Chemical Reviews

Volume 80, Number 6 December 1980

Stereochemical and Base Species Dichotomies in Olefin-Forming E2 Eliminations

RICHARD A. BARTSCH*

Department of Chemistry, Texas Tech University, Lubbock, Texas 79409

JIŘÍ ZÁVADA

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague 6, Czechoslovakia

Received May 22, 1980

Contents

I. Introduction

A. Scope of Review

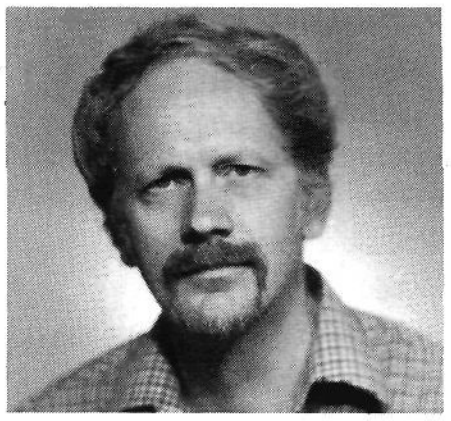
According to the account of N. S. Isaacs[1] in the Annual Reports of the Chemical Society, "The subject of polar elimination reactions has, in recent years, become blurred and fraught with controversy". Important contributors to the confusion have been dichotomies of stereochemistry (anti vs. syn) and of base species (free ions vs. associated bases) which may occur within a broad spectrum of polar eliminations.

Because of the central position occupied by base-promoted 1,2-eliminations within the fundamental framework of both theoretical and synthetic organic chemistry, it is important to establish how the stereochemical and base species dichotomies operate in such mechanistically variegated reactions. The prime goal of this review is to assess the two dichotomies in olefin-forming E2 reactions.

In order to gain maximum insight into the rather complex interrelationships between the nature of the base species, stereochemistry, kinetics, and orientation, this review is confined

0009-2665/80/0780-0453$05.00/0

Richard A. Bartsch received B.A. (with Honors) and M.S. (under Professor J. L. Kice) degrees in chemistry from Oregon State University in 1962 and 1963, respectively. His doctoral studies in organic chemistry at Brown University (1963–1966) were supervised by Professor J. F. Bunnett. Following a temporary teaching position at the University of California, Santa Cruz, he was a NATO Postdoctoral Fellow in the laboratories of Professor S. Hünig at the University of Würzburg. During the period 1968–1973, he was Assistant Professor of Chemistry at Washington State University. After serving for 1 year as an Assistant Program Administrator for the Petroleum Research Fund, he joined the faculty at Texas Tech University as Associate Professor of Chemistry in 1974. He was promoted to Professor in 1978. His research interests are in mechanistic and synthetic organic chemistry. Current projects include base-promoted eliminations which form carbon–carbon and carbon–heteroatom multiple bonds; diazonium ion chemistry; and the synthesis of novel multidentate macrocyclic compounds for cation complexation.



Jiří Závada was born in Prague on February 16, 1935. He studied chemistry at the Charles University of Prague (1954–1958), receiving a RNDr degree under Professor V. Horák. In 1959–1962 he continued his studies in the Institute of Organic Chemistry and Biochemistry of Czechoslovak Academy of Sciences in Prague under Professor J. Sicher and received a C.Sc. degree in chemical sciences in 1963. His main research interests are reaction mechanisms and conformational analysis, with occasional excursions to the area of organic synthesis.

to alkoxide-promoted eliminations. "Weak-base"-promoted eliminations (the so-called E2C mechanism) will not be discussed. Also eliminations involving attack of base on an ion pair rather than on the unionized substrate (the ion-pair mechanism) will not be taken into account.

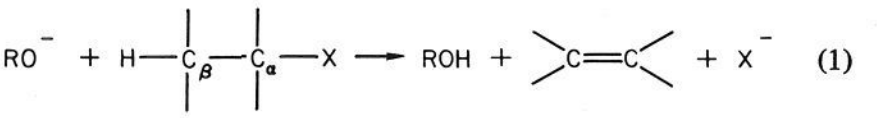
Primarily attention will be focused upon reactions for which an E2 mechanism has been demonstrated or seems certain. These include eliminations from alkyl, cycloalkyl, and bicyclic halides, tosylates, and onium ions and from the corresponding substrates containing moderately activating β substituents (aryl, vinyl, and halogen). Consequences of the base dichotomy under conditions where only one stereochemical pathway (anti) operates are assessed first in section II. The stereochemical dichotomy under conditions where only one base species (free) is involved is then examined in section III.C. This is followed by the more complex situation with dichotomies of both stereochemistry and base species (section III.D). In these sections, the discussion is confined to unactivated E2 reactions from alkyl, cycloalkyl, and bicyclic substrates. In section IV, the perturbations induced by moderately activating β substituents (phenyl, vinyl, halogen) are examined.

Finally, selected recent examples of stereochemical and base species dichotomies in E1cB reactions are discussed in section V.

Literature coverage for this review includes publications which appeared prior to or during December of 1979.

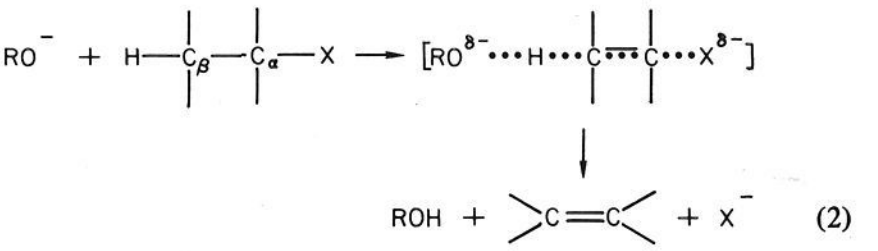
B. Mechanisms of Olefin Formation by Alkoxide-Promoted 1,2-Elimination Reactions

During the past decade, the mechanisms for base-promoted 1,2-elimination reactions have been reviewed by Bordwell,[2] Saunders and Cockerill,[3] Saunders,[4] Cockerill and Harrison,[5] and Aleskerov, Yufit, and Kucherov.[6] Mechanistic possibilities for olefin formation by alkoxide-promoted 1,2-eliminations (eq 1) include the E2 and three E1cB mechanisms.



$$RO^- + H-C_\beta-C_\alpha-X \longrightarrow ROH + >C=C< + X^- \qquad (1)$$

In the E2 mechanism (eq 2), both the C_α–H and C_β–X bonds cleave simultaneously via a single transition state. Customarily,

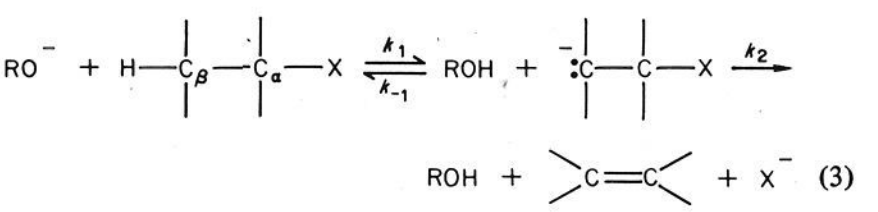


$$RO^- + H-C_\beta-C_\alpha-X \longrightarrow [RO^{\delta-}\cdots H\cdots C\cdots C\cdots X^{\delta-}]$$

$$\downarrow$$

$$ROH + >C=C< + X^- \qquad (2)$$

it is observed that the reaction follows second-order kinetics, first order in base and first order in substrate. However, in several instances, marked deviations from the integral-order kinetics due to base association have been recently observed (section II.B.2.d.5). Also, salt effects may obscure the kinetic pattern, especially in reactions between oppositely charged ions (onium salt eliminations; cf. Section III.C.1). In E1cB mechanisms, the C_β–H bond is ruptured prior to scission of the C–X bond (eq 3). Depending upon the relative magnitudes of k_1,



$$RO^- + H-C_\beta-C_\alpha-X \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ROH + {}^{-}\!:C-C-X \xrightarrow{k_2}$$

$$ROH + >C=C< + X^- \qquad (3)$$

k_{-1}, and k_2, three distinct possibilities for alkoxide-promoted olefin formation by E1cB mechanisms exist: reversible E1cB or $(E1cB)_R$; irreversible E1cB or $(E1cB)_I$; and $(E1)_{anion}$.

If ROH in eq 3 is considerably more acidic than the substrate ($k_1 \gg k_{-1}[ROH]$), the substrate is ionized to only a small extent and application of the steady-state treatment to the carbanion concentration produces the rate expression shown in eq 4. If

$$\text{rate} = \frac{k_1 k_2 [RX][RO^-]}{k_{-1}[ROH] + k_2} \qquad (4)$$

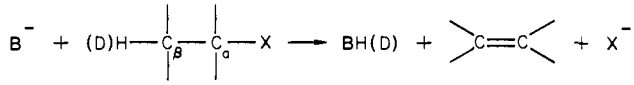
$k_{-1}[ROH] \gg k_2$, the reaction involves a rapid preequilibrium step followed by a slow unimolecular elimination from the carbanion, and the mechanism is termed "reversible" E1cB. For most alkoxide-promoted 1,2-elimination reactions ROH is the solvent, so the $(E1cB)_R$ mechanism (eq 5) should exhibit

$$\text{rate}(E1cB)_R = \frac{k_1 k_2 [RX][RO^-]}{k_{-1}[ROH]} \qquad (5)$$

kinetics which are first order in both substrate and alkoxide (identical with the concerted E2 mode).

If in eq 4 $k_2 \gg k_{-1}[ROH]$, proton abstraction is rate limiting and the resulting carbanion decomposes unimolecularly to alkene more rapidly than it undergoes protonation by the solvent. For this "irreversible" E1cB process, the rate expression in eq 4 becomes that shown in eq 6. Therefore, second-order ki-

Table I. Criteria for Base-Promoted 1,2-Elimination Reactions



mechanism[a]	kinetic order	β-protium exchange faster than elimination	general or specific base catalysis	k_H/k_D	electron withdrawal at C_β	electron release at C_α	leaving group isotope effect or element effect
E2[b]	2	no	general	2-8	rate increase	small rate increase	small to substantial
$(E1cB)_R$	2	yes	specific	1.0	small rate increase	small rate increase	substantial
$(E1cB)_I$	2	no	general or specific[c]	2 → 8	rate increase	little effect	negligible
$(E1)_{anion}$	1	yes	general	1.0	rate decrease	rate increase	substantial

[a] All mechanisms exhibit first-order kinetics in substrate. [b] For E2 transition states with considerable carbanion character. [c] Depending upon the relative magnitudes of k_{-1} and k_2.

$$\text{rate}(E1cB)_I = k_1[RX][RO^-] \quad (6)$$

netics, first order in substrate and in base, are again anticipated for the $(E1cB)_I$ mechanism.

For the third type of E1cB mechanism, the substrate and conjugate acid of the base are of similar acidity and the leaving group is not very labile ($k_{-1}[ROH] > k_2$). In the presence of excess base, the substrate is essentially converted into its conjugate base which then undergoes a rate-determining unimolecular decomposition to form the alkene. If conversion of the substrate to its carbanion is complete or nearly so, further increases in base concentration will have little effect upon reaction rate. Therefore, the elimination will exhibit a first-order dependence in substrate but a zero-order dependence in alkoxide. This mechanism is identified as $(E1)_{anion}$.

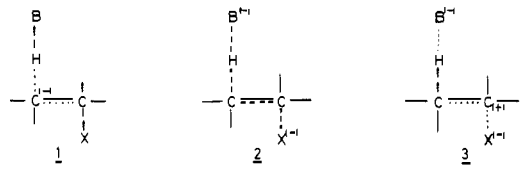
Criteria which allow for the differentiation among E2 and the three E1cB mechanisms have been summarized by Bordwell,[2] Saunders and Cockerill,[3] and Cockerill and Harrison[5] and are presented in Table I. However, in such mechanistic differentiation, possible complications due to base association must also be taken into account. For examples of reactions which proceed via the various E1cB mechanisms, the reader is directed to reviews.[2,5,8]

Except for section V, this review is confined to reactions for which the E2 mechanism has been demonstrated or seems certain (according to the Saunders analysis[4]).

C. The Variable E2 Transition State

The E2 mechanism involves concerted, but not necessarily synchronous, making and breaking of the four affected bonds in the transition state. Different timing of bond making and breaking may give rise to transition states with carbanionic character at C_β, carbonium ion character at C_α, and varying degrees of double bond character. Since most recent reviews[3-8] of 1,2-elimination reactions give detailed coverage of this topic, only a limited discussion with emphasis upon the use of More O'Ferrall plots will be given here.

Bunnett's original concept[7] of the variable E2 transition state involved a spectrum of transition states ranging from "E1cB-like", **1**, to "central", **2**, to "E1-like", **3**. (In **1**-**3**, dotted lines



indicate almost completely ruptured or slightly formed bonds and heavy dashed lines represent only slightly cleaved or almost completely formed bonds.) This theory has been extended to include concepts such as "reactant-like" and "product-like" transition states by the use of More O'Ferrall plots.[5,6,8]

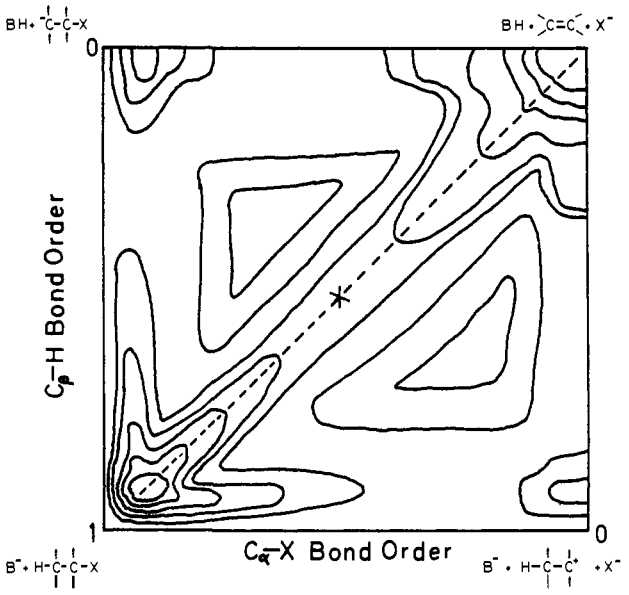


Figure 1. Contour map for the potential-energy surface of an E2 reaction with a "central" transition state.

The More O'Ferrall approach for describing transition states in base-promoted 1,2-elimination reactions which occur by the E2 mechanism is illustrated by the diagram in Figure 1. Along the *y* and *x* axes are presented the C_β–H and C_α–X bond orders, respectively. The out of plane axis is the potential energy, which is represented by contour lines. The substrate and base are located at the bottom left corner (origin) and the reaction products are at the top right corner of the diagram. Rupture of the C_β–H bond corresponds to a vertical motion along the *y* axis which ultimately leads to formation of a carbanion and the conjugate acid of the base at the top left corner. For an E1cB elimination, this step is combined with a subsequent horizontal motion from carbanion to products. Cleavage of the C_α–X bond is depicted by horizontal motion to the right of the origin which ultimately forms the carbonium ion and anion X^-. In an E1 elimination, this horizontal motion is followed by a vertical motion from the carbonium ion to products. Breaking the C_β–H and C_α–X bonds simultaneously corresponds to a diagonal motion from reactants to products. Figure 1 represents an E2 elimination in which the rupture of these two bonds is synchronous.

Alternatively, a simpler plot may be constructed by deleting the contour lines and indicating the reaction coordinate and saddle point (dashed line and cross mark, respectively, in Figure 1). In this manner, transition states of different character may be represented by the reaction coordinates and letters in Figure 2. For example, in "reactant-like" transition state A, there is slight, but equal, rupture of the C_α–H and C_β–X bonds and only a slightly developed C_α–C_β double bond. In "product-like"

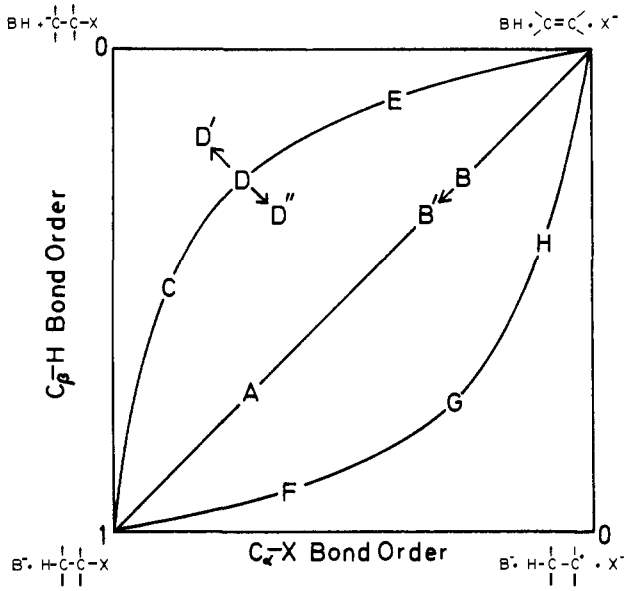


Figure 2. More O'Ferrall plot for E2 elimination reactions.

transition state B, scission of the C_β–H and C_α–X bonds is synchronous and extensive with a high degree of double bond character. Transition states C, D, and E are all "E1cB-like" because cleavage of the C_β–H bond has progressed considerably further than scission of the C_α–X bond in the transition state. Similarly, for F, G, and H, rupture of the C_α–X bond in the transition state has surpassed the breakage of the C_β–H bond, and the transition states are of the "E1-like" variety.

The conceptual advance provided by the More O'Ferrall approach lies in the fact that possible intermediates are included in the potential-energy diagram. Thus, it is possible to translate substituent effects on intermediate stability into effects on the potential-energy surface (and transition-state structure) even when the intermediate is not involved in the reaction.[9]

Perturbations in transition-state character wrought by changes in substrate structure (leaving group, α substituents, β substituents) may be predicted by use of More O'Ferrall plots and the application of three simple rules:[9] (1) if species corresponding to a corner *along* the reaction coordinate (e.g., the lower left corner or origin in Figure 2) are stabilized, the effect is to move the transition state along the reaction coordinate *away* from the stabilized corner (a Hammond effect); (2) if species corresponding to a corner *perpendicular* to the reaction coordinate (e.g., the upper left corner in Figure 2) are stabilized, the effect is to move the transition state *toward* the stabilized corner; (3) if the stabilization is both along and perpendicular to the reaction coordinate, the transition-state movement will be the resultant of vectors for the movements prescribed in rules 1 and 2.

Thus, for a reaction with transition state B in Figure 2, if the substrate were modified to produce a more stable alkene, rule 1 would apply and the transition state should shift to B′. Compared with B, B′ would have less rupture of the C_β–H and C_α–X bonds and less double bond character. For a reaction passing through transition state D in Figure 2, if an electron-withdrawing substituent were attached to C_β, rule 2 would be applicable and the transition state would become more "E1cB-like" by shifting to position D′. Alternatively, if transition state D were modified by changing to a better leaving group, the transition state would shift to D″ in which there is a better balance between the timing of C_β–H and C_α–X bond rupture.

It is important to emphasize that the character of E2 transition states is dependent not only upon the substrate structure but also upon the base and solvent. Effects of base and solvent variation upon E2 transition-state structure are a priori not as easy to assess as those of substrate structure modification. Concomitant variation of both base and solvent (e.g., comparison of EtOK–EtOH with *t*-BuOK–*t*-BuOH) makes prediction very difficult.

II. Dichotomy of Base Species in Unactivated Anti Elimination

A. Alkoxide Base Species

It is now well established that alkoxide ion pairing interactions are important even in such polar solvents as ethanol and dimethyl sulfoxide. For example, Brandstrom[10] reports that 1.0 M EtONa in EtOH contains only about 20% of dissociated ethoxide ions. Therefore, the various base species which may be present in a given base–solvent solution must be considered.

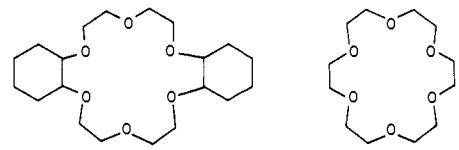
The situation may be most simply viewed according to the equilibria given in eq 7. Thus, the dissociated alkoxide ion **4**

$$\underset{\mathbf{4}}{RO^-} + M^+ \rightleftharpoons \underset{\mathbf{5}}{(RO^-M^+)} \rightleftharpoons \underset{\mathbf{6}}{(RO^-M^+)_2} \rightleftharpoons \underset{\mathbf{7}}{(RO^-M^+)_n} \quad (7)$$

and cation may associate to form ion pair **5**. Ion pairs may further interact to form dimers of ion pairs, **6**, and higher ion pair aggregates, **7**. The position of these multiple equilibria will depend upon the alkyl portion of the alkoxide, the cation, the solvent, the temperature, and the total base concentration.

The influence of metal cations and structure of the alkyl group of the alkoxide upon the equilibrium between dissociated alkoxide **4** and the ion-paired species **5** in Me_2SO has been investigated by Exner and Steiner.[11] Ion-pairing constants for the equilibrium **4** ⇌ **5** of lithium, sodium, potassium, and cesium *tert*-butoxides are 10^6, 10^6, 270, and 200 M^{-1}, respectively. Metal methoxides were found to associate more strongly than the corresponding alkoxides of *t*-BuOH.

In solvents of low polarity, alkoxide association should be even more pronounced. Thus, Saunders, Bushman, and Cockerill[12] observed that the conductivity of 0.1 M *t*-BuONa–*t*-BuOH is only 6% greater than that of pure *t*-BuOH. Conductivity changes caused by addition of the crown ether, dicyclohexano-18-crown-6, **8**, to solutions of *t*-BuOK in di-



8 **9**

methylformamide (DMF), *t*-BuOH, and benzene have been measured by Hapala, Svoboda, and Závada.[13] Crown ethers are strong cation solvators and would be expected to strongly shift the equilibria in eq 7 to the left. The conductivity of the solutions of *t*-BuOK in DMF, *t*-BuOH, and benzene increased by factors of 2, 10, and 34, respectively, when 1 equiv of **8** was added. Even in the presence of **8**, the conductivity of *t*-BuOK in *t*-BuOH and benzene was lower than that in DMF. Thus, the crown ether does not convert *t*-BuOK totally to free ions in benzene or *t*-BuOH. However, in Me_2SO, ion pairing of *t*-BuOK has been completely removed in the presence of 18-crown-6, **9**.[14]

The dominant associated alkoxide species which are present in aprotic solvents of low polarity have been assessed by a variety of physical techniques. Ebullimetric, thermoelectric, and cryoscopic measurements[15,16] show that *t*-BuOK exists as a tetramer in toluene, benzene, diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, and pyridine. *t*-BuONa ranges from a tetramer in diethyl ether, tetrahydrofuran, and pyridine to approximately an octamer in benzene, carbon tetrachloride, and cyclohexane. In agreement with these measurements, X-ray

and mass spectrometric evidence[17-19] has been obtained for tetrameric aggregates of *t*-BuOK, but hexameric to nonameric aggregates for *t*-BuONa.

Much less information is available concerning the associated alkoxide species present in solutions of metal alkoxides in hydroxylic solvents of low polarity. Unpublished partial molar volume studies by Liotta[20] indicated that *t*-BuOK in *t*-BuOH is monomeric only at concentrations below 10^{-3} M. However, very recent measurements by Czechoslovak researchers[21] using ebulliometric and thermoelectric methods reveal that monomeric ion pairs are still the dominant base species present in 0.1–0.5 M solutions of *t*-BuOK in *t*-BuOH.

Actually the situation may be far more complex than presented in eq 7. In addition to the dissociated and the contact ion-paired base species visualized in the equation, solvent-separated ion pairs as well as multiple ions such as $(RO^-)_2M^+$ and $RO^-(M^+)_2$ are also conceivable. Although it has been possible to differentiate among dissociated ions and the different types of ion pairs through spectroscopic examinations of fluorenyl salts,[22] such a convenient probe of ion pairing has not been developed as yet for alkoxide ions. *In the absence of specific evidence regarding the actual alkoxide base species present, contact ion pairs and higher ion-pair aggregates shall therefore be referred to as the associated species and the dissociated alkoxide, solvent-separated ion pairs, and negatively charged ion triplets as the free base.*

Independent of which base species may predominate in a given reaction medium, it is important to focus attention upon the active base species. This active base species may be present in only minor concentration. Often it has been assumed that dissociated alkoxides **4** are the only active base species. Later in this review evidence will be presented which demonstrates that this assumption is often invalid in solvents of low polarity such as *t*-BuOH and benzene and even in highly polar solvents such as DMF and Me_2SO in certain instances.

B. Elimination from 2-Substituted Alkanes

1. Stereochemistry

Formation of internal alkenes in eliminations from 2-alkyl bromides and tosylates usually occurs with exclusive anti-elimination stereochemistry. Within the limits of experimental error, both *trans*-2-butene and *cis*-2-butene arise by stereospecific anti elimination for reactions of 2-butyl-*3-d* bromide with EtOK–EtOH, *sec*-BuOK–*sec*-BuOH, *t*-BuOK–*t*-BuOH, *t*-BuOK–Me_2SO, *t*-BuOK–THF, and *n*-Bu_4NF–DMF.[23,24] Similar observations have been recorded for the formation of *trans*-2-butene and *cis*-2-butene from 2-butyl-*3-d* tosylate induced by EtONa EtOH, EtOK–Me_2SO, and *t*-BuOK–Me_2SO.[25,26] More recently Chiao and Saunders[27] reported the incursion of 12% syn elimination for *trans*-2-hexene formation in reactions of 2-hexyl-*3-d* tosylate with *t*-BuONa–*t*-BuOH. However, evidence from this and other studies[28] suggests that the tendency for syn elimination would have been significantly lower if *t*-BuOK had been employed.

The stereochemistry of 2-alkyltrimethylammonium salt eliminations has also been explored. (2-Butyl-*3-d*)trimethylammonium tosylate reacts with EtOK–EtOH to form *trans*-2-butene and *cis*-2-butene principally by anti elimination.[29] Similarly, elimination from (2-hexyl-*3-d*)trimethylammonium iodide yields *trans*-2-hexene via an anti stereochemistry either exclusively (with *n*-BuOK–*n*-BuOH) or at least predominantly (15% of syn stereochemistry with *t*-BuOK–*t*-BuOH).[30]

Thus, a strong propensity for anti stereochemistry is observed in eliminations from 2-alkyl halides, tosylates, and trimethylammonium ions.

Table II. Olefinic Products from Reactions of 2-Substituted Butanes[a] with 0.05 M *t*-BuOK–*t*-BuOH at 50 °C

leaving group	dicyclohexano-18-crown-6 present[b]	% of 1-butene in total alkenes	*trans*-2-butene: *cis*-2-butene
Br	no	44.1	1.66
Br	yes	32.5	2.92
OTs	no	63.5	0.40
OTs	yes	53.6	1.88

[a] [2-BuX] = 0.10 M. [b] [Crown ether] = 0.28 M.

Table III. Olefinic Products from Reactions of 2-Alkyl Tosylates with 0.37 M *t*-BuOM–*t*-BuOH at 80 °C

	t-BuOK		*t*-BuONa	
alkyl group	% 1-alkene	*trans*-2-alkene: *cis*-2-alkene	% 1-alkene	*trans*-2-alkene: *cis*-2-alkene
2-heptyl	80.5	0.27	74.2	0.22
2-octyl	80.4	0.29	74.5	0.26

2. Base Association and Orientation for 2-Alkyl Halides and Tosylates

a. Effects of Crown Ether and Cation

Strong evidence for a dichotomy of active base species is provided by the influence of dicyclohexano-18-crown-6, **8**, upon orientation in reactions of 2-butyl bromide and tosylate with *t*-BuOK–*t*-BuOH (Table II).[31,32] Both positional (relative amounts of 1-butene and 2-butenes) and geometrical (relative amounts of *trans*-2-butene and *cis*-2-butene) orientation are affected. For both 2-butyl bromide and tosylate, addition of crown ether decreases the percent of 1-butene and increases the *trans*-2-butene:*cis*-2-butene ratio. Since dicyclohexano-18-crown-6 is a powerful potassium ion complexing agent, the base species equilibria represented in eq 7 should be strongly shifted toward the left in its presence. Therefore, it was proposed that the orientation observed in the presence of this crown ether results from free *tert*-butoxide ion base whereas in the absence of crown ether both free and associated base forms are active base species.

Further support for the proposal that free *tert*-butoxide is the active base species in the presence of crown ether is derived from the orientation observed in eliminations from 2-bromobutane promoted by *t*-$BuO^-{}^+N$-*n*-Pr_4 in *t*-BuOH.[31,32] The orientation (31.3% of 1-butene and *trans*-2-butene:*cis*-2-butene = 2.99) is within experimental error of that found for crown-ether-complexed *t*-BuOK (Table II). Since tetraalkylammonium salts are highly dissociated even in solvents of low polarity, the orientation must be that for free *tert*-butoxide base species in both systems.

In general, production of the free base species by crown ether complexation of potassium alkoxides is preferable to the use of tetraalkylammonium alkoxides. Destruction of ammonium ions by Hofmann elimination to give alkene and trialkylamine or by alkyl group displacement occurs under the strongly basic conditions and temperatures used for most base-promoted 1,2-elimination reactions.

The effect upon orientation of changing the alkali metal cation has also been examined for reactions of 2-heptyl and 2-octyl tosylates with *t*-BuOK and *t*-BuONa in *t*-BuOH (Table III).[33] Change from *t*-BuOK to *t*-BuONa produces parallel decreases in both the percentages of 1-alkene and the *trans*-2-alkene:*cis*-2-alkene ratios. It was not possible to study further variation of the cation to lithium since *t*-BuOLi is such a weak base in *t*-BuOH that concurrent solvolytic processes become important. Although the reasons for the orientation changes

Table IV. Olefinic Products from Reactions of 2-Butyl and 2-Decyl Halides and Tosylates with *t*-BuOK-*t*-BuOH

		0.10 M *t*-BuOK		0.25 M *t*-BuOK		0.50 M *t*-BuOK		1.00 M *t*-BuOK	
2-alkyl group	leaving group	% 1-alkene	trans:cis[c]	% 1-alkene	trans:cis[c]	% 1-alkene	trans:cis[c]	% 1-alkene	trans:cis[c]
2-butyl[a]	I	24.4	2.36	28.6	2.14	29.9	2.09	33.3	1.95
	Br	37.7	1.86	41.6	1.78	44.1	1.66	50.6	1.47
	OTs	52.9	0.70	60.4	0.37	62.9	0.35	63.5	0.39
2-decyl[b]	I	66.7	1.89	68.8	1.81	69.7	1.78	74.5	1.68
	Br	77.0	1.44	76.5	1.37	79.7	1.25	84.1	1.12
	Cl	83.1	1.17	84.0	1.11	84.5	1.10	87.2	1.00
	OTs	76.7	0.36	78.7	0.30	79.9	0.28	81.8	0.24

[a] Reactions at 50 °C. [b] Reactions at 120 °C. [c] 2-Alkenes.

cannot be unambiguously explained at present, they provide additional evidence that the associated base species take part in the elimination reactions.

b. Effect of Base Concentration

The equilibrium between free and associated base species should be concentration dependent,[26,32] with the proportion of associated base being enhanced by increases in the total base concentration. Support for this prediction is provided by orientation data for eliminations from 2-butyl and 2-decyl halides and tosylates using different concentrations of *t*-BuOK in *t*-BuOH (Table IV).[35] Thus, increases of total base concentration produce a uniform shift to greater percentages of 1-alkene and lower *trans*-2-alkene:*cis*-2-alkene ratios. As may be seen from the data in Table IV, the effect is operative for both secondary alkyl groups and for several different leaving groups. The observed changes in orientation produced by increased total base concentration are consistent with a shift to an enhanced contribution by the associated base species.

An influence of the base species competition upon the magnitude of isotope effects in anti elimination has been observed.[38] The primary kinetic deuterium isotope effect for formation of 1-hexene from 1-deuterio-2-bromohexane smoothly increases as the total base concentration of *t*-BuOK in *t*-BuOH is enhanced. The k_H/k_D value of 3.7 observed with 0.1 M *t*-BuOK increases to 6.1 with 1.0 M *t*-BuOK. Sensitivity of the magnitude of the deuterium isotope effect to the total base concentration suggests that the extent of C_β–H bond rupture may be very different in reactions with the free and associated base species. However, an alternative explanation must also be considered. The propensity for proton tunneling by the free and associated bases may be different, giving rise to a change in the deuterium isotope effect as the balance between free and associated base species varies. Although Miller and Saunders[37] have recently demonstrated the importance of tunneling contributions to measured deuterium isotope effect values for eliminations from 3-methyl-2-butyl *p*-nitrobenzenesulfonate induced by EtONa-EtOH and *t*-BuOK-*t*-BuOH, it remains to be seen if the tunneling corrections will be the same or different for free and associated forms of the same base in a common solvent.

An interesting aspect of the study by Miller and Saunders[37] is the effect of proton tunneling upon positional orientation in eliminations from 3-methyl-2-butyl *p*-nitrobenzenesulfonate promoted by EtONa-EtOH and *t*-BuOK-*t*-BuOH. In both base-solvent combinations, tunneling was found to be more important in the formation of the terminal alkene. When corrected for tunneling, the proportion of 3-methyl-1-butene obtained with EtONa-EtOH decreased from the observed 18% to 6% and that produced with *t*-BuOK-*t*-BuOH diminished from 68% to 47%. It is noteworthy that the changes in both the observed and corrected positional orientation for base-solvent variation from EtONa-EtOH to *t*-BuOK-*t*-BuOH are quite similar. Therefore, although the results of Miller and Saunders suggest that proton tunneling may moderately influence observed positional orientation (and possibly geometrical orientation) in eliminations from 2-substituted alkanes, it appears that the observed orientation changes caused by variation of the base-solvent combination are a good approximation of the true (corrected for proton tunneling) shifts in relative product proportions.

Table V. Olefinic Products from Reactions of 2-Halodecanes with *t*-BuOK in Different Solvents

2-decyl-X, X =	in Me_2SO[a] at 20 °C		in *t*-BuOH[b] at 100 °C		in benzene[c] at 120 °C	
	% 1-decene	trans:cis[d]	% 1-decene	trans:cis[d]	% 1-decene	trans:cis[d]
I	32.1	5.7	68.2	1.8	66.1	1.5
Br	48.0	5.3	79.4	1.3	79.9	0.8
Cl	59.4	5.1	84.5	1.1	86.0	0.7
F	96.8	3.0	92.4	0.8	94.0	0.5

[a] [*t*-BuOK] = 0.5 M. [b] [*t*-BuOK] = 0.33 M. [c] [*t*-BuOK] = 0.13 M. [d] 2-Decenes.

Table VI. Olefinic Products from Reactions of 2-Bromobutane with *t*-BuOK in Different Solvents

solvent (temp, °C)	% 1-butene	*trans*-2-butene: *cis*-2-butene
Me_2SO[a] (50)	31	3.0
THF[b] (25)	34	3.6
t-BuOH[a] (50)	51	1.47

[a] [*t*-BuOK] = 1.0 M. [b] Saturated solution.

c. Effect of Solvent and Additives Other Than Crown Ethers

As was noted in section II.A, the relative concentrations of free and associated base species should be strongly solvent dependent. Table V records the orientation observed for eliminations from the 2-halodecanes induced by a common base *t*-BuOK in Me_2SO, *t*-BuOH, and benzene.[38] With exception of the very poor fluoro leaving group, there is a uniform increase in the percentages of 1-decene and a sharp decline in *trans*-2-decene:*cis*-2-decene ratios as the solvent is changed from Me_2SO to *t*-BuOH or benzene. Such changes in orientation are entirely consistent with the increased participation of associated base species in solvents of low polarity. The different reaction temperatures required for convenient reaction rates in the three solvents underscore a decrease in reactivity as the base species becomes more associated.

Although *t*-BuOH and benzene are solvents of low polarity (ϵ = 10.9 at 30 °C and 2.28 at 20 °C,[39] respectively) and are poor cation solvators, there are other solvents of low polarity which are good cation solvators. Tetrahydrofuran (THF), for instance, has a dielectric constant of 7.6 at 20 °C,[40] but is well-known for its ability to solvate cations. Table VI records the orientation observed[24] in eliminations from 2-bromobutane promoted by *t*-BuOK in Me_2SO, THF, and *t*-BuOH. Thus, even though the polarity of THF is lower than that of *t*-BuOH, the observed orientation closely resembles that which is obtained in the polar solvent Me_2SO.

