

# Mechanisms of Elimination Reactions Catalyzed by Weak Bases

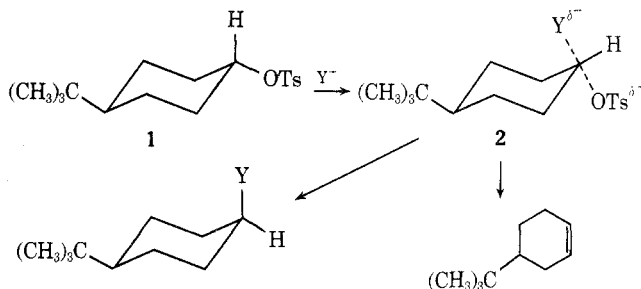
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Since 1956<sup>1,2</sup> there have been many reports that weak proton bases, such as thiophenoxide and chloride ions in polar aprotic solvents, promote faster elimination from certain alkyl halides and sulfonates than strong bases, such as alkoxide ions in alcohols. The synthetic utility of weak base catalyzed eliminations is now well recognized, but their mechanisms are still controversial.

Winstein<sup>1</sup> originally suggested that "nucleophilic attack of halide ion on *trans*-4-*t*-butylcyclohexyl *p*-toluenesulfonate (1) gives rise to an actual intermediate 2, with the electronic and geometrical structure generally ascribed to the transition state in S<sub>N</sub>2 substitution." In his "merged" mechanism, 2 led to both

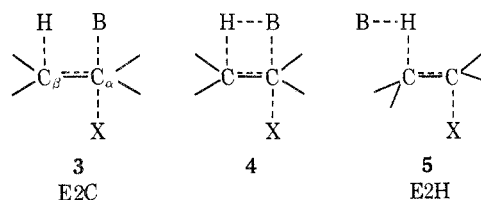


substitution and elimination products. Later experiments in Winstein's laboratory<sup>3</sup> conclusively ruled out any common transition state for these competitive substitution and elimination reactions and eventually led to the proposal by Parker and Winstein<sup>4</sup> of an "E2C" transition state for elimination which resembles, but is not identical with, an S<sub>N</sub>2 transition state.

On the other hand, Bunnett<sup>5</sup> suggested that eliminations catalyzed by weak bases were merely a special class of concerted E2 reactions in which no bonding of base to carbon is required. This Account will evaluate the E2C and E2 mechanisms for weak base catalyzed eliminations and also consider a carbonium ion pair mechanism, hopefully from the viewpoint of an impartial critic.<sup>6</sup>

## The E2C Mechanism

Parker<sup>7</sup> contends there is a spectrum of E2 transition states ranging from E2C (3) to intermediate cases (4) to E2H (5). The E2C extreme is characterized by high nucleophilicity but weak basicity of



base B, concurrent substitution of B for X, and preference for Saytzeff elimination products (most substituted olefins). The E2H extreme is characterized by strong basicity of B and preference for Hofmann elimination products (least substituted olefins).

## The E2H Mechanism

In contrast, Bunnett<sup>5</sup> maintains that weak base catalyzed eliminations do not involve bonding between base and C<sub>α</sub>. He considers them to be part of the concerted reaction class in the theory of the variable E2 transition state.<sup>5</sup> For clarity I will adopt Parker's notation E2H to describe a bimolecular elimination mechanism in which the base does not interact with carbon. Bunnett<sup>5</sup> suggests that thioalkoxide ions are effective elimination catalysts only when a good leaving group X makes possible a transition state in which H<sub>β</sub> is just slightly transferred.

## The Ion-Pair Mechanism

An alternate mechanism, rejected by both Parker and Bunnett, appears in Scheme I. It involves reversible ionization of an alkyl halide or sulfonate to form a tight ion pair, which may be captured by the base at C<sub>α</sub> or at H<sub>β</sub>. If the base participates in the reversible ionization step, the same base ion must eventually remove H<sub>β</sub> or bond to C<sub>α</sub> in the irreversible second stage of the reaction. On the other hand, the base might be required only in the irreversible stage.

As long as the ion-pair concentration does not build up during the reaction, these two possible roles

(1) S. Winstein, D. Darwish, and N. J. Holness, *J. Amer. Chem. Soc.*, **78**, 2915 (1956).

(2) P. B. D. de la Mare and C. A. Vernon, *J. Chem. Soc.*, 41 (1956); E. L. Eliel and R. S. Ro, *Chem. Ind. (London)*, 251 (1956).

(3) S. Winstein, P. Beltrame, G. Biale, R. Cetina, D. Darwish, S. Smith, I. D. R. Stevens, and J. Takahashi, 144th National Meeting of the American Chemical Society, Los Angeles, Calif., 1963, Abstract 8-M.

(4) A. J. Parker, M. Ruane, G. Biale, and S. Winstein, *Tetrahedron Lett.*, 2113 (1968).

