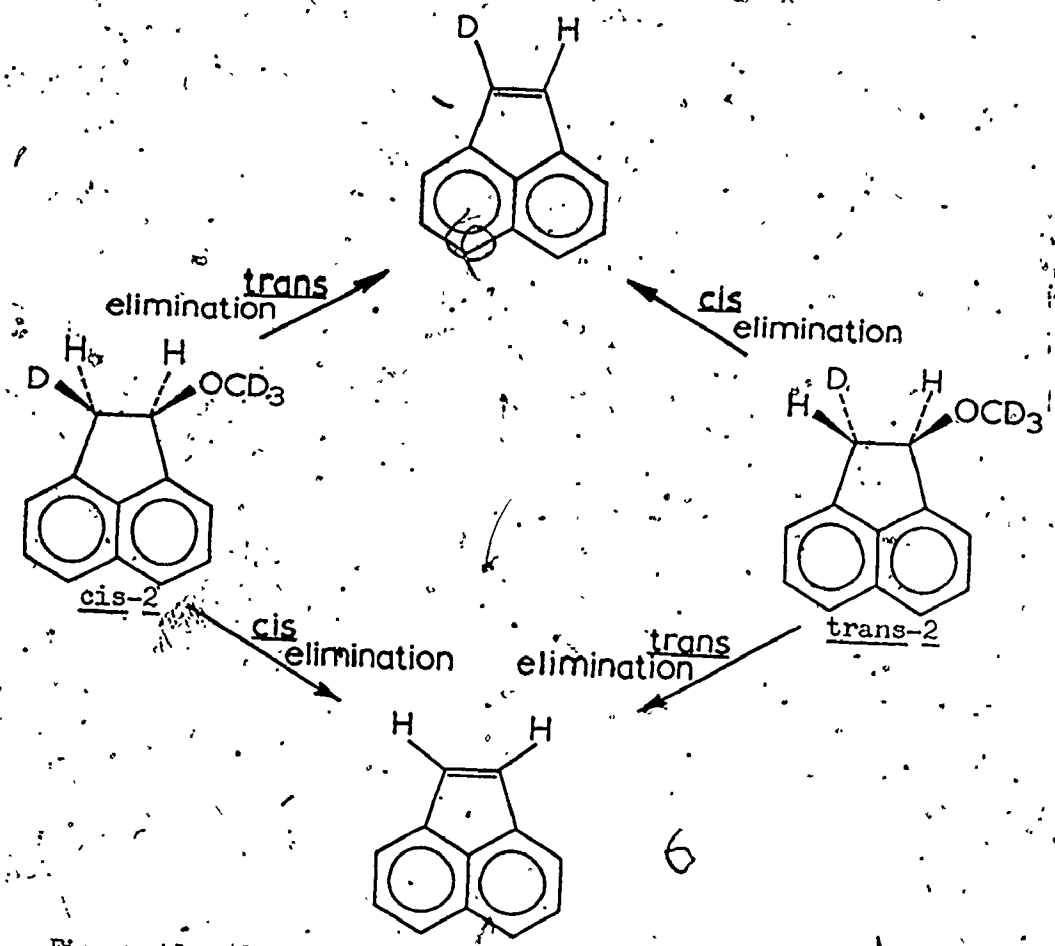


Figure 41 - Scheme for Elimination of cis-2 and trans-2

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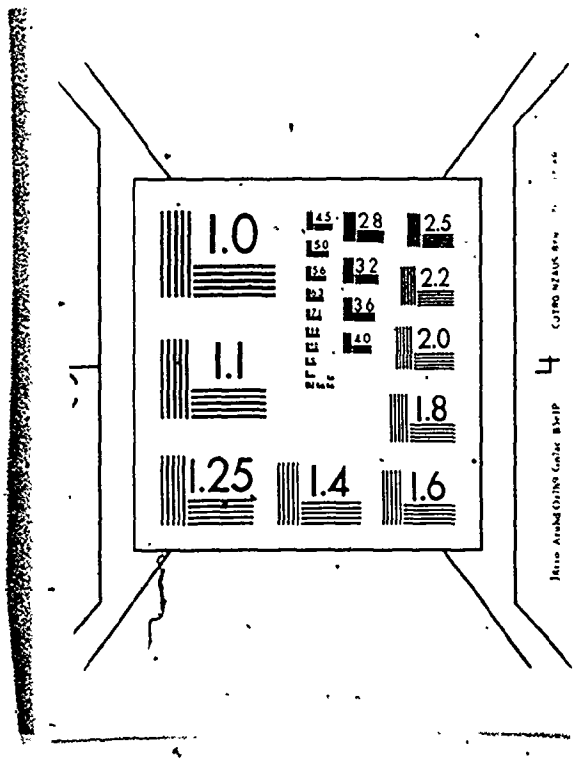

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the elimination reaction was run to varying extents (glpc analysis). The ether and olefin were separated by elution chromatography, and both recovered ether and olefin were analyzed for exchange by nmr and mass spectrometry.

Table 5 contains the calculated percentages of olefin, 4, α-2, cis-2 and trans-2 present in the reaction mixture after trans-2 was treated with base. Table 6 contains the calculated percentages of olefin, 4, cis-2 and trans-2 present in the reaction mixture after cis-2 was treated with base.

It was demonstrated that acenaphthylene does not exchange significantly under the elimination reaction conditions with potassium tert-butoxide in tert-butyl alcohol. Exchange at the 1- and 2-positions occurred with a rate constant per deuteron of 10^{-4} mol^{-1} sec^{-1} at 150.5°. This roughly corresponds to a rate difference of 10^{3} between acenaphthylene exchange and elimination of 1-methoxyacenaphthene.

In the runs at higher temperature, lithium tert-butoxide and potassium methoxide at 152.4°, recoveries of olefin were low. Using dibenzyl as an internal standard for glpc analysis, it appeared acenaphthylene rather than substrate was being lost as described in the exchange study. A sample of partially deuterated acenaphthylene also was subjected to the same reaction conditions

TABLE 5

Effect of Counterion on Relative Elimination Rates of trans-2

Run	Temp. (°C)	Base Conc. (M)	Time (min.)	Olefin				Ether					k_{d_0}/k_{d_1}
				Mole %	$\%d_0$	$\%d_1$	$\%d_2$	Mole%	$\%_4$	$\%\alpha$-2	$\%$(cis-2 + trans-5)	$\%$(trans-2 + cis-5)	
i) Potassium tert-butoxide in tert-butyl alcohol													
22	85.6 ± 0.1	0.43 ± 0.01	74 ± 1	15 ± 1	2.0 ± 0.1	12.5 ± 0.4	0.5 ± 0.1	85 ± 1	13 ± 1	1 ± 2	2 ± 11	69 ± 8	0.168 ± 0.007
23	85.6	0.43	182	32	6.0 ± 0.2	25 ± 1	1.0 ± 0.2	68	15 ± 1	5 ± 2	1 ± 8	47 ± 5	0.228
24	85.6	0.43	330	50	12.5 ± 0.3	37 ± 2	1.5 ± 0.3	50	15 ± 1	5 ± 2	1 ± 5	29 ± 3	0.310
25	65.0	0.37	38,800	>99.7	43.0	54.0	2.7	<0.3	-	-	-	-	0.790 ± 0.017
26	65.0	0.37	38,800	>99.7	43.6	54.0	2.2	<0.3	-	-	-	-	0.805
27	65.0	0.37	585	5	0.6	4.0	0.1	95	-	-	-	-	0.162 ± 0.007
ii) Lithium tert-butoxide in tert-butyl alcohol													
28	152.4	0.14	462	21[a]	2.0	18.0	1.0	79	6	9	15	49	0.090
29	152.4	0.14	1020	40[a]	4.0	35.0	1.0	60	6	6	0	49	0.115
30	152.4	0.14	1535	50[a]	6.0	43.0	1.0	50	5	7	0	38	0.141

TABLE 5 (contd.)

Run	Temp. (°C)	Base Conc.(M)	Time (min.)	Olefin Mole %	Olefin %d_o	Olefin %d_1	Olefin %d_2	Ether Mole%	Ether %4	Ether % α-2	Ether %(cis-2 + trans-5)	Ether %(trans-2 + cis-5)	%d_o/%d_1
iii) Cesium tert-butoxide in tert-butyl alcohol													
31	85.6	0.22	31	15	3	11.5	0.5	85	17	8	0	60	0.276
32	85.6	0.22	104	40	13	26	1.0	60	26	7	3	24	0.508
33	85.6	0.22	149	52	21	30	1.0	48	24	6	4	14	0.702

a) Extensive loss of product due to side reactions
b) % Olefin-d_o = % Acenaphthylene-d_o
% Olefin-d_1 = % Acenaphthylene-d_1
% Olefin-d_2 = % Acenaphthylene-d_2

$$\% d_o/\%d_1 = \frac{\% \text{ Acenaphthylene-}d_o}{\% \text{ Acenaphthylene-}d_1}$$

TABLE 6

Effect of Counterion on Relative Elimination Rates of cis-2

Run	Temp. (°C)	Base Conc. (M)	Time (min)	Olefin Mole %	Olefin %d_o	Olefin %d_1	Olefin %d_2	Ether Mole %	Ether %4	Ether %cis-2	Ether %trans-2	k_H/k_D
i) Potassium tert-butoxide in tert-butyl alcohol												
°34	65.0 ± 0.1	0.37 ± 0.01	50,200 ± 1	>99.7	87.6 ± 0.1	11.8 ± 0.4	0.6 ± 0.1	<0.3	-	-	-	7.4 ± 0.4
35	65.0	0.37	50,200	>99.7	85.9	12.4	1.7	<0.3	-	-	-	6.9 ± 0.3
36	65.0	0.37	734	6 ± 1	4.9	1.2	0.0	94 ± 1	-	-	-	4.2 ± 0.1
37	60.0	0.021[a] ± 0.001	90	12	4.5	7.5	0.0	88	8.3 ± 1	71.0 ± 1	8.9 ± 1	0.60 ± 0.01
38	60.0	0.021[a]	333	16	5.7	10.3	0.0	84	14.0	61.0	9.3	0.57 ± 0.01
39	45.0	0.021[a]	617	5	1.2	3.7	0.1	95	10.9	75.3	8.7	0.32 ± 0.01
40	45.0	0.021[a]	1645	11	3.1	7.9	0.0	89	14.6	63.5	10.6	0.40 ± 0.01
ii) Cesium tert-butoxide in tert-butyl alcohol												
41	85.6	0.20	31	11	7.8	2.6	0.1	89	17.8	64.1	6.8	3.0 ± 0.08

TABLE 6 (contd.)

Run	Temp. (°C)	Base Conc.(M)	Time (min.)	Olefin Mole %	%d_o	%d_1	%d_2	Ether Mole %	4	cis-2	trans-2	k_{d_o}/k_{d_1}
iii) Tetramethylammonium tert-butoxide in tert-butyl alcohol												
42	45.0	0.10	90	10	2.4	7.5	0.1	90	-	-	-	0.32 ± 0.01
43	45.0	0.10	90	8	1.6	6.3	0.1	92	10.4	68.8	12.6	0.26 ± 0.01
44	45.0	0.10	300	20	5.5	14.4	0.1	80	20.1	48.5	11.3	0.38 ± 0.01
45	45.0	0.10	607	29	10.2	18.8	0.0	71	25.1	37.2	8.7	0.54 ± 0.01
iv) Potassium methoxide in methanol												
46	152.4	0.48	45	7[b]	3.3	3.7	0.0	93	19	53	21	0.91 ± 0.02
47	152.4	0.48	150	15[b]	8.4	6.6	0.0	85	38	27	20	1.28 ± 0.03
48	152.4	0.48	350	32[b]	22	9.9	0.0	68	50	9	9	2.22 ± 0.05

a) Added equivalent of dicyclohexyl-18-crown-6 ether
b) Extensive loss of product due to side reactions
c) % Olefin-d_o = % Acenaphthylene-d_o
   % Olefin-d_1 = % Acenaphthylene-d_1
   % Olefin-d_2 = % Acenaphthylene-d_2
   $\%\ d_o/\%d_1 = \dfrac{\%\ \text{Acenaphthylene-}d_o}{\%\ \text{acenaphthylene-}d_1}$

resulting in a significant loss of olefin. However, analysis of recovered acenaphthylene showed that its isotopic composition was unchanged and thus the side reaction(s) will not affect the validity of the elimination experiments.

