Table I. Effect of Metallic Purity on the Products of the Reaction between Cycloheptyl Bromide and Magnesium in the Presence of TMPO• and *tert*-Amyl Alcohol[a]

Mg type[c]	% yield[b] TMPOR	RH	R(-H)	RR
Alfa, 99.9%	81	10	9	0
Baker, 99.8%	82	8	9	0
triply sublimed	87	5	8	0
Mg-4%Fe-3%Zn	83	8	9	0
Alfa + $FeCl_3$[d]	72	21	6	<1

[a] RBr (0.010 M) was allowed to react with Mg turnings (25 mg-atom) at 20 °C in a solvent containing TMPO• (0.50 M), *tert*-amyl alcohol (5.0 M), and LiBr (0.5 M) in Et_2O; R = c-C_7H_{13}. [b] Yields were determined by GLC analysis. [c] Sources of magnesium are given in the General Procedure section. [d] The solution contained ca. 1% (wt/v) of anhydrous $FeCl_3$.

actions with $[TMPO^•]_0 \leq 0.10$ M). Addition of reagents, sampling, extraction, and GLC analysis of the aliquots were performed as described above. A survey of the influence of the origin of the magnesium and of added $FeCl_3$ showed no significant variation (Table I).

Reaction of Cycloheptyl Bromide with Magnesium in the Presence of $TMPO^-$ and *tert*-Amyl Alcohol. After preparation of magnesium turnings (0.61 g, 25 mg-atom) as described above, a solution containing TMPO• (0.469 g, 3.0 mmol), *tert*-amyl alcohol (8.2 mL, 75 mmol), and LiBr (7.5 mmol) in Et_2O was added to the reaction vessel by cannula. The initial volume of the solution was 15.0 mL: $[TMPO^•]_0 = 0.20$ M; $[tert\text{-amyl alcohol}]_0 = 5.0$ M; [LiBr] = 0.50 M. A cool water bath (20 °C) was placed beneath the flask, and vigorous stirring was begun. Dibromoethane (45 μL, 0.5 mmol) was injected into the solution after 1 min. The orange color of TMPO• was no longer evident after 20 min, and the solution was slightly turbid. Five milliliters of the solution was removed to another flask and was used to test the reactivity of $TMPO^-$ toward c-C_7H_{13}Br. To the mixture remaining in the reaction vessel was added 0.50 mL of a solution containing cycloheptyl bromide (0.10 mmol), heptane (3.64 mg, internal GLC standard), and pentadecane (4.35 mg, internal GLC standard) in Et_2O, followed by 1,2-dibromoethane (45 μL, 0.5 mmol). The reaction was allowed to proceed for 25 min at 20 °C. A sample was withdrawn, extracted, and analyzed by GLC, as described above.

Preparation of *N*-Cycloheptoxy-2,2,6,6-tetramethylpiperidine (TMPO-c-C_7H_{13}). A 300-mL round-bottomed flask was capped with a septum, flame dried, and allowed to cool under a stream of argon. TMPO• (3.90 g, 25 mmol) and a magnetic stirring bar were placed in the flask. The septum was replaced and wired down, and the vessel was further flushed with argon. Diethyl ether (50 mL) was added to the flask, an ice bath was placed beneath the flask, and stirring was begun. Cycloheptylmagnesium bromide (1.0 M in Et_2O) was added dropwise until the orange color of TMPO• had disappeared. The colorless, turbid solution was washed with three 50-mL portions of deoxygenated H_2O. The aqueous layers were combined and extracted with Et_2O (50 mL). The organic layers were combined, dried with anhydrous $MgSO_4$, and concentrated to 5 mL by rotary evaporation. The crude product was distilled through a short-path head at reduced pressure (0.02–0.03 Torr). The fraction having a boiling range of 65–70 °C (0.96 g) was a clear, colorless, viscous liquid and was analyzed by GLC: TMPO-c-C_7H_{13}, 85%; bicycloheptyl, 15%. TMPO-c-C_7H_{13} that remained in the pot (0.3 mL, >98% pure by GLC) was separated from gummy residues by molecular distillation (bath temperature 60–75 °C; 0.04 Torr): ^1H NMR ($CDCl_3$) δ 3.80 (m, 1 H), 1.98 (m, 2 H), 1.75–1.16 (m, 16 H), 1.10 (s, 12 H) ppm; mass spectrum (relative abundance) parent ion *m/e* 253 (<1), fragments *m/e* 238 (<1), 157 (11), 142 (100), 69 (9), 55 (11), 41 (16). Anal. ($C_{16}H_{31}NO$): C, H, N.

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Registry No. TMPO•, 2564-83-2; TMPOH, 7031-93-8; c-C_7H_{13}MgBr, 78378-12-8; c-C_5H_9MgBr, 137-43-9; c-C_7H_{13}Br, 2404-35-5; TMPO-*c*-C_7H_{13}, 120881-31-4; Mg, 7439-95-4; *tert*-amyl alcohol, 75-85-4; bicycloheptyl, 23183-11-1; cycloheptane, 291-64-5; cycloheptene, 628-92-2.

Supplementary Material Available: A treatment of the influence of changing surface area of the magnesium on the kinetics of disappearance of alkyl halides (6 pages). Ordering information is given on any current masthead page.