An extensive investigation of the base concentration effect

Table VII. Olefinic Products from Reactions of 2-Decyl Halides and Tosylate with *t*-BuOK in THF at 50 °C

	0.10 M *t*-BuOK		0.25 M *t*-BuOK		0.50 M *t*-BuOK		1.00 M *t*-BuOK	
leaving group	% 1-decene	trans:cis[a]	% 1-decene	trans:cis[a]	% 1-decene	trans:cis[a]	% 1-decene	trans:cis[a]
I	36.3	5.51	37.5	5.44	39.5	5.30	42.2	4.90
Br	52.5	4.86	54.0	4.61	55.6	4.09	58.8	3.72
Cl	66.2	4.04	69.5	3.48	70.5	3.15	72.8	2.36
OTs	83.2	1.47	84.1	1.30	84.5	1.18	85.7	1.10

[a] 2-Decenes.

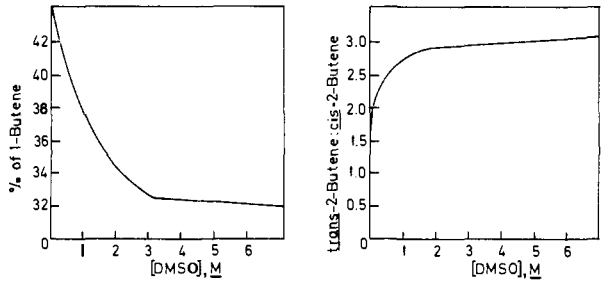
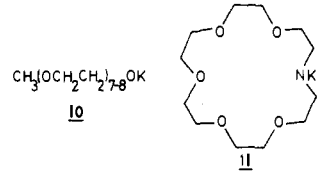


Figure 3. Effect of Me_2SO upon orientation in eliminations from 2-bromobutane induced by 0.50 M *t*-BuOK–*t*-BuOH.

upon positional and geometrical orientation in eliminations from 2-decyl halides and tosylate induced by *t*-BuOK–THF has recently been completed.[35] The results recorded in Table VII show that, irrespective of the leaving group identity, both positional and geometrical orientation are influenced by the total base concentration. The changes in % 1-decene and *trans*-2-decene:*cis*-2-decene with enhanced *t*-BuOK concentration follow the same trends established earlier in *t*-BuOH solvent (Table IV). However, the uniformly higher *trans*-2-decene:*cis*-2-decene ratios observed in THF suggest the operation of a less associated base species than in *t*-BuOH.

Figure 3 illustrates the effect of varying amounts of Me_2SO upon positional and geometrical orientation in eliminations from 2-butyl bromide induced by *t*-BuOK–*t*-BuOH.[31] Marked sensitivity of orientation to the amount of added Me_2SO is observed until a concentration of 2 to 3 M is reached. Further increases produce only very small changes in orientation. These results are readily understandable if the effect of Me_2SO is to increase the proportion of free base species through solvation of potassium cations. In correlation with their donicity numbers, hexamethylphosphortriamide and dimethylformide have a greater influence in producing the free base species than has Me_2SO. Tetramethylene sulfone (sulfolane) has a lesser influence than Me_2SO.

Although pronounced changes in both positional and geometrical orientation are usually noted as the solvent is changed from a good cation solvating solvent, such as Me_2SO, to a poor one, such as benzene or toluene, there are some notable exceptions. The "self-solvating" bases **10** and **11** exhibit the

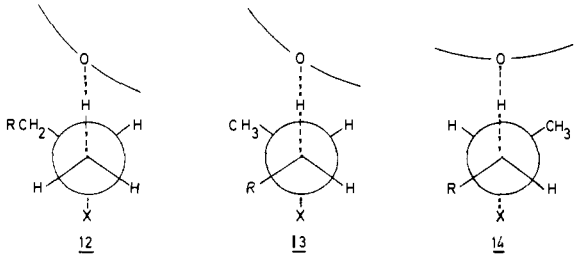


same orientation in eliminations from 2-butyl iodide in Me_2SO and in toluene.[41] In both cases, association of the cation with the basic site is unimportant even in toluene due to the "solvation" of the potassium cation by the polyether portion of the base.

d. Models for Effects of Base Association upon Orientation

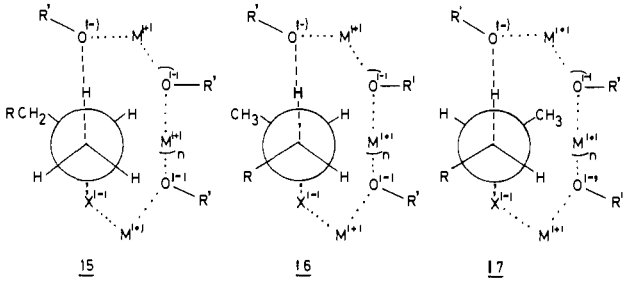
From the preceding evidence and discussion, it is clear that eliminations from 2-alkyl halides and tosylates which are induced by associated base species produce substantially higher proportions of 1-alkene and lower *trans*-2-alkene:*cis*-2-alkene ratios than do those of the corresponding free base. Four models have been proposed to rationalize this general observation. These shall be identified as the clump aggregate model, the belt aggregate model, the ion-pair model, and substrate dielectric model.

(*1*) *Clump Aggregate Model.* In this model, which was proposed by Bartsch,[31,32] the associated base species is thought to be a clump aggregate of ion pairs which has large steric dimensions. In going from the free base to the associated base species, transition states for formation of 1-alkene, **12**, and *cis*-2-alkene, **13**, are less affected than that for



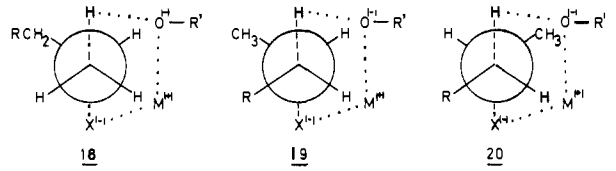
trans-2-alkene formation, **14**, because of the possibility of tilting the base aggregate in **12** and **13** to relieve steric interactions between the bulky base and α- and/or β-alkyl groups. Since the destabilizing steric interactions should increase in the order **12** $\leq$ **13** $<$ **14** as one goes from the free base to the clump aggregate, the relative percentage of 1-alkene should increase and the *trans*-2-alkene:*cis*-2-alkene ratio should decrease, as observed.

(*2*) *Belt Aggregate Model.* For the belt aggregate model advanced by Schlosser,[42,43] a nonmonomeric associated base species is also involved. Because of poor solvolytic stabilization of the departing leaving group in solvents of low polarity, it is deemed important to "solvate" the leaving group in the transition state by concomitant coordination of the cation of the base with the leaving group and the end of a belt of aggregated ion pairs, as illustrated in **15**, **16** and **17**. In the cyclic arrangement required for the coordination, steric interactions between the belt aggregate and the alkyl groups should be important only in the transition state for *trans*-2-alkene (**17**) formation. Thus, for the associated base species, transition state **17** would be destabilized relative to those for formation of 1-alkene and *cis*-2-alkene, **15** and **16**, respectively.



(*3*) *Ion Pair Model.* Zāvada and Schlosser[44,45] have proposed a variation of the belt aggregate model in which "solvation" of the leaving group is still important, but the associated base species is only an ion pair, as illustrated in **18**,

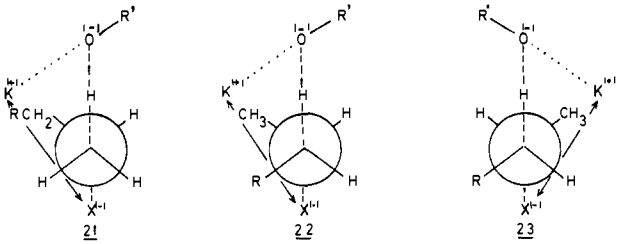
19, and **20**. Such stabilizing "solvation" of the leaving group should be seriously inhibited by the alkyl groups only in the



18 **19** **20**

transition state leading to *trans*-2-alkene. Therefore, when base association is important, an increased proportion of the elimination should proceed through transition states **18** and **19**, producing enhanced percentages of 1-alkene and *cis*-2-alkene.

(*4*) *Substrate Dielectric Model*. It was postulated by Saunders[46] that the base may not avoid alkyl group congestion in the substrate, but actually seek it out as providing the most favorable medium of conduction for electrostatic interaction of an ion-paired base with the leaving group. The attractive interactions may operate almost entirely through the substrate skeleton in transition states for *cis*-2-alkene formation, **22**, but have to pass in part through the solvent in those forming *trans*-2-alkene and 1-alkene, **21** and **23**, respectively. Ac-



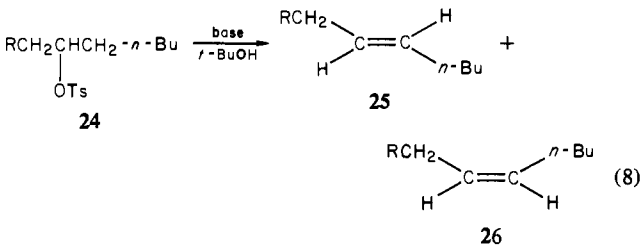
21 **22** **23**

cording to this model, an increase in the relative proportion of *cis*-2-alkene but decreases in the percentages of both *trans*-2-alkene and 1-alkene should be anticipated for the associated base species.

(*5*) *Assessment of Models*. The clump aggregate, belt aggregate, and ion-pair models all predict the observed increase in relative percentage of 1-alkene and decrease in *trans*-2-alkene:*cis*-2-alkene ratio for associated base species. However, the substrate dielectric model suggests simultaneous decreases in the percentage of 1-alkene and the *trans*-2-alkene:*cis*-2-alkene ratio. Since these predictions are not in accord with the observations for associated base species, the substrate dielectric model is discounted.

There exists a fundamental difference between the clump aggregate model on the one hand and the belt aggregate and ion-pair models on the other. In the clump aggregate model, there should be a large difference in the size of the associated and free base species with regards to their interactions with α- and/or β-alkyl groups. On the other hand, the relative dimensions of the associated and free base species are unimportant to the operation of the belt aggregate and ion-pair models.

Very recent work by Závada and Pánková[47] using 18-crown-6 to effect the associated → free *t*-BuOK base conversion provides important insight into the steric requirements of the two alternative species. Rates of anti elimination for the reactions shown in eq 8 and 9 were determined (cf. section III.D.2.a.4) with *t*-BuOK–*t*-BuOH in the absence[46] and in the



24 **25** **26** (8)

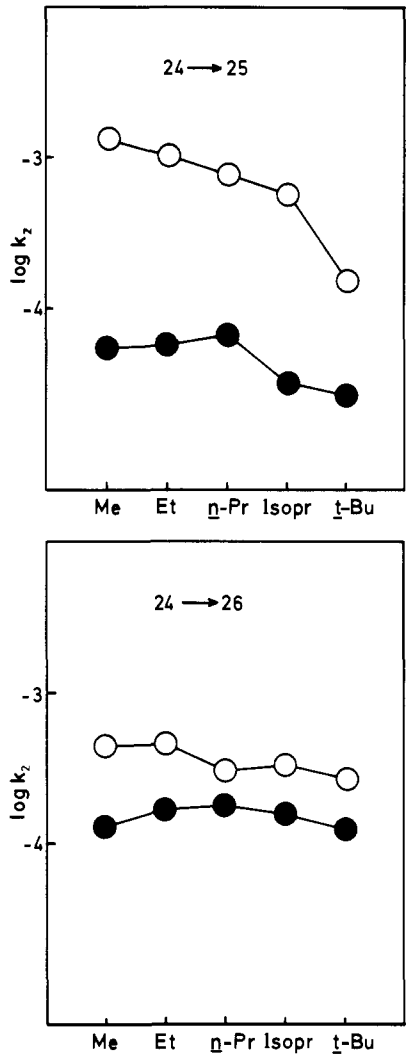
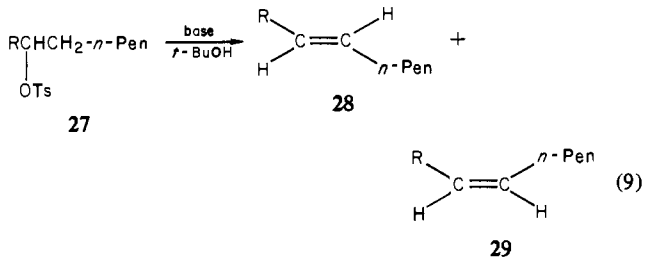


Figure 4. Effect of R variation upon rates of anti elimination from tosylates **24** (filled circles, reaction with 0.43 M *t*-BuOK–*t*-BuOH in the absence of crown ether at 80.7 °C; open circles, reaction with 0.23 M *t*-BuOK–*t*-BuOH in the presence of 0.23 M 18-crown-6 at 25.4 °C).



27 **28** **29** (9)

presence[47] of the crown ether. The observed variations in rates of the individual anti-elimination processes promoted by the associated and free base as the group R was changed in the order Me, Et, *n*-Pr, *i*-Pr and *t*-Bu are presented graphically in Figures 4 and 5.

As is readily evident, the variation of elimination rates with R found for the associated and free base (i.e., in the absence and in the presence of crown ether, respectively) are quite similar. This indicates similar steric requirements for the two types of base species. Transition states for the formation of *trans*-alkenes **25** and **28** from substrates **24** and **27** using the clump-aggregate base model are represented in **30** and **31**. Steric repulsions in these transition states should be very sensitive to variation of R. However, the anticipated sharp decline in rate of formation of **25** and **28** for the associated base as the steric requirements of R are increased is not observed. This

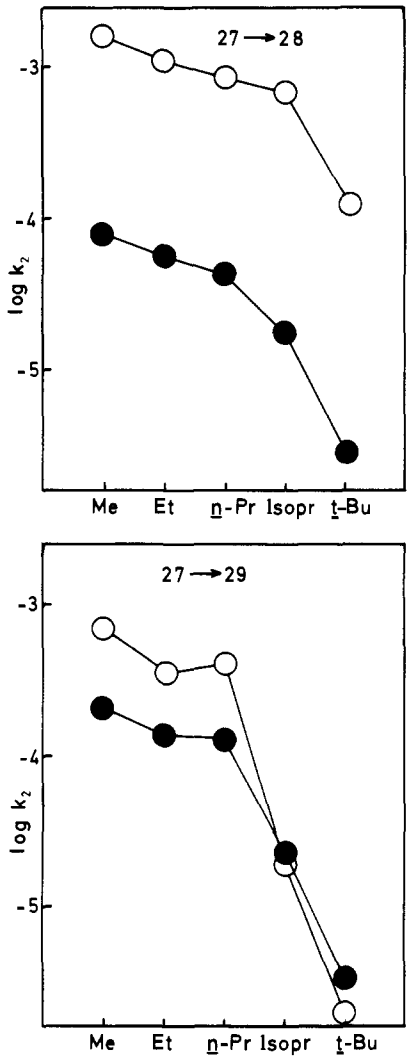
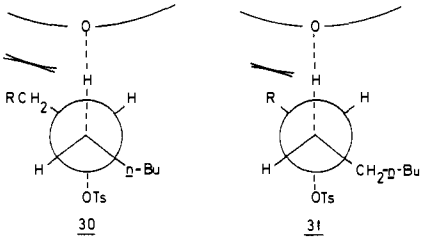


Figure 5. Effect of R variation upon rates of anti elimination from tosylates **27** (filled circles, reaction with 0.43 M *t*-BuOK–*t*-BuOH in the absence of crown ether at 80.7 °C; open circles, reaction with 0.23 M *t*-BuOK–*t*-BuOH in the presence of 0.23 M 18-crown-6 at 25.4 °C).

provides strong evidence against the operation of the clump aggregate model.



The remaining belt aggregate and ion-pair models differ in the degree of association of the active base species. The ion-pair model involves a monomeric base whereas the belt aggregate model utilizes a dimer or higher aggregate of ion pairs.

In principle, it should be possible to kinetically differentiate between these alternatives. Assuming that there is one dominant base species in solution and that the equilibrium between this dominant species D and the active species A is rapid compared to the rate of elimination, the rate of elimination from substrate S is given by eq 10 and [A] is given by eq 11 where

$$\text{rate} = k[\text{A}][\text{S}] \tag{10}$$

$$[\text{A}] = (K[\text{D}]^d)^{1/a} \tag{11}$$

Table VIII. Kinetic Dependence upon Overall Base Concentration Expected for Various Combinations of Dominant and Active Base Species

dominant base	active base				
	$M^+ + B^-$	(M^+B^-)	$(M^+B^-_2)^-$	$(M^+B^-)_2$	$(M^+B^-)_4$
$M^+ + B^-$	1	2	3	4	8
(M^+B^-)	$^1/_2$	1	$^3/_2$	2	4
$(M^+_2B^-)^+$ or $(M^+B^-_2)^-$	$^1/_3$	$^2/_3$	1	$^4/_3$	$^8/_3$
$(M^+B^-)_2$	$^1/_4$	$^1/_2$	$^3/_4$	1	2
$(M^+B^-)_4$	$^1/_8$	$^1/_4$	$^3/_8$	$^1/_2$	1

K is the equilibrium constant and a and d are stoichiometric coefficients for A and D, respectively, in the rapid equilibrium between the two base species: If the concentration of the

$$d\text{D} \underset{}{\overset{K}{\rightleftharpoons}} a\text{A} \tag{12}$$

dominant base species, [D], is approximately equal to the overall base concentration, $[B_{tot}]$, the rate of elimination can be rewritten (eq 13) and the kinetic dependence upon overall

$$\text{rate} = k'[B_{tot}]^{d/a}[\text{S}] \tag{13}$$

base concentration expected for different combinations of dominant and active base species can be calculated (Table VIII). For example, if a tetramer of ion pairs is the dominant species present but the ion-pair monomer is the active species, a one-fourth kinetic order in base should be observed. In the reverse case, when the tetramer is the active base and the monomer is the dominant base species, a fourth order in base would be obtained. Another important point is also illustrated by the data in Table VIII. A first-order dependence upon base concentration will be observed any time the dominant and active base species are the same.

As described in section II.A, thermoelectric measurements have established that the dominant *t*-BuOK species present in *t*-BuOH is the monomeric ion pair. In THF, benzene, and toluene the dominant base species is the tetramer of ion pairs.

Until very recently, little information was available concerning the base concentration dependence of eliminations from 2-substituted alkanes induced by *t*-BuOK in solvents of low polarity. Brown and Klimisch[49] studied eliminations from 2-butyl halides induced by *t*-BuOK–*t*-BuOH under pseudo-first-order conditions (excess base) and assumed a first-order dependence upon *t*-BuOK concentration. Very recently, Závada and his colleagues[50] determined the effects of base concentration upon rates of olefin formation in *t*-BuOK-promoted eliminations from 2-bromodecane in *t*-BuOH and THF. The orders in base found for reactions forming 1-decene, *cis*-2-decene, and *trans*-2-decene are listed in Table IX. The nearly first-order dependence upon base concentration observed in *t*-BuOH identifies the active base species as the dominant base species, a monomeric ion pair. On the other hand, in THF the active base species is not the dominant species (tetramer of ion pairs). On the basis of the kinetic order in *t*-BuOK, the active base species in THF appears to be a mixture of monomeric and dimeric ion pairs. Ion triplets are also conceivable base species.

It is interesting to compare these results for unactivated 1,2-elimination with those for substrates bearing moderately activating β substituents, such as aryl and halogen groups.

Several kinetic studies of olefin formation by anti elimination from β-aryl-activated halides and arenesulfonates promoted by *t*-BuOK in *t*-BuOH have been reported.[51-58] A first-order dependence in concentration of base has been uniformly observed. This kinetic behavior is consistent with monomeric ion pairs as the effective base species.

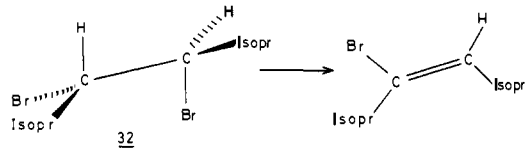
Schlosser, Jan, Byrne, and Sicher[43] have investigated *t*-BuOK-promoted eliminations from β-halogen-activated substrates in toluene. Eliminations from *meso*-3,4-dibromo-2,5-

Table IX. Base Concentration Dependence for Olefin Formation from 2-Bromodecane Promoted by *t*-BuOK in *t*-BuOH and THF

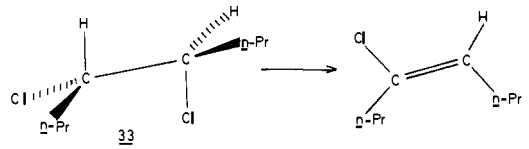
solvent	order in base for formation of 1-decene	*cis*-2-decene	*trans*-2-decene
t-BuOH[a,b]	1.17	1.10	1.02
THF[c,d]	0.44	0.49	0.33

[a] At 80.1 °C. [b] Range of base concentrations was 0.07-0.66 M. [c] At 20.0 °C. [d] Range of base concentrations was 0.10-1.00 M.

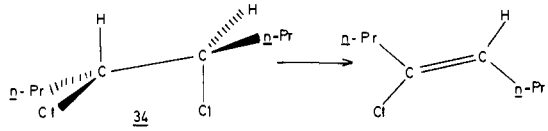
dimethylhexane (**32**), *meso*- and *dl*-4,5-dichlorooctanes (**33**, **34**), and *cis*-1,2-dichlorocyclodecane were examined. For anti elimination from **32** (eq 14), a first-order dependence in base



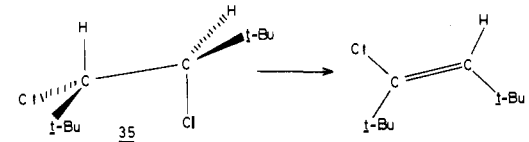
(14)



(15)



(16)



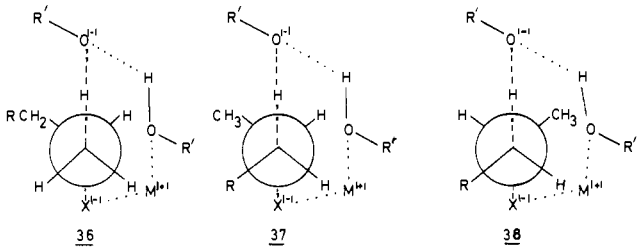
(17)

concentration was observed. Since the predominant base is the *t*-BuOK tetramer, the first-order dependence upon base concentration identifies the tetramer as the active base species. For the anti dehydrochlorinations of **33**, **34**, and *cis*-1,2-dichlorocyclodecane, the kinetic order in base varied between 0.7 and 0.9. Divergence of these values from unity reveals that tetramers and also less associated base species are active in eliminations from these substrates. Quite recently, anti dehydrochlorination from *meso*-3,4-dichloro-2,2,5,5-tetramethylhexane (**35**) was subjected to an analogous kinetic scrutiny.[57] With *t*-BuOK-THF and *t*-BuOK-*t*-BuOH, apparent orders in base of 0.8 and 0.9-1.2, respectively, were found.

Thus, the available data concerning active base species in *t*-BuOK-induced eliminations from unactivated substrates are qualitatively consistent with those for eliminations from substrates bearing moderately activating groups in the β position. In *t*-BuOH the main active base species is the monomeric ion pair. However, in nonhydroxylic solvents of low polarity, such as THF, benzene, and toluene, higher aggregates of ion pairs appear to be the effective base species.

With such information in hand the remaining ion pair and belt aggregate models for effects of base association upon orientation may be reconsidered.

For eliminations induced by *t*-BuOK-*t*-BuOH, the belt aggregate model is clearly inappropriate because the active base is the monomeric ion pair. A somewhat bothersome[46] (but not prohibitive[45]) feature of the residual ion pair model **18-20** is the nonlinear approach of the base to the C_β-H bond which is postulated[44,45] in order to minimize the distance between the metal ion and its sites of interaction (the leaving group and the oxygen of the base). In view of the well-known propensity of *t*-BuOK to form a very strong solvate with one molecule of *t*-BuOH,[58,59] it is suggested[50] that the original ion-pair model be modified to an electrostatic model involving solvated ion pairs **36-38**. This beltlike arrangement allows a nearly collinear



approach of the alkoxide to the C_β-H bond as well as promixity of the cation and the leaving group X.

For eliminations promoted by *t*-BuOK in solvents such as benzene and toluene, operation of the belt aggregate model **15-17** is in accord with the active base species indicated by the kinetic studies.

Because of similarities in beltlike structures for the solvated ion-pair and belt-aggregate models, it might be anticipated that orientation should be similar for *t*-BuOK-promoted eliminations in *t*-BuOH and benzene. The orientation data for reactions of 2-halodecanes with *t*-BuOK in *t*-BuOH and benzene presented in Table V bear out this expectation.

However, *t*-BuOK-induced elimination in THF would appear to be anomalous. Although there is kinetic evidence for involvement of an active base with a degree of association greater than monomeric ion pairs, the orientation observed for reactions of 2-halodecanes with *t*-BuOK-THF (Table VII) is very different from that noted in *t*-BuOH and benzene (Table V). It is proposed[21] that the cation-solvating abilities of THF considerably disrupt operation of the belt-aggregate model. Therefore, leaving group interactions with a beltlike base aggregate becomes less important, and the orientation is more similar to that obtained in Me_2SO (Table V).

3. *Effect of Base Strength and Size upon Orientation*

a. Free Bases

Recognition of the strong influence of base association upon orientation in oxyanion-promoted eliminations has allowed Bartsch and co-workers[60] to settle a long-standing controversy concerning the relative influence of base strength and size in controlling positional orientation. For reactions of oxyanion bases with 2-butyl iodide in Me_2SO, an excellent linear free energy relationship is observed between positional orientation and the base strength (Figure 6). The relationship covers a greater than 20 p*K* unit variation in base strength and includes carboxylates, phenolates, and primary, secondary, and tertiary alkoxides. This result demonstrates a fundamental control of positional orientation by base strength in eliminations induced by oxyanion bases. More recent work[61] extends this conclusion to free anionic nitrogen and carbon bases as well.

The increased proportion of terminal alkene obtained by enhancing the strength of dissociated oxyanion bases may be readily interpreted using the variable E2 transition-state theory (section I.C). Increasing the base strength should stabilize the upper left corner of the More O'Ferrall plot in Figure 2 and thereby increase the carbanion character of the transition state. A fundamental difference between transition states forming 1-alkene and 2-alkenes in eliminations from 2-substituted alkanes is the presence of a β-methyl group in the latter but its absence in the former. Due to the presence of this electron-donating methyl group, transition states for formation of 2-alkenes are destabilized when the amount of negative charge on C_β is increased (i.e., enhanced carbanion character). Similar

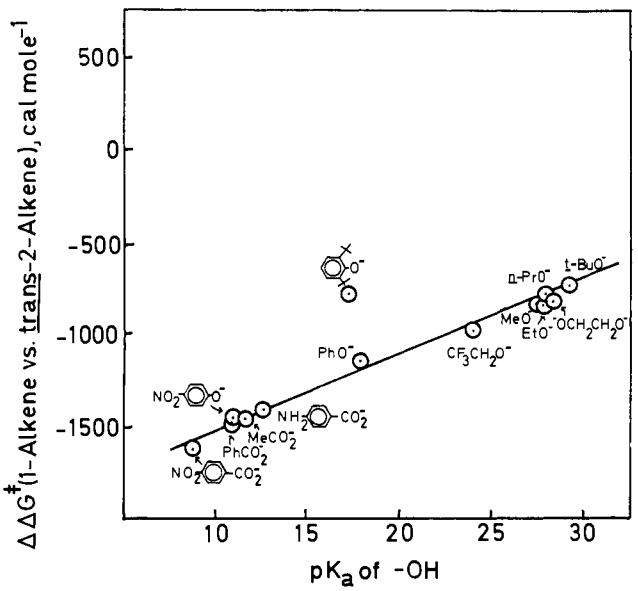


Figure 6. Plot of free-energy difference for formation of 1-butene and *trans*-2-butene vs. the pK_a of the conjugate acid of the base for eliminations from 2-iodobutane.

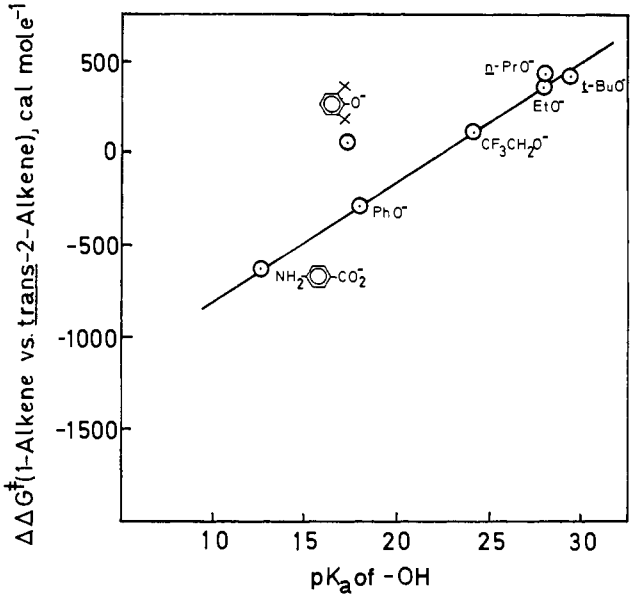


Figure 7. Plot of free-energy difference for formation of 1-butene and *trans*-2-butene vs. the pK_a of the conjugate acid of the base for eliminations from 2-butyl tosylate.

destabilization of the 1-alkene-forming transition state with increasing carbanion character does not occur. Therefore, increasing base strength enhances the relative proportion of terminal olefin by changing the transition-state character.

In the plot presented in Figure 6, only one base, the highly ramified 2,6-di-*tert*-butylphenoxide, is divergent. For this base, more 1-butene is formed than would be predicted according to the base strength. This is exactly the result anticipated for the onset of base steric factors which favor removal of sterically more accessible methyl β-hydrogens than the more congested methylene β-hydrogens. Therefore, a base steric effect may be superimposed upon the base strength control of positional orientation for highly ramified free bases. In subsequent work,[82,83] it has been demonstrated that tricyclohexylmethoxide, tri-2-norbornylmethoxide, and di-*tert*-butyl-*n*-octadecylmethoxide, but not triphenylmethoxide, exhibit base steric effects upon orientation in eliminations from 2-iodobutane in Me_2SO. Recent calculations[64] confirm the importance of steric effects in influencing orientation for eliminations from secondary alkyl

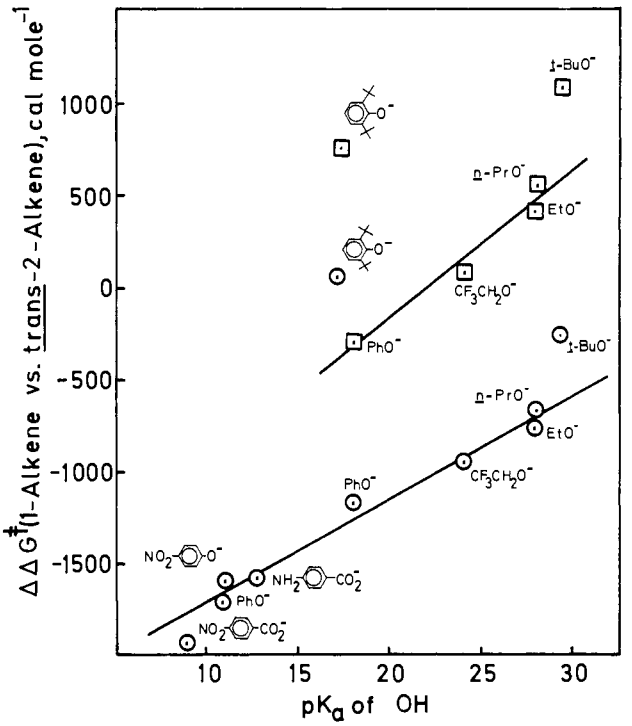


Figure 8. Plots of free-energy difference for formation of 4-methyl-1-pentene and *trans*-2-methyl-2-pentene vs. the pK_a of the conjugate acid of the base for eliminations from 4-methyl-2-pentyl iodide (circles) and tosylate (squares).

halides promoted by ramified oxyanion bases.

For reactions of 2-butyl tosylate with oxyanion bases in Me_2SO (Figure 7) positional orientation is again controlled by base strength for all except an outsized base.[65] Difference in correlation line slopes in Figures 6 and 7 reveals that orientation in eliminations from 2-butyl tosylate is more sensitive to base strength variation than that in the 2-butyl iodide reactions. It is interesting to note that the vertical displacements from the correlation line for the bulky base 2,6-di-*tert*-butylphenoxide is the same with 2-butyl iodide and tosylate. Therefore, in eliminations from 2-butyl halides and arenesulfonates, steric hindrance to base attack at the methylene hydrogens is independent of leaving group identity.

The influence of substrate structure upon the threshold of base steric effects has recently been probed by Bartsch and co-workers.[65] Figure 8 shows the relationships between positional orientation and base strength for oxyanion-promoted eliminations from 4-methyl-2-pentyl iodide and tosylate. As may be seen, *tert*-butoxide ion base is now divergent from the relationships. Thus, for substrates of moderate complexity, all free tertiary alkoxides may be anticipated to exert both base strength and steric effects upon positional orientation. In agreement with predictions made with the use of molecular models, calculations reported by Tremelling and co-workers[84] confirm that base steric effects should become more important as the size of the β-alkyl group is increased.

As previously observed with 2-substituted butanes, the vertical displacement of points from the correlation line in Figure 8 for bases exhibiting steric interactions is independent of leaving group identity. Also, sensitivity of positional orientation to base strength variation is again greater with a tosyloxy leaving group than with an iodo group.

Both associated bases and ramified free bases produce greater proportions of the thermodynamically least stable 1-alkene in eliminations from 2-alkyl halides and tosylates than do free bases of moderate dimensions. Since ramified free bases possess the advantage of considerably higher reactivity than associated base species, it was of interest to compare the

Table X. Olefinic Products from Reactions of 2-Iodobutane with 0.25 M Potassium *tert*-Alkoxides in Me_2SO at 50 °C

base	% 1-butene	*trans*-2-butene: *cis*-2-butene
tert-butoxide	20.7	2.99
triethylmethoxide	20.9	3.13
di-*tert*-butyl-*n*-octadecylmethoxide	24.5	3.31
tricyclohexylmethoxide	27.2	3.04
tri-2-norbornylmethoxide	29.4	3.41
tert-butoxide (0.25 M in *t*-BuOH)	29.9	2.09

positional orientation control provided by the two types of bases. In order to examine this question, orientation in reactions of 2-butyl iodide with a number of tertiary alkoxides in Me_2SO was determined.[63] Results are recorded in Table X. None of the sterically congested free bases eclipse the orientation control provided by *t*-BuOK–*t*-BuOH (last entry in Table X). Similar results were obtained for eliminations from 4-methyl-2-pentyl iodide.[65] Therefore, the concept of sterically hindered free bases which combine the orientation control of associated bases with high reactivity appears to be untenable.

The orientation data in Table X reveal an important difference between ramified free bases and associated bases. For associated bases, the increase in percentage of 1-alkane (when compared with the corresponding free base of moderate size) is accompanied by a decrease in the *trans*-2-alkene:*cis*-2-alkene ratio. However, comparison of a ramified free base with a free base of moderate size shows an increase in the relative proportion of terminal olefin, but no effect upon geometrical orientation.

b. Associated Bases

Froemsdorf and co-workers[66–68] have reported orientations for reactions of several oxyanion bases with 2-butyl tosylate in *t*-BuOH and Me_2SO (Table XI). The gradual decreases in percentage of terminal olefin in the order *t*-BuOK > EtOK > PhOK observed in these two extreme solvents suggest an important effect of base strength upon orientation for reactions promoted by the ion-paired (in *t*-BuOH) as well as by the free (in Me_2SO) oxyanion bases. Interestingly, the trans:cis ratios in *t*-BuOH are unity or less, which indicates a general reluctance of the associated bases to participate in *trans*-olefin formation.