To make comparisons easier, the elimination results for each run of trans-2 have been further organized by also listing in Table 5 the ratios of % olefin-d_0 to % olefin-d_1. Similarly, for cis-2, the ratios of % olefin-d_0 to % olefin-d_1 are included in Table 6.

The ratios of % olefin-d_0 to % olefin-d_1 were extrapolated to zero time and the intercept used to calculate the ratio k_{cis}/k_{trans} for elimination. Figure 42 shows a typical extrapolation for trans-2 with potassium tert-butoxide in tert-butyl alcohol. The k_{cis}/k_{trans} elimination ratios are listed in Table 7. The exchange results for 1 are included for comparison.

3.2 Simulation of Results

In order to verify the validity of the extrapolation to obtain k_{cis}/k_{trans} for elimination, both the exchange and elimination results for cis-2 and for trans-2 were simulated using the scheme in Figure 43. The mathematical expressions for this kinetic scheme are a simplification of a more complicated scheme described by Hunter and Mair (115). Separately for cis-2 and trans-2 using reasonable relative values for each rate constant

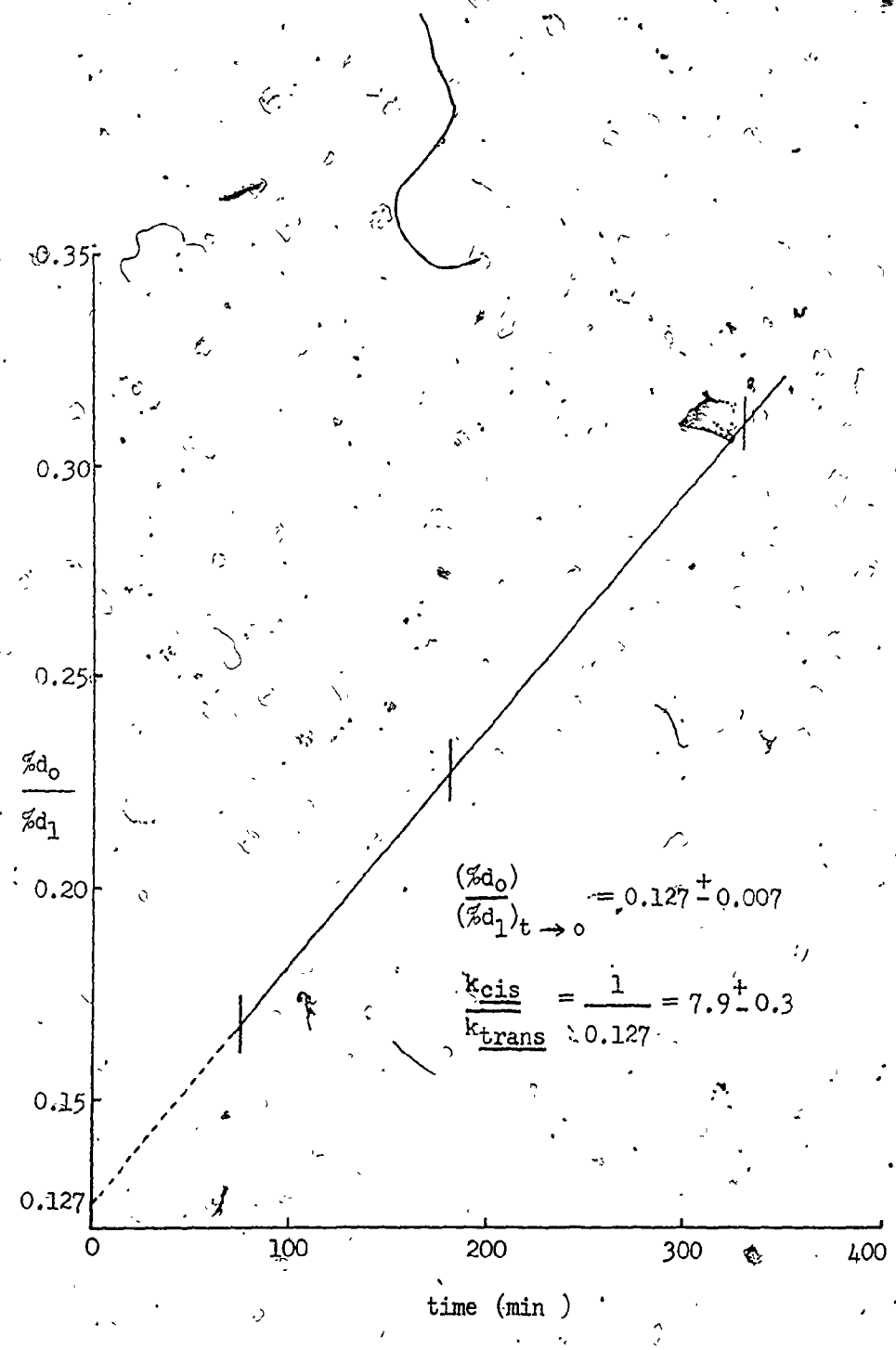

Figure 42 - Extrapolation of % Olefin-d_o to % Olefin-d_1 for trans-2 with Potassium tert-Butoxide

TABLE 7

Effect of Counterion on Relative Elimination Rates of cis-2 and trans-2[a]

Base[b]	T(°C)[c]	Ex./Elim.	Exchange k_{cis}/k_{trans}	Elimination k_{cis}/k_{trans}
LiO*t*-Bu	152	0.3 ± 0.1	31 ± 6	15 ± 1
KO*t*-Bu	86	1.2 ± 0.3	1.6 ± 0.2	7.9 ± 0.3
KO*t*-Bu	65	7 ± 2	1.6 ± 0.3	-
CsO*t*-Bu	86	2.0 ± 0.5	1.0 ± 0.1	6.5 ± 0.1
$(CH_3)_4$NO*t*-Bu	45	2.8 ± 0.8	0.30 ± 0.05	0.20 ± 0.01
KO*t*-Bu[d]	60	2.2 ± 0.6	0.56 ± 0.1	-
KO*t*-Bu[d]	45	3.2 ± 1.4	0.62 ± 0.1	0.25 ± 0.1
$KOCH_3$	152	3.4 ± 0.7	1.0 ± 0.1	0.70 ± 0.05

a) Extrapolated to zero time when more than one run involved
b) The solvent is the alcohol corresponding to the base
c) Temperature of the elimination study
d) With added equivalent of dicyclohexyl-18-crown-6 ether

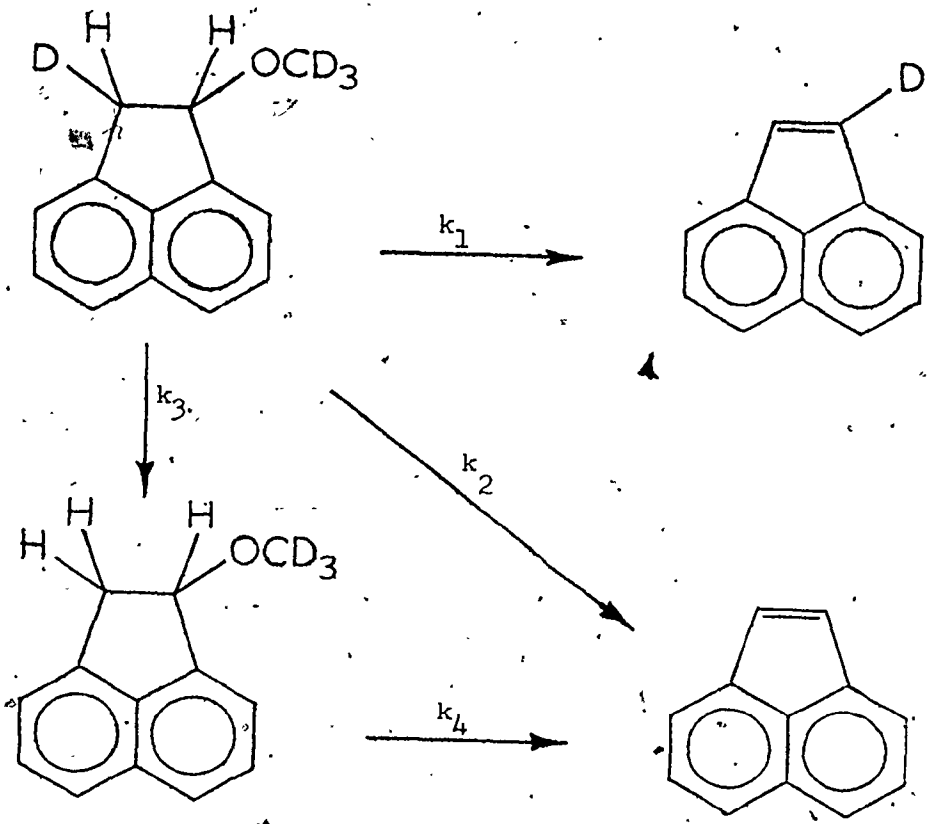

Figure 43 - Scheme for Simulation of Exchange and Elimination Results

as shown in Table 8, and varying each by a factor of four, it was apparent that for the percentages of reaction observed experimentally, the extrapolation should be valid. In all cases the observed olefin and ether compositions fit the experimental results.

The possibility of acenaphthylene arising by an α- elimination mechanism was tested using α-2 with potassium tert-butoxide in tert-butyl alcohol at 85.6° for 90 hours. Recovered acenaphthylene was isolated and analyzed for deuterium showing 97% d_1, ruling out significant contribution by α- elimination.

3.3 Effect of Cation on the Elimination Stereochemistry

As is clear from the results summarized in Table 7, the relative rates of cis and trans elimination varied by about a factor of 75 when the base was changed from lithium to tetramethylammonium tert-butoxide in tert-butyl alcohol. The elimination results using cis-2 and trans-2 roughly parallel the exchange results obtained using 1, with lithium tert-butoxide showing high cis selectivity and both tetramethylammonium and potassium tert-butoxide-crown ether showing preferential trans reaction. Potassium and cesium tert-butoxide show intermediate behavior but with a higher selectivity for cis elimination than for cis exchange. A most dramatic change occurs upon the addition of crown ether to potassium tert-butoxide where k_{cis}/k_{trans} changes by a factor of about 30 from mostly cis elimination to

TABLE 8

Results of Simulation of Exchange and Elimination Results for cis-2 and trans-2

Base[a]	Substrate	k_1	k_2	k_3	k_4
LiOt-Bu[b]	trans-2	0.80	0.054	0.15	1.0
KOt-Bu	trans-2	0.76	0.096	0.57	1.0
CsOt-Bu	trans-2	0.74	0.11	0.93	1.0
$(CH_3)_4NOt$-Bu	cis-2	0.70	0.15	1.23	1.0
KOt-Bu[c,d]	cis-2	0.54	0.26	0.32	1.0
KOt-Bu[c,e]	cis-2	0.59	0.16	0.82	1.0
$KOCH_3$[b]	cis-2	0.46	0.32	1.0[b,f]	1.0

a) The solvent is the alcohol corresponding to the base
b) Extensive loss of product due to side reactions
c) Added equivalent of dicyclohexyl-18-crown-6 ether
d) 60°C
e) 45°C
f) Total exchange and inversion components
g) k_1, k_2, k_3, k_4 as defined in Figure 43

to mostly trans elimination (1C2).

