

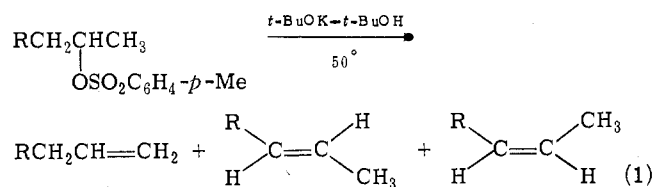
# Ionic Association in Base-Promoted $\beta$ -Elimination Reactions

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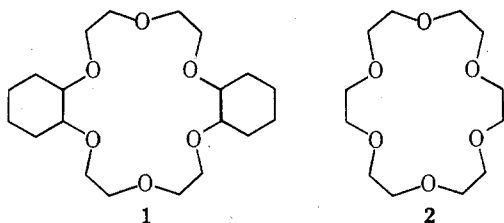
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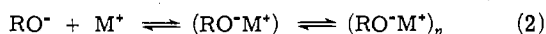
The influence of ionic association in base-promoted  $\beta$ -elimination reactions<sup>1</sup> is dramatically demonstrated by the effect of crown ether<sup>2</sup> upon geometrical orientation<sup>3</sup> in eliminations from 2-alkyl arenesulfonates promoted by potassium *tert*-butoxide (*t*-BuOK) in *tert*-butyl alcohol (*t*-BuOH) (eq 1).



Eliminations from 2-alkyl arenesulfonates induced by *t*-BuOK-*t*-BuOH produce more *cis*-2-alkene than *trans*-2-alkene.<sup>4-8</sup> This is intriguing since the more stable *trans*-2-alkene is preferentially formed in reactions of 2-alkyl halides with numerous base-solvent combinations, including *t*-BuOK-*t*-BuOH,<sup>9</sup> and of 2-alkyl arenesulfonates with base-solvent systems such as EtOK-EtOH and *t*-BuOK in dimethyl sulfoxide (Me<sub>2</sub>SO).<sup>8,10</sup> For instance, *trans*:*cis*-2-butene ratios of 0.40, 1.8, and 2.2 are reported for reactions of 2-butyl tosylate with *t*-BuOK-*t*-BuOH,<sup>8</sup> EtOK-EtOH,<sup>4</sup> and *t*-BuOK-Me<sub>2</sub>SO,<sup>8</sup> respectively, at 50°. However, when the reaction of 2-butyl tosylate with *t*-BuOK-*t*-BuOH is conducted in the presence of the crown ether<sup>2</sup> dicyclohexyl-18-crown-6 (1), the observed *trans*:*cis*-2-butene ratio increases to 1.9.<sup>8</sup>



Rationalization of these results requires careful consideration of the actual base species involved. For potassium and sodium alkoxides, significant base-counterion pairing (eq 2) exists at synthetically use-



ful base concentrations even in such polar solvents as EtOH<sup>11</sup> and Me<sub>2</sub>SO.<sup>12</sup>

Richard A. Bartsch was born in Portland, Oregon, and studied at Oregon State University for his B.A. and M.S. degrees. He obtained the Ph.D. degree from Brown University in 1967, though the year 1966-1967 was spent at UC Santa Cruz. After a year as NATO Postdoctoral Fellow with S. Hünig at the University of Würzburg, he served on the faculty of Washington State University, was Assistant Program Administrator of the Petroleum Research Fund, administered by the American Chemical Society, and was appointed Associate Professor of Chemistry at Texas Tech University in 1974. Professor Bartsch's primary research interests lie in elimination reactions forming carbon-carbon and carbon-heteroatom multiple bonds and the use of neutral cation carriers in organic synthesis and mechanistic studies.

Evidence for the predominant presence of associated base<sup>3</sup> species in solvents of low polarity is provided by physical measurements. The conductivity of 0.1 M *t*-BuONa-*t*-BuOH is only 6% greater than that of pure *t*-BuOH.<sup>14</sup> Partial molar volume studies indicate that *t*-BuOK in *t*-BuOH is monomeric only at concentrations below 10<sup>-3</sup> M.<sup>15</sup> Molecular weight measurements reveal *t*-BuOK exists as a tetramer in toluene, benzene, Et<sub>2</sub>O, tetrahydrofuran, and dimethoxyethane;<sup>16,17</sup> *t*-BuONa ranges from a tetramer in Et<sub>2</sub>O, tetrahydrofuran, and pyridine to approximately an octamer in CCl<sub>4</sub>, benzene, and cyclohexane.<sup>17</sup>

Association of potassium alkoxides is markedly diminished by addition of an appropriate crown ether which strongly complexes with the potassium cation. The conductivity<sup>18</sup> of *t*-BuOK in *t*-BuOH and benzene increases considerably upon addition of 1. Ion-pairing effects in the *t*-BuOK-catalyzed isomerization of 2-methylbicyclo[2.2.1]hepta-2,5-diene to 5-methylenebicyclo[2.2.1]hepta-2-ene in Me<sub>2</sub>SO<sup>19</sup> are completely removed in the presence of 18-crown-6, 2.

Thus in the 2-alkyl tosylate eliminations, *t*-BuOK in *t*-BuOH undoubtedly exists to a large extent as ion pairs and aggregates of ion pairs heavily solvated by *t*-BuOH.<sup>20</sup> The steric requirements of such an as-

(1) Unless specifically noted, evidence for concerted E2 mechanisms has been presented for all reactions to be discussed.

(2) Macrocyclic polyethers. For a review, see C. J. Pederson and H. K. Frensdorff, *Angew. Chem.*, 84, 16 (1972); *Angew. Chem., Int. Ed. Engl.*, 11, 16 (1972).

(3) Positional orientation refers to the relative proportions of 1- and 2-alkenes which are formed, whereas geometrical orientation compares the relative amounts of *trans*-2-alkene and *cis*-2-alkene which are produced.

