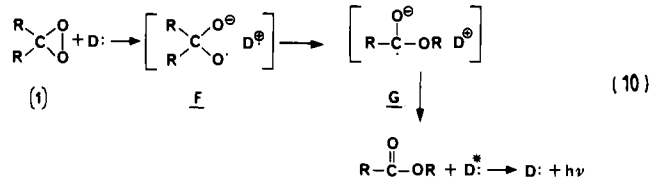

(10)

the dioxirane 1 from the fluorophor, resulting in the radical ion pair F. Conversion of the dioxirane radical anion to its ketyl radical and electron back transfer would generate electronically excited fluorophor. The latter would display its characteristic fluorescence. Such transformations have been postulated for putative dioxirane intermediates[46] and need to be rigorously established.

Quite generally speaking, it is possible that a number of the oxidations observed with dioxiranes that are outlined in the rosette in Figure 2 might proceed via electron transfer, but of course this does not necessarily entail production of excited states. A likely candidate appears to be the quadricyclane–norbornadiene isomerization,[47] which is efficiently catalyzed by dimethyldioxirane (**1a**).[26]

While dioxirane chemistry has been slowly maturing over the last 15 years into a prominent branch of oxidation processes, still numerous fascinating mechanistic and synthetic problems need to be attended.[1b] It is our contention that the fun has just begun!

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(45) Schuster, G. B. *Acc. Chem. Res.* **1979**, *12*, 366 and references therein.
(46) Steinfatt, M. F. D. *J. Chem. Res., Synop.* **1985**, 140.
(47) (a) Bishop, K. C., III *Chem. Rev.* **1976**, *76*, 461. (b) Gassman, P. G.; Hirschberger, J. W. *J. Org. Chem.* **1987**, *52*, 1337 and references.

Base-Promoted, Imine-Forming 1,2-Elimination Reactions

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Base-promoted, bimolecular 1,2-eliminations are one of the fundamental reactions of organic chemistry. Synthetically, they are a common method for the introduction of π-bonds into saturated molecules. Mechanistically, they provide an important testing ground for methods and constructs with which bonding changes that take place during chemical reactions may be described in terms of detailed activated complexes.

The E2 transition state of a base-promoted 1,2-elimination is reached by the making/breaking of four bonds between five atomic centers in a concerted process. The activated complex is characterized structurally by the extents to which making/breaking of the four bonds have progressed. As shown in Figure 1, bond-making events include bond formation between the base and the β-proton and π-bond formation, while bond-breaking processes involve cleavage of the C_β–H bond and rupture of the C_α–leaving group bond. The variable E2 transition state theory[1,2] was developed to

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(1) (a) Bartsch, R. A.; Zavada, J. *Chem. Rev.* **1980**, *80*, 453. (b) Baciocchi, E. *Acc. Chem. Res.* **1979**, *12*, 430. (c) Cockerill, A. F.; Harrison, R. G. *The Chemistry of Double-Bonded Functional Groups, Supplement No. 1*; Patai, S., Ed.; Wiley-Interscience: London, 1977; pp 149–222. (d) Saunders, W. H., Jr.; Cockerill, A. F. *Mechanisms of Elimination Reactions*; Wiley: New York, 1973. (e) Banthorpe, D. V. *Elimination Reactions*; Elsevier: New York, 1963. (f) Baciocchi, E. In *Supplement D, The Chemistry of Halides, Pseudo-Halides, and Azides, Part 2*; Patai, S., Rappoport, Z., Eds.; Interscience: London, 1983; p 1173.
(2) Bunnett, J. F. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 225.

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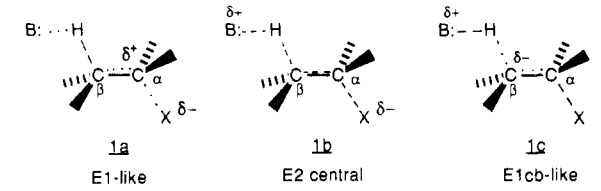


Figure 1. Variable E2 transition states for base-promoted 1,2-eliminations.

Table I
Kinetic Parameters for Alkoxide-Promoted Eliminations from $ArCH_2N(X)CH_3$[6]

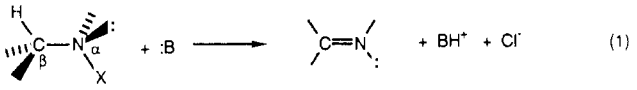
$$ArCH_2N(X)CH_3 \xrightarrow[ROH,\ 39.0\ °C]{RO^-} ArCH{=}NCH_3 + ROH + X^-$$

kinetic parameter	MeONa–MeOH	*t*-BuOK–*t*-BuOH
order	second	second
ρ^a	1.52	1.68
$k_H/k_D{}^{a,b}$	6.0	5.9
$k_{Br}/k_{Cl}{}^b$	11.9	10.8

[a] X = Cl. [b] For Ar = Ph.

account for different degrees of bond making/breaking possible at the transition state. If the bonding changes proceed synchronously[3] (as depicted in **1b**, Figure 1), the elimination is designated E2 central. If loss of the leaving group is more advanced than proton removal by the base, the activated complex is termed E1-like (**1a**), whereas if proton removal is more advanced than loss of the leaving group, the activated complex is described as E1cb-like (**1c**). Alkene-forming eliminations are the most common type of 1,2-elimination reaction and have been the subject of numerous investigations.[1] The result of these studies is a good general understanding of how structural and environmental factors influence the mechanism of elimination as well as the structure of the activated complex.

