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Reactions of *N*-Chloro-*N*-alkylbenzylamines with Amines in Acetonitrile. Origin of Steric Effect in Imine-Forming Elimination

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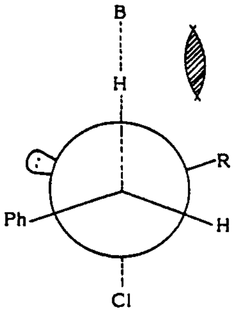
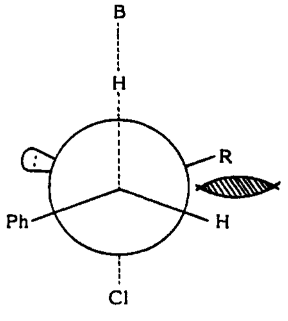
Reactions of *N*-chloro-*N*-alkylbenzylamines in which the alkyl group is Me, Et, *i*-Pr, *sec*-Bu, and *t*-Bu with $\mathrm{MeNH_2}$ and $\mathrm{Et_2NH}$ in MeCN have been studied kinetically. The eliminations are quantitative and regiospecific, producing only *N*-benzylidenealkylamines. The relative rates of elimination for Me/Et/*i*-Pr/*sec*-Bu/*t*-Bu alkyl substituents are 1/0.6/0.4/0.3/0.1 with $\mathrm{MeNH_2}$ and 1/0.5/0.3/0.2/0.03 with $\mathrm{Et_2NH}$, respectively. Comparison with published data reveals that Charton's $|\psi'|$ value for the imine-forming elimination decreases with the variation of the base-solvent from MeONa–MeOH to $\mathrm{MeNH_2}$–MeCN but increases when the base is changed from $\mathrm{MeNH_2}$ to $\mathrm{Et_2NH}$. For a given base, Hammett ρ and k_H/k_D values decrease and the ΔH^* and ΔS^* values increase with bulkier alkyl substituents. From these results, the origin of the steric effect in imine-forming elimination is attributed to the repulsive interaction between the alkyl group and the base in the transition state.

Recently we reported that the rate of elimination from *N*-chloro-*N*-alkylbenzylamines promoted by MeONa–MeOH decreased as the steric requirement of the *N*-alkyl group was increased.[1] The result has been attributed to the repulsive interaction between the *N*-alkyl group and the base in the transition state I. However, the possibility that the eclipsing interaction between the C_β–H and N_α–R bonds in the transition state II may also play an important role in the observed steric effect has not been rigorously ruled out.



I

or



II

Base-promoted imine-forming eliminations from *N*-haloamines are known to proceed by a normal E2 mechanism via an E2-central type of transition state with appreciable C_β–H and N_α–X bond cleavage and significant double-bond character.[2-6] Therefore, the C_β–H and N_α–R bonds must be partially eclipsed in the transition state. A bulkier R group would increase the eclipsing interaction between the two bonds and thus may hinder the formation of the partial double bond in the transition state. This would increase the energy of the transition state and retard the rate.

In order to determine which of these factors (I or II) may be more important in the alkyl group steric effect in imine-forming eliminations it seems necessary to conduct the reaction under conditions where the transition-state double-bond character and the base steric effect may be varied. Accordingly, we have investigated the reactions of *N*-chloro-*N*-alkylbenzylamines **1–5** with $\mathrm{MeNH_2}$ and $\mathrm{Et_2NH}$ in MeCN (eq 1).

$$\mathrm{XC_6H_4CL_2N(Cl)R} + \mathrm{MeNH_2}\ \text{or}\ \mathrm{Et_2NH} \xrightarrow{\mathrm{MeCN}} \mathrm{XC_6H_4CL{=}NR} \qquad (1)$$

1: R = Me
2: R = Et
3: R = *i*-Pr
4: R = *t*-Bu
5: R = *sec*-Bu

6a: X = H; L = H
b: X = H; L = D
c: X = *p*-$\mathrm{CH_3O}$; L = H
d: X = *m*-Br; L = H
e: X = *m*-$\mathrm{NO_2}$; L = H
f: X = *p*-$\mathrm{NO_2}$; L = H

