Study on the Effect of the Structure of the Leaving Group in the E1cb Mechanism of Base-Promoted β-Elimination Reactions from *N*-[2-(*p*-Nitrophenyl)ethyl]alkylammonium Ions

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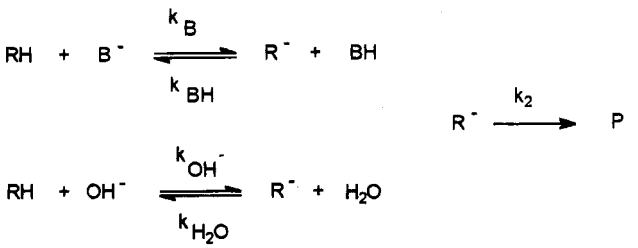
Studies of acid–base catalysis, H/D exchange, and solvent isotope effect on the β-elimination reactions with formation of *p*-nitrostyrene in acetohydroxamate/acetohydroxamic acid buffers at pH 9.05, H_2O, μ = 1 M KCl, 25 °C, from *N*-[2-(*p*-nitrophenyl)ethyl]alkylammonium ions with different leaving groups, such as *N*-methylpyrrolidine **1**, *N*-ethylpyrrolidine **2**, *N*-isopropylpyrrolidine **3**, *N*-methylpiperidine **4**, *N*-isopropylpiperidine **5**, and *N*-methylazepane **6**, show a change from a partially reversible E1cb mechanism with **1**, **2**, and **4** to an irreversible E1cb mechanism with **3**, **5**, and **6**. The change in the rate-determining step is related to the increased steric requirement of the leaving group. A steric acceleration from the carbanion intermediate to product step is proposed.

The β-phenylethyl system has played an important role in elucidating the mechanisms of elimination reactions.[1] It has been shown[2,3] that the β-elimination reaction from *N*-[2-(*p*-nitrophenyl)ethyl]alkylammonium ions induced by $CH_3CONHO^-/CH_3CONHOH$ buffers with formation of *p*-nitrostyrene proceeds by the E1cb mechanism, as shown in Scheme 1. In order to obtain information on

Scheme 1

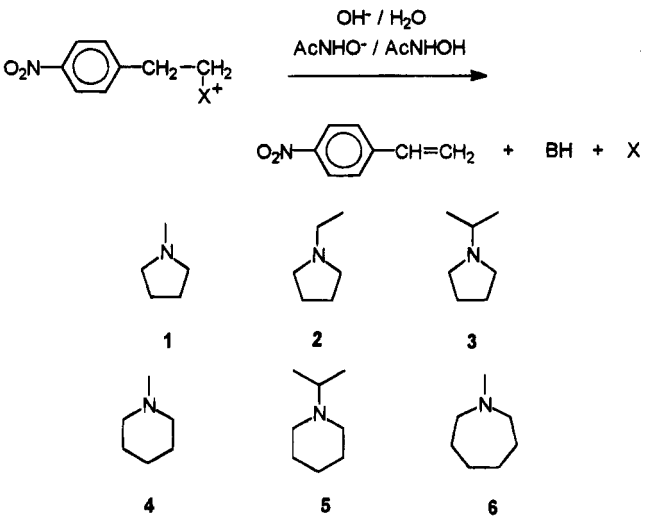


the relationship between changes in the structure of the leaving group and the mechanism of the reaction, we have studied the process of Scheme 2.