Any direct comparison of exchange and elimination rate ratios requires consideration of kinetic deuterium isotope effects on the elimination processes. As will be discussed in more detail later, kinetic isotope effects were measured for the reaction in tert-butyl alcohol with potassium tert-butoxide (Figure 46 and Table 9). The feature of importance here is the small magnitude of both the primary and secondary isotope effects. Thus, the corrections to the elimination ratios (k_{cis}/k_{trans}) will only be of the order of 20%.

As was detailed earlier, the effect of cation on the exchange rates shows that lithium, potassium and cesium tert-butoxide exist primarily as ion pairs or aggregates in tert-butyl alcohol. Since these cations also affect the relative rates of cis and trans elimination, the cations must also be present in the intermediates or transition states responsible for elimination (41b, 66, 116-119).

3.4 Model for the Elimination Reaction

Since α-elimination has been shown to be unimportant in this system, two types of β- elimination mechanisms seem most likely; ElcB or paenecarbanion E2. The observation of concurrent and parallel carbanion formation strongly suggests an $(ElcB)_R$ mechanism in which the carbanion partitions itself between exchange

and elimination. Positive activation volumes for 1-methoxyacenaphthene with potassium tert-butoxide and potassium tert-butoxide-crown ether in tert-butyl alcohol indicate the presence of an ElcB reaction (120). Thus, the model postulated for the exchange process is readily adaptable to the elimination process as well (figure 44).

Bonding of the cation in the base ion pair to substrate then serves two purposes in the cis intermediate. The barrier to cis proton removal and exchange is reduced and bonding to the methoxyl oxygen should produce a better leaving group. This could account for the higher cis selectivity in elimination than in exchange when potassium and cesium cations are present.

Another way of looking at it is possible when dealing with solvents of low dielectric constant where ion pairing is highly favoured. The cis elimination process results in both the negatively charged leaving group and the cationic center being generated in close proximity. In trans elimination, they are separated by the olefin being produced (i.e. product separated ion pairs), (121). The difference in electrostatic energy between the two processes is then the determining factor.

Although the rationale has been developed around an ElcB model, such charge-dipole interactions could apply equally well to a paenecarbanion E2 or to elimination reactions in general.

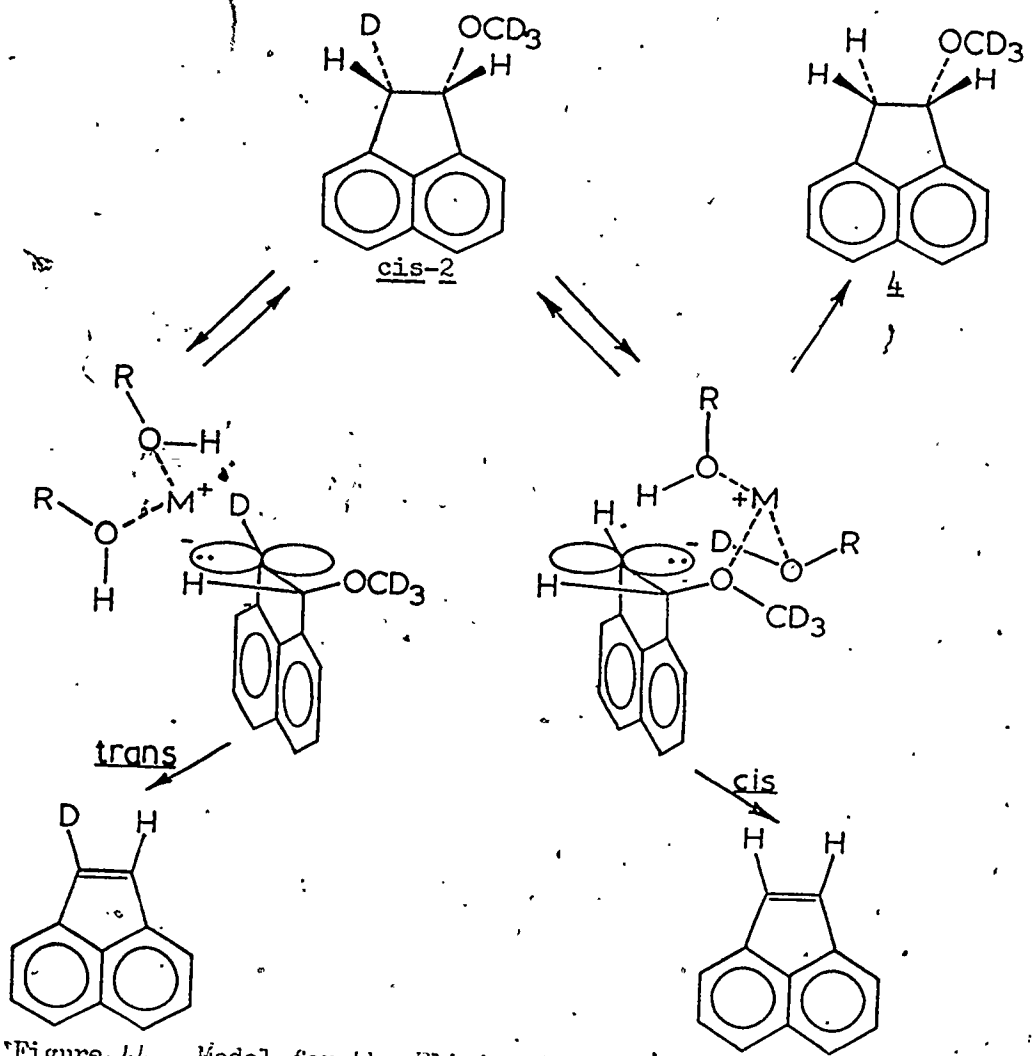

Figure 44 - Model for the Elimination Reaction of cis-2

Thus ion pairing may be of general importance in elimination reactions.

The results with 1-methoxyacenaphthene seem to corroborate a recent explanation for the syn-anti elimination dichotomy based upon ionic association (122-124). The syn-elimination pathway to trans olefin is preferred for acyclic substrates because of simultaneous coordination in the transition state of the metal counterion with the base and leaving group in ion-pairing solvents such as tert-butyl alcohol. The anti pathway to trans olefin has a transition state which is sterically destabilized by the large alkali metal-alkoxide ion pair aggregates present. However, the anti pathway to cis olefin has a transition state which is less affected because the large base can be tilted to that side of the developing double bond where only base-hydrogen interactions occur (125-127), (see Figure 45).

The syn-anti dichotomy for medium-ring compounds has been shown to be caused by ionic association as well as steric accessibility (124, 128, 129). Positional and geometrical orientation in elimination from acyclic substrates also has been shown to be affected by ionic association (124, 130 - 137). Recent studies of β-elimination in the gas phase indicate that ionic association is observed under these conditions as well (138).

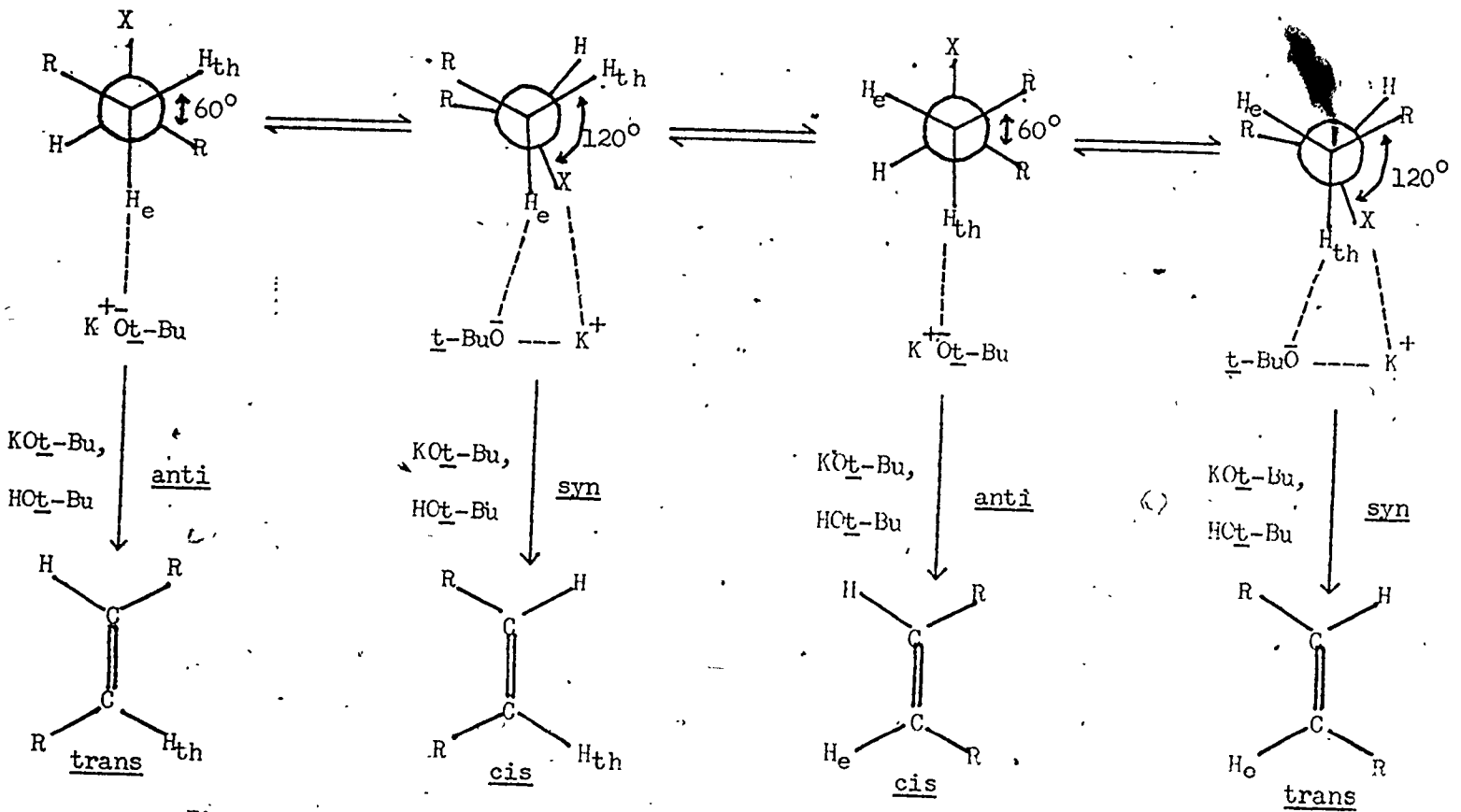

Figure 45 - Explanation of syn-anti Dichotomy Based Upon Ioric Association

3.5 Isotope Effects for cis Elimination

To be able to relate the deuterium content of olefin produced from either cis-2 or trans-2 to the stereochemistry of elimination, it is necessary to know the magnitude of the primary and secondary kinetic deuterium isotope effects on the elimination processes (139 - 141). These were evaluated by comparing the rates of elimination of 4, cis-2, trans-2, α-2, and 1 to 3 with 0.37M potassium tert-butoxide in tert-butyl alcohol at 64.3°. In this medium cis elimination is the major reaction pathway and thus cis-2 should yield the primary isotope effect and the other deuterium labeled compounds will give various secondary isotope effects.