(4) H. C. Brown and R. L. Klimisch, *J. Am. Chem. Soc.*, 87, 5517 (1965).

(5) D. H. Froemsdorf, W. Dowd, and K. E. Leimer, *J. Am. Chem. Soc.*, 88, 2345 (1966).

(6) I. N. Feit and W. H. Saunders, Jr., *J. Am. Chem. Soc.*, 92, 1630 (1970).

(7) R. A. Bartsch, G. M. Pruss, R. L. Buswell, and B. A. Bushaw, *Tetrahedron Lett.*, 2621 (1972).

(8) R. A. Bartsch, G. M. Pruss, D. M. Cook, R. L. Buswell, B. A. Bushaw, and K. E. Wiegiers, *J. Am. Chem. Soc.*, 95, 6745 (1973).

(9) R. A. Bartsch, C. F. Kelly, and G. M. Pruss, *J. Org. Chem.*, 36, 662 (1971).

(10) D. H. Froemsdorf and M. D. Robbins, *J. Am. Chem. Soc.*, 89, 1737 (1967).

(11) A. Brandstrom, *Ark. Kemi*, 11, 567 (1957).

(12) J. H. Exner and E. C. Steiner, *J. Am. Chem. Soc.*, 96, 1782 (1974).

(13) In the absence of specific evidence regarding the actual base species present, contact ion pairs and aggregates of contact ion pairs shall be referred to as the associated species and free ions and separated ions as the dissociated base.

(14) W. H. Saunders, Jr., D. G. Bushman, and A. F. Cockerill, *J. Am. Chem. Soc.*, 90, 1775 (1968).

(15) C. L. Liotta, personal communication.

(16) V. A. Bessonov, P. R. Alikhanov, E. N. Gur'yanova, A. P. Simonov, I. O. Shapiro, E. A. Yakovleva, and A. L. Shalenshtein, *J. Gen. Chem. USSR*, 37, 96 (1967).

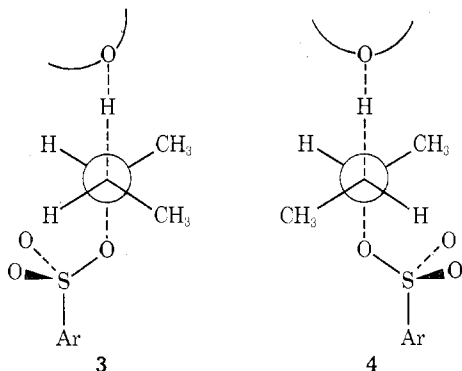
(17) V. Halaska, L. Lockman, and D. Lim, *Collect. Czech. Chem. Commun.*, 33, 3245 (1968).

(18) M. Svoboda, J. Hapala, and J. Závada, *Tetrahedron Lett.*, 265 (1972).

(19) M. J. Maskornik, *Tetrahedron Lett.*, 1797 (1972).

sociated<sup>13</sup> base should be very large indeed. In contrast, the presence of the crown ether, 1, which drives the equilibrium in eq 2 to the left, should produce the much smaller dissociated<sup>13</sup> *tert*-butoxide ions as the active base.

The effect of base association upon geometrical orientation in 2-butyl tosylate eliminations may be interpreted by considering the large steric demands of the associated base in the transition states 3 and 4 to form internal olefins.<sup>21a</sup> Preferential formation of *cis*-2-butene is readily explained since both the bulky base and asymmetrical tosylate leaving group may be arranged so as to relieve steric interactions with the  $\alpha$ - and  $\beta$ -alkyl groups in 3, but not in 4.



That both dissociated and associated base species may be kinetically important reactants in base-promoted reactions has been realized for some time.<sup>11,22,23</sup> However, recognition of the special steric and complexing properties of the associated species in base-induced  $\beta$  eliminations is a new development. Both orientation and stereochemistry are affected.

Because of dissimilar interactions of associated bases with substrates which bear leaving groups of different charge types, eliminations involving initially neutral and positively charged leaving groups are discussed separately in this Account.

### Neutral Leaving Groups

**Orientation in Anti Eliminations from 2-Haloalkanes.** The effects of base association upon positional and geometrical orientation<sup>3</sup> have been further probed in our laboratories through investigations of anti eliminations<sup>24</sup> from 2-alkyl halides.<sup>7,8</sup> For eliminations from 2-bromobutane induced by *t*-BuOK-*t*-BuOH, positional and geometrical orientation are dependent upon base concentration, as illustrated in Table I (entries 1-4). Similar sensitivity of orientation to base concentration is not observed for reactions with MeOK-MeOH, EtOK-EtOH, or *t*-BuOK-Me<sub>2</sub>SO.

It is proposed<sup>8</sup> that both dissociated and associated<sup>25</sup> base species are important in the *t*-BuOK-*t*-BuOH base-solvent system. Although anticipated to be present in only small concentration, dissociated

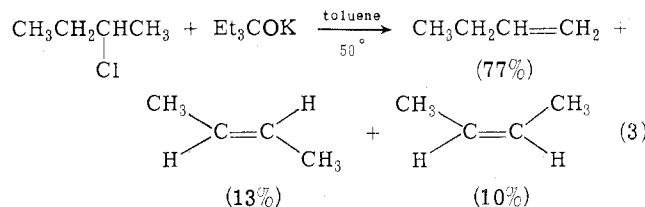
**Table I**  
Olefinic Products from Reactions of 2-Bromobutane with Various Base-Solvent Systems at 50°

Entry	Base-solvent	[Base], M	% 1- <i>cis</i> -2- butene	<i>trans</i> -: <i>cis</i> -2- butene
1	<i>t</i> -BuOK- <i>t</i> -BuOH	0.10	37.7	1.86
2	<i>t</i> -BuOK- <i>t</i> -BuOH	0.25	41.6	1.78
3	<i>t</i> -BuOK- <i>t</i> -BuOH	0.50	44.1	1.66
4	<i>t</i> -BuOK- <i>t</i> -BuOH	1.00	50.6	1.47
5	MeOK-MeOH	0.50	15.4	3.34
6	EtOK-EtOH	0.50	17.9	3.21
7	<i>t</i> -BuOK-Me <sub>2</sub> SO	0.50	30.6	3.16
8	<i>t</i> -BuOK- <i>t</i> -BuOH <sup>a</sup>	0.50	32.5	2.92
9	<i>t</i> -BuON- <i>n</i> -Pr <sub>4</sub> - <i>t</i> -BuOH	0.25	31.3	2.99

<sup>a</sup> Dicyclohexyl-18-crown-6 present.

