DOI: 10.1002/ejoc.200901327

Selectivity of Stabilized Benzhydrylium Ions

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Keywords: Kinetics / Solvolysis / Microsolvation / Stabilized benzhydrylium ions

Methyl carbonates (**1**–**4**–OCO_2Me) and phenyl carbonates (**2**–**4**–OCO_2Ph) were subjected to solvolysis in the series of aqueous ethanol, the product ratios were determined and the selectivities (k_E/k_W) of the corresponding stabilized benzhydrylium ions **1**–**4** were calculated. The individual rate constants for ethanolysis (k_E) and hydrolysis (k_W) have been calculated. Ethanolysis proceeds via earlier more carbocation-like transition state than hydrolysis. Due to more important solvation, k_E decreases slower than k_W if the fraction of the water in the binary solvent increases, which net effect is pronounced dependence of the selectivity on the solvent polarity. The selectivities of less stable carbocations **5**–**8** are reduced and influenced by the leaving group because of pairing and bending of the log k vs. E plot.

Introduction

Carbocation intermediate formed by heterolysis reaction in a binary solvent reacts with different rates with each component of the mixture. The pseudo first-order rate constant of such reaction represents the sum of the individual pseudo first-order rate constants. Thus, if the carbocation is generated in aqueous ethanol, the corresponding first-order rate constant is presented with Equation (1).

$$k' = k'_E + k'_W = k_E\,[EtOH] + k_W\,[H_2O] \tag{1}$$

in which k' is the pseudo first-order rate constants for reaction with aqueous ethanol, k'_E and k'_W are the pseudo first-order individual rate constants with ethanol and water, resp., while k_E and k_W are the second-order individual rate constants.

A selectivity is defined as a ratio of the individual second-order rate constants (k_E/k_W) for the reaction of a given carbocation with individual components of the binary solvent.[1,2] Since the molar ratio of the alcohol and ethyl ether ([ROH]/[ROEt]) formed in reaction of carbocation R^+ with aqueous ethanol indicates the ratio of the individual first-order rate constants (k'_E/k'_W), the selectivity can easily be derived from Equation (2).

$$S = \frac{k_E}{k_W} = \frac{[ROEt]\times[H_2O]}{[ROH]\times[EtOH]} \tag{2}$$

Generally, it has been accepted that in aqueous solvents the selectivity of the substrates that solvolyze via formation of the free carbocation is $S > 1$ and increases as the fraction of water increases, while that of substrates that yield the products from the solvent-separated ion pairs is $S < 1$.[3,4] If more species exist as intermediates, the observed selectivity was interpreted as weighted average of the individual selectivity values. The observations that the selectivity increases with the ionizing power of the solvent and that better leaving groups produce higher selectivities have been rationalized as a change in the relative population of the free ions and the solvent-separated ions.[5–7]

Our investigations presented here rely on Mayr's results obtained with substituted benzhydrylium ions. First, it has been shown that the stabilized benzhydrylium ions in aqueous ethanol can be treated as thermally equilibrated free ions, since the reaction with the solvent is slow enough to allow the counterion to diffuse away.[8] Therefore, the selectivity values reflect the ratio of two rate constants only (k_E/k_W). Secondly, Mayr et al. determined the nucleophilicities of different solvents and solvent mixtures by measuring the pseudo first-order rate constants for combination of the substituted benzhydrylium ions with the series of binary solvents, providing numerous experimental rate constants (k').[9] It has been shown that, similarly as was previously demonstrated for the reaction of carbocations with variety of nucleophiles,[10] the first-order rate constants for combination of the carbocation with the solvent follow the special LFER relationship, see Equation (3).

$$\log k_{20\,°C} = s(E + N) \tag{3}$$

in which E represents the empirical electrophilicity parameter of the cation, N is an empirical nucleophilicity parameter of the solvent, and s is an nucleophile-specific parameter.

The above results prompted us to study the selectivities of substrates that produce stable benzhydrylium ions, extract the individual rate constants for ethanolysis (k_E) and hydrolysis (k_W) in a given aqueous ethanol, and interpret

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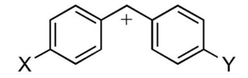
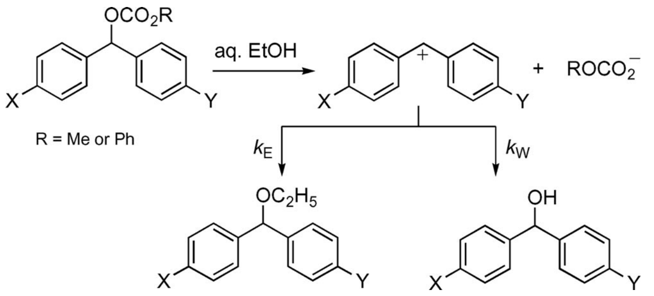
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.200901327.



