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Amine Base Promoted β-Elimination in α-Bromo Ester Substrates. Evidence for Permutational Isomerism in the TBP Carbon Intermediate

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Amine bases show reaction rates and activation parameters that suggest close similarity to the E2C mechanism previously identified for the Br^--promoted reaction with α-bromo ester. Proton Sponge (PS), an amine base, which cannot participate in an S_N2 process, nonetheless, is an effective promoter of the E2C. This is confirmed by applying the temperature-dependent isotope effect (TDKIE) criteria of transition-state geometry[10] to PS and other amine reactions with α-bromo esters with the general result that $[\Delta E_a]_D{}^H$ is found to be temperature independent and $A_H/A_D \gg 1.2$. The α-secondary deuterium isotope effect, $(k_H/k_D)_\alpha = 1.27$, is the largest value ever found (thus far) for either S_N2-like or β-elimination processes. On these and other grounds it is concluded that the E2C mechanism is *not* S_N2 like but is regarded as a precedented nucleophilic trigger mechanism.[6] The virtual identity of intra- and intermolecular isotope effects among amine base promoters cannot be explained by the formation of a symmetrical trigonal-bipyramid (TBP) intermediate, as was the case for the Br^--promoted reaction with α-bromo ester substrates. But the obviously equal availability of abstractable H and D in the transition states of the intramolecular competition isotope effect is possibly to be explained by invoking permutational isomerism in the precursor trigonal-bipyramid (TBP) intermediate. The reasoning which seems to justify this proposal is considered in detail.

One of the more distinctive factors controlling the incidence of the E2C mechanism is the relationship between the basicity and nucleophilicity of the promoter reagent. When the reagent is a strong carbon nucleophile such as thiourea of triphenylphosphine, which have only dimly basic properties, it apparently cannot function to promote the E2C.[1] On the other hand, the question of how little nucleophilic activity on the part of a sufficiently strong base which can still serve to effect the E2C process has not as yet been investigated.[2]

It is known from the work of Bunnett[3] that halide ions in aprotic solvents are sufficiently basic and, at the same time, sufficiently nucleophilic to bring about the E2C elimination in cases that are highly hindered to S_N2 substitution at C_α. However, it has also been contended that the approach of the promoter reagent is rigidly confined to a nucleophilic pathway directed at C_α. Furthermore, Winstein and co-workers have convincingly demonstrated cases of this "cleanest reaction known to man",[4] in which the weak base promoted elimination cannot be made to occur when the trans, antiperiplanar requirement cannot be fulfilled.[5]

This type of reaction has been called a nucleophilic trigger mechanism[6,7] because only a small fraction of the nucleophilic "power" of the promoter is utilized; i.e., only a small degree of covalent bonding is realized in bringing about the electron displacements necessary to reach to nearby transition state (TS). One of the principal purposes of the present study is to probe the threshold of nucleophilic activity required for triggering the E2C mechanism.

In this undertaking, a promoter was utilized which is incapable of forming a covalency to carbon but may still be regarded as a base, namely, 1,8-bis(dimethylamino)naphthalene, so-called Proton Sponge (PS) (Aldrich). The substrates chosen for this study, ethyl 2-bromo-3-phenylpropionate (**1**) and methyl 2-bromo-2-methyl-3-phenylpropionate (**2**), have been shown to have loose transition states in their E2C reactions with bromide ion as promoter base.[8] The angle of H-transfer tends to be small and therefore, the degree of ionization (extension) of the C_β–$H^{\delta+}$ bond is greater in this type of TS due to the acidifying influence of the –COOEt group conjugating with the incipient double bond. With these substrates, the PS reagent, which is incapable of establishing the required degree of covalent bonding in an S_N2 TS, still manages to

Table I. Rates as a Function of Temperature and Activation Parameters in the E2C β-Elimination Reactions of Substrates 1 and 2 with a Weak Neutral PS and an Anionic Br^- Base in Acetonitrile Solution