*tert*-butoxide ions compete effectively because of the much greater basicity of *tert*-butoxide ion than of associated *t*-BuOK in *t*-BuOH.<sup>26,27</sup> The greater percentage of 1-butene and the reduced *trans*:*cis*-2-butene ratios observed at higher base concentrations are postulated to arise from a greater proportion of elimination being promoted by associated *t*-BuOK. Inasmuch as the equilibrium represented in eq 2 should be strongly shifted to the left by complexing of potassium ions with an appropriate crown ether or by changing to a tetraalkylammonium counterion,<sup>26</sup> entries 8 and 9 in Table I especially support this hypothesis. Virtual identity of orientation for reactions of 2-bromobutane with *t*-BuOK-1-*t*-BuOH, *t*-BuON-*n*-Pr<sub>4</sub>-*t*-BuOH, and *t*-BuOK-Me<sub>2</sub>SO indicates that dissociated *tert*-butoxide is the reactive base in all three base-solvent systems.

Recognition of base association effects provides the key to understanding a dichotomy of orientation for base-induced dehydrohalogenation of 2-haloalkanes in alcoholic and in dipolar aprotic solvents.<sup>9</sup> Reactions of 2-haloalkanes with several bases in dipolar aprotic solvents produce high (3.4-4.0) *trans*:*cis*-2-butene ratios, which are independent of the percent of 1-butene.<sup>9,28</sup> However, an inverse relationship between percent of 1-butene and *trans*:*cis*-2-butene ratios obtains for reaction of 2-butyl halides with ROK-ROH,<sup>8</sup> as recorded in Table II. In contrast, eliminations promoted by ROK-ROH in the presence of crown ether 1 provide orientation quite similar to that observed in dipolar aprotic solvents (Table II). Therefore, the high relative proportions of terminal olefin and low *trans*:*cis*-2-alkene ratios from reactions of 2-haloalkanes with alkali metal alkoxides in alcoholic solvents of low polarity and in



(20) D. J. Cram, C. A. Kingsbury, and B. Richborn, *J. Am. Chem. Soc.*, **83**, 3688 (1961).

(21) For an earlier version of this explanation in which the large steric demands of associated bases were not recognized see: (a) ref 4; (b) H. C. Brown and R. L. Klimisch, *J. Am. Chem. Soc.*, **88**, 1425 (1966).

(22) R. P. Bell and J. E. Prue, *J. Chem. Soc.*, 362 (1949).

(23) D. J. McLennan, *J. Chem. Soc., Perkin Trans. 2*, 1577 (1972).

(24) R. A. Bartsch, *J. Am. Chem. Soc.*, **93**, 3683 (1971).

(25) Kinetic evidence for a trimeric or tetrameric base species in dehydrohalogenations of *meso*-3,4-dibromo-2,5-dimethylhexane and *meso*- and *dl*-4,5-dichlorooctane with *t*-BuOK-toluene has been presented: M. Schlosser, G. Jan, E. Byrne, and J. Sicher, *Helv. Chim. Acta*, **56**, 1630 (1973).

(26) D. Bethel and A. F. Cockerill, *J. Chem. Soc. B*, 913 (1966).

(27) J. N. Roitman and D. J. Cram, *J. Am. Chem. Soc.*, **93**, 2231 (1971).

(28) R. A. Bartsch, *J. Org. Chem.*, **35**, 1023 (1970).

**Table II**  
Olefinic Products from Reactions of 2-Bromobutane with 0.25 M ROK in ROH at 50° in the Presence and Absence of 0.25 M Dicyclohexyl-18-crown-6

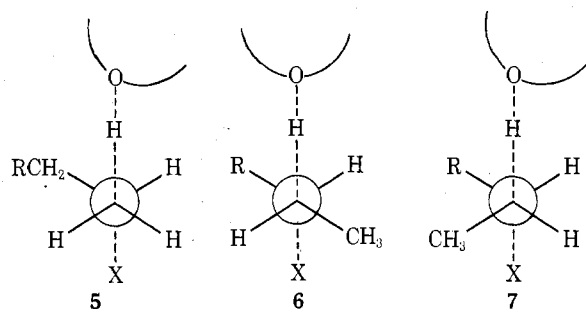
ROH of ROK-ROH	Crown ether absent		Crown ether present	
	<i>trans</i> -:		<i>trans</i> -:	
	% 1-butene	% <i>cis</i> -2-butene	% 1-butene	% <i>cis</i> -2-butene
Methanol	15.4	3.34	16.3	3.43
Ethanol	17.9	3.23	17.6	3.31
2-Propanol	23.7	2.72	23.8	2.95
2-Methyl-2-propanol	41.6	1.78	31.2	3.20
3-Ethyl-3-pentanol	63.1	1.04	37.3	2.82

**Table III**  
Primary Deuterium Isotope Effect and Hammett  $\rho$  Values for Syn Elimination in Reactions of *trans*-2-Arylcyclopentyl Tosylates with ROK-ROH-1

Base-solvent	$k_H/k_D$	$\rho$
<i>n</i> -BuOK- <i>n</i> -BuOH	1.2	+0.3
<i>t</i> -BuOK- <i>t</i> -BuOH	5.1	+3.1

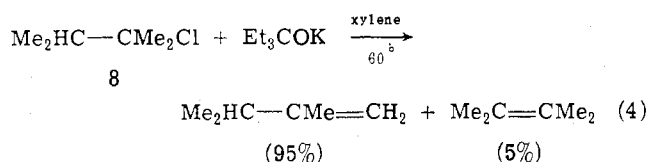
hydrocarbons<sup>9,29</sup> (eq 3) are attributable to base association.