(5) J. F. Bunnett, *Surv. Progr. Chem.*, **5**, 53 (1969), and references therein.

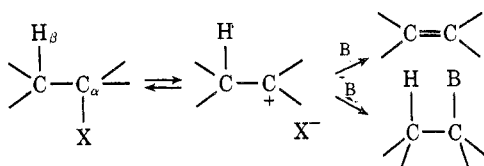
(6) More details and supporting arguments will be presented for the ion-pair mechanism than for the others because it has not received much attention in earlier papers. For further details of the E2C and E2 mechanisms consult the references.

(7) G. Biale, D. Cook, D. J. Lloyd, A. J. Parker, I. D. R. Stevens, J. Takahashi, and S. Winstein, *J. Amer. Chem. Soc.*, **93**, 4735 (1971).

Warren T. Ford was born in Kalamazoo, Mich., in 1942. He earned an A.B. from Wabash College and a Ph.D. from UCLA with D. J. Cram. After a year as a National Science Foundation postdoctoral fellow with P. D. Bartlett at Harvard, he took his present position as Assistant Professor of Chemistry at the University of Illinois in 1968. His major research interests are carbanion chemistry and the influence of solvents on chemical structures and reactions.

of the base are kinetically indistinguishable. This proposal resembles the ion-pair mechanism advocated by Sneen<sup>8</sup> for borderline SN1/SN2 substitutions and fits into the E2<sub>ip</sub> category of Bordwell's<sup>9</sup> spectrum of elimination mechanisms.

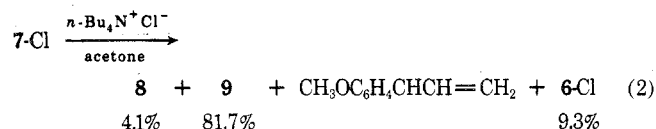
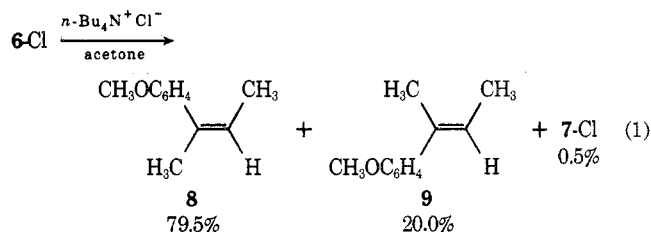
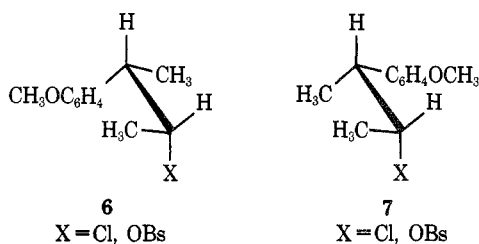
## Scheme I



Keeping in mind that the E2C, E2H, and ion-pair mechanisms are really extremes of what is likely a wide range of elimination mechanisms, let us now relate some representative experimental results to each.<sup>10</sup>

## Stereochemistry and Orientation of Eliminations

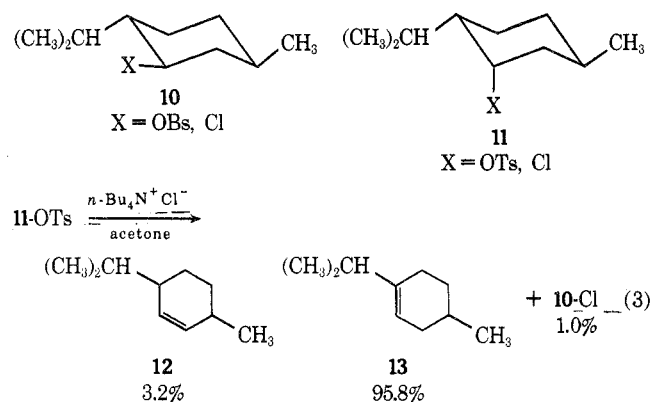
Reaction of *threo*-3-*p*-anisyl-2-butyl chloride (6-Cl) with tetra-*n*-butylammonium chloride in acetone at 75° produced the olefins shown in eq 1 after ten half-lives.<sup>11</sup> Reaction of the erythro isomer (7-Cl) with tetra-*n*-butylammonium chloride in acetone at 50° proceeded by concurrent substitution to 6-Cl and elimination to the olefins shown in eq 2 (after 1% conversion).<sup>11</sup>