Results and Discussion

Acid–base catalysis was studied by following the formation of *p*-nitrostyrene at 336 nm (initial rates), 25 °C, in $CH_3CONHO^-/CH_3CONHOH$ buffers, pH = 9.05, H_2O, μ = 1 M KCl. The k_{obs} (s^{-1}) was calculated from the $A_t = A_0 + k_{obs}(A_\infty - A_0)t$.[2,4] The plots of k_{obs} (s^{-1}) against [$AcNHO^-$] showed curvature with 1-methyl-1-[2-(4-nitrophenyl)ethyl]pyrrolidinium ion (**1**),1-ethyl-1-[2-(4-nitrophenyl)ethyl]pyrrolidinium ion (**2**), and 1-methyl-1-[2-(4-nitrophenyl)ethyl]piperidinium ion (**4**). With 1-isopropyl-1-[2-(4-nitrophenyl)ethyl]pyrrolidinium ion (**3**), 1-isopropyl-1-[2-(4-nitrophenyl)ethyl]piperidinium ion (**5**) and 1-methyl-1-[2-(4-nitrophenyl)ethyl]azepanium ion (**6**) linearity, corresponding to general base catalysis, was observed (Figures 1 and 2).

Scheme 2



The curvatures are consistent with a partially reversible E1cb mechanism in which the term k_{BH}[BH], related to the protonation of the carbanion intermediate by BH, competes with k_2, the rate constant for the expulsion of the leaving group (LG) from the intermediate. In this system the following equations hold.[2]

$$k_{obs} = k_2 \frac{k_{OH^-}[OH^-] + k_B[B]}{k_{H_2O} + k_{BH}[BH] + k_2} \quad (1)$$

$$\frac{k_{obs} - k_0}{[BH]} \frac{k_{H_2O} + k_2}{k_2} = \frac{[B]}{[BH]} k_B - k_{obs} \frac{k_{BH}}{k_2} \quad (2)$$

$$k_\infty = \frac{k_B}{k_{BH}} k_2 \frac{[B]}{[BH]} \quad (3)$$

$$\frac{k'_0 + k_\infty}{k_\infty} = \frac{k_{H_2O} + k_2}{k_2} \quad (4)$$

$$k'_0 = k_{OH^-}[OH^-] \quad (5)$$

$$k_0 = k_{OH}[OH^-] = k_{OH^-}[OH^-] \frac{k_2}{k_{H_2O} + k_2} \quad (6)$$

B = $AcNOH^-$; BH = AcNHOH

By a first approximation of the ratio $(k_{H_2O} + k_2)/k_2$ =

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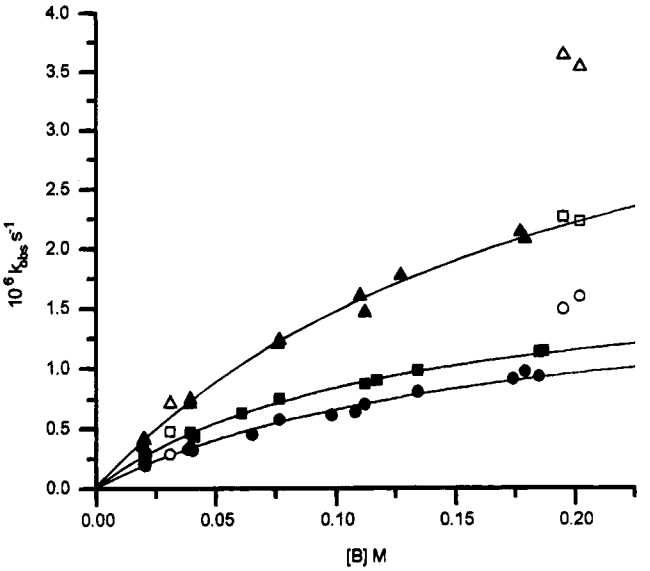


Figure 1. Dependence of the k_{obs} (s^{-1}) for compounds **1**, **2**, and **4** on [AcNHO$^-$]. Solid symbols: $k_{obs}(H_2O)$. Open symbols: $k_{obs}(D_2O)$. Solid lines are calculated from eq 2 and the appropiate rate constants from Table 1. Circle: substrate **1**. Square: substrate **2**. Triangle: substrate **4**.