As with 2-alkyl tosylates, effects of base association upon orientation in eliminations from 2-alkyl halides are attributable to the steric destabilization introduced by large alkali metal-alkoxide ion pair aggregates in transition states 5-7 for formation of the isomeric olefinic products.<sup>21b</sup> Steric interactions of a bulky associated base with  $\alpha$ - and  $\beta$ -alkyl groups should increase in the order 5 < 7 < 6. Transition

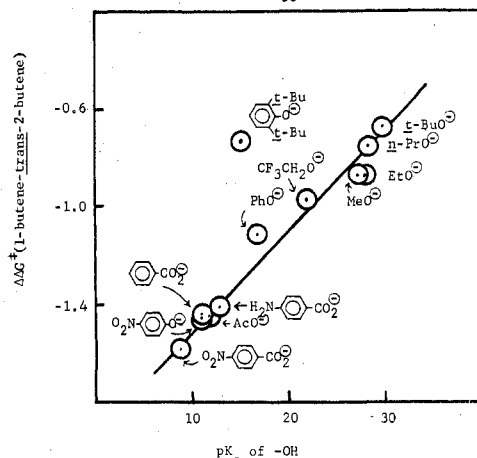
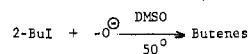


state 7 is less affected than 6 because the large base can be tilted to that side of the developing double bond where only base-hydrogen interactions occur. Change from a dissociated base to a bulky associated one should increase the proportion of 1-alkene and decrease the *trans*:-*cis*-2-alkene ratio, as observed.

Large steric requirements of an associated base also explain the almost exclusive removal of a more accessible methyl hydrogen in reactions of 8 with Et<sub>3</sub>COK in xylene.<sup>30</sup>



(29) D. L. Griffith, D. L. Meges, and H. C. Brown, *Chem. Commun.*, 90 (1968).



**Figure 1.** Plot of the free-energy difference in kcal/mol for formation of 1-butene and *trans*-2-butene vs. the  $pK_a$  of the conjugate acid of the base.

Realization of the effects of base association allowed resolution of an old controversy concerning the relative importance of base strength and base size in determining orientation. A wide variety of anionic oxygen, nitrogen, and carbon bases in Me<sub>2</sub>SO (a solvent which should suppress complicating base association) promote dehydrohalogenation of 2-iodobutane.<sup>31,32</sup> Linear relationships between free energy differences for formation of 1-butene and *trans*-2-butene (or *cis*-2-butene) and the  $pK_a$  of conjugate acids of the bases in Me<sub>2</sub>SO are obtained for nearly all bases (Figure 1). These linear correlations demonstrate a fundamental control of positional orientation by base strength, not size, for *dissociated* bases.

Certain oversized bases, such as 2,6-di-*tert*-butylphenoxide and anions from diphenylamine and diphenylmethane, deviate from the relationships in the direction anticipated for the onset of base steric interactions. Examination of models reveals that steric effects of dissociated anionic bases become important when impingement of the residual base portion upon a plane passed through the basic atom cannot be avoided. Therefore, steric effects of the base are demonstrated to be important only for *associated* bases and highly ramified *dissociated* bases. These findings suggest the synthesis of new sterically hindered dissociated bases which combine the orientation control of an associated base with the higher reactivity of a dissociated one.

Interpreting the effects of base association upon eliminations from secondary alkyl halides and arenesulfonates other than 2-alkyl derivatives becomes more complicated because of the onset of syn elimination pathways (*vide infra*).

**Competitive Syn and Anti Eliminations from Cyclopentyl, Cyclohexyl, and Norbornyl Systems.** Sicher, Závada, and coworkers<sup>33</sup> proposed that syn elimination is facilitated by base association which

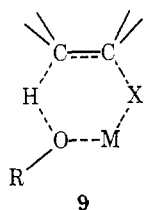
(30) S. P. Acharyan and H. C. Brown, *Chem. Commun.*, 305 (1968).

(31) R. A. Bartsch, G. M. Pruss, B. A. Bushaw, and K. E. Weigers, *J. Am. Chem. Soc.*, 95, 3405 (1973).

(32) R. A. Bartsch, K. E. Weigers, and D. M. Guritz, *J. Am. Chem. Soc.*, 96, 430 (1974).

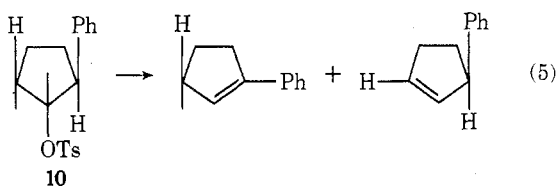
(33) J. Sicher, *Angew. Chem.*, 84, 177 (1972); *Angew. Chem., Int. Ed. Engl.*, 11, 200 (1972), and references cited therein.

allows simultaneous coordination of the metal counterion with the base and leaving group, as depicted in 9, where X is the leaving group, RO is the base, and

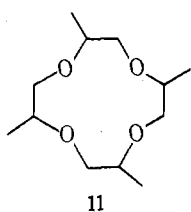


M is the alkali metal counterion. A similar cyclic pathway is obviously impossible for a coplanar anti elimination, and a noncoplanar anti elimination is inconsistent with observed isotope effects.<sup>34</sup>