Since exchange at the β-position occurred competitively with elimination, the rate constants were measured at small percentages of reaction ($\leq 3\%$) by following the rate of appearance of acenaphthylene spectrophotometrically. Under these conditions exchange should be minimized. The initial rate constants were converted to kinetic isotope effects by making the individual rates relative to 4. The relative rates are shown in Table 9 and illustrated in Figure 46.

The most striking feature of the kinetic isotope effects on this cis elimination is their low magnitude (142), even the primary isotope effect is only 40%. The observed k_{cis}/k_{trans} ratio

TABLE 9

Kinetic Isotope Effects for 1-Methoxyacenaphthene at 64.3° in 0.37M KOt-Bu-HOt-Bu

Runs	Substrate	$\frac{\text{slope} \times 10^3}{\text{Conc(m)}}$	k(rel)	$k_H(d_0)/k_D$	$k_H(d_3)/k_D$
49 - 51	1	3.04 ± 1.3%	1.00	2.15	1.79 ± 4.2%
52 - 54	α- 2	5.26 ± 5.3%	1.73	1.24	1.04 ± 8.2%
55 - 57	4	5.45 ± 2.9%	1.79	1.20	1.00 ± 2.9%
58 - 60	trans -2	4.64 ± 5.2%	1.52	1.41	1.17 ± 8.1%
61 - 63	cis -2	3.89 ± 3.9%	1.28	1.68	1.40 ± 6.8%
64 - 66	3	6.54 ± 3.8%	2.15	1.00	0.83 ± 6.7%

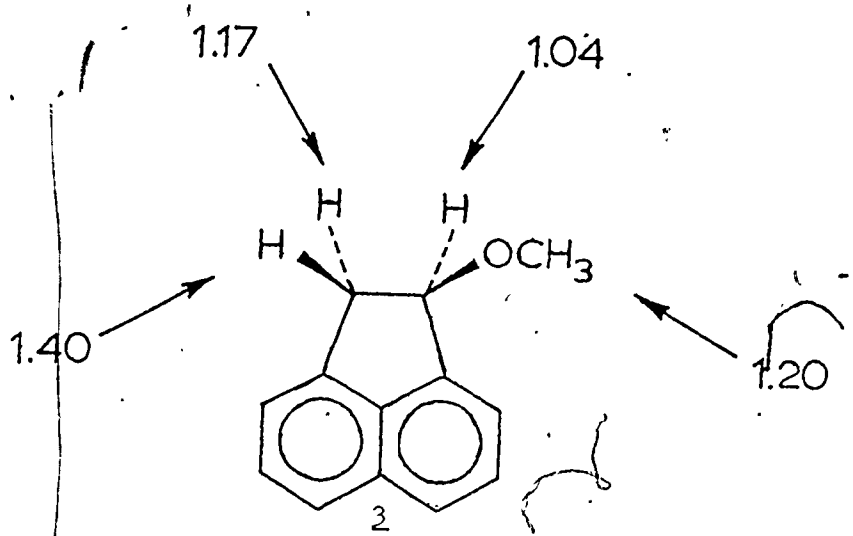

Figure 46 - Kinetic Isotope Effects for Elimination of 3 at 64.3° in 0.37 M KOt-Bu-HOt-Bu

for elimination using cis-2 should then be reduced by a factor of $1.2=\frac{(1.40)}{(1.17)}$ if the trans elimination has a similar pattern of kinetic isotope effects. A primary kinetic deuterium isotope effect of 32 for trans elimination in potassium tert-butoxide on cis-2 in this medium could be obtained indirectly by simulation similar to that illustrated in Table 8.

A second feature of interest is the unique leaving group isotope effect of 20% which can be correlated with an inductive effect. Analogously, trideuterioacetic acid is about 18% less acidic than acetic acid (143).

The observed pattern of isotope effects is certainly consistent with an $(ElcB)_R$ mechanism but a paenecarbanion E2 process cannot be ruled out although such a small primary isotope effect on an E2 reaction is not normally observed (139, 144, 145).

3.6 Relative Rate Constants for the Exchange and Elimination Processes.

The exchange and elimination results for cis-2 and trans-2 in tert-butyl alcohol-potassium tert-butoxide at 65° were analyzed according to the kinetic scheme in Figure 43 assuming each step is of the same order in base. The data obtained for trans-2 allowed a straightforward determination of the rate constants. An approximate value for $k_1/k_2=6.2$ was given by the short elimination time value for olefin-d_1/olefin-d_0 (run 27, Table 5). The ratio, $k_1/(k_2+k_3)=1.25$, was given by the infinite time value (runs 25 and 26) for olefin-d_1/olefin-d_0.

The ratio, $k_4/(k_1+k_2) = 1.17$, is the observed initial elimination rate constant ratio for trans-2 and 4 (see Table 9). Relative rate constants were determined by setting $k_4=1.0$ and yielded $k_1 = 0.74$, $k_2 = 0.12$, $k_3 = 0.47$. The results for cis-2 were similarly analyzed using an approximate value for $k_1/k_2 = 0.24$ (run 36, Table 6), with $k_1/(k_2+k_3) = 0.14$ and $k_4/(k_1+k_2) = 1.40$. Setting $k_4 = 1.0$, yields $k_1 = 0.14$, $k_2 = 0.58$ and $k_3 = 0.41$.

This analysis has two main uses. These rate constants were used as parameters to simulate the reaction profile and to show that the extrapolations are justified. The simulation involved computing expected ether and olefin compositions at various times using a simplified version of a more complex kinetic scheme described by Hunter and Mair (115).

These parameters also provided an estimate of the kinetic deuterium isotope effect for trans elimination. A comparison of k_1 for cis-2 (0.14) and k_2 for trans-2 (0.12) yields a composite of the primary and secondary isotope effect for the β-position of 1.2 for trans elimination. A similar composite isotope effect of 1.3 (0.74/0.58) is obtained for cis elimination and verifies that neither isotope effect is large and that both are of the same magnitude.

3.7 Stereochemistry of the Exchange Process

Two different carbanionic intermediates (cis and trans) have been proposed (Figure 44) to account for the exchange and elimination results for cis-2 and trans-2.

As was discussed earlier, if these two intermediates do not interconvert these exchanges will occur with retention, as interconversion would provide a pathway for inversion. As for 1, such an inversion component could be detected if cis-2 were converted to trans-2 or vice-versa by proton removal and reprotonation on the opposite face.

While conclusions are only qualitative it is interesting to note that when trans-2 was used as substrate, the relative percentage of cis-2 isolated was always lower than in starting material. Similar results were observed with cis-2 as substrate except for methanol-methoxide where significant amounts of interconversion seem to be occurring. It would seem that inversion does not play a major role in tert-butyl alcohol and that two intermediate are involved. Methanol acts as if one carbanionic intermediate (or two equilibrating intermediates) is being produced which reacts with similar ease at both faces of the carbanion. No attempt has been made to make a quantitative analysis of the exchange results but a consistent qualitative picture is apparent.

CHAPTER 4

EXPERIMENTAL

4.1 Reagents and Chemicals

The reagents and chemicals used in the present study were obtained from various commercial sources as indicated below :

Aldrich Chemical Co., Inc., Milwaukee, Wisconsin : acenaphthenequinone, acenaphthylene; m-chloroperbenzoic acid.

Alfa Inorganics, Inc., Beverly, Mass. : 1M borane-tetrahydrofuran solution, calcium hydride, cesium metal, lithium aluminum hydride, phenyllithium solution, sodium hydride oil dispersion.

Anachemia Chemicals Ltd., Montreal, Quebec : anhydrous potassium carbonate, anhydrous sodium bicarbonate, anyhdrous sodium sulphate, anhydrous sodium sulphite, calcium oxide.

Canadian Laboratory Supplies Limited (J. T. Baker) : acenaphthylene, anhydrous potassium acetate, methyl iodide, naphthalic anhydride, potassium dihydrogen phosphate, tetrapropylammonium bromide.

The British Drug Houses (Canada) Ltd., Toronto, Ont. : acetic anhydride, anhydrous sodium carbonate, benzene, N-bromosuccinimide, tert-butyl alcohol, dimethylformamide, magnesium turnings, mercuric chloride, molecular sieves type 4A, petroleum ether 30°- 60°, petroleum ether 60°- 80°, petroleum ether 80°- 100°, phosphorus pentoxide, phosphorus tribromide,

phosphoryl chloride, potassium bicarbonate, potassium hydroxide, potassium metal, silica gel 60 - 120 mesh, sodium chloride, sodium hydroxide, sulphuryl chloride.

Chromatographic Specialties Ltd., Brockville, Ont. : Chromsorb A 40 - 60 mesh, silicone gum rubber SE30.

Commercial Alcohols Limited, Scarborough, Ont. : 95% ethanol

E. I. du Pont de Nemours and Co., Wilmington, Del. : dicyclohexyl-18-crown-6 ether.

Eastman Organic Chemicals, Rochester, N.Y. : acenaphthene, acetonitrile, benzonitrile, boron trifluoride etherate, dibenzyl, tetramethylammonium hydroxide solution, p-toluenesulphonic acid.

Fisher Scientific Co. Ltd. : aluminum chloride, barium oxide, carbon disulphide, carbon tetrachloride, cellulose powder, hydrogen peroxide 30%, hydrogen peroxide 50%, methanol, methylene chloride, mossy zinc, oxalic acid, pyridine, tetrabutylammonium bromide, tetrahydrofuran, thionyl chloride, trimethylamine.

Foote Mineral Company, Exton, Pa. : lithium ribbon

Liquid Carbonic Canadian Corp. Ltd., Toronto, Ont. : argon, nitrogen.

Mallinckrodt Chemical Works Ltd., Pointe Claire, Que. : anhydrous diethyl ether, carbon tetrachloride tech.

Canadian Laboratory Supplies Ltd. (Matheson Coleman and Bell) : 1-naphthaleneacetic acid.

McArthur Chemical Company Ltd., Montreal, Que. : toluene.

E. Merck AG, Darmstadt (Germany) : silica gel 30 - 70 mesh.

Nuclear Magnetic Resonance Specialties, Inc., New Kensington, Pa. : deuteriochloroform, deuterium oxide, tetramethylsilane.

Phillips Petroleum Co., Bartlesville, Okla. : normal pentane tech.

Stohler Isotope Chemicals, Rutherford, N.J. : lithium aluminum deuteride, methanol-d_4, methyl iodide-d_3.

Union Carbide Canada Ltd., Scarborough, Ont. : Ucon lubricant 50-HB-260.

M. Woelm, Eschwege, Germany : acidic alumina, basic alumina, neutral alumina.

Most reagents were freshly distilled or recrystallized before use.

4.2 Melting Points and Boiling Points.

All melting and boiling points are uncorrected. Melting points were taken on a Callerkamp MF-370 instrument.

4.3 Infrared Spectra (ir).

All ir spectra were obtained using an IR 10 double-beam recording spectrometer.

4.4 Mass Spectra (ms).

Mass spectra reported herein were taken on a Varian M-66, double focussing mass spectrometer.