4. Effect of Leaving Group upon Orientation for Free and Associated Bases

a. Halide Leaving Groups

The influence of the identity of the halogen leaving group upon positional and geometrical orientation has been determined for 18 combinations of 2-alkyl group and base–solvent system (Table XII). For both free (MeONa–MeOH, EtONa–EtOH, *t*-BuOK–Me_2SO) and associated (*t*-BuOK–*t*-BuOH, *t*-BuOK–THF, *t*-BuOK–benzene) bases, the same shifts in orientation are noted as the leaving group is changed from iodo to bromo to chloro to fluoro. Thus, there are uniform shifts toward the production of a higher percentage of 1-alkene and a lower *trans*-2-alkene; *cis*-2-alkene ratio as the halogen leaving group becomes poorer. Such data provide strong evidence for a coupling of positional and geometrical orientation in these eliminations. More quantitative evidence for this coupling comes from kinetic studies of Bartsch and Bunnett[69] for eliminations from 2-hexyl halides induced by MeONa–MeOH. Excellent linear free energy relationships between log k_2(1-hexene) vs. log k_2(*trans*-2-hexene) and log k_2(1-hexene) vs. log k_2(*cis*-2-hexene) are observed for the four halogen leaving groups. Thus, for the four halogen leaving groups there is an excellent correlation between orientation and leaving group reactivity.

Table XI. Orientation in Oxyanion-Promoted Eliminations from 2-Butyl Tosylate in *t*-BuOH and Me_2SO at 55 °C

	in *t*-BuOH		in Me_2SO	
base	% 1-butene	*trans*-2-butene: *cis*-2-butene	% 1-butene	*trans*-2-butene: *cis*-2-butene
t-BuOK	64	0.58	61 (59)[a]	2.53 (2.32)[a]
EtOK	54	0.80	54 (56)	2.34 (2.41)
KOH	50	0.83		
PhOK	34	1.24	31 (46)	1.96 (2.00)

[a] Values in parentheses are more recent measurements at 50 °C reported in ref 65.

The coupling of positional and geometrical orientation may be readily rationalized within the framework of the variable E2 transition-state theory (section I.C). A gradual increase in the percentage of 1-alkene is assumed to be diagnostic for a shift in transition-state character toward the E1cB extreme. This is consistent with a prediction based upon the More O'Ferrall plot (Figure 2) in which increasing the C_α–X bond strength should destabilize the bottom right-hand corner and thereby increase the carbanionic character of the E2 transition state.

A gradual increase in values of *trans*-2-alkene:*cis*-2-alkene isomer ratios is anticipated on passing from the nearly E1 to the central region (where alkyl–alkyl interactions due to more advanced double bond development are more pronounced), followed again by a decrease of the ratio on going toward the nearly E1cB extreme from the central region.

The distribution of positional isomers in eliminations from 2-alkyl iodides induced by free base–solvent systems suggests that the transition states lie near central. The gradual, but very regular, increase in the relative percentage of 1-alkene which results from replacement of iodo by the other halogen leaving groups indicates a corresponding shift toward the E1cB region. For the fluoro leaving group, the transition state must be close to the E1cB extreme. The shift in transition-state character with halide leaving group variation is also in complete accord with the observed changes in *trans*-2-alkene:*cis*-2-alkene ratios from high values for the iodides (3.6–5.7) to lower values with the fluorides (2.3–3.0).

With the extensive data collected in Table XII, one may now ask if all halogen leaving groups are influenced by base association in the same manner as previously demonstrated for the bromo leaving group (section II.B.2). With the exception of positional orientation for fluoro, the change from a free base to the corresponding associated species produces a marked increase in the percentage of 1-alkene and a corresponding sharp diminution of the *trans*-2-alkene:*cis*-2-alkene ratio for all of the halogen leaving groups. For the fluoro group, the percentage of terminal olefin appears to be insensitive to base association (compare systems 5 and 6, 13 and 14).

It is advantageous to examine the orientation data for eliminations from the 2-decyl halides[38] induced by *t*-BuOK–benzene in the presence and absence of crown ether (systems 13 and 14) more closely. Table XIII presents ratios of different pairs of alkenes formed by the free and associated base species. In order to reveal the effect of base association upon the free-energy differences between pairs of isomers, the ratio for the associated base is divided by the ratio for the free base in the fourth, seventh, and tenth columns of the table. Data for 2-decyl fluoride are omitted from the correlation because of the low percentages of *trans*- and *cis*-2-decenes formed. A small experimental error in one of these percentages would introduce a large error in the ratios.

Focusing attention upon the ratio of ratios for the pair of olefins 1-decene and *cis*-2-decene, values near unity are calculated for the three halogen leaving groups. This means that the competition between formation of 1-decene and *cis*-2-decene is unaffected by base association. In contrast, the

Table XII. Olefinic Products from Reactions of 2-Alkyl Halides and Tosylates with Different Base-Solvent Systems

				X = I		X = Br		X = Cl		X = F		X = OTs	
system	2-alkyl-X	base-solvent	temp, °C	% 1-alkene	trans:cis[i]	% 1-alkene	trans:cis[i]	% 1-alkene	trans:cis[i]	% 1-alkene	trans:cis[i]	% 1-alkene	trans:cis[i]
1[a]	2-hexyl	MeONa-MeOH	100	19	3.6	28	3.0	33	2.9	70	2.3	39	1.7
2[b]	2-pentyl	EtONa-EtOH	reflux	20	4.1	25	3.8	35	3.5	82	2.6		
3[c]	2-butyl	*t*-BuOK-*t*-BuOH	50	33	2.2	54	1.4	67	1.3			62	0.6
5[d]	2-hexyl	*t*-BuOK-*t*-BuOH	100	69	1.8	80	1.4	88	1.1	97	1.2	80	0.4
5[e]	2-decyl	*t*-BuOK-*t*-BuOH	100	68	1.8	79	1.3	85	1.1	92	0.8	77	0.4
6[e]	2-decyl	*t*-BuOK-18-Crown-6-*t*-BuOH	100	42	5.4	53	5.1	65	3.6	91	2.9	75	2.2
7[f]	2-butyl	Et_3COK-Et_3COH	50	49	1.5	71	1.3	80	1.1				
8[f]	2-butyl	*t*-BuOK-DMSO	25	20	3.5	32	3.8	41	4.1				
9[g]	2-hexyl	*t*-BuOK-DMSO	25	35	5.2	47	4.9	59	4.9			73	2.9
10[e]	2-decyl	*t*-BuOK-DMSO	20	32	5.7	48	5.3	59	5.1	97	3.0	75	3.2
11[e]	2-decyl	*t*-BuOK-18-Crown-6-DMSO	20	31	5.5	47	5.7	59	5.3	97	3.0	79	6.0
12[f]	2-butyl	Et_3COK-DMSO	25	21	3.8	33	3.9	44	4.2				
13[e]	2-decyl	*t*-BuOK-Benzene	130	66	1.5	80	0.8	86	0.7	94	0.5	88	0.7
14[e]	2-decyl	*t*-BuOK-18-Crown-6-Benzene	20	47	3.2	62	2.7	71	2.8	95	1.4	82	1.7
15[f]	2-butyl	*t*-BuOK-Toluene	50	36	1.7	52	1.4	67	1.0				
16[f]	2-butyl	*t*-BuOK-THF	25	20	3.6	34	3.3	49	2.9				
17[h]	2-decyl	*t*-BuOK-THF	50	40	5.3	56	4.0	70	3.2				
18[f]	2-butyl	Et_3COK-THF	25	25	4.1	34	3.1	49	2.7				

[a] Reference 69. [b] Reference 70. [c] Reference 71. [d] Reference 72. [e] Reference 38. [f] Reference 73. [g] Reference 74. [h] Reference 35. [i] 2-Alkenes.

Table XIII. Ratios of Isomeric Alkenes Formed in Eliminations from 2-Decyl Halides Induced by *t*-BuOK-Benzene and by *t*-BuOK-18-Crown-6-Benzene

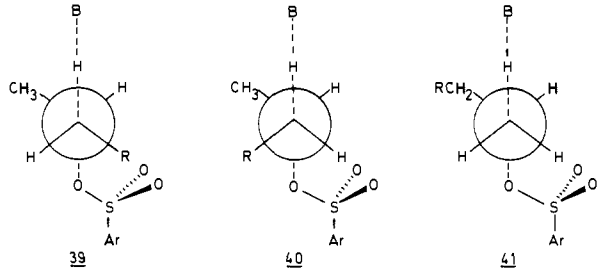
leaving group	% 1 / % *t*-2	$(\% 1/\% t\text{-}2)_{CE}$	(% 1/% *t*-2) / $(\% 1/\% t\text{-}2)_{CE}$	% 1 / % *t*-2	$(\% 1/\% c\text{-}2)_{CE}$	(% 1/% *c*-2) / $(\% 1/\% c\text{-}2)_{CE}$	% *t*-2 / % *c*-2	$(\% t\text{-}2/\% c\text{-}2)_{CE}$	(% *t*-2/% *c*-2) / $(\% t\text{-}2/\% c\text{-}2)_{CE}$
I	3.2	1.1	2.8	4.8	3.6	1.3	1.5	3.2	0.46
Br	8.9	2.2	4.0	7.1	6.1	1.2	0.8	2.7	0.29
Cl	15.4	3.2	4.8	10.2	9.2	1.1	0.6	2.8	0.21

ratio of ratios for the pair of olefins 1-decene and *trans*-2-decene is considerably greater than unity. These numbers demonstrate that base association has a much greater retarding influence on *trans*-2-decene formation than on the production of 1-decene. Therefore, it may be concluded that the general effect of base association is a repression of *trans*-2-alkene formation which results in proportional increases in the production of 1-alkene and *cis*-2-alkene. The observable result is an increase in the percentage of 1-alkene and a decrease in the *trans*-2-alkene:*cis*-2-alkene ratio.

b. Comparison of Halogen with Other Leaving Groups

(*1*) *Tosyloxy*. From the available kinetic evidence concerning base-promoted eliminations from secondary alkyl halides and tosylates,[89] it appears that tosyloxy and bromo leaving groups are removed at approximately the same rate. For this reason, orientation in eliminations from 2-alkyl bromides and tosylates might be anticipated (cf. section II.B.4.a) to be quite similar. That this is not the case is readily apparent from the data presented in Table XII. For the tosyloxy leaving group, positional orientation lies between that exhibited by chloro and fluoro in all systems except those involving eliminations induced by *t*-BuOK–*t*-BuOH (entries 3, 4, and 5). In these exceptions, tosyloxy is similar to the bromo leaving group. Observed *trans*-2-alkene:*cis*-2-alkene ratios for tosyloxy are lower than those for any of the halogens, including fluoro, in the alcoholic solvents (entries 1, 3–6). In the aprotic solvents Me_2SO and benzene, geometric orientation for 2-decyl tosylate eliminations usually lies between that observed for 2-decyl chloride and fluoride.

This divergence of orientation for tosyloxy leaving groups from the scale ascribed by the halogens may be attributed to the onset of steric interactions between the tosyloxy group and adjacent alkyl groups. Felt and Saunders[75] suggest that interactions between tosyloxy leaving groups and adjacent alkyl functions influence *trans*-2-alkene:*cis*-2-alkene ratios. A simple conformational model was proposed (**39** and **40**) in which in-



39 40 41

teractions between the leaving group and R disfavor the formation of *trans*-2-alkene. It seems reasonable to extend this arrangement to include the transition state for 1-alkene formation (**41**). Therefore, in going from 2-alkyl halide eliminations to the corresponding reactions of tosylates, steric interactions between tosyloxy leaving group and the substrate alkyl groups should increase in the order 1-alkene ≤ *cis*-2-alkene < *trans*-2-alkene. This would produce an elevated proportion of 1-alkene and a lower *trans*-2-alkene:*cis*-2-alkene ratio than that found with a halogen leaving group of comparable reactivity, in agreement with the observations. Thus, the threshold for steric interactions of the leaving group with alkyl groups of the substrate appears to lie between halogen and tosyloxy.

As mentioned above, the shift in geometrical orientation for tosyloxy away from that for bromo is stronger in protic than in aprotic solvents. This observation is consistent with extra steric bulk being attributed to[78,77] hydrogen bonding of protic solvents to the sulfonyl oxygens as the arenesulfonoxy leaving group

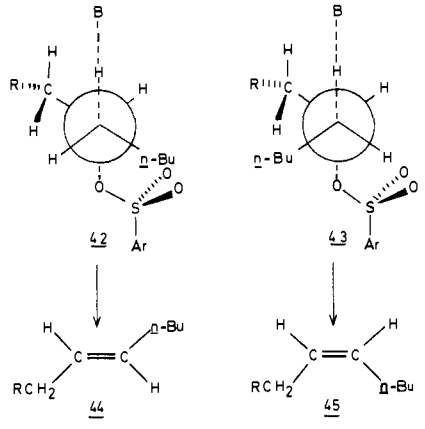
Table XIV. Product and Rate Data for Eliminations from 2-Pentyl Arenesulfonates Promoted by 1.0 M *t*-BuOK-*t*-BuOH at 50 °C

Ar of 2-PenOSO$_2$Ar	% 1-pentene	*trans*-2-pentene: *cis*-2-pentene	relative rate
p-MeOC$_6$H$_4$	73.8	0.77	1.0
p-MeC$_6$H$_4$	73.7	0.53	1.3
C$_6$H$_5$	73.8	0.38	1.7
p-BrC$_6$H$_4$	75.8	0.35	5.9
mesityl	79.0	0.33	0.45

develops negative charge in the transition state.

Supportive evidence for this proposal is provided by studies of Klimisch[49b] in which eliminations from a series of 2-pentyl arenesulfonates induced by *t*-BuOK-*t*-BuOH were examined. Relative rates and observed orientation are recorded in Table XIV. Although no trend is evident for positional orientation, the *trans*-2-pentene:*cis*-2-pentene ratios decrease steadily with increasing reactivity. If enhanced reactivity indicates more C_α–X rupture in the transition state, the amount of negative charge borne by the leaving group should also increase. Increased charge would be accompanied by enhanced hydrogen bonding with solvent molecules and an effectively larger leaving group. Thus, the sensitivity of geometrical orientation to changes in para-substituted arenesulfonoxy leaving group ability may be rationalized. Although the reactivity of 2-pentyl 2,4,6-trimethylbenzenesulfonate is less than that for any of the other 2-pentyl arenesulfonates, it forms more 1-pentene and has a lower *trans*-2-pentene:*cis*-2-pentene ratio. These results are consistent with an increased bulk of the leaving group itself and indicates the sensitivity of orientation to rather minor changes in the size of the arenesulfonate leaving group.

Further insight into the effect of alkyl–arenesulfonyloxy interactions upon the formation of geometrical isomers has been provided by Závada and Pánková.[77] Anti elimination from RCH$_2$CH(OTs)-*n*-C$_5$H$_{11}$ promoted by *t*-BuOK-DMF and EtOK-EtOH was investigated by using a homologous series of alkyl R groups (eq 18). The influence of R variation upon the ob-



(18)

served *trans*:*cis* ratios *44*:*45* is recorded in Table XV. The trans:cis ratios are essentially the same when R is methyl, ethyl, or *n*-propyl, but decrease markedly on going to isopropyl and become lower than unity when R is a *tert*-butyl group. The remarkable changes in the geometrical orientation may be explained by considering transition states **42** and **43** in which the R group is oriented anti with respect to the C_α–C_β bond in order to minimize steric strain. Examination of models indicates that when R is a straight-chain alkyl group, the *p*-toluenesulfonyl residue in **42** can rotate around the C–O bond away from R, so that it interferes only with *n*-butyl group. However, when R is isopropyl or *tert*-butyl, a similar rotation in **42** does not avoid severe interactions between the tosyl and the branched alkyl

Table XV. Trans:Cis Ratios for the Formation of RCH$_2$CH=CH-*n*-C$_4$H$_9$ in Reaction of RCH$_2$CH(OTs)-*n*-C$_5$H$_{11}$ with *t*-BuOK-DMF at 20 °C and EtOK-EtOH at 110 °C

R	*trans*:*cis*-RCH$_2$CH=CH-*n*-C$_4$H$_9$	
	t-BuOK-DMF	EtOK-EtOH
Me	3.9	2.0
Et	3.4	1.6
n-Pr	3.7	1.7
i-Pr	2.0	1.1
t-Bu	0.6	0.6

group. In **43**, on the other hand, the interactions can be avoided irrespective of R because the rotation of the tosyl residue is not opposed by the *n*-butyl group. Under such circumstances, transition state **43** may become of lower energy than **42**, even though it suffers from repulsion between the C_α–R and C_β–*n*-butyl bonds.

A possible additional contributing factor is a selective shielding of base approach. In **42**, the base must approach between flanking α- and β-alkyl groups, whereas in **43** the approaching base has free access from that side of substrate where only hydrogens are located.

In addition to this β-alkyl group effect, it is also found that for a given R group the trans:cis ratio is usually lower in reactions with EtOK-EtOH than with *t*-BuOK-DMF. Hydrogen bonding of the alcoholic solvent with the tosyloxy leaving group should increase the leaving group bulk, thereby disfavoring transition state **42** vs. **43** and producing lower trans:cis ratios.

(*2*) *Trimethylammonio*. Although the incursion of syn eliminations pathways often complicates studies for this leaving group, clean anti elimination has been demonstrated or seems certain[29,30,76] for several eliminations from 2-alkyltrimethylammonium salts. In these systems, there is a strong preference for formation of the terminal alkene and *trans*-2-alkene:*cis*-2-alkene ratios less than unity are observed. For example, reaction of 2-hexyltrimethylammonium ion by *n*-BuOK-*n*-BuOH at 85 °C yields 96.2% 1-hexene and *trans*-2-hexene:*cis*-2-hexene = 0.28.[30] The high proportion of 1-alkene is consistent with the poor leaving group ability of trimethylammonio and its acidifying effect on the β hydrogen.

Because of the E1cB-like character of the transition state for eliminations involving the trimethylammonio group, trans:cis ratios near unity would be normally anticipated. Since the observed trans:cis ratios are significantly lower than unity, the operation of some additional factor is indicated. That the low trans:cis ratios do not arise from base association effects, as is observed with 2-alkyl halides and tosylates, has been demonstrated by Bartsch.[79] In eliminations from 2-butyltrimethylammonium ion promoted by *t*-BuOK-*t*-BuOH, positional and geometrical orientation are insensitive to changes in the total base concentration or to the addition of dicyclohexano-18-crown-6. Apparently the free base species is being produced by metathical gegen ion exchange, as illustrated in eq 19. For

$$t\text{-BuO}^-\text{K}^+ + \text{RNMe}_3^+ + \text{X}^- \rightleftarrows \text{K}^+\text{X}^- + \text{RNMe}_3^+ + t\text{-BuO}^- \quad (19)$$

this reason, associated bases cannot play an important role in eliminations from substrates with onium ion leaving groups.

Saunders[30] has proposed a model by which geometrical orientation in eliminations from alkyltrimethylammonium salts may be rationalized. The explanation is illustrated for the 2-hexyl case in transition states **46** and **47**. The bulky trimethylammonio leaving group forces the alkyl group attached to the γ position of the alkyl chain (the ethyl group) into a position where it can hinder access of the base to the β-hydrogen. The β-hydrogen is shielded on both sides in **46**, but on only one in **47**. It is postulated that the selective hindrance to base approach which thus arises sufficiently disfavors **46** relative to **47** that trans:cis ratios of less than unity are observed.

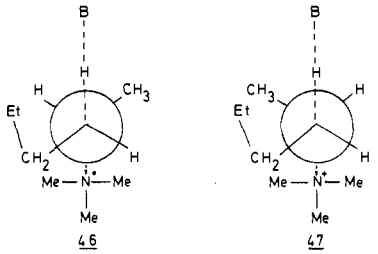
Table XVI. Olefinic Products from Reactions of 3α-Chloro-3β-methyl-5α-cholestane (48) with *t*-BuOK-*t*-BuOH at 100 °C

[*t*-BuOK], M	49:50
0.19	0.91
0.53	1.67
0.98	2.69
0.012 + 0.024 M 18-crown-6	0.81

Table XVII. Olefinic Products from Reactions of 1-Chloro-1-methylcyclohexane with Various Base-Solvent Systems

base-solvent	olefin yield	52:53
c-Pen$_3$COK-c-Pen$_3$COH-undecane[a,c]	100	3.0
Et$_3$COK-Et$_3$COH[a]	100	1.63
Et$_3$COK-xylene[a]	99	1.32
t-BuOK-benzene[b]	100	0.79
t-BuOK-*t*-BuOH[b]	100	0.55
NaOH-polypropylene glycol 400[b]	100	0.21
2-PrOK-2-PrOH[b]	100	0.14
KOH-tetraglyme dimethyl ether[b]	100	0.12
EtOK-EtOH[b]	92	0.063
MeOK-MeOH[b]	100	0.051
t-BuOK-Me$_2$SO[b]	100	0.018

[a] Reference 83. [b] Reference 84. [c] c-Pen, cyclopentyl.



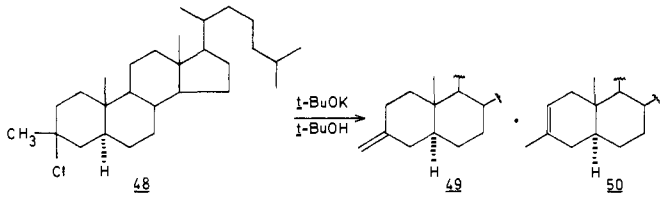
46 47

However, since it is difficult to extend this argument to the simplest 2-alkyl system, 2-butyl, some additional factor such as that postulated by Felkin[80] must also be involved (section III.C.2).

C. Synthetic Applications

It is now well established that associated bases provide the highest possible proportions of the least thermodynamically stable alkenes in eliminations from 2-alkyl halides and tosylates.

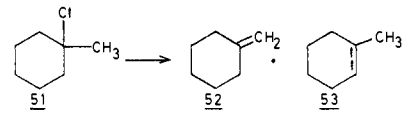
That base association is also important in controlling positional orientation in eliminations from tertiary halides has been demonstrated by Baciocchi and co-workers[82] in eliminations from 3α-chloro-3β-methyl-5α-cholestane (**48**) promoted by



48 49 50 (20)

t-BuOK-*t*-BuOH (Table XVI). Thus, the proportion of product with the exocyclic double bond is enhanced as the total base concentration and base association are increased. Addition of 18-crown-6, which reduces base association, decreases the relative proportion of product with the exocyclic double bond.

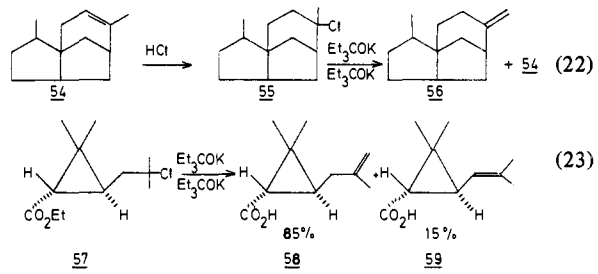
Rather extensive studies of exocyclic vs. endocyclic double bond formation in eliminations from 1-chloro-1-methylcyclohexane (**51**) have been made by Acharya and Brown[83] and by Schlosser and Tarchini.[84] Their results are recorded in Table XVII. Highest yields of the thermodynamically less stable **52** are obtained with alkoxides of ramified tertiary alcohols in al-



51 52 53 (21)

coholic or aprotic solvents of low polarity. Similar position orientation control is observed for 1-chloro-1-methylcyclopentane, 1-chloro-1-methylcycloheptane, and 1-chloro-2,3-dimethylbutane eliminations.[83]

Two applications[83,85] in organic synthesis are shown in eq 22 and 23.



54 55 56 + 54 (22)

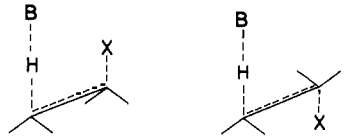
57 58 59 (23)

III. Dichotomy of Stereochemical Pathways in Unactivated E2 Reactions

A. Alternative Stereochemical Modes

Facility of a concerted 1,2-elimination depends upon the dihedral angle θ between the C$_\beta$–H and C$_\alpha$–X bonds being broken in the activated complex. Experiments on rigid ring systems have shown that the activation energy for elimination is not a monotonous function of θ but exhibits two minima corresponding to the anti-periplanar (θ = 180°) and syn-periplanar (θ = 0°) arrangements of the departing groups[86-88] (Figure 9).

Both optimal arrangements are attainable in conformationally mobile systems. Therefore, in the mechanistic analysis of E2 reactions of such substrates, the possibility of alternative syn and anti stereochemical modes, **60** and **61**, respectively, must be considered.



60 61

The principle of least motion,[89] quantum mechanical calculations,[90-96] and conceptual dissection[97] of the E2 reaction into S$_N$ and S$_E$ components all predict a preference of the anti over the syn elimination mode. However, for E1cB-like transition states, a favoring of the syn mode has been postulated.[96,97]

Steric interactions are different in the two alternative modes. Syn elimination requires eclipsing of the three pairs of substituents on C$_\alpha$ and C$_\beta$ in the transition state whereas anti elimination permits a staggered arrangement. Such conformational energy differences favor anti elimination. However, steric interactions of C$_\alpha$ or C$_\beta$ alkyl substituents with the leaving group and/or the approaching base will be greater in anti-elimination transition states than in those for corresponding syn-elimination processes. When such factors become important, the relative proportion of syn elimination will be enhanced.

Electrostatic interactions[44,45,96-102] between the attacking base and the leaving group may also influence the balance between the alternative elimination processes. Because of the proximity of the base and leaving group in the syn-elimination mode, the interactions will always be stronger than in the anti mode. Attractive interactions[44,45,96-100] occur between a free alkoxide base and an onium leaving group (ion–ion interaction)

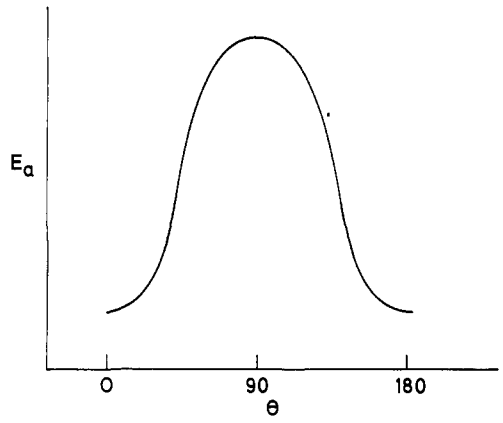


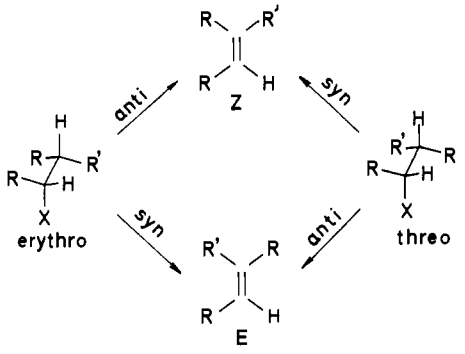
Figure 9. Dependence of activation energy for elimination upon the dihedral angle θ between the C_β–H and C_α–X bonds.

and also between an associated base and a neutral leaving group (ion–dipole interaction) and increase the propensity for syn elimination. On the other hand, repulsive[44,45,101,102] interactions arise between a free alkoxide base and a neutral leaving group (with unshared electron pairs) and also between an associated base and an onium leaving group. Such unfavorable interactions are minimized in anti-elimination transition states.

During the past decade, the competition between the alternative stereochemical modes (syn–anti dichotomy) has been intensively probed. A pattern of syn–anti variation has gradually emerged from systematic investigation of the effects of base, solvent, alkyl group structure, and the leaving group. As will be shown, any of these four variables is capable of completely reversing the stereochemical course of a concerted elimination reaction.

B. Determination of Elimination Stereochemistry

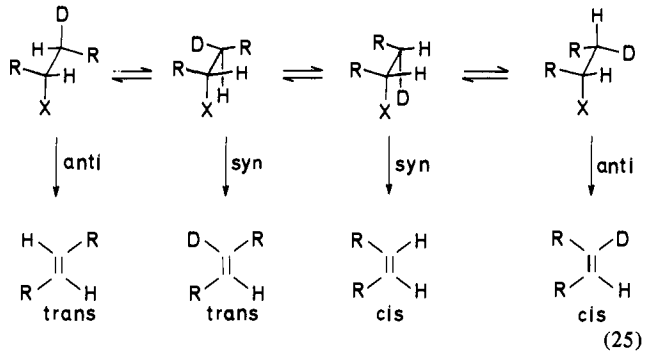
Determination of elimination stereochemistry is based primarily on configurational correlation between reactant and olefinic products. When the reactant is a diastereoisomer with C_α and C_β the chiral centers, the contributions of syn and anti elimination modes may be directly evaluated from the proportions of alternative *E* and *Z* isomeric olefins arising in the elimination reaction (eq 24). This simple procedure may be used



(24)

when certain trisubstituted olefins are the elimination products.

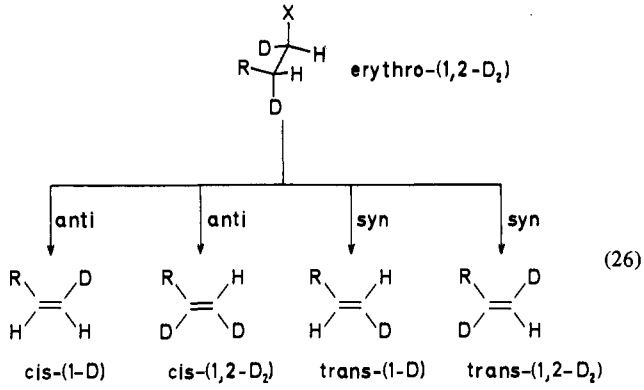
In the more common case of disubstituted olefins, the prerequisite diastereoisomerism is introduced by a stereospecific β-deuterium labeling. Then, contributions from the syn and anti pathways may be evaluated from the deuterium content of the individual (cis and trans) olefinic isomers (eq 25). However, in order to determine the syn and anti contributions in eliminations from the parent unlabeled compounds, a correction for the operation of the kinetic deuterium isotope effect must be applied. The correction is imperative since the isotope effect retards only one of the two alternative pathways (syn or anti)



(25)

and thereby obscures the outcome of the mechanistic competition. Several procedures for the correction have been proposed.[103-106] In some instances, the complex problem has been simplified by determining only apparent isotope effects in the reaction of the erythro and threo deuterated compounds. When apparent isotope effect values are used, syn and anti contributions can be estimated,[107-109] even without determining the deuterium content of the olefinic products.

Elimination stereochemistry in formation of monosubstituted olefins (1-alkenes) from 1-alkyl compounds presents an even more complicated problem. The stereochemical determination now requires stereospecific introduction of two deuterium labels into the reactant and a quantitative spectroscopic analysis of complex olefinic mixture (eq 26). However, the analytical



(26)

problem has been resolved with remarkable ease by using NMR[110] and IR[111,112] spectroscopic methods.

The stereochemistry of 1-alkene formation from 2-alkyl compounds poses a practically insurmountable experimental problem. Configurational correlation would now require a tritium label in addition to the two deuterium atoms.

C. Stereochemical Dichotomy in Onium Salt Eliminations: The Domain of Dissociated Base

1. Mechanistic Assumptions

Attempts to determine the nature of the active base species by kinetic methods (section II.B.2.d.5) in onium salt eliminations are complicated by strong, rate-depressing salt effects which make it difficult to draw unambiguous conclusions.[12,113] Therefore, nonkinetic evidence must be employed.

As was previously discussed (section II.B.4.b.2), a fast metathesis occurs between a metal alkoxide and onium salt (eq 19), giving rise to an onium alkoxide with an extremely low propensity for ionic association even in nonpolar solvents. Therefore, it seems reasonable that the dissociated base is the primary active base species in the olefin-forming reaction. This assumption greatly simplifies the mechanistic analysis of onium salt eliminations. The stereochemical dichotomy may then be examined in the absence of complicating variations of the active

base species. Experimental support for this assumption, as well as possible exceptions, will be presented later in this section.

Considerable experimental evidence is available for a wide variety of alkyl group structures, bases, and solvents which establishes that two-step, olefin-forming processes such as reversible E1cB,[105] α eliminations,[105] and α',β (ylide) eliminations[30,103-105,109,114,115] do not participate significantly in alkoxide-promoted eliminations from ammonium salts. (In contrast, ylide mechanisms may prevail for anionic nitrogen and carbon bases.[116]) Deuterium as well as leaving group isotope effects[117,118] are consistent with concerted processes for both syn and anti eliminations from ammonium salts. The syn-elimination transition states are presumably shifted more[119] toward the E1cB-like side of the variable E2 transition-state spectrum than are those for the anti mode.

2. Ammonium Salt Eliminations

Practically all reported studies of the stereochemistry of ammonium salt eliminations involve a trimethylammonium leaving group. However, recent findings[120] suggest that the replacement of the $-NMe_3^+$ group by $-NMe_2^+CO_2Et$, $-NMe_2^+CO_2H$, or $-NMe_2^+CH_2Br$ does not substantially affect the stereochemical course of the elimination, at least in protic solvents.

a. Acyclic Systems

(1) Effect of Alkyl Group upon Elimination Stereochemistry. The alkyl group effect upon the syn–anti competition has been probed in complementary studies by the Prague and Rochester groups. Pertinent results for disubstituted *trans*-alkene formation in two base–solvent systems are summarized in Table XVIII.

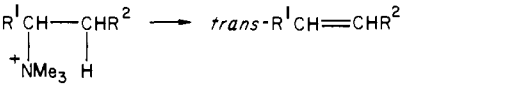
As is readily evident, the elimination stereochemistry for *trans*-alkene formation is strongly influenced by the substituents R^1 and R^2 for both base–solvent combinations. When R^1 = D or Me and R^2 is an unbranched alkyl group, the *trans*-olefin is formed predominantly by anti elimination. This result is in accord with the strong preference for anti elimination observed in eliminations from 2-alkyltrimethylammonium salts (section II.B.4.b.2). However, with lengthening or branching of R^1 (entries 3–6) or R^2 (entry 7), syn elimination increases in importance and may become the dominant reaction pathway.

In contrast, no alkyl group effect on the syn–anti competition is found in the formation of the corresponding *cis*-alkenes (Table XIX). The contribution of the syn pathway is negligibly small regardless of alkyl group structure.

When a trisubstituted alkene instead of a trans-disubstituted olefin is the elimination product, the contribution of the syn pathway is also relatively low. This is apparent in the data for eliminations from *erythro*- and *threo*-5-methyl-6-decyltrimethylammonium salts[122] presented in Table XX. Noteworthy is the marked difference in elimination stereochemistry for the two diastereomers. The percentage of syn elimination from the threo reactant is much smaller for both base–solvent combinations.

Consideration of alkyl group eclipsing interactions provides a simple rationale for the differing propensities of syn eliminations yielding geometrically isomeric di- and trisubstituted alkenes. In contrast to syn eliminations forming trans-disubstituted olefins (Table XVIII), eclipsing between α- and β-alkyl groups cannot be avoided in syn-elimination transition states leading to either the cis-disubstituted (Table XIX) or the *E* and *Z*-trisubstituted (Table XX) alkenes. For the formation of (*E*)- and (*Z*)-5-methyl-5-decenes, eclipsing interactions are presumably greater in the transition state for formation of the *Z* isomer which arises by syn elimination from the threo reactant (cf. eq 24). In agreement, the proportion of syn elimination is substantially less from the threo substrate than from the corresponding erythro compound.

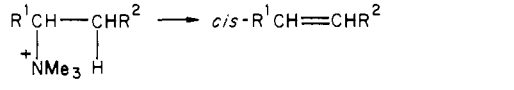
Table XVIII. Syn-Anti Competition in *trans*-Alkene Formation



		syn elimination,[a] %		
R^1	R^2	*t*-BuOK/ *t*-BuOH	MeOK/ MeOH	ref
D	*n*-Oct	7	–[b]	111
Me	*n*-Pr	15	0	30
Et	Et	80	20	30
n-Bu	*n*-Bu	89	24	105
t-Bu	*n*-Pen	>97	83	121
neo-Pen	*n*-Bu	>99	89	121
n-Pen	*t*-Bu	>90	>90	121

[a] % syn + % anti = 100%. [b] Not determined.