Reactions of *trans*-2-phenylcyclopentyl tosylate (10) with *t*-BuOK-*t*-BuOH demonstrate the importance of interactions represented in 9.<sup>36</sup> In this elimination, 1-phenylcyclopentene is produced by activated syn elimination and 3-phenylcyclopentene by



unactivated anti elimination. Reaction of 10 with 0.10 M *t*-BuOK-*t*-BuOH, yields 89% of syn-elimination product. The presence of equimolar crown ether 1, which should disrupt simultaneous coordination of potassium ions with the base and leaving group, sharply reduces the relative proportion of 1-phenylcyclopentene to 30%. That this effect results specifically from potassium ion complexing is corroborated by the observation that the presence of equimolar tetramethyl-12-crown-4, 11, for which the crown ether



cavity is too small to accommodate potassium ions,<sup>2</sup> yields a percentage of 1-phenylcyclopentene nearly identical with that formed in the absence of crown ether 1.<sup>36</sup>

Transition-state differences for syn eliminations promoted by associated and dissociated *tert*-butoxide ion bases are revealed from reactions of *trans*-2-arylcyclopentyl tosylates with *t*-BuOK-*t*-BuOH in the absence and presence of crown ether 1.<sup>36</sup> With *t*-BuOK,  $k_H/k_D$  (primary) = 5.3 and  $\rho = +2.2$ ; but with *t*-BuOK-*t*-BuOH-1, values of 5.1 and +3.1, respectively, are calculated.

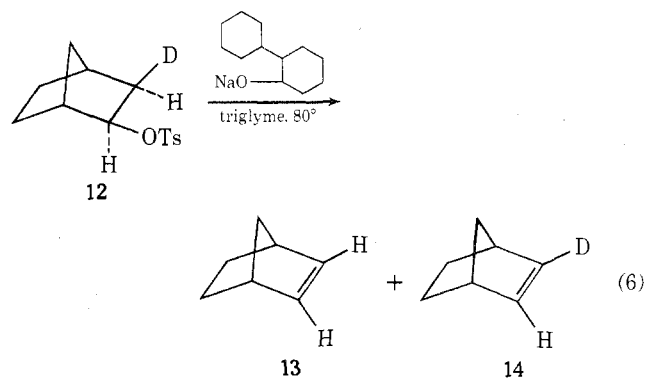
Change from an associated to a dissociated base should result in a stronger base and a poorer leaving group. To judge from anti eliminations of  $\beta$ -phenylethyl compounds, stronger bases<sup>37</sup> and poorer leav-

ing groups<sup>38</sup> lead to transition states with greater carbanionic character.<sup>39</sup> Since the  $k_H/k_D$  values suggest quite similar relative transition-state force constants for the O...H and H...C $_{\beta}$  bonds in eliminations induced by the associated and dissociated bases, the more carbanionic transition states observed for the latter apparently result from a dominant leaving group effect.<sup>40</sup>

Calculated primary deuterium isotope effects and  $\rho$  values for syn eliminations from *trans*-2-arylcyclopentyl tosylates induced by two dissociated base-solvent combinations<sup>36</sup> are presented in Table III. A marked influence of the base-solvent system upon syn-elimination transition-state character is evident.

The changes in  $k_H/k_D$  and  $\rho$  may be explained within the framework of the variable E2 transition-state theory.<sup>38,39</sup> According to this theory, wide variations in relative amounts of C $_{\beta}$ -H and C $_{\alpha}$ -leaving group bond rupture and C-C double bond formation may exist in concerted, bimolecular  $\beta$ -elimination transition states. Changing from *t*-BuO<sup>-</sup>-*t*-BuOH to *n*-BuO<sup>-</sup>-*n*-BuOH provides a weaker base but a better solvent for a leaving group which bears partial negative charge in the transition state. Both factors produce transition states with less C $_{\beta}$ -H bond scission, more C $_{\alpha}$ -leaving group bond cleavage, and less carbanion character,<sup>39,42</sup> as indicated by the sharply decreased  $k_H/k_D$  and  $\rho$  values.

Base association also affects the stereochemistry of elimination from norbornyl compounds.<sup>43</sup> Brown and Liu<sup>44</sup> report that reaction of *exo*-2-norbornyl-*exo*-3-*d* tosylate (12) with the sodium salt of 2-cyclohexylcyclohexanol in triglyme produces norbornene (13) but no 2-deuterionorbornene (14). The exclusive syn-*exo*



elimination is consistent with previous investigations in which a favoring of syn-*exo* over anti-*endo*-H elimination by a factor of 100 or greater was noted.<sup>45</sup>

We reasoned that an associated base species might be enhancing the syn-*exo* pathway. Both stabilization of the syn-elimination transition state by base association, 9, and the large steric requirements of an associated base directing removal of the less hin-

(38) W. H. Saunders, Jr., and A. F. Cockerill, "Mechanisms of Elimination Reactions", Wiley-Interscience, New York, N.Y., 1973, Chapter 2.

(39) J. F. Bunnett, *Angew. Chem.*, 74, 731 (1962); *Angew. Chem., Int. Ed. Engl.*, 1, 225 (1962); J. F. Bunnett, *Surv. Prog. Chem.*, 5, 53 (1969).

(40) This conclusion is made somewhat less certain by the double-valued nature of the primary deuterium isotope effect.<sup>41</sup>

(41) F. H. Westheimer, *Chem. Rev.*, 61, 265 (1961).

(42) For an opposing view, see E. R. Thornton, *J. Am. Chem. Soc.*, 89, 2915 (1967).

(43) R. A. Bartsch and R. H. Kayser, *J. Am. Chem. Soc.*, 96, 4346 (1974).