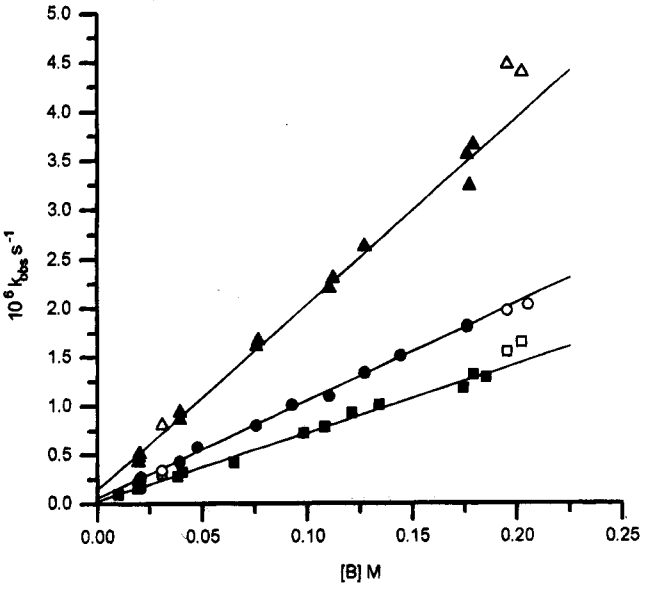


Figure 2. Dependence of the k_{obs} (s^{-1}) for compounds **3**, **5**, and **6** on [AcNHO$^-$]. Solid symbols: $k_{obs}(H_2O)$. Open symbols: $k_{obs}(D_2O)$. Solid lines are from linear regression analysis. Square: substrate **3**. Circle: substrate **5**. Triangle: substrate (**6**).

1, k_B and k_{BH}/k_2 are evaluated from the intercept and the slope of the plot of $(k_{obs} - k_0)/[BH]$ against k_{obs}, eq 2. Using eq 3, a value for k_∞ (k_{obs} at [buffer] that makes the deprotonation step completely reversible) can be estimated. With the approximation that $k_0 = k'_0$, a value for $(k_{H_2O} + k_2)/k_2$ was calculated from eq 4 and used in eq 2 to obtain better values of k_B, k_{BH}/k_2, and k_∞. Following an iterative procedure until convergence allows the final values of k_B, k_{BH}/k_2, k_2/k_{H_2O}, and k_∞ to be calculated. In our case, no more than two iterations were necessary. The calculated rate constants are reported in Table 1.

The k_{BH}/k_2 ratio decreased from **1** to **3** (in which general base catalysis was observed) by a factor of >4 (from the absence of curvature the k_{BH}/k_2 ratio was estimated to be <1 for **3**). The observed variation is consistent with a change from a partially reversible E1cb mechanism for compounds **1** and **2** to an irreversible E1cb mechanism for compound **3**. It is to be noted that the pK_a of the leaving group increases from **1**, $pK_a(LG) = 10.77$, to **3**, $pK_a(LG) = 11.25$. An increase in the k_{BH}/k_2 ratio is expected[2] with the associated increase in the pK_a of the leaving group. In our case the observed decrease in the k_{BH}/k_2 ratio from **1** to **3** can then be related to the increased steric requirements of the LG. The results from a study of H/D exchange are consistent with the conclusion of a change in the rate-determining step. When the elimination was carried out in D_2O with acetohydroxamate/acetohydroxamic acid buffers, compounds **1** and **2** incorporated deuterium in the β-position, while H/D exchange was not observed with compound **3**. (The degree of deuterium incorporation was measured on the *p*-nitrostyrene, see the Experimental Section.) In a typical experiment, **1** was reacted with buffers in D_2O at 42 °C, [B] = 0.381 M, and [BD] = 0.589 M. When the *p*-nitrostyrene product was 55% of the starting substrate, the H/D exchange was 12%. For compound **2**, at 42 °C, [B] = 0.352 M, and [BD] = 0.453 M, at 67% of *p*-nitrostyrene formed, the H/D exchange was 10%. Similar experiments carried out with **3** showed no H/D exchange. Results from a study of solvent isotope effect are also consistent. Carrying out the elimination reactions in buffers in D_2O, the $k_{obs}(D_2O)$ were significantly higher than the $k_{obs}(H_2O)$ at the same [B] for **1** and **2**, while for **3** the $k_{obs}(D_2O)$ values substantially fit a linear correlation for a general base catalysis, (Figures 1 and 2). This is in agreement with a partially reversible E1cb mechanism for **1** and **2** and an irreversible E1cb mechanism for **3**. In fact, the term related to the protonation of the intermediate carbanion, $k_{BH}[BH]$, is lower in D_2O due to the presence of a primary deuterium kinetic isotopic effect that makes $k_{BD} < k_{BH}$. In a partially reversible E1cb mechanism, this term is significant in eq 1, and an increase in $k_{obs}(D_2O)$ with respect to $k_{obs}(H_2O)$ is expected. The effect is greater at higher buffer concentrations because the $k_{BH}[BH]$ term is larger.