Proton Sponge		bromide ion	
reaction temp, °C ± 0.05 °C	second-order k_2, L $mol^{-1} \cdot s^{-1}$	reaction temp, °C ± 0.05 °C	second-order k_2, L $mol^{-1} \cdot s^{-1}$
Ethyl 2-Bromo-3-phenylpropionate (**1**)			
66.90	$1.40 \pm 0.05 \times 10^{-6}$	66.90	$4.5 \pm 0.2 \times 10^{-6}$
100.60	$1.89 \pm 0.04 \times 10^{-5}$	101.20	$11.0 \pm 1.0 \times 10^{-5}$
132.20	$1.81 \pm 0.09 \times 10^{-4}$	130.00	$11.0 \pm 0.6 \times 10^{-4}$
Methyl 2-Bromo-2-methyl-3-phenylpropionate (**2**)			
66.90	$3.16 \pm 0.8 \times 10^{-6}$	66.90	$18.1 \pm 0.7 \times 10^{-6}$
100.60	$3.4 \pm 0.1 \times 10^{-5}$	102.00	$51 \pm 1.0 \times 10^{-5}$
132.20	$2.6 \pm 0.1 \times 10^{-4}$	132.20	$72 \pm 4.0 \times 10^{-4}$

computed activation parameters	Proton Sponge	bromide ion
Ethyl 2-Bromo-3-phenylpropionate (**1**)		
$\Delta H^\ddagger$, kcal/mol	19.3 ± 0.05	22.9 ± 0.05
$\Delta S^\ddagger$, eu	-28.9 ± 0.1	-16.0 ± 0.1
$\Delta G^\ddagger$, kcal/mol (T, 100.60 °C)	30.0 ± 0.7	28.8 ± 0.4
correl coeff[a]	0.9996	0.9999
Methyl 2-Bromo-2-methyl-3-phenylpropionate (**2**)		
$\Delta H^\ddagger$, kcal/mol	17.3 ± 0.05	24.3 ± 0.05
$\Delta S^\ddagger$, eu	-33.1 ± 0.1	-9.2 ± 0.1
$\Delta G^\ddagger$, kcal/mol (T, 100.60 °C)	29.6 ± 0.8	27.7 ± 0.2
correl coeff[a]	0.9997	0.9997

[a] The correlation coefficient determined in calculations of the Arhennius plot slope and intercept when computing the activation parameters listed.

[†] Deceased, March 31, 1983.

(1) Pearson, R. G.; Sobel, H.; Songstad, J. *J. Am. Chem. Soc.* **1968**, *90*, 319.

(2) See for discussion: McLennan, D. J. *Tetrahedron* **1975**, *31*, 2999.

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Table II. Intramolecular Isotope Effect in the DBN[11] Promoted β-Elimination Reaction[a] of $C_6H_5CHDCHBrCOOEt$

reaction temp, °C ± 0.05 °C	corrected[b,c] $(M_D/M_H)_{corr}$ $(=k_H/k_D)$	mean k_H/k_D
68.4	2.54 ± 0.01	2.53 ± 0.01, ΔT = 60.2 °C
76.9	2.54 ± 0.01	
88.8	2.527 ± 0.007	
100.0	2.543 ± 0.001	
114.9	2.517 ± 0.003	
128.6	2.525 ± 0.001	

[a] A tenfold excess of DBN in DMF solution, approximately 0.007 M in substrate. [b] See Table II in reference 8 for correction calculations and procedure. [c] 20 000 determinations of mass ratio at each temperature.

Table III. Intramolecular Isotope Effect in the β-Elimination Reaction of $C_6H_5CHDC(CH_3)BrCOOCH_3$ (2a) Promoted by Amine Bases[a] in DMF Solution

amine base	reaction temp, 0 °C ± 0.05 °C	corrected[b,c] $(M_D/M_H)_{corr}$ $(=k_H/k_D)$	mean k_H/k_D
Dabco[12]	66.3	2.06 ± 0.03	2.06 ± 0.01, ΔT = 54.8 °C
	79.0	2.064 ± 0.006	
	101.5	2.060 ± 0.007	
	110.7	2.080 ± 0.003	
	121.1	2.054 ± 0.008	
DBN[11]	66.3	1.561 ± 0.005	1.561 ± 0.007, ΔT = 67.2 °C
	101.5	1.555 ± 0.008	
	110.7	1.572 ± 0.005	
	121.1	1.556 ± 0.002	
	133.5	1.561 ± 0.007	