Borderline between E1 and E2 Mechanisms. Bimolecular Base-Promoted Elimination via Ion Pairs Competing with Concerted E2 Elimination

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Abstract: The solvolysis of 2-chloro-2-methyl-1-phenylpropane (**1**) in methanol or in 25 vol % acetonitrile in water at 25 °C yields substitution product **2** (ether or alcohol) and the two elimination products **3** and **4**. The olefin fraction in the aqueous solution does not increase significantly in the presence of 0.75 M sodium hydroxide. In methanol, on the other hand, the fraction of **3** and **4**, the ratio [**3**]/[**4**], and the rate of disappearance of **1** increase with methoxide ion concentration. The kinetic isotope effects $(k_{12}{}^{H} + k_{13}{}^{H} + k_{14}{}^{H})/(k_{12}{}^{d_2} + k_{13}{}^{d_2} + k_{14}{}^{d_2}) = 1.41$ and 1.42, measured for the solvolysis of the dideuterated analogue d_2-**1** in water/acetonitrile and in methanol, respectively, are too large to be secondary effects on a rate-limiting ionization step, but they suggest reaction via a reversibly formed carbocationic intermediate. The solvolysis of the hexadeuterated analogue d_6-**1** exhibits "normal" secondary kinetic isotope effects, $(k_{12}{}^{H} + k_{13}{}^{H} + k_{14}{}^{H})/(k_{12}{}^{d_6} + k_{13}{}^{d_6} + k_{14}{}^{d_6}) = 1.79$ and 1.81 in water/acetonitrile and methanol, respectively. The presence of 2 M NaOMe increases the isotope effect for d_2-**1** to 2.4 but decreases the effect for d_6-**1** to 1.35. These results indicate that **3** is formed by a parallel methoxide-promoted one-step concerted route (E2) and that such a route is not significant for the formation of **4**. The isotope effect for the E2 reaction is estimated as $k^H/k^{d_2} = 4.9$ (on the basis of the assumption that the elimination product ratio [**3**]/[**4**] for the carbocationic route is not affected by MeO^-).

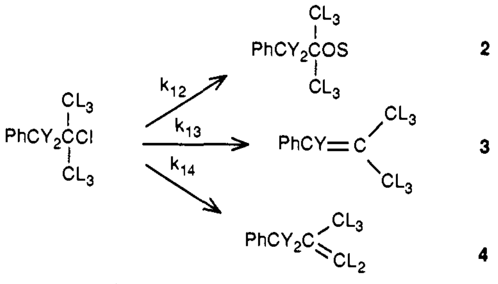
It is conceivable that some elimination reactions that have been classified as E2 with carbocationlike transition states consist, in fact, of a mixture of concerted elimination (E2) and elimination from a reversibly formed carbocation ion-pair intermediate ("$E2_{ip}$"). The measured kinetic deuterium isotope effect for the elimination reaction is then composed of a substantial isotope effect on the E2 route and a small isotope effect on the carbocationic path. A large proportion of the stepwise route, which exhibits

Table I. Rate Constants for the Reactions of **1** in 25 vol % Acetonitrile in Water at 25.00 ± 0.03 °C

substrate[a]	salt[b]	$10^6(k_{12} + k_{13} + k_{14})$, s^{-1}	$10^6 k_{12}$, s^{-1}	$10^6 k_{13}$, s^{-1}	$10^6 k_{14}$, s^{-1}	k_{13}/k_{12}	k_{14}/k_{12}
h-**1**	none	296	219	43.3	33.4	0.20	0.15
	$NaClO_4$	330	235	54.6	39.8	0.23	0.17
	NaCl	290	209	46.2	34.4	0.22	0.16
	NaBr	357	261	40.2	56.5	0.22	0.15
	NaN_3	~400					
	NaOAc	182	127	30.6	24.4	0.24	0.19
	NaOH	167	115	29.1	22.8	0.25	0.20
d_2-**1**	none	209	166	14.6	28.6		
	$NaClO_4$	234	181	18.4	34.6		
	NaOH	120	90	10.8	19.7		
d_6-**1**	none	165	129	28.8	7.7		
	$NaClO_4$	183	138	36.4	9.2		
	NaOH	97	71	20.6	6.4		

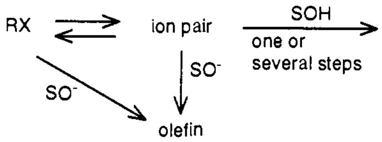
[a] 0.3 mM. [b] 0.75 M.

Scheme I



1: Y = ¹H, L = ¹H
d₂-1: Y = ²H, L = ¹H
d₆-1: Y = ¹H, L = ²H

the same bimolecular kinetics as the E2 reaction, yields a small overall kinetic isotope effect.



(1)

This hypothesis is in accord with Bordwell's suggestion that, in systems which undergo ionization,[1] lyate ions promote elimination from ion pairs rather than from the substrate itself. The reason for this is that ion pairs are far superior to covalent substrates as proton donors.

Base-promoted elimination reactions of the chloride **1** are expected to have mechanisms near the borderline E1–E2 and may constitute appropriate reactions for testing the hypothesis of competing E2 and bimolecular carbocationic elimination as the cause of small elimination isotope effects. Several research groups have studied base-promoted elimination from **1**.[2-4] Thus, Bunnett and co-workers have found that first-order processes that give **2–4** compete with second-order reactions that yield olefins **3** and **4** (Scheme I).[3] It was concluded that the methoxide-promoted eliminations are of E2 type despite the small isotope effect $k_{13}^{H}/k_{13}^{d_2} = 2.6$ (76 °C) for formation of product **3** from d_2-**1**.

