The Role of Ion–Molecule Pair Intermediates in Acid-Catalyzed Solvolysis. General Base-Catalyzed Formation of 4-Methylbenzyl Carbocation and Its Trapping by Nucleophiles

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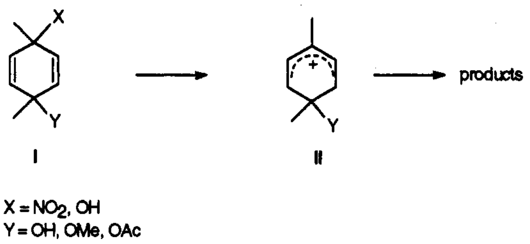
The specific acid-catalyzed hydrolysis of 3,6-dimethoxy-3,6-dimethyl-1,4-cyclohexadiene (**1**) in 25 vol % acetonitrile in water at 25 °C provides 2,4-dimethylphenol (**2a**), 2,5-dimethylphenol (**2b**), 2,4-dimethylanisole (**3a**), 4-methylbenzyl alcohol (**4**), and small amounts of 2,5-dimethylanisole (**3b**) and 4-methylbenzyl methyl ether (**5**). The formation of **3b** and **5** is proposed to involve intramolecular rearrangement of carbocation–molecule pair intermediates. The formation of 4-methylbenzyl alcohol (**4**) is catalyzed by general bases, indicating that dehydronation of the cyclohexadienyl carbocation is rate-limiting in its reaction to benzylic products. The Brønsted parameter was measured with carboxylate anions as $\beta = 0.28$. The 4-methylbenzyl carbocation, which is postulated to be an intermediate in this reaction, discriminates between added nucleophiles and solvent water: $k_{SCN}/k_{HOH} = 37$, $k_{Cl}/k_{HOH} = 9.8$, $k_{EtOH}/k_{HOH} = 1.9$, and $k_{MeOH}/k_{HOH} = 2.1$ (ratios of second-order rate constants). The rate constant for reaction of the carbocation with solvent water is estimated as $k_{HOH} = 1.4 \times 10^8$ M^{-1}s^{-1} (5.6×10^9 s^{-1}), assuming a diffusion-controlled rate constant of 5×10^9 M^{-1}s^{-1} for its reaction with thiocyanate anion. The nucleophilic selectivity values are considerably smaller than those exhibited by 4-methylbenzyl bromide under the same reaction conditions: $k_{Cl}/k_{HOH} = 210$, $k_{EtOH}/k_{HOH} = 3.8$, and $k_{MeOH}/k_{HOH} = 5.3$. These differences are concluded to be due to different mechanisms. The bromide reacts by a concerted bimolecular S_N2 mechanism with chloride anion. With alcohols and water, the reactions occur either by a concerted uncoupled mechanism or via the ion pairs.

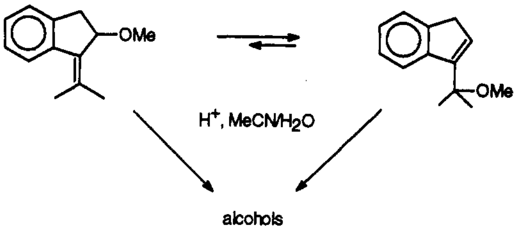
Introduction

The mechanisms of solvolysis of 3,6-dimethyl-1,4-cyclohexadiene derivatives (**I**) and similar substrates have received considerable attention during the past two decades.[1–6] The usefulness of these compounds in synthesis has also been examined.[7] The solvolysis mechanisms of the uncatalyzed or acid-catalyzed reaction of **I** have generally been assumed to involve ionization to the cyclohexadienyl carbocation **II** as the first step. Subsequent nucleophilic substitution, rearrangement, and aromatization processes give rise to a rather broad spectrum of products. Our interest in these mechanisms originates from interest in ion–molecule pair intermediates in solvolytic reactions.[8,9] An example of a previously studied system is the acid-catalyzed solvolysis of the allylic methyl ethers shown in Scheme II.[9] Intramolecular allylic rearrangement of the ethers accompanies formation of the corresponding allylic alcohols. This was considered as strong evidence for the intermediacy of carbocation–molecule pairs having substantial lifetimes.

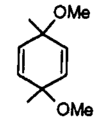
Scheme I



Scheme II



The chance that such processes also occur in the cyclohexadienyl system was considered to be good. In the present work, the mechanisms of the acid-catalyzed solvolysis of the diether **1** in aqueous acetonitrile have been studied. Evidence for intramolecular 1,3- and 1,5-



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[•] Abstract published in *Advance ACS Abstracts*, November 1, 1993.

(1) Kasperek, G. J.; Bruice, T. C.; Yagi, H.; Kaubisch, N.; Jerina, D. M. *J. Am. Chem. Soc.* **1972**, *94*, 7876–7882.

(2) Fischer, A.; Ramsay, J. N. *Can. J. Chem.* **1974**, *52*, 3960–3970.

(3) Banwell, T.; Morse, C. S.; Myhre, P. C.; Vollmar, A. *J. Am. Chem. Soc.* **1977**, *99*, 3042–3051.

(4) Gibbs, H. W.; Moodie, R. B.; Schofield, K. *J. Chem. Soc., Perkin Trans. 2* **1978**, 1145–1147.

(5) Geppert, J. T.; Johnson, M. W.; Myhre, P. C.; Woods, S. P. *J. Am. Chem. Soc.* **1981**, *103*, 2057–2062.

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(7) Alonso, F.; Barba, I., Yus, M. *Tetrahedron Lett.* **1990**, 2069–2080.