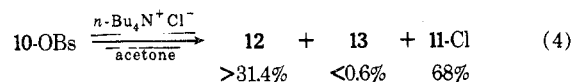
Extrapolation of these product distributions to zero time showed that the eliminations were more (but not completely) stereoselectively anti than indicated in eq 1 and 2. Moreover, treatment of the corresponding *threo*- and *erythro*-*p*-bromobenzenesulfonates (6-OBs and 7-OBs) with tetra-*n*-butylammonium chloride in acetone produced olefins 8 and 9, respectively, with >99% anti stereoselectivity. Microscopic reversibility requires that the reactions 6-Cl → 7-Cl and 7-Cl → 6-Cl proceed *via* the same transi-

tion state. Since 6-Cl and 7-Cl lead to the same transition state for substitution and yet give grossly different elimination products, at least one and probably both of them cannot undergo elimination and substitution *via* a single transition state. This rules out a transition state for elimination which is identical to the SN2 transition state, but allows formation of an intermediate similar to 2 prior to the irreversible stage of the reaction.<sup>12</sup>

Another pair of isomers which provides insight to the stereochemistry of weak base catalyzed eliminations are the menthyl (10) and neomenthyl (11) derivatives. Reaction of 11-OTs with tetra-*n*-butylammonium chloride in acetone at 75° gave mostly 3-menthene (13), apparently formed by anti-diaxial elimination of *p*-toluenesulfonic acid.<sup>11</sup> The product distribution in eq 3 was invariant from 20% reaction



to 20 half-lives. Under the same conditions 10-OBs gave predominantly neomenthyl chloride (which reacts with chloride ion more slowly than 10-OBs) and lesser amounts of olefins, of which >98.2% was 2-menthene (12, eq 4).<sup>11</sup>



The lack of 3-menthene from 10-OBs indicates that the preference for anti elimination is stronger than the preference for formation of the most substituted olefin in cyclohexyl systems. In contrast, strong base catalyzed eliminations form preferentially the Hofmann (least substituted) olefin and may proceed with syn as well as anti stereochemistry.<sup>13</sup> How does the anti stereochemical requirement fit the three mechanisms proposed for weak base catalyzed eliminations?

Both E2C and E2H mechanisms, which involve concerted removal of a proton and an anion, can explain anti elimination. A 180 or 0° dihedral angle between the breaking C<sub>β</sub>-H and C<sub>α</sub>-X bonds maximizes their overlap, which leads to the new π bond in the product. The preferred anti stereochemistry of weak base catalyzed eliminations is consistent with previous observations of alkoxide-initiated eliminations in which the syn course is favored only by very strong proton bases, which lead to transition states with considerable carbanionic character.<sup>13</sup>

(8) R. A. Sneen, *Accounts Chem. Res.*, **6**, 46 (1973).

(9) F. G. Bordwell, *Accounts Chem. Res.*, **5**, 374 (1972).

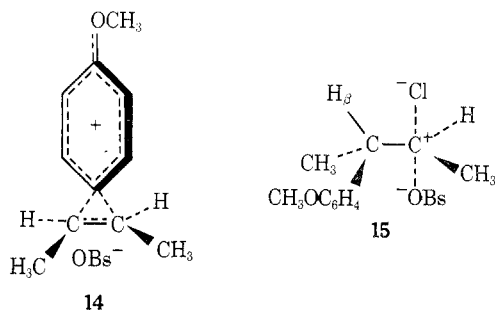
(10) Attention will be restricted to eliminations which proceed as fast or faster with halide ions in aprotic solvents or thioalkoxide ions in alcohols than they do with alkoxide ions in alcohols.

(11) G. Biale, A. J. Parker, S. G. Smith, I. D. R. Stevens, and S. Winstein, *J. Amer. Chem. Soc.*, **92**, 115 (1970).

(12) In the original merged mechanism Winstein<sup>4</sup> called 2 an intermediate, not a transition state. Some more recent papers have failed to make this distinction.

(13) For the latest reviews see J. Sicher, *Angew. Chem., Int. Ed. Engl.*, **11**, 200 (1972); S. Wolfe, *Accounts Chem. Res.*, **5**, 102 (1972).

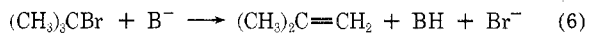
The anti elimination requirement is more difficult to rationalize with an ion-pair mechanism. Ionization *via p*-anisyl participation in chloride ion induced elimination of *p*-bromobenzenesulfonic acid from *threo*-3-*p*-anisyl-2-butyl brosylate (6-OBs) to give phenonium ion pair 14<sup>14</sup> may be ruled out kinetically because optically active 6-OBs reacts at nearly identical polarimetric and titrimetric rates, and stereochemically because 8 is the sole olefin produced. However, reaction of 6-OBs at 75° in acetone containing 2,6-lutidine, but no other base, proceeds *via* 14 because the polarimetric rate greatly exceeds the titrimetric rate.<sup>15</sup> If chloride ion induced elimination from 6-OBs proceeds *via* an ion pair, the chloride ion must assist ionization to bypass 14 and produce 15, and H<sub>β</sub> must be removed only from the anti conformation (shown) of 15. This stereochemical path is reasonable if both overlap between the breaking C-H bond and the carbonium ion p orbital in 15 and H<sub>β</sub>-Cl<sup>-</sup> interaction are required for proton removal.