4.5 Nuclear Magnetic Resonance Spectra (nmr).

Nmr spectra were recorded using a Varian HA-100 spectrometer on undegassed samples using field sweep mode. All chemical shifts are expressed in ppm relative to tetramethylsilane (TMS) used as an internal standard. Measurement of the cis β-hydrogen to trans β-hydrogen ratio of the deuterated ethers was made by planimeter integration of the peaks recorded on slow sweep of the δ 3.2 - 3.4 ppm region at a sweep width of 100 Hz.

4.6 Gas Liquid Phase Chromatographic Analyses (glpc).

All glpc analyses were performed on a Varian Aerograph A90 - P3 gas chromatographic instrument with thermal conductivity detector and helium as carrier gas.

A Leeds and Northrup Speedomax W recorder with dish integrator was used to measure the area percent of the ether and

and olefin. The area percentage measurements were converted to mole percentage by calibration using known mixtures of ether and olefin. A silicone gum rubber SE 30 on Chromsorb W (45 - 60 mesh) column was used with injector temperature 192°, column temperature 155°, detector temperature 240° and collector temperature 210°. The helium flow rate was 100 ml/min.

4.7 Constant Temperature Oil Bath.

UCON lubricant 50-HB-260 was used with a Fisher Model 77 Proportional Temperature Controller and probe. Temperatures were measured with a calibrated thermometer to ± 0.1°. All reaction times were measured with a Precision Scientific "time it" timer. A "Lightnin" Model high speed stirrer was used to maintain uniform temperatures.

4.8 1-Methoxyacenaphthene (3).

(a) A mixture of acenaphthene (7.7g; 50 mmol) and N-bromosuccinimide (9.8g; 55 mmol) was refluxed for 15 minutes in 100 ml of carbon tetrachloride. After cooling and filtration, the solvent was evaporated leaving crude 1-bromoacenaphthene. This oily material, which showed mainly one component by thin layer chromatography (tlc), was used immediately without further purification.

To the crude 1-bromoacenaphthene and 6.0g (60 mmol) sodium bicarbonate was added 5 ml of acetonitrile. This mixture was rapidly stirred and 1.7g (55 mmol) of methanol were added. After stirring for 30 hours, the reaction mixture was treated with pentane and washed four times with water. After drying and removing the solvent, the residual oil was chromatographed on 500g of silica gel using 10% ether in pentane. The later fractions containing 3 (146) were combined and vacuum distilled. The fraction boiling at 72° at 0.01 mm Hg was collected (7.7g; 84%) and analyzed by glpc to contain less than 0.1% acenaphthylene (literature (146) bp 160-1° at 16 mm Hg).

(b) A mixture of 1-acenaphthenol (147) (5.0g; 29 mmol), barium oxide (17.6g; 115 mmol), methyl iodide (4.9g; 34 mmol), water (0.4 ml) and 30 ml of N, N-dimethylformamide (freshly distilled from CaO) were shaken for 18 hours in a degassed, argon-filled, light-shielded flask (148). The reaction mixture was dissolved in

300 ml of methylene chloride and 300 ml of water. The water layer was extracted with methylene chloride and the organic layers combined. These were washed with water until neutral to litmus paper, indicating removal of all dimethylformamide. After drying over anhydrous sodium sulphate, the solvent was removed on a steam bath. The resulting oil was triturated with pentane to remove the unreacted alcohol. After filtration, the filtrate was concentrated on a steam bath and chromatographed on silica gel using 10% ether in pentane. The appropriate fractions were combined and distilled, collecting the material of boiling point. 72° at 0.01 mm Hg (3.3g; 62%), (146).

4.9. 1-Methoxy-d_3-acenaphthene (4).

Following procedure (a) for 3 described above, 15.4g (100 mmol) of acenaphthene were reacted and the crude 1-bromoacenaphthene was treated with 12.0g (120 mmol) sodium bicarbonate and 3.8g (110 mmol) methanol-d_4 in 10 ml of acetonitrile. A yield of 6.4g (34%) of material containing less than 0.05% acenaphthylene was obtained.

In the nmr the aromatic protons appeared as a multiplet (6 protons at δ = 7.3 ppm) and the remaining three protons were analyzed as an ABX (δ_{cis} = 3.14 ppm, δ_{trans} = 3.36 ppm, δ_{α} = 5.11 ppm, $J_{cis,\,trans}$ = -17.7 Hz, $J_{cis,\alpha}$ = 2.6 Hz, $J_{trans,\alpha}$ = 7.1 Hz), (89).

Mass spectrometry using low electron energy indicated <2% of d_2 material and >98% of d_3 material.

4.10 1-Methoxy-d_3- acenaphthene-1, 2, 2-d_3 (1).

Procedure (a)

Acenaphthene-1-one. A sample of 1-naphthylacetyl chloride, prepared from 56g (0.3 mol) of 1-naphthaleneacetic acid and 60g (0.5 mol) of thionyl chloride, was reacted at room temperature for 3 hours with 66g (0.5 mol) of aluminum chloride in 500 ml of methylene chloride. Work up using 1l of dilute hydrochloric acid, and washes of water, sodium bicarbonate, water twice more, drying and solvent evaporation yielded a crude dark product. Vacuum sublimation yielded 29.8g (59%) of light yellow product of melting point (mp) 119.5 - 120.5°.

Acenaphthene-1-one-2,2-d_2.

A mixture of 17.0g (0.10 mol) of acenaphthene-1-one, 50.0 ml (2.7 mol) of deuterium oxide and 5.0g of potassium carbonate was degassed and flushed with nitrogen in a 250 ml round-bottomed flask fitted with a reflux condenser. After refluxing and stirring for two hours, the mixture was cooled, filtered and the ketone air dried and vacuum sublimed. The sublimed ketone (15.5g, mp 117 - 118°) was refluxed two hours under nitrogen with a further 50.0 ml of deuterium oxide and 5.0g of potassium carbonate. After work up and sublimation there resulted 14.5g (85% yield) mp 119 - 120° of acenaphthene-1-one-2,2-d_2. Nmr analysis in chloroform-d indicated only a small peak at $\delta = 3.20$ ppm which corresponds to 95% d_2 material.

1-Acenaphthenol-1,2,2-d_3. In a 500 ml 3-necked round-bottomed flask was placed 14.5g (85 mmol) of acenaphthene-1-one-2,2-d_2 with 1.2g (29 mmol) of lithium aluminum deuteride in a side arm. The system was degassed and flushed with argon and then 250 ml of tetrahydrofuran, which had been freshly distilled from lithium aluminum hydride, was added. The system was degassed again flushed with argon. The solid lithium aluminum deuteride was added portionwise while cooling the mixture with an ice bath. An orange color formed and after stirring overnight at room temperature, the mixture was refluxed for three hours prior to work up. To the cold mixture was added slowly 125 ml of 1M hydrochloric acid and the tetrahydrofuran was removed by film evaporation. The residue was dissolved in 500 ml of methylene chloride and then washed with saturated sodium bicarbonate solution, dried and solvent removed. A crude yellow solid weighing 14.0g crystallized out during the evaporation. This solid was recrystallized from benzene. The filtrate was chromatographed on 300g of alumina using methylene chloride. The total yield of alcohol was 10.1g (68%) mp 146-147°. Nmr analysis in pyridine solvent showed no absorption for the β-hydrogens at δ= 3.4 and 3.7 ppm and no absorption for the α-hydrogen at δ= 5.9 ppm (89).

1-Methoxy-d_3-acenaphthene-1,2,2-d_3 (1). Following procedure (b) for 3, 5.9g (34 mmol) of the 1-acenaphthenol-1,2,2-d_3 and 5.0g (34.5 mmol) of methyl iodide-d_3 yielded 8.8g (82%) of product

containing less than 0.1% of acenaphthylene. Nmr analysis in carbon tetrachloride indicated the absence of α-hydrogens at δ = 5.1 ppm and less than 1% β-hydrogens and methoxyl hydrogens at δ = 3.2 ppm (1a, 89). Isotopic analysis by ms at low electron energy indicated 1% d_4, 8% d_5 and 91% d_6 material. Thus the ether was an isotopic mixture of 1% α-2, 8% cis-5 and trans-5 and 91% 1.

Procedure (b)

$\alpha,\alpha,\alpha^1,\alpha^1$-$d_4$-1,8-di(hydroxymethyl)naphthalene (84).

A 1l 3-necked round-bottomed flask fitted with reflux condenser and side arm was evacuated, flamed out and flushed with argon. Naphthalic anhydride (43.5g; 0.22 mol) was added and 10.0g (0.239 mol) of lithium aluminum deuteride added to the side arm. The system was evacuated and flushed with argon again. Tetrahydrofuran (500 ml), which had been freshly distilled from lithium aluminum hydride, was added followed by degassing and flushing with argon. The lithium aluminum deuteride was added portionwise to the suspension over a 30 minute period while cooling with an ice bath. After refluxing 16h, to the cold mixutre was added 250 ml of 2M hydrochloric acid with stirring. After removing the solvent, and filtration, the resulting solid was washed four times with 150 ml of water and dried under vacuum overnight. Recrystallization from 2l of benzene yielded a first crop of diol mp 152 - 157° (84). The filtrate was chromatographed

on 1 kg of silica gel with 2% methanol in methylene chloride. The early fractions contained a lactone, α,α-d_2-1,8-naphthalide (84), mp 152 - 153°. The later fractions contained further diol. The lactone could be reduced further with lithium aluminum deuteride by the same procedure to give diol. The overall yield of diol was 28 g (66%).

$\alpha,\alpha,\alpha^1,\alpha^1$-$d_4$-1,8-di(bromomethyl) naphthalene (84).

To a cold, stirred solution of 20.1g(0.1 mol) of $\alpha,\alpha,\alpha^1,\alpha^1$-$d_4$--1,8-di(hydroxymethyl)-naphthalene and 50 g (1.6 mol) of tetrabutylammonium bromide in 500 ml of methylene chloride was added rapidly 83g (0.3 mol) of phosphorous tribromide. Following a one hour reflux, the methylene chloride was washed twice with water, once with sodium bicarbonate, once with water, dried and evaporated. The residue was chromatographed on silica gel with 10% ether in pentane to yield 28.4g (90%) of material mp 124 - 127° (149). On further elution a small amount of cyclic ether, 1H,3H-naphtho-[1,8-c,d]-pyran, was obtained mp 78 - 79° (150). Addition of tetraalkylammonium bromide minimizes the amount of cyclic ether that is produced.

Acenaphthene -1,1,2,2-d_4 (84). To a 1l 3-necked flask containing 300 ml of benzene and 150 ml of diethyl ether, freshly distilled from lithium aluminum hydride, was added 28.6g. (90 mmol) of $\alpha,\alpha,\alpha^1,\alpha^1$-$d_4$-1,8-di(bromomethyl)naphthalene. The solution was degassed twice, flushed with argon and cooled to -10° by means of a salt-ice freezing mixture. To the cold, stirred

solution slowly was added 130 ml of 0.9M pheryllithium solution (120 mmol). After stirring overnight at room temperature and refluxing for 2 hours, deuterium oxide (3 ml) was added and the mixture extracted 3 times with 300 ml of water. After drying and solvent removal, the residue was chromatographed on 600g of silica gel with 1% ether in pentane. The later fractions were combined to give acenaphthene-d_4 contaminated with biphenyl. Upon recrystallization from 200 ml of methanol, 9.8g (69%) of acenaphthene-d_4 resulted which could be sublimed under vacuum mp 89 - 90° (84). Nmr analysis indicated the absence of an absorption for the ethano bridge protons at δ= 3.20 ppm.