(8) (a) Sneen, R. A.; Felt, G. R.; Dickason, W. C. *J. Am. Chem. Soc.* **1973**, *95*, 638. (b) Katritzky, A. R.; Brycki, B. E. *J. Phys. Org. Chem.* **1988**, *1*, 1–20. (c) Szele, I.; Zollinger, H. *J. Am. Chem. Soc.* **1978**, *100*, 2811–2815. Hashida, Y.; Landells, R. G. M.; Lewis, G. E.; Szele, I.; Zollinger, H. *J. Am. Chem. Soc.* **1978**, *100*, 2816–2823. (d) Thibblin, A. *J. Chem. Soc., Chem. Commun.* **1990**, 697–699. (e) Thibblin, A. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1195–1198. (f) Thibblin, A.; Sidhu, H. *J. Am. Chem. Soc.* **1992**, *114*, 7403–7407. (g) Thibblin, A. *J. Phys. Org. Chem.* **1993**, *6*, 287–292. (h) Thibblin, A. *J. Phys. Org. Chem.* **1993**, *6*, 374–375.

(9) Thibblin, A. *J. Chem. Soc., Perkin Trans. 2* **1987**, 1629–1632.

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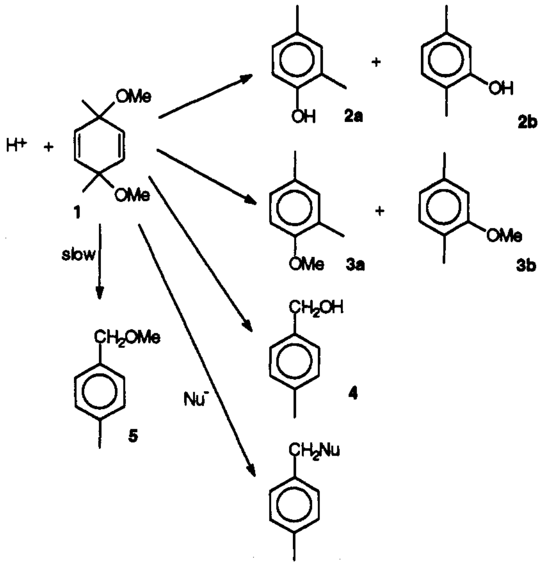
Scheme III



rearrangements will be presented. However, the allylic rearrangement is much less important in this system. Possible reasons will be discussed.

One of the products is 4-methylbenzyl alcohol (4). The formation of this product was found to be catalyzed by general bases. The mechanism is postulated to involve the 4-methylbenzyl carbocation. The cation is formed by base-catalyzed dehydronation of the cyclohexadienyl carbocation, followed by specific acid-catalyzed expulsion of methanol to give the 4-methylbenzyl carbocation that reacts with solvent water and added nucleophiles.

This route generates a "free" 4-methylbenzyl carbocation that is not associated to any leaving group, which otherwise may be a problem in studies of reactivity and selectivity of short-lived carbocations. Moreover, reactions of 4-methylbenzyl derivatives with moderately efficient nucleophiles are bimolecular S_N2 processes, or involve reaction of the ion pair with a pool of solvent molecules that are present when the ion pair is born, which complicates studies of solvolytically generated carbocation. The "azide clock" method[10] to estimate the lifetime of the carbocation formed from solvolysis is therefore not applicable. The results of the present work show that the 4-methylbenzyl carbocation has a significant lifetime in nucleophilic solvents.

Results

The reaction of an *E*/*Z*-mixture of 3,6-dimethoxy-3,6-dimethyl-1,4-cyclohexadiene (1) (*E*/*Z* ratio 27/73) in 25 vol % acetonitrile in water at 25 °C in the presence of perchloric acid yields the six products shown in Scheme III. The kinetics and the products were studied by a sampling high-performance liquid chromatography procedure. The kinetics of the reactions was also studied by following the increase in the absorbance at 277 nm with UV spectrophotometry. The measured rate constant, product compositions, and reaction conditions are shown in Table I.

Table I. Rate Constant, Product Compositions, and Reaction Conditions for the Acid-Catalyzed Solvolysis of 1[a] at 25 °C

solvent[b]	k_{obs},[c] M^{-1} s^{-1}	products,[c] mol %					
		2a	**2b**	**3a**	**3b**	**4**	**5**
25 vol % MeCN[d]	0.24	64	32	2.3	0.07	1.8	0.02
97 vol % MeCN[e]		74	*f*	24	0.2	1.1	0.2
50 vol % MeOH[e]		33	17	5	41	2.1	2.0

[a] Initial concentration: ≤1 mM. [b] In water. [c] Measured by HPLC. [d] Formate buffer added, $[HCOOH]/[HCOO^-]$ = 3.1, pH 3.36. [e] $[HClO_4]$ = 1 mM, $[NaClO_4]$ = 2 mM. [f] A trace may be formed (<10% of **2a**); see Experimental Section.

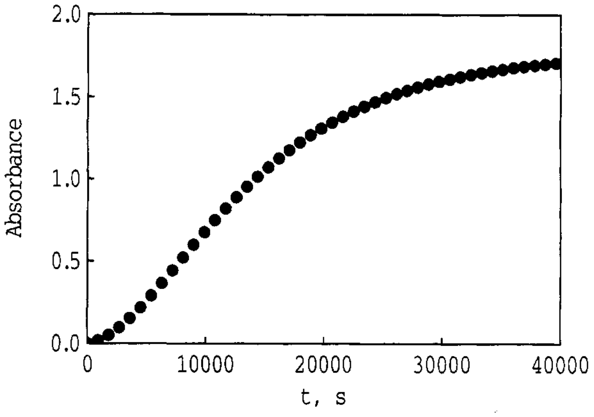


Figure 1. Increase in absorbance at 277 nm for the reaction of 1 in 25 vol % acetonitrile in water at pH 3.36.