Table 1. Rate Constants for the β-Elimination Reaction from Compounds 1–6 (in acetohydroxamate/acetohydroxamic acid buffers, H_2O, pH = 9.05, μ = 1 M KCl, 25 °C)

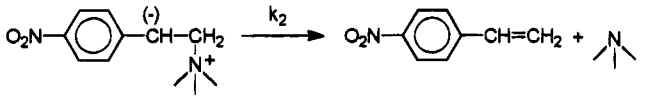
substrate	$10^3 k_{OH}$[a] (M^{-1} s^{-1})	$10k_B$ (M^{-1} s^{-1})	k_{BH}/k_2 (M^{-1})	k_2/k_{H_2O}	$10^6 k_\infty$ (s^{-1})	$pK_a(LG)$[b]
1	0.67	1.55	3.67	156	1.81	10.77
2	0.48	1.05	2.58	213	1.75	11.06
3	0.34	0.702[c]	<1			11.25
4	1.06	2.19	2.12	238	4.43	10.53
5	0.49	1.01[c]	<1			10.92
6	1.20	1.92[c]	<1			10.88

[a] Observed second-order rate constant for the elimination reaction in KOH (0.1 M), μ = 1 M KCl, 25 °C. [b] At 25 °C, H_2O, μ = 1 M KCl; the error on $pK_a(LG)$ is ±0.05. [c] Slope of the line from linear regression analysis of the plot k_{obs} (s^{-1}) vs [B], Figure 2.

The structural change from **4** to **5** is similar to that from **1** to **3**. A methyl group in the leaving group is substituted by an isopropyl group. The study of acid–base catalysis and solvent isotope effect (Figures 1 and 2, data of Table 1) shows that, also in this case, there is a change from a partially reversible E1cb mechanism with **4** to an irreversible E1cb mechanism with **5**. The decrease in the k_{BH}/k_2 ratio can also be related to the increased steric requirement in the leaving group as the pK_a of the LG increases from **4** to **5** (Table 1).

Finally, a comparison of the k_{BH}/k_2 ratios of substrates **1**, **4**, and **6** allows evaluation of the effect of leaving group ring size. It can be seen from Figures 1 and 2 and the data of Table 1 that the k_{BH}/k_2 ratio decreases from **1** to **4** to **6**. In this series too, there is a change from a partially reversible E1cb mechanism for **1** and **4** to an irreversible E1cb mechanism for **6**, as shown by the acid–base catalysis and solvent isotope effect studies. The small increase in the pK_a of the LG (Table 1) from **1** to **6** indicates that the observed variation in mechanism is not related to the electronic effect but to a steric effect.