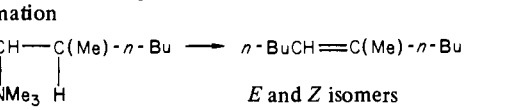
Table XIX. Syn-Anti Competition in *cis*-Alkene Formation



		syn elimination,[a] %		
R^1	R^2	*t*-BuOH/ *t*-BuOK	MeOK/ MeOH	ref
Me	*n*-Pr	≤5[b]	≤5[b]	30
Et	Et	≤5[b]	≤5[b]	30
n-Bu	*n*-Bu	4.7	6.3	105
neo-Pen	*n*-Bu	≤5[b]	≤5[b]	121
t-Bu	*n*-Pen	≤5[b]	≤5[b]	121

[a] % syn + % anti = 100%. [b] Estimated from the apparent isotope effects for *cis*-alkene formation. The isotope effects were calculated from isomer distribution data by a standard procedure (ref 107).

Table XX. Syn-Anti Competition in Trisubstituted Alkene Formation



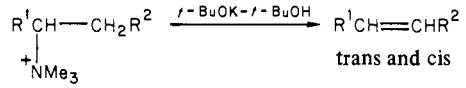
reactant	base-solvent	% (*E*)-methyl-5-decene	% (*Z*)-5-methyl-5-decene	syn elimination, %
erythro	*t*-BuOK-*t*-BuOH	1.2 (syn)	1.8 (anti)	40
threo	*t*-BuOK-*t*-BuOH	4.4 (anti)	0.2 (syn)	4.4
erythro	MeOK-MeOH	2.2 (syn)	42.1 (anti)	5
threo	MeOK-MeOH	53.3 (anti)	0.2 (syn)	0.4

The discriminating role of eclipsing effects is also dramatically illustrated by comparison of the stereoselectivities of the competing syn and anti elimination modes. Stereoselectivities of the syn and anti pathways can be calculated from the overall trans:cis ratios arising in the dichotomous reaction when contributions of the syn and anti pathways to the formation of the individual olefinic isomers are known. The stereoselectivities, $(trans:cis)^{syn}$ and $(trans:cis)^{anti}$, calculated[121] for reactions of alkyltrimethylammonium salts with *t*-BuOK–*t*-BuOH are summarized in Table XXI.

The calculated values of $(trans:cis)^{syn}$ ratios are imposingly high in most instances and are usually in excess of those which would correspond to the difference in thermodynamic stability of the geometrical isomers. It has been suggested[30] that since the rotational barriers in simple alkanes are in the range 1.0–2.7 kcal/mol, reactant-like syn-elimination transition states could produce the observed trans:cis ratios.

In striking contrast, values for the $(trans:cis)^{anti}$ ratios are always lower than unity and practically independent on the steric bulk of R^1 and R^2 alkyl groups. Both observations are in sharp

Table XXI. Stereoselectivities of Competing Syn and Anti Pathways



R^1	R^2	$(trans:cis)^{syn}$	$(trans:cis)^{anti}$
Me	*n*-Pr	≥1.3	0.4
Et	Et	≥17	0.4
n-Bu	*n*-Bu	45	0.3
t-Bu	*n*-Pen	≥260	≤0.8
neo-Pen	*n*-Bu	≥310	≤0.4

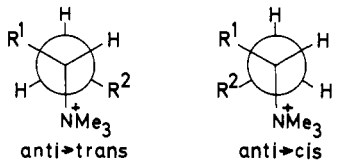


Figure 10. Conformations for formation of geometrical isomers by anti elimination.

disagreement with the expected operation of repulsive interactions between R^1 and R^2 groups which should disfavor *cis*-olefin formation (Figure 10). Apparently, some other factor controls geometrical orientation.

As already mentioned in section II.B.4.b.2, Saunders[30] proposed a model of selective hindrance to base approach which explains why $(trans:cis)^{anti}$ ratios in eliminations from alkyltrimethylammonium salts are lower than unity. Modified models for selective hindrance to base approach which lead to similar conclusions have also been advanced by other authors.[45,105] In the model proposed by Felkin and Sicher,[105,123] which seems to be in the best accord with the majority of results, dominant repulsive interaction between C_β–R^2 and C_α–NMe_3^+ in anti elimination forces some deviation from strict anti-periplanarity (Figure 11). This has opposite consequences for the transition states leading to the *trans*- and to the *cis*-alkene. In the former, the deviation moves the reactive hydrogen on C_β into a position which is shielded by R^1 whereas in the latter, the hydrogen moves out of the congested environment. In this way, a selective retardation of the *trans*-alkene formation arises. The magnitude of this effect depends on the steric size of R^1. The repulsive interactions for *cis*-olefin formation depicted in Figure 10 also depend on R^1. These parallel retarding factors in the anti → trans and anti → cis pathways may well explain why $(trans:cis)^{anti}$ ratios in alkyltrimethylammonium salt eliminations are lower than unity and nearly independent of R^1.

According to Saunders,[30,76] the selective hindrance to base approach theory also accounts for the alkyl group effect on syn–anti competition in the formation of *trans*-alkenes (Table XVIII) because retardation of the anti → trans pathway provides the opportunity for the proportion of syn elimination to increase gradually and eventually become the dominant stereochemical mode.

Thus, a very simple and consistent rationale can be provided for the observed stereochemistry of trimethylammonium salts eliminations. However, the following examinations of elimination reaction rates and base–solvent effects will reveal that the concept of selective hindrance to base approach is not devoid of flaws.

(*2*) *Effect of Alkyl Group upon Elimination Rates.* The effect of alkyl group upon elimination rates has been investigated for several alkyltrimethylammonium ion series.[124–126] However, only in some instances was the syn–anti dichotomy taken into account.

For reactions of homologous alkyltrimethylammonium salts (Figure 12) with *t*-BuOK–*t*-BuOH, Závada and Pánková[125,126] determined the overall (syn plus anti) rates of formation of the

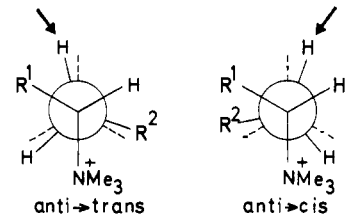


Figure 11. Model of steric hindrance to base approach proposed by Felkin and Sicher.

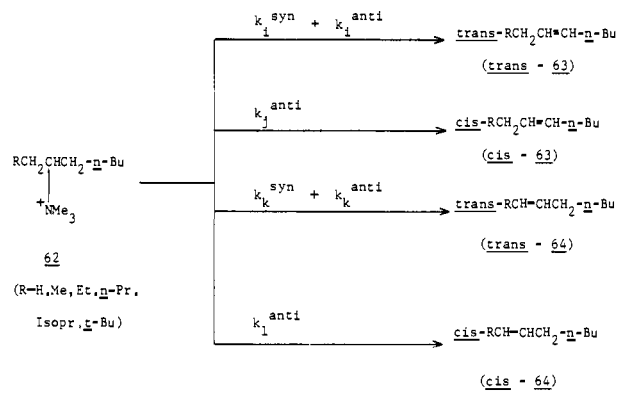


Figure 12. Dissection of elimination pathways for reactions of alkyltrimethylammonium chlorides **62** with *t*-BuOK–*t*-BuOH.

individual olefinic isomers. The overall rates were then dissected into syn and anti partial rates by using estimated contributions of the competing stereochemical pathways to the formation of the individual olefin. The dependence of partial reaction rates upon the substituent R ("rate profile") which was thus obtained for all the main contributing processes (Figure 12) allows a very through analysis of steric as well as polar effects of alkyl groups to be made for this reaction.

In the formation of the alkenes *trans*- and *cis*-**63** which arise by elimination "away" from R, the R group is insulated from the reaction centers by a methylene unit. In this way, any polar influence of R is highly attenuated, and the observed effect of R on the dissected processes syn → *trans*-**63** may be assumed to be predominantly steric. The rate profiles for these processes are shown in Figure 13.

An impressive increase of rate (factor of 400) with increasing steric bulk of R in the order H < Me < Et ~ *n*-Pr < *i*-Pr < *t*-Bu is found for the syn- → *trans*-**63** pathway. In contrast, the anti → *trans*-**63** and anti → *cis*-**63** processes show little sensitivity to variation of R. Only when R = *t*-Bu, the bulkiest group, is there a significant (factor of 3–4) rate decrease in the anti pathways.

In the rationalization of these three rate profiles, steric congestion induced by the extremely bulky trimethylammonium group plays the key role. In the steric model provided in Figure 14, the sterically outsized trimethylammonium group forces the alkyl groups on C_α and C_β as far as possible from the leaving group and into a position where steric interaction between R and the *n*-Bu group occurs (**65**). Because of this alkyl group interaction, the ground-state conformation is assumed to be strained, with the degree of strain increasing as the steric size of R is enhanced.

When the reaction proceeds from the staggered ground state **65** to the eclipsed arrangement **66** which is required for the *syn* → *trans*-**63** path, repulsion between the alkyl groups is relieved, which provides the driving force for the observed steric acceleration. In contrast, from **65** to the staggered conformation **67** which is required for the *anti* → *cis*-**63** process, the repulsion between the alkyl groups remains practically unchanged, in accord with the near independence of the rates with R variation. The gauche interaction between the *n*-Bu and NMe_3^+

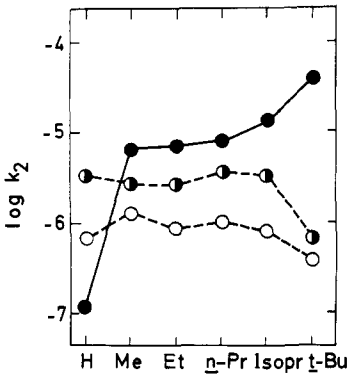


Figure 13. Rate profiles for the processes *syn* → *trans*-**63** (filled circles), *anti* → *trans*-**63** (half-filled circles), and *anti* → *cis*-**63** (open circles) for reactions of alkyltrimethylammonium chlorides **62** with *t*-BuOK-*t*-BuOH at 35 °C.

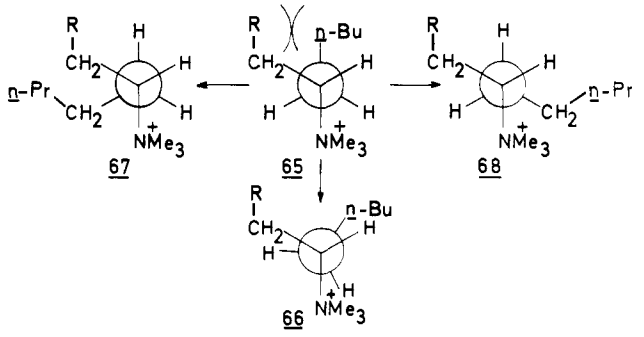


Figure 14. Steric model for base-promoted eliminations from alkyltrimethylammonium chlorides **65**.

groups which is also introduced in **67** does not apparently affect the alkyl group interactions, but does produce low rates of anti elimination.

However, on the path from **65** to the arrangement **68** which is required in the *anti* → *trans*-**63** pathway, the repulsion between the alkyl groups disappears, being replaced by the gauche *n*-Bu and NMe_3^+ group interaction. Therefore, a gradual increase of rates with increasing bulk of R, similar to that found for the *syn* → *trans*-**63** process, would be expected for the anti → *trans*-**63** reaction mode. This prediction is inconsistent with the observations (Figure 13).

As a possible resolution for this lack of agreement between the conformational analysis and the kinetic results, it was suggested that selective hindrance to base approach may be involved in the *anti* → *trans*-**63** pathway. Both the selective hindrance to base approach (Figure 11) and relief of alkyl group repulsion in the transition state **65** → **68** should be sensitive to steric effects of R, but in opposite directions. A fortuitous superposition of the two counteracting factors may well lead to kinetic results which are more or less independent of R.

Completely different rate profiles were found for the corresponding processes which proceed "toward" the group R in **62**, affording the alkenes *trans*- and *cis*-**64** (Figure 15). A gradual decrease of rates in the order Me > Et ~ n-Pr > i-Pr > t-Bu occurs in the *syn* → *trans*-**64** as well as the *anti* → *trans*-**64** and *anti* → *cis*-**64** pathways. It is believed that the retardation originates either mainly (in the *syn* → *trans*-**64** process) or at least partly (in the *anti* → *trans*-**64** and *anti* → *cis*-**64** pathways) from the polar influence of R as it affects the acidity of the C_β–H bond.

Extension of the study to a corresponding series of positionally isomeric alkyltrimethylammonium salts **69** (R = H, Me, Et, *n*-Pr, *i*-Pr, *t*-Bu) provided additional support for the conclusions drawn for eliminations from **62**.[126]

In further studies,[126] analogous kinetic investigations were performed for the reactions of the quaternary salts **62** and **69**

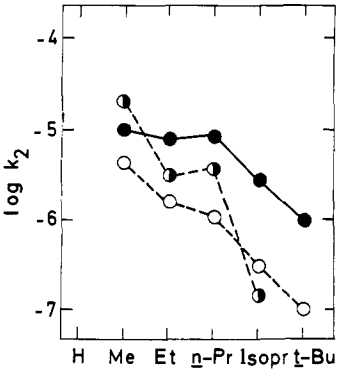
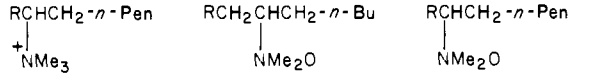


Figure 15. Rate profiles for the processes *syn* → *trans*-**64** (filled circles), *anti* → *cis*-**64** (half-filled circles), and *anti* → *trans*-**64** (open circles) for reactions of alkyltrimethylammonium chlorides **62** with *t*-BuOK-*t*-BuOH at 35 °C.

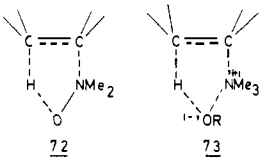
with MeOK-MeOH. A striking resemblance between the rate profiles for reactions of a given series of substrates with *t*-BuOK-*t*-BuOH and MeOK-MeOH was almost invariably found.

A comparison was also made between the rates of bimolecular elimination from **62** and **69** and the thermal intramolecular



69 **70** **71**

syn elimination (Cope elimination) which was previously investigated[127] for the corresponding alkyldimethylamine oxide series **70** and **71**. A close similarity of the steric effects of R but a complete dissimilarity of the polar influences of R was found when the intramolecular and bimolecular syn-elimination processes **72** and **73**, respectively, were compared.[126]



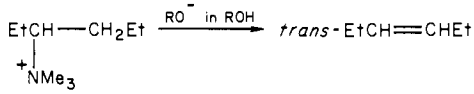
72 **73**

(*3*) *Effects of Base and Solvent upon Elimination Stereochemistry*. It has already been established from the data in Tables XVIII and XX that irrespective of alkyl structure of the ammonium ion substrate the proportion of syn elimination is always significantly higher when *t*-BuOK-*t*-BuOH is the base-solvent system than with MeOK-MeOH. Impressive results reported by Saunders and co-workers[30,78] for a wider range of RO^- in ROH systems are summarized in Table XXII.

Proceeding down the series of base-solvent combinations in Table XXII, the intrinsic strength of the base increases and, concomitantly, the ability of the alcohol to solvate the oxygen anion by hydrogen-bonding decreases. The resulting sharp increase in basicity may well account for the increasing proportion of syn pathway. The two explanations which have been proposed for this trend assume alternatively that enhancement of basicity increases the E1cB-like[98,99] or reactant-like[30] character of the transition state. Quite recently, theoretical support for the former proposal has been advanced by Bach.[128] In either case, it is argued that the stereochemical preference for anti elimination becomes weakened by the shift in transition-state character.

A complementary explanation[99] has been advanced in terms of the ion-ion attractive interaction between an alkoxide anion and the positively charged trimethylammonium group which favors a pseudocyclic arrangement in the syn-elimination mode **73**. This interaction should be strongest when the charges on the anion and cation are as great as possible. Solvation of the ions results in partial charge dissipation and the Coulombic

Table XXII. Effect of Base and Solvent on the Syn-Anti Competition



R of RO^- in ROH	% syn elimination	R of RO^- in ROH	% syn elimination
H	9.5	*sec*-Bu	67.5
Me	~20	*t*-Bu	80.0
n-Bu	16.6	*t*-Pen	83.0

Table XXIII. Effect of Solvent on the Syn-Anti Competition in *tert*-Butoxide-Promoted Reactions of Alkyltrimethylammonium Salts

	% syn elimination in formation of		
solvent	1-decene[a]	5-decene[b,c]	5-methyl-5-decene[d]
benzene	20	84	89
Me_2SO	13[e]	76	8
t-BuOH	8	64	4

[a] From *erythro*-1,2-dideuterio-1-decyltrimethylammonium ion.[111] [b] From 5-decyltrimethylammonium ion.[105] [c] Mixture of trans and cis isomers. [d] From *threo*-5-methyl-6-decyltrimethylammonium ion.[122] [e] In DMF.

attraction of the two ions becomes less. Therefore, the proportion of syn elimination should be highest in poor solvents for ions. Support for this explanation is derived from the data collected in Table XXIII. Thus, for eliminations from alkyltrimethylammonium salts induced by a common base, *tert*-butoxide, the proportion of syn elimination is greatest in benzene, a solvent which poorly solvates both ionic centers. On the other hand, in solvents which efficiently solvate either the cation (Me_2SO) or anion (*t*-BuOH), the proportion of syn elimination is invariably smaller.

In contrast to the pronounced effect of base and solvent upon the relative propensities for syn and anti elimination, observed changes in the stereoselectivity of the individual syn and anti pathways are surprisingly small (Tables XXIV and XXV).

Assuming that the steric size of the base increases as one goes down the base-solvent series in Table XXV, the selective hindrance to base approach in the anti → trans elimination mode should increase and values of $(trans/cis)^{anti}$ should decrease for the base-solvent combinations which appear lower in the table. Clearly this is not the case. The apparent lack of correlation with the predictions of the selective hindrance to base approach theory has led to the suggestion[99,129] that some other factor may be dominant.

It has been proposed by Sicher and Závada[99,129] and also by Wolfe[130] that differing reactivities of the diastereotopic hydrogens on C_β might be responsible for the *cis*-olefin stereoselectivity observed in the anti elimination. Several examples of stereoselective behavior due to different reaction rates for diastereotopic hydrogens are known.[131-133] It is significant that all of the examples involve transition states with considerable carbanion character. To date, this explanation has not been sufficiently developed to challenge the elaborate concept of the selective hindrance to base approach.

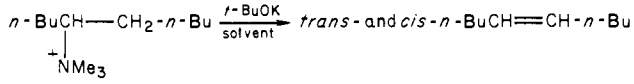
(4) Effects of Cation and Crown Ether. Irrespective of solvent ion separating capability, the effects of cation and crown ether on the syn-anti competition in the alkoxide-promoted elimination from alkyltrimethylammonium salts are usually negligibly small (Table XXVI). This provides important support for the assumption that counterion metathesis between a metal alkoxide and the trimethylammonium salt suppresses involvement of the ion-paired (associated) base species in these elimination reactions.

In sharp contrast to the prevailing evidence for alkoxide-induced eliminations, Borchardt and Saunders[108] report a pronounced cation effect on the syn-anti competition for a quaternary ammonium salt elimination promoted by metal phenoxides (Table XXVII). Addition of the inert tetramethylammonium iodide to potassium phenoxide (entry 2) should shift the equilibrium between associated and dissociated phenoxide (eq 27) further to the right and thereby increase the concen-

$$PhO^-M^+ + RNMe_3^+ + X^- \rightleftarrows M^+X^- + RNMe_3^+ + PhO^- \quad (27)$$

tration of the dissociated species. Therefore, the increase of syn pathway from 34% in entry 1 to 67% in entry 2 is attributed to an increased participation by the dissociated base species. This is in complete accord with the prediction[98,99] (cf. previous section) that free base should be more effective than the associated species in promoting syn elimination due to the favorable electrostatic interactions between a dissociated oxygen anion and trimethylammonium cation. For the differences among the individual metal phenoxides (entries 1, 3, 4) it is suggested that reactivity of the associated phenoxide species decreases in the order $PhO^-K^+ > PhO^-Na^+ > PhO^-Li^+$ so that

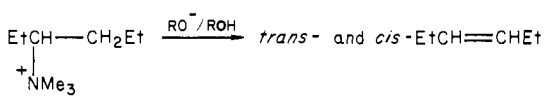
Table XXIV. Effect of Solvent on Stereoselectivity of the Competing Syn and Anti Pathways



solvent	$(trans/cis)^{syn}$[a]	$(trans/cis)^{anti}$[a]
benzene	46	0.9
Me_2SO	62	0.3
t-BuOH	45	0.3

[a] From ref 105.

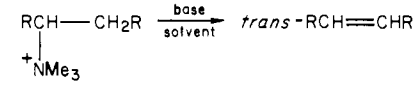
Table XXV. Effect of Base on Stereoselectivity of the Anti Pathway



R of RO^- in ROH	$(trans/cis)^{anti}$[a]
H	0.48
Me	0.27
n-Bu	0.30
sec-Bu	0.34
t-Bu	0.40
t-Pen	0.46

[a] Calculated from data in ref 30 with the simplifying assumption that a syn → cis pathway is absent.

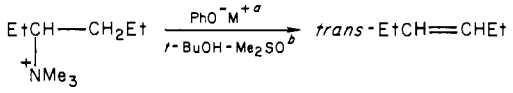
Table XXVI. Effects of Cation and Crown Ether upon the Syn-Anti Competition for Alkoxide-Promoted Eliminations



R	base-solvent	% syn elimination	ref
Et	*n*-BuOK-*n*-BuOH	16.6	106
Et	*n*-BuOK-*n*-BuOH + CE[a]	16.9	106
Et	*n*-BuONa-*n*-BuOH	17.4	106
Et	*t*-BuOK-*t*-BuOH	83.4	106
Et	*t*-BuOK-*t*-BuOH + CE[a]	82.1	106
Et	*t*-BuONa-*t*-BuOH	89.6	106
n-Bu	*t*-BuOK-benzene	76.4[b]	45
n-Bu	*t*-BuOK-benzene + CE[a]	73.8[b]	45
n-Bu	*t*-BuOK-benzene	99[c]	45
n-Bu	*t*-BuOK-benzene + CE[a]	99[c]	45

[a] CE = dicyclohexano-18-crown-6. [b] For the reaction of the *threo*-6-*d* derivative. [c] For the reaction of the *erythro*-6-*d* derivative.

Table XXVII. Effect of Cation on the Syn-Anti Competition of Phenoxide-Promoted Elimination



base	% syn elimination
PhO^-K^+	34
$PhO^-K^+ + NMe_4I^-$	67
PhO^-Na^+	55
PhO^-Li^+	74

[a] A 50% excess of phenol over phenoxide was present. [b] In an 80:20 ratio by volume.

the participation of the dissociated base increases in the same order.

The incursion of associated bases in phenoxide-promoted eliminations from tetraalkylammonium salts and the presence of only free bases in alkoxide-induced eliminations remain to be rationalized. In the former reactions, as studied by Borchardt and Saunders, phenol was always present. Závada, Pánková, and Svoboda[45] have suggested that hydrogen bonding by phenol may make the reactivities of the dissociated and associated phenoxide base species comparable. Phenol should be an efficient hydrogen-bonding agent for dissociated phenoxide, but not for the associated base species. It is known[134] that associated potassium phenoxide is a stronger base than is the dissociated species, which is hydrogen bonded by the conjugate acid. Therefore, the unusual counterion effects observed with phenoxide bases may be attributed to a reduced reactivity of the free base species by hydrogen bonding with phenol which allows associated bases to play an important role in the elimination reactions.

b. Monocyclic Systems

Elimination stereochemistry has been investigated for a wide range of cycloalkyltrimethylammonium salts differing in ring size (n = 4–14, 16) and also in alkyl substitution. However, in contrast to acyclic systems, only a limited portion of the reported evidence is derived from investigations of stereospecifically deuterium-labeled substances. The majority of the evidence has been inferred from the effects of ring size, base, and solvent upon elimination rates and isomeric olefin distribution in homologous cycloalkyltrimethylammonium series (n = 5–14, 16).

(*1*) *Evidence from Deuterium-Labeled Substrates: Effects of Ring Size and Alkyl Substitution*. The most consistent set of evidence from deuterium-labeled substrates available is for eliminations from cycloalkyltrimethylammonium hydroxides performed under pyrolytic conditions. The results reported by Cope and co-workers[103,135-137] for the formation of five homologous *cis*-cycloalkenes differing in ring size (n = 4–8) are summarized in Table XXVIII. Under comparable conditions, the percentage of syn elimination in the formation of a corresponding acyclic analogue, *cis*-5-decene, was very low (4%).[105]

Conformational differences among the individual reactants account for the remarkable effect of ring size. For the cyclobutane ring, syn-periplanarity is easy to attain whereas anti-periplanarity requires very severe distortion. This situation is reversed for the cyclohexane ring system in which syn-periplanarity would require an eclipsed boatlike arrangement. In agreement with the intermediate elimination stereochemistries observed in cyclopentane, cycloheptane, and cyclooctane rings, attainment of the syn- as well as of the anti-periplanarity arrangement of vicinal bonds is relatively easy.[137,138]

Unfortunately, no corresponding evidence can be obtained concerning the stereochemistry of *cis*-cycloalkene formation with ring sizes greater than eight under the pyrolytic conditions

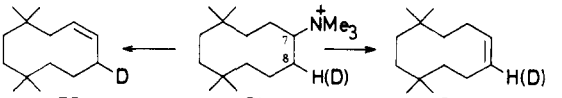
Table XXVIII. Effect of Ring Size upon Stereochemistry of *cis*-Cycloalkene Formation in the Pyrolysis of Cycloalkyltrimethylammonium Hydroxides

ring size	% syn elimination
4	~90[a]
5	39 ± 7[b]
6	2 ± 2[b]
7	30 ± 2[b]
8	~50[b]

[a] At 50 °C (10^{-7} torr). [b] At 110–114 °C (20–40 torr).

since trans isomers then represent the predominant reaction product.

The stereochemistry of *trans*-cycloalkene formation from deuterium-labeled cyclooctyltrimethylammonium hydroxide[103] and from the 1,1,4,4-tetramethylcyclodecyl homologue **74**[109]



(28)

75 (trans and cis) **74** (trans- or cis-8-D) **76** (trans and cis)

was found to be remarkably uniform. Both *trans*-cyclooctene and the *trans*-cyclodecene **76** were formed stereospecifically by syn elimination under the pyrolytic conditions. The same complete preference for syn elimination stereochemistry was also found[109] in the formation of the *trans*-cyclodecene **76** even under conditions which are less favorable for syn elimination (as indicated by comparison with data obtained[105] for formation of an acyclic analogue, *trans*-5-decene; see Table XXIX).

In marked contrast, no incursion of syn elimination was detected[109] in the formation of the corresponding *cis*-cyclodecene **76** from **74**. Thus, in elimination from the cyclodecylammonium salt **74** a complete divergence of competing syn and anti elimination mechanisms occurs. The former leads exclusively to *trans*-olefin formation and the latter only to the production of *cis*-alkene.

Indirect evidence[98-100] obtained in investigations of elimination reaction rates and base–solvent effects in homologous series (cf. next section) indicate that the divergent syn → trans, anti → cis behavior is not unique for eliminations from the cyclodecylammonium ion **74**. Although probably less pronounced, the dichotomous behavior also exists for eliminations from other medium- and large-ring cycloalkyltrimethylammonium salts.

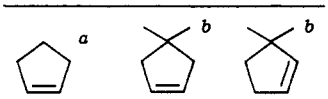
In addition to ring size, limited evidence[103,122,136,139-141] indicates that alkyl substituents on the ring also influence the elimination stereochemistry. In the cyclopentyl system, the introduction of geminal dimethyl groups[103,136,137,140] substantially increases the contribution of the syn-elimination pathway (Table XXX). Retardation of the anti-elimination pathway by interactions between the bulky trimethylammonium group and one of the geminal dimethyl groups was deemed to be the factor responsible for the alkyl group effect. In the cyclodecyl system **74** the effects of the more remote geminal dimethyl groups must be less important since the *cis*-cyclodecene **76** arises by clean anti elimination.

(*2*) *Evidence from the Effect of Ring Size upon Elimination Rates*. The effect of ring size upon elimination rate ("rate profile") in homologous cycloalkyl series has been employed by Sicher and Závada[98-100,139,142,143] as an efficient tool for the qualitative determination of E2 reaction stereochemistry. This approach rests upon the fortunate circumstance that the rate profiles for processes proceeding in the syn and in the anti fashion are fundamentally different in the medium and large ring region (Figures 16 and 17). Thus, it is known from independent kinetic studies that syn elimination of cycloalkyldimethylamine oxides (the Cope elimination) is facile[142] in the medium- and

Table XXIX. Stereochemistry of *trans*-Olefin Formation from 74 and from 5-Decyltrimethylammonium Salt

conditions	% syn elimination in formation of *trans*-76	*trans*-5-decene
pyrolysis	100	95.5
t-BuOK-Me_2SO	100	93.4
t-BuOK-*t*-BuOH	100	88.9
MeOK-MeOH	100	24.3

Table XXX. Stereochemistry of Cyclopentene and Dimethylcyclopentene Formation

conditions	% syn elimination in formation of 		
	a	b	b
pyrolysis	39 ± 7	70 ± 6	97
t-BuOK-Me_2SO	45	71	*c*
t-BuOK-*t*-BuOH	17	63	*c*
NaOH-H_2O	4 ± 3	10	*c*

[a] From cyclopentyltrimethylammonium salt. [b] From 3,3-dimethylcyclopenthyltrimethylammonium salt. [c] Not determined.

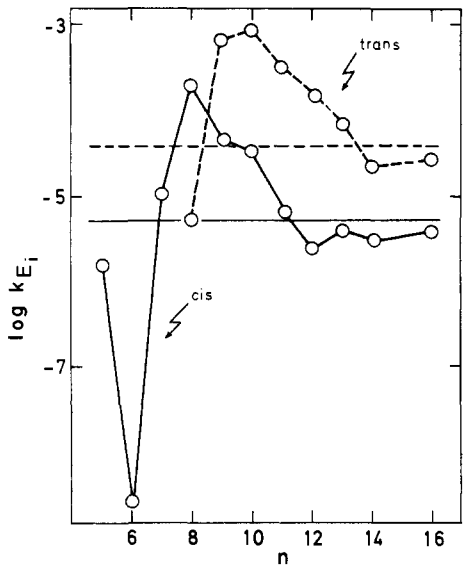


Figure 16. Effect of ring size, *n*, upon rates of *trans*- and *cis*-cycloalkene formation by syn elimination from cycloalkyldimethylamine oxides in *t*-BuOH at 70.6 °C.[142] (Corresponding rates of *trans*- and *cis*-4-nonene formation from 5-nonyldimethylamine oxide under the same conditions are included for comparison: dotted and solid horizontal lines, respectively.)

large-ring region (*n* = 8–13), particularly for formation of the *trans*-cycloalkene (Figure 16). On the other hand, anti elimination leading to either *trans*- or *cis*-cycloalkenes is difficult[100] in this region (Figure 17) because the hydrogens required for these reactions point into the ring and are thereby shielded from base attack (cf. section III.D.3.e for a detailed discussion). Therefore, by comparison of the rate profile for the elimination reaction under investigation with those for reactions of known stereochemical courses (Figures 16 and 17), the stereochemistry of the new reaction may be readily assessed.

The rate profiles measured[139] for the reaction of cycloalkyltrimethylammonium chlorides (*n* = 5–14, 16) with *t*-BuOK-*t*-BuOH are shown in Figure 18. An immediately apparent feature of Figure 18 is the complete dissimilarity of the rate profiles for *trans*- and *cis*-cycloalkene formation. The rate profile observed for the *tert*-butoxide-promoted production of the *trans*-cycloalkenes is almost identical with that noted for *trans*-cycloalkene formation in the syn elimination of cycloalkyldimethylamine oxides (Figure 16). A logarithmic plot for

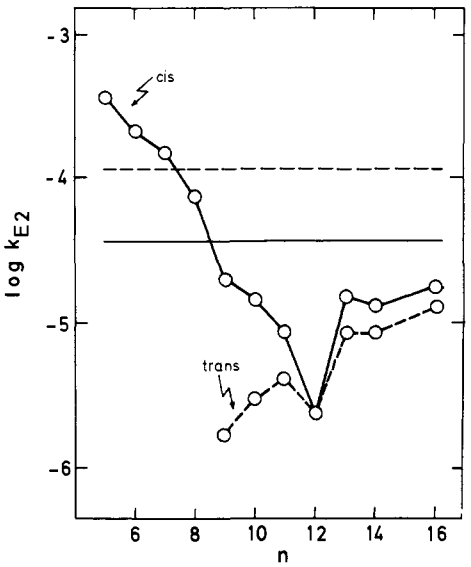


Figure 17. Effect of ring size, *n*, upon rates of *trans*- and *cis*-cycloalkene formation by anti elimination from cycloalkyl bromides promoted by EtOK-EtOH at 58.5 °C.[100] (Corresponding rates of *trans*- and *cis*-4-nonene formation from 5-bromononane under the same conditions are included for comparison: dotted and solid horizontal lines, respectively.)

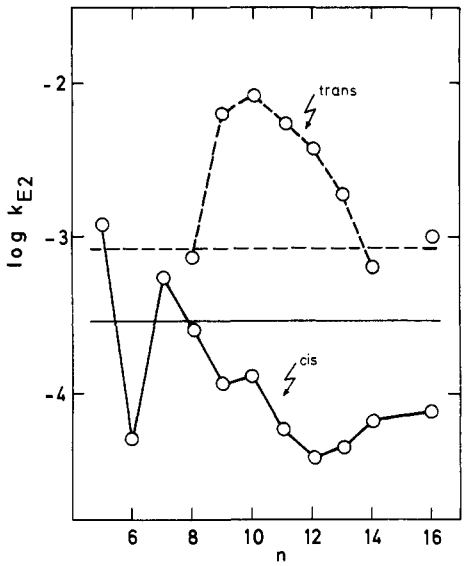


Figure 18. Effect of ring size, *n*, upon rates of *trans*- and *cis*-cycloalkene formation in reactions of cycloalkyltrimethylammonium chlorides with *t*-BuOK-*t*-BuOH at 55 °C. (Corresponding rates of *trans*- and *cis*-4-nonene formation from 5-nonyltrimethylammonium chloride under the same conditions are included for comparison: dotted and solid horizontal lines, respectively.)

these two reactions gives a good linear fit (Figure 19a). However, a corresponding plot for *cis*-cycloalkene formation gives no correlation (Figure 19b).

An exactly opposite situation is found when the analogous comparison is made between the rate profiles for *trans*- and *cis*-cycloalkene formation in the *tert*-butoxide-promoted eliminations from cycloalkyltrimethylammonium ions and in the E2 reactions of cycloalkyl bromides with EtOK-EtOH.[100,143] The latter are assumed to proceed via anti elimination. Now, the correlation for *trans*-olefin production gives a scatter plot (Figure 20a) whereas a very reasonable fit is obtained for *cis*-cycloalkene formation (Figure 20b).

On the basis of these and subsidiary results, the conclusion was drawn that for the cycloalkyltrimethylammonium salt reactions with *t*-BuOK-*t*-BuOH the *trans*- and *cis*-cycloalkenes arise by different stereochemical pathways. The former is

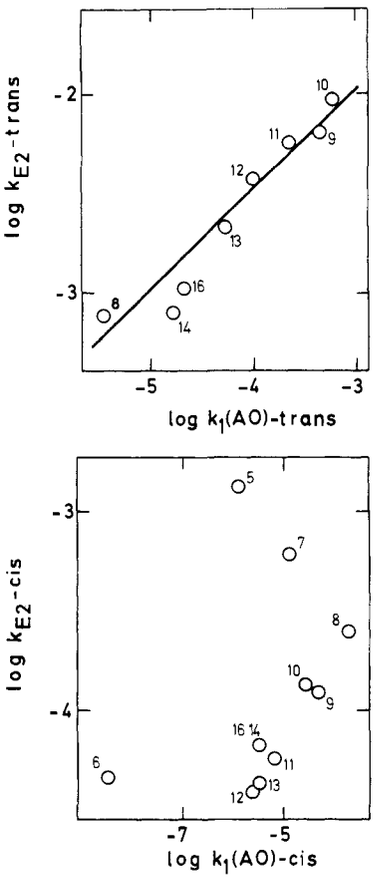


Figure 19. (a) Plot of log k_1(AO)-trans for *trans*-cycloalkene formation from cycloalkyldimethylamine oxides (*t*-BuOH; 70.6 °C) against log k_{E2}-trans for *trans*-cycloalkene formation from cycloalkyltrimethylammonium chlorides (*t*-BuOK-*t*-BuOH; 55 °C). (b) Plot of log k_1(AO)-cis for *cis*-cycloalkene formation from cycloalkyldimethylamine oxides (*t*-BuOH; 70.6 °C) against log k_{E2}-cis for *cis*-cycloalkene formation from cycloalkyltrimethylammonium chlorides (*t*-BuOK-*t*-BuOH; 55 °C).