[a] A tenfold excess of amine base in DMF solution at approximately 0.007 M substrate concentration. [b] The correction to be applied and the procedure for computation is given in Table V of reference 8. [c] 20 000 determinations of mass ratio at each temperature.

bring to bear sufficient nucleophilic "power" to meet the demand for rearward approach in triggering the E2C, as is shown in the ensuing report.

Results and Discussion

The reactivity of PS in the weak base promoted β-elimination of **1** is found to be quite similar to that effected by bromide ion.[8] Table I contains the rate data as a function of temperature, comparing the reactivity of Br^- and PS with **1** in acetonitrile; it also presents a comparison of the activation parameters computed from these data. Apparently, the change of promoter reagent from Br^- to PS, which results in the lowering of $\Delta H^\ddagger$ by ca. 2.5 kcal/mol, is accompanied by an almost compensating decrease in $\Delta S^\ddagger$ (13 e.u. more negative). This is readily explained by the charge development in both the intermediate and the nearby TS by the neutral base reagent transforming to $PS^{\delta+}$ and thus creating solvent striction consequences.[9]

The effect of a methyl substituent at C_α on the rates and activation parameters is realized in comparing PS and Br^- in reaction with substrate **2** (see Table I). In this case, the lowering of $\Delta H^\ddagger$ accompanying the change of promoter reagent from Br^- to PS is even greater (ca. 8 kcal/mol), as is the compensating disparity in $\Delta S^\ddagger$ (24 eu more negative). What these data appear to tell is that a steric hindrance effect of α-CH_3 is not operating; the methyl substituent at C_α affords no serious obstruction to the course of the approaching nucleophile promoter. Instead, what is observable is the hyperconjugative effect of methyl tending to stabilize the incipient double bond in a product-resembling TS. That is to say, the C_β–$H^{\delta+}$ bond is more ionized and thus more extensively abstracted by PS in the TS. Thus, the positive charge on $PS^{\delta+}$ is developed to a greater extent in the looser TS supported by methyl hyperconjugation. This produces a larger dipole moment between $PS^{\delta+}$ and the leaving $Br^{\delta-}$ in the TBP intermediate, thereby, intensifying the solvent striction[9] from which the lower $\Delta H^\ddagger$ and larger negative $\Delta S^\ddagger$ originate. It is possible, also, that the bifunctional nature of the PS may be a factor in the large, negative $\Delta S^\ddagger$.

For purposes of calibrating amines, in general, as a class of weak base nucleophiles as to their abilities in the E2C mechanism, several popular amine reagents, often used in β-elimination reactions, were tried in reactions with substrates **1** and **2**. The results of applying the TDKIE criteria[10] to the reactions with DBN[11] and Dabco[12] in the aprotic solvent are very informative in this regard (see Tables II and III).

Changing the nature of the base promoter from anionic bromide to a neutral nitrogen, base nucleophile, like DBN in DMF, appears to be without a profound effect on the TS structure. The KIE parameters ($[\Delta E_a]_D^H = 0$, $A_H/A_D = 2.53$) vs. LiBr in DMF[8] ($[\Delta E_a]_D^H = 0$, $A_H/A_D = 2.52$) testify to the fact that the DBN TS is still that of an E2C mechanism and is unaltered in its geometry compared to the LiBr case in the reaction with substrate **1**. But the much stronger base, DBN, exerts a large effect (ca. a 50% lowering of A_H/A_D) compared to LiBr (ca. a 5% lowering) when the α-methyl substituent is present. Dabco, a weaker base than DBN but stronger than bromide ion, shows a value of A_H/A_D in reaction with **2** which is intermediate.