(44) H. C. Brown and K.-J. Liu, *J. Am. Chem. Soc.*, 92, 200 (1970).

(45) N. A. LeBel, *Adv. Alicycl. Chem.*, 3, 279-288 (1971).

(34) W. H. Saunders, Jr., *J. Chem. Soc., Chem. Commun.*, 850 (1973).

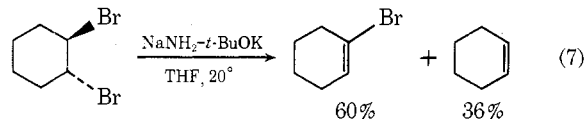
(35) R. A. Bartsch and K. E. Wieggers, *Tetrahedron Lett.*, 3819 (1972).

(36) R. A. Bartsch, E. A. Mintz, and R. M. Parlman, *J. Am. Chem. Soc.*, 96, 4249 (1974).

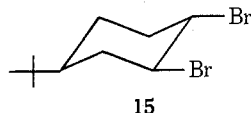
(37) S. Alunni and E. Baciocchi, *Tetrahedron Lett.*, 4665 (1973).

dered exo  $\beta$  hydrogen should favor syn-exo elimination. Repeating Brown and Liu's experiment, but now in the presence of **2**, forms norbornenes which contain 72% of **13** and 28% of **14**. After correction for a primary deuterium isotope effect in the formation of **13**, relative rates of syn-exo and anti-endo-H elimination of  $\sim 15:1$  are calculated,<sup>43</sup> in contrast to a ratio of  $>100:1$  for the associated base.<sup>44</sup>

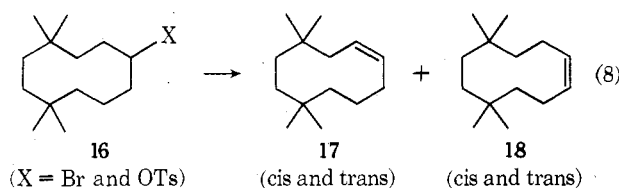
Special favoring of syn elimination by sodamide-containing complex bases is used to advantage in synthesis by Caubère and coworkers.<sup>46-48</sup> Thus, *trans*-1,2-dibromocyclohexane reacts with  $\text{NaNH}_2$ -*t*-BuOK in tetrahydrofuran (THF) to produce 1-bromocyclohexene, a product of syn elimination, and cyclohexene (eq 7). Under similar conditions, nei-



ther  $\text{NaNH}_2$  nor *t*-BuOK in THF is effective.<sup>46</sup> The same reaction converts conformationally locked **15** almost quantitatively into 1- and 2-bromo-4-*tert*-butylcyclohexenes.<sup>47,48</sup>



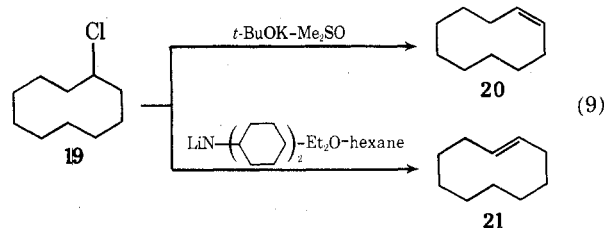
**Competitive Syn and Anti Eliminations in Conformationally Mobile Systems.** Závada and coworkers<sup>18,49</sup> investigated base-associated effects in eliminations from the cyclodecyl bromide and tosylate **16**. Early studies demonstrated formation of *trans* olefins **17** and **18** principally by syn elimination and production of *cis* olefins **17** and **18** almost exclusively by anti elimination (i.e., the syn-anti dichotomy).<sup>50</sup>



Relative proportions of *cis*- and *trans*-**17** and **18** formed in reactions of **16** (X = OTs) with *t*-BuOK-DMF (DMF, dimethylformamide) are dependent upon the base concentration, suggesting that both dissociated *tert*-butoxide and associated *t*-BuOK are effective even in the polar solvent DMF. In agreement, addition of crown ether **1** to reactions of **16** (X = Br and OTs) with *t*-BuOK-DMF produces reduced *trans*-:*cis*-olefin ratios. Also consistent with this hypothesis is the decrease in *trans*-:*cis*-cyclodecene ratio previously noted for a base change from *t*-BuOLi to *t*-BuOK for eliminations from cyclodecyl bromide in DMF.<sup>51</sup> These findings indicate that the

dissociated base yields predominately *cis* olefin by anti elimination, while the associated base furnishes nearly exclusively *trans* olefin by syn elimination through transition states similar to **9**. This duality of participating base is felt to be a dominant factor in the syn-anti dichotomy.<sup>18,49</sup>

Seemingly consistent with this proposal is the striking orientation control reported by Traynham and coworkers<sup>52</sup> in eliminations from chlorocyclodecane, **19** (eq 9). Reaction of **19** with *t*-BuOK pro-



duces 97% *cis*-cyclodecene (**20**); but lithium dicyclohexylamide yields 96% *trans*-cyclodecene (**21**). That the dissociated *tert*-butoxide ion base favors anti elimination and formation of **20**, but the associated lithium dicyclohexylamide promotes syn elimination and production of **21**, seems reasonable. However, further studies<sup>53</sup> reveal that the overwhelming predominance of the thermodynamically more stable **20** obtained with *t*-BuOK- $\text{Me}_2\text{SO}$  is caused by isomerization of initially formed mixtures of **20** and **21**. Evidence for a significant, but not overpowering, effect of base association in elimination from **19** is provided by the increase in proportion of **20** from 13% found with lithium dicyclohexylamide in  $\text{Et}_2\text{O}$ -hexane to 32% in the presence of **11**, a crown ether for lithium cations.<sup>53</sup>

Research groups of Závada and Sicher<sup>54,55</sup> and of Saunders<sup>56</sup> investigated the effects of base association upon elimination stereochemistry for acyclic halides and tosylates, other than 2-substituted alkanes. For these compounds, significant formation of *trans*-alkenes by syn elimination occurs, particularly with poor leaving groups<sup>57</sup> in solvents of low polarity.<sup>54,56</sup> However, *cis*-alkenes remain almost exclusively ( $>90\%$ ) the products of anti elimination.