Using the spectrophotometric method, the kinetics revealed that a long-lived intermediate is rapidly formed in the beginning of the reaction (Figure 1). Computer simulation (see Experimental Section) yields an approximate rate constant for the disappearance of the substrate 1 which has a value close to that obtained by the HPLC method (Table I). The intermediate disappears slightly faster than the substrate itself. Consistently, there is a small peak in the LC chromatograms, which disappears completely after a long reaction time and which has a UV spectrum quite similar to that of the starting material. This compound is concluded to be 3,6-dihydroxy-3,6-dimethyl-1,4-cyclohexadiene (6) (Scheme V), i.e., the hydroxy analogue of the ether 1. The formation of 6 is faster than formation of the phenols **2a** and **2b** and the anisoles **3a** and **3b**.

The disappearance of the substrate is specific acid catalyzed rather than general acid catalyzed since acetic acid or formic acid buffers up to a concentration of 0.75 M do not enhance the reaction rate at constant pH and ionic strength. The product composition is not constant throughout the reaction (Table I). The fraction of the phenols **2a** and **2b** increases during the reaction because these products are the only products from the diol 6 (possibly along with a small amount of 4). However, the product ratio of the two isomers **2a** and **2b** did not change, within experimental error, during the reaction. The solvolysis of 1 in acidified pure methanol gave exclusively **3a**, **3b**, and **5**.

The reaction of 1 in 97 vol % acetonitrile in water provided, within experimental error, only one of the phenols (**2a**, Table I). Reaction in 50 vol % methanol in water gave, as expected, a large fraction of anisoles.

A substantial increase in the amount of the benzylic product 4 (Scheme III) was found when buffer bases were added to the solution. Figure 2 shows the effect of increasing acetic acid buffer on the fraction of 4. The Brønsted plot has a slope of β = 0.28 (Figure 3). Traces of products from reaction of the nucleophilic carboxylate anions (to give benzylic and ring-substituted aromatic products) were seen. However, this competition between

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[10] Richard, J. P.; Rothenberg, M. E.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1361–1372.

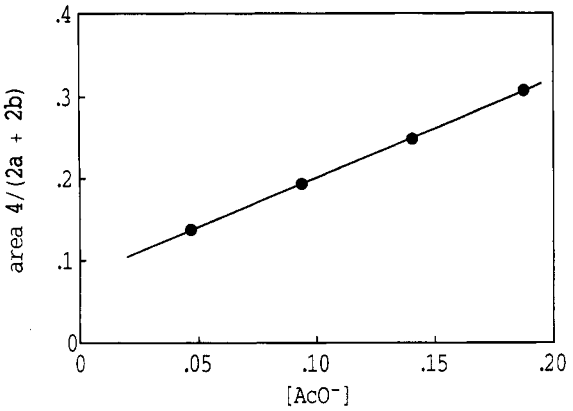

Figure 2. Increase in 4-methylbenzyl alcohol (4), expressed as the area ratio 4/(2a + 2b), as a function of buffer base concentration ([HOAc]/[OAc⁻] = 3) in 25 vol % acetonitrile in water; ionic strength maintained constant with sodium perchlorate.

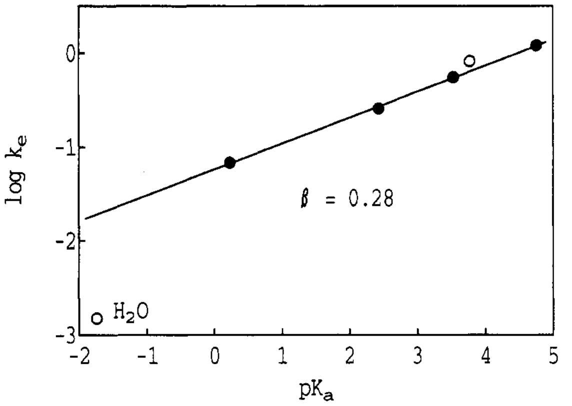

Figure 3. Brønsted plot for the dehydronation of the cyclohexadienyl carbocation by carboxylate anions in 25 vol % acetonitrile in water. The bases are in the order of decreasing basicity: $MeCOO^-$, $HCOO^-$, $MeOCH_2COO^-$, $CNCH_2COO^-$, and CF_3COO^-. The pK_a values refer to water.

water and carboxylate anions for the benzyl carbocation should have a negligible effect on the measured Brønsted parameter.

Other benzylic products were obtained when nucleophiles were added to the aqueous solution. The observed product ratio is a measure of the competition between nucleophile and water for the benzylic carbocation. The measured product ratio was used to calculate the discrimination between reaction of the carbocation intermediate with X^- and water by using eq 1:

$$k_X/k_{HOH} = ([4\text{-MePhCH}_2X]/[4\text{-MePhCH}_2OH])([H_2O]/[X^-]) \quad (1)$$

The ratio k_X/k_{HOH} is thus a ratio of second-order rate constants for reaction of nucleophile X and water with the carbocation. The ratios are listed in Table II. The product ratio for the chloride anion and ethanol could not be measured in the same experiment since the two products coeluted from the LC column. Bromide anion yields the corresponding benzylic product but, owing to its fast reaction to alcohol, it was difficult to measure the discrimination ratio. The chloride adduct also reacts with solvent under these reaction conditions but much more slowly, and only a small correction for this solvolysis was necessary for calculation of the k_{Cl}/k_{HOH} ratio.

A small amount of the benzylic ether 5 was obtained in 25 vol % acetonitrile in water. Decrease of the water content of the solvent from 75 vol % down to 3 vol % increased the amount of benzylic ether 10 times (Table I).