This isotope effect appears too small for an E2 reaction of this type since, for example, the lyate-promoted elimination of DCl from the related $ArCD_2CH_2X$ (X = Br, Cl, or F) in alcohols shows isotope effects of 5–8.[5,6] Moreover, a more acidic tertiary chloride, 9-(2-chloro-2-propyl)fluorene, exhibits an E2 isotope effect k^{H}/k^{D} = 6.6 in $MeO^-/MeOH$ (25 °C).[7] Accordingly, it was of interest to reexamine the reaction of **1** to ascertain whether an ion-pair mechanism (eq 1) could be the cause of the small isotope effect. The present investigation has also employed the hexadeuterated substrate d_6-**1**.

Table II. Rate Constants for the Reactions of **1** in Methanol[a] at 25.00 ± 0.03 °C

substrate[b]	salt	$10^6(k_{12} + k_{13} + k_{14})$, s^{-1}	$10^6 k_{12}$, s^{-1}	$10^6 k_{13}$, s^{-1}	$10^6 k_{14}$, s^{-1}
h-**1**	none	0.461	0.307	0.081	0.071
	NaOAc[c]	0.520	0.312	0.115	0.094
	NaOMe[d]	1.208	0.171	0.837	0.200
d_2-**1**	none	0.324	0.230	0.032	0.062
	NaOAc[c]	0.355	0.230	0.045	0.080
	NaOMe[d]	0.506	0.117	0.215	0.174
d_6-**1**	none	0.255	0.181	0.054	0.021
	NaOAc[c]	0.287	0.181	0.078	0.028
	NaOMe[d]	0.898	0.116	0.722	0.059

[a] 3.74 vol % water. [b] 0.3 mM. [c] 0.98 M. [d] 2.00 M.

Table III. Isotope Effects for the Reactions of **1** in 25 vol % Acetonitrile in Water at 25.00 ± 0.03 °C

salt[a]	$(k_{12}^{H} + k_{13}^{H} + k_{14}^{H})/(k_{12}^{i} + k_{13}^{i} + k_{14}^{i})$	k_{12}^{H}/k_{12}^{i}	k_{13}^{H}/k_{13}^{i}	k_{14}^{H}/k_{14}^{i}
		i = d_2		
none	1.41	1.32	2.97	1.17
$NaClO_4$	1.41	1.30	2.97	1.15
NaOH	1.39	1.29	2.69	1.16
		i = d_6		
none	1.79	1.70	1.50	4.34
$NaClO_4$	1.80	1.71	1.50	4.33
NaOH	1.72	1.63	1.41	3.56

[a] 0.75 M.

Another reason for studying the reaction system of Scheme I is that it may contribute to knowledge of the possible role of ion pairs as reaction intermediates in a highly aqueous solvent, which is one of our main interests in this laboratory.[8-12]

Results

Syntheses. Highly deuterated 1-phenyl-(1,1-$^2H_2$)-2-propanone (98.5 atom % ^2H) was prepared from the undeuterated compound by slight modification of a method by Winnik.[13] Otherwise, standard methods were used for the synthesis of the substrates (see the Experimental Section).

Kinetic and Product Studies. The solvolysis of 2-chloro-2-methyl-1-phenylpropane (**1**) in methanol or in 25 vol % acetonitrile

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Table IV. Isotope Effects for the Reactions of **1** in Methanol[a] at 25.00 ± 0.03 °C

Salt	$(k_{12}^{H} + k_{13}^{H} + k_{14}^{H})/(k_{12}^{i} + k_{13}^{i} + k_{14}^{i})$	k_{12}^{H}/k_{12}^{i}	k_{13}^{H}/k_{13}^{i}	k_{14}^{H}/k_{14}^{i}
		i = d_2		
none	1.42	1.33	2.53	1.15
NaOAc[b]	1.46	1.36	2.56	1.18
NaOMe[c]	2.39	1.46	3.89	1.15
		i = d_6		
none	1.81	1.70	1.50	3.4
NaOAc[b]	1.81	1.72	1.47	3.4
NaOMe[c]	1.35	1.47	1.16	3.4

[a] 3.74 vol % water. [b] 0.98 M. [c] 2.00 M.

in water at 25 °C provides the substitution product (**2**) which is 2-methoxy-2-methyl-1-phenylpropane or 2-hydroxy-2-methyl-1-phenylpropane along with the elimination products 2-methyl-1-phenyl-1-propene (**3**) and 2-methyl-3-phenyl-1-propene (**4**) (Scheme I). The kinetics of the reactions were studied at 25 °C by a sampling high-performance liquid-chromatography (HPLC) procedure. The measured rate constants and reaction conditions are shown in Tables I and II.

The effect of bases on the product composition is very small in the aqueous solution (Table I). Addition of sodium azide (0.75 M) yields a product ratio for azide to alcohol of ~0.35 and 25 vol % methanol in water gives a product ratio for ether to alcohol of 0.13. From these results, the discrimination between water and other nucleophiles for reaction with the carbocationic intermediate may be calculated as $k_{N_3}/k_{H_2O} \approx 19$ and $k_{MeOH}/k_{H_2O} = 0.8$ (ratio of second-order rate constants).

The results of the kinetic experiments with the deuterated substrates 2-chloro-2-methyl-1-phenyl-(1,1-$^2H_2$)-propane (d_2-**1**) and 2-chloro-2-($^2H_3$-methyl)-1-phenyl-(3,3,3-$^2H_3$)-propane (d_6-**1**) are also reported in Tables I and II. The measured isotope effects are collected in Tables III and IV.

