diffusion and electron transfer occur *laterally* within the membrane. The results reported here describe a system where the donor and acceptor are bound at different depths within the membrane. Thus, while diffusion is still primarily lateral in nature, electron transfer occurs in the *transverse* direction. It is the vectorial arrangement of the system which permits the distance change in passing through the phase transition to overcome the effects of diffusion, allowing the exponential dependence of the reaction on distance to become the dominant factor. This results in the opposite dependence of the PET reaction on the membrane physical state from that reported in the earlier work.

In conclusion, liposomal membranes have been used as media for photoinduced electron transfer reactions. The donor and acceptor were conveniently separated by binding at different depths within the bilayer membrane. This is particularly important for hydrophobic molecules such as the borates employed in this study. The aqueous complexes formed by these anions with water-soluble cationic dyes have intricate photophysical and photochemical pathways open to them, resulting in relatively inefficient PET. Solubilization within phospholipid membranes prevents this association, thereby reducing the number of pathways open to the excited cyanine and enhancing PET from borate to dye. Moreover, the donor–acceptor separation and, therefore, electron-transfer efficiency are dependent on the physical state of the membrane. The strong distance dependence of PET reactions leads to dramatic effects on the photobleaching and fluorescence quenching efficiencies. In fact, these types of experiments may provide a means of accurately determining the locations of membrane-bound donors and acceptors, provided the binding site of one of the redox partners is known and one can quantitatively account for diffusion and the variable dielectric. An additional appealing feature of the system is that back electron transfer appears to be a very minor process within the membrane. This permits the liposomal system to store the excitation energy as redox products for potentially useful amounts of time. This general strategy could in principle be used to generate a large number of reduced acceptors at or near the surface of a liposome. The stored energy could then be used to drive subsequent chemical transformations, a system which is made even more attractive by the high surface area afforded by liposomes. In fact, Willner and associates have incorporated many of these features into a colloidal-based system which effectively hydrogenates ethylene.[16] However, in that system the chemical processes were confined to the colloid surface or bulk aqueous medium, whereas the system described here is based on redox processes occurring within the membrane itself. Finally, the results obtained in this study suggest that the design of membrane-based systems for the harvest and conversion of light energy should include an investigation of the role of the lipid bilayer in promoting or inhibiting the desired photochemistry.

Acknowledgment. The authors thank the National Science Foundation for partial support of this research.

Kinetic Deuterium Isotope Effects as Evidence for a Common Ion-Pair Intermediate in Solvolytic Elimination and Substitution Reactions of 1,1-Diphenylethyl Chloride

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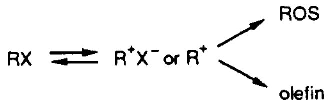
Abstract: Solvolysis of 1,1-diphenyl-1-chloroethane (**1**-Cl) in acetonitrile at 25 °C provides the elimination product 1,1-diphenylethene (**3**). Addition of water or methanol to the acetonitrile increases the rate of elimination and gives rise to a second product, 1,1-diphenyl-1-hydroxyethane (**1**-OH) or 1,1-diphenyl-1-methoxyethane (**1**-OMe). The deuteriated analogue, 1,1-diphenyl-1-chloro[2,2,2-$^2H_3$]ethane (d-**1**-Cl), reacts slower. The overall kinetic deuterium isotope effect was found to decrease from $(k_{12}^H + k_{13}^H)/(k_{12}^D + k_{13}^D) = 1.73$ in pure acetonitrile to 1.34 in 20 vol % methanol in acetonitrile. This isotope effect is composed of a substitution isotope effect k_{12}^H/k_{12}^D and an elimination isotope effect k_{13}^H/k_{13}^D, which simultaneously change from 0.84 to 0.96 and from 2.2 to 3.2, respectively, when the methanol concentration is increased from 1.96 to 9.09 vol %. These results indicate a branched mechanism involving an almost rate-limiting formation of a common carbocationic intermediate. The acid-catalyzed solvolysis of 1,1-diphenyl-1-phenoxyethane (**1**-OPh) in acetonitrile containing 0.4 vol % aqueous 2 M sulfuric acid quickly provides the alcohol **1**-OH, $k_{12}/k_{13} \approx 11$, which in a subsequent fast reaction yields the olefin **3** as the final product. In contrast, the solvolysis of the chloride **1**-Cl in 0.4 vol % water in acetonitrile yields almost exclusively olefin **3**, $k_{12}/k_{13} = 0.003$. The results strongly indicate that the leaving chloride anion is involved in the elimination process and that the common intermediate is the contact ion pair. The isotope effect of the acid-catalyzed elimination of the alcohol **1**-OH in 0.4 vol % water in acetonitrile is $k_{13}^H/k_{13}^D = 5.3$, which increases to $k_{13}^H/k_{13}^D = 6.5$ in 25 vol % acetonitrile in water. The possibility of an ion–molecule pair intermediate in the acid-catalyzed solvolysis is discussed.