In conclusion, this system shows a decrease in the k_{BH}/k_2 value related to an increased steric requirement of the leaving group. This decrease in the k_{BH}/k_2 ratio can be traced back to an increase in the k_2 rate constant, since the k_{BH} rate constant is not expected to be strongly affected by this structural variation of the leaving group in the β-position with respect to the site of protonation of the intermediate by AcNHOH. In fact variations on the electronic effect of the leaving group have little influence on the k_{BH} rate constant,[2] and the increased steric requirements of the leaving group from **1** to **3** and from **4** to **5** have a limited effect on the k_{OH} and k_B rate constants (from Table 1, it can be seen that the total variation in k_{OH} and k_B is a factor of ca. 2, and it is the sum of the electronic and steric contributions). We suggest that the increase in the k_2 rate constant can be



explained by a relief of steric strain (this effect has also been reported in S_N1-type reactions[5,6] and β-elimination reactions[7]), since the steric requirements on the intermediate are larger than in the products, and/or by a different solvation[8] of the intermediate.

Experimental Section

Materials. Glass-distilled and freshly boiled water was used throughout. Reagent grade potassium chloride, 2-(*p*-nitrophenyl)ethyl bromide, and acetohydroxamic acid (Aldrich) were used without further purification. *p*-Nitrostyrene was prepared and purified as previously described.[4]

1-[2-(4-Nitrophenyl)ethyl]pyrrolidine (7). A mixture of (*p*-nitrophenyl)ethyl bromide (2.1 g, 9.13 mmol) and pyrrolidine (6.6 g, 92 mmol) in 2 mL of acetonitrile was kept at 45 °C for 2 h and at room temperature for 8 h. The reaction mixture was hydrolyzed with potassium carbonate and the amine extracted with Et_2O and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the resulting crude product was purified by crystallization with petroleum ether at −20 °C to give 1.83 g (8.3 mmol) of yellow solid: mp 43 °C; ^{1}H-NMR (80 MHz, $CDCl_3$) δ 1.8 (m, 4H), 2.7 (m, 8H), 7.25–8.3 (m, AA'BB' system, 4H); MS *m*/*z* 220 (M^+), 84 (100). Anal. Calcd: C, 65.43; H, 7.30; N, 12.72. Found: C, 65.42; H, 7.53; N, 12.50.

1-[2-(4-Nitrophenyl)ethyl]piperidine (8). The procedure for the synthesis of the amine **8** was the same as the one for amine **7**. From 4 g (17 mmol) of (*p*-nitrophenyl)ethyl bromide and 13 g (153 mmol) of piperidine in 10 mL of acetonitrile was obtained 2.5 g of crude product, and then it was chromatographed on silica gel (eluent Et_2O/CH_3OH, 85/15) to give 1.2 g (5.1 mmol) of amine **8** as a yellow oil: ^{1}H-NMR (80 MHz, $CDCl_3$) δ 1.6 (m, 6H), 2.7 (m, 8H), 7.25 −8.4 (m, AA'B' system, 4H); MS *m*/*z* 234 (M^+), 98 (100). Anal. Calcd: C, 66.64; H, 7.74; N, 11.96. Found: C, 66.56; H, 7.75; N, 11.86.

1-[2-(4-Nitrophenyl)ethyl]azepane (9). The procedure for the synthesis of the amine **9** was the same as the one for amine **8**. From 3.6 g (15.6 mmol) of (*p*-nitrophenyl)ethyl bromide and 18 g (180 mmol) of azepane was obtained 1.2 g (4.8 mmol) of amine **9** as a yellow oil: ^{1}H-NMR (80 MHz, $CDCl_3$) δ 1.6 (m, 8H), 2.7 (m, 8H), 7.25–8.3 (m, AA'BB' system 4H); MS *m*/*z* 248 (M^+), 112 (100). Anal. Calcd: C, 67.72; H, 8.12; N, 11.28. Found: C, 67.88; H, 8.03; N, 11.19.

1-Ethylpyrrolidine (10). An equimolar amount of ethyl bromide was added dropwise to a solution of pyrrolidine in methanol keeping the temperature at 20 °C by an ice–water bath. The mixture was hydrolyzed with potassium carbonate, extracted with ether, and dried over Na_2SO_4. The solution was fractionally distilled and the fraction with bp 104–105 °C[9] was collected. **10**: ^{1}H-NMR (80 MHz, $CDCl_3$) δ 1.12 (t, J = 7 Hz, 3H), 1.78 (m, 4H), 2.50 (m, 6H); MS *m*/*z* 99 (M^+), 84 (100).