It has been demonstrated that the change of base–solvent from MeONa–MeOH to $\mathrm{Bu_2NH}$–MeCN increases the transition-state double-bond character for elimination from **1** without much affecting the extent of C_β–H bond cleavage.[5] Since the $\mathrm{p}K_a$ values of $\mathrm{MeNH_3^+}$ and $\mathrm{Bu_2NH_2^+}$ in MeCN are nearly the same,[6] a similar increase in the transition-state double-bond character is anticipated with $\mathrm{MeNH_2}$–MeCN as the base–solvent system. Moreover, the steric requirements of $\mathrm{MeO^-}$ and $\mathrm{MeNH_2}$ are expected to be similar. Thus, a comparison of the Charton's $|\psi'|$ value[7,8-10] for the reactions of **1–5** with $\mathrm{MeNH_2}$ in MeCN with the existing data for the same substrates and MeONa–MeOH would provide a valuable insight into the effect of the transition-state double-bond character upon the steric effect. Furthermore, the base steric effect may also be determined by varying the base from $\mathrm{MeNH_2}$ to $\mathrm{Et_2NH}$. The results of these studies are now reported.

Results

N-Benzylidenealkylamines **6**, *N*-alkylbenzylamines, and *N*-chloro-*N*-alkylbenzylamines **1–5** were prepared as described before.[1-6] Reactions of **1–5** with $\mathrm{MeNH_2}$ and $\mathrm{Et_2NH}$ in MeCN produced only *N*-benzylidenealkylamine **6**. Excellent pseudo-first-order kinetic plots, which covered at least 2 half-lives (usually more than 3), were obtained. Pseudo-first-order rate constants were divided by the base concentration to provide second-order rate constant, which remained constant for 10-fold variations in base concen-

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[1] Cho, B. R.; Maeng, J. H.; Yoon, J. C.; Kim, T. R. *J. Org. Chem.* **1987**, *52*, 4753–4756.

[2] Bartsch, R. A.; Cho, B. R. *J. Org. Chem.* **1979**, *44*, 145–146.

[3] Bartsch, R. A.; Cho, B. R. *J. Am. Chem. Soc.* **1979**, *101*, 3587–3591.

[4] Cho, B. R.; Yoon, J. C.; Bartsch, R. A. *J. Org. Chem.* **1985**, *50*, 4943–4946.

[5] Cho, B. R.; Namgoong, S. K.; Bartsch, R. A. *J. Org. Chem.* **1986**, *51*, 1320–1324.

[6] Cho, B. R.; Namgoong, S. K.; Kim, T. R. *J. Chem. Soc., Perkin Trans. 2* **1987**, 853–856.

[7] Coetzee, J. F. *Prog. Phys. Org. Chem.* **1965**, *4*, 45–92.

[8] Charton, M. *J. Am. Chem. Soc.* **1975**, *97*, 1552–1556.

[9] Charton, M. *J. Am. Chem. Soc.* **1975**, *97*, 3694–3697.

[10] Charton, M. *J. Am. Chem. Soc.* **1975**, *97*, 6159–6161.

0022-3263/89/1954-2855$01.50/0

Table I. Rate Constants for Elimination from $XC_6H_4CL_2N(Cl)R$ Promoted by $MeNH_2$ in MeCN[a]

				10^3k,[b] M^{-1} s^{-1}			
entry	temp, °C	X	L	R = Me	R = Et	R = *i*-Pr	R = *t*-Bu
1[c]	25.0	H	H	3.75	2.24	1.62	0.447
2	35.0	H	H	5.98	3.14	2.46	0.970
3	45.0	H	H	8.19	5.12	4.23	1.48
4	25.0	H	D	0.493	0.339	0.306	0.140
5	25.0	*p*-CH_3O	H	2.16	1.24	0.816	0.377
6	25.0	*m*-Br	H	7.59	3.73	1.86	0.528
7	25.0	*m*-NO_2	H	13.2	8.14	3.49	0.984
8	25.0	*p*-NO_2	H	36.6	16.7	6.86	1.41

[a] $[MeNH_2] = (3.5 \times 10^{-2})–(3.5 \times 10^{-1})$ M; [substrate] = $(1.8–6.7) \times 10^{-5}$ M. [b] Estimated uncertainty, ±3%. [c] $k_2 = 9.46 \times 10^{-4}$ M^{-1} s^{-1} for R = *sec*-Bu.