Introduction

Solvolytic reactions of substrates having at least one hydron in the β position generally give both a substitution product, by reaction with the solvent or added nucleophile, and an elimination product. The substitution product is usually the dominant product in nucleophilic solvents. When the experimental results indicate stepwise solvolysis, the substitution and the elimination have frequently been postulated for the sake of mechanistic simplicity to occur via a common carbocationic intermediate (eq 1). Kinetic deuterium isotope effects for the separate reactions have provided experimental evidence for branching via a common ion pair in the solvolysis of the relatively unreactive 9-(2-chloro-2-propyl)fluorene[1] in a highly aqueous medium and strong support for branching in some other systems.[2-5]



(1)

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[1] Thibblin, A. *J. Am. Chem. Soc.* **1987**, *109*, 2071–2076.
[2] Thibblin, A. *J. Chem. Soc., Perkin Trans. 2* **1986**, 321–326.
[3] Thibblin, A. *J. Am. Chem. Soc.* **1989**, *111*, 5412–5416.

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Table I. Rate Constants[a] and Reaction Conditions for the Solvolysis of **1**-Cl in Acetonitrile and in Mixtures of Acetonitrile with Methanol at 25 °C

substrate[b]	addition	$10^6(k_{12} + k_{13})$,[c] s^{-1}	$10^6 k_{12}$,[d] s^{-1}	$10^6 k_{13}$,[d] s^{-1}
h-**1**-Cl		628		628
d-**1**-Cl		364		364
h-**1**-Cl	6 mM TEA[e]	630		630
h-**1**-Cl	[$^2H_3$]MeCN[f]	578		578
d-**1**-Cl	[$^2H_3$]MeCN[f]	337		337
h-**1**-Cl	1.96% MeOH	1796	229	1567
d-**1**-Cl	1.96% MeOH	992	272	720
h-**1**-Cl	3.85% MeOH	3462	801	2661
d-**1**-Cl	3.85% MeOH	2009	936	1073
h-**1**-Cl	5.66% MeOH	5740	1819	3921
d-**1**-Cl	5.66% MeOH	3512	2074	1438
h-**1**-Cl	7.41% MeOH	8550	3294	5256
d-**1**-Cl	7.41% MeOH	5398	3630	1768
h-**1**-Cl	9.09% MeOH	11985	5277	6708
d-**1**-Cl	9.09% MeOH	7580	5486	2094
h-**1**-Cl	20% MeOH	43000		
d-**1**-Cl	20% MeOH	32180		

[a] Defined in Scheme I. [b] Substrate concentration 0.1 mM. [c] Observed rate constants measured by UV spectroscopy (see the Experimental Section). [d] Calculated from $k_{12} + k_{13}$ and the product ratio measured by HPLC (see the Experimental Section). [e] Triethylamine. [f] 100% of the heavy acetonitrile (Glaser, 99.8 atom % ^{2}H).

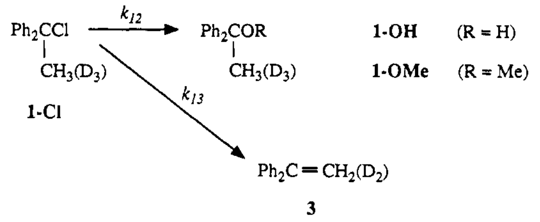
As indicated in eq 1, the common intermediate may be an ion pair or a free, solvent-equilibrated carbocation which is formed by reversible or irreversible ionization. It may also be a carbocation–molecule pair formed from a substrate with a neutral leaving group, e.g., an ammonium salt or a protonated ether or alcohol. However, most often the solvolysis of this type has been discussed in terms of a free carbocation, and the possibility of a carbocation–molecule pair has been ignored. There are a few reports on substitution and/or rearrangement reactions which have been concluded to involve such intermediates. Elimination reactions have very seldom been discussed in terms of elimination from an ion–molecule pair.[6,7]

Recent results suggest that the acid-catalyzed solvolysis of 1,1-diphenylethyl methyl ether (**1**-OMe) in highly aqueous medium (20 vol % dimethyl sulfoxide in water) involves reversible formation of an ion–molecule pair, which may be trapped by the strongly nucleophilic iodide anion.[8] The present study was started with the intention to investigate whether the elimination from the methyl ether also occurs via the carbocation–molecule pair. The reaction was run in nearly 100% acetonitrile to keep the competing substitution to a minimum. The acid-catalyzed solvolytic elimination of the corresponding alcohol was employed as a reference reaction.

In this paper we also describe the solvolysis of the very reactive 1,1-diphenyl-1-chloroethane (**1**-Cl) in mixtures of acetonitrile with methanol. Analysis of the kinetic deuterium isotope effects for the separate reactions of the chloride **1**-Cl, i.e., the elimination and the substitution, strongly indicates that the reactions have a common intermediate. Very significant base catalysis from the leaving group indicates that this intermediate is the contact ion pair.