Discussion

The Solvolysis Reactions. The solvolysis of the chloride **1** is nearly 700 times faster in the aqueous solution than in methanol, consistent with a carbocationic mechanism. There are several indications that the ionization step is reversible in both solvents. Thus, the solvolysis in water/acetonitrile is somewhat faster in the presence of azide anion or bromide anion than with perchlorate anion. The opposite behavior was found for the solvolysis of 9-(2-chloro-2-propyl)fluorene, which has been concluded to undergo rate-limiting ionization.[11] The reason for the rate enhancement is presumably a fast reaction of the carbocationic intermediate with azide anion and bromide anion that decreases the amount of ion-pair return. About 18% of azide product is formed with 0.75 M NaN_3 in water/acetonitrile, which agrees with the observed rate increase from $k_{obs} = 330 \times 10^{-6}$ s^{-1} ($NaClO_4$) to $k_{obs} \approx 400 \times 10^{-6}$ s^{-1} (NaN_3). The bromide product is expected to react rapidly with solvent water to yield the same products as the chloride. Addition of chloride anion does not have a substantial depressing effect on the solvolysis rate (Table I). Accordingly, external return should not be of importance.

Reversible ionization is also suggested by the size of the isotope effect $(k_{12}^{H} + k_{13}^{H} + k_{14}^{H})/(k_{12}^{d_2} + k_{13}^{d_2} + k_{14}^{d_2})$. The measured values of 1.41 and 1.42 for reaction in water/acetonitrile and methanol, respectively, correspond to an isotope effect of 1.19 per deuterium, which is too large for a secondary β-deuterium isotope effect.[14] The values are consistent with reversible ionization followed by rate-limiting reaction of the ion pair to substitution and elimination products. The isotope effect $(k_{12}^{H} + k_{13}^{H} + k_{14}^{H})/(k_{12}^{d_6} + k_{13}^{d_6} + k_{14}^{d_6})$ has a value close to 1.8 in both solvents. The magnitude does not give any information about reversibility.

The very similar isotope effects measured on the total solvolysis reaction rates in the two solvents argue against different degrees of reversibility but suggests that internal return is much faster than reaction to products ($k_{-1} \gg k_2$, k_3, k_4, eq 2). Partial

$$\begin{tikzcd} \mathbf{1} \arrow[r, shift left, "k_1"] & \text{ion pair} \arrow[l, shift left, "k_{-1}"] \arrow[r, "k_2"] \arrow[d, "k_3"] \arrow[dr, "k_4"] & \mathbf{2} \\ & \mathbf{3} & \mathbf{4} \end{tikzcd} \qquad (2)$$

reversibility of the ionization step should have been reflected in observed isotope effects of different magnitude in the two solvents since more internal return is expected in methanol. The solvolysis of *tert*-butyl chloride has also been discussed in terms of reversible ionization.[15]

An alternative, but not likely, explanation for the large isotope effects on the rate of disappearance of d_2-**1** might be hydrogen participation by one of the benzylic hydrogens.[16] Neighboring-group participation from the phenyl group has been ruled out by Bunnett; solvolysis of **1** is somewhat slower than that of *tert*-butyl chloride.[3] Another unlikely cause of the large isotope effects might be that part of **3** is formed by a separate, one-step solvent-promoted elimination with a substantial primary isotope effect.

The carbocationic intermediate shows relatively small selectivity toward different nucleophiles. The azide anion is about 19 times more reactive than a water molecule. In accord with substrate structure, this value is higher than that exhibited by the highly reactive ion pair formed from 9-(2-chloro-2-propyl)fluorene ($k_{N_3}/k_{H_2O} = 5$),[11] but it is smaller than the selectivity shown by the more stable intermediates formed from 2-chloro-2-phenylpropane ($k_{N_3}/k_{H_2O} = 42$)[12] and 3-(2-chloro-2-propyl)indene ($k_{N_3}/k_{H_2O} = 50$, 35 °C)[8] in the same reaction medium, and it is also smaller than the selectivity shown in the reaction of 1-chloro-1-(4-methylphenyl)ethane in 50% trifluoroethanol in water ($k_{N_3}/k_{H_2O} = 40$).[17] The selectivity between methanol and water for reaction with the intermediate, measured in 25 vol % methanol in water, is also small, $k_{MeOH}/k_{H_2O} = 0.8$ (ratio of second-order rate constants), and is within the interval measured for more reactive and less reactive carbocationic intermediates.[8-12,17]

The small k_{N_3}/k_{H_2O} and k_{MeOH}/k_{H_2O} values suggest that nucleophilic attack occurs to a significant extent at the ion-pair stage, i.e., diffusional separation is not much faster than direct reaction of the reactive ion pair. This conclusion is based upon the assumption that the intermediate reacts with azide anion with a diffusion-controlled rate.[8-12,17] A rate constant of $k_d = 5 \times 10^9$ M^{-1} s^{-1} for this diffusion yields a rate constant for reaction with solvent water to form **2** as $k_{H_2O} \approx 1.1 \times 10^{10}$ s^{-1}. This rate constant is of the same magnitude as the value for the diffusional separation of the ion-pair intermediate, $k_{-d} = 2.5 \times 10^{10}$ s^{-1}, that could be estimated from k_d and an association constant (K_{as}) for formation of ion pairs from the free ions of $K_{as} = 0.2$ M^{-1}.[18]

The fraction of elimination products is larger in methanol than in the more ionizing aqueous medium. It seems to be a general phenomenon that elimination is favored relative to substitution when the ionizing power of the solvent is decreased. The reason is presumably that the elimination products are formed mainly from the contact ion pair in a one-step process; dissociation to solvent-separated and free ions favors ether or alcohol formation.