Percentages of syn elimination for formation of *trans*-3-hexene in reactions of 3-hexyl-4-*d* tosylate with phenoxide ion bases in 95%  $\text{Me}_2\text{SO}$ -5% *t*-BuOH<sup>56</sup> are presented in Table IV. Although the tendency of this tosylate to undergo syn elimination is low, appreciable variations are observed. That the greater proportion of syn elimination prevails with PhOLi, the most tightly ion-paired base, shows that base association facilitates syn elimination. Interaction of  $\text{Me}_4\text{NI}$  with PhOLi, which should sharply decrease base association, completely suppresses syn elimination. Greater tendency of PhOK than *p*-NO<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>OK to exist in the associated form<sup>58</sup> is probably

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(51) J. Závada, J. Krupická, and J. Sicher, *Collect. Czech. Chem. Commun.*, **33**, 1393 (1968).

**Table IV**  
Stereochemistry of *trans*-3-Hexene Formation in Eliminations from 3-Hexyl-4-*d* Tosylate

Base	% syn elimination
PhOLi	16
PhOLi + NMe <sub>4</sub> I	0
PhOK	9
<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> OK	3

**Table V**  
Stereochemistry of *trans*-5-Decene Formation in Eliminations from 5-Decyl-6-*d* Tosylate

Conditions	% syn elimination
<i>t</i> -BuOK-benzene	27
<i>t</i> -BuOK-benzene-1	6
<i>t</i> -BuOK- <i>t</i> -BuOH	15
<i>t</i> -BuOK- <i>t</i> -BuOH-1	7
<i>t</i> -BuOK-DMF	4
<i>t</i> -BuOK-DMF-1	4

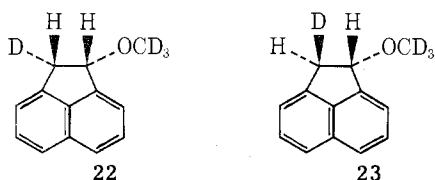
**Table VI**  
Effect of Cation on Relative Elimination Rates from 22 and 23

Conditions	$k_{syn}/k_{anti}$
<i>t</i> -BuOLi- <i>t</i> -BuOH, 152°	≥13
<i>t</i> -BuOK- <i>t</i> -BuOH, 86°	≥7
<i>t</i> -BuOCs- <i>t</i> -BuOH, 86°	≥5
<i>t</i> -BuONMe <sub>4</sub> - <i>t</i> -BuOH, 45°	0.3
<i>t</i> -BuOK-1- <i>t</i> -BuOH, 45°	0.3

responsible for the greater proportion of syn elimination with the former base.

Effects of adding crown ether 1 in reactions of 5-decyl-6-*d* tosylate with *t*-BuOK in benzene, *t*-BuOH, and DMF<sup>55</sup> are recorded in Table V. The presence of 1, which should favor dissociated bases, reduces the proportion of *trans*-5-decene resulting from syn elimination in benzene and *t*-BuOH. In DMF, there is no discernible effect of 1. These results further substantiate the favoring of *trans*-olefin formation by associated base species through transition states such as 9.

**Stereochemistry of an E1cB Reaction.** Variation of the base counterion produces marked changes in elimination stereochemistry for reactions of *cis*- and *trans*-1-methoxy-*d*<sub>3</sub>-2-*d*-acenaphthenes, 22 and 23,



respectively, with alkali metal and trimethylammonium *tert*-butoxides in *t*-BuOH (Table VI).<sup>59</sup> Propensity for syn elimination decreases as the cation is varied, Li > K > Cs > NMe<sub>4</sub> = K-1. Base association is also anticipated to decrease in this order. Evidence for an E1cB mechanism includes detectable hydrogen-deuterium exchange, and  $k_H/k_D = 1.6$ –1.8.

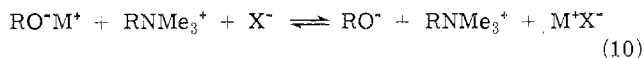
(58) H. E. Zaugg and A. D. Schaefer, *J. Am. Chem. Soc.*, **87**, 1857 (1965).

(59) D. H. Hunter and D. J. Shearing, *J. Am. Chem. Soc.*, **93**, 2348 (1971).

The preference for syn elimination with associated bases suggests strong coordination between the base metal ion and the substrate ether oxygen in the carbanion intermediate.

### Positively Charged Leaving Groups

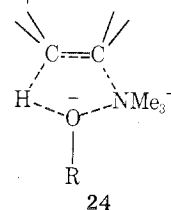
The possibility of an ion-pair exchange equilibrium, as illustrated in eq 10, makes ionic association



effects more complicated for substrates with charged leaving groups. Evidence for the occurrence of this equilibrium is provided by the unusual kinetic behavior observed in reactions of 2-phenylethyltrimethylammonium bromide with *t*-BuONa-*t*-BuOH and *t*-BuOK-*t*-BuOH.<sup>14</sup> With respect to the quaternary ammonium salt, the kinetic order is 1.5 rather than 1.0. If dissociated alkoxide were the only effective base (equilibrium in eq 10 far to the right), a second-order dependence upon quaternary ammonium salt concentration would be anticipated (1.0 in its role as substrate and 1.0 in its role in determining base concentration).<sup>60</sup> A kinetic order of 1.5 therefore implicates both dissociated and associated base species.