In contrast, mechanisms of elimination reactions in which the π-bond is formed between carbon and a heteroatom, such as nitrogen, oxygen, or sulfur, have received much less attention. Of particular interest are eliminations in which the α-atom is nitrogen and the products of elimination are imines (eq 1). Imine-


(1)

forming eliminations are known to be facile,[4] and a study of *N*-(benzoyloxy)amine reactions with weak bases suggested that an E2 mechanism was operative.[5] Research programs were initiated at New Mexico State University and Texas Tech University and subsequently at Korea University to examine the changes wrought by the atomic substitution of nitrogen for carbon in base-promoted 1,2-elimination reactions.

Base-Promoted 1,2-Eliminations from *N*-Chloramines

Alkoxide-induced, imine-forming eliminations from *N*-chloro-*N*-methylbenzylamines have many features

Table II
Activation Parameters for Alkoxide-Promoted Eliminations from $PhCH_2N(Cl)CH_3$ and $PhCH_2CH(Cl)CH_3$

substrate	temp, °C	base–solvent	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu	ref
$PhCH_2N(Cl)CH_3$	29.6	MeONa–MeOH	16.6	−12.1	6
		t-BuOK–*t*-BuOH	11.7	−21.1	6
$PhCH_2CH(Cl)CH_3$	25.0	EtONa–EtOH	22.3	−10.1	9
		t-BuOK–*t*-BuOH	17.9	−19.4	9

Table III
Eliminations from $ArCH(R)N(Cl)CH_3$ Promoted by MeONa–MeOH at 39.0 °C

R	rel rate	ρ	$k_H/k_D{}^a$	$k_{Br}/k_{Cl}{}^a$	ref
Me	0.5	1.36	4.4	28.8	12
H	1.0	1.52	6.0	11.9	6
Ph	3.1	1.67	5.1	11.1	12

[a] For Ar = Ph.

in common with alkene-forming E2 reactions (Table I).[6] They are bimolecular reactions, first order in both alkoxide and chloramine substrate. Hammett studies indicate that electron density increases at the β-carbon in going to the transition state. There is a substantial primary kinetic deuterium isotope effect that further implicates partial rupture of the C_β–H bond at the transition state. A large leaving group element effect requires that cleavage of the N_α–X bond is occurring in the activated complex.[6,7] Taken together, these data provide convincing evidence for an E2 type elimination.[8]

There are, however, several important differences between these reactions and olefin-forming eliminations. Most noticeably, base-promoted eliminations from chloramines are much faster ($\sim 10^4$). This rate difference is primarily due to the significantly lower $\Delta H^{\ddagger}$ values for the chloramine elimination; the $\Delta S^{\ddagger}$ values are comparable (Table II). The reduced $\Delta H^{\ddagger}$ values arise from two factors. The N–Cl bond which must be broken is weaker than a C–Cl bond by about 24 kcal/mol, and the resultant C–N double bond is stronger than a C–C double bond by about 10 kcal/mol.[10]

Another difference between imine- and alkene-forming eliminations is the magnitudes of ρ values determined for $ArCH_2N(Cl)CH_3$ and $ArCH_2CH(Cl)CH_3$. In general, the ρ values are smaller for alkoxide-promoted eliminations from *N*-chloramines ($\rho \sim 1.5$) than for analogous alkene-forming eliminations ($\rho \sim 2.2$).[6] This implies that there is less proton transfer and/or more π-bond formation in the former. Thus the transition state is nearer to E2 central in imine-forming eliminations and more E1cb-like in alkene-forming eliminations.

(3) Dewar, M. J. S. *J. Am. Chem. Soc.* **1984**, *106*, 209.
(4) (a) Dayagi, S.; Degani, Y. *The Chemistry of Carbon-Nitrogen Double Bonds*; Patai, S., Ed.; Wiley-Interscience: New York, 1970; pp 117–124. (b) Brauman, S. K.; Hill, M. E. *J. Org. Chem.* **1969**, *34*, 3381; (c) *J. Am. Chem. Soc.* **1967**, *89*, 2131.
(5) Oae, S.; Sakurai, T. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 730.
(6) Bartsch, R. A.; Cho, B. R. *J. Am. Chem. Soc.* **1979**, *101*, 3587.
(7) Cho, B. R.; Yoon, J. C.; Bartsch, R. A. *J. Org. Chem.* **1985**, *50*, 4943; **1986**, *51*, 4326.
(8) The possibility of an $(E1cb)_{irr}$ mechanism for imine-forming eliminations is highly unlikely. Examples of this mechanism in alkene-forming eliminations are observed only for cases in which the leaving group is quite poor and/or the C_β–H bond is highly activated. In contrast, in similar systems where better leaving groups are employed or where the C_β–H bond is made slightly less acidic, an E2 mechanism is found. See, for example: Thibblin, A. *J. Am. Chem. Soc.* **1988**, *110*, 4582. Gandler, J. R.; Jencks, W. P. *Ibid.* **1982**, *104*, 1937. Since the substrates used for imine-forming eliminations have very good leaving groups and do not have unusually acidic C_β–H protons, an $(E1cb)_{irr}$ process is highly improbable. We thank Professor Joseph R. Gandler for a preprint of an excellent review article on alkene-forming eliminations which discusses these points in detail.
(9) Koch, H., unpublished data.
(10) Kerr, J. A. *Chem. Rev.* **1966**, *66*, 465.