Results

Scheme I



Scheme II

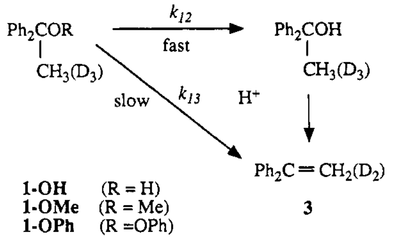


Table II. Rate Constants[a] for the Acid-Catalyzed Solvolysis of **1**-OH, **1**-OMe, and **1**-OPh in Acetonitrile–Water at 25 °C

substrate[b]	solvent[c]	$10^6 k_{13}$,[d] s^{-1}	$k_{13}/[H^+]$, $M^{-1}\,s^{-1}$	k_{12}/k_{13}[e]
h-**1**-OH	75% 1 M $HClO_4$	41.7	56×10^{-6}	
d-**1**-OH	75% 1 M $HClO_4$	6.4	8.5×10^{-6}	
h-**1**-OH	0.4% 2 M H_2SO_4	725	0.045	
d-**1**-OH	0.4% 2 M H_2SO_4	136.3	0.0085	
h-**1**-OMe	0.4% 2 M H_2SO_4			11
h-**1**-OPh	0.4% 2 M H_2SO_4			10

[a] Defined in Scheme II. [b] Substrate concentration 0.1 mM. [c] Volume % aqueous acid in acetonitrile. [d] Observed rate constants measured by UV spectroscopy (see the Experimental Section). [e] Calculated from the product ratio measured by HPLC (see the Experimental Section).

Table III. Kinetic Deuterium Isotope Effects for the Reactions of **1**-Cl and **1**-OH at 25 °C

substrate	addition	$(k_{12}^H + k_{13}^H)/(k_{12}^D + k_{13}^D)$[a]	k_{12}^H/k_{12}^D[b]	k_{13}^H/k_{13}^D[c]
1-Cl		1.73		1.73
1-Cl		1.72[d]		1.72[d]
1-Cl	1.96% MeOH	1.81	0.84	2.18
1-Cl	3.85% MeOH	1.72	0.86	2.48
1-Cl	5.66% MeOH	1.63	0.88	2.73
1-Cl	7.41% MeOH	1.58	0.91	2.97
1-Cl	9.09% MeOH	1.58	0.96	3.20
1-Cl	20% MeOH	1.34		
1-OH	75% 1 M $HClO_4$[e]	6.5[f]		6.5[f]
1-OH	0.4% 1 M H_2SO_4[e]	5.3[f]		5.3[f]

[a] Estimated maximum error ±3%. [b] Estimated maximum error ±0.06. [c] Estimated maximum error ±0.12. [d] In [$^2H_3$]MeCN. [e] Volume % aqueous acid in acetonitrile. [f] Estimated maximum error ±0.2.

The solvolysis of 1,1-diphenyl-1-chloroethane (**1**-Cl) in acetonitrile at 25 °C provides the elimination product 1,1-diphenylethene (**3**) as the sole product. Solvolysis in mixtures of acetonitrile with water or methanol yields a substitution product, 1,1-diphenyl-1-hydroxyethane (**1**-OH) or 1,1-diphenyl-1-methoxyethane (**1**-OMe), along with the olefin **3** (Scheme I). The kinetics of the reaction was studied by following the increase in the absorbance at 250 nm with UV spectrophotometry. Product compositions were measured by high-performance liquid chromatography (HPLC). Addition of triethylamine (6 mM) to neutralize the small amount of HCl that is formed during the reactions has no significant effect on the kinetics. The measured rate constants and reaction conditions are shown in Table I. The solvolysis of **1**-Cl in acetonitrile containing 0.4 vol % water yields very little alcohol product, $k_{12}/k_{13} = 0.003$.

The acid-catalyzed solvolysis of **1**-OH in acetonitrile containing 0.4 vol % 2 M aqueous sulfuric acid converts all of the substrate to olefin **3**. Under the same reaction conditions, **1**-OMe or 1,1-diphenyl-1-phenoxyethane (**1**-OPh) reacts very rapidly to form **1**-OH, which in a subsequent reaction yields **3** (Scheme II). The rate constant ratios k_{12}/k_{13} were measured as 11 and 10, re-

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(4) Thibblin, A. *J. Phys. Org. Chem.* **1989**, 15–25.
(5) Thibblin, A.; Ahlberg, P. *Chem. Soc. Rev.* **1989**, *18*, 209–224.
(6) Bordwell, F. G. *Acc. Chem. Res.* **1972**, *5*, 374–381.
(7) Thibblin, A.; Sidhu, H. *Ion Pairs and Ion-Molecule Pairs in Solvolytic Reactions in Aqueous Solvent*, presented at the Fifth International Conference on Mechanisms of Reactions in Solution, The Royal Society of Chemistry, Canterbury, 1990.
(8) Thibblin, A. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1195–1198.