1: X = Y = OMe
2: X = OMe, Y = OPh
3: X = OMe, Y = Me
4: X = OMe, Y = H
5: X = Me, Y = Me
6: X = Me, Y = H
7: X = Y = H
8: X = Y = Cl

selectivity values obtained on quantitative basis (Table 1). The main criterion was to choose substrates that produce carbocations that react with the series of aqueous ethanol with the rates that are way bellow the diffusion controlled processes. X,Y-Substituted benzhydrylium (Bh) ions **1**–**4** turned out to be suitable substrates for determination of the selectivities. In order to avoid mixing problems, which may cause inconsistent product ratios, it was necessary to use substrates whose rates of the carbocation formation were not too fast. This was achieved by adjusting the nucleofugality of the leaving group. We found that methyl and phenyl carbonates ($MeOCO_2$ and $PhOCO_2$) were suitable leaving groups for these investigations.[11] The overall process investigated here is presented in Scheme 1.



Scheme 1.

Results and Discussion

In order to measure the ether/alcohol product ratio ([X,Y-BhOEt]/[X,Y-BhOH]) and derive the corresponding selectivity values, the series of methyl carbonates (**1**–OCO_2Me, **2**–OCO_2Me, **3**–OCO_2Me, and **4**–OCO_2Me) and the series of phenyl carbonates (**2**–OCO_2Ph, **3**–OCO_2Ph, and **4**–OCO_2Ph) were solvolyzed for approximately 10 reaction half-lives in aqueous ethanol mixtures (90–60% v/v) at 20 °C with and without base added. The products were analyzed by means of NMR spectroscopy. Product ratios and the selectivity values are presented in Table 1.

As expected, the selectivities obtained for solvolysis of both carbonates are $k_E/k_W > 1$. The following trends can be seen from Table 1. First, the *S* values increase considerably without exception as the polarity of the solvent mixture increases. Secondly, the *S* values obtained with the phenyl carbonates are virtually equal to those obtained with the methyl carbonates, supporting the formation of the free ions. Furthermore, the selectivity values slightly but consistently decrease as the stability of the carbocations decrease.

From Equations (1) and (2), taking the pseudo first-order rate constants for reaction of the X,Y-substituted benzhydrylium ions with the series of aqueous ethanol[9] and the selectivity values shown in Table 1, the second-order individual rate constants for ethanolysis and hydrolysis can be determined straightforwardly, see Equation (4).

$$k_E = k'\times\frac{S}{S\times[\mathrm{EtOH}]+[\mathrm{H_2O}]} \qquad k_W = \frac{k'}{S\times[\mathrm{EtOH}]+[\mathrm{H_2O}]} \tag{4}$$

The calculated second-order individual rate constants k_E and k_W along with the corresponding pseudo first-order rate constants are presented in Table 2.

Table 1. Product ratios and selectivities (k_E/k_W) for solvolysis of benzhydryl carbonates in ethanol/water mixtures at 20 °C.

Cation (X,Y)	Solvent[a]	Methyl carbonate		Phenyl carbonate	
		[X, Y-BhOEt]/[X, Y-BhOH] [b]	S[c]	[X, Y-BhOEt]/[X, Y-BhOH] [b]	S[c]
1 (MeO,MeO)	90E	12.2 ± 0.2 (4)	4.4 ± 0.1		
	80E	7.2 ± 0.4 (6)	5.8 ± 0.3		
	70E	5.2 ± 0.2 (7)	7.2 ± 0.2		
	60E	4.1 ± 0.2 (6)	8.8 ± 0.2		
2 (MeO,PhO)	90E	12.1 ± 0.2 (3)	4.4 ± 0.1	12.1 ± 0.1 (3)	4.4 ± 0.1
	80E	6.8 ± 0.1 (3)	5.5 ± 0.1	6.7 ± 0.2 (4)	5.4 ± 0.2
	70E	4.9 ± 0.1 (3)	6.8 ± 0.1	4.9 ± 0. 1 (3)	6.8 ± 0.1
	60E	3.9 ± 0.1 (3)	8.5 ± 0.2	4.2 ± 0.1 (3)	9.1 ± 0.2
3 (MeO,Me)	90E	10.8 ± 0.2 (4)	3.9 ± 0.1	12.3 ± 0.2 (5)	4.4 ± 0.1
	80E	6.3 ± 0.2 (4)	5.1 ± 0.1	6.8 ± 0. 1 (4)	5.5 ± 0.1
	70E	4.6 ± 0.1 (4)	6.5 ± 0.2	4.8 ± 0.1 (4)	6.7 ± 0.1
	60E	3.7 ± 0.1 (5)	8.0 ± 0.2	3.7 ± 0. 1 (4)	8.0 ± 0.1
4 (MeO,H)	90E	11.5 ± 0.2 (5)	4.1 ± 0.1	11.5 ± 0.2 (4)	4.1 ± 0.1
	80E	6.3 ± 0.1 (3)	5.1 ± 0.1	6.2 ± 0.4 (5)	5.0 ± 0.1
	70E	4.5 ± 0.1 (3)	6.2 ± 0.1	4.5 ± 0.1 (4)	6.2 ± 0.1
	60E	3.1 ± 0.1 (4)	6.8 ± 0.1	3.4 ± 0.1 (4)	7.4 ± 0.2