Table II. Nucleophilic Selectivities for the Reaction of 4-Methylbenzyl Carbocation at 25 °C

solvent[a]	k_{SCN}/k_{HOH}[b]	k_{Cl}/k_{HOH}[b]	k_{EtOH}/k_{HOH}[b]	k_{MeOH}/k_{HOH}[b]
25 vol % MeCN	37	9.8		
50 vol % EtOH			1.9	
50 vol % MeOH				2.1
25 vol % MeOH 25 vol % EtOH			1.7	2.3

[a] In water. [b] Ratios of second-order rate constants calculated from the measured product ratios and the concentrations of the nucleophiles using eq 1.

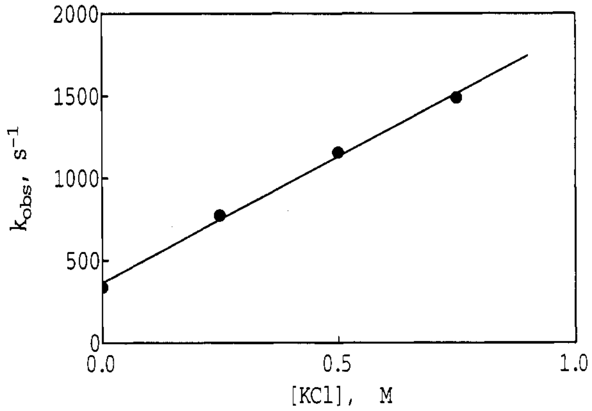

Figure 4. Dependence of observed rate constant of the reaction of 4-methylbenzyl bromide on the concentration of chloride anion in 25 vol % acetonitrile in water.

Table III. Rate Constants, Nucleophilic Selectivities, and Reaction Conditions for the Solvolysis of 4-Methylbenzyl Bromide at 25 °C

solvent[a]	$10^6 k_{obs}$, s^{-1}	$10^6 k_{Cl}$,[b] $M^{-1} s^{-1}$	k_{Cl}/k_{HOH}[c]	k_{EtOH}/k_{HOH}[c]	k_{MeOH}/k_{HOH}[c]
25 vol % MeCN	338	1535	210		
50 vol % EtOH	104			3.8	
50 vol % MeOH	330				5.3
25 vol % MeOH 25 vol % EtOH	190			7.5	2.9

[a] In water. [b] Calculated from the slope of the linear plot shown in Figure 4. [c] Ratios of second-order rate constants calculated from the measured product ratios and the concentrations of the nucleophiles using eq 1.

The reaction of 4-methylbenzyl bromide, using the same conditions as for 1, has been studied by a sampling high-performance liquid chromatography procedure. The reaction with added chloride anion is bimolecular, as shown in Figure 4. The data are presented in Table III. The product data yield k_{Cl}/k_{HOH} = 210. The kinetic data, treating the reaction with water as a second-order rate constant, give a slightly lower value, k_{Cl}/k_{HOH} = 189. This is presumably due to a negative specific salt effect of the chloride anion on the S_N2 reaction having a carbocation-like transition state.[11]

Discussion

The solvolysis of 1 is specific acid catalyzed since it is catalyzed by H_3O^+ but not by general acids, such as formic acid or acetic acid. This is in accord with what has been found for other acid-catalyzed heterolytic reactions of methyl ethers, for example, anthranylic and allylic

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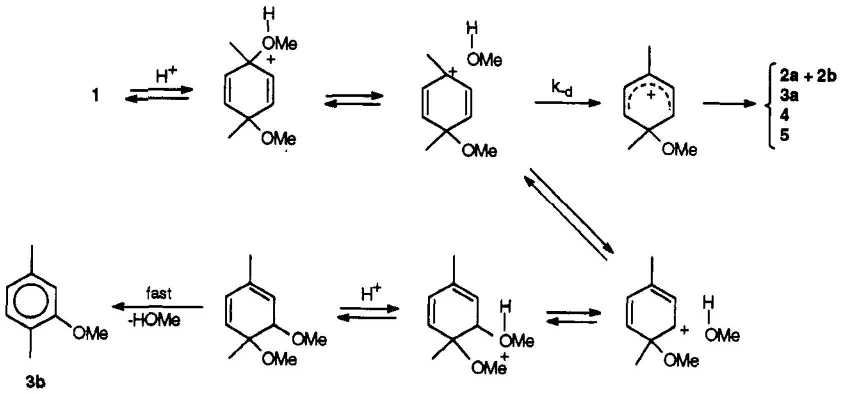
[11] Maskill, H. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1241–1246.

Scheme IV



derivatives,[8d,9] which ionize to relatively stable carbocation intermediates. However, general base catalysis has been reported for addition of weakly basic alcohols to moderately stable 1-phenylethyl carbocations, which corresponds to general acid catalysis in the reverse direction.[12]

The ionization step of the hydronated substrate should be rate limiting or partially rate limiting. The solvolysis reactions of **I** ($X = NO_2$, $Y = OAc$) and of **I** ($X = NO_2$, $Y = OH$) in aqueous solvents (Scheme I), which involve cleavage of the bond to the nitro group, have been discussed in terms of stepwise $D_N + A_N$ (S_N1) mechanisms.[5,6] It has been found that a single diastereomer of **I** ($X = NO_2$, $Y = OH$) in 50% methanol in water yields a diastereomeric mixture of **I** ($X = NO_2$, $Y = OH$) as well as of **I** ($X = OMe$, $Y = OH$). These were the major products under neutral conditions.