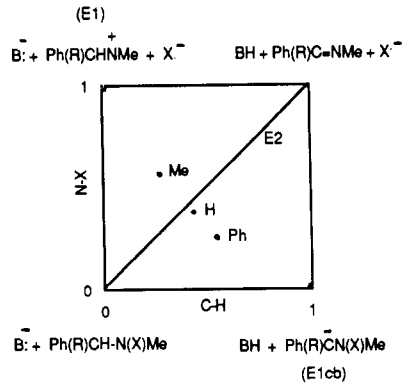


Figure 2. MOFJ diagram for base-promoted, imine-forming 1,2-elimination reactions.

Transition states for base-promoted, alkene-forming E2 reactions are known to be influenced by changes in substrate structure and the base–solvent system employed. It was therefore of interest to probe the influence of structural and environmental factors in imine-forming eliminations. There are several advantages to using imine-forming reactions as models for the study of bimolecular elimination processes. They are well-behaved kinetically and do not suffer from competing substitution on nitrogen. Due to the high rates of elimination, they can be studied under mild conditions using bases of widely varying strengths and charge types. Finally, the reactants are easily prepared from the corresponding amines by reaction with halogenating agents to attach chloride or bromide leaving groups[6] or with arylsulfonyl peroxides to attach arenesulfonate leaving groups to nitrogen.[11]

Variation of β-Substituents

Attachment of substituents to the β-position of *N*-chloro-*N*-methylbenzylamine leads to small rate differences (Table III)[12] which are primarily attributable to electronic effects. An electron-donating methyl group destabilizes proton removal and slows the reaction, while a phenyl group stabilizes the developing negative charge on C_β and increases the reaction rate. As the β-substituent is changed from Me to H to Ph, the extent of proton transfer is enhanced as shown by the increased ρ values and the deuterium isotope effect values, while the extent of leaving-group loss decreases as seen in the decreasing values for k_{Br}/k_{Cl}, the leaving group element effect. The deuterium isotope effect values bracket a maximum value of 6.0 as the extent of proton removal increases in the series.

When a Me group was substituted on the β-carbon of 2-phenylethyl tosylate and bromide, decreased ρ values were also noted.[13] Hence imine- and alkene-forming transition states appear to respond similarly to the introduction of a β-Me substituent.

A very effective method for visualizing these changes in transition-state structure is to use a More-O'Ferrall–Jencks (MOFJ) diagram.[14,35] For these reaction-coordinate diagrams, elimination reactions have proton removal as the abscissa, leaving-group loss as the ordinate, and free energy as the third coordinate (Figure 2). A diagonal connection between the reactants and products represents a synchronous E2 process, and the opposite corners represent E1 and E1cb mechanistic extremes. The transition state for an elimination reaction can be moved parallel to the diagonal for concerted elimination or perpendicular to it. The amount and direction of movement depend on structural and electronic features which can change the energies of reactants, products, and the E1 and E1cb corners.

Table IV
Eliminations from $PhCH_2N(Cl)R$ Promoted by NaOMe–MeOH at 25.0 °C[16]

R	rel rate	ρ	k_H/k_D
Me	1	1.58	6.4
Et	0.5	1.52	5.1
i-Pr	0.3	1.47	3.0
s-Bu	0.2	–	–
t-Bu	0.01	1.36	2.8

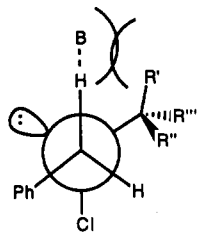


Figure 3. Steric effects of alkyl groups in eliminations from $PhCH_2N(Cl)R$.

The data from Table III are used qualitatively in Figure 2 to show that β-substituents produce perpendicular shifts in the transition state.[15] When R = Me, the transition state is more E1-like with less proton transfer and greater leaving-group loss. When R = H, the transition state is more central. Enhanced proton