[a] Aqueous ethanol mixtures are v/v at 25 °C; E = ethanol. [b] Data with standard deviation; entries in the parentheses present the number of determinations; Bh = benzhydryl. [c] Data with standard deviation.

Table 2. The pseudo-first-order rate constants (k') for reaction of the benzhydrylium ions with the series of aqueous ethanols at 20 °C and the derived second and first-order individual rate constants for ethanolysis (k_E) and hydrolysis (k_W).

Substrate	Solvent[a]	$k'/10^4$ s^{-1} [b]	$k_E/10^4$ s^{-1}M^{-1}	$k'_E/10^4$ s^{-1}	$k_W/10^4$ s^{-1}M^{-1}	$k'_W/104$ s^{-1}
1 (MeO,MeO)	E	433[c,d]	27.7			
	90E	253	14.8	234	3.37	19.1
	80E	151	9.34	132	1.60	18.4
	60E	71.3	2.25	57.3	0.255	14.0
	W	9.44				
3 (MeO,Me)	E	868[c,d]	55.6			
	90E	947	54.8	866	14.1	80.2
	80E	788	47.9	680	9.39	108
	60E	655	48.1	516	6.03	139
	W	78[d]			1.4	
4 (MeO,H)	80E	1220	74.1	1053	14.5	167
	60E	1060	74.9	801	11.1	258
	W	190[d]				

[a] Aqueous ethanols mixtures are v/v at 25 °C; E = ethanol, W = water. [b] Rate constants k' are taken from ref.[9] [c] 91% in acetonitrile. [d] Rate constants are taken from ref.[13]

Effect of Microsolvation on Selectivity

Very pronounced changes in selectivities have been observed if the ratio of the solvents has been changed. Thus, the selectivities are about twice higher if the content of the ethanol decreases from 90% to 60%, indicating that the individual rate constants change differently with changing polarity. We plotted the logarithms of k_E and of k_W against the solvent ionizing power (Y_{OTs}).[12] The rate constants obtained earlier with pure water and ethanol (91% in acetonitrile) have also been taken in account.[9,13] The plots obtained for cations **1** and **3** are presented in Figure 1, while those for **4** are shown in the Supporting Information.

The rates for combination of the cations **1**–**4** with both solvents decrease as the content of water increases, because of the lower nucleophilicity of the solvent. However, the trends of decreasing rates for hydrolysis and ethanolysis are not the same. Parts a and b of Figure 1 show essentially the same phenomenon that the individual rates for ethanolysis in the series of aqueous ethanol depend considerably less on the solvent content than the individual rates for hydrolysis, hence different slopes of log k_E vs. Y_{OTS} and logk_W vs. Y_{OTS} plots cause pronounced changes of the selectivities.

Beside the nucleophilicity of the solvent, the solvation of a transition state also influences the reaction rate to some degree. Different slopes of logk_E vs. Y_{OTS} and logk_W vs. Y_{OTS} lines can be rationalized if the different microsolvation of the two transition states is assumed. Since ethanolysis is more rapid than hydrolysis, the transition state for combination of a given benzhydrylium ion with ethanol is more carbocation-like than the TS for the reaction of the same cation with water. The solvation of the earlier carbocation-like TS is important. On the other hand, because of the more advanced hydrolysis in the TS, a transfer of the positive charge, which is delocalized additionally to oxygen, is more developed, so the importance of solvation is diminished, causing more pronounced decrease of the reaction rate, i.e., steeper logk_W vs. Y_{OTS} plot. This conclusion is in line with the results of Van Pham and McClelland, who on the basis of kinetic and equilibrium isotope effects showed that in the TS of hydrolysis of cation **1** in aqueous acetonitrile the formation of C–O bond is already 50–65% advanced.[13]