The reaction of **I** ($X = NO_2$, $Y = OH$) in 50% methanol in water has been found to provide up to 20% of 2,5-dimethylnitrobenzene.[2] This result strongly indicates an intramolecular 1,3-rearrangement through the ion pair R^+ NO_2^-, followed by fast elimination of water to give the nitroaromatic product. A most interesting question is whether an analogous mechanism is possible for the ether **1** employing an ion–molecule pair instead of the ion pair. The product of such a mechanism is the anisole **3b** (Scheme III). As mentioned in the Introduction, a similar type of mechanism through ion–molecule pair intermediates has been concluded for the acid-catalyzed rearrangement of allylic ethers (Scheme II).[9]

The anisoles **3a** and **3b** are formed in 2.4% yield from **1** in 25 vol % acetonitrile in water (Table I). Only 3% of the anisole mixture consists of the isomer **3b**. The formation of **3b** indicates that the methanol molecule of the ion–molecule pair undergoes a 1,3-migration to give the isomeric ether, which, in acidic solution, rapidly expels methanol (Scheme IV). The small fraction of **3b** is presumably due to steric hindrance from the methyl and methoxyl groups of the adjacent carbon, which makes allylic rearrangement relatively slow as compared with diffusional separation to free carbocation. Accordingly, data for the reaction in 97 vol % acetonitrile in water shows that the nucleophilic attack of water on carbon 1 (k_1) is much faster than attack on carbon 3 (k_3) since only one of the phenol isomers (**2a**) was obtained (Scheme V, Table I). Consistent with the interpretation that allylic rearrangement of the ion–molecule pair is responsible for the formation of the anisole isomer **3b** is the fact that this isomer is the *dominant* product in reaction in 50 vol % methanol in water (Table I). The large concentration of methanol results in a greatly enhanced concentration of the ion–molecule pair. However, much of **3b** is expected to result from nucleophilic attack of methanol from the solvent on carbon 3, and it is not possible to distinguish between intramolecular and intermolecular isomerization.

It is plausible that the Me shift occurs to a substantial extent before the diffusional separation and that this process also competes successfully with migration of the methanol molecule. In fact, the methyl group might facilitate the ionization by neighboring group participation. Surprisingly, no anisole products were produced from acid-catalyzed hydrolysis of **I** ($X = OH$, $Y = OMe$) despite the fact that the carbocation **II** ($Y = OMe$) is expected to be formed under these conditions.[1]

The mechanistic interpretation of the results is complicated by the fact that **3b** may, in principle, be formed also by a 1,2-shift of the methoxyl group. However, Fischer and co-workers have found that migration of the methyl group in the carbocation **II** ($Y = OH$) is at least 50 times faster than migration of the hydroxyl.[6] Myhre's group has also arrived at a similar conclusion.[5] The preference for methyl migration to migration of a methoxyl group should be of about the same magnitude.[6] If this large preference in migration is correct, it may be inferred that **3b** is subsequently formed mainly or exclusively via an intramolecular 1,3-rearrangement through the ion–molecule pairs (Scheme IV). In analogy with what has been concluded for the allylic system shown in Scheme II, which gives a substantial amount of isomerization under the same reaction conditions,[9] it is suggested that *two* discrete intermediates of ion–molecule pair type are involved in the isomerization. The methanol molecule in these intermediates is associated to carbon 1 and 3 of the allylic system, respectively. Another example of isomerization through ion–molecule pair intermediates is the formation of 4-methylbenzyl methyl ether (**5**) by a 1,5-intramolecular rearrangement (see below).

It is likely that some internal return from the ion–molecule pair (1^+OMeH) accompanies product formation. It has been suggested that internal return is faster than product formation in the reaction of **I** ($X = NO_2$, $Y = OH$) in aqueous ethanol.[5]

The reaction of **1** to the observed products is consistent with the mechanistic model of Scheme V.

Formation of Benzylic Products. The general base-catalyzed formation of the benzylic products is mechanistically interesting. The studies by Myhre and Fischer and their co-workers of **I** ($X = NO_2$, $Y = OH$) or **I** ($X = NO_2$, $Y = OAc$) in mixtures of organic solvents with water have not revealed any products of this type.[5,6] Moreover, Bruice has not found benzylic products from acid-catalyzed