1-Methoxy-d_3-acenaphthene-1,2,2-d_3 (1). Following procedure (a) for 3, 4.0g (25 mmol) of acenaphthene-d_4 were reacted and the crude bromo compound was treated with 3.7g (44 mmol) sodium bicarbonate and 2.0g (56 mmol) methanol-d_4 in 3 ml of acetonitrile. A yield of 1.2g (26%) of material containing less than 0.1% acenaphthylene was obtained. Nmr analysis in carbon tetrachloride indicated the absence of β-hydrogens and methoxy hydrogens at δ= 3.2 ppm and α-hydrogens at δ = 5.1 ppm (1a, 89). Isotopic analysis by ms at low electron energy indicated 6% d_5 and 94% d_6 material. Thus the ether was an isotopic mixture of 6% cis-5 and trans-5 and 94% 1.

4.11 cis-1-Methoxy-d_3-acenaphthene-2-d (cis-2).

Procedure (a)

Trimethylamine-borane. To a cooled solution of 14.0g (200 mmol) of trimethylamine in 100 ml of tetrahydrofuran, which had been freshly distilled from lithium aluminum hydride, was added dropwise with rapid stirring 100 ml of 1.0M borane--tetrahydrofuran solution (100 mmol). After warming to room temperature and removal of solvent, the crude product was sublimed under vacuum to yield 7.0g (95%) of trimethylamine--borane mp 80 - 85° (151).

Trimethylamine-borane-d_3 (87). Distilled sulphuryl-chloride (5 ml; 0.062 mol) was stirred vigorously with 200 ml (11 mol) of deuterium oxide for 20 minutes. The resulting acid mixture of 0.3M D_2SO_4 and 0.6M DCl contained approximately 0.45% H_2O as determined by nmr. One hundred ml of the acid solution was stirred with 10.0g (0.137 mol) of trimethylamine-borane in 500 ml of diethyl ether which had been freshly distilled from lithium aluminum hydride. After 5 hours the aqueous layer was extrated three times with 500 ml of ether and the ether layers combined. After drying over anhydrous potassium carbonate, the ether was removed. The exchange was repeated twice more with 50 ml of the acid solution and 250 ml of ether each time. The resulting crude product was vacuum sublimed to yield 3.2g (31%) of trimethylamine--borane-d_3. The product had approximately 97% deuterium incorporation in the borane as determined by ir at 2270 and 2372 cm^{-1}.

cis-1-acenaphthenol-2-d. Trimethylamine-borane-d_3 (0.76g; 10 mmol) and 4.55g (30 mmol) of acenaphthylene were sealed in an evacuated tube. After heating at 127° for 12 hours in an explosion-proof oven, the contents were dissolved in 100 ml of tetrahydrofuran which had been freshly distilled from lithium aluminum hydride. This mixture then was oxidized with basic peroxide (0.4g; 9 mmol of sodium hydroxide; 3.6 ml; 36 mmol of 30% hydrogen peroxide). After stirring 2.5 hours, the solvent was removed and the residue dissolved in methylene chloride. The solution was washed with dilute hydrochloric acid followed by 10% sodium carbonate solution, dried and the solvent removed. The crude yellow product was chromatographed on 400 g of alumina with 1% methanol in methylene chloride. The later fractions were combined to yield 2.5g (48%) of alcohol product. After recrystallization from benzene and sublimation under vacuum, a white material mp 143.5° (147) was obtained. Nmr analysis in pyridine for relative amounts of cis and trans β-hydrogens indicated a substantial amount of deuterium incorporation in both positions as well as α to the hydroxyl group (89). Isotopic analysis by ms at low electron energy indicated 8.5% d_0, 28% d_1, 37% d_2, 21.5% d_3, 4.5% d_4 and 0.5% d_5 material. Ir in chloroform indicated C-D stretching bands at 2180, 2230 and 2280 cm^{-1}. These results indicate the probability of deuteration on the aromatic ring.

Procedure (h)

cis-1-Acenaphthenol-2-d (88). Under an argon atmosphere, to 1.14g (8 mmol) of boron trifluoride etherate (freshly distilled from calcium hydride) and acenaphthylene (3.65g; 24 mmol) in 60 ml of ether slowly was added 0.25g (6 mmol) of lithium aluminum deuteride. The mixture was stirred at ambient temperature for 12 hours and then worked up by adding saturated sodium sulphate and extracting with ether. After solvent removal, the residue was dissolved in 10 ml of 90% ethanol containing 0.27g (5 mmol) of sodium hydroxide. Upon addition of 2.3 ml of 30% hydrogen peroxide (23 mmol), the temperature rose to 70° and was maintained for 10 min. After cooling and extraction using ether-water, the solvent was dried and evaporated to yield 3.6g of crude material. After chromatography on alumina using 1% methanol-methylene chloride and recrystallization from benzene, material (1.4g; 34%) of mp 143.0 - 143.5° (147) was obtained. Nmr analysis in pyridine indicated >90% cis-β-deuterium (89). Isotopic analysis by ms at low electron energy indicated >90% monodeuterated alcohol.

cis-1-Methoxy-d_3-acenaphthene-2-d (cis-2) (148). Following procedure (b) for 3, 6.5g (38 mol) of cis-1-acenaphthenol-2-d and 5.0g (34.5 mmol) of methyl iodide-d_3 yielded 3.3g (62%) of cis-2 (146) which contained less than 0.25% acenaphthylene. Nmr analysis in carbon tetrachloride indicated 87% β-hydrogen trans to the methoxy and 13% cis for a total of 1.05 atoms H/molecule (1a, 89).

Isotopic analysis by ms at low-electron energy indicated 4 d_3 and 96 d_4 material. This corresponds to an isotopic mixture of 4 4, 12 trans-2 and 84 cis-2.

4.12 trans-1-Methoxy-d_3-acenaphthene-2-d (trans-2).

Acenaphthylene. Commercial acenaphthylene which has been sublimed under vacuum contains approximately 13 acenaphthene impurity according to glpc analysis. Acenaphthylene which is acenaphthene-free can be prepared from 1-acenaphthenol (152). 1-Acenaphthenol (147), (20g; 12 mmol) and 6.0g of oxalic acid in 100 ml of water were refluxed for 3 hours and the sublimed acenaphthylene collected, dissolved in pentane, washed with water, dried and the solvent removed. Acenapthene-free acenaphthylene resulted upon sublimation under vacuum.

1,2-Epoxyacenaphthene. The epoxidation of acenaphthylene with m-chloroperbenzoic acid was run as a two phase reaction consisting of acenaphthene-free acenaphthylene (19g; 0.125 mol) in 200 ml of methylene chloride and a buffer solution (pH = 8) of 170g (1.25 mol) potassium dihydrogen phosphate and 46g (1.15 mol) sodium hydroxide in 1.5l of water. To an efficiently stirred mixture slowly was added 48.3g (0.25 mol) of m-chloroperbenzoic acid in 800 ml of methylene chloride. The temperature was maintained at 25° for 3.5h and then 15g sodium sulphite was added to destroy the excess peracid. The methylene chloride layer then was washed three times with water, dried and the solvent removed. This material was recrystallized

from petroleum ether to yield 60% of material of mp 81.5 - 82.5° (86). Nmr analysis in carbon tetrachloride indicated a singlet (2H) at δ= 4.56 ppm and a multiplet (4H) at 7.0 - 7.7 ppm. The presence of 10% acenaphthene-1-one impurity was also indicated. If commercial acenaphthylene was used, an additional impurity of 13% acenaphthene in the 1,2-epoxyacenaphthene is observed. This greatly complicates purification. The crude product from commercial acenaphthylene was chromatographed on cellulose powder using petroleum ether. This was followed by repeated recrystallization from petroleum ether.

trans-1-acenaphthenol-2-d (86, 153). 1,2-epoxyacenaphthene (9.0g; 53 mmol), (containing ca. 10% acenaphthene-1-one) in 100 ml of tetrahydrofuran, which had been freshly distilled from lithium aluminum hydride, was added dropwise to a stirred mixture of 1.13g (27 mmol) of lithium aluminum deuteride in 100 ml of tetrahydrofuran all in an argon atmosphere. After stirring for 16 hours at reflux, the reaction mixture was worked up using 100 ml of saturated sodium sulphate. Solvent was removed and the residue taken up in ether and water after extraction four times with 50 ml of ether, the combined ether layers were washed with water and saturated sodium chloride solution. After drying and solvent removal, there resulted 7.1g (78%) of crude alcohol mp 134 - 138° (147). Nmr analysis in pyridine showed approximately 10% deuterium incorporated α to the hydroxyl group and approximately 90% deuterium incorporation

in one of the positions β to the hydroxyl group (89). It was also determined by nmr that the ratio of β-protons cis and trans to the hydroxyl was approximately 85/15 respectively. Mass spectrometry showed approximately 6% d_2 material and a significant amount of non-deuterated product which could not be measured accurately due to an (M-1) peak which occurred even at low electron energy.

trans-1-Methoxy-d_3-acenaphthene-2-d (trans-2) (148). Following procedure (b) for 3, 5.5g (32 mmol) of trans-1-acenaphthenol-2-d and 5.0g (34.5 mmol) of methyl iodide-d_3 yielded 3.4g (56%) of trans-2. Nmr analysis in carbon tetrachloride for relative amounts of protons cis and trans to the methoxyl group indicated 85% cis-H to 15% trans-H of the total (1.09 H) β to the methoxyl group and approximately 11% deuterium α to the methoxyl group (1a, 89). Isotopic analysis by ms at low electron energy indicated 8% d_3, 86% d_4 and 6% d_5 material. This corresponds approximately to an isotopic mixture of 8% 4, 3% α-2, 3% cis-2, 6% cis-5 and trans-5 and 80% trans-2.

4.13 1-Methoxy-d_3-acenaphthene-1-d (α-2).

Acenaphthene-1-one (154). To a solution of 300g (200 mmol) of acenaphthylene, 3.0g (30 mmol) of potassium bicarbonate and 21.0g (210 mmol) of benzonitrile in 150 ml of methanol slowly was added 15.0g (210 mmol) of 50% hydrogen peroxide. The solution was

stirred and spontaneously rose to reflux temperatures over a one hour period. After two hours the cold solution was diluted with 300 ml of water and 300 ml of methylene chloride. Sodium sulfite was added to destroy any remaining peroxides. The organic layer was washed with water and dried. The 1,2-epoxyacenaphthene solution was stirred with 50g of silica gel for 24 hours to isomerize it to the ketone. After filtration and removal of solvent, the resulting crude ketone was recrystallized twice from 95% ethanol to yield 4.5g (12%) of acenaphthene-1-one mp 117 - 119°.

1-Acenaphthenol-1-d: A mixture of 160g (95 mmol) of acenaphthene-1-one, 1.0g (24 mmol) of lithium aluminum deuteride and 125 ml of tetrahydrofuran was allowed to react and then worked up. The crude yellow product was recrystallized from benzene and the filtrate chromatographed and the resulting alcohol recrystallized. The total yield of pale yellow alcohol was 11.5g (71%) mp 140.5° - 141.5° (147). Nmr analysis in pyridine showed an AB quartet for the β-hydrogens at $\delta = 3.4$ and 3.7 ppm and showed no absorption for the α-hydrogen indicating complete α-deuteration (89).

1-Methoxy-d_3-acenaphthene-1-d (α-2) (148). Following procedures (b) for 3, 6.5g (38 mmol) of 1-acenaphthenol-1-d and 5.0g (34.5 mmol) of methyl iodide-d_3 yielded 5.4g (80%) of ether containing less than 0.25% of acenaphthylene. Nmr analysis in carbon tetrachloride indicated 51% cis-H and 49% trans-H of the total hydrogens β to the methoxyl group. There was complete deuterium incorporation α to

the methoxyl group as no absorption was observed $\delta = 5.11$ ppm (1a, 89). Isotopic analysis by ms at low electron energy indicated 4% d_3 and 96% d_4 material. That is, the ether was an isotopic mixture of 4% 4 and 96% 2-2.