(11) Hoffman, R. V.; Belfoure, E. L. *Synthesis* **1983**, 34.
(12) Bartsch, R. A.; Cho, B. R. *J. Am. Chem. Soc.* **1989**, *111*, 2252.
(13) DePuy, C. H.; Storm, D. L.; Frey, J. T.; Naylor, C. G. *J. Org. Chem.* **1970**, *35*, 2746.
(14) (a) More-O'Ferrall, R. A. *J. Chem. Soc. B* **1970**, 247. (b) Jencks, W. P. *Chem. Rev.* **1972**, *72*, 705.
(15) (a) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper and Row: New York, 1987, pp 211–228. (b) Thornton, E. R. *J. Am. Chem. Soc.* **1967**, *89*, 2915. (c) Winey, D. A.; Thornton, E. R. *J. Am. Chem. Soc.* **1975**, *97*, 3102.
(16) Cho, B. R.; Maeng, J. H.; Yoon, J. C.; Kim, T. R. *J. Org. Chem.* **1987**, *52*, 4752.
(17) Charton, M. *J. Am. Chem. Soc.* **1975**, *97*, 6159.
(18) MacLaury, M. R.; Saracino, A. *J. Org. Chem.* **1979**, *44*, 3344.
(19) Thibblin, A. *J. Am. Chem. Soc.* **1984**, *106*, 183.
(20) Thibblin, A. *J. Am. Chem. Soc.* **1988**, *110*, 4582.
(21) Coetzee, J. F.; Padmanabhan, G. R. *J. Am. Chem. Soc.* **1965**, *87*, 5005.
(22) Cho, B. R.; Namgoong, S. K.; Bartsch, R. A. *J. Org. Chem.* **1986**, *51*, 1320.
(23) Brown, K. C.; Romano, F. J.; Saunders, W. H., Jr. *J. Org. Chem.* **1981**, *46*, 4242.
(24) McLennan, D. T.; Wong, R. J. *Tetrahedron Lett.* **1972**, 2887.
(25) Cook, D. J.; Hutchinson, R. E. J.; MacLeod, J. K.; Parker, A. *J. Org. Chem.* **1974**, *39*, 534.
(26) Hoffman, R. V. *J. Am. Chem. Soc.* **1976**, *98*, 6702.
(27) Reference 1c, pp 180–181.
(28) Cho, B. R.; Pyun, S. Y.; Kim, T. R. *J. Am. Chem. Soc.* **1987**, *109*, 8041.
(29) Hoffman, R. V.; Belfoure, E. L. *J. Am. Chem. Soc.* **1982**, *104*, 2183; **1979**, *101*, 5687.
(30) Bartsch, R. A.; Cho, B. R. *J. Org. Chem.* **1979**, *44*, 145.
(31) (a) Shiner, V. J.; Smith, M. L. *J. Am. Chem. Soc.* **1961**, *83*, 593. (b) DePuy, C. H.; Storm, D. L.; Frey, J. T.; Naylor, C. G. *J. Org. Chem.* **1970**, *35*, 2746. (c) Alunni, S.; Baciocchi, E. *J. Chem. Soc., Perkin Trans. 2* **1976**, *2*, 877.
(32) Hoffman, R. V.; Cadena, R. *J. Am. Chem. Soc.* **1977**, *99*, 8226.
(33) Hoffman, R. V.; Cadena, R.; Poelker, D. J. *Tetrahedron Lett.* **1978**, 203.
(34) Hoffman, R. V.; Shankweiler, J. M. *J. Am. Chem. Soc.* **1986**, *108*, 5536.
(35) For example, see: Gandler, J. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1982**, *104*, 1937. Jencks, W. P. *Acc. Chem. Res.* **1980**, *13*, 161.

Table V
Eliminations from $ArCH_2N(Cl)CH_3$ Promoted by Neutral and Charged Bases at 25.0 °C

	MeONa–MeOH[7]	Bu_2NH–MeCN[22]
pK_a of base	18.3	18.3
ρ	1.58	0.96
k_H/k_D[a]	6.4	8.8
k_{Br}/k_{Cl}[a]	15.8	24.1
$\Delta H^{\ddagger}$,[a] kcal/mol	14.2	7.6
$\Delta S^{\ddagger}$,[a] eu	−19.9	−45.1
$\Delta G^{\ddagger}$,[a] kcal/mol	20.1	21.0

[a] For Ar = Ph.

removal and diminished leaving-group loss produce a more E1cb-like transition state when R = Ph.

Variation of α-Substituents

Variation of the alkyl substituents on the α-nitrogen also produces distinct changes in the activated complex.[16] Increases in steric bulk cause decreases in rate (Table IV), which indicates that steric effects are of primary importance (since the electronic effects would be similar for all of the alkyl groups). Taken together, the ρ and deuterium isotope effect values suggest that the degree of C_β–H bond rupture is lessened as the steric bulk of the α-alkyl group increases.

The effect of increasing steric bulk might be to hinder the approach of the base to the C_β–H bond (Figure 3), which would decrease the extent of proton removal at the transition state. Support for this interpretation is found in the correlation between the rates of elimination and the steric parameters for the *N*-alkyl groups.[17] Although data for leaving-group variation are not available in this series, it is reasonable to expect that rupture of the N_α–Cl bond would increase (i.e., the transition state becomes more E1-like) as proton transfer is lessened by the steric effect.

Variation of Base–Solvent System

The ease with which *N*-chloramines underwent bimolecular elimination with alkoxide bases suggested that neutral amine bases might also be used to promote imine-forming elimination. Products of this elimination would be the imine and an ammonium salt. Alkene-forming eliminations of this charge type (neutral reactants giving charged products) have been recently reported only for highly activated substrates such as 2,2-diaryl-1,1,1-trichloroethanes (DDT),[18] 9-(chloromethyl)fluorene,[19] 1-(2-X-2-propyl)indene,[19] and 9-(2-chloro-2-propyl)fluorene.[20]

Dibutylamine in acetonitrile was chosen as the base since its pK_a value (18.3)[21] matched that of MeONa in MeOH, which provides a constant base strength. The results presented in Table V demonstrate a marked change in the transition-state structure with the neutral base.[22]

Although large k_H/k_D values are observed for both base–solvent combinations, which indicates similar extents of C_β–H bond breaking, there is much greater cleavage of the N_α–Cl bond with dibutylamine in acetonitrile and much less negative charge development at C_β, probably due to increased π-bond formation. Of further note is the fact that the activation entropy is the most important component of the free energy of activation. The development of partial charges at the transition state results in increased solvent organization around the activated complex and a large decrease in entropy. Increased π-bond formation would reduce the overall charge development.