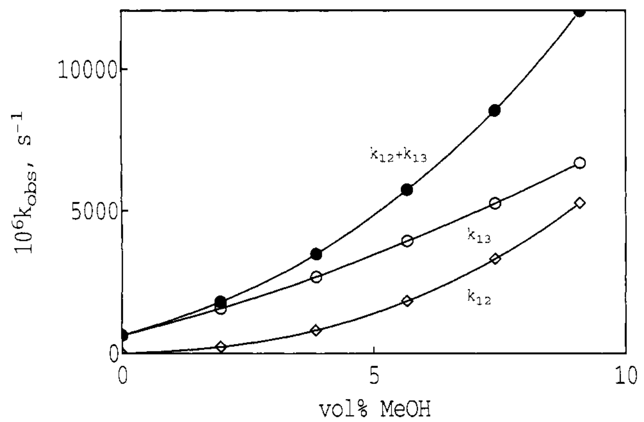


Figure 1. Rate constants measured for the reactions of **1**-Cl (Scheme I) as a function of methanol concentration in acetonitrile at 25 °C.

spectively. Also solvolysis of **1**-OPh in "anhydrous" acetonitrile solution, i.e., acetonitrile dried with 4-Å molecular sieves and containing 0.04 vol % 100% sulfuric acid, rapidly provides a substitution product which reacts to the final product **3**. Therefore, it was not possible to measure k_{13} (Scheme II) accurately. The measured rate constants and reaction conditions are recorded in Table II, which also includes data for the reaction of **1**-OH to **3** in 25 vol% acetonitrile in water, [HClO$_4$] = 0.75 M.

The results of the kinetic experiments with the [2,2,2-^{2}H$_3$]-deuteriated substrates d-**1**-Cl and d-**1**-OH are reported in Tables I and II. The measured isotope effects are collected in Table III.

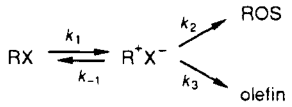
Solvolysis of **1**-Cl in a methanolic solution of 2 M sodium methoxide significantly increases the olefin to substitution product ratio compared with solvolysis in pure methanol. Work is proceeding in our laboratory to study this base-promoted reaction.

Discussion

The solvolysis of 1,1-diphenylethyl derivatives in highly aqueous solvents has recently been studied.[8,9] The products, mainly substitution product but also some olefin, were concluded to be formed via carbocation intermediates. For example, the acetate **1**-OAc was inferred to undergo rate-limiting ionization to an ion pair in 20 vol % dimethyl sulfoxide in water.[9] Most of the olefin was found to be formed directly from the ion pair in a process which is catalyzed by the leaving acetate anion.

The solvolytic elimination of HCl from **1**-Cl in acetonitrile seems to follow the same type of mechanism. The measured isotope effect is small, $k_{13}{}^{H}/k_{13}{}^{D} = 1.73$ (Table III), which indicates that the ionization is almost rate-limiting. The reaction in [^{2}H$_3$]-acetonitrile is slower, $k_{CH_3CN}/k_{CD_3CN} = 1.09$. The overall reaction rate, as well as the elimination reaction rate, increases with the addition of methanol to the acetonitrile solvent, as expected for a reaction with rate-limiting ionization (Figure 1). However, the ionization in pure acetonitrile is not completely free of internal return since the measured isotope effect of 1.73 (corresponding to $k^H/k^D = 1.20$ per deuteron) is considerably larger than the maximum secondary kinetic deuterium isotope effect for a CD$_3$ group, which has been estimated as 1.52 (corresponding to $k^H/k^D = 1.15$ per deuteron).[10] The overall isotope effect decreases when methanol is added to the acetonitrile down to a value of $k^H/k^D = 1.34$ in 20 vol % methanol in acetonitrile (Table III). This decrease is probably caused by a decreased amount of internal return and is not due to a change in the ionization isotope effect, $k_1{}^H/k_1{}^D$. The amount of internal return is expected to decrease by the methanol addition, owing to a faster reaction of the ion pair to elimination product and owing to reaction of the ion pair with methanol. The substitution product may be formed both via direct attack of methanol on the ion pair and via predissociation of the ion pair to a solvent-separated ion pair or to a "free" solvent-equilibrated carbocation followed by substitution.

The measured isotope effects on the competing elimination and substitution reactions constitute strong support for a coupled mechanism via a common ion-pair intermediate. The mechanistic model of eq 2 corresponds to the relations between phenomenological and microscopic rate constants that follow it.