1-Isopropylpyrrolidine (11). The procedure for the synthesis of amine **11** was the same as the one for amine **10**. Isopropyl iodide was used as reagent. **11**: bp 112–113 °C;[10] ^{1}H-NMR (80 MHz, $CDCl_3$) δ 1.1 (d, J = 7 Hz, 6H), 1.85 (m, 4H), 2.4 (m, 1H), 2.65 (m, 4H); MS *m*/*z* 113 (M^+), 98 (100).

1-Isopropylpiperidine (12). The procedure for the synthesis of amine **12** was the same as the one for amine **10**. Isopropyl iodide and piperidine were used as reagents. **12**: bp 149–150 °C;[11] ^{1}H-NMR (80 MHz, $CDCl_3$) δ 1.05 (d, J = 7 Hz, 6H), 1.6 (m, 6H), 2.4 (m, 4H), 2.7 (m, 1H); MS *m*/*z* 127 (M^+), 112 (100).

1-Methylazepane (13). The procedure for the synthesis of amine **13** was the same as the one for amine **10**. Methyl iodide and azepane were used as reagents. However, in this case the fraction distilled at 136 °C was a mixture of azepane and amine **13**. Separation of the secondary and tertiary amine was accomplished by standard Hinsberg procedure. The amine **13** was purified by distillation: bp 138 °C;[12] ^{1}H-NMR (80 MHz, $CDCl_3$) δ 1.6 (m, 8H), 2.3 (s, 3H), 2.55 (m, 4H); MS *m*/*z* 113 (M^+), 84 (100).

1-Methyl-1-[2-(4-nitrophenyl)ethyl]pyrolidinium iodide (1). An excess of methyl iodide was added to a solution of amine **7** (600 mg, 2.7 mmol) in 5 mL of acetonitrile. The mixture was stirred for 2 h at 40 °C. The reaction mixture was then evaporated to dryness and the solid washed with Et_2O. The salt was dissolved in 2 mL of ethanol and precipitated with Et_2O. The solid was washed with Et_2O and crystallized twice from 2-propanol–ethanol at −20 °C to give salt **1**, 250 mg (0.69 mmol): mp 123–133 °C dec; ^{1}H-NMR (80 MHz, D_2O) δ 2.1 (m, 4H), 3.0 (s, 3H), 3.5 (m, 8H), 7.35–8.15 (m, AA'BB' system, 4H). Anal. Calcd: C, 43.11; H, 5.29; N, 7.73. Found: C, 42.98; H, 5.40; N, 7.82.

1-Ethyl-1-[2-(4-nitrophenyl)ethyl]pyrrolidinium Bromide (2). The procedure for the synthesis of salt **2** was the same as the one for salt **1**. From 760 mg (3.5 mmol) of amine **7** and an excess of ethyl bromide was obtained 290 mg (0.88 mmol) of salt **2**. The salt was crystallized from 2-propanol at −20 °C: mp 119–129 °C dec; ^{1}H-NMR (80 MHz, D_2O) δ 1.3 (t, 3H), 2.1 (m, 4H), 3.35 (m, 10H), 7.35–8.15 (m, AA'BB' system, 4H). Anal. Calcd: C, 51.07; H, 6.43; N, 8.51. Found: C, 51.17; H, 6.48; N, 8.36.