The deprotonation of the carbocation intermediates has been found in several studies to be catalyzed by general bases.[9,11,12,17] Thus, the elimination from the very unstable intermediate formed from 9-(2-chloro-2-propyl)fluorene shows a Brønsted β = 0.05 with substituted acetate anions in aqueous solution,[11] and β = 0.13 was measured in the reaction of 2-chloro-2-phenylpropane.[12] Water was found to be about 10 times less efficient as a proton

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(14) Values of 1.10 ± 0.05/β-D have been reported: Westaway, K. C. *Isotopes in Organic Chemistry*; Buncel, E., Lee, C. C., Eds.; Elsevier: Amsterdam, 1987; Chapter 5.

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acceptor than predicted by the Brønsted relation for substituted acetate anions.[9,11,12] However, the reaction with **1** does not show any substantial increase in the fraction of elimination product with 0.75 M NaOAc and not even with 0.75 M NaOH. Why is water a much more efficient proton acceptor in the reaction of **1**? The results do not give any answer to this important question.

Equation 2 seems to represent the simplest mechanistic model that accounts for all experimental data of the solvolytic reactions. The steady-state approximation yields the following relations between phenomenological and microscopic rate constants for the eq 2 model:

$$k_{12} = k_1k_2/(k_{-1} + k_2 + k_3 + k_4) \quad (3)$$

$$k_{13} = k_1k_3/(k_{-1} + k_2 + k_3 + k_4) \quad (4)$$

$$k_{14} = k_1k_4/(k_{-1} + k_2 + k_3 + k_4) \quad (5)$$

$$k_{12} + k_{13} + k_{14} = k_1(k_2 + k_3 + k_4)/(k_{-1} + k_2 + k_3 + k_4) \quad (6)$$

Since it has been concluded that $k_{-1} \gg k_2$, k_3, and k_4, the expressions for the isotope effects are

$$k_{12}{}^{\mathrm{H}}/k_{12}{}^{\mathrm{D}} = (K_{\mathrm{eq}}{}^{\mathrm{H}}/K_{\mathrm{eq}}{}^{\mathrm{D}})(k_2{}^{\mathrm{H}}/k_2{}^{\mathrm{D}}) \quad (7)$$

$$k_{13}{}^{\mathrm{H}}/k_{13}{}^{\mathrm{D}} = (K_{\mathrm{eq}}{}^{\mathrm{H}}/K_{\mathrm{eq}}{}^{\mathrm{D}})(k_3{}^{\mathrm{H}}/k_3{}^{\mathrm{D}}) \quad (8)$$

$$k_{14}{}^{\mathrm{H}}/k_{14}{}^{\mathrm{D}} = (K_{\mathrm{eq}}{}^{\mathrm{H}}/K_{\mathrm{eq}}{}^{\mathrm{D}})(k_4{}^{\mathrm{H}}/k_4{}^{\mathrm{D}}) \quad (9)$$

$$(k_{12}{}^{\mathrm{H}} + k_{13}{}^{\mathrm{H}} + k_{14}{}^{\mathrm{H}})/(k_{12}{}^{\mathrm{D}} + k_{13}{}^{\mathrm{D}} + k_{14}{}^{\mathrm{D}}) = (K_{\mathrm{eq}}{}^{\mathrm{H}}/K_{\mathrm{eq}}{}^{\mathrm{D}})(k_2{}^{\mathrm{H}} + k_3{}^{\mathrm{H}} + k_4{}^{\mathrm{H}})/(k_2{}^{\mathrm{D}} + k_3{}^{\mathrm{D}} + k_4{}^{\mathrm{D}}) \quad (10)$$

where $K_{\mathrm{eq}}{}^{\mathrm{H}}/K_{\mathrm{eq}}{}^{\mathrm{D}} = (k_1{}^{\mathrm{H}}/k_1{}^{\mathrm{D}})/(k_{-1}{}^{\mathrm{H}}/k_{-1}{}^{\mathrm{D}})$.

Reaction branching in accord with eq 2 may cause enlarged and attenuated overall isotope effects. Branching as the cause of unusually large and unusually small kinetic isotope effects has been discussed previously for reactions that are coupled via a common carbanion intermediate[19,20] and for solvolysis reactions.[9,11,12,20]

In the reactions with d_6-**1**, the isotope effect $k_{14}{}^{\mathrm{H}}/k_{14}{}^{d6}$ (eq 9) is a product of a secondary isotope effect on the first reversible step ($K_{\mathrm{eq}}{}^{\mathrm{H}}/K_{\mathrm{eq}}{}^{d_6}$) and a primary isotope effect on the deprotonation step ($k_4{}^{\mathrm{H}}/k_4{}^{d_6}$).[21] On the other hand, according to eq 8, the isotope effect $k_{13}{}^{\mathrm{H}}/k_{13}{}^{d_6}$ shows only a secondary isotope effect $K_{\mathrm{eq}}{}^{\mathrm{H}}/K_{\mathrm{eq}}{}^{d_6}$ multiplied by a secondary isotope effect on the deprotonation step ($k_3{}^{\mathrm{H}}/k_3{}^{d_6}$). The latter should be very small, i.e., close to unity. The isotope effect $k_{12}{}^{\mathrm{H}}/k_{12}{}^{d_6}$ is also a product of two secondary isotope effects (eq 7); $k_2{}^{\mathrm{H}}/k_2{}^{d_6}$ is expected to be small. The magnitude of the isotope effect on the total reaction of d_6-**1** (eq 10) is dependent on the relative amounts of products. Thus, a large amount of elimination product **4** corresponds to a large isotope effect, but a large amount of **3** yields a smaller value.