### Rate Correlations

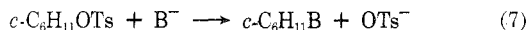
A Brønsted plot (eq 5) of rate constants for elimination of HBr from *tert*-butyl bromide catalyzed by weak bases (B<sup>-</sup>) in acetone at 50° (eq 6) and pK<sub>a</sub>'s

$$\log k_E = \beta pK_a + \text{constant} \quad (5)$$



of their conjugate acids (BH) in dimethylformamide gave no correlation whatsoever.<sup>16</sup> The rate constants covered a range of about 2.7 log units, while pK<sub>a</sub>'s covered a range of 11 units. Clearly rates of elimination are not related to the proton basicity of the catalyst. The E2C mechanism explains this fact with an SN2-like transition state;<sup>16</sup> the ion pair mechanism explains it by involving base with proton only in a strongly exothermic reaction step; the E2H mechanism explains it by delaying most of the B-H bond formation until after the transition state.

Correlations between rates of bimolecular substitution and elimination reactions have been used to support the E2C mechanism.<sup>16,17</sup> A plot of log *k<sub>E</sub>* for elimination of HBr from *tert*-butyl bromide catalyzed by weak bases in acetone at 50° (eq 6) against log *k<sub>S</sub>* for substitution with the same bases and cyclohexyl tosylate in acetone at 75° (eq 7) gives a



reasonably good correlation and has been used to justify bonding of base to C<sub>α</sub> in the elimination transition state.<sup>16</sup> However, if correlation of eq 6 and eq 7 is to be used in support of a general mechanism, then data with similar substrates should correlate well too. In ten similar attempted correlations between logarithms of substitution and elimination rate constants for *tert*-butyl bromide (*k<sub>E</sub>*), cyclohexyl tosylate (*k<sub>E</sub>* and *k<sub>S</sub>*), and cyclohexyl bromide (*k<sub>E</sub>* and *k<sub>S</sub>*) using all rate data available in ref 16 and 17, only three give correlation coefficients of 0.85 or more. (Data points for azide ion, which gives unusually high substitution rates, are omitted.) Good correlation between elimination and substitution rates is the exception, not the rule. Parker<sup>17</sup> contends that cyclohexyl bromide is a more E2H-like substrate than cyclohexyl tosylate, but this position leaves only unhindered tertiary alkyl halides and cyclohexyl tosylates as E2C-like substrates.

### The Leaving Group

Relative rates of substitution and elimination reactions with tetra-*n*-butylammonium chloride are rather insensitive to the nature of the leaving group. For C<sub>6</sub>H<sub>11</sub>X (X = Br and OTs in acetone; X = Cl, I, and <sup>+</sup>S(CH<sub>3</sub>)<sub>2</sub> in DMF; C<sub>6</sub>H<sub>11</sub> = cyclohexyl) the per cent cyclohexene formed varies over only 50–73%.<sup>17</sup> These results suggest great similarity between substitution and elimination transition states.

However, the leaving group affects markedly relative rates of elimination with strong and weak base catalysts. In reactions of benzyldimethylcarbinyl derivatives (C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>C(CH<sub>3</sub>)<sub>2</sub>X) the rate ratio *k<sub>E</sub>*<sup>EtS<sup>-</sup></sup>/*k<sub>E</sub>*<sup>MeO<sup>-</sup></sup> varies from 6.5 with a good leaving group, Cl<sup>-</sup>, to 0.8 with S(CH<sub>3</sub>)<sub>2</sub>, to 0.05 with a poor leaving group, CH<sub>3</sub>SO<sub>2</sub><sup>-</sup>.<sup>18</sup> These results were interpreted in terms of variable E2H transition states in which EtS<sup>-</sup> is the better elimination catalyst when C<sub>α</sub>-X is highly broken and H<sub>β</sub> is little transferred, and MeO<sup>-</sup> is the better catalyst when C-X is less broken and transfer of H<sub>β</sub> is more advanced.<sup>18</sup>

### Bulky Substituents at C<sub>α</sub>

The size of alkyl groups bound to C<sub>α</sub> dramatically affects rates of bimolecular substitution. If weak base-catalyzed eliminations proceed *via* an E2C transition state (3 or 4), which resembles an SN2 transition state, their rates should be affected similarly. After suitable statistical corrections cyclohexyl tosylate undergoes elimination six times faster than 2,2-dimethylcyclohexyl tosylate (16), and isopropyl bromide undergoes elimination faster than 2-bromo-3,3-dimethylbutane (17) by factors of 6.8 with methoxide ion and ≤2.2 with thioethoxide ion. Because bulky substitution at C<sub>α</sub> has so little effect on elimination rates, Bunnett and Eck<sup>19</sup> contend there cannot be bonding between C<sub>α</sub> and the base in the elimination transition state. In defense of the E2C mechanism Parker says that an E2C transition state is "looser"<sup>20</sup> than an SN2 transition state, and that the greater distance between C<sub>α</sub> and base in an E2C

(14) S. Winstein and G. C. Robinson, *J. Amer. Chem. Soc.*, **80**, 469 (1958).