Table II. Rate Constants for Elimination from $XC_6H_4CL_2N(Cl)R$ Promoted by Et_2NH in MeCN[a]

				10^3k,[b] M^{-1} s^{-1}			
entry	temp, °C	X	L	R = Me	R = Et	R = *i*-Pr	R = *t*-Bu
1[c]	25.0	H	H	7.40	3.52	1.91	0.217
2	35.0	H	H	11.0	5.70	3.21	0.399
3	45.0	H	H	17.3	8.71	5.26	0.813
4	25.0	H	D	0.954	0.852	0.487	0.140
5	25.0	*p*-CH_3O	H	4.75	2.03	1.25	0.188
6	25.0	*m*-Br	H	14.5	7.80	4.31	0.376
7	25.0	*m*-NO_2	H	28.0	13.5	8.67	0.522
8	25.0	*p*-NO_2	H	105	37.2	16.9	0.970

[a] $[Et_2NH] = (3.0 \times 10^{-3})–(3.0 \times 10^{-2})$ M; [substrate] = $(1.9–6.7) \times 10^{-5}$ M. [b] Estimated uncertainty, ±3%. [c] $k_2 = 1.71 \times 10^{-3}$ M^{-1} s^{-1} for R = *sec*-Bu.

Table III. Effect of Base-Solvent upon Imine-Forming Elimination from $ArCH_2N(Cl)CH_3$

	base–solvent		
	MeONa–MeOH[a]	Bu_2NH–MeCN[a]	$MeNH_2$–MeCN
pK_a	18.3[b]	18.3[c]	18.4[c]
ρ	1.58	0.96	0.83 ± 0.3
k_H/k_D	6.4	8.8	7.6
k_{Br}/k_{Cl}	15.8	24.1	
$\Delta H^{\ddagger}$, kcal/mol	14.2	7.6	6.8 ± 0.3
$\Delta S^{\ddagger}$, eu	−19.9	−45.1	−46.8 ± 2.2
$\Delta G^{\ddagger}$, kcal/mol	20.1	21.0	20.8 ± 1.0

[a] Reference 5. [b] Reference 14. [c] Reference 7.

trations. The rate constants for eliminations from **1**–**5** promoted by $MeNH_2$ and Et_2NH in MeCN are summarized in Tables I and II. Relative rates of elimination for **1a**/**2a**/**3a**/**5a**/**4a** are 1/0.6/0.4/0.3/0.1 with $MeNH_2$ and 1/0.5/0.3/0.2/0.03 with Et_2NH, respectively.

The influence of *N*-alkyl groups upon the rates correlated reasonably well with the Charton's equation using ν' values.[1,8–10] The Charton's plots for elimination from **1a**–**5a** promoted by $MeNH_2$ and Et_2NH in MeCN are compared with that for the same substrate and MeONa-MeOH in Figure 1.

Rates of elimination from **1a**–**4a** promoted by $MeNH_2$ and Et_2NH in MeCN were measured at three temperature spanning 20 °C. The Arrhenius plots were linear with excellent correlation. Calculated enthalpies and entropies of activation are presented in Tables III–V.

The influence of aryl substituents upon elimination rates correlated satisfactorily with the Hammett equation using σ^- values (Figures 2 and 3). Hammett ρ values are given in Tables III–V.

From the rate coefficients for eliminations from **1a**–**4a** and their deuterated analogues **1b**–**4b** at 25.0 °C, primary deuterium isotope effect values were calculated. The values are listed in Tables III–V.