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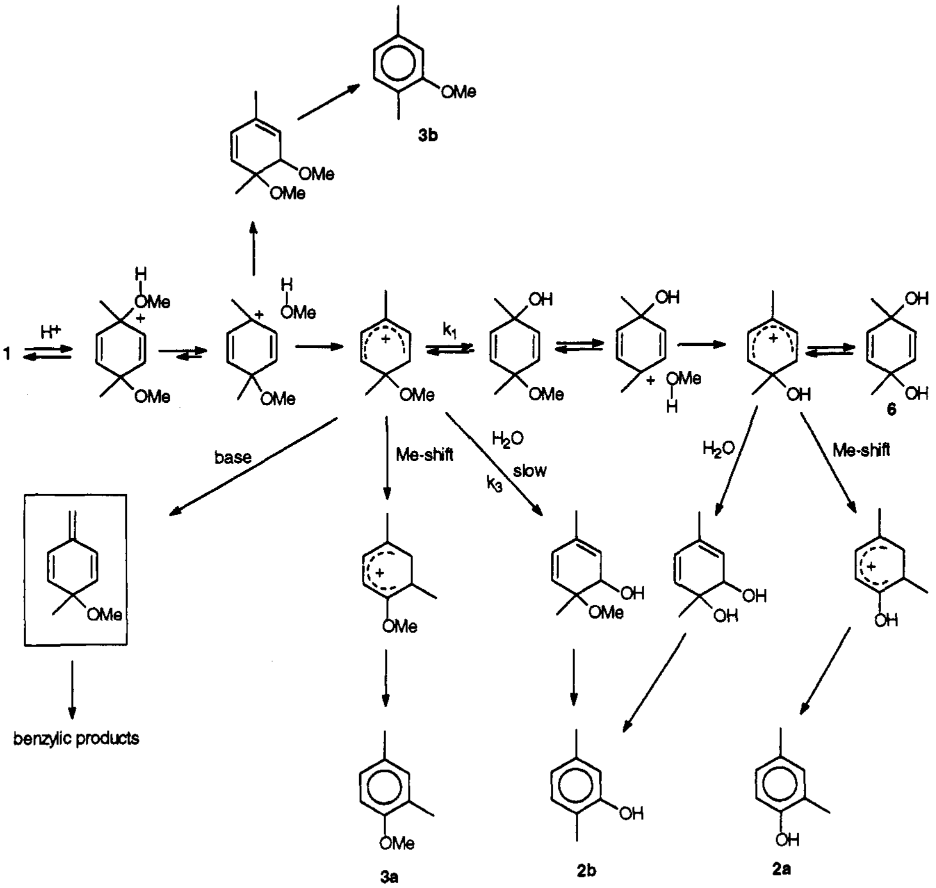
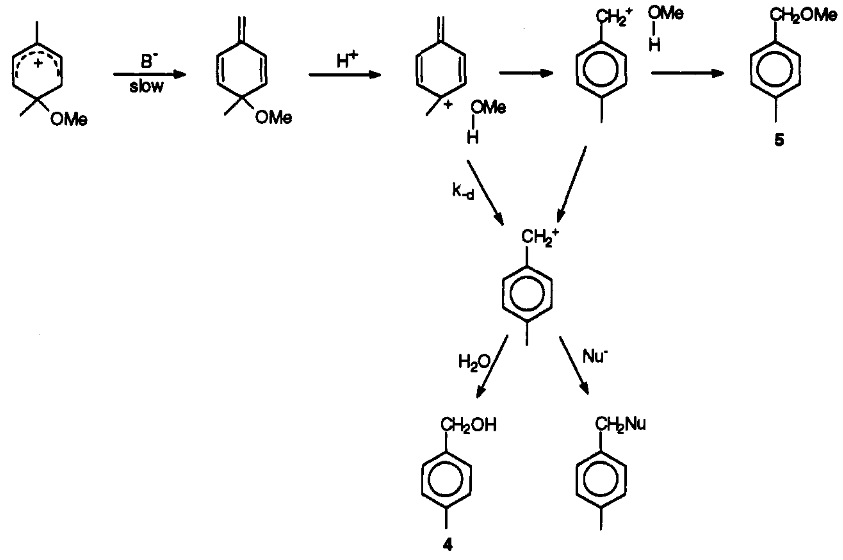
[12] Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* 1984, *106*, 1396–1401.

Scheme V



Scheme VI



solvolysis of **I** (X = OH, Y = OMe).[1] This is the reason why no route to benzylic derivatives from the diol **6** has been indicated in Scheme V.

The mechanism should involve dehydronation of the cyclohexadienyl carbocation to give a triene, followed by rapid acid-catalyzed expulsion of methanol to give the benzylic carbocation (Scheme VI). A related, but more stable, triene, 1-methylene-2,3,4,4,5,6-hexamethyl-2,5-cyclohexadiene, has been isolated.[13] The carbocation may be trapped by the nucleophilic solvent or by any other nucleophile present in the solution. The abstraction of a hydron from the carbocation is, as shown by the presence of general base catalysis in 25 vol % acetonitrile in water (Figure 3), the rate-limiting step. This is not unexpected since hydron transfer to and from carbon is usually relatively slow.[14] The Brønsted parameter of $\beta = 0.28$ (Figure 3) corresponds to an early transition state in which the hydron is transferred less than 50% to the oxyanion base. The β parameter is substantial because of the relatively high stability of the cyclohexadienyl carbocation and the relatively low stability of the elimination product, which corresponds to a transition state that is more symmetric than it usually is in this type of reaction.

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[13] von E. Doering, W.; Saunders, M.; Boyton, H. G.; Earhart, H. W.; Wadley, E. F.; Edwards, W. R.; Laber, G. *Tetrahedron* **1958**, *4*, 178–185.

[14] See, for example: Caldin, E.; Gold, V. *Proton-Transfer Reactions*; Chapman and Hall: London, 1975.

Dehydronation by water is about 10 times less efficient. Similar behavior has been found previously.[15]

There are very few studies in the literature on dehydronation of "free" carbocations. Abstraction of a hydron from stabilized carbocations has been studied in 50 vol % water–acetonitrile.[16] A Brønsted parameter of $\beta = 0.32$ and a kinetic deuterium isotope effect of $k_H/k_{D_2} = 6.7$ were measured for a substrate stabilized with one ferrocenyl group, with tertiary amines used as hydron abstractors. Two ferrocenyl groups resulted in a Brønsted parameter of $\beta = 0.45$. Some acid-catalyzed elimination of water and alcohols has been found to exhibit large kinetic deuterium isotope effects. For example, $Ph_2C(CD_3)OH$ reacts to give alkene in 25 vol % acetonitrile in water with $k_H/k_{D_3} = 6.5$.[8f] However, these solvolytic isotope effects include contribution from preequilibrium steps and do not entirely measure the degree of hydron transfer in the transition state of the rate-limiting step.

The dehydronation step of some solvolytic elimination reactions of substrates with negatively charged leaving groups has been examined with help of Brønsted plots.[15,17–19] For example, $\beta = 0.13$ and $k_H/k_{D_6} = 3.5$ were measured for the dehydronation of the intermediate formed from heterolysis of $PhCMe_2Cl$ in 25 vol % acetonitrile in water, with substituted acetate anions used as bases.[15] The carbocations are presumably not diffusionally equilibrated in these reactions but are associated to the leaving groups as ion pairs. A very small Brønsted parameter ($\beta = 0.05$) and a kinetic isotope effect of moderate size ($k_H/k_{D_6} = 2.8$) have been reported for the elimination of HCl from a very short-lived carbocation ion pair under the same reaction conditions as above.[19]

Work at Myhre's laboratory has provided evidence for the operation of a mechanism similar to that of Scheme VI in the solvolysis of I ($X = NO_2$, $Y = OAc$) in concentrated sulfuric acid solutions.[5] Under these conditions, the acetoxy group is hydronated and the substrate reacts by departure of acetic acid. Abstraction of a hydron followed by departure of NO_2^- provides the benzylic cation, which, in the subsequent step, reacts with the solvent to give 4-methylbenzyl alcohol. A smaller yield of this product was obtained from the corresponding d_6-substrate having the methyl groups deuterated.