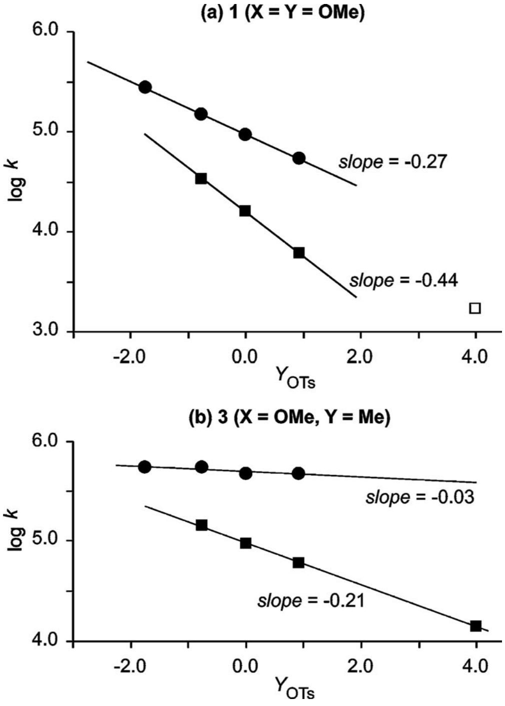


Figure 1. Correlation plots of the logarithms of the individual rate constants for ethanolysis (black circle) and hydrolysis (black square) of cation **1** (a) and cation **3** (b) against the ionizing power (Y_{OTs})[12] for the series of aqueous ethanols.

In accord with the above considerations are the steeper slopes of the log$k$ vs. Y_{OTS} plots for cation **1** in comparison to the slopes obtained for cation **3** (Figure 1). While logk_E vs. Y_{OTS} for **1** has a slope of ca. –0.3, the slope of k_E vs. Y_{OTS} plot for **3** is almost parallel to the abscissa. Similarly, the slope of the logk_W vs. Y_{OTS} plot for **1** is steeper for ca. 0.2 in comparison to the slope for **3**. Since cation **3** is more reactive than cation **1**, the reactions with both solvents proceed via earlier TS than for **1**, the reactions with solvents are less advanced and both transition states are more carbocation-like than the transition states for cation **1**. Because of more important solvation of the early TS, the trends of decreasing $\log k_E$ vs. Y_{OTS} and $\log k_W$ vs. Y_{OTS} plots for cation **3** with decreasing nucleophilicity of the solvent (increased water content) are diminished. It should be noted that the relative differences of the slopes that correspond to ethanolysis and hydrolysis for both cations **1** and **3** are almost same, causing similar changes of selectivity with solvent polarity.

Selectivity of Less Stabilized Benzhydrylium Ions

At this point some selectivity values presented earlier in the literature can be rationalized using the above approach. We plotted $\log S$ obtained for cations **1**–**4** against the electrophilicity of the given carbocations (E) and obtained good linear correlation. This is not surprising, since, according to definition [Equation (2)], $\log S$ equals the difference between two variables, $\log k_E$ and $\log k_W$, which both correlate linearly with E; see Equation (3). The $\log S$ vs. E plot obtained in 80% aq. ethanol is presented in part b of Figure 2 (all other plots see in the Supporting Information). For the purpose of comparison, logarithms of some selectivities obtained earlier with X,Y-substituted benzhydrylium chlorides[5] and *p*-nitrobenzoates[7] are also added to Figure 2. Good $\log S$ vs. E correlation provides reference selectivities expected for free cations if followed the route presented on Scheme 1, whose values in turn can be compared with the S values obtained experimentally for cations **5**–**8**.

There are some striking differences between the selectivities of the stable cations **1**–**4** and those of less stable (**5**–**8**) determined earlier. First, the selectivities of cations **1**–**4** are almost invariant with the structure, while those of **5**–**8** decrease considerably with decreasing stability of the cation (Figure 2, b). Also the S values for **5**–**8** are lower than expected for free cation.[5,7] Secondly, an increase of the selectivities of less stable ions with solvent polarity is less pronounced (e.g. an increase of the water content from 90% to 60% in ethanol causes an increase in selectivities of **7**–Cl for only $\Delta S = 1.0$ at 25 °C).[7] Furthermore, our results presented in Table 1 indicate that the selectivities of the benzhydrylium ions **1**–**4** are independent of the nucleofugality of the leaving group, while those obtained with less stable ions indicate that substrates with better nucleofuges produce higher selectivity. For example, **7**–Br is more selective than **7**–Cl ($S_{Br} = 3.69$ vs. $S_{Cl} = 2.60$ in 80% aq. ethanol at 25 °C).[7]