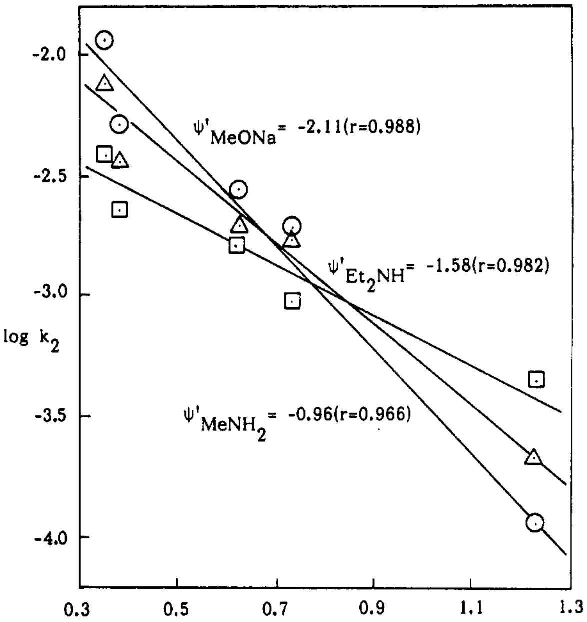

Figure 1. Charton's plots for base-promoted eliminations from $ArCH_2N(Cl)R$; base–solvents are the following: MeONa–MeOH (⊙), Et_2NH–MeCN (▲), and $MeNH_2$–MeCN (▣).

Table IV. Transition-State Parameters for Eliminations from $ArCH_2N(Cl)R$ Promoted by $MeNH_2$ in MeCN

R	ρ	k_H/k_D	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
Me	0.83 ± 0.03	7.6	6.8 ± 0.3	−46.8 ± 2.2
Et	0.77 ± 0.05	6.6	7.2 ± 0.5	−46.6 ± 3.2
i-Pr	0.60 ± 0.07	5.3	8.4 ± 0.4	−43.0 ± 2.7
t-Bu	0.41 ± 0.05	3.2	10.7 ± 0.7	−37.7 ± 3.5

Table V. Transition-State Parameters for Eliminations from $ArCH_2N(Cl)R$ Promoted by Et_2NH in MeCN

R	ρ	k_H/k_D	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
Me	0.92 ± 0.04	7.8	7.4 ± 0.2	−43.4 ± 1.5
Et	0.86 ± 0.03	4.1	7.9 ± 0.1	−43.0 ± 0.5
i-Pr	0.80 ± 0.05	3.9	8.9 ± 0.1	−40.9 ± 0.1
t-Bu	0.51 ± 0.02	1.6	11.8 ± 0.4	−35.5 ± 2.6

Discussion

Transition State for Elimination from 1 Promoted

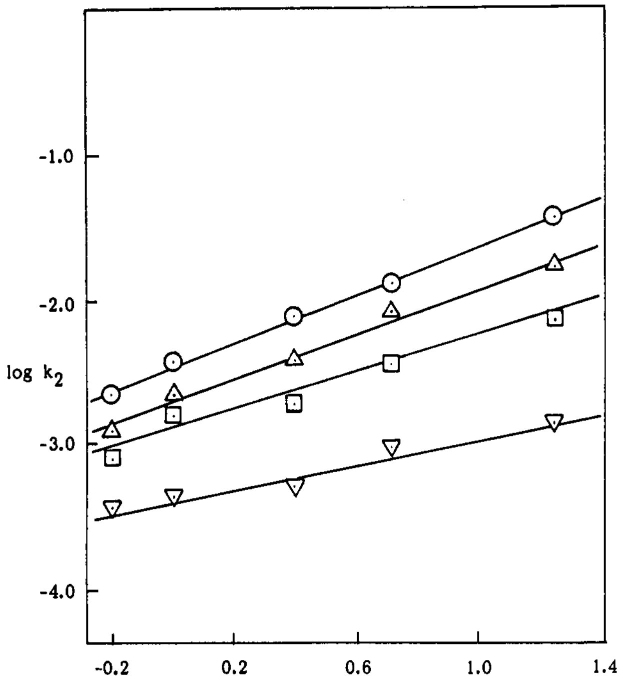

Figure 2. Hammett plots for eliminations from $ArCH_2N(Cl)R$ promoted by $MeNH_2$ in MeCN; R = Me, Et, *i*-Pr, and *t*-Bu in descending order.