The intramolecular formation of the ether **5** shows that the 1,5-migration of methanol can compete with diffusional separation of the complex (k_{-d} in Scheme VI), although not very successfully. The measured product ratio of **4** and **5** for reaction in 25 vol % acetonitrile in water shows that the intramolecular reaction is about 100 times slower than the diffusional separation of the ion–molecule complex. The methanol molecule has a long distance to migrate, which results in this low yield of benzyl ether **5**. The ratio decreases when the water content of the solvent decreases. Thus, the intramolecular reaction is only five times slower than the reaction with solvent water in 97 vol % acetonitrile in water.

Alternative mechanisms for formation of benzylic products involve nucleophilic attack on the exocyclic carbon of the triene followed by expulsion of methanol. This may occur either concerted or stepwise through a carbanion. However, such mechanisms do not seem very likely, e.g., addition of a nucleophile to the exocyclic double bond yields a nonaromatic carbanion. Expulsion of methanol, on the other hand, yields the 4-methylbenzyl carbocation and should be favored energetically since it involves aromatization. This conclusion is supported by a work by Suzuki and co-workers which suggests that a pentamethylbenzyl carbocation–nitrite anion ion pair is formed in the first step of the reaction of the corresponding nitrotriene.[20]

Trapping of 4-Methylbenzyl Carbocation. The formation of the 4-methylbenzyl carbocation from **1** constitutes a new alternative to ordinary solvolysis of 4-methylbenzyl derivatives for generation of the carbocation (Scheme VI). The method has the advantage that the carbocation is free from any interactions or shielding from a leaving group. Effects of association of a carbocation to the leaving group as an ion pair or ion–molecule pair are often a problem in the mechanistic interpretation of results of stepwise solvolytic reactions. Moreover, 4-methylbenzyl derivatives with efficient leaving groups yield bimolecular S_N2 reactions with moderately strong nucleophiles, which does not make studies of the carbocation easier.

The carbocation reacts 37 times faster with SCN^- than with a solvent water molecule (Table II). This relatively high selectivity shows that the lifetime of the carbocation is significant and that, to some extent, it has time to diffuse through the solvent before reaction. A rate constant for reaction with solvent water of $k_{HOH} = 5.6 \times 10^9\ s^{-1}$, or $k_{HOH} = 1.35 \times 10^8\ M^{-1}\ s^{-1}$, is estimated on the basis of the assumption that the reaction with thiocyanate anion is diffusion controlled, with a rate constant of $5 \times 10^9\ M^{-1}\ s^{-1}$. This assumption is in accord with data of Richard and co-workers, who have found that thiocyanate and azide anion react with 1-(4-methoxyphenyl)-2,2,2-trifluoroethyl carbocation at the same rate. They concluded that both reactions are diffusion limited.[21] The rate constant for reaction of 4-methylbenzyl carbocation with water is very similar to the rate constant for reaction of 1-(4-methylphenyl)ethyl carbocation with solvent water measured as $k_{HOH} = 0.9 \times 10^8\ M^{-1}\ s^{-1}$ in 20 vol % acetonitrile in water and as $k_{HOH} = 1.3 \times 10^8\ M^{-1}\ s^{-1}$ in 50 vol % trifluoroethanol in water.[10,22] A roughly 50% larger rate constant was estimated by taking into account reaction directly from the ion pair.[17]

The methyl group is expected to stabilize the secondary cation, which should result in a significantly smaller rate constant k_{HOH} for 1-(4-methylphenyl)ethyl carbocation than for the 4-methylbenzyl carbocation. The very similar rate constants for reaction with solvent shown by the two carbocations support the assumption that the thiocyanate anion reacts at a diffusion-controlled rate with the 4-methylbenzyl carbocation (since an even smaller k_{HOH} value is obtained if the reaction rate with thiocyanate is not diffusion-limited).

The absence of a significant difference in k_{HOH} for the primary and the secondary carbocation may be due to the fact that the rate constant for the latter is evaluated from solvolysis data. The leaving group might have the effect of decreasing the ratio of azide product to alcohol, on which

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the calculation of k_{HOH} is based, and accordingly to yield a too large k_{HOH} for 1-(4-methylphenyl)ethyl carbocation. A shielding effect from the negatively charged leaving group that decreases the rate constant for attack of negatively charged nucleophiles, even the potent azide anion, more than attack of a neutral nucleophile is reasonable. This shielding effect may introduce a general systematic positive error in the estimated rate constants for the water reaction of short-lived carbocation generated in solvolysis.

The thiocyanate ion is only about four times more reactive than chloride anion toward the carbocation (Table II). This shows that the ion pair R^+Cl^- collapses rapidly to covalent material, i.e., the barrier for internal return from any ion pair formed from heterolysis of the chloride is very small.