Table VI
Eliminations from $ArCH_2N(Cl)CH_3$ Promoted by Secondary Amines in MeCN at 25.0 °C[22]

base	pK_a	k_H/k_D[a]	ρ
piperidine	18.9	6.6	0.84
Et_2NH	18.7	8.6	0.89
n-Bu_2NH	18.3	8.8	0.96
i-Bu_2NH	17.9	6.4	0.86
$PhCH_2NHMe$	17.1	5.0	0.82

[a] For Ar = Ph.

When a series of five different amine bases covering a 1.8 pK_a unit range were used to promote eliminations from *N*-chloro-*N*-methylbenzylamines, a smooth variation in the extent of proton transfer was noted[22] (Table VI). The measured deuterium isotope effect values pass through a maximum value of 8.8 and suggest that changes in the transition-state structure are larger in the parallel than perpendicular direction. For the limited range of base strengths, only a small variation in the ρ values was evident. It is interesting to note that for eliminations from *N*-chloro-*N*-methylbenzylamines, a change from MeONa–MeOH to *t*-BuOK–*t*-BuOH produced only a small variation in transition-state structure (Table I).

A parallel shift of transition-state character with base-strength variation has been advocated for alkene-forming transition states that proceed via highly carbanionic E2 transition states.[23-25] In contrast, for eliminations which proceed through E2 central transition states (e.g., 2-arylethyl substrates with ArO^-–DMF), the changes in k_H/k_D and ρ values with base-strength variation have been interpreted by assuming similar effects on parallel and perpendicular motion in the reaction-coordinate diagram.[1b]

The differing effects of base strength for imine- and alkene-forming eliminations which utilize E2 central transition states arise from the lower free energy of activation of the former (vide supra). If the free energy of activation is lowered without changing the relative energy of any corner in the reaction coordinate diagram, the parallel effect will predominate.

Base-Promoted 1,2-Eliminations from *N*-(Arylsulfonoxy)amines (NAS)

N-(Arylsulfonoxy)amines are highly reactive substrates in base-promoted, imine-forming elimination reactions.[26] In alkene-forming eliminations, bromide and arenesulfonate leaving groups have comparable leaving-group abilities[27] and the C_α–leaving group bond strengths are nearly the same.[10] On the other hand, in imine-forming eliminations, the N_α–leaving group bond strength is some 30 kcal/mol weaker for arenesulfonate leaving groups than for bromide,[28] which provides an extremely good leaving group in NAS. The enhanced leaving-group ability of arenesulfonates in imine-forming elimination produces a rich diversity of transition-state structures that lie between E2 central and E1-like, which is an inaccessible region in alkene-forming eliminations.

Shift from E2 Central toward E1-like Transition States

For bimolecular eliminations from NAS, the transition-state character is distinctly different from those

Table VII
Base-Promoted Eliminations from $ArCH_2N(X)R$ in Methanol at 25.0 °C

	$ArCH_2N(Cl)CH_3$,[a] MeONa–MeOH	$ArCH_2N(OAs)CH_3$,[b,c] MeONa–MeOH	$ArCH_2NH(OAs)$,[c,d] $PhCH_2NH_2$–MeOH
rel rate[e]	1	175	0.3
ρ	1.73	1.15	0.11
k_H/k_D[e]	6.4	3.6	1.2
ρ_{lg}[e]	–	1.3	1.65
$\Delta H^{\ddagger}$,[e] kcal/mol	14.9	12.2	14.5
$\Delta S^{\ddagger}$,[e] eu	−16.8	−16.2	−34.8

[a] Reference 7. [b] Reference 28. [c] OAs = $OSO_2C_6H_4$-*m*-CF_3. [d] Reference 29. [e] For Ar = Ph.

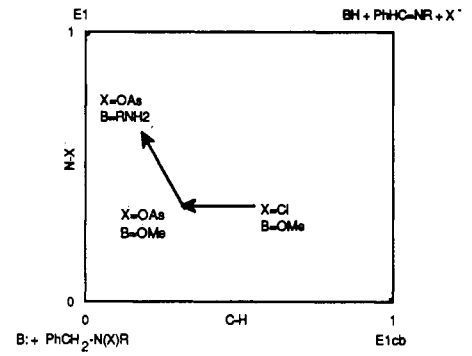


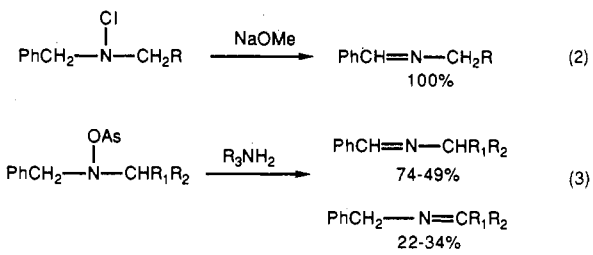
Figure 4. MOFJ diagram for imine-forming elimination reactions shown in Table VII.

for eliminations from *N*-chloramines (Table VII). For eliminations induced by MeONa–MeOH, the change from a chloride leaving group to *m*-(trifluoromethyl)-benzenesulfonate (OAs) markedly diminishes the degree of proton transfer at the transition state, and there is substantial charge development on the leaving group (ρ_{lg}). The transition state has been shifted toward E1-like.