**Orientation in Anti Elimination.** In order to assess the influence of base association upon orientation for eliminations of charged "onium" leaving groups, we investigated anti eliminations<sup>61</sup> from 2-butyltrimethylammonium tosylate promoted by *t*-BuOK-*t*-BuOH.<sup>62</sup> In sharp contrast to results observed for 2-butyl bromide and tosylate (*vide supra*), olefin orientation is insensitive to changes in base concentration and to the presence of crown ether 1. Apparently for eliminations from 2-butyltrimethylammonium ions, the effective base is dissociated *tert*-butoxide formed via eq 10. Therefore, base association is unimportant in determining orientation for anti eliminations from "onium" compounds.

**Competitive Syn and Anti Eliminations.** Závada and Sicher<sup>63,64</sup> predicted that a dissociated base should be more effective than an associated one in promoting syn eliminations from "onium" salts. Electrostatic interaction of the anionic base with the positively charged leaving group places the base in a favorable position for attack upon a syn  $\beta$  hydrogen, as in 24. Thus, syn elimination should be favored by



dissociated bases for substrates with positively charged leaving groups, but by associated base species for neutral leaving groups.

(60) J. K. Borchardt and W. H. Saunders, Jr., *J. Am. Chem. Soc.*, **96**, 3912 (1974).

(61) D. S. Bailey, F. C. Montgomery, G. W. Chodak, and W. H. Saunders, Jr., *J. Am. Chem. Soc.*, **92**, 6911 (1970).

(62) R. A. Bartsch, *J. Org. Chem.*, **38**, 846 (1973).

(63) J. Závada and J. Sicher, *Collect. Czech. Chem. Commun.*, **32**, 3701 (1967).

(64) J. Sicher and J. Závada, *Collect. Czech. Chem. Commun.*, **33**, 1278 (1968).

Borchardt and Saunders<sup>60</sup> examined the influence of ion association upon the syn-anti dichotomy (*vide supra*) for eliminations from quaternary ammonium salts. In order to provide substantial, but not exclusive, formation of trans olefin by syn elimination<sup>65</sup> and the possibility for base strength variation, reactions of 3-hexyl-4-*d*-trimethylammonium iodide with alkali metal phenoxides in *t*-BuOH-Me<sub>2</sub>SO mixtures were studied (Table VII).

That the proportion of *trans*-3-hexene resulting from syn elimination decreases as the phenoxide cation is varied (Li ~ NMe<sub>4</sub> > Na > K (Table VII, entries 1-4)) may be understood by considering eq 10 and structure 24. For PhONMe<sub>4</sub>, the equilibrium in eq 10 is shifted to the right and the high concentration of dissociated base favors syn elimination. If this interpretation is correct, entries 1-3 indicate increases in the dissociated base concentration in the order Li > Na > K for alkali metal phenoxides. This ordering may be rationalized if the stability of M<sup>+</sup>X<sup>-</sup> is assumed to control the equilibrium position in eq 10. An alternative explanation involves decreased reactivity of the associated base in the order PhOK > PhONa > PhOLi so that the proportion of reaction with dissociated phenoxide decreases in the same order.

Data for substituted potassium phenoxides (entries 5-7) are interpreted in similar fashion. The equilibrium in eq 10 would be farther to the right for the more weakly associated bases, such as *p*-nitrophenoxide, enhancing syn elimination.

These results are all compatible with a mechanism

(65) Reactions of 3-hexyl-4-*d*-trimethylammonium iodide with PhOK in *t*-BuOH and *t*-BuOH-Me<sub>2</sub>SO form *cis*-3-hexene by 94-98% anti elimination. However, *trans*-3-hexene originates via both syn and anti elimination processes.<sup>60</sup>

Table VII  
Percent *trans*-3-Hexene Formed by Syn Elimination  
from 3-Hexyl-4-*d*-trimethylammonium Iodide

Entry	Base	Solvent	% syn elimination
1	PhOLi	<i>a</i>	74
2	PhONa	<i>a</i>	55
3	PhOK	<i>a</i>	34
4	PhONMe <sub>4</sub>	<i>a</i>	67
5	PhOK	<i>b</i>	38
6	<i>o</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> OK	<i>b</i>	59
7	<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> OK	<i>b</i>	69

<sup>a</sup> 80% *t*-BuOH-20% Me<sub>2</sub>SO. <sup>b</sup> 5% *t*-BuOH-95% Me<sub>2</sub>SO.

in which associated phenoxide favors anti elimination, but dissociated phenoxide facilitates syn elimination, in agreement with the predictions of Závada and Sicher.<sup>62,63</sup>

### Summary

The investigations described above amply illustrate an important influence of ionic association upon orientation and stereochemistry in base-promoted  $\beta$  elimination. Dependence of these effects upon the charge type of the leaving group is underscored. Recognition of these factors will provide new mechanistic insight into base-induced  $\beta$ -elimination reactions and may lead to improved reagents for alkene synthesis.

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## Too Many Rearrangements of Cyclohexadienones

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Molecular rearrangements have long entranced the romantic spirits among organic chemists. While their colleagues plodded away, measuring minute rate differences and defining the structures of transition states for common reactions ever more precisely, students of molecular rearrangements raced ahead, hap-

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pily anticipating that molecules would turn themselves inside out, rings would shrink or expand, chains would entwine and rearrange, all apparently at the whim of an imaginative and unfettered nature.

This undisciplined license was abhorrent to chemical puritans, who determined to restrict organic molecules to a small set of allowed reactions, and to forbid all others. The puritans have largely prevailed. Their rules, "thou shalt not undergo suprafacial [1,3] shifts; thou shalt not undergo antarafacial [3,3] shifts . . .",<sup>1</sup> are now among the familiar bedrocks of the theory of organic chemistry.

(1) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry", Academic Press, New York, N.Y., 1971; see also, M. J. S. Dewar, *Angew. Chem., Int. Ed. Engl.*, 10, 761 (1971).