(2)

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

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

$$k_{12} + k_{13} = k_1(k_2 + k_3)/(k_{-1} + k_2 + k_3) \tag{5}$$

The expressions for the isotope effects are the following:

$$k_{12}{}^H/k_{12}{}^D = (k_1{}^H/k_1{}^D)(k_2{}^H/k_2{}^D)(k_{-1}{}^D + k_2{}^D + k_3{}^D)/(k_{-1}{}^H + k_2{}^H + k_3{}^H) \tag{6}$$

$$k_{13}{}^H/k_{13}{}^D = (k_1{}^H/k_1{}^D)(k_3{}^H/k_3{}^D)(k_{-1}{}^D + k_2{}^D + k_3{}^D)/(k_{-1}{}^H + k_2{}^H + k_3{}^H) \tag{7}$$

$$(k_{12}{}^H + k_{13}{}^H)/(k_{12}{}^D + k_{13}{}^D) = (k_1{}^H/k_1{}^D)[(k_2{}^H + k_3{}^H)/(k_2{}^D + k_3{}^D)][(k_{-1}{}^D + k_2{}^D + k_3{}^D)/(k_{-1}{}^H + k_2{}^H + k_3{}^H)] \tag{8}$$

Reaction branching may cause enlarged and attenuated isotope effects, as will be discussed below. Let us assume for simplicity that internal return is negligible ($k_{-1} \ll k_2, k_3$). The isotope effect $k_1{}^H/k_1{}^D$ is a secondary isotope effect and is expected to have a rather small value ($1.16 < k_1{}^H/k_1{}^D < 1.52$).[10] Also $k_2{}^H/k_2{}^D$ is a secondary isotope effect; the value should be close to unity. The primary isotope effect $k_3{}^H/k_3{}^D$, on the other hand, should have a substantial value.[11]

It can be inferred from eq 7 that the isotope effect on the elimination reaction attains a maximum value of $k_{13}{}^H/k_{13}{}^D = (k_1{}^H/k_1{}^D)(k_3{}^H/k_3{}^D)$ when elimination is much slower than substitution ($k_3{}^H \ll k_2{}^H$). The isotope effect on the substitution reaction (eq 6) attains, under these conditions, a maximum value of $k_{12}{}^H/k_{12}{}^D = k_1{}^H/k_1{}^D$. On the other hand, fast elimination, i.e., $k_3{}^H \gg k_2{}^H$, yields a minimum elimination isotope effect of $k_{13}{}^H/k_{13}{}^D = k_1{}^H/k_1{}^D$ and a minimum substitution isotope effect of $k_{12}{}^H/k_{12}{}^D = (k_1{}^H/k_1{}^D)(k_2{}^H/k_2{}^D)(k_3{}^D/k_3{}^H)$, which can be approximated as $k_{12}{}^H/k_{12}{}^D = (k_1{}^H/k_1{}^D)(k_3{}^D/k_3{}^H)$. Branching as the cause of unusually large and unusually small isotope effects on competing reactions has been discussed previously for carbocation reactions[1-4] and carbanion reactions[12] and has been generalized and reviewed.[5]

Fast internal return ($k_{-1} \gg k_2, k_3$) yields $k_{13}{}^H/k_{13}{}^D = (k_1{}^H/k_1{}^D)(k_3{}^H/k_3{}^D)(k_{-1}{}^D/k_{-1}{}^H)$, i.e., $k_{13}{}^H/k_{13}{}^D \approx (k_1{}^H/k_1{}^D)(k_3{}^H/k_3{}^D)$. This has the same effect on the elimination isotope effect as fast substitution. Thus, the observed elimination isotope effect is enlarged due to multiplication with a factor which is larger than unity.

The trends in measured deuterium isotope effects for the reactions of **1**-Cl (Table III) seem to agree with the analysis given above. Thus, the elimination isotope effect $k_{13}{}^H/k_{13}{}^D$ increases from 1.73 to 3.20 when the fraction of substitution increases from 0 to 44%. The substitution isotope effect $k_{12}{}^H/k_{12}{}^D$ increases with increasing methanol content from 0.84 to 0.96 corresponding to 13 and 44% substitution, respectively. It does not seem possible to accommodate these isotope effect values and trends in isotope effect values in a reaction scheme with two competing parallel reactions which do not have an intermediate in common. However, branching via a common intermediate as shown in eq 2 may

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(9) Thibblin, A. *J. Phys. Org. Chem.* **1992**, *5*, 367–371.

(10) 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.

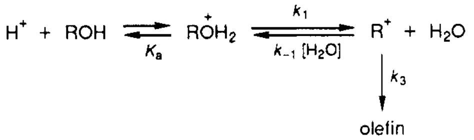
(11) The isotope effect $k_3{}^H/k_3{}^D$ is not a purely primary isotope effect since the methyl group has three deuteriums. Thus, $k_3{}^H/k_3{}^D$ includes a small secondary isotope effect with an expected value of >1.

(12) See the references given in ref 5.

account for the results. The intermediate undergoes some internal return as discussed above.

Addition of a strong base increases the fraction of olefin product; the fraction is larger for solvolysis in 2 M sodium methoxide than in methanol. Catalysis from added base has been found in some other solvolysis reactions via carbocationic intermediates.[1-4,13] The solvolytic elimination from $Ph_2CH_2C(Me)_2Cl$ shows catalysis from NaOMe in methanol but not from NaOH in water.[3]

The acid-catalyzed elimination of water from the alcohol **1**-OH in 25 vol % acetonitrile in water exhibits a substantial isotope effect of 6.5 (Table III), which implies rate-limiting hydron transfer. The results are consistent with the mechanistic model of eq 9, from which the rate and isotope effect expressions of eqs 10 and 11 can be derived. The carbocation intermediate may alternatively be formed directly from the alcohol by a one-step, general-acid-catalyzed route.