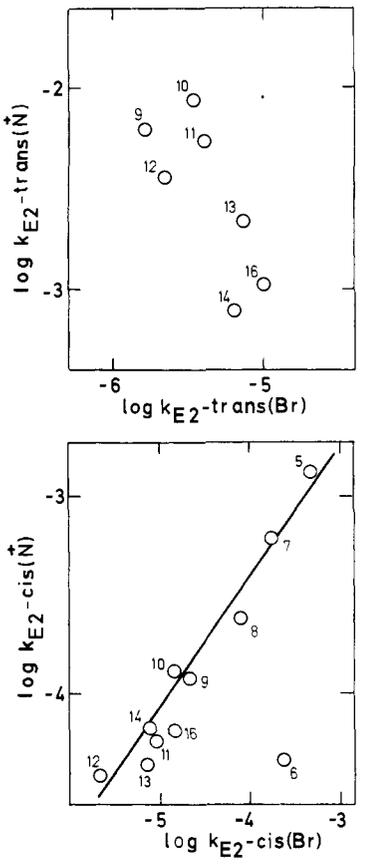


Figure 20. (a) Plot of log k_{E2}-trans (Br) for *trans*-cycloalkene formation from cycloalkyl bromides (EtOK-EtOH; 58.5 °C) against log k_{E2}-trans (N^+) for *trans*-cycloalkene formation from cycloalkyltrimethylammonium chlorides (*t*-BuOK-*t*-BuOH; 55 °C). (b) Plot of log k_{E2}-cis (Br) for *cis*-cycloalkene formation from cycloalkyl bromides (EtOK-EtOH; 58.5 °C) against log k_{E2}-cis (N^+) for *cis*-cycloalkene formation from cycloalkene formation from cycloalkyltrimethylammonium chloride (*t*-BuOK-*t*-BuOH; 55 °C).

produced predominantly or perhaps exclusively by syn elimination and the latter by an anti elimination pathway.

The rate profile approach has been extended[96,99] to other base–solvent systems. A total of 12 different combinations were investigated for reactions with the cycloalkyltrimethylammonium salts. For each case, the conclusion was the same: formation of *trans*-cycloalkenes by syn elimination and production of *cis*-cycloalkenes by anti elimination.

By its very nature, the rate profile method lacks sufficient sensitivity to be quantitative. The incursion of some anti elimination in *trans*-olefin formation or syn elimination in *cis*-cycloalkene production would escape notice, particularly in the n = 5–8 region (cf. Tables XXVIII and XXX). In spite of this flaw, the kinetic method provides a basically correct picture of the stereochemical reaction course. Historically, the analysis of rate profiles posed the first major challenge to the then-prevailing assumption that E2 reactions proceeded only with anti stereochemistry.

(*3*) *Evidence from the Effects of Base and Solvent upon Trans:Cis Ratios*. Table XXXI summarizes the effects of base and solvent on *trans*- to *cis*-cycloalkene ratios[99] in E2 reactions of medium (n = 8–11) and large (n = 12–14) ring quaternary ammonium salts. The corresponding data for an open-chain analogue, 5-nonyltrimethylammonium chloride, are included for comparison.

A pronounced effect of base strength is immediately apparent. Regardless of solvent and alkyl structure, a truly dramatic decrease in the value of the *trans*:*cis* ratio is noted on going from the strong base *tert*-butoxide to the weak base phenoxide.

Table XXXI. Effects of Base and Solvent on the *trans*- to *cis*-Alkene Ratio in E2 Reactions of Cycloalkyltrimethylammonium Chlorides (n = 8–14) and 5-Nonyltrimethylammonium Chloride

		trans:cis ratio in			
ring size	base	benzene	Me_2SO	*t*-BuOH	MeOH
8	*t*-BuOK	5.7	4.9	3.0	
	MeOK	2.3	1.7	1.4	0.14
	PhOK	0.25	0.04	0.14	0.07
9	*t*-BuOK	~100	40	50	
	MeOK	32	10	13	0.8
	PhOK	3.2	0.7	1.3	0.9
10	*t*-BuOK	~200	65	65	
	MeOK	50	19	24	2.0
	PhOK	5.2	1.3	1.8	1.4
11	*t*-BuOK	~330	~100	~100	
	MeOK	100	32	24	1.6
	PhOK	4.5	1.1	1.7	1.2
12	*t*-BuOK	200	32	100	
	MeOK	11.5	3.3	8.1	0.8
	PhOK	1.3	0.2	0.5	0.3
13	*t*-BuOK	250	65	50	
	MeOK	32	10	11.5	0.7
	PhOK	1.3	0.3	0.7	0.4
14	*t*-BuOK	50	9	11.5	
	MeOK	6.2	1.2	2.7	0.15
	PhOK	0.3	0.1	0.15	0.10
5-nonyl	*t*-BuOK	19	3.3	2.9	
	MeOK	4.5	1.1	1.0	0.25
	PhOK	0.5	0.35	0.35	0.28

A distinct trend in *trans*-alkene:*cis*-alkene composition with change of solvent is also observed. Independent of the em-

Table XXXII. *trans*-Alkene:*cis*-Alkene Ratios for Eliminations from Alkyldimethylsulfonium and Alkyltrimethylammonium Salts

	trans-alkene:*cis*-alkene			
	t-BuOK-*t*-BuOH		EtOK-EtOH	
alkyl group	$-SMe_2^+$	$-NMe_3^+$	$-SMe_2^+$	$-NMe_3^+$
5-nonyl	10.1[a]	2.84[a]	0.54[a]	0.35[a]
3-pentyl	5.0[b]	0.88[c]	0.84[b]	0.38[c,d]
2-pentyl	3.5[b]	0.42[c]	0.64[b]	0.31[c,d]

[a] Reference 145. [b] Reference 146. [c] Reference 30. [d] In *n*-BuOK-*n*-BuOH.

Table XXXIII. *trans*-Cycloalkene:*cis*-Cycloalkene Ratios in Eliminations from Cycloalkyldimethylsulfonium and Cycloalkyltrimethylammonium Salts[a]

	trans-cycloalkene:*cis*-cycloalkene			
	t-BuOK-*t*-BuOH		EtOK-EtOH	
ring size	$-SMe_2^+$	$-NMe_3^+$	$-SMe_2^+$	$-NMe_3^+$
10	~50	~50	0.7	4.0
12	⩾100	⩾100	0.8	1.1
14	11.5	11.5	0.3	0.3

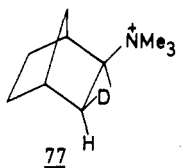
[a] Reference 98.

ployed base, the trans:cis ratio always decreases in the order benzene > Me_2SO ~ *t*-BuOH > MeOH.

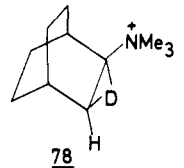
This pattern of trans:cis ratio variation provides strong additional support to the assumption that the *trans*-olefins are formed mainly by syn elimination but the *cis*-alkenes are produced chiefly by anti elimination. As was discussed earlier in this section, syn:anti variation with base and solvent follows exactly the same pattern (cf. Tables XXII and XXIII).

c. Bicyclic Systems

In the rigid bicyclo[2.2.1]heptyl and somewhat more flexible bicyclo[2.2.2]octyl systems **77** and **78**, respectively, a dihedral



77



78

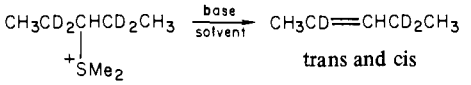
angle close to zero exists in the ground state for the deuterium and trimethylammonium groups whereas the β-hydrogen is almost fixed in an anticlinal position with respect to the leaving group. In full accord with this conformational assessment, a clean syn elimination was demonstrated for both the bicyclic systems **77** and **78** under pyrolytic[114] as well as homogeneous conditions (*t*-BuOK-Me_2SO).[104]

3. Sulfonium Salt Eliminations

Extreme steric requirements, positive charge, and an ability to convert associated alkoxide base into dissociated species are common features of trimethylammonium and dimethylsulfonium leaving groups. Although only scanty evidence concerning elimination stereochemistry in alkoxide-promoted reactions of sulfonium salts has been reported,[98,144,148] the data in Tables XXXII and XXXIII clearly indicate similarity in elimination behavior of acyclic as well as cyclic dimethylsulfonium and trimethylammonium salts.

With EtOK-EtOH as the base-solvent system, the trans:cis ratios from acyclic as well as cyclic dimethylsulfonium salts are always lower than unity, which suggests, by analogy with the established behavior of trimethylammonium salts (vide supra), that cis-stereoselective anti elimination predominates in the reaction. On the other hand, for reactions induced by *t*-BuOK-*t*-BuOH, the trans:cis ratios from the sulfonium salt

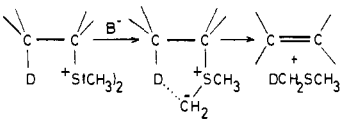
Table XXXIV. Effect of Base-Solvent System upon Incursion of Ylide Mechanism in Sulfonium Salt Eliminations



base-solvent	% ylide mechanism	base-solvent	% ylide mechanism
n-BuOK-*n*-BuOH	1.7	*t*-BuOK-Me_2SO-*t*-BuOH	73.0
t-BuOK-*t*-BuOH	65.2		

eliminations are always much higher than unity, which indicates, again by analogy with the trimethylammonium salts, that trans-stereoselective syn elimination is now the predominant course.

An important difference between the two types of onium leaving groups is the incursion of the ylide mechanism (eq 29)



(29)

in alkoxide-promoted elimination involving the dimethylsulfonium group. According to results reported by Saunders and coworkers for β,β,β′,β′-tetradeuterated 3-pentyldimethylsulfonium salt (Table XXXIV), the ylide mechanism contribution[147,148] increases as the basicity of the medium is enhanced. In the *t*-BuOK-*t*-BuOH system, the ylide mechanism represents two-thirds of the overall reaction. Less than 0.5% of ylide mechanism was detected in an elimination involving a trimethylammonium group[105] under comparable conditions. This difference probably explains why the values of trans:cis ratios for elimination of dimethylsulfonium group collected in Table XXXII are higher than those for the trimethylammonium group. It has been shown[120] that the ylide mechanism preferentially yields *trans*-alkenes.

D. Stereochemical Dichotomy in Eliminations from Neutral Compounds: The Domain of Dissociated and Associated Bases

1. Introduction

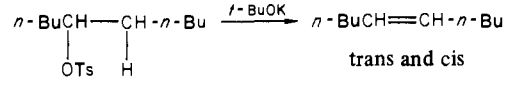
When compared with the preceding onium salt eliminations, the corresponding reactions of neutral substrates, such as sulfonates or halides, are mechanistically more complex. In addition to the stereochemical (syn-anti) dichotomy, the dichotomy of base species must now also be considered.

The experimental approach which allows for the solution of this complex problem is relatively simple. The syn-anti dichotomy is first assessed for base-solvent combinations of differing ion-pairing ability by the methods employed earlier for the onium salt eliminations (section III.C). At the same time, the base species dichotomy is probed by the techniques already described in section II. Predominance of free base species is effected by use of dipolar aprotic solvents and/or crown ethers, whereas prevalence of the associated base is achieved by use of nonpolar solvents which have very low cation-solvating ability, e.g., benzene or *t*-BuOH.

2. Acyclic Systems

In this section, eliminations from open-chain tosylates, for which the most complete set of experimental results is available, will be initially discussed. Then the more limited information regarding dehydrohalogenation and the effect of halide group polarity on elimination stereochemistry will be examined.

Table XXXV. Effect of Solvent and Crown Ether on Syn and Anti Contributions for *t*-BuOK-Promoted Eliminations from 5-Decyl Tosylate



conditions	% anti → trans	% syn → trans	% anti → cis	% syn → cis
C_6H_6	33.6	12.4	50.4	3.6
C_6H_6 + CE[a]	63.9	4.1	29.2	2.8
t-BuOH	24.8	4.2	68.2	2.8
t-BuOH + CE[a]	67.1	4.7	26.7	1.5
DMF	73.2	2.8	22.6	1.4

[a] CE = dicyclohexano-18-crown-6.

Table XXXVI. Effect of Base Association on Syn:Anti and Trans:Cis Ratios in the Formation of 5-Decene by *t*-BuOK-Promoted Elimination from 5-Decyl Tosylate

conditions	(syn:anti)^{trans}	(syn:anti)^{cis}	(trans:cis)^{anti}	(trans:cis)^{syn}
C_6H_6	0.37	0.07	0.67	3.5
C_6H_6 + CE[a]	0.06	0.09	2.19	1.5
t-BuOH	0.17	0.04	0.36	1.5
t-BuOH + CE[a]	0.07	0.06	2.51	3.1
DMF	0.04	0.06	3.24	2.0

[a] CE = dicyclohexano-18-crown-6.

a. Elimination from Tosylates

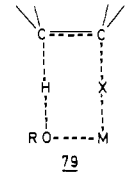
(1) Effect of Base Association upon Elimination Stereochemistry. The detailed analysis of *t*-BuOK-promoted elimination from 5-decyl tosylate reported by Závada, Svoboda, and Pánková[149] shows that base association affects the relative propensities of the individual pathways participating in *trans*- and *cis*-5-decene formation in a rather selective fashion (Table XXXV). Suppression of the associated base species by the presence of crown ether or by using DMF as solvent markedly increases the propensity for anti → trans elimination but decreases, in most instances, contributions of the concomitant anti → cis, syn → trans, and syn → cis pathways. As a consequence, the effect of base association upon the syn–anti competition is pronounced only in the formation of the *trans*-alkene for which an approximately tenfold increase of the proportion of syn pathway is found (Table XXXVI).

In addition, the effect of base association on geometrical orientation (trans:cis ratios) in the competing syn and anti eliminations is entirely different (Table XXXVI). A strong influence is noted for the anti elimination, with the associated species favoring the formation of *cis*-5-decene, whereas the free base facilitates trans-isomer formation. On the other hand, no clear effect of base association is found in the trans:cis ratios for the syn elimination component. For both types of base species, formation of the trans isomer is preferred.

Remarkably similar results have been obtained by Chiao and Saunders[27] who investigated the effect of added Me_2SO in reactions of 3-hexyl tosylate with *t*-BuONa–*t*-BuOH (Table XXXVII). Addition of Me_2SO lowered the contribution of syn elimination in formation of *trans*-3-hexene and increased the trans:cis ratio for anti elimination.

A simple rationalization for such results has been advanced[45] in terms of electrostatic interactions between an associated base and leaving groups which possess unshared electron pairs. As was already discussed in section II.B.2.d, the operation of such interactions in anti eliminations from open-chain tosylates and halides accounts for the enhanced formation of *cis*-alkenes in reactions with associated bases.

For syn elimination, electrostatic interactions are also thought to be involved.[98,150] In fact, such interactions are considered to be more important[45] for syn elimination than in anti elimination pathways. For the former, a pseudocyclic six-membered arrangement (**79**) is easily attainable due to the proximity of the

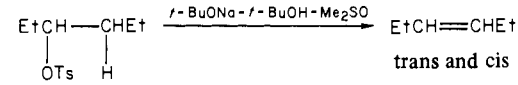


79

interacting groups. Therefore, the facilitation of syn elimination by base association can be explained on simple geometrical grounds.

For syn elimination, ion pairs are sufficient to allow nearly collinear approach of the base to the C_β–H bond in **79**. In contrast, ion-pair oligomers (**15–17**) or solvent-bridged ion pairs (**36–38**) are necessary in order to achieve an essentially collinear attack of the base upon the C_β–H bond in transition states for anti elimination (section II.B.2.d.5).

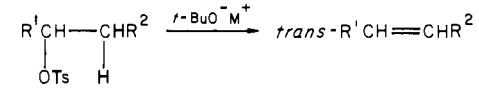
Table XXXVII. Effect of Me_2SO on Syn:Anti and Trans:Cis Ratios in Formation of 3-Hexene by *t*-BuONa-Promoted Elimination from 3-Hexyl Toslyate in *t*-BuOH–Me_2SO



% Me_2SO	(syn:anti)^{trans}	(trans:cis)^{anti}
0	0.40	0.25[a]
5	0.25	0.53[a]
10	0.10	1.15[a]
90	0.07	3.52[a]

[a] Calculated from data in ref 27 under the assumption that the cis isomer is formed exclusively by anti elimination.

Table XXXVIII. Effect of Alkyl Groups on the syn:anti Competition in *trans*-Alkene Formation



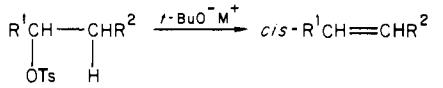
R[1]	R[2]	% syn elimination[a] associated base	free base	ref
Me	Me	*b*	⩽2[c]	26
Me	*n*-Pr	12.3[d]	*b*	27
Et	Et	20.3,[e] 28[d]	6.4[f]	27
n-Pr	Me	16.6[d]	*b*	27
n-Bu	*n*-Bu	14.5,[e] 27[g]	3.7[h]	105
neo-Pen	*n*-Bu	70[e,g]	~0[h]	105
t-Bu	*n*-Pen	70[g]	~0[h]	105

[a] % syn + % anti = 100. [b] Not determined. [c] *t*-BuOK–Me_2SO. [d] *t*-BuONa–*t*-BuOH. [e] *t*-BuOK–*t*-BuOH. [f] *t*-BuONa–Me_2SO–*t*-BuOK (9:1). [g] *t*-BuOK–C_6H_6. [h] *t*-BuOK–DMF.

(2) Effect of Alkyl Group on Elimination Stereochemistry. The syn:anti competition has been investigated in *tert*-butoxide-promoted eliminations from various acyclic tosylates with different alkyl group structures. Table XXXVIII summarizes the influence of alkyl group structure on the stereochemistry of *trans*-alkene formation and compares the results obtained under conditions when associated and free base species should prevail.

The data in Table XXXVIII demonstrate that the fundamental differences between associated and free base species noted in the previous section occur for a variety of alkyl group structures. Thus, for the elimination promoted by free base species, the proportion of syn pathway is always small, and no alkyl group effect is observed. However, when the elimination is promoted by the associated base species, the syn contribution is significant and increases gradually with increasing bulk

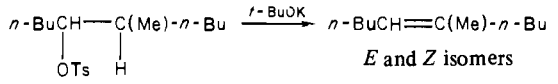
Table XXXIX. Effect of Alkyl Groups on Syn:Anti Competition in *cis*-Alkene Formation



		% syn elimination[a]		
R¹	R²	associated base	free base	ref
Me	Me	*b*	<2	26
Me	*n*-Pr	~5[d]	*b*	27
Et	Et	~2.5[d]	<5[d]	27
n-Pr	Me	~5[d]	*b*	27
n-Bu	*n*-Bu	3.9[e]	5.8[h]	105
neo-Pen	*n*-Bu	<5[e,g]	<5[h]	105

[a] See the corresponding footnotes in Table XXXVIII.

Table XL. Syn:Anti Competition in Trisubstituted Alkene Formation



erythro or threo

reactant	conditions	% E isomer	% Z isomer	% syn elimination
erythro	C_6H_6	2.0 (syn)	35.0 (anti)	5.4
	C_6H_6-CE[a,b]	0.3 (syn)	60.7 (anti)	0.5
	t-BuOH	2.4 (syn)	51.3 (anti)	4.5
	t-BuOH-CE[a,b]	0.5 (syn)	47.4 (anti)	1.0
	DMF	0.2 (syn)	38.3 (anti)	0.5
	DMF-CE[a,b]	0.2 (syn)	43.2 (anti)	0.5
threo	C_6H_6	17.6 (anti)	0.8 (syn)	4.3
	C_6H_6-CE[a,b]	42.2 (anti)	0.6 (syn)	1.4
	t-BuOH	35.5 (anti)	3.7 (syn)	9.4
	t-BuOH-CE[a,b]	44.2 (anti)	0.5 (syn)	1.1
	DMF	41.6 (anti)	0.2 (syn)	0.5
	DMF-CE[a,b]	40.8 (anti)	0.2 (syn)	0.5

[a] CE = dicyclohexano-18-crown-6. [b] Reference 151.

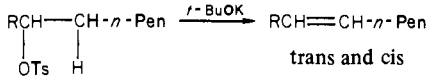
of the alkyl group. A qualitatively similar, but more pronounced, trend was observed earlier in the reactions of the corresponding trimethylammonium salts (Table XVIII).

In contrast to the situation for *trans*-alkenes, the contribution of syn elimination to the formation of the cis isomers is always negligibly small, irrespective of alkyl group structure (Table XXXIX). Apparently, eclipsing between the R^1 and R^2 groups (cf. section III.C.2.a.1) is responsible for this difference. In agreement with this postulated role of eclipsing effects, the proportion of syn elimination observed[122] for trisubstituted alkene formation in *t*-BuOK-promoted reactions of *erythro*- and *threo*-5-methyl-6-decyl tosylates is also small. Nevertheless, a significant effect of base association on the proportion of syn elimination is evident (Table XL).

In addition to the complex effect of alkyl group structure on the syn–anti competition, a remarkable influence on geometrical orientation in the major (anti) stereochemical pathway has been found.[47,77] Table XLI shows the alkyl group effect on (trans:cis)[anti] ratios evaluated for eliminations from homologous open-chain tosylates promoted by free (*t*-BuOK–crown ether–*t*-BuOH or *t*-BuOK–DMF) and associated (*t*-BuOK–*t*-BuOH) alkoxide bases. Values of (trans:cis)[anti] in reactions induced by free base are invariably higher than unity and increase dramatically with branching of the alkyl group R. On the other hand, for reaction with associated base, the ratios are always less than unity and do not change substantially with branching of the R group. Thus, alkyl group effects are completely different for reactions induced by the two alternative base species.

(3) Models for the Observed Effects of Alkyl Groups and Base Association upon syn:anti and trans:cis Ratios. The

Table XLI. Effect of Alkyl Groups and Base Association on Trans:Cis Ratios in the Anti Pathway

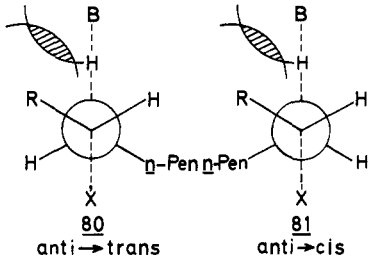


	(trans:cis)[anti]		
R	*t*-BuOK-*t*-BuOH[a]	*t*-BuOK-CE-*t*-BuOH[b]	*t*-BuOK-DMF[a]
Me	0.38	2.3	2.7
Et	0.42	3.1	4.7
n-Pr	0.36	2.1	2.9
i-Pr	0.75	35.6	24.0
t-Bu	0.90	54.5	54.5

[a] Reference 77. [b] Reference 47; CE = 18-crown-6.

intriguing pattern of alkyl group effects on the syn:anti competition (Table XXXVIII) and orientation (Table XLI) observed in the reactions promoted by associated base gives rise to two interrelated questions: (a) Why does the proportion of syn elimination increase with increasing bulk of the alkyl group? (b) Why do the trans:cis ratios for anti elimination not increase with the increasing bulk of the alkyl group?

Two plausible explanations can be provided for the initial question. First, the tosyloxy group may have sufficient steric bulk to produce a ground-state conformation similar to that proposed for a trimethylammonium group (cf. **65**). As previously mentioned (section III.C.2.a.2), relief of strain from such a conformation leads to acceleration of syn elimination, with the magnitude of the effect depending on steric bulk of R. Alternatively, hindrance to base approach by the group R retards both anti → trans and anti → cis pathways, **80** and **81**, re-

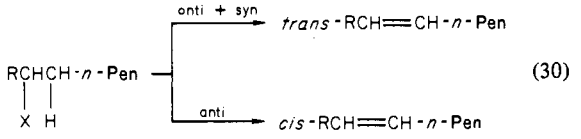


spectively, and thereby provides an opportunity for the less hindered syn elimination to gradually prevail in the reaction.

With regard to the second question, a routine conformational analysis of the anti elimination transition states which considers the repulsive interactions between the adjacent R and *n*-Pen groups in **80** and **81** leads to the prediction that the trans:cis ratio should always be greater than unity and increase gradually with the increasing bulk of R. While the values of (trans:cis)[anti] in Table XLI for free base follow this prediction, the ratios observed with associated base are clearly anomalous. Thus, with associated base, some additional factor must either retard the anti → trans pathway or accelerate the anti → cis route as the steric bulk of the R group is increased.

In the following section, evidence is presented which allows one to distinguish between the alternative answers to both questions.

(4) Model Verification by Kinetic Studies. In order to probe the alkyl group effect on syn:anti and (trans:cis)[anti] ratios, Pánková and Závada[47,128] determined rates of the individual pathways (eq 30) for eliminations from the homologous tosy-



(30)

82 R = Me, Et, *n*-Pr, *i*-Pr, *t*-Bu

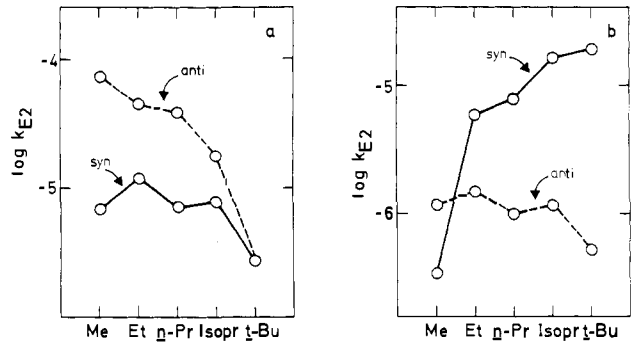


Figure 21. Effect of alkyl group R upon rates of the competing syn → trans and anti → trans pathways: (a) elimination of tosylates **82** (X = OTs) with 0.43 M *t*-BuOK-*t*-BuOH at 80.7 °C (ref 47); (b) elimination of trimethylammonium salts **82** (X = N^+Me_3) with 0.43 M *t*-BuOK-*t*-BuOH at 35 °C (ref 126).

lates and trimethylammonium salts **82** (X = OTs and NMe_3^+, respectively). Approximate rates for the syn → trans and anti → trans pathways from the reaction of the tosylates **82** with *t*-BuOK-*t*-BuOH are graphically presented in Figure 21a and compared with the corresponding rate data for the elimination of the trimethylammonium salts (X = NMe_3^+) in Figure 21b.

The comparison reveals entirely different rate patterns for eliminations from the tosylates and from the trimethylammonium salts. In the tosylate series, the rates for the syn pathway are more or less independent on R whereas the rate for the anti pathway decreases markedly with increasing bulk of R. On the other hand, in the onium series, the rates for the syn pathway show parallel increases with the bulk of R, but the rates for the anti pathway do not change substantially with the variation of the alkyl group. Thus, the kinetic studies demonstrate that the steric model proposed for the syn-anti competition in trimethylammonium salt (section III.C.2.a.2) is not applicable to the reactions of tosylates. Apparently, the unsymmetrical tosyloxy group is not sufficiently bulky to accelerate the syn elimination process. Therefore, retardation of anti elimination by hindrance of base approach due to R (**80** and **81**) is judged to be the controlling factor. Using a less extensive series of 2- and 3-hexyl tosylates and *t*-BuONa-*t*-BuOH as the base-solvent system, Chiao and Saunders[27] reached essentially the same conclusion.

Whether the anomalous insensitivity of $(trans:cis)^{anti}$ ratios to R group variation in eliminations involving associated base is due to retardation of the anti → trans pathway or acceleration of the anti → cis processes is also answered by the kinetic studies.[47] Ratios of rate constants for the anti → trans pathway promoted by associated (*t*-BuOK-*t*-BuOH) and free (*t*-BuOK-crown ether-*t*-BuOH) base, respectively, as well as comparable ratios for the anti → cis process are summarized in Table XLII.

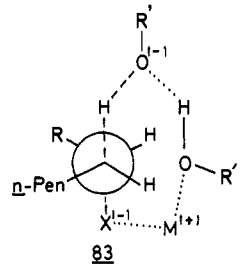
Values of k^{assoc}/k^{free} for the *trans*-alkene formation decrease slightly whereas those for the *cis*-alkene increase markedly with branching of the alkyl group. Therefore, in going from free to associated base, a stabilization of the anti → cis pathway, rather than a destabilization of the anti → trans course, occurs. This pattern of results agrees well with the earlier qualitative conclusion (section II.B.2.d.5) that electrostatic attraction between an associated base and a leaving group which possesses unshared electron pairs operates selectively in anti elimination and facilitates the anti → cis, but not the anti → trans, pathway.

One conceivable explanation for the relative favoring of the anti → cis pathway by associated base is that the base-leaving group interactions illustrated in transition state **83** (or **18–20**) may force a nonlinear approach of the base to the C_β–H bond. This deviation from collinearity would decrease steric interference between the base and the R group. Since a linear C_β···H···O arrangement is anticipated for the free base, destabilizing steric interactions between the base and large R group would

Table XLII. Ratios of Rate Constants[a] for Anti Elimination Induced by Associated and by Free *t*-BuOK Base in Tosylate Series 82

R	$\frac{k^{assoc}(anti \rightarrow trans)}{k^{free}(anti \rightarrow trans)}$	$\frac{k^{assoc}(anti \rightarrow cis)}{k^{free}(anti \rightarrow cis)}$
Me	0.042	0.29
Et	0.040	0.37
n-Pr	0.043	0.30
i-Pr	0.025	1.15
t-Bu	0.021	1.65

[a] k^{assoc} = partial second-order rate constants from the reaction with *t*-BuOK-*t*-BuOH at 80.7 °C; k^{free} = partial second-order rate constants from the reaction with *t*-BuOK-CE-*t*-BuOH at 25.4 °C; CE = 18-crown-6.



83

be expected. Therefore, as the steric requirements of the R group become large, the anti → cis process for associated base becomes favored when compared with the anti → cis pathway for free base.

b. Elimination from Halides

(*1*) *Interrelation of Leaving Group, Base Association, and Syn:Anti Competition.* The Prague group has investigated[45,152] the syn:anti competition in reactions of three 5-decyl halides with associated (in benzene) and free (in Me_2SO) *t*-BuOK base. The results obtained for *trans*-5-decene formation are summarized in Table XLIII. For the *cis*-5-decene-forming reactions, the proportion of syn elimination was found to be uniformly low.

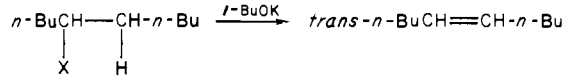
For the data in Table XLIII, regular trends in the syn:anti ratios are noted in both solvents as the leaving group becomes more electronegative. A plausible explanation for this effect has been advanced in terms of the variable E2 transition-state theory. A gradual shift from central to E1cB-like transition states presumably occurs as the leaving group electronegativity is increased in the order Br < Cl < F. According to the theoretical arguments presented earlier (section III.A), such a shift is advantageous for syn elimination.

In addition to the leaving group polarity, base association also strongly affects the syn:anti competition in the halide eliminations. In agreement with the situation previously observed for the tosyloxy group, the syn:anti ratio in dehydrohalogenations induced by associated base species (in benzene) is always much higher than that in the reaction with free base (in Me_2SO).

An interesting dependence of the magnitude of the base association effect upon the leaving group is also apparent. The complex ratio $(syn:anti)^{C_6H_6}/(syn:anti)^{Me_2SO}$ in Table XLIII shows that the effect of base association increases in the order Br < Cl < F, i.e., with increasing electronegativity of the halide group. This trend agrees well with the suggestion[100,143] that interaction between the leaving group and metal counterion of the associated base provides driving force for syn elimination. It was recently demonstrated by Bartsch's group[153] that the interaction becomes stronger with increasing electronegativity of halogen group and that this factor may become the dominating leaving group property in activated syn elimination (cf. section IV.C.3).

Corroborative evidence for the effects of base association and leaving group identity in eliminations from 3-hexyl fluoride

Table XLIII. Effect of Leaving Group and Base Association on Syn:Anti Competition in Eliminations from 5-Decyl Halides



X	$(syn:anti)^{C_6H_6}$	$(syn:anti)^{Me_2SO}$	$\frac{(syn:anti)^{C_6H_6}}{(syn:anti)^{Me_2SO}}$
Br	0.5	0.03	15
Cl	1.9	0.06	30
F	7.3	0.12	60

and tosylate has been reported by Saunders' group.[154]

(2) *Interrelation of Leaving Group, Base Association, and Orientation.* The trans:cis ratios evaluated[45,152] for the competing syn and anti pathways in the reactions of 5-decyl halides with the associated (in benzene) and the free (in Me_2SO) *t*-BuOK base are summarized in Table XLIV.

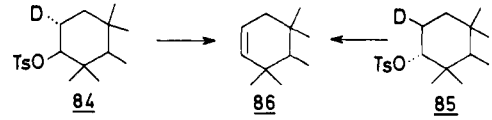
The rather small changes in orientation which are produced by leaving group variation may be readily rationalized in terms of the variable E2 transition-state theory. On the other hand, the effect of base association in the elimination of 5-decyl halides is strong, leading in the anti pathway to preferential *cis*-olefin formation. A quite analogous effect of base association was noted earlier (section II.B.4.a), in the eliminations from 2-decyl and 2-hexyl halides which presumably proceed by clean anti elimination.

3. Monocyclic Systems

Stereochemistry of elimination for monocyclic substrates differing in ring size, alkyl substitution, and leaving group has been studied extensively during the past two decades. Only a limited number of these studies involve the investigation of deuterium-labeled compounds. A considerable portion of our knowledge in this area has been only inferred (similar to the case of cyclic onium salts, section III.C) from examination of the effects of ring size, base, and solvent on rates and orientation in appropriate reaction series.

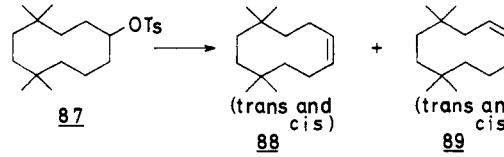
a. Evidence from Deuterium-Labeled Models

In agreement with the previously noted reluctance of cyclohexyl derivatives to undergo syn elimination (section III.C), kinetic isotope effect values determined by Finley and Saunders[155] indicate that E2 reactions of cyclohexyl tosylate with *t*-BuOK–*t*-BuOH, as well as with EtOK–EtOH, proceed mainly or exclusively in the anti fashion. Similarly, Levisalles and Pete[156] report that eliminations from the pentamethyl-substituted cyclohexyl tosylates **84** and **85** with $NaCH_2SOCH_3$–Me_2SO are stereospecifically anti. However, in the reaction of these two tosylates with *t*-$C_5H_{11}ONa$–benzene, syn elimination played an important role (78% for **84** and 39% for **85**).



84 **86** **85** (31)

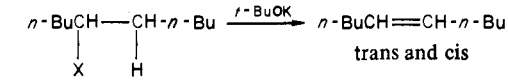
Very different results were obtained by Svoboda, Závada, and Sicher[157] for eliminations from the tetramethylcyclodecyl tosylate **87** induced by *t*-BuOK–DMF, *t*-BuOK–*t*-BuOH, and



87 **88** (trans and cis) **89** (trans and cis) (32)

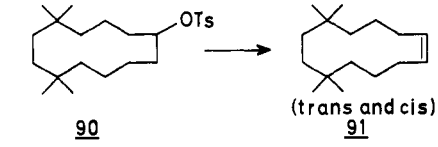
t-BuOK–benzene. In all three base-solvent systems, the *cis*-cyclodecene **88** arose almost exclusively (>95%) by anti elimination whereas the corresponding trans isomer **88** was formed predominantly (>95%) by syn elimination. Unpublished results[151] reveal that the dichotomous situation does not change substantially even when dicyclohexano-18-crown-6 is added to these three base-solvent systems. Less complete evidence[157] indicates that the same dichotomy also holds for the formation of the positionally isomeric olefin pair of *trans*-**89** and *cis*-**89**. Such a clear-cut syn → trans, anti → cis dichotomy was demonstrated earlier[109] only in the case of eliminations from the corresponding cyclodecyltrimethylammonium salt **74** (section III.C.2.b).