These changes in transition-state character may be readily rationalized with a MOFJ diagram (Figure 4). Starting with the assumption that the transition state for methoxide-promoted elimination from the chloramine is close to E2 central, a change to a better leaving group would lower the upper edge of the diagram and cause a shift of the transition state toward the leftmost edge.

Now considering the change in transition-state character on going from reaction of $ArCH_2NH(OAs)CH_3$ with MeONa to reaction of $ArCH_2NH(OAs)$ with benzylamine in the common solvent of methanol, the values of ρ, k_H/k_D, and ρ_{lg} (Table VII) demonstrate a further shift toward E1-like. These results clearly demonstrate that the E2 central transition state can be shifted toward E1-like by utilizing a better leaving group and a weaker base. For an explanation of the base shift in terms of a MOFJ diagram, the reader is directed to ref 28.

The magnitudes of the parallel and perpendicular components which produce the shifts shown in Figure 4 are purely qualitative, being derived from consideration of the transition-state parameters given in Table VII. Other evidence suggests that these changes are, in fact, quite reasonable. When *N*-alkyl-*N*-chlorobenzylamines are treated with sodium methoxide, only the conjugated imines are formed,[7,30] which is typical of an E2 central process (eq 2).[31] On the other hand, treatment of *N*-alkyl-NAS with amine bases gives mixtures of regioisomers. The product ratios are dependent on the chain branching in the *N*-alkyl group (eq 3).[32] The change in regioselectivity for the NAS



is due to the E1-like transition state with a substantial positive charge on nitrogen and little proton removal by base. Thus conjugative interactions with the phenyl ring are of lesser importance in the activated complex, and the tendency to form the more highly substituted, and thus more stable, imine becomes competitive. In a few cases, an E1 process in imine-forming eliminations has been found to give rise to competing cationic skeletal rearrangement.[33]

Transition-State Mapping for NAS Eliminations

Two defined coordinates are required for the MOFJ diagram of imine-forming eliminations: the extent of proton transfer and the extent of nitrogen–leaving group bond cleavage. A method that has proven successful to quantitate these bonding changes at the transition state is the use of Brønsted coefficients.[29,34] For proton transfer, correlation of the rate of elimination with the pK_a of the base gives the Brønsted parameter β, whose values vary between 0 and 1 for no and complete proton transfer, respectively, at the transition state. While these limits need not hold universally, they have been widely used as acceptable descriptors of bonding change.[35]

Cleavage of the nitrogen–leaving group bond can be approached similarly. Correlation of the rate of elimination with the pK_a of the leaving group gives the Brønsted parameter of β_{lg}, the extent of leaving-group loss at the transition state. Recent work suggests that this approach is valid if the leaving groups are similar.[36,37] Arylsulfonoxy groups are quite suitable since aryl substitution gives minimal structural change for leaving groups with different pK_a values. When this Brønsted treatment was applied to eliminations from NAS, β_{lg} values > 2.5 were observed, while application of the method to literature data for other reaction types gave β_{lg} values up to 3.[29] Therefore the equilibrium acidity of arenesulfonic acids is not a suitable model equilibrium, and β_{lg} is not a suitable parameter for leaving-group loss in MOFJ diagrams since the upper limit is not defined.

An equilibrium which better models the changes taking place when an arylsulfonoxy group acts as a leaving group is the methyl transfer equilibrium between arenesulfonates. When the data of Lewis[38] were used, methyl transfer equilibrium constants, pK_{lg}, were correlated with rates of elimination to give the modified Brønsted parameter $\beta_{lg}^{CH_3}$.[34,39] For a variety of elim-

(36) Stirling, C. J. M. *Acc. Chem. Res.* **1979**, *12*, 198.
(37) Boyd, D. B. *J. Org. Chem.* **1985**, *50*, 885.
(38) Lewis, E. S.; Hu, D. D. *J. Am. Chem. Soc.* **1984**, *106*, 3292.
(39) The designation $\beta_{lg}^{CH_3}$ denotes the dependence on methyl transfer equilibria.