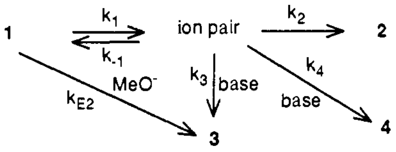
The isotope effects for the reaction of d_2-**1** may be analyzed in an analogous way. For example, $(k_{12}{}^{\mathrm{H}} + k_{13}{}^{\mathrm{H}} + k_{14}{}^{\mathrm{H}})/(k_{12}{}^{d_2} + k_{13}{}^{d_2} + k_{14}{}^{d_2})$ is a function of the relative amounts of product **3**; the isotope effect increases with the yield of **3** and has a maximum equal to the isotope effect $k_{13}{}^{\mathrm{H}}/k_{13}{}^{d_2}$.

Let us examine the isotope effects of the solvolytic reactions (Tables III and IV) with the help of eq 7–10, assuming $k_3{}^{\mathrm{H}}/k_3{}^{d_6}$ and $k_4{}^{\mathrm{H}}/k_4{}^{d_2}$ are equal to unity. A value of $k_{14}{}^{\mathrm{H}}/k_{14}{}^{d_2} = 1.16$ for the reaction of d_2-**1** in water/acetonitrile yields $K_{\mathrm{eq}}{}^{\mathrm{H}}/K_{\mathrm{eq}}{}^{d_2} = 1.16$. This value gives $k_2{}^{\mathrm{H}}/k_2{}^{d_2} = 1.31/1.16 = 1.13$ and $k_3{}^{\mathrm{H}}/k_3{}^{d_2} = 2.97/1.16 = 2.6$. The following isotope effects are calculated for d_6-**1**: $K_{\mathrm{eq}}{}^{\mathrm{H}}/K_{\mathrm{eq}}{}^{d_6} = 1.50$, $k_2{}^{\mathrm{H}}/k_2{}^{d_6} = 1.71/1.50 = 1.14$, and $k_4{}^{\mathrm{H}}/k_4{}^{d_6} = 4.33/1.50 = 2.9$. The results with sodium hydroxide yield $k_3{}^{\mathrm{H}}/k_3{}^{d_2} = 2.69/1.16 = 2.3$ and $k_4{}^{\mathrm{H}}/k_4{}^{d_6} = 3.56/1.41 = 2.5$.

An analogous treatment of the data for reaction in methanol yields $K_{\mathrm{eq}}{}^{\mathrm{H}}/K_{\mathrm{eq}}{}^{d_2} = 1.15$, $k_2{}^{\mathrm{H}}/k_2{}^{d_2} = 1.33/1.15 = 1.16$, $k_3{}^{\mathrm{H}}/k_3{}^{d_2} = 2.53/1.15 = 2.2$, $K_{\mathrm{eq}}{}^{\mathrm{H}}/K_{\mathrm{eq}}{}^{d_6} = 1.50$, $k_2{}^{\mathrm{H}}/k_2{}^{d_6} = 1.70/1.50 = 1.13$, and $k_4{}^{\mathrm{H}}/k_4{}^{d_6} = 3.4/1.50 = 2.3$.

The isotope effects on the separate steps are obviously very similar in the two solvents. However, the isotope effects on the deprotonation steps are somewhat larger in the aqueous medium than in methanol. The isotope effect has been estimated for deprotonation of other ion pairs and ions.[9,11,12] For example, k^{H}/k^{d_6} has been calculated as ~2.8 for 9-(1,1,1,3,3,3-^{2}H$_6$)-9-(2-chloro-2-propyl)fluorene[11] and ~3.5 for (1,1,1,3,3,3-^{2}H$_6$)-2-chloro-2-phenylpropane in water/acetonitrile.[12]

Base-Promoted Elimination. There are several substantial and significant changes in measured rate constants and isotope effects when sodium methoxide is added to the methanol. These changes cannot be accommodated in the mechanistic model of eq 2. The large increases in total rate and in the rate of elimination forming **3**, combined with a large increase in the isotope effects $(k_{12}{}^{\mathrm{H}} + k_{13}{}^{\mathrm{H}} + k_{14}{}^{\mathrm{H}})/(k_{12}{}^{d_2} + k_{13}{}^{d_2} + k_{14}{}^{d_2})$ and $k_{13}{}^{\mathrm{H}}/k_{13}{}^{d_2}$, strongly indicate a parallel, competing methoxide-promoted reaction of E2 type (eq 11). Further indications are the decreases in $(k_{12}{}^{\mathrm{H}} + k_{13}{}^{\mathrm{H}} + k_{14}{}^{\mathrm{H}})/(k_{12}{}^{d_6} + k_{13}{}^{d_6} + k_{14}{}^{d_6})$ and $k_{13}{}^{\mathrm{H}}/k_{13}{}^{d_6}$.