In connection with consideration of a possible carbonium ion E2C mechanism[2], the finding the amine bases can effectively promote a reaction path, which is similar in rate and TS structure to that of the bromide-promoted reaction, can be construed as incongruent with the McLennan model.[2] Since the nitrogen seat of basicity acquires positive charge in the act of abstraction the C_β-H, its dipole–dipole interaction with the putative carbonium ion center at C_α should be destabilizing, which is not the case.

The TDKIE criteria have also been applied to the PS promoted β-elimination reaction of **1** and **2** in the intermolecular competition mode (Tables IV and V) for comparison with the KIE parameters summarized in Table VI for the β-elimination reactions of the amines and bromide reagents. This comparison indicates that an E2C mechanism is operating with PS in much the same manner as with weak bases, possessing recognizable nucleophilic properties. The isotope effect, k_H/k_D, of the PS reaction is temperature independent, i.e., shows no perceptible trends with temperature, and A_H/A_D is greater than the practical limit for linear H-transfer,[10] 1.2, as it is for all the promoter base reagents listed in Table VI. It can be

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(3) Bunnett, J. F.; Eck, D. L. *J. Am. Chem. Soc.* **1973**, *95*, 1897, 1900.

(4) Winstein, S. Accad. Naz. Lincei, Corso Estivo Chim. 9th, 1965, 327.

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(7) Kwart, H.; Brechbiel, M. W.; Miles, W.; Kwart, L. D. *J. Am. Chem. Soc.* **1981**, *103*, 1757.

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(9) Kwart, H.; Lilley, T. H. *J. Org. Chem.* **1978**, *43*, 2374.

(10) For a full discussion and other references see: Kwart, H. *Acc. Chem. Res.* **1982**, *15*, 401.

(11) DBN is 1,5-diazabicyclo[4.3.0]non-5-ene; see: Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 0000; Vol. 1, p 189 and Vol. 2, p 98.

(12) Dabco is 1,4-diazabicyclo[2.2.2]octane. Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 0000; Vol. 1, p 1203 and Vol. 2, p 99.

Table IV. The Intermolecular Primary Deuterium Isotope Effect in the β-Elimination Reaction of a Mixture of $C_6H_5CD_2CHBrCOOEt$ and $C_6H_5CH_2CHBrCOOEt$ Promoted by PS[a] in CH_3CN Solution

reaction temp, °C ± 0.05 °C	fraction of reaction completed, f	corrected[b,c] isotope ratio, R_{A_f}	isotope effect,[d] k_H/k_D	mean k_H/k_D at reaction temp	mean k_H/k_D over reaction temp range
66.9	0.092	0.4285 ± 0.0002	2.365 ± 0.001	2.364 ± 0.002	2.37 ± 0.01, ΔT = 63.1 °C
66.9	0.15	0.4403 ± 0.0005	2.362 ± 0.003		
100.6	0.07	0.4227 ± 0.0002	2.3750 ± 0.0009	2.365 ± 0.005	
100.6	0.15	0.4404 ± 0.0004	2.362 ± 0.001		
132.2	0.05	0.4173 ± 0.0005	2.386 ± 0.003	2.385 ± 0.002	
132.2	0.09	0.425 ± 0.001	2.383 ± 0.008		
80.0	1.00	R_{A_0} = 0.946 ± 0.001			

[a] A tenfold excess of PS and approximately 0.007 M substrate was used. [b] See Table II in reference 8 for correction calculations and for procedures for calculation of k_H/k_D; see Table III of reference 8, footnote *b*. [c] See Table III of reference 8, footnote *b*, for calculations of k_H/k_D. [d] 20 000 determinations of mass ratio at each temperature.