(15) The data in ref 11 which indicate nearly equal polarimetric and titrimetric rates under these conditions are wrong: S. G. Smith, personal communication.

(16) A. J. Parker, M. Ruane, D. A. Palmer, and S. Winstein, *J. Amer. Chem. Soc.*, **94**, 2228 (1972).

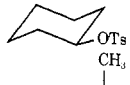
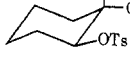
(17) P. Beltrame, G. Biale, D. J. Lloyd, A. J. Parker, M. Ruane, and S. Winstein, *J. Amer. Chem. Soc.*, **94**, 2240 (1972).

(18) J. F. Bunnett and E. Baciocchi, *J. Org. Chem.*, **32**, 11 (1967).

(19) J. F. Bunnett and D. L. Eck, *J. Amer. Chem. Soc.*, **95**, 1897, 1900, 4473 (1973).

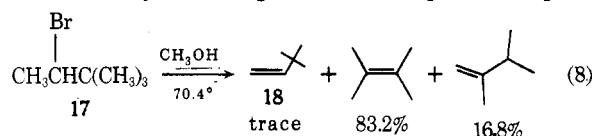
(20) E. C. F. Ko and A. J. Parker, *J. Amer. Chem. Soc.*, **90**, 6447 (1968).

Table I  
Rates of Reaction of Secondary Alkyl Bromides and Tosylates with Bases at 69.9°<sup>19</sup>

Reactant	Base	Solvent	10 <sup>9</sup> k <sub>E</sub> , M <sup>-1</sup> sec <sup>-1</sup>	10 <sup>5</sup> k <sub>S</sub> , M <sup>-1</sup> sec <sup>-1</sup>
	<i>n</i> -Bu <sub>4</sub> N <sup>+</sup> Cl <sup>-</sup>	(CH <sub>3</sub> ) <sub>2</sub> CO	25.6	6.8
 (16)	<i>n</i> -Bu <sub>4</sub> N <sup>+</sup> Cl <sup>-</sup>	(CH <sub>3</sub> ) <sub>2</sub> CO	2.16	0.0
CH <sub>3</sub> CHBrCH <sub>3</sub>	NaOCH <sub>3</sub>	CH <sub>3</sub> OH	23.8	22.4
CH <sub>3</sub> CHBrC(CH <sub>3</sub> ) <sub>3</sub> (17)	NaOCH <sub>3</sub>	CH <sub>3</sub> OH	1.74	0.0
CH <sub>3</sub> CHBrCH <sub>3</sub>	NaSC <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub> OH	≤ 13	860
CH <sub>3</sub> CHBrC(CH <sub>3</sub> ) <sub>3</sub> (17)	NaSC <sub>2</sub> H <sub>5</sub>	CH <sub>3</sub> OH	2.91	0.0

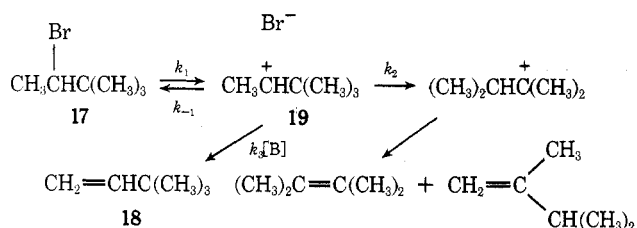
transition state lessens the rate-retarding effect of bulky substituents.

Let us now consider how the data in Table I relate to the ion-pair mechanism. Methanolysis of 17 produced only rearranged olefins (eq 8) as expected



from a carbonium ion intermediate with an appreciable lifetime.<sup>19</sup> But when sodium methoxide or sodium thioethoxide was employed as base in methanol, the major product (>91%) was 3,3-dimethyl-1-butene (18), and the rearranged olefins (<9%) could be attributed to competing solvolysis. Bunnett and Eck<sup>19</sup> rejected an ion-pair mechanism for base-catalyzed reactions of 17 because elimination gave no rearranged products. However, if the ion pair reacts much faster with strong nucleophiles than with methanol, lack of rearrangement would not rule out an ion-pair intermediate. In other reactions thought to proceed *via* a 3,3-dimethyl-2-butyl cation-anion pair (such as 19), trifluoroacetic acid added to 18 with extensive but not complete rearrangement,<sup>21</sup> and addition of hydrogen chloride to 18 in acetic acid produced chlorides and acetates which were less than half rearranged.<sup>22</sup> Hence, as the counterion in an intimate pair, chloride in acetic acid can capture the 3,3-dimethyl-2-butyl cation as fast as the cation can rearrange. To explain base-catalyzed elimination of HBr from 17 by an ion-pair mechanism, we must abandon only the preconception that  $k_2 > k_3$  in Scheme II and consider that  $k_3 > k_2$  is possible. The similar elimination rates for hindered and unhindered substrates (Table I) in an ion-pair mechanism would be due to a balance between acceleration of ionization and retardation of base attack by bulky substituents.