As expected, the nucleophilic selectivity of the carbocation toward methanol, ethanol, and water favors reaction with the alcohols more than reaction with water, and methanol is slightly more reactive than ethanol. The selectivity value $k_{MeOH}/k_{HOH} = 2.1$ is considerably smaller than that exhibited by the 1-(4-methylphenyl)ethyl carbocation, $k_{MeOH}/k_{HOH} = 4.7$.[17] This large difference is a further indication that the estimated value of k_{HOH} for the latter carbocation, based upon trapping with azide anion, is too large owing to the above-discussed shielding effect. Other nucleophilic selectivity values previously reported include $k_{MeOH}/k_{HOH} = 6.4$ for the 1,1-diphenylethyl carbocation and $k_{MeOH}/k_{HOH} = 2.9$ for the 1-methyl-1-phenylethyl carbocation.[8e,15]

The solvolysis of 4-methylbenzyl bromide with chloride ion is a bimolecular concerted reaction (Figure 4). Accordingly, the selectivity value $k_{Cl}/k_{HOH} = 210$ given in Table III does not reflect trapping of a carbocation intermediate. The reactions with solvent and alcohols, on the other hand, may occur either stepwise, as suggested by Pross and co-workers,[23] or concerted. It is not possible to make a clear-cut distinction between these two mechanistic alternatives. The different nucleophilic selectivities shown by the cation and 1-(4-methylphenyl)ethyl bromide for these neutral nucleophiles may be caused by concerted reactions of the bromide but may also reflect reactions through ion pair. Selectivities of $k_{EtOH}/k_{HOH} = 2.6$ and $k_{EtOH}/k_{HOH} = 2.0$ have been reported for reaction of the bromide and the chloride, respectively, at 50 °C.[23b]

Studies of reactions of "free" 4-methylbenzyl or benzyl carbocation have not been reported previously. Recent results suggest that the latter has a far too short lifetime to allow it to react with other nucleophiles than those that are present when the carbocation is born. Thus, the lifetime of unsubstituted benzyl carbocation in 50% trifluoroethanol–water has been estimated to be so short, $k_s = 4 \times 10^{11}\ s^{-1}$, that it reacts faster with solvent than the ion pair diffuses apart.[11,24,25] Selectivity values of $k_{SCN}/k_{HOH} = 452$, $k_{Cl}/k_{HOH} = 26$, and $k_{EtOH}/k_{HOH} = 2.8$ have been measured for solvolysis of benzyl tosylate in 50 vol % trifluoroethanol in water.[11] The reactions were discussed in terms of coupled and uncoupled S_N2 mechanisms.

Experimental Section

General Procedures. The NMR analyses were performed with a Varian XL 300 spectrometer. The high-performance liquid chromatography (HPLC) analyses were carried out with a Hewlett-Packard 1090M liquid chromatograph equipped with a diode-array detector and a C18 reversed-phase column (3 × 100 mm). The mobile phase was a solution of acetonitrile in water or, in some experiments, methanol in water. A Kontron Uvicon 930 spectrophotometer equipped with an automatic cell changer thermostated with water from a Heto 01 PT 623 thermostat bath was used for the kinetic experiments.

Materials. The ether 3,6-dimethoxy-3,6-dimethyl-1,4-cyclohexadiene (**1**) was received as a gift from Miguel Yus. ^1H NMR analysis showed an *E*/*Z* ratio of 27/73. The phenols 2,4-dimethylphenol (**2a**, Aldrich, 99+ %) and 2,5-dimethylphenol (**2b**, Supelco), 2,4-dimethylanisole (**3a**, Janssen Chimica, 99%), and 2,5-dimethylanisole (**3b**, Janssen Chimica, 99%) were used for calibration purposes. 4-Methylbenzyl bromide was purchased from Aldrich. Acetonitrile, ethanol (99.5 %), and methanol were of spectroscopic quality and were used as solvents without further purification. All other chemicals were of reagent grade.

Kinetics and Product Studies. The reaction solutions were prepared by mixing the acetonitrile with the cosolvent at room temperature, ca. 22 °C. The reaction vessel was either a thermostated 3-mL UV cell or a 2-mL HPLC flask, sealed with a gas-tight PTFE septum, which was placed in an aluminum block in the water thermostat. The reactions were initiated by fast addition of a few μL, by means of a syringe, of the substrate dissolved in acetonitrile. The absorbance increase at 277 nm of the reactions, measured with the spectrophotometer, or the decrease in peak area of the substrate, measured with the HPLC apparatus, were followed for at least 10 half-lives. The rate constants of the disappearance of the substrate were calculated by means of a non-linear least-squares regression computer program.

The product compositions were calculated from peak areas measured by HPLC employing the relative response factors, which were determined in separate experiments. The phenols did not separate on the column but eluted as one peak. However, the isomer ratio was determined from comparison of the UV spectrum of the phenol peak (obtained with the diode-array LC detector) with the UV spectra of the pure compounds. This method is not very sensitive for detection of a small amount of 2,5-dimethylphenol (**2b**) mixed with a large amount of the 2,4-isomer. Thus, a small amount of **2b** (<10% of **2a**) may be hidden in the large phenol peak in the solvolysis experiment using 97 vol % acetonitrile in water (Table II).

The kinetic data from the UV kinetics (Figure 1) were computer simulated using the integrated rate constant expressions for the system of eq 1,[26] where **B** is a long-lived intermediate and **C** is products absorbing at 277 nm (phenols and anisoles). The model is rather crude since it does not take into account the formation of benzylic products.

$$\begin{tikzcd}
\mathbf{1} \arrow[rr, "k_{AB}"] \arrow[dr, "k_{AC}"'] & & \mathbf{B} \arrow[dl, "k_{BC}"] \\
& \mathbf{C} &
\end{tikzcd} \qquad (1)$$

The simulation gave approximate values for the rate constants k_{AB}, k_{AC}, and k_{BC} of (110, 5, and 144) × $10^{-6}\ s^{-1}$, respectively, at pH 3.36. A maximum concentration of **B** was attained after a reaction time of about 2 h, the same as was obtained from the HPLC kinetics.

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