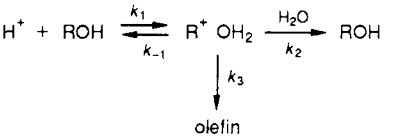
(9)

$$k_{obsd} = (1/K_a)k_1k_3/(k_{-1}[H_2O]) \quad (10)$$

$$k_{obsd}^H/k_{obsd}^D = (K_a^D/K_a^H)(k_1^H/k_1^D)(k_{-1}^D/k_{-1}^H)(k_3^H/k_3^D) \quad (11)$$

The rate of elimination is 800 times slower in this solvent than in acetonitrile containing 0.4 vol % 2 M sulfuric acid due to very fast return ($k_{-1}[H_2O] \gg k_3$). Thus, the second-order rate constant of elimination in the highly aqueous solvent is 56×10^{-6} M^{-1} s^{-1}, while in the acetonitrile solution the rate constant is 45×10^{-3} M^{-1} s^{-1} (Table II). The faster rate might also be due in part to an increase in the acidity of the medium on moving from aqueous perchloric acid to sulfuric acid in acetonitrile. The isotope effect is larger in the highly aqueous solvent (6.5 versus 4.5, Table III), which may also be the result of the larger degree of return, as will be discussed below, but may be due to other reasons.

The difference in observed isotope effects in the two solvents may reflect different degrees of external return, i.e., return from the free carbocation. However, the rate constant ratios k_{12}/k_{13} of 10 and 11 measured for **1**-OPh and **1**-OMe, respectively, in 0.4% water in acetonitrile cannot explain more than 8% of the total difference of 23%. Internal return from a carbocation–molecule pair may account for the isotope effect difference:



(12)

The rate constant k_1 corresponds to a one-step process (general-acid-catalyzed ionization) or to a two-step process in which the protonated alcohol is formed in a preequilibrium. The alcohol may be formed directly from the ion–molecule pair or via a predissociation of the ion–molecule pair. The isotope effect expression is the same as that given in eq 7. Accordingly, some internal return from the carbocation–molecule pair may explain the observation of a smaller isotope effect in the acetonitrile solvent. An ion–molecule pair has recently been suggested to be an intermediate in the acid-catalyzed solvolysis of **1**-OMe in 20 vol % dimethyl sulfoxide in water to provide **1**-OH, since it was found that iodide anion accelerates the reaction.[8]

The carbocationic intermediate(s) formed in the acid-catalyzed solvolysis of the ethers **1**-OMe and **1**-OPh reacts extremely fast in acetonitrile to give substitution product. This process is much faster than elimination. No conclusion about the intermediacy of ion–molecule pairs in the solvolysis of the ethers can be made since the elimination to substitution ratios for the reactions of **1**-OMe and **1**-OPh are similar. Different product ratios had been strong evidence for ion–molecule pairs having significant lifetimes. On the other hand, the results do not exclude ion pairs as intermediates.

The quite different ratios k_{12}/k_{13} obtained in acetonitrile containing 0.4% water with **1**-Cl (0.003) and **1**-OPh (10) or **1**-OMe (11) show that the chloride ion pair and the free carbocation (or ion–molecule pair) have quite different reactivities in formation of the elimination product. Let us assume that the ion pair and the carbocation provide alcohol **1**-OH with the same rate.[14] The data then yield that the ion pair produces olefin >3000 times faster than does the free carbocation. In the highly aqueous solution, the reactivity difference is of course much smaller owing to the higher dissociating ability of the solvent and to the higher concentration of the reactant water. Thus, the acetate ion pair is only about 3 times more reactive than the carbocation or carbocation–methanol pair in the elimination reaction in 20 vol % dimethyl sulfoxide in water.[9] The carbocation exhibits a very high selectivity toward different nucleophiles. For example, the reaction with azide anion is about 1200 times faster than with a solvent water molecule.[9]

The leaving chloride anion obviously has a great "catalytic" effect on the elimination reaction of **1**-Cl. Catalysis from the leaving group has been found in several other systems,[1,2,4,9,13,15] but such a large acceleration of the elimination that is found for **1**-Cl does not seem to have been observed previously.

It is presumably a general phenomenon that a more stable carbocation intermediate corresponds to a smaller fraction of elimination. Accordingly, the elimination (abstraction of a methyl hydron) to substitution ratios measured for the solvolysis of the tertiary chlorides 9-(2-chloro-2-propyl)fluorene, $PhCH_2C(Me)_2Cl$, and $PhC(Me)_2Cl$ in 25 vol % acetonitrile in water were 1.8,[1] 0.15,[3] and <0.005,[4] respectively. The rate of solvolysis increases roughly 1000 times in the same series. Also, other factors, such as steric factors, are of course important in controlling the product ratio.