Table XLIV. Effects of Leaving Group and Base Association upon Orientation



X	in C_6H_6 $(trans:cis)^{syn}$	in C_6H_6 $(trans:cis)^{anti}$	in Me_2SO $(trans:cis)^{syn}$	in Me_2SO $(trans:cis)^{anti}$
Br	6.7	0.56	2.2	6.5
Cl	7.1	0.48	2.5	6.7
F	21.5	0.74	2.5	5.1

A less pronounced syn–anti dichotomy was found by the Prague group[157] in the elimination of the tetramethylcyclododecyl homologue **90**. *trans*-Cyclododecene **91** was formed by

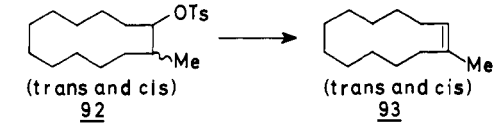


90 **91** (trans and cis) (33)

a predominant (about 95%) syn elimination only when the base–solvent combination was *t*-BuOK–benzene. In the reaction with *t*-BuOK–*t*-BuOH, anti elimination already competed to some extent (15%), and with *t*-BuOK–DMF it became the principal reaction mode (70%) for the *trans*-olefin formation.

No experimental data are available concerning the mode of *cis*-cyclododecene **91** formation from the tosylate **90**, but by analogy with the formation of *cis*-cyclodecene **88** from **87** and other related cases, it is suggested[157] that this olefin is formed mainly, if not exclusively, by anti elimination.

Intermediate results were obtained[122] in the corresponding reactions of *trans*- and *cis*-2-methylcyclododecyl tosylates (**92**).



(trans and cis) **92** **93** (trans and cis) (34)

The proportion of syn pathway observed in the formation of the trisubstituted olefin **93** varied between 1% and 75%, depending upon the substrate isomer and, primarily, upon the base-associating ability of the solvent employed.

b. Effects of Ring Size and Solvent upon Elimination Rates

The rate profile method for assessing elimination stereochemistry which has already been described for cycloalkyltrimethylammonium salts (section III.C.2.b) was used by the Prague group also for the corresponding series of cycloalkyl bromides with differing ring sizes (n = 5–14, 16). The rate profiles determined[100] for the *t*-butoxide-promoted eliminations in benzene, *t*-BuOH, and DMF solvents are presented in Figure 22a–c.

In the solvents of low polarity, benzene and *t*-BuOH (Figure 22a,b), the rate profiles for both the *trans*- and *cis*-olefin formation closely resemble those which were found for the corresponding trimethylammonium salt series (Figure 18). A pronounced rate maximum is again noted for the *trans*-olefin-

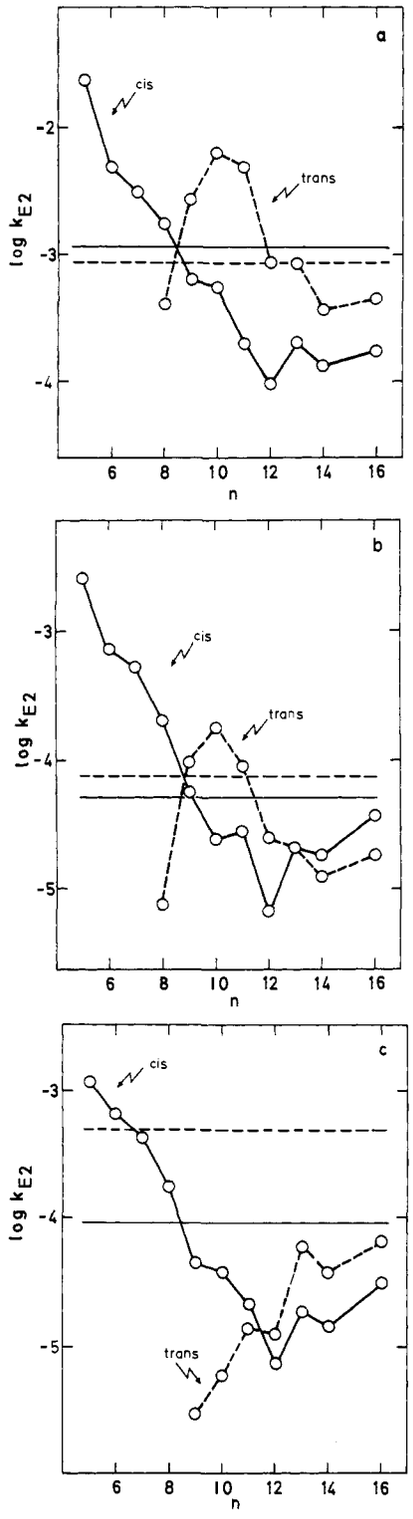


Figure 22. Effect of ring size, *n*, upon rates of *cis*- and *trans*-cycloalkene formation from cycloalkyl bromides: (a) reaction with *t*-BuOK–benzene at 100 °C; (b) reaction with *t*-BuOK–*t*-BuOH at 82.5 °C; (c) reaction with *t*-BuOLi–DMF at 40 °C. (Corresponding rates of *cis*- and *trans*-4-nonene formation from 5-nonyl bromide are included for comparison: solid and dotted horizontal lines, respectively.)

forming process in the 9–13-membered-ring region, whereas a rate minimum simultaneously occurs in this region for the cis isomers. The syn → trans, anti → cis dichotomy which has been earlier inferred from this rate pattern for the medium- and large-ring onium salts thus apparently also holds for eliminations of the corresponding bromides in base-associating solvents.

On the other hand, in the base-dissociating solvent DMF (Figure 22c), rate minima are found in the 9–13-membered-ring region for both the *cis*- and *trans*-olefin formation. This is the same rate pattern as that found in the reaction of cycloalkyl bromides with EtOK–EtOH (Figure 17) and has been shown[100,143] to be diagnostic of a homogeneous anti → cis, anti → trans elimination.

Thus, the kinetic evidence for the bromide series leads to stereochemical conclusions which are similar to those previously reached in investigation of eliminations from the deuterium-labeled tosylates **87** and **90**.

c. Base Association Effects

The observation that *tert*-butoxide-promoted elimination of 5,5,8,8-tetramethylcyclodecyl tosylate (**87**) always follows the unique syn → trans, anti → cis dichotomous course makes this reaction a very useful mechanistic model for the investigation of base association effects. In particular, the effect of base association on the syn:anti competition can be deduced immediately from the observed variation in trans:cis isomer ratios produced by changing the base counterion, the base concentration, and the solvent or by adding crown ether.

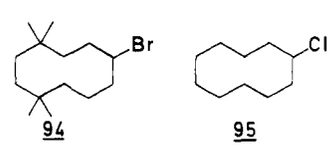
(*1*) *Effect of Base Counterion*. The effect of cation on the syn:anti competition was investigated by Svoboda and Závada[28] in reactions of tosylate **87** with *t*-BuO$^-$M$^+$–*t*-BuOH. A very marked decrease in the values of *trans-88*:*cis-88*, as well as *trans-89*:*cis-89*, was found (Table XLV) on changing the base counterion in the order $Na^+ > K^+ > Rb^+ \gg NMe_4^+$. The proportion of associated alkoxide species in solution should vary inversely with the ionic diameter of the cation following the order $Na^+ > K^+ > Rb^+ \gg NMe_4^+$. The variation of trans:cis ratios (Table XLV) is postulated[28] to arise from a cation-dependent competition between the associated and the free base species, the former preferring syn → trans, but the latter anti → cis elimination.

(*2*) *Effect of Base Concentration*. As was established in section II.B.2.b, competition between associated and free base in elimination reactions is also concentration dependent. The contribution of the free species is increased by lowering the total base concentration. Therefore, the observation by the Czech researchers[34] that trans:cis ratios in *t*-BuOK–DMF-induced elimination of the cyclodecyl tosylate **87** decrease gradually with diminishing base concentration (Table XLVI) provides additional support for the proposal[158] that the syn → trans, anti → cis dichotomy in the cyclic system originates from a competition between associated and free base species.

(*3*) *Effects of Solvent, Crown Ether, and Leaving Group*. The dramatic effects of solvent and dicyclohexano-18-crown-6[158] in *t*-BuOK-promoted eliminations from tetramethylcyclodecyl tosylate **87** are recorded in Table XLVII. The *trans*-olefins **88** and **89** are practically the sole products when the associated base species prevails (in benzene, in the absence of crown ether). However, the cis isomers **88** and **89** are highly favored when the associated base species has been suppressed by the use of DMF as the solvent or the addition of crown ether to any of the three base–solvent combinations. When combined with the evidence presented in the previous two subsections, these findings demonstrate that the syn:anti dichotomy in this particular system is a direct consequence of a dichotomy of the participating base.

Almost identical effects of solvent and crown ether presence upon isomer distribution was found[158] in eliminations of the bromo analogue **94**. Thus, the elimination behavior of bromo and tosyloxy leaving groups is again shown to be quite similar.

Traynham, Stone, and Couvillion[159] have investigated the



94 95

Table XLV. Effect of Base Counterion upon Trans:Cis Ratios in Eliminations from 87

cation	*trans*-88:*cis*-88	*trans*-89:*cis*-89
Na^+	52	1.0
K^+	24	0.98
Rb^+	17	0.95
NMe_4^+	0.46	0.18

Table XLVI. Effect of Base Concentration upon Trans:Cis Ratios in Eliminations from 87

[*t*-BuOK], M	*trans*-88:*cis*-88	*trans*-89:*cis*-89
1.0	1.31	0.32
0.8	1.17	0.25
0.5	1.01	0.23
0.2	0.79	0.17
0.1	0.73	0.15

Table XLVII. Effects of Solvent and Crown Ether upon Trans:Cis Ratios in Eliminations from 87

conditions	*trans*-88:*cis*-88	*trans*-89:*cis*-89
C_6H_6	63.4	8.8
C_6H_6 + CE[a]	0.2	0.02
t-BuOH	9.8	1.1
t-BuOH + CE[a]	0.40	0.14
DMF	0.94	0.20
DMF + CE[a]	0.08	0.01

[a] Dicyclohexano-18-crown-6 present; equimolar with respect to *t*-BuOK.

effects of solvent and base in eliminations from chlorocyclodecane **95**. The dehydrochlorination induced by *t*-BuOK–Me_2SO produced 97% *cis*-cyclodecene whereas with lithium dicyclohexylamide in ether–hexane, 96% *trans*-cyclodecene was obtained. However, later studies revealed[160] that a substantial trans → cis isomerization occurred when the dehydrochlorination was promoted by *t*-BuOK–Me_2SO. The results suggest that the effect of base association in eliminations from cyclodecyl chloride is probably less pronounced than that observed in the eliminations of the tosyloxy and bromo group from **87** and **94**, respectively.

d. Product Stability and Orientation

Equilibration experiments and heat of hydrogenation measurements show that the relative stabilities of *trans*- and *cis*-cyclodecenes and of the corresponding 1,1,4,4-tetramethylcyclodec-7-enes are remarkably different.[161] Thus, the enthalpy of hydrogenation of *cis*-cyclodecene is lower than that of *trans*-cyclodecene by more than 3 kcal/mol. By contrast, for the tetramethylated pair of cyclodecenes **88**, the relationship is reversed, the enthalpy of hydrogenation of the cis isomer being higher than that of the trans isomer by 2.7 kcal/mol. This disparate situation persists also for the corresponding cyclododecenes[162] (Table XLVIII).

Despite these differences, the trans:cis ratios for cycloalkenes arising from eliminations of the unsubstituted and of the tetramethylated reactants are always remarkably similar (Tables XLIX and L). This constancy shows, surprisingly, that product stability is an entirely unimportant factor in the elimination, regardless of the nature of base species involved. Possible reasons of this behavior are considered in the following subsection.

e. Conformational Aspects of Elimination Stereochemistry in Medium- and Large-Ring Systems

The 1,1,4,4-tetramethylcyclodecanes and corresponding dodecanes represent conformationally biased systems which are believed to possess structures (**96** and **97**, respectively) very similar to those which have been established by X-ray studies for the parent, nonmethylated compounds.[163,164]

Table XLVIII. Enthalpies of Hydrogenation (kcal/mol) of Cycloalkenes

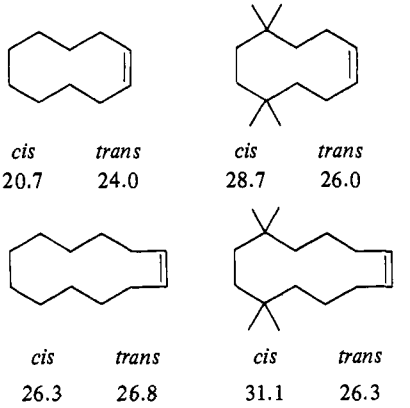


Table XLIX. Trans:Cis Ratios in Elimination from Cyclodecyl[a] and 1,1,4,4-Tetramethyl-7-cyclodecyl Bromides[b]

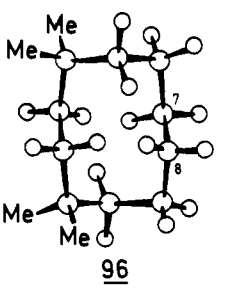
conditions	*trans*-:*cis*-cyclodecene	*trans*-:*cis*-1,1,4,4-tetramethylcyclodec-7-ene
t-BuOK–C_6H_6	8.1	55
t-BuOK–*t*-BuOH	7.3	9.0
t-BuOK–DMF	0.06	0.1

[a] From ref 100. [b] From ref 158.

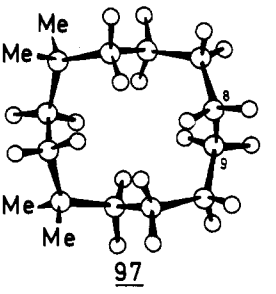
Table L. Trans:Cis Ratios in Eliminations from Cyclodecyl and 1,1,4,4-Tetramethyl-8-cyclododecyl Tosylates[a]

conditions	*trans*-:*cis*-cyclododecene	*trans*-:*cis*-1,1,4,4-tetramethyl-8-cyclododecene
t-BuOK–C_6H_6	11.8	21.6
t-BuOK–DMF	1.4	2.3

[a] From ref 157.



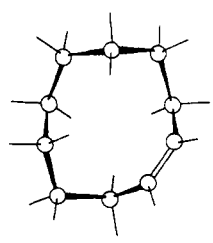
96



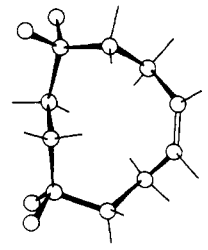
97

A plausible explanation for the elimination stereochemistry observed in *trans*-cycloalkene formation has been advanced in terms of these conformations. Consider the two alternative pathways which may lead to the *trans*-7-cyclodecene **88** and to the *trans*-8-cyclododecene **91**. The anti elimination pathway always involves an intraannular hydrogen, whereas for the syn path an extraannular hydrogen is removed. The intraannular hydrogen is located in the overcrowded inside of the ring, and the approach of base is therefore hindered.[30,99,123] Evidently this hindrance is greater in the 10- than in the 12-membered-ring substrate. On the other hand, the extraannular hydrogen sticks out from the ring and is open to attack by base. A quite analogous situation seems reasonable for *trans*-olefin formation from the corresponding nonmethylated compounds, which explains why syn:anti ratios in these reactions are so high.

The conformational situation concerning cis isomer formation is more involved. Dunitz[165] and Sicher[166] point out that the conformation for the *cis*-cyclodecene **98** resembles the stable



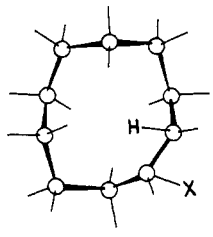
98



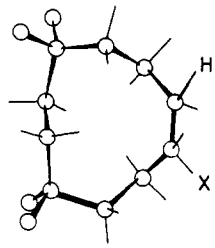
99

conformation of the cyclodecane ring whereas that for *cis*-1,1,4,4-tetramethylcyclodec-7-ene (**88**) involves a rather extreme distortion, **99**, which accounts for the low thermodynamic stability of this compound. Quite analogous conformational differences have been suggested[182] to exist between the *cis*-cyclododecene and *cis*-1,1,4,4-tetramethylcyclododec-8-ene, **91**.

Therefore, the different conformational arrangements shown in **100** and **101** might be expected for the eliminations which lead to the unsubstituted and to the tetramethylated *cis*-cycloalkenes, respectively. In the former, more stable, arrangement, **100**, the reactive hydrogen for anti elimination occupies an



100



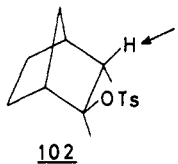
101

intraannular position and is therefore prohibitively hindered in the same fashion as it was in the formation of the trans isomer. However, in the latter, distorted arrangement, **101**, the reactive hydrogen is turned out from an intraannular position and is accessible for base attack.

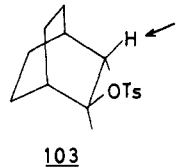
Thus, it seems reasonable to assume that both the tetramethyl-substituted and the nonmethylated reactants utilize the distorted conformation for the formation of *cis*-olefin. This explains[151] why no correlation exists between product stability (Table XLVIII) and product composition (Tables XLIX and L) in the eliminations from these cycloalkyl compounds.

4. Bicyclic Systems

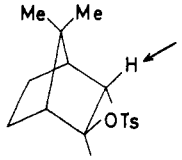
In agreement with the stereochemical behavior of the bicyclic onium salts **77** and **78** mentioned in section III.C.2.c, the corresponding tosylates **102** and **103** exhibit a very strong



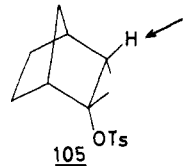
102



103



104



105

preference for syn elimination, particularly under conditions which favor base association. In the presence of crown ether or when polar solvents are used, a more balanced competition between syn and anti pathway is observed (Table LI).

Table LI. Stereochemistry of Elimination from Bicyclic Tosylates

reactant	conditions	syn:anti elimination	ref
102	2-CCONa[a]-triglyme	98:2[c]	167
102	2-CCONa[a]-triglyme + CE[b]	15:1[c] (11:1)[c,d]	168
104	2-CCONa[a]-triglyme	95:1[c]	167
105	2-CCONa[a]-triglyme	1:9[c]	167
102	*t*-HexONa-*p*-cymene	65:35[e]	170
102	*t*-HexONa-*t*-HexOH	18:72[e]	170
103	*t*-BuOK-benzene	89:11[c]	104
103	*t*-BuOK-triglyme	85:15[c]	104
103	*t*-BuOK-Me_2SO	64:36[c]	104
103	*t*-BuOK-DMF	61:39[c]	104

[a] Sodium salt of 2-cyclohexylcyclohexanol. [b] 18-Crown-6. [c] Corrected for the operation of the deuterium isotope effect. [d] Revised value, ref 169. [e] Uncorrected data from elimination of the *endo*-3-*d*-reactant.

Under the same reaction conditions very similar stereochemical results were obtained for eliminations from *exo*-norbornyl tosylate (**102**) and 7,7-dimethyl-*exo*-norbornyl tosylate (**104**). This demonstrates that the *syn*-7-methyl substituent does not substantially shield base approach to the exo-3 hydrogen.

In a marked contrast, elimination from the *endo*-tosylate **105** proceeds (Table LI) in a predominantly anti fashion, in spite of the unfavorable dihedral angle between the departing groups. Whether the suggested[187] steric hindrance to base approach at the endo hydrogen is responsible for this difference remains unclear.

Elimination stereochemistry was also investigated in the reactions of the chloro- and/or bromo analogues[171-173] of **102**, **103**, and **105**, with similar results.

IV. Dichotomies of Stereochemistry and Base Species in Activated E2 Eliminations

In previous sections, the dichotomies of base species and stereochemistry have been examined for unactivated E2 elimination reactions. Attention is now focused upon the corresponding dichotomies for base-promoted eliminations from substrates which bear moderately activating (aryl, vinyl, halogen) substituents. For the reactions presented in this section, E2 mechanisms have been established or are the most reasonable mechanistic alternatives.

A. Aryl-Activated Ammonium Salt Eliminations

1. Stereochemistry

The stereochemistry of eliminations from α- and/or β-arylated salts is compared with that for structurally similar unactivated ammonium salts in Table LII.

It is readily apparent that the syn elimination propensity is considerably lower for the reactions of α- as well as β-phenyl-activated substrates than for the related alkyltrimethylammonium salts. This tendency also extends to α,β-diphenyl-activated substrates except for the reaction of (*erythro*-1,2-diphenyl-1-propyl)trimethylammonium ion with *t*-BuOK-*t*-BuOH. This anomalous result was originally attributed[175] to a change into nonconcerted mechanistic channel caused by the strong *tert*-butoxide ion base. Later arguments[178] in support of concertedness for this unusual reaction are not conclusive, because a conceivable $(E1cB)_I$ mechanism was not disproven.

In agreement with the earlier observations for unactivated ammonium salt eliminations (section III.C.2.a.3), changing the base-solvent system from a primary alkoxide–primary alcohol combination to a tertiary alkoxide–tertiary alcohol system for

Table LII. Stereochemistry of Base-Promoted Eliminations from Ammonium Salts

substrate	product compared	% syn elimination: MeONa-MeOH	% syn elimination: *t*-BuOK-*t*-BuOH	ref
PhCHCH$_2$CH$_3$ (+NMe$_3$)	*trans*-PhCH=CHMe	1	29	174
CH$_3$CH$_2$CH$_2$CHCH$_2$CH$_3$ (+NMe$_3$)	*trans*-2-Hexene	10[a]	70[b]	30
PhCH$_2$CHCH$_3$ (+NMe$_3$)	*trans*-PhCH=CHMe	5	10	174
CH$_3$CH$_2$CH$_2$CH$_2$CHCH$_3$ (+NMe$_3$)	*trans*-2-Hexene	~0[a]	15	30
PhCHDCHO (+NMe$_3$)	*trans*-PhCH=CHO	~0	~0	110
CH$_3$(CH$_2$)$_7$CHOCHO (+NMe$_3$)	1-Decene-1,2-D$_2$	*c*	7	111
erythro-PhCHCHPh (+NMe$_3$)	PhC(CH$_3$)=CHPh	0[d]	100	175
erythro-*n*-BuCHCH-*n*-Bu (+NMe$_3$)	*n*-BuC(CH$_3$)=CH-*n*-Bu	5.0	40	122
threo-PhCHCHPh (+NMe$_3$)	PhC(CH$_3$)=CHPh	0[d]	0	175
threo-*n*-BuCHCH-*n*-Bu (+NMe$_3$)	*n*-BuC(CH$_3$)=CH-*n*-Bu	0.4	4.4	122

[a] *n*-BuOK-*n*-BuOH. [b] *t*-PenOK-*t*-PenOH. [c] Not determined. [d] EtOK-EtOH.

phenyl-activated ammonium salt eliminations enhances the propensity for syn elimination. It seems reasonable to extend the explanations previously advanced for the unactivated eliminations to the phenyl-activated elimination processes.

2. Geometrical Orientation

A sizable difference between the geometrical orientation observed in anti elimination components for aryl-activated and for unactivated ammonium salt eliminations is evident from the data in Table LIII. As previously mentioned, trans:cis ratios in eliminations from alkylammonium ions are always less than unity. However, for eliminations from α- as well as β-aryl-activated ammonium ions, very high trans:cis ratios are found. The ratios are insensitive to changes in the base–solvent system, as would be anticipated if the free alkoxide is the active base species. This is consistent with metathetical gegenion exchange to give the free base species even in solvents of low polarity (section II.B.4.b.2).

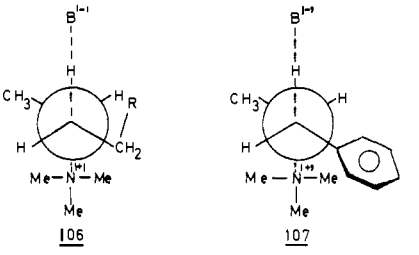
In comparing geometrical orientation for the aryl-activated and unactivated systems, it is important to keep in mind the differences in thermodynamic stability between pairs of geometrical isomers. For 1-phenyl-1-propene the equilibrium trans:cis ratio is reported by different workers to be 62 at 55 °C[177] and 18 at 97 °C.[178] On the other hand, equilibrium trans:cis ratios for 2-alkenes are usually in the range 3–5.[65] Thus, in eliminations from aryl-activated substrates, the observed trans:cis ratios are close to the equilibrium value, but for unactivated substrates, observed trans:cis ratios are far below the equilibrium values.

Rationalization of trans:cis ratios less than unity for eliminations from alkyltrimethylammonium salts has been made in terms of Saunder's model in which the bulky leaving group

Table LIII. Geometrical Orientation in Anti Eliminations from Ammonium Salts

substrate	product	trans:cis ratio: MeOH-MeOK	trans:cis ratio: *t*-BuOK-*t*-BuOH	ref
PhCHCH$_2$CH$_3$ (+NMe)	PhCH=CHMe	13	10	174
CH$_3$CH$_2$CH$_2$CHCH$_2$CH$_3$ (+NMe)	*n*-PrCH=CHMe	0.3	0.3	30
PhCH$_2$CHCH$_3$ (+NMe)	PhCH=CHMe	23	15	174
CH$_3$CH$_2$CH$_2$CHCH$_3$ (+NMe)	*n*-PrCH=CHMe	0.3	0.4	30

forces α- and β-alkyl groups into conformations (e.g., **106**) where approach of the base to the β hydrogen is hindered. The hindrance is greater in transition states for *trans*-alkene formation, and *cis*-alkene predominates (section II.B.4.b.2).



106 107

However, for eliminations from aryl-activated trimethylammonium salts, the aryl group is rigid and cannot bend upward to alleviate interactions with the leaving group (cf., e.g., **107**). Therefore, a "normal" preference for forming a large proportion of the thermodynamically more stable trans isomer is observed for elimination from the (1-phenyl-2-propyl)trimethylammonium ion **107** and from the (1-phenyl-1-propyl)trimethylammonium ion.[174]

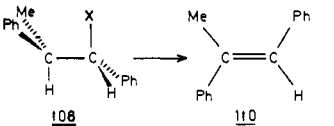
The apparent absence of hindrance to base approach in eliminations from the arylated ammonium salts may also explain why the contribution of syn elimination to the overall reaction is rather low for these substrates (Table LII). As pointed out in section III.C.2.a.1, there is a correlation between the amount of hindrance to base approach and the percentage of syn elimination.

B. β-Aryl- and β-Vinyl-Activated Elimination Reactions Involving Neutral Leaving Groups

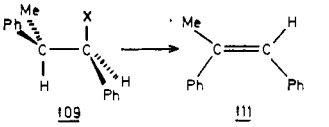
1. Acyclic Systems

a. Stereochemistry

The stereochemistry of β-aryl-activated eliminations from acyclic systems was reported in the classic paper by Cram, Greene, and DePuy more than 30 years ago.[175] Using *threo*- and *erythro*-1,2-diphenyl-1-propyl bromide and chloride, **108** and **109**, respectively, and a variety of base–solvent systems, only anti elimination stereochemistry was observed. Thus, the



108 110 (35)



109 111 (36)

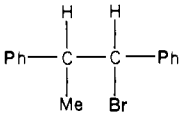
threo isomer **108** gave only (*E*)-α-methylstilbene (**110**) and the erythro isomer **109** produced only (*Z*)-α-methylstilbene (**111**) with EtONa-EtOH, 1-octONa-1-octOH, 2-octOK-2-octOH, *t*-BuOK-*t*-BuOH, $EtMe_2COK$-$EtMe_2COH$, and 2-octOK-benzene.

More recently, the stereochemistry of eliminations from 2-chloro-1-phenylpropane and β-phenylethyl tosylate and chloride has been investigated by Alunni, Baciocchi, Nicoletti, and Tinqoli[179] and by Bayne and Snyder,[180] respectively. Elimination from DL-*erythro*-2-chloro-1-deuterio-1-phenylpropane occurs by an anti mechanism with EtONa-EtOH and with *t*-BuOK-*t*-BuOH (in the presence of dicyclohexano-18-crown-6), whereas a small amount of syn elimination (<6%) is observed with *t*-BuOK-*t*-BuOH. Only anti stereochemistry is observed for eliminations from DL-*threo*-2-chloro-1-deuterio-1-phenylpropane. Reactions of PhCHDCHDOTs with *t*-BuOK in Me_2SO, *t*-BuOH, and benzene proceed with 4, 7, and 19% syn elimination, respectively. Elimination from the corresponding chloride promoted by *t*-BuOK-benzene involves 25% syn elimination.

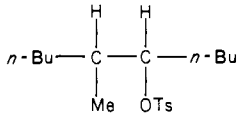
Very recently, Saunders[181] has confirmed the earlier report by Cram[182] of no significant syn elimination in reactions of 3-phenyl-2-butyl tosylate with EtONa-EtOH. Within experimental uncertainty (a few percent), Saunders observed only anti elimination for the eliminations induced by either EtONa-EtOH or *t*-BuONa-*t*-BuOH.

From the studies described above, it appears that significant contributions from syn elimination pathways need be anticipated only in reactions of β-aryl-activated acyclic halides and tosylates with the most highly associated base-solvent systems (e.g., tertiary alkoxides in hydrocarbon solvents).

Reasonably similar systems for the comparison of relative propensities for syn stereochemistry in aryl-activated and unactivated eliminations from acyclic substrates are 1,2-diphenyl-1-propyl bromide (**112**) and 5-methyl-6-decyl tosylate (**113**). For the latter, small amounts of syn elimination (4–10%)



112



113

are observed with *t*-BuOK-*t*-BuOH and *t*-BuOK-benzene.[122] Under similar conditions, the aryl-activated elimination gave no detectable syn elimination product.[175] Therefore, it appears that the same diminished propensity for syn stereochemistry noted for aryl-activated trimethylammonium salts (compared with unactivated compounds) also holds for neutral leaving groups.

b. Geometrical Orientation

(*1*) *β-Aryl-Activated Eliminations*. The tendency for elimination toward an activating β-aryl substituent (compared with unactivated elimination in another direction as in $PhCH_2CHXCH_3$) is so strong that positional orientation becomes meaningless. However, geometrical orientation in the formation of internal olefins may be compared between β-aryl-activated and unactivated eliminations (Table LIV).

When the geometrical orientation for iodo, bromo, chloro leaving groups vs. tosyloxy are examined, a parallel between β-aryl-activated and unactivated eliminations is clearly evident. For both types of elimination, significantly lower trans:cis ratios are observed with tosyloxy than with the ordinary halogen leaving groups. Apparently the asymmetric tosyloxy leaving group has a similar steric influence (section II.B.4.b.1) upon the β-aryl-activated and unactivated eliminations.

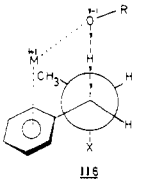
Further comparisons reveal some rather striking contrasts between geometrical orientation for activated and unactivated eliminations. In unactivated eliminations from the 2-alkyl halides, change to a poorer halogen leaving group produces a decrease in *trans*-2-alkene:*cis*-2-alkene ratio for all base-solvent systems. On the other hand, for eliminations from 1-phenyl-2-propyl iodide, bromide, and chloride, there is essentially no influence of the halogen leaving group upon geometrical orientation for eliminations induced by EtONa-EtOH or *t*-BuOK-*t*-BuOH and a possible trend toward higher trans:cis ratios for poorer leaving groups with *t*-BuOK-dicyclohexano-18-crown-6-*t*-BuOH. The extremely high trans:cis ratio observed in reactions of 1-phenyl-2-propyl fluoride with EtONa-EtOH could not be verified in the other base-solvent systems because of product isomerization under the conditions required to eliminate this poor leaving group. Such observations indicate considerable differences between transition states for unactivated and β-aryl-activated elimination reactions.

Elimination from 1-phenyl-1-bromopropane promoted by *t*-BuOK-*t*-BuOH[177] gives a trans:cis ratio of 66. The trans:cis ratios of similar magnitude for eliminations involving either an α- or β-phenyl group indicate that the phenyl groups primarily exert a conjugative effect and produce transition states with a high degree of double bond character.

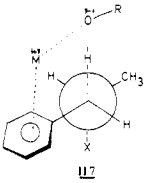
Also in contrast with the unactivated eliminations, the change from EtONa-EtOH to *t*-BuOK-*t*-BuOH causes higher trans:cis ratios in eliminations from 1-phenyl-2-propyl halides and tosylate. When the base-solvent system is *t*-BuOK-*t*-BuOH, addition of dicyclohexano-18-crown-6 lowers the trans:cis ratios for eliminations from 1-phenyl-2-propyl halides but has no effect in the reactions of 1-phenyl-2-propyl tosylate. Thus, base association has entirely different effects upon geometrical orientation in β-aryl-activated and in unactivated eliminations.

The sharply contrasting effects of base association upon geometrical orientation in β-aryl-activated and unactivated eliminations indicates the introduction of some new factor in the former which augments those previously discussed for unactivated eliminations. A model in which attractive interactions between the counterion of the associated base and the π electrons of the aromatic ring supplement the solvated ion pair model (section II.B.2.d.5) is now advanced.

If only solvated ion pair interactions of associated bases were important in the β-phenyl-activated eliminations (cf. transition states **114** and **115**), the effect of base association should

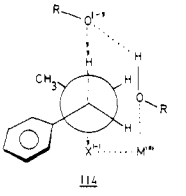


116

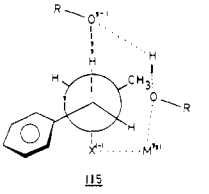


117

be to favor cis alkene formation and lower the trans:cis ratio. However, attractive interactions between the counterion of an associated base with the β-aryl group are also conceivable (cf. transition states **116** and **117**). These interactions should be



114



115

much stronger in the *trans*-alkene-forming transition state **117** because of the disruptive α-methyl group in **116**.

Considering only the more favorable attractive interactions, the trans:cis ratio will be determined by the relative stabilities of transition states **117** and **114**, respectively. The presence of the attractive interactions postulated in transition state **117** cannot be probed by the addition of crown ether since the strong metal ion complexing agent would also disrupt the favorable associations in transition state **114**.

Indication of interactions between the counterion of an associated base and a β-aryl group is provided by the geometrical

Table LIV. Geometrical Orientation as a Function of Leaving Group and Base-Solvent System in β-Aryl-Activated and Unactivated Eliminations

substrate	base-solvent	temp, °C	trans:cis ratio I	Br	Cl	F	OTs	ref
$PhCH_2\underset{X}{\underset{\vert}{C}}HCH_3$	*t*-BuOK-*t*-BuOH	60	74	78.5	72		21	183, 184
$PhCH_2\underset{X}{\underset{\vert}{C}}HCH_3$	*t*-BuOK-dicyclohexano-18-crown-6-*t*-BuOH	60	28.5	30	45		22.5	183, 184
$PhCH_2\underset{X}{\underset{\vert}{C}}HCH_3$	EtONa-EtOH	60	28	25	25	112	10	183, 184, 185
$n\text{-}C_7H_{15}CH_2\underset{X}{\underset{\vert}{C}}HCH_3$	*t*-BuOK-*t*-BuOH	100	1.8	1.3	1.1	0.8	0.4	38
$n\text{-}C_7H_{15}CH_2\underset{X}{\underset{\vert}{C}}HCH_3$	*t*-BuOK-dicyclohexano-18-crown-6-*t*-BuOH	100	5.4	5.1	3.6	2.9	2.2	38
$n\text{-}C_3H_7CH_2\underset{X}{\underset{\vert}{C}}HCH_3$	MeONa-MeOH	100	3.6	3.0	2.9	2.3	1.7	69
$n\text{-}C_3H_7CH_2\underset{X}{\underset{\vert}{C}}HCH_3$	*t*-BuOK-*t*-BuOH	100	1.8	1.4	1.1	1.2	0.4	72

Table LV. Geometrical Orientation in Reactions of $ArCH_2CH(X)CH_3$ with EtONa-EtOH and *t*-BuOK-*t*-BuOH

substrate Ar	X	*trans*-:*cis*-1-aryl-1-propene EtONa-EtOH	*t*-BuOK-*t*-BuOH
Ph	Br	34	90
π-$Cr(CO)_3Ph$	Br	35	36
Ph	OTs	9	20
π-$Cr(CO)_3Ph$	OTs	10	42

Table LVI. Olefinic Products from Reactions of $CH_2{=}CHCH_2CH(X)CH_3$ with Several Base-Solvent Systems[a] at 50 °C

base-solvent	*s-trans*-piperylene:*s-cis*-piperylene ratio when X is Br	Cl	OTs
t-BuOK-*t*-BuOH	5.7	5.4	1.9
EtONa-EtOH	4.7	4.7	2.8
MeONa-MeOH	4.6	4.6	2.6

[a] [Base] = 0.26-0.28 M, [RX] = 0.10 M.

orientation reported by Ceccon and Catelani[186] for base-promoted eliminations from 1-phenyl-2-propyl bromide and tosylate and the corresponding chromium tricarbonyl complexed species (Table LV).