Scheme II

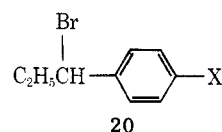


(21) V. J. Shiner, Jr., R. D. Fisher, and W. Dowd, *J. Amer. Chem. Soc.*, **91**, 7748 (1969).

(22) R. C. Fahey and C. A. McPherson, *J. Amer. Chem. Soc.*, **91**, 3865 (1969).

### Electron Demand at C<sub>α</sub>

Variation of substituents at C<sub>α</sub> provides a way to estimate charge at C<sub>α</sub> in elimination transition states. Rates of reaction of 1-aryl-1-bromopropanes (20) under typical solvolysis, bimolecular nucleophil-



ic substitution, and weak base catalyzed elimination conditions appear in Table II.<sup>23</sup> The solvolysis data correlate well with  $\sigma^+$  and  $\rho = -4.7$ , as expected for a carbonium ion reaction. The nucleophilic substitutions with tetra-*n*-butylammonium chloride in dimethylformamide proceed faster with both 20-NO<sub>2</sub> and 20-CH<sub>3</sub> than with the unsubstituted 20-H. The tetra-*n*-butylammonium bromide initiated eliminations follow the substituent order expected of a reaction which develops positive charge at C<sub>α</sub>, but the substituent effects are very small and do not fit a Hammett equation with either  $\sigma$  or  $\sigma^+$ .

These failures of substitution and elimination rates to fit a Hammett equation mean that the substitution and elimination transition states do not depend on substituents in the same way as the reference reactions of the  $\sigma$  and  $\sigma^+$  scales.<sup>24</sup> In either an E2C mechanism or an E2H mechanism variation of the degree of C-Br bond breakage and the degree of double bond formation in the transition state can rationalize the small substituent effects on elimination rates in Table II. However, these substituent effects are the strongest evidence against an ion-pair mechanism for bromide ion catalyzed elimination, because the transition state for an ion-pair mechanism would be expected to have substantial carbonium

Table II  
Rates of Reactions of 1-Aryl-1-bromopropanes (20)<sup>23</sup>

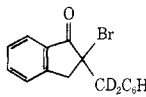
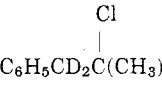
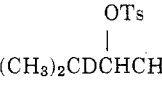
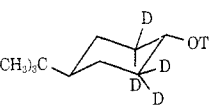
	10 <sup>2</sup> k <sub>S</sub> , M <sup>-1</sup> sec <sup>-1a</sup>	10 <sup>4</sup> k <sub>E</sub> , M <sup>-1</sup> sec <sup>-1b</sup>	k <sub>1</sub> , sec <sup>-1c</sup>
NO <sub>2</sub>	1.78	2.60	5 × 10 <sup>-8</sup> (est)
H	0.66	4.33	9.1 × 10 <sup>-5</sup>
CH <sub>3</sub>	1.74	12.3	3.35 × 10 <sup>-3</sup>
OCH <sub>3</sub>			1.3 (est)

<sup>a</sup> 0.04 M Bu<sub>4</sub>N<sup>+</sup>Cl<sup>-</sup>, DMF, 25°. <sup>b</sup> 0.10 M Bu<sub>4</sub>N<sup>+</sup>Br<sup>-</sup>, 0.05 M 2,6-lutidine, acetone, 75°. <sup>c</sup> 90% acetone-water, 75°.

(23) D. J. Lloyd and A. J. Parker, *Tetrahedron Lett.*, 5029 (1970).

(24) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley, New York, N. Y., 1963, pp 190-191.

Table III  
Kinetic Isotope Effects on Elimination (E) and Substitution (S) Reactions

Substrate	Solvent	Base	Temp, °C	Reaction	$k_H/k_D^a$	Ref
	CH <sub>3</sub> CN	Et <sub>4</sub> N <sup>+</sup> Br <sup>-</sup>	59.8	E	3.4	31
(CD <sub>3</sub> ) <sub>3</sub> CCl	CH <sub>3</sub> CN	Et <sub>4</sub> N <sup>+</sup> Cl <sup>-</sup>	45.0	E	3.81	32
	CH <sub>3</sub> OH	C <sub>2</sub> H <sub>5</sub> S <sup>-</sup> Na <sup>+</sup>	75.8	E	2.4	33
	(CH <sub>3</sub> ) <sub>2</sub> CO	Bu <sub>4</sub> N <sup>+</sup> Cl <sup>-</sup>	75.0	S E	1.1 2.3	34
	(CH <sub>3</sub> ) <sub>2</sub> CO	Bu <sub>4</sub> N <sup>+</sup> Cl <sup>-</sup>	75.0	S E	1.4 3.2	34