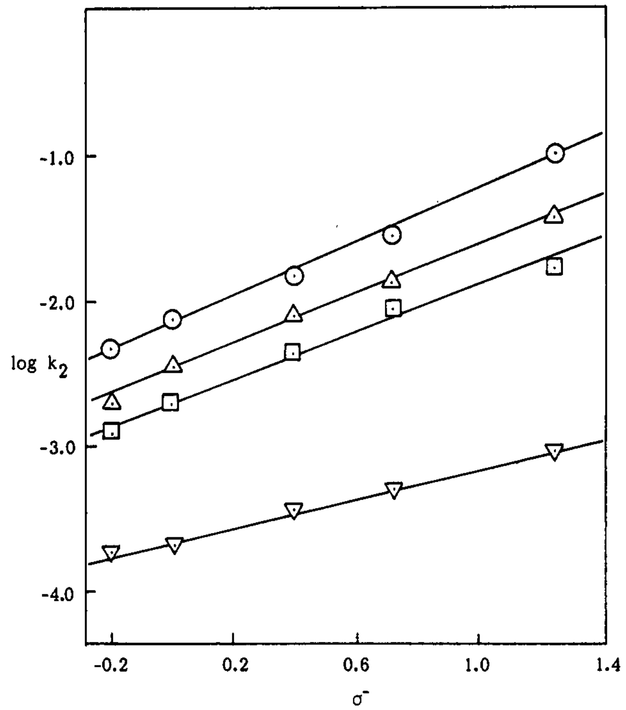

Figure 3. Hammett plots for eliminations from $ArCH_2N(Cl)R$ promoted by Et_2NH in MeCN; R = Me, Et, *i*-Pr, and *t*-Bu in descending order.

by $MeNH_2$–MeCN. Earlier we reported that the reactions of **1**–**5** with MeONa–MeOH and **1** with R_2NH and Et_3N in MeCN proceed by a normal E2 mechanism.[1-6] The results of kinetic investigation and control experiments reveal that the reactions of **1**–**5** with $MeNH_2$ and Et_2NH in MeCN also proceed by the same E2 mechanism. Since **1**–**5** were stable in MeCN and the reactions exhibited second-order kinetics, all except bimolecular pathways can be ruled out.[11] Although the element effect of the leaving group could not be determined because of the competing substitution reaction on *N*-bromoamine,[4] an Elcb mechanism can be negated by the similarities in the transition-state parameters to those obtained for the E2 reactions of the same substrates under similar conditions.[5,6]

The transition-state parameters for base-promoted eliminations from **1** changed significantly when the base–solvent was changed from MeONa–MeOH to amine–MeCN but remained nearly the same when the amine base was changed from Bu_2NH to $MeNH_2$ (Table III). Previously the change of the transition-state parameters with the variation of the base–solvent from MeONa–MeOH to Bu_2NH–MeCN was interpreted with similar extent of proton transfer, decreased carbanionic character, and increased N–Cl bond cleavage and π-bond formation in the transition state for the Bu_2NH-promoted eliminations.[5] Since the transition-state parameters are nearly the same for both amine bases, the structures of the transition states can also be assumed to be similar for both reactions. Thus it appears that the reaction of **1** with $MeNH_2$ in MeCN proceeds through E2-central type of transition state with significant C_β–H bond cleavage, little carbanionic character, and well-developed double-bond character.