Table V. The Intermolecular Primary Deuterium Isotope Effect in the β-Elimination Reaction of a Mixture of $C_6H_5CD_2C(CH_3)BrCOOCH_3$ and $C_6H_5CH_2C(CH_3)BrCOOCH_3$ Promoted by PS[a] in CH_3CN Solution

reaction temp, °C ± 0.05 °C	fraction of reaction, completed, f	corrected[b,c] isotopic ratio, R_{A_f}	isotope effect[d] k_H/k_D	mean k_H/k_D at reaction temp	mean k_H/k_D over reaction
66.9	0.092	0.5126 ± 0.0003	1.4140 ± 0.0009	1.41 ± 0.01	1.411 ± 0.007, ΔT = 65.3 °C
66.9	0.15	0.5241 ± 0.0003	1.3964 ± 0.0007		
100.6	0.094	0.5130 ± 0.0006	1.413 ± 0.002	1.412 ± 0.002	
100.6	0.15	0.5192 ± 0.0002	1.4106 ± 0.0006		
132.2	0.100	0.5139 ± 0.0003	1.4123 ± 0.0009	1.412 ± 0.002	
132.2	0.138	0.5177 ± 0.0005	1.412 ± 0.001		
132.2	1.00	R_{A_f} = 0.7131 ± 0.0005			

[a] A tenfold excess of PS and approximately 0.007 M substrate was used. [b] The correction to be applied and the procedure for computation is given in Table V of reference 8. [c] 20 000 mass ratio determinations at each temperature. [d] See Table III of reference 8, footnote *b*, for calculations of k_H/k_D.

Table VI. Summary of Temperature Independent Isotope Effects in the Weak Base Promoted β-Elimination Reactions of Ethyl 2-Bromo-3-phenylpropionates (1) and Methyl 2-Bromo-2-methyl-3-phenylpropionates (2)

substrate	promoter reagent/solvent	mode of measurement	A_H/A_D	approx. angle of H transfer
1	Et_4NBr/CH_3CN	intramolecular	2.61	100°
1	Et_4NBr/CH_3CN	intermolecular	2.73	100°
1	LiBr/DMF	intramolecular	2.52	95°
1	PS/CH_3CN	intermolecular	2.37	90°
1	DBN/DMF	intramolecular	2.53	95°
2	DBN/DMF	intramolecular	1.56	70°
2	Dabco/DMF	intramolecular	2.03	82°
2	Et_4NBr/CH_3CN	intermolecular	1.91	80°
2	LiBr/DMF	intramolecular	2.37	90°
2	PS/CH_3CN	intermolecular	1.41	60°

concluded, therefore, that even though PS does not have the ability to attain the degree of covalent bonding to carbon that is characteristic of an S_N2 TS, it still possesses sufficient nucleophilic activity to trigger the formation of a bent E2C TS; that is to say, it can cause sufficient displacement of the leaving group and bring about formation of a TBP structured intermediate similar to what has been suggested for the other amines (above) and for the Br^- promoted case.[8]

Focusing on the A_H/A_D values of PS and Br^- in their respective reactions with substrates 1 and 2 in the intermolecular competition mode (Table VI) confirms again that the reagent of higher basicity (PS), despite its considerably reduced nucleophilic ability vs. Br^-, has a somewhat looser TS. Moreover, there is a greater decline in the angle of H abstraction observed for the PS reagent than for the Br^- reagent in reaction with the α-CH_3 substituted substrate 2. Part of the unusually large effect of the α-CH_3 may be due to a slightly closer rearward approach to C_α by the PS which is permitted by the flattening of C_α attending the effect of methyl hyperconjugation on top of –COOEt conjugation with the incipient double bond in the TS. Reenforcement of these influences may also stem from an increase in the degree of ionization of the C_β–$H^{\delta+}$ due to the presence of a second amine function in PS, which is not even weakly bonded to C_α, as seen in Figure 1.

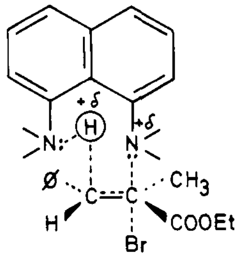

Figure 1. Proposed TS‡ in the PS-promoted β-elimination of 2.