4.14 Bases and Solvents.

The tert-butyl alcohol was fractionally distilled from calcium hydride onto freshly baked molecular sieves (4A) and contained less than 0.002 M water. The methanol was distilled from magnesium turnings onto molecular sieves (0.002M H_2O).

The lithium, potassium and cesium tert-butoxide solutions were prepared by stirring the freshly cleaned metal at room temperature with degassed tert-butyl alcohol under an argon atmosphere. These solutions then were titrated for water (0.002M using a Photovolt Aquatest) and for total base (pH meter) which is reported with the results. Potassium methoxide in methanol was prepared similarly except the methanol was cooled during reaction. The solutions containing dicyclohexyl-18-crown-6 ether (90c) were prepared by adding a weighed amount of the crown ether to the base solution. The solution of crown ether with potassium tert-butoxide in tert-butyl alcohol was not indefinitely stable and seemed to have decomposed within two months. Neither did the crown ether solution survive when heated to 180°.

The solution of tetramethylammonium tert-butoxide in tert-butyl

alcohol was prepared by dissolving freeze-dried tetramethylammonium hydroxide in tert-butyl alcohol and then freeze drying. This procedure was repeated three times to remove the bulk of the water. Molecular sieves were added to the final solution which was typically 0.25 M in water. After about two days the solution contained 0.05 M water and was 0.11 M in base. This base solution must be used immediately since it decomposes within days to a weaker base (presumably trimethylamine and tert-butyl methyl ether).

4.15 Exchange and Elimination Procedure.

The routine was effectively the same for all base solutions and substrates. Usually about 200 mg of substrate and 10 ml of base solution were twice degassed and sealed under vacuum in a Carius tube. After immersing in a constant temperature bath for the indicated time, the tube was cooled, opened and the contents dissolved in pentane and water. The pentane layer was washed four times with water, dried and evaporated through a Vigreaux column.

The mixture was analyzed by glpc (2.5m x 6.3mm column of 10% SE-30 on 45 - 60 Chromsorb W; injector 192°; column 155°; detector 240°; helium 100 ml/min). The area % of acenaphthylene and 1-methoxyacenaphthylene was converted to mole % using a calibration curve. Figure 47 shows a typical plot of the pseudo first order reaction of trans-2 with potassium tert-butoxide in tert-butyl alcohol (runs 22 - 24 in Table 11).

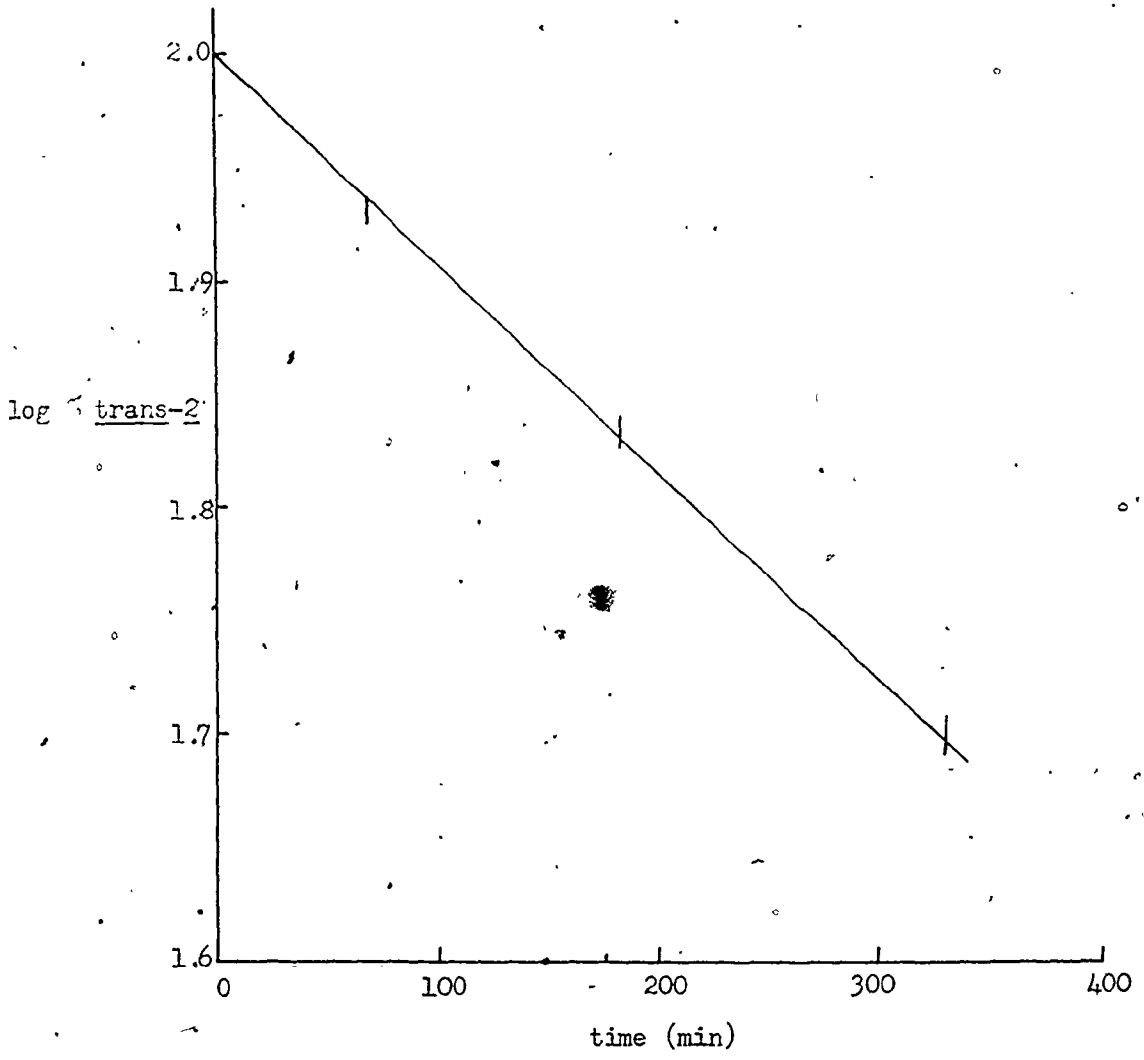

Figure 47 - Pseudo First Order Reaction of trans-2 with Potassium tert-Butoxide

The mixture of olefin and ether then was separated on silica gel (60 - 120 mesh) eluting with 10% diethyl ether in pentane. The early fractions containing acenaphthylene were combined and sublimed (approximately 70° at 16 mm Hg) with greater than 85% recovery. The later fractions containing ether were distilled (at 0.05 mm hg) with greater than 75% recovery.

The olefin was analyzed for deuterium content by both proton nmr and mass spectrometry at low electron energy. The composition of the ether mixture was determined by a combination of nmr and mass spectroscopic techniques. Nmr analysis of 10 - 15 weight solutions in carbon tetrachloride allowed determination of the ratios of cis (3.14 ppm) and trans (3.36 ppm) protons β to the methoxyl-d_3 group (89). Mass spectrometric analysis at low electron energy allowed determination of the relative amounts of material containing zero, one or two hydrogens for the case of 1. These two types of data allowed extraction of the percentages of the four ethers. For the case of cis-2 or trans-2, mass spectrometric analysis allowed determination of the relative amounts of material containing one, two or three hydrogens. The percentages of the four ethers in the case of trans-2 and the three ethers in the case of cis-2 were extracted from these data. Tables 10 - 12 contain the raw data of this study organized according to counterion and substrate.

Complications were encountered in the reactions at 150 - 160°

TABLE 10

Raw Data (nmr and ms) for the Exchange of 1

Run	Temp. (°C)	Base Conc. (M)	Time (Min.)	Olefin					Ether					
				Mole%	Olefinic H by nmr	Olefinic H by ms h_o	h_1	h_2	Mole%	β-H by nmr	cis-β-H/trans-β-H	β-H by ms h_o	h_1	h_2
i) Potassium tert-butoxide in tert-butyl alcohol														
1	85.0 ± 0.1	0.43 ± 0.01	90 ± 1	10 ± 1	-	92.5 ± 0.5	7.5 ± 0.5	0.0 ± 0.5	90 ± 1	0.25 ± 0.01	67 ± 1/ 33 ± 1	78.9 ± 0.5	21.1 ± 0.5	0.0 ± 0.5
2	85.0	0.43	188	23	0.11 ± 0.01	86.8	13.0	0.2	77	0.65	63/37	57.3	38.3	4.4
3	85.0	0.43	500	57	0.28	76.5	23.0	0.5	43	1.00	66/34	25.9	50.1	24.0
4	85.0	0.43[a]	135	17	-	-	-	-	83	0.52	65/35	-	-	-
5	85.6	0.022	1830	8	-	-	-	-	92	-	68/32	72.3	24.4	3.3
6	65.0	0.37	700	4	-	-	-	-	96	-	64/36	66.4	28.7	4.9
7	65.0	0.37	1600	10	-	-	-	-	90	-	67/33	63.8	30.2	6.2
8	60.0	0.021[b] ± 0.001	107	8	-	-	-	-	92	-	37/63	70.0	23.0	6.5
9	45.0	0.021[b]	1818	4	-	-	-	-	96	-	39/61	76.0	22.0	1.9

TABLE 10 (contd.)

Run	Temp. (°C)	Base Conc. (M)	Time (Min.)	Olefin Mole %	Olefinic H by nmr	Olefinic H by ms h_o	h_1	h_2	Ether Mole %	β-H by nmr	cis-β-H/trans-β-H	β-H by ms h_o	h_1	h_2
ii) Lithium tert-butoxide in tert-butyl alcohol														
10	160 ± 1	0.14 ± 0.01	1010	34[c]	0.0	96.0	3.8	0.2	66	0.24	97/3	76.0	24.0	0.0
11	160	0.14	1900	51[c]	0.0	94.1	4.2	1.7	49	0.61	95/5	61.0	39.0	0.0
12	160	0.14	4023	76[c]	0.0	92.4	7.6	0.0	24	0.84	93/7	29.3	63.3	7.4
iii) Cesium tert-butoxide in tert-butyl alcohol														
13	85.6 ± 0.1	0.20	37	11	-	-	-	-	89	-	48/52	60.5	32.5	7.0
14	85.6	0.20	124	30	-	-	-	-	70	-	50/50	31.5	46.5	22.0
15	85.6	0.20	241	54	-	-	-	-	46	-	48/52	13.0	42.0	42.5

TABLE 10 (contd.)