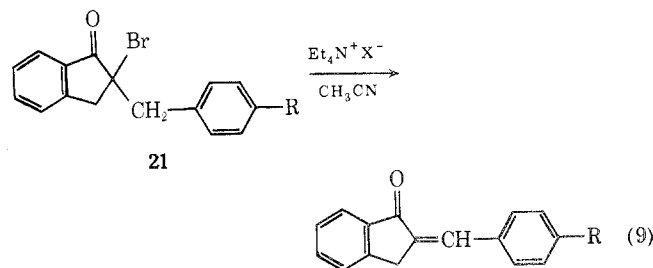
<sup>a</sup> Ratios of rate constants for compounds shown to rate constants for undeuterated analogs.

ion character (but not as much as a transition state for solvolysis of the same substrate).

The electronic nature of C<sub>α</sub> in weak base catalyzed elimination transition states has also been probed by substitution of a second halogen atom at C<sub>α</sub>. Substitution of a second bromine or chlorine at C<sub>α</sub> greatly accelerates unimolecular substitution of benzyl chloride,<sup>25</sup> greatly retards bimolecular substitution of methyl bromide,<sup>26</sup> and speeds bimolecular elimination from 1,1-diaryl-2-chloroethanes.<sup>27</sup> Rates of reaction of 1,1-dibromocyclohexane and 1,1-dichlorocyclohexane with para-substituted sodium thiophenoxides in ethanol at 55° are comparable to those of their monohalocyclohexane analogs, but the dihalocyclohexane rates are more sensitive to the basicity of the thiophenoxides.<sup>28</sup> The *gem*-dihalides give 100% elimination, while the monohalides give 33–59% elimination.<sup>28</sup> These rates are inconsistent with an S<sub>N</sub>2-like mechanism and fit well into the theory of the variable E2 transition state with the *gem*-dihalides nearer the carbanionic end of the transition state spectrum than the monohalides.

### Substituents at C<sub>β</sub>

In simple alkyl bromides and tosylates replacement of one or two (but not all three) hydrogens at C<sub>β</sub> by methyl groups promotes weak base catalyzed eliminations but has little effect on the concurrent substitution rates. This reflects the preferred Saytzeff orientation and suggests that there is no carbanionic character and appreciable double bond character at C<sub>β</sub> in the elimination transition states. Charge development at C<sub>β</sub> has been investigated in elimination of hydrogen bromide from substituted 2-benzyl-2-bromo-1-indanones (21, eq 9).<sup>29</sup> Plots of log  $k_2$  (eq



9) vs.  $\sigma_p^-$  gave  $\rho = 0.42$  and  $0.16$  for the chloride- and bromide-catalyzed reactions respectively. The small  $\rho$  values indicate that little charge develops at C<sub>β</sub> in the transition states for elimination from 21, a concept consistent with all mechanisms proposed.

Reactions of 1,1-diaryl-2,2,2-trichloroethanes with tetra-*n*-butylammonium chloride in acetone and with lithium chloride in DMF proceed with rate constants which fit Hammett plots with  $\rho = 1.31$  and  $0.99$ , respectively.<sup>30</sup> Unlike all the other alkyl halides discussed here, the 1,1-diaryl-2,2,2-trichloroethanes react faster with alkoxide ions in alcohols than with chloride ion in acetone.<sup>30</sup> With two aryl groups and one trichloromethyl group bound to C<sub>β</sub>, even chloride ion in acetone can lead to an elimination transition state with carbanionic character. This supports the concept of variable E2 transition states.

### Kinetic Isotope Effects

Substitution of deuterium for hydrogen at C<sub>β</sub> enables determination of primary kinetic isotope effects  $k_H/k_D$  for elimination and secondary isotope effects for substitution of alkyl halides and sulfonates. Representative measurements appear in Table III.<sup>31–34</sup>

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The different isotope effects for substitution and elimination in one substrate (3-methyl-2-butyl tosylate or *trans*-4-*tert*-butylcyclohexyl tosylate) require that substitution and elimination have different transition states.

More than one interpretation of the primary isotope effects for elimination is possible. If base, proton, and carbon lie in a linear configuration, and the proton does not move in the symmetric stretching vibration of the transition state, an isotope effect of 7 at 25° is predicted.<sup>35</sup> Lesser values are predicted if the proton is more tightly bound to either base or carbon such that the proton moves in the symmetric stretching vibration of the transition state.<sup>35</sup> Data in Table III and the assumption of a linear configuration of base, proton, and carbon thus lead to the conclusion that H<sub>β</sub> is either slightly or highly transferred, and the lack of correlation of rates with pK<sub>a</sub>'s of bases indicates little transfer of H<sub>β</sub> in the transition states. In contrast, primary isotope effects of 4.5–8.5 have been found for sodium ethoxide and potassium *tert*-butoxide catalyzed eliminations from cyclohexyl tosylate.<sup>36</sup> Alternatively, if the configuration of base, proton, and carbon is assumed to be bent as envisioned in the E2C mechanism (3 or 4), model calculations predict  $k_H/k_D$  to lie in the 2.5–4.2 range.<sup>37</sup> Thus the isotope effects in Table III cannot help distinguish between E2C and E2H transition states for elimination.