These results verify that, beyond a low threshold of nucleophilic ability required of the promoter reagent, basicity is one of the essential characteristics determining the structural features of the E2C TS. Moreover, the rationale of the bent E2C and its success depend on the promoter base being only weakly bonded to the rear of the C_α–L bond in order to retain most of its basicity for effective abstraction of neighboring hydrogen in the TS. The small amount of nucleophilic bonding at C_α provides both the triggering of electron displacement and the orientation for effective H bond abstraction. The other important characteristics of the promoter reagent, which have been recognized in these studies,[8,13] are the leaving group ability[13] and the acidifying effect on the β-H[8] exerted through substitution at C_α and C_β (hyperconjugation, resonance, inductive effects).

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(13) Kwart, H.; Wilk, K. A.; Chatellier, D. *J. Org. Chem.* **1983**, *48*, 756.

Table VII. α-Secondary Deuterium Isotope Effect in the PS (in CH_3CN Solution) Promoted β-Elimination Reaction of a Mixture of $C_6H_5CH_2CDBrCOOEt$ and $C_6H_5CH_2CHBrCOOEt$

reaction temp, °C ± 0.05, °C	fraction of reaction completed, *f*	corrected[a] isotopic ratio, R_{A_f}	isotope effect k_H/k_D	mean[c] k_H/k_D
100.6	0.050	0.7173 ± 0.0003	1.2760 ± 0.0006	1.27 ± 0.01
100.6	0.15	0.738 ± 0.001	1.255 ± 0.003	
101.2	1.00	R_{A_0} = 0.8826 ± 0.0002		

[a] The correction equation applied here is identical to that described in footnote *b* of Table II. [b] The method of computation is the same as that discussed in footnote *b* of Table III in reference 8. [c] A total of 40 000 mass ratio determinations were used in deducing this value.

Finally, the opportunity to confirm the essential similarity in mechanism of the Br^- and PS promoted reactions, as well as the somewhat looser structure and more product-like nature of the PS transition state, presents itself through measurement of $(k_H/k_D)_\alpha$. The data in Table VII indicate that this value of the α-secondary KIE for the PS reaction ($(k_H/k_D)_\alpha$ = 1.27) is even greater than in the Br^- case ($(k_H/k_D)_\alpha$ = 1.21)[8], which hitherto was the largest value ever found for an S_N2 or β-elimination process. These results give further support to the contention that the basicity of PS contributes strongly to the ionization of the C_β–$H^{\delta+}$ bond, once the geometry of the bent E2C TS is established with formation of the TBP intermediate (see Figure 1).

Symmetry Properties of the Intermediate Structure. The PS-catalyzed product composition is devoid of any *cis*-cinnamate. Recalling[8] that this is also the case in the Br^- promoted reaction and that the stereochemistry of the weak base promoted eliminations are nearly exclusively anti,[4,5,14] the symmetry of the TS where Br^- is both nucleophile and nucleofuge was invoked previously[8] to account for the virtual identity of the intramolecular and intermolecular isotope effects. In fact, it is found that all the weak nitrogen base catalyzed eliminations in aprotic media show the same temperature independence and identity of intramolecular and intermolecular isotope effects when corrected for secondary isotope effects. Moreover, as can be seen above, the PS reaction TS under discussion is similar in all respects to the E2C previously identified for the Br– promoted reactions of **1** and **2** except, possibly, for the symmetry of the apical bonds to C_α in the intermediate. One is thus required to explain how such unsymmetrically structured TBP intermediates as the initially formed **3A** and **3B** can give rise to a TS in which the ease of subsequent H and D removal by the weakly bonded PS promoter is in proportion to their zero point energy differences rather than the diastereomeric composition of the ground precursors.

One possible explanation for the apparently equal availability of the H and D to the bonded base, B: in the intermediates, **3A** and **3B**, assumes that an actual S_N2 displacement of the leaving group has occurred rapidly and the resulting substance undergoes E2C elimination equally well with rates that are comparable to that of the initial substrate. However, this explanation seems both contrived and far fetched for three reasons: (a) No such reaction intermediate has ever been detected at any stage of the E2C reaction, which would correspond to such a displacement of Br^- by B:, where this could be expected on the basis of (known) diminished reactivity of the displacement reaction product. (b) In the particular case where PS is the promoter reagent, the formation of such a displacement reaction product as an intermediate is not possible for lack of ability to form a covalency to carbon.