(11)

base = methanol or MeO$^-$

The data provide no indication of a parallel reaction route to give product **4**. Thus, it is concluded that **4** is not formed significantly by an E2 reaction. The reason is most likely the low kinetic acidity of the methyl hydrons; the benzylic hydrons are much more acidic.[22] In the aqueous medium there is no indication of any significant contribution from any parallel E2 reaction with hydroxide anion to product **3**. This can be rationalized by the large ionization rate in water/acetonitrile. A competing E2 reaction is not expected to be very much faster in this solvent than in methanol.[7]

The isotope effect $k_{13}{}^{\mathrm{H}}/k_{13}{}^{d_2} = 3.89$ (Table IV) is, of course, the isotope effect on formation of **3** both via the E2 route and the carbocationic path. How can the value be divided into isotope effects for the separate reaction routes? It seems reasonable to assume that the rate constant ratio k_3/k_4 (eq 11, pseudo-first-order rate constants) is approximately the same with or without added base. Calculation of the separate rate constants based upon this assumption and the data of Table II yields, for example, a rate constant k_3 for the carbocationic route to product **3** as $(0.081 \times 10^{-6}/0.071 \times 10^{-6})(0.200 \times 10^{-6})$ s^{-1} = 228×10^{-9} s^{-1}. The results of such a calculation may be summarized as shown in eq 12. It should be noted that the calculation is not based upon the conclusion about reversible ionization. However, the increase in the solvolysis rate constant with sodium methoxide, 599×10^{-9} s^{-1}, compared with 461×10^{-9} s^{-1} (Table II) without base is in accord with reversible ionization. The total rate of reaction has been found to be a linear function of methoxide anion concentration.[3,4]

The isotope effects on the E2 reaction are $k_{\mathrm{E2}}{}^{\mathrm{H}}/k_{\mathrm{E2}}{}^{d_2} = 4.9$ and $k_{\mathrm{E2}}{}^{\mathrm{H}}/k_{\mathrm{E2}}{}^{d_6} = 1.07$.[23] Experiments with lower methoxide concentration gave similar results. An even higher value for the E2 isotope effect $k_{\mathrm{E2}}{}^{\mathrm{H}}/k_{\mathrm{E2}}{}^{d_2}$ is obtained if k_3/k_4 is larger for reaction

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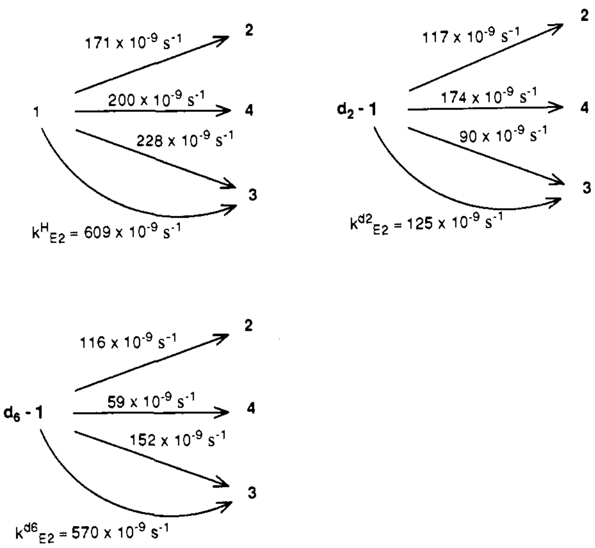
(19) Ölwegård, M.; McEwen, I.; Thibblin, A.; Ahlberg, P. *J. Am. Chem. Soc.* **1985**, *107*, 7494–7499 and references therein.

(20) Ahlberg, P.; Thibblin, A. *Synthesis and Applications of Isotopically Labeled Compounds*, Proceedings of the Second International Symposium, Kansas City, MO, 1985; Elsevier Science Publishers B. V.: Amsterdam, 1986; pp 89–94.

(21) The isotope effect $k_4{}^{\mathrm{H}}/k_4{}^{d_6}$ is not a purely primary isotope effect since the methyl groups have three deuteriums. Thus, $k_4{}^{\mathrm{H}}/k_4{}^{d_6}$ includes a small secondary isotope effect with an expected value of >1.

(22) The pK_a of toluene has been estimated to be 41 in cyclohexylamine and 42 in dimethyl sulfoxide. Streitwieser, A., Jr.; Granger, M. R.; Mares, F.; Wolf, R. A. *J. Am. Chem. Soc.* **1973**, *95*, 4257–4261. Matthews, W. S.; Bares, J. E.; Bartmess, J. E.; Bordwell, F. G.; Cornforth, F. J.; Drucker, G. E.; Margolin, Z.; McCallum, R. J.; McCollum, G. J.; Vanier, N. R. *J. Am. Chem. Soc.* **1975**, *97*, 7006–7014. Bordwell, F. G.; Algrim, D.; Vanier, N. R. *J. Org. Chem.* **1977**, *42*, 1817–1819.

(23) Treatment of the data of Bunnett and co-workers measured at 76 °C in the same way as above results in an E2 isotope effect k^{H}/k^{d_2} considerably larger than the reported value of 2.6.[3]



(12)

with MeO^- than with MeOH. Moreover, the isotope effects on the carbocationic route to **3** are 2.5 and 1.5 for d_2-**1** and d_6-**1**, respectively, similar to those obtained without added base (Table IV).

The effect of substituents in the phenyl group has been studied in methanol. A Hammett plot gave $\rho = 1.0$ for the bimolecular methoxide-promoted reaction and $\rho = -1.1$ for the solvolysis at 66 °C.[4a] The elimination from 2-aryl-1-chloroethane in EtO^-/EtOH has shown a Hammett parameter of $\rho = 2.6$.[24]

Mechanistic Borderline. A presumably rather common type of change of mechanism for a reaction involves two concurrent mechanisms having different transition-state structures.[7,11] A change in experimental conditions or structure of the reactants lowers the energy of one of the transition states relative to the energy of the other, which may induce a shift in the major reaction path. Accordingly, the reaction product may, in principle, be formed simultaneously by two parallel reactions, "reaction channels".[25] At the borderline, both transition states are of equal energy. Owing to a large difference in energy between the transition states, one of the mechanisms frequently dominates and is the only mechanism observed.