Origin of Steric Effect in Imine-Forming Elimination. The present study was undertaken to determine the origin of the steric effect in imine-forming eliminations from **1**–**5**. As mentioned above, there are two possibilities by which the alkyl group steric effect may operate in these reactions. If the repulsive interaction between the base and the alkyl group (I) were the dominant factor of the steric effect, the susceptibility of the reaction rate to the alkyl group steric effect, as represented by Charton's $|\psi'|$ value,[1,8-10] is expected to decrease as the transition-state double-bond character increases, because the base and alkyl group will be further away in the transition state under such condition. However, the $|\psi'|$ value would increase with increasing base steric effect because a bulkier base would increase the repulsive interaction between the base and the alkyl group in the transition state. On the other hand, if the eclipsing interaction (II) were more important, the $|\psi'|$ value is anticipated to increase substantially with the increase in the transition-state double-bond character but increase only slightly with a bulkier base.

To determine which of these factors may be more important we have measured the Charton's $|\psi|$ values for the reactions of **1**–**5** and $MeNH_2$ and Et_2NH (Figure 1). The $|\psi'|$ value decreased from 2.11 to 0.96 when the base–solvent was changed from MeONa–MeOH to $MeNH_2$–MeCN but increased from 0.96 to 1.58 with the variation of the amine base from $MeNH_2$ to Et_2NH. Thus the susceptibility of the reaction to the alkyl group steric effect decreases substantially with increasing transition-state double-bond character but increases significantly with a bulkier base. These results clearly indicate that the steric effects observed in the eliminations from **1**–**5** results from the repulsive interaction between the base and *N*-alkyl group in the transition state (I).

The change of the transition-state parameters with the variations of *N*-alkyl group and the base is consistent with this conclusion. For a given base the ρ and k_H/k_D values decreased and the $\Delta H^\ddagger$ and $\Delta S^\ddagger$ values increased with increasing substrate steric effect (Tables IV and V). If a bulky alkyl substituent hinders the approach of the base to the C_β–H bond in the transition state I, the extent of

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[11] Cockerill, A. F.; Harrison, R. G. *The Chemistry of Double-Bonded Functional Groups*, Patai, S., Ed.; Wiley-Interscience: New York, 1977; Supplement A, Part 1, p 725.

C_β–H bond cleavage and negative charge development on the benzylic carbon are anticipated to decrease. This would predict that the ρ and k_H/k_D values should decrease with a bulkier *N*-alkyl group, as observed.[1,12] On the other hand, the $\Delta H^\ddagger$ and $\Delta S^\ddagger$ values are expected to increase because less of the base–proton bond and the π-bond will be formed in the transition state, and the transition state will be less associated with respect to base–proton bond.[1]

When the base was changed from $MeNH_2$ to Et_2NH the Hammett ρ, $\Delta H^\ddagger$, and $\Delta S^\ddagger$ values remained nearly within experimental error, but the k_H/k_D values for **2–4** decreased slightly (Table IV and V). Since Et_2NH is bulkier than $MeNH_2$ it would be more difficult to approach the C_β–H bond, decreasing the extent of C_β–H bond cleavage in the transition state.[13] Moreover, this effect would become more important for a sterically more hindered substrate. Therefore, the smaller k_H/k_D values for **2–4** with Et_2NH as the base undoubtedly result from the base steric effect. It should be noted, however, that the structure of the imine-forming transition state is relatively insensitive to the variation of the amine bases, despite the large change in the base steric effect.

The present results reveal that the origin of the steric effect in imine-forming elimination is the repulsive interaction between the base and the *N*-alkyl group in the transition state I. A bulky alkyl group appears to hinder the approach of the base to the C_β–H bond to decrease the extent of C_β–H bond cleavage and negative charge development in the transition state.

Experimental Section

Materials. *N*-Benzylidenealylamine **6**, *N*-alkylbenzylamines, and *N*-chloro-*N*-alkylbenzylamines **1–5** were either available from previous work or prepared as before.[1-6] Reagent grade acetonitrile, $MeNH_2$, and Et_2NH were fractionally distilled from CaH_2. The MeCN solution of amine was prepared by adding appropriate amounts of amine to MeCN.