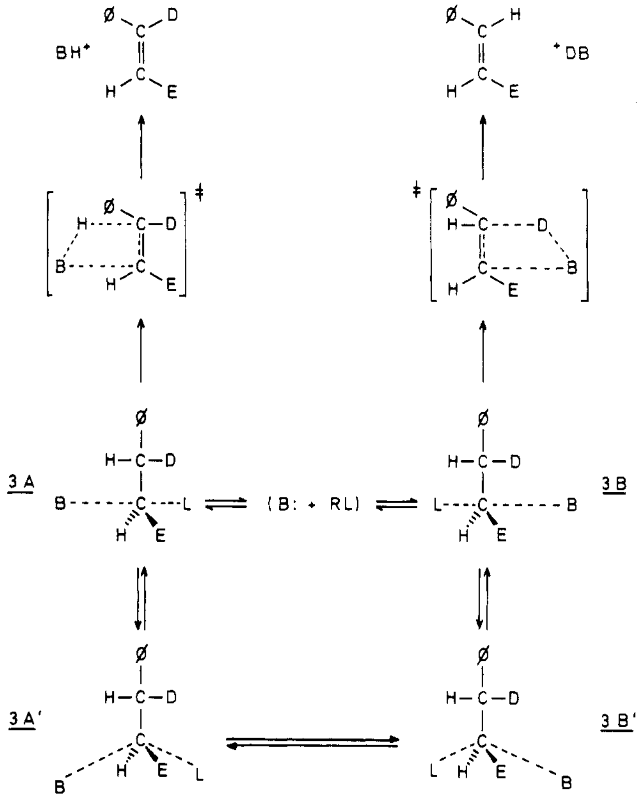

Figure 2. Permutational isomerism in the E2C mechanism of β-elimination.

(c) Nor can it be assumed that a displacement reaction product forms in the case of neopentyl type substrates,[3] which are inert to S_N2 displacement but very active in the E2C elimination.

The most attractive explanation is that the TBP intermediates **3A** and **3B**, shown in Figure 2, undergo polytopal rearrangement[15] by some mode of permutational isomerism which equilibrates the apically bonded promoter base and nucleofuge in rapid steps of racemization, i.e., **3A** $\rightleftharpoons$ **3A′** and **3B** $\rightleftharpoons$ **3B′** as represented and discussed in Figure 2. These events serve effectively to equalize, at all times during the reaction, the populations of the intermediates **3A** and **3B** which can subsequently experience the elimination reaction TS, shown in Figure 2, leading to expulsion of the conjugate acids (BH^+ and BD^+) and L^-.

It must be emphasized that the apical bond to the promoter reagent B: in the intermediate is both longer and weaker than the other apical bond to the leaving group; in other words, the assumption is being made that the TBP intermediate is a highly unsymmetrical structure

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[14] Parker, A. J. *Chem. Tech.* **1971**, *1*, 297.

[15] (a) Berry, R. J. *J. Chem. Phys.* **1960**, *32*, 933. (b) Lauterbur, P. C.; Ramirez, F. *J. Am. Chem. Soc.* **1968**, *90*, 6722. (c) Gillespie, P.; Hoffman, P.; Klusacek, H.; Marquarding, D.; Pfohl, S.; Ramirez, F.; Tsolis, E. A.; Ugi, I. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 687.

from which it would not be expected that return to starting material, after permutational isomerization, could result in a buildup of a (displacement product) second substrate, which has been sought but never found to date (as started above).

Experiments are currently in progress to test this possibility. Though Forbus and Martin[16] have convincingly demonstrated the existence of a long lived pentacovalent, pentacoordinate carbon compound, in a case where such a structure is compelled by the nature and stereochemistry of the five substituent groups; the property of permutational isomerism has not been demonstrated. It is conceivable that this property is associated only with cases where at least one of the apical bonds of the trigonal bipyramid structure surrounding a carbon center are extraordinarily long and weak, a possibility which suggests how and why the permutational isomerism may be taking place. It has already been shown that if, indeed, a tightly structured S_N2 intermediate[17] could be formed, it would not be expected to manifest permutational isomerism.[18] The lengthy, weak, apical bonds in the E2C intermediate apparently permit permutational isomerism over a low barrier quite as readily as do long and weak bonds in pentacoordinate phosphorus,[19] for example.