Conclusions. Analysis of the kinetic deuterium isotope effects for the separate elimination and substitution reactions of **1**-Cl shows that the solvolysis proceeds via a branched mechanism (eq 2) having a common carbocationic intermediate. The large catalytic effect of the leaving chloride anion on the elimination reaction strongly indicates that the intermediate is of the contact ion-pair type. The ion pair is estimated to eliminate >3000 times faster than the free carbocation in 0.4 vol % water in acetonitrile.

The 23% difference in observed kinetic isotope effect on the acid-catalyzed elimination from **1**-OH in highly aqueous solution compared with 0.4% water in acetonitrile may suggest internal return from a reversibly formed ion–molecule pair.

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 C8 reversed-phase column (2.1 × 100 mm). The mobile phase was a solution of acetonitrile in water. A Kontron Uvicon 930 spectrophotometer equipped with an automatic cell changer thermostated with water from a Heto 01 PT 623 thermostat was used for the kinetic experiments.

Materials. The alcohol, 1,1-diphenyl-1-hydroxyethane (**1**-OH), purchased from Aldrich, was purified by recrystallization from pentane. The olefin, 1,1-diphenylethene (**3**) (Aldrich), was used for calibration purposes. Acetonitrile and methanol were of spectroscopic quality and were used as solvents without further purification. In some experiments, acetonitrile dried over 4-Å molecular sieves was used. All other chemicals were of reagent grade. The synthesis of the ether, 1,1-diphenyl-1-methoxyethane (**1**-OMe), has been described previously.[9,16]

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(13) Richard, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 1373–1383.

(14) Ritchie, C. D.; Hofelich, T. C. *J. Am. Chem. Soc.* **1980**, *102*, 7039–7044.

(15) (a) Seib, R. C.; Shiner, V. J., Jr.; Sendijarevic, V.; Humski, K. *J. Am. Chem. Soc.* **1978**, *100*, 8133–8137. (b) Cram, D. J.; Sahyun, M. R. V. *J. Am. Chem. Soc.* **1963**, *85*, 1257–1263. (c) Dannenberg, J. J.; Goldberg, B. J.; Barton, J. K.; Dill, K.; Wienwurzel, D. H.; Longas, M. O. *J. Am. Chem. Soc.* **1982**, *103*, 7764–7768. (d) Cocivera, M.; Shiner, V. J., Jr. *J. Am. Chem. Soc.* **1963**, *85*, 1702–1703.

(16) Ziegler, K.; Schnell, B. *Ann. Chem.* **1924**, *437*, 242.

1,1-Diphenyl-1-hydroxy[2,2,2-$^{2}H_{3}$]ethane (d-1-OH) was prepared from benzophenone and CD_3MgI (Aldrich, 1 M, 99+% ^{2}H) under dry nitrogen. Recrystallization from pentane gave pure product. The deuterium content in the methyl group was 99.6 ± 0.4 atom % (^{1}H NMR).

1,1-Diphenyl-1-phenoxyethane (1-OPh) was synthesized from 1-OH by a modification of a previously published method.[17] Phenol (1.5 g, 16 mmol) and methylene chloride (0.5 mL) were added to 100 mg (0.5 mmol) of 1-OH. After addition of zinc iodide (100 mg, 0.5 mmol), the mixture was stirred for 15 min under dry nitrogen. The reaction was stopped by adding pentane to the reaction flask. The filtered pentane solution was washed several times with water to remove the phenol and once with brine. Analysis by HPLC showed 52% conversion of the alcohol to give 78% of the ether and 22% of olefin 3. A longer reaction time reduces the ratio of ether to olefin quite quickly. The required ether was purified by semipreparative HPLC.

1,1-Diphenyl-1-chloroethane (1-Cl). Method 1. A total of 15 mg of 1-OH partially dissolved in 0.6 mL of hexane was shaken with 0.6 mL of concentrated hydrochloric acid. After 2 min, the organic phase was separated from the water phase. The chloride was not isolated but kept in the hexane solution. The purity was checked by spectrophotometry and HPLC analysis of an aliquot which had been solvolyzed in methanol. A trace of olefin but no starting material or other impurities was found. A stock solution of the substrate in hexane was kept in the freezer. **Method 2.** Recrystallized alcohol (4.0 mg) dissolved in 2 mL of dichloromethane containing some $CaCl_2$ was cooled to ca. −10 °C. Dry HCl gas was bubbled through the solution for 2 min and then dry nitrogen for 1 min. The dichloromethane solution was filtered, but the product was not isolated. The purity was checked as above. The chloride is less stable in dichloromethane than in hexane. Method 2 is not good for preparing the deuteriated chloride since some H–D exchange occurs during the synthesis.