Table VIII
Brønsted Coefficients β and $\beta_{lg}^{CH_3}$ for Proton Removal and Leaving-Group Loss in Base-Promoted Eliminations from N-Substituted (Arylsulfonoxy)amines in TEW[a]

$$R_1R_2CHN(OAs)H + B: \rightarrow R_1R_2C{=}NH + BH^+ + AsO^-$$

entry	substrate R_1	substrate R_2	β^b	$\beta_{lg}^{CH_3\,b}$	ref
1	H	C_5H_{11}	0.24 ± 0.04	0.51 ± 0.06	41
2	CH_3	C_4H_9	0.22 ± 0.02	0.55 ± 0.07	41
3	H	CF_3CH_2	0.22 ± 0.04	0.49 ± 0.06	41
4	H	Ph	0.30 ± 0.09	0.42 ± 0.05	29
5	H	p-$CH_3C_6H_4$	0.32 ± 0.07	0.45 ± 0.07	41
6	H	m-$CF_3C_6H_4$	0.35 ± 0.06	0.49 ± 0.05	41
7	H	p-$NO_2C_6H_4$	0.43 ± 0.06	0.41 ± 0.07	41

[a] TEW is 2.25 M aqueous THF–ethyl acetate. [b] The reported errors are 1 standard deviation from the least-squares value.

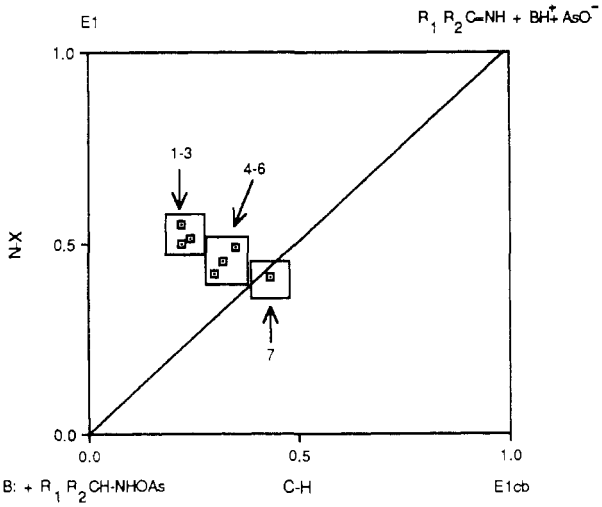


Figure 5. MOFJ diagram for imine-forming elimination reactions shown in Table VIII.

ination and substitution reactions, $\beta_{lg}^{CH_3}$ varies between 0.40 and 0.61, appears to be a well-behaved and informative descriptor of the extent of leaving-group loss for arenesulfonate groups,[40] and is consistent with the limits of 0 and 1 for the extent of nitrogen–leaving group bond cleavage.

A method is now in hand to map the positions of transition states for imine-forming eliminations on the MOFJ energy surface. Rates of elimination for a group of NAS were measured by using a standard series of cyclic, secondary amine bases to obtain β and a series of arenesulfonate leaving groups to obtain $\beta_{lg}^{CH_3}$. The results are presented in Table VIII, and a MOFJ plot of the data is shown in Figure 5.[41]

Effect of β-Substituents on E1-like Transition States

The results indicate that substituents at the β-carbon have a significant effect on both the extent of proton removal and the amount of leaving-group loss. Alkyl substituents (entries 1–3, Table VIII) have E1-like transition states with little proton removal, but significant rupture of the nitrogen–leaving group bond.

(40) The use is restricted to arenesulfonates. Mesylate does not fit the same correlations as arenesulfonates, and halides most certainly would not. See: Crumrine, D. S.; Shankweiler, J. M.; Hoffman, R. V. *J. Org. Chem.* **1986**, *51*, 5013.

(41) Hoffman, R. V.; Shankweiler, J. M. *J. Am. Chem. Soc.* **1988**, *110*, 401∂.

Table IX
Transition-State Parameters β and $\beta_{lg}^{CH_3}$ for Base-Promoted, Imine-Forming Elimination Reactions

entry	substrate	base–solvent	β	$\beta_{lg}^{CH_3}$	ref
1	$C_6H_5CH_2NHOAs$	R_2NH–MeOH	0.10	0.57	29
2	$C_5H_{11}CH_2NHOAs$	R_2NH–TEW[a]	0.24	0.51	41
3	$C_6H_5CH_2NHOAs$	R_2NH–TEW[a]	0.30	0.42	41
4	$C_6H_5CH_2N(CH_3)OAs$	MeONa–MeOH	~0.25[b]	0.43	28
5	$C_6H_5CH_2N(CH_3)Cl$	Bu_2NH–MeCN	0.41	0.41[d]	22
6	$C_6H_5CH_2N(CH_3)Cl$	MeONa–MeOH	>0.41[c]	<0.41[d]	28

[a] TEW is 2.25 M aqueous THF–ethyl acetate (3:1). [b] Estimated by comparison of the deuterium isotope effect values from entries 2 and 3. [c] Estimated from deuterium isotope effect values. [d] Estimated from leaving group element effect values.

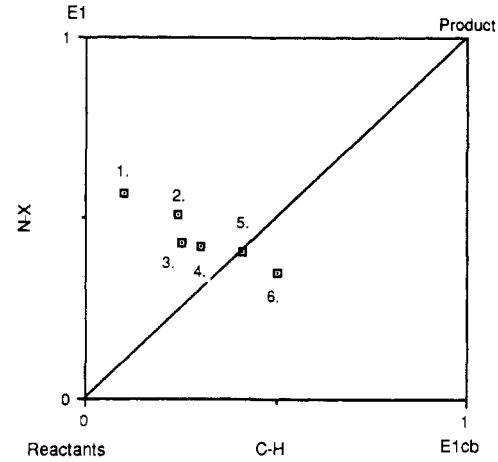


Figure 6. MOFJ diagram for imine-forming elimination reactions given in Table IX.