The question naturally arises as to why one should expect rapid permutational isomerism in structures like **3A** and **3B**. The mechanisms of permutational isomerism usually discussed for trigonal bipyramid (TBP) and tetragonal pyramid (TP) structures having normal apical bonds, namely, Berry pseudorotation[15a] and Ugi turnstile rotation,[15c] require 5 acts of permutational isomerism to interconvert enantiomers.[15b] One possible answer to this question originates in the fact that the apical bonds in **3A** and **3B** are far from their equilibrium configurations. In such circumstances, the bending vibrations of these bonds, which are involved in both the Berry and Ugi mechanisms of isomerization, become inseparable and undergo rapid energy exchanges. If it can be presumed that the facility for energy exchange between these weak bonds also prevails in a highly unsymmetrical tetragonal pyramid, derivable in the course of appropriate bending vibrations, then positional interchange should also be greatly facilitated in a process that circumvents the normal, higher activation-demanding mechanisms of permutational isomerism.[15]

Another way of expressing this is from the viewpoint of the extraordinarily long apical bond to B: and the lengthened bond to $L^{\delta-}$ in the TBP (see **3A** and **3B**). Thus, the bending amplitudes of these far-out groups are not seriously limited by collisions or interaction with atoms or groups closely bonded to the central C_α, around which all the groups are clustered in both the TBP and TP structures.

Experimental Section

Substrates 1 and 2 and their deuterated analogues used in the kinetic experiments, the data for which are summarized in Tables I–VII, were prepared as described previously.[8] Instrumentation used in the kinetic experiments and kinetic procedures have also been described in the preceeding article[8] and discussed, as well, in references cited therein.

Registry No. 1, 39149-82-1; 2, 18197-77-8; Et_4NBr, 71-91-0; LiBr, 7550-35-8; PS, 20734-58-1; DBN, 3001-72-7; Dabco, 280-57-9; bromide anion, 24959-67-9; carbon, 7440-44-0; deuterium, 7782-39-0.

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(16) Forbus, T. R.; Martin, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 5057.

(17) The results of both experimental and theoretical studies tend to the conclusion that a metastable TBP intermediate cannot intervene in the simplest cases of S_N2 displacement; see for data and discussions: (a) Olmstead, W. M.; Brauman, J. I. *J. Am. Chem. Soc.* **1977**, *99*, 4219. (b) Gillespie, R. J. *J. Chem. Soc.* **1952**, *1002*. (c) Schlegel, H. B.; Milsow, K.; Bernardi, F.; Bottoni, A. *Theor. Chim. Acta* **1977**, *44*, 245. (d) Firestone, R. A. *Tetrahedron* **1977**, *33*, 3009. (e) Wolfe, S.; Kost, D. *Nouv. J. Chim.* **1978**, *2*, 441.

(18) The stereochemical factors relevant to this expectation are discussed in: (a) El Gomati, T.; Lenoir, D.; Ugi, I. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 59. (b) Eckert, H.; Lenoir, D.; Ugi, I. *J. Organomet. Chem.* **1977**, *141*, C23. (c) Gray, R. W.; Chapleo, C. B.; Vergnani, T.; Dreiding, A. S.; Liesner, M.; Seebach, D. *Helv. Chim. Acta* **1976**, *59*, 1547. (d) Schaffler, J.; Retey, J. *Angew. Chem.* **1978**, *90*, 906. (e) Kunz, H. *Z. Naturforsch. B* **1976**, *31*, 1676. (f) Kirmse, W.; Engbert, T. *Angew. Chem.* **1979**, *91*, 240. (g) Maryanoff, C. A.; Ogura, F.; Mislow, K. *Tetrahedron Lett.* **1975**, 4095.

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