Kinetic Studies of Eliminations from 1–5. Kinetic studies of eliminations from **1–5** were carried out as before[1-6] by using a Cary 170 or Perkin-Elmer 552 UV–vis spectrophotometer with thermostated cuvette holders. The pseudo-first-order rate constant was divided by the base concentration to afford the second-order rate constant, k_2.

Product Studies of Reactions of 1–5 with Amine–MeCN. For reactions of **1–5** with $MeNH_2$ or Et_2NH in MeCN, the absorbance of infinity samples from the kinetic reactions were compared with those of authentic samples of **6**. Based upon the starting benzylalkylamines, the yields of **6** were 84–99%.

The products of reactions of **1a** with $MeNH_2$ and Et_2NH in MeCN were identified by using more concentrated solutions and gas chromatographic analysis outlined previously.[5] *N*-Benzylidenemethylamine was obtained as the only product in 95–97% yields with both amine bases.[5]

Control Experiment. The stability of *N*-chloroamines and *N*-benzylidenealkylamines under the experimental conditions were demonstrated by the previously used method.

Acknowledgment. This investigation was supported by grants from Korea Science and Engineering Foundation and Korea Ministry of Education.

Registry No. $C_6H_5CH_2N(Cl)$*sec*-Bu, 120332-04-9; $C_6H_5CH_2N(Cl)Me$, 3555-71-3; $C_6H_5CH_2N(Cl)Et$, 110079-23-7; $C_6H_5CH_2N(Cl)Pr$-*i*, 110079-24-8; $C_6H_5CH_2N(Cl)Bu$-*t*, 33863-73-9; CH_3O-*p*-$C_6H_4CH_2N(Cl)Me$, 70972-89-3; CH_3O-*p*-$C_6H_4CH_2N(Cl)Et$, 110079-25-9; CH_3O-*p*-$C_6H_4CH_i$NnCl)Pr-*i*, 110079-26-0; CH_3O-*p*-$C_6H_4CH_2N(Cl)Bu$-*t*, 110079-27-1; Br-*m*-$C_6H_4CH_2N(Cl)Me$, 70972-94-0; Br-*m*-$C_6H_4CH_2N(Cl)Et$, 110079-28-2; Br-*m*-$C_6H_4CH_2N(Cl)Pr$-*i*, 110079-29-3; Br-*m*-$C_6H_4CH_2N(Cl)Bu$-*t*, 110079-30-6; NO_2-*m*-$C_6H_4CH_2N(Cl)Me$, 70972-96-2; NO_2-*m*-$C_6H_4CH_2N(Cl)Et$, 110079-31-7; NO_2-*m*-C_6H_4CH2N(Cl)Pr-*i*, 110079-32-8; NO_2-*m*-$C_6H_4CH_2N(Cl)Bu$-*t*, 110079-33-9; NO_2-*p*-$C_6H_4CH_2N(Cl)Me$, 70972-95-1; NO_2-*p*-$C_6H_4CH_2N(Cl)Et$, 110079-34-0; NO_2-*p*-$C_6H_4CH_2N(Cl)Pr$-*i*, 110079-35-1; NO_2-*p*-$C_6H_4CH_2N(Cl)Bu$-*t*, 110079-36-2; $MeNH_2$, 74-89-5; Et_2NH, 109-89-7; D_2, 7782-39-0.

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(12) Smith, P. J. *Isotopes in Organic Chemistry*; Buncel, E., Lee, C. C., Eds.; Elsevier: Amsterdam, 1976; pp 239–241.

(13) The pK_a value of $Et_2NH_2^+$ is greater than that of $MeNH_3^+$ by 0.3 pK_a units.[7] The faster rate of elimination from **1–3** with Et_2NH apparently results from its greater basicity. Although the increased ρ value with Et_2NH as the promoting base may also be explained with the increased basicity, the difference is too small to suggest appreciable changes in the transition state carbanionic character.

(14) Rochester, C. H.; Rossall, B. *Trans. Faraday Soc.* **1969**, *65*, 1004–1013.