### Influence of Solvent

A comparison of rates of solvolysis, bimolecular elimination, and bimolecular substitution of *trans*-4-*tert*-butylcyclohexyl tosylate with tetra-*n*-butylammonium chloride in five solvents is shown in Table IV.<sup>17</sup> In all five solvents initial pseudo-first-order tetra-*n*-butylammonium chloride catalyzed rates exceed solvolysis rates by at least a factor of eleven (excluding possible positive salt effects on solvolyses). The large difference between solvolytic and base-catalyzed rates in acetone illustrates the value of acetone as a solvent for base-catalyzed eliminations. None of the rates takes ion pairing of tetra-*n*-butylammonium chloride into account. For each reaction variation of solvent affects the rate constant by a factor of <10 (except for solvolysis in DMF). The fraction of olefin produced by base catalysis covers a range of only 30–50% in the five solvents. These similarities suggest that the solvent does not participate in the elimination or substitution processes in any specific way.

Rates of substitution and elimination in reactions of tetra-*n*-propylammonium thiophenoxide with cyclohexyl bromide have been measured in three solvents with greatly different solvating properties: methanol, a good hydrogen bond donor and acceptor; dimethylformamide, a good solvator of cations but poor solvator of anions; and triethyl-*n*-hexyl-

Table IV  
Rates of Solvolysis and Rates of Initial 0.03 M *n*-Bu<sub>4</sub>N<sup>+</sup>Cl<sup>-</sup> Catalyzed Substitution and Elimination of *trans*-4-*tert*-Butylcyclohexyl Tosylate at 75°<sup>17</sup>

Solvent	Solvolysis 10 <sup>7</sup> k <sub>1</sub> , sec <sup>-1</sup>	Substitu- tion, 10 <sup>7</sup> k <sub>1</sub> , sec <sup>-1</sup>	Elimina- tion, 10 <sup>7</sup> k <sub>1</sub> , sec <sup>-1</sup>
Acetone	1.5	600	250
Dimethylformamide	48	550	240
Acetonitrile	9.5	190	97
Nitromethane	9.5	60	60
<i>tert</i> -Butyl Alcohol	12	72	61

ammonium triethyl-*n*-hexylboride (N<sub>2226</sub>B<sub>2226</sub>), an ionic liquid which cannot hydrogen bond or specifically coordinate to solutes. Under conditions of negligible solvolysis relative rates at 25° were methanol, 1.00; N<sub>2226</sub>B<sub>2226</sub>, 41.0; and DMF, 492. The fraction of cyclohexene in the products varied with the solvent and temperature from 46 to 58%.<sup>38</sup> This insensitivity of the substitution–elimination product distribution to solvent and temperature is strong evidence that the substitution and elimination transition states have very similar charge distributions.

### Conclusions

None of the three extreme mechanisms considered here is consistent with all the reliable data, but each explains some of it well. Although a few reactions may fit one or another of the three extreme mechanisms, most weak base catalyzed eliminations probably proceed *via* transition states which are compromises between the extremes. Bunnett and Parker both have proposed spectra of elimination transition states in which the extent of bond formation between base and H<sub>β</sub> increases progressively as the proton basicity of the catalyst increases from halide and thioalkoxide ions to alkoxide ions. Their disagreement centers on whether halide and thioalkoxide ions interact with C<sub>α</sub>.

I agree that there is a broad spectrum of elimination transition states which are highly dependent on substrate structure and on the base–solvent system, and suggest that all weak base-catalyzed eliminations<sup>10</sup> may be described by elaboration of the following scheme. First the C<sub>α</sub>-X bond stretches markedly with assistance from the base when the base is a good carbon nucleophile and C<sub>α</sub> is not too hindered. If the substrate is hindered, relief of strain accelerates breakage of the C<sub>α</sub>-X bond, compensating for decreased nucleophilic assistance. Only after the initial deformation of C<sub>α</sub>-X does the base bond strongly enough to H<sub>β</sub> or C<sub>α</sub> to reach the respective transition states for elimination and substitution.<sup>39</sup> This scheme necessarily is very general because eliminations proceed *via* such a wide range of transition states that no more specific mechanism is likely to agree with all the reliable data.

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(39) Tertiary and hindered secondary alkyl halides and sulfonates should lead to transition states with more ion-pair character than do more open secondary substrates, and consequently should show more carbonium ion like substituent effects on elimination rates. This possibility deserves experimental testing.