Inductive effects appear to play an insignificant role since one (entry 1) or two (entry 2) alkyl groups or an electron-withdrawing alkyl group (entry 3) all give transition states that are, within experimental error, identical. Aromatic groups produce a decided perpendicular shift in the E1cb direction (entries 4–6). Increased proton transfer and decreased leaving-group scission are clearly distinguishable for these substrates and probably result from resonance interaction of the developing charge with the aromatic ring. Inductive effects again are shown to be of little consequence when the ring substituent is varied from electron donating to electron withdrawing (entries 5 and 6, respectively). However, a p-nitrophenyl substituent (entry 7) gives a synchronous transition state with proton removal and leaving-group loss equally advanced. In this case, resonance stabilization of the developing negative charge is even greater, which causes an additional perpendicular shift.

Some noteworthy points are demonstrated in Figure 5. The first is that very significant changes in transition-state character are produced by structural variation: from E1-like to E2 central for eliminations from NASs. Second, inductive effects are of minor importance in the transition states, while resonance effects are quite effective in influencing the structure of the activated complexes. Finally, the transition states are located on the energy surface with fair certainty.

Factors That Influence the Structure of Imine-Forming Transition States

With the results for the NAS eliminations serving as reference points, it is possible to estimate the positions of transition states for other imine-forming eliminations.

From the data collected in Table IX, a spectrum of transition-state structure variations is readily evident. As shown in Figure 6, the elimination transition states vary from E1-like through E2 central toward E1cb-like. The transition-state position is influenced by both structural and environmental factors.

The effects of β-substituents differ depending upon the structure of the transition state. For *N*-chloramine eliminations which proceed via E2 central transition states, a β-alkyl substituent shifts the transition state toward E1-like and a β-aryl substituent shifts the transition state in the E1cb direction (Figure 1). For NAS eliminations which proceed through E1-like transition states, however, inductive effects of β-substituents are negligible and resonance effects are appreciable. A β-alkyl substituent does not change the structure of the transition state significantly, but a β-aryl substituent, which can stabilize the developing negative charge on the β-carbon by resonance, causes a shift in the E1cb direction with enhanced C_β–H bond rupture and diminished N–leaving group bond scission (Table IX). In both cases, the effects are perpendicular; parallel shifts are not apparent. Alkene-forming eliminations should be influenced in a similar fashion by variation of β-substituents. However, due to their fundamentally E1cb-like nature, the latter effect has not been observed.

Variation of the alkyl substituents on the α-nitrogen also produces changes in the activated complex. A bulky alkyl substituent hinders the approach of the base to the C_β–H bond, shifting the transition toward E1-like (Table IV). Except for large substituents, this steric effect is only modest.

Identity of the leaving group strongly affects the transition-state character of base-promoted, imine-forming elimination reactions. The most important factor is the strength of the nitrogen–leaving group bond. The leaving ability is found to be OAs > Br > Cl, which parallels the N_α–X bond strengths.[28] Better leaving groups give significantly more E1 character to the transition state (compare entries 4 and 6 in Table IX) by stabilizing the E1 corner of the MOFJ diagram. Similar arguments should hold for alkene-forming eliminations, keeping in mind that leaving-group abilities are Br > OAs > Cl, which parallel the C_α–X bond strengths. Since the differences in C_α–X bond strengths are considerably smaller than those of the corresponding N_α–X bonds, leaving-group effects should be smaller in alkene-forming eliminations.

Variation of the base–solvent combination is another factor that exerts a strong influence in imine-forming elimination reactions. As expected, stronger bases lead to more E1cb-like transition states (Table VI). The differences are rather small, although only a limited range of base strengths were examined. Of much greater importance is solvent polarity, particularly when the elimination reaction forms charged products from uncharged reactants. When neutral bases are used, the change to a more polar solvent produces a dramatic shift toward the E1 domain (compare entries 1 and 3 in Table IX). In some cases, a change to an E1 mechanism has been observed for imine-forming eliminations induced by neutral bases in a highly polar solvent. For anionic bases, less dramatic changes in transition-state structure are likely with variations of solvent polarity.

Conclusion

The study of base-promoted, imine-forming elimination reactions has led to methods for the systematic evaluation of factors that cause variations in transition-state structures. Valuable insight into the relative importance of structural and environmental factors has been obtained through the use of transition-state parameters. Development of methods to locate transition states in MOFJ diagrams allows changes in transition-state structures to be clearly described. The result is that base-promoted, imine-forming elimination reactions can be reasonably discussed and understood. As such, these reactions constitute an interesting and valuable model system, since the structure–reactivity insight gained here is directly applicable to other π-bond-forming elimination reactions.

This work was brought to fruition by the efforts of talented and enthusiastic students whose names appear in the references. We heartily applaud their contributions and their dedication. The research carried out at New Mexico State University was supported by the donors of the Petroleum Research Fund, administered by the American Chemical Society, and by the National Science Foundation. Research conducted at Texas Tech University was supported by the Robert A. Welch Foundation. The work completed at Korea University was supported by the Korea Science and Engineering Foundation, the Korea Research Foundation, and the Korea Ministry of Education.