Run	Temp. (°C)	Base Conc. (M)	Time (Min.)	Olefin Mole%	Olefinic H by nmr	Olefinic H by ms h_o	Olefinic H by ms h_1	Olefinic H by ms h_2	Ether Mole%	Ether β-H by nmr	Ether cis-β-H/trans-β-H	Ether β-H by ms h_o	Ether β-H by ms h_1	Ether β-H by ms h_2
iv) Tetramethylammonium tert-butoxide in tert-butyl alcohol.														
16	44.8	0.11	100	6	-	-	-	-	94	0.37	22/78	71.0	29.0	0.0
17	44.8	0.11	500	9	-	86.6	13.2	0.2	91	0.45	29/71	60.0	38.0	2.0
18	44.8	0.11	4842	8	-	87.5	12.0	0.5	92	0.52	31/69	59.0	39.0	2.0
19	44.9	0.11	319	24	-	77.5	22.0	0.5	76	0.93	31/69	27.0	58.0	15.0
v) Potassium methoxide in methanol														
20	150.3	0.40	200	8[c]	-	-	-	-	92	0.53	50/50	-	-	-
21	150.3	0.40	810	30[c]	0.48	-	-	-	70	1.42	50/50	-	-	-

a) 0.06M in potassium acetate
b) Added equivalent of dicyclohexyl-18-crown-6 ether
c) Extensive loss of product due to side reactions

TABLE II

Raw Data (nmr and ms) for the Exchange and Elimination of trans-2

Run	Temp. (°C)	Base Conc.(M)	Time (Min.)	Olefin Mole%	Olefinic H by nmr	Olefinic H by ms h_o	h_1	h_2	Ether Mole%	β-H by nmr	cis-β-H/ trans-β-H	β-H by ms h_1	h_2	h_3
i) Potassium tert-butoxide in tert-butyl alcohol														
22	85.6 ± 0.1	0.43 ± 0.01	74 ± 1	15 ± 1	-	3.0 ± 0.5	83 ± 0.5	14 ± 0.5	85 ± 1	1.23 ± 0.01	81 ± 1/ 19 ± 1	4.5 ± 0.5	80 ± 0.5	15.5 ± 0.5
23	85.6	0.43	182	32	1.12 ± 0.01	3.0	79.0	18.0	68	1.44	76/24	2.5	74.5	23.0
24	85.6	0.43	330	50	1.23	3.0	74.0	23.0	50	1.61	71/29	3.0	66.0	30.0
25	65	0.37	38,800	99.7	-	2.7	54.2	43.0	0.3	-	-	-	-	-
26	65	0.37	38,800	99.7	-	2.2	54.2	43.6	0.3	-	-	-	-	-
27	65	0.37	585	5	-	1.8	84.6	13.6	95	-	-	-	-	-
ii) Lithium tert-butoxide in tert-butyl alcohol														
28	152.4	0.14	462	21[a]	1.03	3.0	89.0	8.0	79	1.48	87/13	6.0	86.0	8.0
29	152.4	0.14	1062	40[a]	0.99	3.0	87.0	10.0	60	1.41	87/13	5.0	85.0	10.0
30	152.4	0.14	1535	50[a]	1.01	3.0	85.0	12.0	50	1.52	85/15	3.5	86.0	10.5

TABLE II (contd.)

Run	Temp. (°C)	Base Conc. (M)	Time (Min.)	Olefin Mole%	Olefinic H by nmr	Olefinic H by ms h_o	h_1	h_2	Ether Mole%	β-H by nmr	cis-β-H/trans-β-H	β-H by ms h_1	h_2	h_3
iii) Cesium tert-butoxide in tert-butyl alcohol														
31	85.6	0.22	31	15	-	3.0	76.0	21.0	85	1.50	79/21	3.0	77.0	20.0
32	85.6	0.22	104	40	1.27	2.0	65.0	33.0	60	1.85	61/39	3.5	53.0	43.5
33	85.6	0.22	149	52	1.42	3.0	5.7	4.0	48	1.94	56/44	2.5	47.0	50.5

a) Extensive loss of product due to side reactions

TABLE 12

Raw Data (nmr and ms) for the Exchange and Elimination of cis-2

Run	Temp. (°C)	Base Conc. (M)	Time (Min.)	Olefin Mole%	Olefinic H by nmr	Olefinic H by ms h_0	h_1	h_2	Ether Mole%	β-H by nmr	cis-β-H/ trans-β-H	β-H by ms h_1	h_2	h_3
i) Potassium tert-butoxide in tert-butyl alcohol														
34	65.0 ± 0.1	0.37 ± 0.01	50,200 ± 1	99.7	-	0.6 ± 0.5	11.8 ± 0.5	87.6 ± 0.5	0.3	-	-	-	-	-
35	65.0	0.37	50,200	99.7	-	1.7	12.4	85.9	0.3	-	-	-	-	-
36	65.0	0.37	734	6 ± 1	-	0.0	19.4	80.6	94 ±1	-	-	-	-	-
37	60.0	0.021[a] ± 0.001	90	12	-	0.0	62.5	37.5	88	1.11 ± 0.01	18 ± 1/ 82 ± 1	0.0 ± 0.5	90.6 ± 0.5	9.4 ± 0.5
38	60.0	0.021[a]	333	16	-	0.0	62.5	34.5	84	1.13	24/76	0.0	83.3	16.7
39	45.0	0.021[a]	617	5	-	1.9	74.3	23.5	95	1.08	19/81	0.0	88.5	11.5
40	45.0	0.021[a]	1645	11	-	0.0	71.6	28.4	89	1.12	24/76	0.0	83.6	16.4
ii) Cesium tert-butoxide in tert-butyl alcohol														
41	85.6	0.20 ± 0.01	31	11	-	1.0	24.7	74.2	89	1.22	23/77	0.6	79.5	19.9

TABLE 12 (contd.)

Run	Temp. (°C)	Base Conc.(M)	Time (Min.)	Olefin Mole%	Olefinic H by nmr	Olefinic H by ms h_0	h_1	h_2	Ether Mole	β-H by nmr	cis-β-H/trans-β-H	β-H by ms h_1	h_2	h_3
iii) Tetramethylammonium tert-butoxide in tert-butyl alcohol														
42	45.0	0.10	90	10	-	1.0	75.2	23.8	90	-	-	-	-	-
43	45.0	0.10	90	8	-	0.8	79.0	20.2	92	1.12	22/78	0.5	88.3	11.2
44	45.0	0.10	300	20	-	0.6	72.0	27.4	80	1.23	31/69	0.0	74.9	25.1
45	45.0	0.10	607	29	-	0.0	64.9	35.1	71	1.37	35/65	0.0	64.6	35.4
iv) Potassium methoxide in methanol														
46	152.4	0.48	45	7[b]	-	0.0	52.5	47.5	93	1.26	36/64	0.0	79.5	20.5
47	152.4	0.48	150	15[b]	-	0.0	44.0	56.0	85	1.49	47/53	0.0	55.0	43.0
48	152.4	0.48	350	32[b]	1.71	0.0	31.0	69.0	68	1.83	50/50	0.0	27.0	70.0

a) Added equivalent of dicyclohexyl-18-crown-6 ether
b) Extensive loss of product due to side reactions

since a substantial loss of material had occurred during the reactions. The reactions were repeated using dibenzyl as internal standard. For example, a mixture of 0.104g (0.76 mmoles) of trans-2 and 0.050g (0.28 mmoles) of dibenzyl were heated at 152.4° with 10 ml of 0.14M LiOt-Bu-HOt-Bu solution (1.4 mmoles) for the same length of time as run 28 in Table II. After work up the mixture was analyzed by glpc and the percentage loss determined. A mixture of 0.060g (0.33 mmoles) of acenaphthylene and 0.050g (0.28 mmoles) of dibenzyl was heated at 152.4° with 10 ml of 0.14M LiOt-Bu-HOt-Bu solution (1.4 mmoles) for the same length of time. After work up the mixture was analyzed by glpc and the percentage loss of acenaphthylene was measured and seemed to account for the loss of material in run 28.

A mixture of 0.015g (0.10 mmoles) of deuterated acenaphthylene and 0.50g (0.28 mmoles) of dibenzyl was heated at 152.4° with 10 ml of 0.14M LiOt-Bu-HOt-Bu solution (1.4 mmoles) for the same length of time. After work up the mixture was analyzed by glpc and the percentage loss of deuterated acenaphthylene was similar to that for the undeuterated acenaphthylene. Isotopic analysis by mass spectrometry at low electron energy of the starting deuterated acenaphthylene and the recovered deuterated acenaphthylene indicated 72% acenaphthylene-d_1 material in both cases. Therefore, negligible deuterium isotope effects occur in the loss of acenaphthylene in this reaction.

A.16 Kinetics of the Exchange and Elimination Processes.

A water jacketed cylindrical quartz cell having a 10 mm path length and a sample volume of approximately 0.7 ml was installed within the sample compartment of a Jasco Model ORD/UV-5 spectrophotometer. The cell was attached to a water bath where the temperature was maintained constant within ±0.1° by means of a proportional temperature controller. The cell was flushed with argon and capped with a Teflon plug. To the cell was added 0.5g of 0.37M KO<u>t</u>-Bu-HO<u>t</u>-Bu solution by means of a syringe and the temperature allowed to equilibrate. To this solution was added 0.05g (0.3 mmoles) of the ether substrate by means of a syringe and the cell tightly capped under an atmosphere of argon. The absorbance at 412 nm was followed over a period of two hours at 64.3°. A least squares plot of absorbance versus time gave the slope and the error in the slope from which the absolute rate constant could be calculated. At 412 nm acenaphthylene, the elimination product, absorbed with an extinction coefficient which was measured to be 138 whereas the substrate, 1-methoxyacenaphthene, and the base solution did not absorb appreciably. Acenaphthylene gave a linear Beer's Law plot of absorbance versus concentration at 412 nm over the concentration range used in this experiment. The density of the 1-methoxyacenaphthene solution in 0.37M KO<u>t</u>-Bu-HO<u>t</u>-Bu was 0.773g/ml at 65°. This was calculated from the specific gravity of the solution at 25° and the density of water at 25° and corrected for the change in density of

tert-butyl alcohol upon heating to 65°.

Table 13 contains the raw data from which the observed pseudo-first order rate constants were calculated.

TABLE 13

Raw Data for the Kinetics of Elimination of 1-Methoxyacenaphthene at 64.3° in 0.37M KOt-Bu-HOt-Bu

Run	Substrate	Conc.(molality)	Conc. (M)	slope x 10^3	slope x 10^3 / conc.(m)	k(abs.) x 10^6 (sec^{-1})
49	1	0.586	0.408	1.814 ± 0.007	3.10	2.00
50	1	0.578	0.403	1.754 ± 0.009	3.04	1.97
51	1	0.580	0.404	1.736 ± 0.008	2.99	1.94
52	α-2	0.577	-	3.257 ± 0.021	5.64	-
53	α-2	0.583	-	3.091 ± 0.017	5.30	-
54	α-2	0.590	-	2.850 ± 0.023	4.83	-
55	4	0.577	-	3.291 ± 0.030	5.70	-
56	4	0.580	-	3.044 ± 0.014	5.25	-
57	4	0.578	-	3.123 ± 0.022	5.41	-
58	trans-2	0.576	-	2.600 ± 0.021	4.51	-
59	trans-2	0.570	-	2.845 ± 0.033	5.00	-
60	trans-2	0.575	-	2.555 ± 0.020	4.42	-
61	cis-2	0.573	-	2.130 ± 0.011	3.72	-

TABLE 13 (cont.)

Raw Data for the Kinetics of Elimination of 1-Methoxyacenaphthene at 64.3° in 0.37M KO*t*-Bu-HO*t*-Bu

Run	Substrate	Conc.(molality)	Conc.(M)	slope x 10^3	slope x 10^3 / conc.(m)	k(abs.)x 10^6 (sec^{-1})
62	*cis*-2	0.580	-	2.384 ± 0.011	4.11	-
63	*cis*-2	0.579	-	2.217 ± 0.021	3.83	-
64	3	0.567	-	3.924 ± 0.029	6.92	-
65	3	0.583	-	3.726 ± 0.030	6.40	-
66	3	0.581	-	3.667 ± 0.045	6.31	-

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