With the dissociated base-solvent system of EtONa-EtOH, π complexation of the phenyl ring of 1-phenyl-2-propyl bromide or tosylate by chromium tricarbonyl has no apparent effect upon geometrical orientation. However, with the associated base-solvent combination of *t*-BuOK-*t*-BuOH, geometrical orientation is markedly affected by π complexation. The phenyl ring π complexation should sharply reduce the base counterion-aryl ring interactions postulated in transition states **116** and **117**. Therefore, the reduced trans:cis ratio observed for the π complexed substrate in the eliminations from 1-phenyl-2-propyl bromide induced by *t*-BuOK-*t*-BuOH supports the proposed attractive base counterion-aryl group interactions. However, for the corresponding system with a tosylate leaving group, π complexation increases the trans:cis ratio. Although the reason for the contrasting behavior of the two neutral leaving groups is not apparent, it is clear that π complexation of the β-aryl ring does markedly influence geometrical orientation for eliminations employing associated bases.

(*2*) *β-Vinyl-Activated Eliminations*. In order to provide a better understanding of the differences in factors which control geometrical orientation in unactivated and β-aryl-activated eliminations, Bartsch and Haines[187] have examined base-promoted, β-vinyl-activated elimination reactions. Geometrical orientations for reactions of 4-penten-2-yl bromide, chloride, and tosylate with MeONa-MeOH, EtONa-EtOH, and *t*-BuOK-*t*-BuOH are recorded in Table LVI. It was not possible to determine orientation in eliminations promoted by *t*-BuOK-18-crown-6-*t*-BuOH or *t*-BuOK-Me_2SO because of rapid isomerization of the diene products by these base-solvent systems. From a diene mixture which had been equilibrated at 50° with *t*-BuOK-Me_2SO, a *s-trans*-piperylene:*s-cis*-piperylene ratio of 6.4 was determined.[187]

Just as in the corresponding unactivated and β-aryl-activated reactions (Table LIV), β-vinyl-activated eliminations exhibit lower trans:cis ratios for the tosyloxy leaving group than for the halogens. Thus the asymmetric tosyloxy leaving group appears to exert the same type of steric influence (section II.B.4.b.1) upon all activated and unactivated eliminations.

The shifts in geometrical orientation produced by changing from a free base (EtONa-EtOH) to an associated base (*t*-BuOK-*t*-BuOH) for the β-vinyl-activated eliminations are intermediate between those found in unactivated and β-aryl-activated eliminations. The changes are summarized in Table LVII.

The intermediate effects of base association upon geometrical orientation in β-vinyl-activated eliminations when compared with those for β-aryl-activated and unactivated elimination reactions lends support to the postulated competitive attractive associated base interactions in the β-aryl-activated processes. For the β-vinyl-activated reactions, attractive interactions between the counterion of the associated base and the π electrons of the double bond should be weaker than those for β-aryl-activated reactions. Therefore, both the attractive solvated ion pair interactions (cf. transition states **114** and **115**) and attractive associated base counterion π-electron interactions (cf. transition states **116** and **117**) are important and roughly cancel each other.

c. Base Association and Transition-State Character

Effects of base association upon the E2 transition-state character of aryl-activated elimination reactions conducted in *t*-BuOH have been probed by Baciocchi and co-workers.[55,56] From the kinetic studies of anti eliminations from 1-bromo-2-arylethanes[55] and 1-chloro-1-phenyl-2-arylethanes[56] promoted by *t*-BuOK-*t*-BuOH and *t*-BuOK-18-crown-6-*t*-BuOH, the Hammett ρ values, β deuterium isotope effect values, and leaving group effect values listed in Table LVIII were obtained. Reactions of these substrates with *t*-BuOK-*t*-BuOH were found to be first order in both aryl halide and base. However, the presence of 18-crown-6 produced reactions which were first

Table LVII. Shifts in Geometrical Orientation Produced by Changing the Base-Solvent System from EtONa-EtOH to *t*-BuOK-*t*-BuOH

substrate	β-activating group	change in trans:cis ratio when the leaving group is	
		Br and Cl	OTs
$CH_3(CH_2)_2CH_2CH(X)CH_3$	none	decrease	decrease
$PhCH_2CH(X)CH_3$	aryl	increase	increase
$CH_2=CHCH_2CH(X)CH_3$	vinyl	small increase	small decrease

Table LVIII. Effects of Base Association upon Transition-State Structure for Anti Elimination Reactions Promoted by *t*-BuOK-*t*-BuOH in the Absence and Presence of 18-Crown-6 at 30 °C

substrate	18-crown-6	ρ	k_H/k_D	k_{Br}/k_{Cl}[a]
$ArCH_2CH_2Br$	absent	2.53	8.16	23
	present	2.77	8.05	19
$ArCH_2CH(Cl)Ph$	absent	2.20	7.93	
	present	3.40	8.04	

[a] The $PhCH_2CH_2Br$:$PhCH_2CH_2Cl$ rate ratio.

order in substrate but 1.4–1.5 order in base. This peculiar kinetic aspect of eliminations induced by crown-ether-complexed *t*-BuOK remains to be rationalized.

Although the rates of *t*-BuOK-promoted eliminations from 1-bromo-2-arylethanes in *t*-BuOH increased about 250-fold in the presence of 18-crown-6, the near constancy of the ρ, k_H/k_D, and k_{Br}/k_{Cl} values in the absence and presence of crown ether reveals that base association has little effect upon the transition-state structure for these anti eliminations. In contrast, the eliminations from 1-chloro-1-phenyl-2-arylethanes which show approximately the same acceleration in the presence of 18-crown-6 appear to have decidedly more carbanionic transition states with the free base species (ρ = 3.40) than for the associated base (ρ = 2.20).

The disparity of base association effects for these two substrates is made even more intriguing by the observation that the introduction of an α-phenyl group does not substantially alter the carbanionic character of the elimination transition state for reactions of β-aryl-activated substrates with EtONa-EtOH.[188] Additional research is clearly needed to delineate the factors responsible for the influence of substrate structure upon the base association effect in anti eliminations.

2. Cyclic Systems

As mentioned in section IV.B.1.a, the propensity for syn elimination from β-aryl-activated acyclic systems is quite low. The facility of syn-elimination pathways can, however, be markedly increased through the use of conformationally restricting ring systems which force a β-hydrogen and the leaving group into a syn-periplanar or nearly syn-periplanar arrangement. Thus, β-aryl-activated syn eliminations occur readily from *trans*-2-arylcyclopentyl,[189] *trans*-2-arylcyclobutyl,[190] *endo*-3-aryl-*exo*-2-norbornyl,[190] and *exo*-3-aryl-*endo*-2-norbornyl[190] tosylates. Base-promoted eliminations from the monocyclic substrates were studied with *t*-BuOK-*t*-BuOH because of concomitant solvolysis when more polar solvents are utilized. On the other hand, eliminations from the bicyclic systems could be investigated with EtONa-EtOH.

In order to assess the relative effects of base association for competitive β-aryl-activated syn elimination and unactivated anti elimination, reactions of *trans*-2-arylcyclopentyl tosylate (**118**) with *t*-BuOK-*t*-BuOH were examined by Bartsch and co-workers[191,192] (eq 37). 1-Arylcyclopentene (**119**) is the product of β-aryl-activated syn elimination whereas 3-arylcyclopentene (**120**) is the product of unactivated anti elimination.

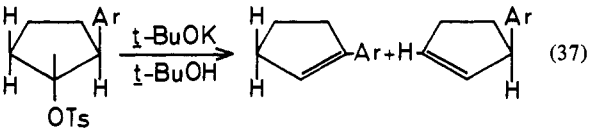
Table LIX. Relative Proportion of Syn Elimination Product formed in Reactions of *trans*-2-Phenylcyclopentyl Tosylate with *t*-BuOK-*t*-BuOH[a] at 50 °C

[dicyclohexano-18-crown-6], M	relative % of 1-phenylcyclopentene
0	89.2
0.031	46.5
0.049	33.0
0.10	30.1
0.17	29.5
0.22	30.8

[a] [*t*-BuOK] = 0.10 M.

Table LX. Effects of Base Association upon Transition-State Structure for Syn Eliminations from *trans*-2-Arylcyclopentyl Tosylates Promoted by *t*-BuOK-*t*-BuOH in the Absence and Presence of Dicyclohexano-18-crown-6 at 50 °C

dicyclohexano-18-crown-6	ρ	k_H/k_D
absent	2.2	5.3
present	3.1	5.1



(37)

118 119 120

Effects of adding dicyclohexano-18-crown-6 upon the relative amounts of **119** and **120** formed in reactions of **118** with *t*-BuOK-*t*-BuOH are recorded in Table LIX. The addition of crown ether (which reduces base association) causes a marked diminution in the relative proportion of syn elimination product until the crown ether and base are present in equal amounts. Further crown ether addition produces no noticeable effect. The presence of 0.10 M tetramethyl-12-crown-4, for which the crown ether cavity is too small to accommodate potassium ions, gave, within experimental error, the same proportion of 1-phenylcyclopentene as found in the absence of any crown ether.

The results clearly demonstrate a greater sensitivity of β-aryl-activated syn elimination to the effects of base association than in unactivated anti elimination. Similar results have been obtained for competition between unactivated syn-elimination and unactivated anti-elimination pathways (section III.D.2.a.1) which indicates that the phenomenon is independent of the presence of a β-aryl-activating group. Therefore, the rationalization previously advanced (i.e., six-centered transitions states such as **79** with associated bases) is valid in this case also.

For meta- and para-substituted phenyl groups, the relative proportions of **119** and **120** were also determined in eliminations from **118** induced by *t*-BuOK-*t*-BuOH and by *t*-BuOK-dicyclohexano-18-crown-6-*t*-BuOH. When the reasonable assumption that variation of the aryl group does not influence the rate of unactivated anti elimination was made, ρ values for the β-aryl-activated syn elimination involving associated and free base were calculated from the relative proportions of **119** and **120**. These values together with the primary deuterium isotope effect for syn elimination (also determined from product proportion measurements) are listed in Table LX.[192] The change from associated to free base has little influence upon k_H/k_D, but produces a substantially more carbanionic syn-elimination transition state.

Combination of these results for β-aryl-activated syn elimination with those previously presented for activated anti elimination from aralkyl halides (Table LVIII) indicates that insensitivity of k_H/k_D to base association effects is a general feature of both syn and anti eliminations. In turn, this suggests that the more carbanionic transition states observed for free base-pro-

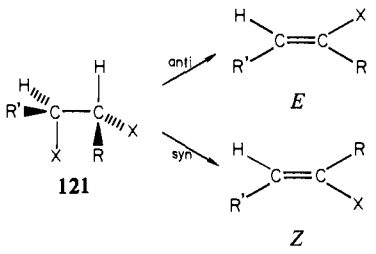
moted transition states with two of the three substrates is associated with changes in the degree of C_α–X bond rupture.

C. β-Halogen-Activated Eliminations

1. Stereochemistry

a. Acyclic Vicinal Dihalides

The stereochemical course of eliminations from acyclic vicinal dihalides may be assessed without the use of deuterium-labeled substrates. When the reactant exists as diastereomers, identity of the elimination products defines the stereochemistry. Thus, for elimination from the erythro dihalide **121**, either the

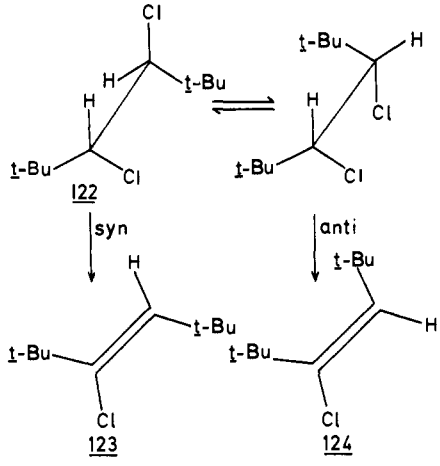


(38)

(*E*)- or (*Z*)-vinyl halide is formed depending on whether the elimination proceeds by an anti or syn reaction stereochemistry. In the earlier literature, reactions of *erythro*-2,3-dichloropentane and homologous *erythro*- and *meso*-*vic*-dichloroalkanes with KOH–*n*-PrOH were reported to give exclusively the (*E*)-vinyl chlorides, showing that the elimination proceeds with anti stereochemistry.[193] More recent studies show that reactions of *meso*- and *dl*-4,5-dichlorooctanes with *n*-BuONa–*n*-BuOH, *t*-BuOK–*t*-BuOH, *t*-BuOK–benzene, and *t*-BuOK–toluene, as well as *meso*-3,4-dibromo-2,5-dimethylhexane with *t*-BuOK–toluene, all exhibit exclusive anti-elimination stereochemistry.[43]

Stereochemical preferences for β-halogen-activated elimination and unactivated dehydrohalogenation are strikingly divergent. A reasonable comparison is for eliminations from 4,5-dichlorooctane and 5-decyl chloride both induced by *t*-BuOK–benzene. For the former, solely anti elimination stereochemistry is observed.[43] However, in elimination from 5-chlorodecane the overall syn-elimination component is 41%.[45] Thus, the previously noted lower propensity for syn elimination from β-aryl-activated substrates than from corresponding unactivated compounds extends also to β-halogen-activated substrates. This suggests that the tendency for activated syn eliminations will, in general, be low for acyclic substrates.

Very recent results by Schlosser and An[57] show that syn elimination from an acyclic vicinal dihalide may be achieved with a sufficiently sterically biased substrate. Depending upon the



(39)

solvent, *meso*-3,4-dichloro-2,5,5-tetramethylhexane (**122**) undergoes base-promoted dehydrochlorination to give predominately (*Z*)-3-chloro-2,2,5,5-tetramethyl-3-hexene (**123**; syn-elimination product) or the thermodynamically less stable (*E*)-3-chloro-2,2,5,5-tetramethyl-3-hexene (**124**; anti-elimination product). Results for *t*-BuOK-promoted eliminations from the dichloride **122** in three solvents are recorded in Table LXI together with the reaction order in base for the competing syn- and anti-elimination pathways.

Table LXI. Reaction Products and Order in Base for Reactions of *meso*-3,4-Dichloro-2,2,5,5-tetramethylhexane with *t*-BuOK in Different Solvents

solvent	temp, °C	% 123:% 124 (with 1.0 M base)	reaction order in base: syn elimination	reaction order in base: anti elimination
THF	60	92:8[a]	0.5	0.8
t-BuOH	80	86:14	0.6[b]	1.0[b]
Me_2SO	20	7:93[c]		

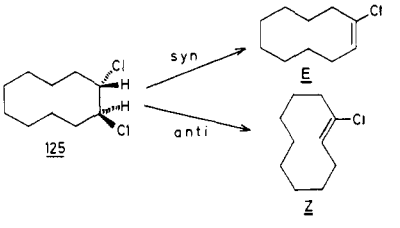
[a] Values of 93:7 and 90:10 were found for 0.83 and 1.5 M base concentrations, respectively. [b] [*t*-BuOK] = 0.37–0.93 M. [c] Values of 13:87 and 8:92 were found for 0.10 and 1.5 M base concentrations, respectively.

From the data in Table LXI, the enhancement of syn elimination by solvents such as THF and *t*-BuOH which favor base association is readily evident. This means that base association favors β-halogen-activated syn elimination in competition with β-halogen-activated anti elimination. It should be recalled that base association also favors the syn pathway in the competition of unactivated syn and anti eliminations (section III.D.2.a.1) and of β-phenyl-activated syn and unactivated anti eliminations (section IV.B.1.a) from acyclic substrates. Therefore, the favoring of syn over anti elimination through base association is demonstrated to be independent of activation or its absence.

The orders in base for competitive syn and anti eliminations from **122** promoted by *t*-BuOK–THF and *t*-BuOK–*t*-BuOH were determined as slopes of log k_{obsd} vs. log base concentration plots and provide information concerning the active base species in the two solvents (see section II.B.2.d.5). Since the tetrameric base species is dominant[16] in THF, slopes of 0.5 and 0.8 indicate that the active base is less associated than the tetramer and is probably a dimer for syn elimination and a mixture of dimers and trimers for anti elimination (cf. Table VIII). For elimination induced by *t*-BuOK–*t*-BuOH, the situation should be quite different than in THF solvent because the dominant base species is probably a monomeric ion pair.[47] Comparison of the slopes for *t*-BuOK-promoted eliminations conducted in both *t*-BuOH and THF indicates that the degree of association for the active base involved in the syn elimination is less than that in anti elimination. The same trend probably also holds for the *t*-BuOK–Me_2SO system since the syn:anti elimination product ratio decreases with increasing base concentration (Table LXI, footnote c). This is surprising because exactly opposite results (syn:anti elimination ratio increases with increasing base concentration) are observed for unactivated eliminations induced by *t*-BuOK–DMF.[34]

b. Medium-Ring Vicinal Dihalides

Assessment of reaction stereochemistry by product analysis is also possible for eliminations from vicinal dihalides in medi-



(40)

Table LXII. Halocycloalkene Products in Eliminations from *trans*-1,2-X_2-Cyclodecanes Promoted by Various Base-Solvent Combinations

base-solvent	temp, °C	E:Z ratio when X = Cl	E:Z ratio when X = Br
EtONa-EtOH	100	5.6[a] 2.5[b]	4,7[a,c]
t-BuOK-*t*-BuOH	100	10,[a] 11[b]	12[a]
t-BuOK-benzene	100	20[a]	23[a]
t-BuOK-toluene	100	18[b]	
t-BuOK-18-crown-6-toluene	100	2.5[b]	
t-BuOK-DMF	20	1.2[b]	

[a] Reference 194. [b] Reference 195. [c] Base-solvent system was 10% KOH in EtOH at 80 °C.

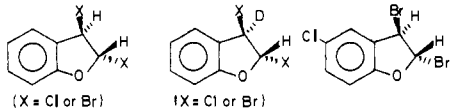
um-sized-ring compounds. For example, *trans*-1,2-dichlorocyclodecane (**125**) yields (*E*)-1-chlorocyclodecene by syn elimination and (*Z*)-1-chlorocyclodecene by anti elimination. Relative contributions from syn and anti elimination pathways (ratio of *E*:*Z*) for eliminations from *trans*-1,2-dibromocyclodecane and *trans*-1,2-dichlorocyclodecane are recorded in Table LXII.[194,195]

Change of the base-solvent system from EtONa-EtOH to *t*-BuOK-*t*-BuOH to *t*-BuOK-toluene (or benzene) produced significant enhancement in the amount of syn elimination. The changes are essentially the same for the dichloride and dibromide. For the common base *t*-BuOK, the proportion of syn elimination is considerably higher with the associated base species (*t*-BuOH, benzene, or toluene) than when the free base species is produced by addition of crown ether or a change to the good cation-solvating solvent DMF. Thus, as observed with acyclic vicinal dihalides, base association enhances the propensity for syn stereochemistry in eliminations from cyclic dihalides.

Kinetic evidence concerning the active associated base species in eliminations from *cis*-1,2-dichlorocyclodecane promoted by *t*-BuOK-toluene has been provided by Schlosser, Jan, Byrne, and Sicher.[43] The slope of the log k_{obsd} vs. log base concentration plot was approximately 0.8 for formation of (*E*)-1-chlorocyclodecene (anti elimination) and 0.5 for production of (*Z*)-1-chlorocyclodecene (syn elimination). Since the tetrameric base species is dominant in toluene, slopes less than unity (section II.B.2.d.5) indicate that the active base is less associated than the tetramer, probably dimers or trimers. The observed lower base reaction order for syn than anti elimination reveals that a less associated base species is also responsible for syn elimination from the cyclic dihalides.

2. Base Association and Transition-State Character

Baciocchi and co-workers[196,197] have recently used reactions of oxyanion bases with *trans*-2,3-dihalo-2,3-dihydrobenzofurans (**126**) to probe base association effects upon transition states



for β-halo-β-aryl-activated syn eliminations. With alkoxide and phenoxide bases, **126** gives the corresponding 3-halogenobenzofurans in quantitative yields.[196,197]

The transition-state for syn eliminations from *trans*-2,3-dibromo-2,3-dihydrobenzofuran was investigated by measuring the primary deuterium isotope effect (with **127**, X = Br) and the influence of an electron-withdrawing aryl substituent (with **128**).[196] Values of k_H/k_D and the substituent effect, k_{Cl}/k_H, as well as relative reaction rates for different base-solvent combinations are recorded in Table LXIII.

No significant variation in transition-state structure is evident when the base-solvent system is changed from EtOK-EtOH to

Table LXIII. Deuterium Isotope Effect and Substituent Effect Values for Elimination Reactions of *trans*-2,3-Dibromo-2,3-dihydrobenzofurans at 30 °C

base-solvent	approximate relative rates	k_H/k_D	k_{Cl}/k_H
EtOK-EtOH	1.0	3.0	12.0
n-BuOK-*n*-BuOH	1.4	3.3	11.0
n-BuOK-18-crown-6-*n*-BuOH	5	2.8	15.8
t-BuOK-*t*-BuOH		1.8[a]	7.1
t-BuOK-*t*-BuOH	150-250	2.0[b]	7.4
t-BuOK-18-crown-6-*t*-BuOH	20 000-70 000	3.0	15.4

[a] [*t*-BuOK] = 0.1 M. [b] [*t*-BuOK] = 5×10^{-3} M.

n-BuOK-*n*-BuOH. Addition of 18-crown-6 to the latter caused only a small rate enhancement which indicates only a low level of base association in *n*-BuOH. The small changes in k_H/k_D and k_{Cl}/k_H might suggest a slight increase in carbanionic character of the transition state (if the proton is more than half transferred).

Change of the base-solvent combination to *t*-BuOK-*t*-BuOH increases the reaction rate but decreases the substituent effect from that observed for eliminations induced by EtOK-EtOH or *n*-BuOK-*n*-BuOH. The decrease in k_{Cl}/k_H indicates less carbanionic character in transition states for eliminations induced by *t*-BuOK-*t*-BuOH. The accompanying decrease in k_H/k_D is anomalous.

Addition of 18-crown-6 to *t*-BuOK-*t*-BuOH produces a marked rate enhancement (10^2-10^3). Increased k_H/k_D and k_{Cl}/k_H values are consistent with more carbanionic character in the transition states for elimination by the free base. Such a shift in transition-state character in the present β-halo-β-aryl-activated reactions is in keeping with those previously noted for β-aryl-activated syn elimination and α,β-diaryl-activated anti elimination (Tables LVIII and LX). However, it should be recalled that the addition of crown ether did not change the k_H/k_D value for eliminations from these other substrates.

Baciocchi, Ruzziconi, and Sebastiani[197] have measured the rates of syn elimination from *trans*-2,3-dichloro-2,3-dihydrobenzofuran (**126**; X = Cl) and its 3-deuterated counterpart, **127** (X = Cl), induced by free phenoxide and by lithium phenoxide ion pairs in Me_2SO. Reactions with the free base were found to be faster than those with the ion-paired base by a factor of approximately 30. It was also determined for anti elimination (from 2-phenylethyl chloride) that the entire reaction proceeded via the free base. These observations led the authors to state: "the frequently reported statement that syn elimination reactions are favored by nucleophile (base) association should be more appropriately replaced by the statement that nucleophile (base) association disfavors syn eliminations much less than anti eliminations".

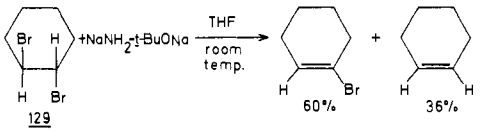
It is interesting that the kinetic deuterium isotope effect values for eliminations from *trans*-2,3-dichloro-2,3-dihydrobenzofuran induced by free phenoxide base and lithium phenoxide ion pairs were found to be 2.5 and 2.4, respectively. Thus, the deuterium isotope effect was insensitive to base ion pairing in phenoxide-promoted eliminations whereas base association had a measurable effect upon k_H/k_D for eliminations induced by *t*-BuOK-*t*-BuOH (vide supra).

3. Complex-Base-Induced Eliminations

Caubère has pioneered the use of sodium amide containing "complex bases" in organic synthesis.[198,199] The reagents are comprised of sodium amide and in situ generated sodium alkoxides or enolates in ethereal solvents, such as THF. Complex bases have proven to be unusually effective in promoting novel alkene, diene, and alkyne-forming reactions, as well as arynic condensations.[198,199]

In 1972, Caubère and Coudert[200] reported that the reaction

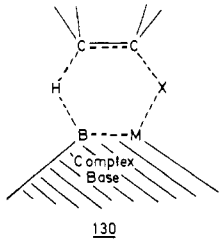
of $NaNH_2$–*t*-BuONa with *trans*-1,2-dibromocyclohexane (**129**) in THF at room temperature produced a 60% yield of 1-bromocyclohexene and a 36% yield of cyclohexene (eq 41).



(41)

Under the same reaction conditions but with either $NaNH_2$ or *t*-BuONa alone as the base, 70–90% of the starting material was recovered and only traces of 1-bromocyclohexene and cyclohexene were observed.

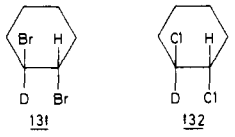
Formation of synthetically useful amounts of the syn-elimination product 1-bromocyclohexene in the reaction of **129** with the heterogeneous complex base–solvent combination is noteworthy, since only very low yields of this product are obtained with ordinary bases, such as NaOH–aqueous in EtOH.[201] Subsequently, Caubère and co-workers[202,203] demonstrated the generality of this syn-elimination process by the formation of 1-bromocyclopentene (47%), 1-bromocycloheptene (90%), and 1-bromocyclooctene (95%) in reactions of the corresponding *trans*-1,2-dibromocycloalkanes with $NaNH_2$–*t*-BuONa in THF at room temperature. It was proposed[196,199,202] that the unusually facile syn elimination results from a two-site interaction of the dihalide on the surface of complex base aggregates, as depicted in **130** (where B is the base, M is the countercation of



130

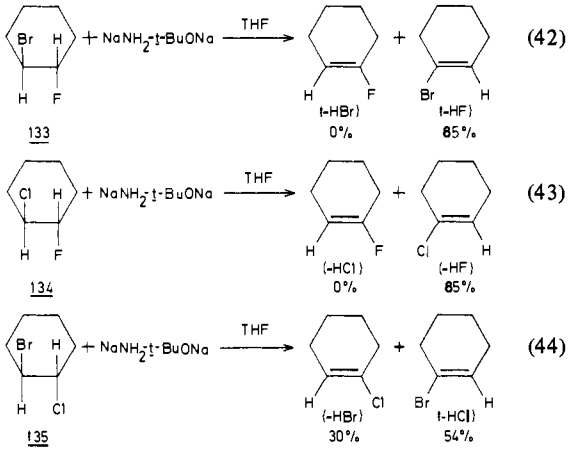
the base, and X is the leaving group). Similar simultaneous interactions of the base with the β-hydrogen and leaving group are probably not possible in an analogous anti elimination with the heterogeneous base.

Consistent with the proposed concerted elimination mechanism, Bartsch and Lee[189] have observed a substantial deuterium isotope effect in complex base-promoted dehydrohalogenation of the monodeuterated *trans*-1,2-dihalocyclohexanes **131** and **132**.



Recently, Lee and Bartsch[153] reported an amazing propensity for removal of the normally poorer halogen leaving group in complex-base-promoted eliminations from *trans*-1,2-dihalocyclohexanes containing two different halogens (eq 42–44). Thus dehydrohalogenation of *trans*-1-bromo-2-fluorocyclohexane (**133**) and *trans*-1-chloro-2-fluorocyclohexane (**134**) involved regiospecific loss of HF. Dehydrochlorination was also favored over dehydrobromination in complex-base-promoted elimination from *trans*-1-bromo-2-chlorocyclohexane (**135**).

The preferential loss of "poorer" halogen leaving groups is confined to reactions with syn stereochemistry. Thus, reactions of 1-bromo-1-chlorocyclohexane and *cis*-1-bromo-2-chlorocyclohexane with $NaNH_2$–*t*-BuONa in THF produced 99% yields of 1-chlorocyclohexene.[153] Therefore, complex-base-induced anti eliminations from 1,1- and *cis*-1,2-dihalocyclohexanes exhibit the same preference for dehydrobromination over dehydrochlorination noted with more ordinary base–solvent combinations.[201]



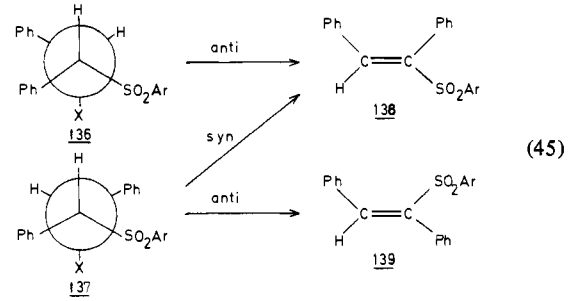
The observed preference for removal of "poorer" halogen leaving groups in complex-base-promoted syn eliminations suggests that leaving group–metal ion interactions in transition state **130** are the dominant leaving group property rather than the customary preeminence of the C–X bond strength.[153] Because of high electronegativity, which favors strong interactions with M, fluoro is the preferred halogen leaving group. Similarly, the chloro leaving group is removed in preference to bromo.

V. Dichotomies of Stereochemistry and Base Species in E1cB Eliminations

Although the previous chapters were confined to dichotomies of stereochemistry and base species in E2 reactions, similar dichotomies have been noted in a few instances for reactions which proceed via E1cB mechanisms. Several of these investigations are now briefly summarized. For a general survey of progress in the study of E1cB mechanisms, the reader is referred to recent reviews.[2,5,6]

Substrate properties which are conducive to elimination by an E1cB mechanism include a β-hydrogen that is acidified by a strongly activating sulfonyl or cyano group and/or a very poor leaving group.

In 1963, Cristol and Pappas[204] reported that reactions of *erythro*- and *threo*-2-*p*-toluenesulfonyl-1,2-diphenyl-1-chloroethanes, **136** and **137** (X = Cl), respectively, with ethanolic KOH



(45)

both produced only (*E*)-2-*p*-toluenesulfonyl-1,2-diphenylethene (**138**). Thus reaction of the erythro substrate **136** proceeds by anti elimination and that of the threo compound **137** results from syn elimination. This "stereoconvergent elimination" was attributed to a change of mechanism. The more rapid anti elimination from **136** was ascribed to an E2 mechanism. Anti elimination from the threo substrate **137** was thought to be prohibited by conformational steric repulsions between the α-phenyl and β-tosyl groups which forced the elimination to proceed with syn stereochemistry via an E1cB mechanism. However, subsequent investigations have cast serious doubt upon this explanation.

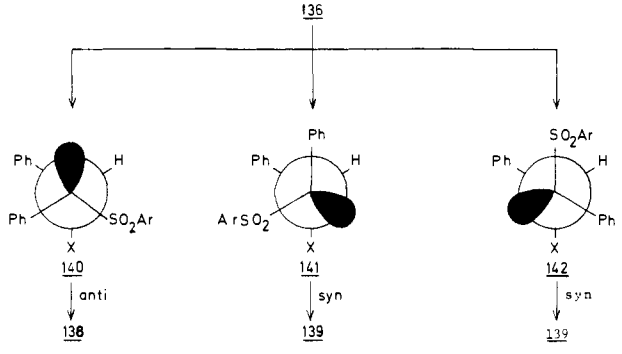
Fiandanese, Maffeo, Naso, and Ronzini have measured the rates of reaction of **136** and **137** (X = Br and Cl) with MeO-

Na-MeOH.[205] For the threo as well as the erythro substrates, the leaving group element effect was uncommonly small ($k_{Br}/k_{Cl} \sim 2$). The extremely small leaving group effect when combined with additional mechanistic evidence indicated an $(E1cB)_I$ mechanism or an E2 mechanism with extremely small amounts of C_α-X bond rupture for eliminations from *both* of the diastereomers **136** and **137**. Strong support for the $(E1cB)_I$ alternative has recently been provided by Stirling and co-workers.[208] Therefore the stereoconvergent elimination does not result from an E2-E1cB dichotomy but rather from a stereochemical syn-anti dichotomy occurring within a single E1cB mechanism.

In another important study, Naso and co-workers[207] demonstrated that the stereoconvergent elimination behavior of the diastereomers **136** and **137** is markedly dependent upon the base-solvent system employed. Reactions of the erythro substrate **136** (X = Cl and Br) with a variety of base-solvent combinations always yielded only **138**, the product of anti elimination. However, in reactions of the threo compounds **137** (X = Cl and Br) widely varying amounts of syn and anti elimination products, **138** and **139**, respectively, were obtained with different base-solvent combinations (Table LXIV).

In Table LXIV, a clear-cut correlation between the percentage of syn elimination and the basicity of the base-solvent combination is evident. Increased basicity provides an enhanced proportion of syn elimination product. A negligible effect of base association is demonstrated by the absence of changes in stereochemistry when the elimination is conducted in the presence of crown ether (compare entry 1 with entries 2 and 6 with 7 in Table LXIV). Thus, the overall pattern of syn-anti variation closely resembles that which was noted earlier in E2 reactions of alkyl- and cycloalkyltrimethylammonium salts (sections III.C.2.a.3 and III.C.2.b.3). It is also noteworthy that for a given base-solvent system the relative proportions of syn- and anti-elimination products formed from **136** are insensitive to leaving-group variation from chloro to bromo. This provides additional evidence for an $(E1cB)_I$ mechanism for reactions of **136** (which contrasts with the E2 mechanism for eliminations from unactivated trimethylammonium salts).

If it is assumed that the $(E1cB)_I$ mechanistic hypothesis is correct, the stereochemical results recorded in Table LXIV may be explained as follows. Proton abstraction from the erythro substrate **136** leads to a mixture of rapidly equilibrating (with respect to leaving group expulsion) pyramidal[208,209] carbanions **140-142** (eq 46). However, elimination proceeds only via



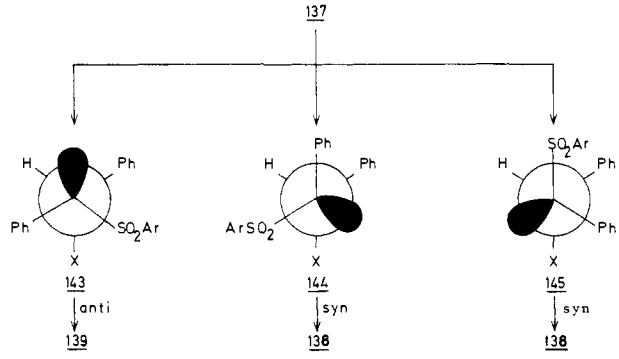
(46)

carbanion **140** because its electron pair is ideally situated for expulsion of the leaving group and, at the same time, Ph-$ArSO_2$ steric interactions are minimized in carbanion **140**. Therefore, a clean anti elimination takes place.