1,1-Diphenyl-1-chloro[2,2,2-$^{2}H_{3}$]ethane (d-1-Cl) was prepared as above by method 1 from d-1-OH but with deuteriated concentrated hydrochloric acid (Glaser, 37% DCl in D_2O, 99.5% ^{2}H).

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, by means of a syringe, of the substrate dissolved in hexane (1-Cl) or acetonitrile (all other substrates). The absorbance increases at 250 nm of the reactions were followed for at least 10 half-lives. The rate constants of the disappearance of the substrates were calculated by means of a nonlinear least-squares regression computer program. Very good pseudo-first-order behavior was seen for all of the reactions studied. The separate rate constants for the elimination and substitution reactions were obtained by combination of product composition data (from HPLC analyses), corrected for the small amount of olefin in the substrate solution, with the observed rate constants obtained as described above.

The rate constant ratios k_{12}/k_{13} for the acid-catalyzed reactions were measured after neutralizing the acidic solution after a very short reaction time with a methanolic solution of sodium hydrogen carbonate followed by analysis of the product composition by HPLC.

The rate constants of the slow acid-catalyzed solvolysis of 1-OH in 25 vol % acetonitrile in aqueous perchloric acid were obtained from initial-rate experiments by following the increase in absorbance at 250 nm for 3% of reaction. The kinetic deuterium isotope effect was calculated as the ratio of the linear slopes (dA/dt) for the reaction of h-1-OH and d-1-OH corrected for a small difference in initial concentration of substrate measured by HPLC. The rate constants were obtained from the linear slopes and the infinity absorbance, A_∞, by the relationship $k_{obsd} = (dA/dt)/(A_\infty - dA/2)$. The infinity absorbance A_∞ was obtained from reaction of 1-OH in acetonitrile containing 0.4 vol % 2 M aqueous sulfuric acid. Division of the rate constant for the reaction of h-1-OH and d-1-OH, respectively, gave the same isotope effect value, within experimental errors, as the division of the corrected slopes as described above. The estimated errors are considered as maximum errors derived from maximum systematic errors and random errors.

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[17] Guindon, Y.; Frerette, R.; Fortin, R.; Rokach, J. *J. Org. Chem.* 1983, *48*, 1357–1359.

Dimensional Analogue of a dA·dT Base Pair Devoid of Propeller Twist

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Abstract: A dimensional analogue of dA·dT, with a covalently linked cross section containing a 10 π-electron core nucleus, has been synthesized from selectively protected 5-methyl-2′-deoxycytidine and 2′-deoxyadenosine. The immediate precursor, 3-(3′,5′-di-*O*-acetyl-2′-deoxy-β-D-ribofuranosyl)-9-(2′-deoxy-β-D-ribofuranosyl)-11-methyl-3*H*-pyrimido[1″,6″:1′,2′]imidazo[4′,5′:4,5]imidazo[2,1-*i*]purin-8(9*H*)-one, with diacetyl protection on the deoxyadenosine side, has a coplanar (±0.03 Å by X-ray) central pentacyclic ring system. Selective 1,1,3,3-tetraisopropyldisiloxanediyl protection on the equivalent of the thymidine side in the analogue now permits differential phosphorylation for directed incorporation in a polydeoxyribonucleotide double helix.

Introduction

The synthesis of substituted 1,3,4,6-tetraazapentalenes,[1] with a core nucleus having 10 π-electrons, has been crucial to the construction of covalently linked cross sections with molecular architecture similar to that of hydrogen-bonded DNA/RNA base pairs for both antiparallel[2] and parallel[3] helical duplexes. These fluorescent covalently-linked cross sections, if phosphorylated and incorporated in a polydeoxynucleotide sequence,[4] for example, are capable of introducing local rigidity as a marker for potential

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[1] (a) Cruickshank, K. A.; Sumoto, K.; Leonard, N. J. *Tetrahedron Lett.* 1985, *26*, 2723. (b) Groziak, M. P.; Wilson, S. R.; Clauson, G. L.; Leonard, N. J. *J. Am. Chem. Soc.* 1986, *108*, 8002. (c) Pereira, D. E.; Neelima; Leonard, N. J. *Tetrahedron* 1990, *46*, 5895.

[2] (a) Devadas, B.; Leonard, N. J. *J. Am. Chem. Soc.* 1986, *108*, 5012. (b) Leonard, N. J.; Devadas, B. *J. Am. Chem. Soc.* 1987, *109*, 623. (c) Devadas, B.; Leonard, N. J. *J. Am. Chem. Soc.* 1990, *112*, 3125.

[3] (a) Bhat, B.; Cruickshank, K. A.; Leonard, N. J. *J. Org. Chem.* 1989, *54*, 2028. Leonard, N. J.; Bhat, B.; Wilson, S. R.; Cruickshank, K. A. *J. Am. Chem. Soc.* 1991, *113*, 1398.

[4] Petrič, A.; Bhat, B.; Leonard, N. J.; Gumport, R. I. *Nucleic Acids Res.* 1991, *19*, 585.

0002-7863/92/1514-7407$03.00/0