The mechanistic change for reaction of **1** to **3** is concluded to be of this type. Accordingly, in pure methanol the E2 transition state (with methanol as hydron acceptor) has much higher energy than the transition state of dehydronation of the ion pair. Accordingly, the reaction exclusively employs the carbocationic path. With methoxide, the E2 transition state has much lower energy and can compete successfully with the dehydronation of the ion pair with methanol as well as with methoxide anion. The E2 reaction should be about four times (Table II and eq 12) faster than the methoxide-promoted reaction via the ion pair. Apparently, the methoxide-promoted reactions are very close to the borderline where both mechanisms possess the same activation energy. This borderline does not correspond to merging of transition state structures.[26]

Experimental Section

General Procedures. The NMR analyses were performed with a JEOL FX 100 spectrometer equipped with a 5-mm ^1H probe or with a Varian XL 300 spectrometer. The high-performance liquid-chromatography (HPLC) analyses were carried out with a Hewlett-Packard 1084 B liquid chromatograph equipped with a variable-wavelength detector on a C18 reversed-phase column (3.0 × 200 mm). The mobile phase was a solution of acetonitrile (far UV grade) in water. The reactions were studied at constant temperature in a HETO 623 thermostat.

Materials. The alcohol 2-hydroxy-2-methyl-1-phenylpropane (Fluka) was recrystallized from pentane. The olefins 2-methyl-1-phenyl-1-propene (**3**) and 2-methyl-3-phenyl-1-propene (**4**) were purchased from Fluka and K + K Labs, respectively, and were used after distillation for calibration purposes. Acetonitrile and methanol were of spectroscopic quality and were used as solvents without further purification. All other chemicals were of reagent grade. A stock solution of sodium perchlorate was prepared from perchloric acid and sodium hydroxide solution. The pH value of the stock solution of sodium acetate was adjusted to ca. 7.

2-Chloro-2-methyl-1-phenylpropane (1)[2,3,4] was prepared by treatment of the alcohol with $ZnCl_2$–HCl in chloroform (reaction time 1 h) according to the method that has been described for other tertiary alcohols.[8,11,27] The crude product was purified by distillation under reduced pressure.

2-Hydroxy-2-($^2H_3$)-methyl-1-phenyl-(3,3,3-$^2H_3$)-propane was prepared from benzylmagnesium chloride and (1,1,1,3,3,3-$^2H_6$)-acetone (99.8 atom % ^2H) in ether. The product was purified by recrystallization from pentane.

2-Chloro-2-($^2H_3$)-methyl-1-phenyl-(3,3,3-$^2H_3$)-propane (d_6-1) was synthesized from the corresponding deuterated alcohol as described for the protium compound. The deuterium content in the methyl groups was 98.0 ± 1.0 atom %.

1-Phenyl-(1,1-$^2H_2$)-2-propanone was prepared from the undeuterated compound by pyridine-catalyzed exchange with heavy water (99.8% ^2H) as a deuterium pool. It was possible to raise the degree of exchange considerably compared with previously reported results[13] by employing a longer reaction time (21 h, 22 °C). The pot temperature during evaporation was 27 °C. The crude product was dried over sodium chloride. Analysis by ^1H NMR showed 1.5 atom % ^1H in the α-position, i.e., 98.5% ^2H was incorporated. The amount of ^2H in the methyl group was found to be <4% (^2H NMR). The product was used for synthesis without further purification.

2-Hydroxy-2-methyl-1-phenyl-(1,1-$^2H_2$)-propane was synthesized from methylmagnesium iodide and 1-phenyl-(1,1-$^2H_2$)-2-propanone in ether. Recrystallization from pentane gave pure product. The deuterium content in the benzylic position was 99.2 ± 1.0 atom % (^1H NMR) and 1.0 ± 1.0 atom % in the methyl groups (^2H NMR).

2-Chloro-2-methyl-1-phenyl-(1,1-$^2H_2$)-propane (d_2-1) were synthesized from the corresponding deuterated alcohols as described for the protium compound. The deuterium content in the benzylic position was 99.2 ± 1.0 atom % (^1H NMR) and 1.0 ± 1.0 atom % in the methyl groups (^2H NMR).

Kinetics and Product Studies. The aqueous reaction solutions were prepared by mixing 3 volumes of the salt (1.00 M in water) with 1 volume of the organic solvent at room temperature, ca. 22 °C. The reaction vessel was either a 2-mL HPLC flask, sealed with a gas-tight PTFE septum, which was placed in an aluminum block in the water thermostat, or in the slower reactions, a 4-mL pear-shaped flask[28] equipped with a PTFE stop cock (high-vacuum type). The reactions were initiated by rapid addition, by means of a syringe, of the substrate dissolved in acetonitrile. At appropriate intervals, samples (300 μL) of the reaction solution were transferred with a thermostated syringe to an HPLC flask (in the experiments with strong base the flask contained a quench solution consisting of a mixture of 1 M $HClO_4$, acetic acid, and acetonitrile) and analyzed. The mol % of the starting material and each of the products were measured by means of the relative response factors measured in separate experiments. The rate constants were calculated from plots of ln (mol % starting material) vs time and product composition. In some of the experiments internal standard (p-xylene) was employed. Plots of ln (area starting material/area internal standard) vs time gave the same values of the rate constants, within the limits of experimental error, as those obtained from the mol % data.

The data with sodium azide are approximate, owing to incomplete chromatographic separation of the peaks from the azide product and **1**, and since the relative response factor of the azide product was not known. The estimated errors are considered as maximum errors derived from maximum systematic errors and random errors.

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