1-Isopropyl-1-[2-(4-nitrophenyl)ethyl]pyrrolidinium Iodide (3). An excess of isopropyl iodide was added to a solution of amine **7** (1 g, 4.5 mmol) in 5 mL of acetonitrile. The reaction mixture was refluxed for 5 h, and then evaporated to dryness. The residual was washed with Et_2O, dissolved in 2 mL of ethanol, and precipitated with Et_2O. The solid was treated with hot 2-propanol. The undissolved solid was crystallized from 2-propanol at room temperature. A second crystallization from 2-propanol–ethanol at room temperature gave 200 mg

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(0.51mmol) of **3**: mp 185–189 °C dec; ^{1}H-NMR (80 MHz, D_2O) δ 1.3 (d, J = 6 Hz, 6H), 2.1 (m, 4H), 3.1 (m, 2H), 3.5 (m, 6H), 3.8 (m, 1H), 7.35–8.15 (m, AA'BB' system, 4H). Anal. Calcd: C, 46.16; H, 5.94; N, 7.18. Found: C, 46.12; H, 5.85; N, 7.32.

1-Methyl-1-[2-(4-nitrophenyl)ethyl]piperidinium Iodide (4). The procedure for the synthesis of salt **4** was the same as the one for salt **1**. From 650 mg (3 mmol) of amine **8** and an excess of methyl iodide was obtained 500 mg (1.3 mmol) of **4**. The salt was crystallized from 2-propanol–ethanol at −20 °C: mp 167–170 °C dec; ^{1}H-NMR (80 MHz, D_2O) δ 1.8 (m, 6H), 3.1 (s, 3H), 3.4 (m, 8H), 7.35–8.3 (m, AA'BB' system, 4H). Anal. Calcd: C, 44.69; H, 5.63; N, 7.45. Found: C, 44.73; H, 5.72; N, 7.33.

1-Isopropyl-1-[2-(4-nitrophenyl)ethyl]piperidinium Iodide (5). The procedure for the synthesis of salt **5** was the same as the one for salt **3**. From 2 g (8.5 mmol) of amine **8** and an excess of isopropyl iodide, was obtained 800 mg (1.98 mmol) of **5**. The salt was crystallized from 2-propanol–ethanol at room temperature: mp 217–219 °C dec; ^{1}H-NMR (80 MHz, D_2O) δ 1.4 (d, J = 6 Hz, 6H), 1.8 (m, 6H), 3.4 (m, 8H), 4.1 (m, 1H), 7.35–8.4 (m, AA'BB' system, 4H). Anal. Calcd: C, 47.53; H, 6.23; N, 6.93. Found: C, 47.46, H, 6.10; N, 6.84.

1-Methyl-1-[2-(4-nitrophenyl)ethyl]azepanium Iodide (6). The procedure for the synthesis of salt **6** was the same as the one for salt **1**. From 700 mg (2.82 mmol) of amine **9** and an excess of methyl iodide was obtained 950 mg of **6**. The salt was crystallized from 2-propanol–ethanol at 0 °C mp 182–184 °C dec; ^{1}H-NMR (80 MHz, D_2O) δ 1.8 (m, 8H), 3.1 (s, 3H), 3.5 (m, 8H), 7.35–8.35 (m, AA'BB' system, 4H). Anal. Calcd: C, 46.16; H, 5.94; N, 7.18. Found: C, 45.98; H, 6.05; N, 7.06.

Kinetic Measurements. The kinetics were studied following the decomposition of the [2-(4-nitrophenyl)ethyl]ammonium ions to *p*-nitrostyrene at 25 °C, with aqueous potassium hydroxide and aqueous acetohydroxamate/acetohydroxamic acid buffers. The ionic strength was maintained at 1 M with potassium chloride. Slight variations in pH within the buffer series required some adjustments of the pH to 9.05. The appearance of *p*-nitrostyrene was followed spectrophotometrically at 336 nm (ϵ = 8298 in H_2O, μ = 1 M KCl, 25 °C) after injection of 50–100 μL of substrate solution (H_2O or H_2O/CH_3CN) into a temperature-equilibrated cuvette containing 2 mL of the buffers or hydroxide solution. The reactions with hydroxide solutions were followed to completion. The pseudo-first-order rate constants were obtained from the slopes of the plot $\ln(A_\infty - A_0)/(A_\infty - A_t)$ vs time.