In eliminations from the threo compound **137**, the situation is different because the stereoelectronic and conformational factors are not cooperative (eq 47). Since expulsion of the leaving group from the stereoelectronically preferred carbanion **143** is rendered difficult by severe Ph-$ArSO_2$ steric interactions,

Table LXIV. Stereochemical Course of Eliminations from *threo*-2-*p*-Toluenesulfonyl-1,2-diphenyl-1-haloethanes 137

	X = Cl		X = Br	
base-solvent	% anti	% syn	% anti	% syn
t-BuOK-*t*-BuOH	0	100		
t-BuOK-dicyclohexano-18-crown-6-*t*-BuOH	0	100		
MeONa-Me_2SO	0	100		
MeONa-MeOH	40	60	35	65
PhOK-Me_2SO	72	28	65	35
PhOK-dioxane	88	12	84	16
PhOK-dicyclohexano-18-crown-6-dioxane	87	13	87	13
p-$NO_2C_6H_4ONa$-Me_2SO	90	10	100	0
$MeCO_2Na$-Me_2SO	100	0	100	0
$Et_3N^+F^-$-MeCN	100	0		



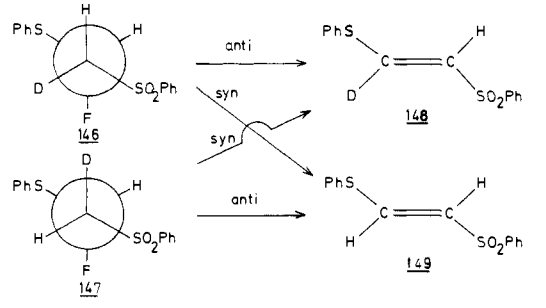
(47)

the anti elimination is slowed down and syn elimination via carbanions **144** and **145** becomes competitive. It has been proposed[97,99] that syn elimination requires a configurational inversion of the C_β atom. The relative amounts of syn- and anti-elimination products formed from **137** may therefore depend upon the configurational stability of the carbanions **144** and **145**.

From the stereochemical data in Table LXIV, it is noted that the base-solvent combinations which favor anti elimination are those in which the conjugate acid of the base (HF, $MeCO_2H$, ArOH) is capable of forming strong hydrogen bonds with carbanions **144** and **145**. The formation of hydrogen-bonded carbanions should enhance their configurational stability and thereby favor elimination via carbanion **143** which forms the product of anti elimination **139**.

Similar reasoning may be used to explain the differing stereochemical results for eliminations from **137** induced by a common base MeONa in MeOH and in Me_2SO. In the latter solvent, only syn elimination is observed, whereas in MeOH, a mixture of syn- and anti-elimination products is formed. A higher acidity of MeOH in MeOH (pK_a = 16.3[210]) than in Me_2SO (pK_a = 27.9[211]) should lead to more anti-elimination product in MeOH than in Me_2SO, as observed.

Fiandanese, Marchese, Naso, and Sciacovelli[212] have also studied eliminations from diastereomeric 1-deuterio-2-fluoro-2-phenylthioethyl phenyl sulfones **146** and **147**. Compared with



(48)

Table LXV. Stereochemical Course of Eliminations from Diastereometric 1-Deuterio-2-fluoro-2-phenylthioethyl Phenyl Sulfones at 25 °C

substrate	base-solvent	dicyclohexano-18-crown-6 present	% anti	% syn
146	PhOK–dioxane	no	13	87
146	PhOK–dioxane	yes	58	42
146	*t*-BuONa-*t*-BuOH–C_6H_6[a]	no	77	23
146	*t*-BuONa-*t*-BuOH–C_6H_6[a]	yes	79	21
147	PhOK–dioxane	no	4	96
147	PhOK–dioxane	yes	50	50
147	*t*-BuONa-*t*-BuOH–C_6H_6[a]	no	33	67
147	*t*-BuONa-*t*-BuOH–C_6H_6[a]	yes	38	62

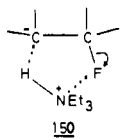
[a] *t*-BuOH–C_6H_6 (20:80).

the substrates **136** and **137**, the β-hydrogens in **146** and **147** are less activated but the leaving group is much poorer. Therefore, the mechanism of elimination from **146** to **147** should also be on the $(E1cB)_I$–E2 (nearly E1cB) borderline. Stereochemical results of eliminations from **146** and **147** induced by PhOK–dioxane and *t*-BuONa–*t*-BuOH–C_6H_6 are recorded in Table LXV.

For these two base–solvent combinations, the effect of adding crown ether is surprisingly different. With PhOK–dioxane, the presence of crown ether causes a sharp reduction in the percentage of syn elimination from both **146** and **147**. However, for *t*-BuONa–*t*-BuOK–C_6H_6, the presence of crown ether has no influence upon the elimination stereochemistry.

These results indicate a change of mechanism for eliminations from **146** and **147** induced by the two different base–solvent systems. The previously mentioned absence of base association effects in eliminations from **136** and **137** for which an $(E1cB)_I$ mechanism was postulated suggests that reactions of **146** and **147** with *t*-BuOK–*t*-BuOH–C_6H_6 also proceed by a stepwise mechanism. On the other hand, the pronounced base association effect for reactions of **146** and **147** with PhOK–dioxane is consistent with competitive syn and anti elimination by E2 mechanisms (sections III.D.2.a.1 and IV.B.2). The weaker phenoxide base could be the cause of a mechanistic change from $(E1cB)_I$ (with *t*-BuOK–*t*-BuOH–C_6H_6) to E2.

Triethylamine-promoted eliminations of HF from **146** and **147** in benzene gave only syn-elimination products.[213] Comparison of elimination rates with those for the corresponding undeuterated substrate gave k_H/k_D = 1.1 for **145** and k_H/k_D = 0.8 for **147**. An E1cB mechanism involving an ion pair, $(E1cB)_{ip}$, was proposed in which interactions such as those depicted in transition state **150** control the elimination stereochemistry.



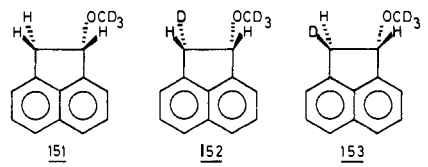
150

That such interactions are especially important for the fluorine leaving group is indicated by studies of eliminations from (2-phenylsulfonyl)ethyl halides promoted by triethylamine in acetonitrile and benzene.[214] The apparent E2 mechanism for eliminations from (2-phenylsulfonyl)ethyl bromide and chloride changes to $(E1cB)_{ip}$ for the fluoro leaving group.

Hunter and Shearing[215,216] describe a somewhat different type of E1cB mechanism which involves ion pairs in studies of *tert*-butoxide-induced eliminations from deuterium-labeled 1-methoxyacenaphthenes in *t*-BuOH. For reactions of **151**, **152**, and **153** with *tert*-butoxide in *t*-BuOH, base-promoted exchange and elimination are in close competition. A combination of rate and product studies allows the carbanionic elimination processes to be dissected.

Table LXVI. Relative Rates of Eliminations from 1-Methoxyacenaphthene Induced by *t*-BuOM in *t*-BuOH

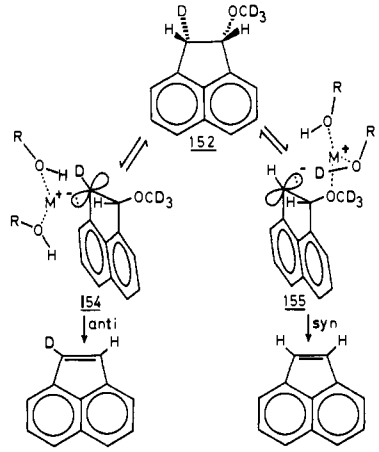
base	substrate	temp, °C	k_{syn}: k_{anti}
t-BuOLi	153	152	15
t-BuOK	153	86	7.9
t-BuOCs	153	86	6.5
t-BuOK + dicyclohexano-18-crown-6	152	45	0.25
t-BuONMe$_4$	152	45	0.20



151 152 153

An effect of the base counterion upon the relative rates of syn and anti elimination is evident from the data presented in Table LXVI. With associated bases, syn elimination is favored, but for free *tert*-butoxide (produced by adding crown ether to *t*-BuOK or by use of a nonassociating tetramethylammonium counterion), anti elimination is preferred.

The effect of base association was explained by the mechanistic model depicted in eq 49. The associated base favors



(49)

syn elimination because the base counterion can coordinate with the oxygen of the leaving group in **155**. Thus, the metal ion acts as an electrophile and assists removal of the leaving group from the carbanion.[217] Such interactions are not possible for geometrical reasons in **154**.

VI. Concluding Remarks

In the fundamental mechanistic concept outlined by Ingold,[97] base-promoted 1,2-elimination reactions are portrayed as a band of mechanisms differing with respect to the timing of bond breaking and bond making. The dichotomies of stereochemistry and of base species which we have now surveyed add a new dimension to this concept since bands of mechanisms differing with respect to stereochemistry and/or ionic association of the participating base evidently must also be considered. Therefore, mechanistic analysis of elimination reactions poses a much more delicate problem than was previously anticipated.

In this review, we have summarized diverse evidence which illuminates various aspects of the complex influence of substrate structure, base association, base strength, and solvent upon the rates, orientation, and stereochemistry of concerted, alkoxide-promoted, 1,2-elimination reactions. Main features of

alternative anti- and syn-elimination modes promoted by associated and free alkoxide base species gradually emerge from the composite evidence. In addition to providing mechanistic insight, this new understanding is of considerable preparative interest.

As noted by Ingold,[97] reaction mechanisms are, in general, elucidated by successive approximation. In most instances, we have had to limit ourselves to drawing a general (and somewhat vague) distinction between associated and free base species. Identification of the individual base species which participate in given elimination reactions represents the next important stage in the mechanistic analysis.

Acknowledgments. This review originated from an exchange of ideas which took place during a National Academy of Sciences (USA)–Czechoslovak Academy of Sciences sponsored visit by R.A.B. to the Institute of Organic Chemistry and Biochemistry of the Czechoslovak Academy of Sciences in Prague in May of 1978. Both authors wish to express their appreciation for this opportunity to initiate collaborative writing and research on base-promoted elimination reactions. R.A.B. also acknowledges the Robert A. Welch Foundation, the National Science Foundation, and the Petroleum Research Fund, administered by the American Chemical Society, for their support of elimination reaction research in his laboratories. Support from the Robert A. Welch Foundation during the period in which this review was written is especially appreciated.

VII. References

(1) Isaacs, N. S. In "Annual Reports on the Progress of Chemistry": The Chemical Society: London, 1970; p 180.
(2) Bordwell, F. G. *Acc. Chem. Res.* **1972**, *5*, 374.
(3) Saunders, W. H., Jr.; Cockerill, A. F. "Mechanisms of Elimination Reactions"; Wiley-Interscience: New York, 1973; Chapter 1.
(4) Saunders, W. H., Jr. *Acc. Chem. Res.* **1976**, *8*, 19.
(5) Cockerill, A. F.; Harrison, R. G. In "The Chemistry of Double-Bonded Functional Groups, Part I"; Patai, S., Ed.; Wiley-Interscience: New York, 1977; pp 155–189.
(6) Alekserov, M. A.; Yufit, S. S.; Kucherov, V. F. *Russ. Chem. Rev.* **1978**, *47*, 134.
(7) Bunnett, J. F. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 225; *Angew. Chem.*, **1962**, *74*, 731.
(8) More O'Ferrall, R. A. *J. Chem. Soc. B* **1970**, 274.
(9) Harris, J. M.; Shafer, S. G.; Moffatt, J. R.; Becker, A. R. *J. Am. Chem. Soc.* **1979**, *101*, 3295.
(10) Brandstrom, A. *Ark. Kemi* **1957**, *11*, 567.
(11) Exner, J. H.; Steiner, E. C., *J. Am. Chem. Soc.* **1974**, *96*, 1782.
(12) Saunders, W. H., Jr.; Bushman, D. G.; Cockerill, A. F. *J. Am. Chem. Soc.* **1968**, *90*, 1775.
(13) Hapala, J.; Svoboda, M.; Závada, J., unpublished results.
(14) Maskornik, M. J. *Tetrahedron Lett.* **1972**, 1797.
(15) Bessonov, V. A.; Alikhanov, P. R.; Gur'yanova, E. N.; Simonov, A. P.; Shapiro, I. O.; Yakovleva, E. A.; Shalenshtein, A. L. *J. Gen. Chem. USSR* **1967**, *37*, 96.
(16) Halaska, V.; Lochman, L.; Lim, D. *Collect. Czech. Chem. Commun.*, **1968**, *33*, 3245.
(17) Weiss, E.; Alsdorf, H.; Kühr, H. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 801; *Angew. Chem.* **1967**, *79*, 816.
(18) Greiser, J.; Weiss, E. *Chem. Ber.* **1977**, *110*, 3388.
(19) Weiss, E.; Alsdorf, H.; Kühr, H.; Grutzmacher, H. F. *Chem. Ber.* **1968**, *101*, 3777.
(20) Liotta, C. L., unpublished results.
(21) Pechanec, V.; Horáček, V.; Halaška, V.; Pánková, M.; Závada, J. *Collect. Czech. Chem. Commun.*, in press.
(22) Hogen-Esch, T. E. *Adv. Phys. Org. Chem.* **1977**, *15*, 154–266.
(23) Skell, P. S.; Allen, R. M. *J. Am. Chem. Soc.* **1959**, *81*, 5383.
(24) Bartsch, R. A. *J. Am. Chem. Soc.* **1971**, *93*, 3683.
(25) Skell, P. S.; Hall, W. H. *J. Am. Chem. Soc.* **1963**, *85*, 2851.
(26) Froemsdorf, D. H.; Dowd, W.; Gifford, W. A.; Meyerson, S. *Chem. Commun.* **1968**, 449.
(27) Chiao, W.-B.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1977**, *99*, 6699.
(28) Svoboda, M.; Závada, J. *Collect. Czech. Chem. Commun.* **1972**, *37*, 3902.
(29) Fromesdorf, D. H.; Pinnick, H. R.; Meyerson, S. *Chem. Commun.* **1968**, 1600.
(30) Bailey, D. S.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1970**, *92*, 6904.
(31) Bartsch, R. A.; Pruss, G. M.; Cook, D. M.; Buswell, R. L.; Bushaw, B. A.; Wiegers, K. E. *J. Am. Chem. Soc.* **1973**, *95*, 6745.
(32) Bartsch, R. A. *Acc. Chem. Res.* **1975**, *8*, 239.
(33) Závada, J., unpublished results.
(34) Závada, J.; Svoboda, M. *Tetrahedron Lett.* **1972**, 23.
(35) Závada, J.; Pánková, M.; Bartsch, R. A.; Cho, B. R. *Collect. Czech. Chem. Commun.*, in press.
(36) Allaway, J. R.; Bartsch, R. A.; Snyder, C. H., unpublished results.
(37) Miller, D. J.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1979**, *101*, 6749.
(38) Pánková, M.; Závada, J. *Collect. Czech. Chem. Commun.* **1977**, *42*, 1981.
(39) "Handbook of Chemistry and Physics", 57th ed.; Weast, R. C., Ed.; CRC Press: Cleveland, 1977; pp E 56–57.
(40) "Tetrahydrofuran as a Reaction Solvent": Technical Bulletin A-39452: Elastomers Department, E. I. du Pont de Nemours & Co., Inc.: Wilmington, DE, 1969; p 2.
(41) Bartsch, R. A.; Roberts, D. K. *Tetrahedron Lett.* **1977**, 321.
(42) Schlosser, M. In Houben-Weyl-Müller, "Methoden der Organischen Chemie"; Thieme Verlag: Stuttgart, 1972; Volume V/1b, p 40.
(43) Schlosser, M.; Jan, G.; Byrne, E.; Sicher, J. *Helv. Chim. Acta* **1973**, *56*, 1530.
(44) Závada, J.; Pánková, M.; Svoboda, M.; Schlosser, M. J. *J. Chem. Soc., Chem. Commun.* **1973**, 168.
(45) Závada, J.; Pánková, M.; Svoboda, M. *Collect. Czech. Chem. Commun.* **1976**, *41*, 3778.
(46) Saunders, W. H., Jr. *J. Chem. Soc., Chem. Commun.* **1973**, 850.
(47) (a) Závada, J.; Pánková, M. *Collect. Czech. Chem. Commun.* **1960**, *45*, 2171. (b) Pánková, M.; Závada, J. *Ibid.*, in press.
(48) Pánková, M.; Závada, J. *Collect. Czech. Chem. Commun.* **1977**, *42*, 3439.
(49) (a) Brown, H. C.; Klimisch, R. L. *J. Am. Chem. Soc.* **1966**, *88*, 1425. (b) Klimisch, R. L., "Structural Effects in Bimolecular Elimination Reactions"; Ph.D. Thesis, Purdue University, 1964; p 31.
(50) Závada, J.; Pánková, M.; Vítek, A. *Collect. Czech. Chem. Commun.*, in press.
(51) Cockerill, A. F.; Rottschaefer, S.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1967**, *89*, 901.
(52) Yoshida, T.; Yano, Y.; Oae, S. *Tetrahedron* **1971**, *27*, 5343.
(53) DePuy, C. H.; Storm, D. L.; Frey, J. T.; Naylor, C. G. *J. Org. Chem.* **1970**, *35*, 2746.
(54) Banger, J.; Cockerill, A. F.; Davis, G. L. O. *J. Chem. Soc. B* **1971**, 498.
(55) Alunni, S.; Baciocchi, E.; Perucci, P. *J. Org. Chem.* **1976**, *41*, 2636.
(56) Alunni, S.; Baciocchi, E.; Perucci, P. *J. Org. Chem.* **1977**, *42*, 2170.
(57) Schlosser, M.; An, T. D. *Helv. Chim. Acta* **1979**, *62*, 1194.
(58) Cram, D. J.; Kingsbury, C. A.; Richborn, B. *J. Am. Chem. Soc.* **1961**, *83*, 3688.
(59) Pritchard, J. G.; Nelson, H. M. *J. Phys. Chem.* **1960**, *64*, 795.
(60) Bartsch, R. A.; Pruss, G. M.; Bushaw, B. A.; Wiegers, K. E. *J. Am. Chem. Soc.* **1973**, *95*, 3045.
(61) Bartsch, R. A.; Roberts, D. K.; Cho, B. R. *J. Org. Chem.* **1979**, *44*, 4105.
(62) Bartsch, R. A.; Wiegers, K. E.; Gurltz, D. M. *J. Am. Chem. Soc.* **1974**, *96*, 430.
(63) Bartsch, R. A.; Ingram, D. D. *J. Org. Chem.* **1975**, *40*, 3138.
(64) Tremelling, M. J.; Hopper, S. P.; Mendelowitz, P. C. *J. Org. Chem.* **1979**, *44*, 4770.
(65) Bartsch, R. A.; Read, R. A.; Larson, D. T.; Roberts, D. K.; Scott, K. J.; Cho, B. R. *J. Am. Chem. Soc.* **1979**, *101*, 1176.
(66) Froemsdorf, D. H.; McCain, M. E. *J. Am. Chem. Soc.* **1965**, *87*, 3983.
(67) Froemsdorf, D. H.; Dowd, W.; Leimer, K. E. *J. Am. Chem. Soc.* **1966**, *88*, 2345.
(68) Froemsdorf, D. H.; Robbins, M. D. *J. Am. Chem. Soc.* **1967**, *89*, 1737.
(69) Bartsch, R. A.; Bunnett, J. F. *J. Am. Chem. Soc.* **1968**, *90*, 408.
(70) Saunders, W. H., Jr.; Fahrenholtz, S. R.; Caress, E. A.; Lowe, J. P.; Schreiber, M. *J. Am. Chem. Soc.* **1965**, *87*, 3401.
(71) Brown, H. C.; Klimisch, R. L. *J. Am. Chem. Soc.* **1965**, *87*, 5517.
(72) Bartsch, R. A.; Bunnett, J. F. *J. Am. Chem. Soc.* **1969**, *91*, 1376.
(73) Griffith, D. L.; Meges, D. L.; Brown, H. C. *Chem. Commun.* **1966**, 90.
(74) Bartsch, R. A.; Bunnett, J. F. *J. Am. Chem. Soc.* **1969**, *91*, 1382.
(75) Feit, I. N.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1970**, *92*, 1630.
(76) Pánková, M.; Závada, J. *Collect. Czech. Chem. Commun.* **1977**, *42*, 2161.
(77) Závada, J.; Pánková, M. *Collect. Czech. Chem. Commun.* **1977**, *42*, 3421.
(78) Bailey, D. S.; Montgomery, F. C.; Chodak, G. W.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1970**, *92*, 6911.
(79) Bartsch, R. A. *J. Org. Chem.* **1973**, *38*, 846.
(80) The steric hindrance model of H. Felkin is reported in ref 81.
(81) Sicher, J.; Závada, J.; Pánková, M. *Collect. Czech. Chem. Commun.* **1971**, *36*, 3162.
(82) Baciocchi, E.; Corsano, S.; Ruzziconi, R. *J. Chem. Soc., Perkin Trans. 2* **1977**, 436.
(83) Acharaya, S. P.; Brown, H. C. *Chem. Commun.* **1968**, 305.
(84) Schlosser, M.; Tarchini, C. *Helv. Chim. Acta* **1977**, *60*, 3060.
(85) Julia, S.; Julia, M.; Linstrumelle, G. *Bull. Soc. Chim. Fr.* **1966**, 3499.
(86) DePuy, C. H.; Thurn, R. D.; Morris, G. F. *J. Am. Chem. Soc.* **1962**, *84*, 1314.
(87) Kreevoy, M. M.; Gilje, J. W.; Ditsch, L. T.; Batorewitz, W.; Turner, M. A. *J. Org. Chem.* **1962**, *27*, 726.
(88) Závada, J.; Krupička, J.; Sicher, J. *Collect. Czech. Chem. Commun.* **1963**, *28*, 1664.
(89) Hine, J. *J. Am. Chem. Soc.* **1966**, *88*, 5525.
(90) Fukui, K. *Tetrahedron Lett.* **1965**, 2427.
(91) Fukui, K.; Fujimoto, H. *Tetrahedron Lett.* **1965**, 4303.
(92) Fukui, K.; Fujimoto, H. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2018.

(93) Fukui, K.; Hao, H.; Fujimoto, H. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 348.
(94) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. "Conformational Analysis": Interscience: New York, 1965; p 483.
(95) Dixon, W. T. *Chem. Ind. (London)* **1967**, 789.
(96) Ahn, N. T. *Chem. Commun.* **1966**, 1089.
(97) Ingold, C. K. *Proc. Chem. Soc., London* **1962**, 265.
(98) Závada, J.; Sicher, J. *Collect. Czech. Chem. Commun.* **1967**, *32*, 3701.
(99) Sicher, J.; Závada, J. *Collect. Czech. Chem. Commun.* **1968**, *33*, 1278.
(100) Závada, J.; Krupička, J.; Sicher, J. *Collect. Czech. Chem. Commun.* **1966**, *33*, 1393.
(101) Hückel, W.; Tappe, W.; Legutke, G. *Liebigs Ann. Chem.* **1940**, *543*, 191.
(102) Cristol, S. J.; Hause, N. L.; Meek, J. S. *J. Am. Chem. Soc.* **1951**, *73*, 674.
(103) Cooke, M. P.; Coke, J. L. *J. Am. Chem. Soc.* **1966**, *90*, 5556.
(104) Sicher, J.; Pánková, M.; Závada, J.; Knlezo, L.; Orahovats, A. *Collect. Czech. Chem. Commun.* **1971**, *36*, 3128.
(105) Sicher, J.; Závada, J.; Pánková, M. *Collect. Czech. Chem. Commun.* **1971**, *36*, 3140.
(106) Borchardt, J. K.; Saunders, W. H. *J. Am. Chem. Soc.* **1974**, *96*, 3912.
(107) Závada, J.; Svoboda, M.; Sicher, J. *Tetrahedron Lett.* **1966**, 1627.
(108) Pánková, M.; Sicher, J.; Závada, J. *Chem. Commun.* **1967**, 394.
(109) Závada, J.; Svoboda, M.; Sicher, J. *Collect. Czech. Chem. Commun.* **1966**, *33*, 4027.
(110) Bourns, A. N.; Frosst, A. C. *Can. J. Chem.* **1970**, *48*, 133.
(111) Pánková, M.; Vítek, A.; Vašíčková, S.; Řeřicha, R.; Závada, J. *Collect. Chem. Czech. Commun.* **1972**, *37*, 3456.
(112) Řeřicha, R.; Vítek, A.; Vašíčková, S.; Pánková, M.; Závada, J. *Collect. Czech. Chem. Commun.* **1972**, *37*, 3749.
(113) Cockerill, A. F.; Kendall, W. J. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1352.
(114) Coke, J. L.; Cooke, M. P. *J. Am. Chem. Soc.* **1967**, *89*, 6701.
(115) Coke, J. L.; Cooke, M. P. *Tetrahedron Lett.* **1968**, 2253.
(116) Bach, R. D.; Knight, J. W. *Tetrahedron Lett.* **1979**, 3815.
(117) Reference 3, pp 79–92.
(118) Smith, P. J.; Bourns, A. N. *Can. J. Chem.* **1974**, *52*, 749.
(119) Sicher, J. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 200; *Angew. Chem.* **1972**, *84*, 177.
(120) Pánková, M.; Závada, J. *Collect. Czech. Chem. Commun.*, In press.
(121) Závada, J.; Pánková, M.; Sicher, J. *Collect. Czech. Chem. Commun.* **1972**, *37*, 2414.
(122) Sicher, J.; Svoboda, M.; Pánková, M.; Závada, J. *Collect. Czech. Chem. Commun.* **1971**, *36*, 3633.
(123) Sicher, J. *Pure Appl. Chem.* **1971**, *25*, 655.
(124) Banthorpe, D. V.; Hughes, E. D.; Ingold, C. K. *J. Chem. Soc.* **1960**, 4054.
(125) Pánková, M.; Závada, J. *Tetrahedron Lett.* **1973**, 2237.
(126) Závada, J.; Pánková, M. *Collect. Czech. Chem. Commun.* **1979**, *44*, 1273.
(127) Závada, J.; Pánková, M.; Svoboda, M. *Collect. Czech. Chem. Commun.* **1973**, *38*, 2102.
(128) Bach, R. D.; Badger, R. C.; Lang, T. L. *J. Am. Chem. Soc.* **1979**, *101*, 2845.
(129) Sicher, J.; Závada, J.; Pánková, M. *Chem. Commun.* **1966**, 1147.
(130) Wolfe, S. *Acc. Chem. Res.* **1972**, *5*, 102.
(131) Wolfe, S.; Rauk, A. *Chem. Commun.* **1966**, 778.
(132) Landsbury, P. T. *Acc. Chem. Res.* **1969**, *2*, 210.
(133) Fraser, R. R.; Schubert, F. J. *Chem. Commun.* **1969**, 1474.
(134) Almy, J.; Garwood, D. C.; Cram, D. J. *J. Am. Chem. Soc.* **1970**, *92*, 4321.
(135) Coke, J. L.; Mourning, M. C. *J. Am. Chem. Soc.* **1966**, *90*, 5561.
(136) Coke, J. L.; Cooke, M. P.; Mourning, M. C. *Tetrahedron Lett.* **1966**, 2247.
(137) Coke, J. L.; Smith, G. D.; Britton, G. H. *J. Am. Chem. Soc.* **1975**, *97*, 4323.
(138) Sicher, J. *Prog. Stereochem.* **1962**, *3*, 229–238.
(139) Sicher, J.; Závada, J. *Collect. Czech. Chem. Commun.* **1967**, *32*, 2122.
(140) Brown, K. C.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1970**, *92*, 4292.
(141) Lamaty, G.; Tapiero, C.; Wylde, R. *Bull. Soc. Chim. Fr.* **1966**, 2039.
(142) Závada, J.; Krupička, J.; Sicher, J. *Collect. Czech. Chem. Commun.* **1966**, *31*, 4273.
(143) Závada, J.; Krupička, J.; Sicher, J. *Chem. Commun.* **1967**, 66.
(144) Závada, J.; Sicher, J. *Proc. Chem. Soc., London* **1963**, 96.
(145) Závada, J.; Sicher, J. *Collect. Czech. Chem. Commun.* **1965**, *30*, 438.
(146) Feit, I. N.; Schadt, F.; Lublnkovski, J.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1971**, *93*, 6606.
(147) Borchardt, J. K.; Hargreaves, R.; Saunders, W. H., Jr. *Tetrahedron Lett.* **1972**, 2307.
(148) Saunders, W. H., Jr.; Bonadies, S. D.; Braunstien, M.; Borchardt, J. K.; Hargreaves, R. T. *Tetrahedron* **1977**, *33*, 1577.
(149) Závada, J.; Svoboda, M.; Pánková, M. *Tetrahedron Lett.* **1972**, 711.
(150) Závada, J.; Pánková, M.; Sicher, J. *Chem. Commun.* **1968**, 1145.
(151) Svoboda, M.; Závada, J., unpublished results.
(152) Pánková, M.; Svoboda, M.; Závada, J. *Tetrahedron Lett.* **1972**, 2465.
(153) Lee, J. G.; Bartsch, R. A. *J. Am. Chem. Soc.* **1979**, *101*, 228.
(154) Borchardt, J. K.; Swanson, J. C.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1974**, *96*, 3918.
(155) Finley, K. T.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1967**, *89*, 898.
(156) Levisalles, J.; Pete, J. P. *Bull. Soc. Chim. Fr.* **1966**, 2912.
(157) Svoboda, M.; Závada, J.; Sicher, J. *Collect. Czech. Chem. Commun.* **1966**, *33*, 1415.
(158) Svoboda, M.; Hapala, J.; Závada, J. *Tetrahedron Lett.* **1972**, 265.
(159) Traynham, J. G.; Stone, D. B.; Couvillion, J. L. *J. Org. Chem.* **1967**, *32*, 510.
(160) Bartsch, R. A.; Shelly, T. A. *J. Org. Chem.* **1973**, *38*, 2911.
(161) Sicher, J.; Svoboda, M.; Závada, J.; Turner, R. B.; Goebel, P. *Tetrahedron* **1966**, *22*, 659.
(162) Sicher, J.; Svoboda, M.; Mallon, B. J.; Turner, R. B. *J. Chem. Soc. B* **1968**, 441.
(163) Huber-Buser, E.; Dunitz, J. D. *Helv. Chim. Acta* **1960**, *43*, 760.
(164) Dunitz, J. D.; Shearer, H. M. *Helv. Chim. Acta* **1960**, *43*, 18.
(165) Dunitz, J. D. *Pure Appl. Chem.* **1971**, *25*, 495.
(166) Sicher, J. *Ind. Chim. Belge* **1967**, *32*, 331.
(167) Brown, H. C.; Liu, K.-T. *J. Am. Chem. Soc.* **1970**, *92*, 200.
(168) Bartsch, R. A.; Kayser, R. H. *J. Am. Chem. Soc.* **1974**, *96*, 4346.
(169) Bartsch, R. A.; Lee, J. G., unpublished results.
(170) Kwart, H.; Takeshita, T.; Nyce, J. L. *J. Am. Chem. Soc.* **1964**, *86*, 2606.
(171) Stille, J. K.; Sonnenburg, F. M.; Kinstle, T. H. *J. Am. Chem. Soc.* **1966**, *88*, 4922.
(172) Stille, J. K.; Sonnenburg, F. M. *Tetrahedron Lett.* **1966**, 4587.
(173) Marchand, A. P.; McBrockway, N. *J. Am. Chem. Soc.* **1970**, *92*, 5801.
(174) Machkova, Z.; Závada, J. *Collect. Czech. Chem. Commun.*, In press.
(175) Cram, D. J.; Greene, F. D.; DePuy, C. H. *J. Am. Chem. Soc.* **1956**, *78*, 790.
(176) Borchardt, J. K.; Saunders, W. H. *J. Org. Chem.* **1974**, *39*, 99.
(177) Biale, G.; Cook, D.; Lloyd, D. J.; Parker, A. J.; Stevens, I. D. R.; Takahashi, J.; Winstein, S. *J. Am. Chem. Soc.* **1971**, *93*, 4375.
(178) Ela, S. W.; Cram, D. J. *J. Am. Chem. Soc.* **1966**, *88*, 5791.
(179) Alunni, S.; Baciocchi, E.; Nicolettl, R.; Tingoli, M. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1669.
(180) Bayne, W. F.; Snyder, E. I. *Tetrahedron Lett.* **1971**, 571.
(181) Chiao, W. B.; Saunders, W. H. *J. Org. Chem.* **1960**, *45*, 1319.
(182) Cram, D. J. *J. Am. Chem. Soc.* **1952**, *74*, 2149.
(183) Alunni, S.; Baciocchi, E. *J. Chem. Soc., Perkin Trans. 2* **1976**, 877.
(184) Alunni, S.; Baciocchi, E.; Ruzziconi, R.; Tingoli, M. *J. Org. Chem.* **1974**, *39*, 3299.
(185) Alunni, S.; Baciocchi, E. *Tetrahedron Lett.* **1973**, 205.
(186) Ceccon, A.; Catelani, G. *J. Organomet. Chem.* **1974**, *72*, 179.
(187) Bartsch, R. A.; Haines, J. C., unpublished results.
(188) Baciocchi, E.; Perucci, P.; Rol, C. *J. Chem. Soc., Perkin Trans. 2* **1975**, 329.
(189) DePuy, C. H.; Morris, G. F.; Smith, J. S.; Smat, R. J. *J. Am. Chem. Soc.* **1965**, *87*, 2421.
(190) DePuy, C. H.; Naylor, C. G.; Beckman, J. A. *J. Org. Chem.* **1970**, *35*, 2750.
(191) Bartsch, R. A.; Weigers, K. I. *Tetrahedron Lett.* **1972**, 3819.
(192) Bartsch, R. A.; Mintz, E. A.; Parlman, R. M. *J. Am. Chem. Soc.* **1974**, *96*, 4249.
(193) Hoff, M. C.; Greenlee, K. W.; Boord, C. E. *J. Am. Chem. Soc.* **1951**, *73*, 3329.
(194) Sicher, J.; Jan, G.; Schlosser, M. *Angew. Chem.* **1971**, *83*, 1012; *Angew. Chem. Int. Ed. Engl.* **1971**, *10*, 926.
(195) Tarchini, C.; An, T. D.; Jan, G.; Schlosser, M. *Helv. Chim. Acta* **1979**, *62*, 635.
(196) Baciocchi, E.; Sebastiani, G. V. *J. Org. Chem.* **1979**, *44*, 28.
(197) Baciocchi, E.; Ruzziconi, R.; Sebastiani, G. V. *J. Org. Chem.* **1979**, *44*, 3718.
(198) Caubère, P. *Acc. Chem. Res.* **1974**, *7*, 301.
(199) Caubère, P. *Top. Curr. Chem.* **1976**, *1*, 49–124.
(200) Caubère, P.; Coudert, G. *J. Chem. Soc., Chem. Commun.* **1972**, 1289.
(201) Goering, H. L.; Epsy, H. H. *J. Am. Chem. Soc.* **1956**, *78*, 1454.
(202) Guillaumet, G.; Lemmel, V.; Coudert, C.; Caubère, P. *Tetrahedron* **1974**, *30*, 1289.
(203) Caubère, P.; Coudert, G. *Bull. Soc. Chim. Fr.* **1973**, 3067.
(204) Cristol, S. J.; Pappas, P. *J. Org. Chem.* **1963**, *28*, 2066.
(205) Fiandanese, V.; Maffeo, C. V.; Naso, F.; Ronzini, L. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1303.
(206) Redman, R. P.; Thomas, P. J.; Stirling, C. J. M. *J. Chem. Soc., Chem. Commun.* **1976**, 43.
(207) Fiandanese, V.; Maffeo, C. V.; Marchese, G.; Naso, F. *J. Chem. Soc., Chem. Commun.* **1975**, 221.
(208) Wolfe, S.; Rauk, A.; Csizmadia, I. *J. Am. Chem. Soc.* **1969**, *91*, 1567.
(209) Bordwell, F. G.; Doomes, E.; Corfield, P. W. R. *J. Am. Chem. Soc.* **1970**, *92*, 2581.
(210) Bunnett, J. F.; Retallick, L. *J. Am. Chem. Soc.* **1967**, *89*, 423.
(211) Arnett, E. M.; Small, L. E. *J. Am. Chem. Soc.* **1977**, *99*, 808.
(212) Fiandanese, V.; Marchese, G.; Naso, F.; Sclacovelli, O. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1336.
(213) Fiandanese, V.; Marchese, G.; Naso, F. *J. Chem. Soc., Chem. Commun.* **1972**, 250.
(214) Fiandanese, V.; Marchese, G.; Naso, F. *J. Chem. Soc., Perkin Trans. 2* **1973**, 1538.
(215) Hunter, D. H.; Shearing, D. J. *J. Am. Chem. Soc.* **1971**, *93*, 2348.
(216) Hunter, D. H.; Shearing, D. J. *J. Am. Chem. Soc.* **1973**, *95*, 8333.
(217) Cram, D. J.; Wingrove, A. S. *J. Am. Chem. Soc.* **1964**, *86*, 5490.