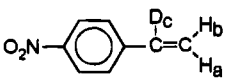
The reactions with buffer solutions (pH = 9.05, 25 °C, H_2O, μ = 1 M KCl) were studied by using ca. 3×10^{-3} M substrate and following the reaction to 2–3% completion. The total concentration of buffer solutions was 0.6–0.06 M. The pseudo-first-order rate constants, k_{obs} (s^{-1}), were obtained from the slopes of the plot A_t vs time divided by $(A_\infty - A_0)$. An association constant of 0.27 M^{-1} was considered for buffer association.[2] The [OH^-] was calculated from the equation[4] $-\log [OH^-] = 14 - (pH + 0.19)$. The p$K_a$ of AcNHOH is 9.4 at 25 °C, H_2O, μ = 1 M KCl.[2] It was shown that *p*-nitrostyrene was stable in the buffer solutions used and under the experimental kinetic conditions. As a control, for all substrates it was confirmed that the k_{obs} (s^{-1}) obtained in 0.1 M KOH, from the initial rates and from following the reactions to completion, were in agreement.

Product Analysis. Experiments carried out with all the substrates in buffers showed that after extraction with *n*-hexane and VPC analysis, the only products were *p*-nitrostyrene and the amine leaving group. Reactions in KOH were also quantitative eliminations to *p*-nitrostyrene as shown by UV analysis of the *p*-nitrostyrene product.

pK_a Determination. The pK_a values of the amine leaving group were determined by titration at 25 °C, H_2O, μ = 1 M KCl.

Solvent Isotope Effect. The elimination reactions were followed in acetohydroxamate/acetohydroxamic acid buffers, D_2O, using the same procedure described for reactions in H_2O. The [B] and [BD] were calculated from the measured pH and the relationships:[13] pD = pH + 0.4 and pD − pK_a = log [B]/[BD]. The ratio [B]/[BD] was always 0.5. Measuring the pH of solutions with different [B]/[BD] ratios, we found a pK_a = 10 ± 0.05 for AcNHOH (D_2O, μ = 1 M KCl, 25 °C), which was in agreement with a previously reported[2] value.

H/D Exchange. Experiments were carried out dissolving the substrate (2×10^{-2} M) in acetohydroxamate/acetohydroxamic acid buffers in D_2O solution at the desired temperature. The reaction mixture was covered with a layer of *n*-hexane, frequently shaken, and extracted. Under these conditions the contribution to deuteration by the addition of the amine leaving group to *p*-nitrostyrene can be excluded.[2] When the reaction mixture reached the desired percentage, the reaction mixture was extracted with *n*-hexane and the residual substrate was treated in KOH (1 M), at 45 °C for 90 min; this reaction mixture was covered with a layer of *n*-hexane, occasionally shaken, and extracted. The degree of deuterium incorporation was determined in the *p*-nitrostyrene formed in this elimination reaction. Mass spectra of this *p*-nitrostyrene show that the ratio of the peaks M/(M + 1), m/e 149/150, decreased when a significant amount of deuterated *p*-nitrostyrene was present (we found that the ratio in the mass



spectra of the *p*-nitrostyrene formed from the reaction of the reagent with KOH was 10.8 ± 2). The percentage of H/D exchange was evaluated from % (H/D) = $100(10.8C - A)/(9.8A + 10.8C)$, where A is the intensity of the peak at *m/e* 149 and C that of the peak at *m/e* 150. The ^{1}H-NMR spectra[14] ($CDCl_3$) of these samples show the expected appearance of the multiplets at δ = 5.9 and 5.5 ppm related to the coupling of the H_a and H_b protons with deuterium. It is to be noted that in the elimination induced by KOH, the transfer of the proton to the base is faster than that of deuterium due to a primary deuterium kinetic isotope effect; however, in this process is expected a limited loss of deuterium.

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Supporting Information Available: Observed rate constants, k_{obs} (s^{-1}), in H_2O or D_2O for the β-elimination reaction at different [B] and [BH(D)], 25 °C, μ = 1 M KCl, for compounds **1–6** (6 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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