In order to examine the trends of the individual processes, we plotted the logarithms of the individual first-order rate constants (k'_E and k'_W) obtained in 80% ethanol against E and obtained linear plots; see Equation (3). Extrapolation of those plots toward higher E indicates that the individual rates for ethanolysis are reaching the diffusion limit. This is in line with Mayr's results that carbocations which are less stable than di-*p*-tolylmetyl cation ($E = 3.6$) predictably undergo diffusion-controlled reaction with 80% ethanol.[14] Numerous data show that $\log k$ vs. E correlation plots are linear if the reaction rates are below 10^8, while for faster reactions the correlation lines bend and asymptotically approach the diffusion limit region.[14,15] Since the differences between k'_E and k'_W related to selectivity [$\log k'_E - \log k'_W = \log S + \log(H_2O)/(EtOH)$, see Equations (1) and (2)], it is clear (Figure 2, a) that in the region of less stable carbocations (stronger electrophiles) the selectivity is reduced.

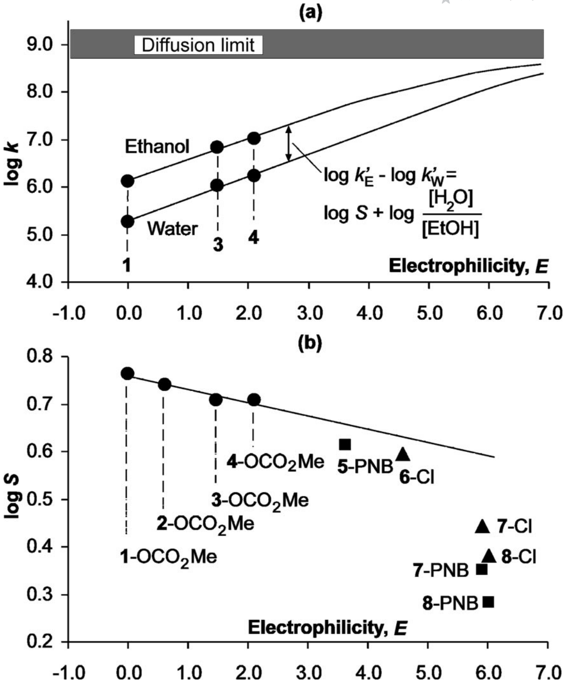


Figure 2. Comparison of the selectivities of stabilized (**1**–**4**) and less stable (**5**–**8**) X,Y-substituted benzhydrylium ions in 80% aqueous ethanol at 25 °C using (a) $\log k'_E$ vs. E and $\log k'_W$ vs. E plots and (b) $\log S$ vs. E plot.

Dependence of the selectivity on the leaving group can be rationalized if the rates of the bond breaking and the bond forming are compared. Stable cations, as are **1**–**4**, react slowly enough with the solvent to allow the nucleofuge to depart leaving free ions, so the reaction rates with the solvent are independent on the leaving group. On the other hand, less stable ions react with the solvent with rates that are approaching the diffusion limit, so the counterion cannot diffuse away. In such cases pairing occurs and the selectivity depends on the nucleofugality of the counterion in a way that better leaving group, which diffuses away faster and therefore increases the fraction of the free ions, produces higher selectivity. It should be emphasized that the selectivities presented in the literature have been determined for such less stable ions.

Experimental Section

General: All substrates were prepared as described previously.[11] Typically, 40–50 mg of substrate was dissolved in 0.10–0.15 mL of dichloromethane and injected into 50 mL of solvent ($2–3 \times 10^{-3}$ M). Solvolyses were carried out under the thermostatted conditions at 20 ± 0.1 °C. After 10 half-lives the solvent was evaporated in vacuo. The residue was dissolved in deuterated chloroform, and NMR spectrum was recorded. The individual S values were calculated according to the Equation (2) from the observed peak area ratios of α-H of ether (5.3–5.4 ppm) and alcohol (5.7–5.8 ppm). Solvolyses were also conducted in the presence of pyridine ($5–11 \times 10^{-3}$ M). The buffered solutions gave individual S values within the experimental error in comparison with the unbuffered solutions. The S values presented are average values obtained from at least three measurements, which included both the buffered and the unbuffered solvolyses.

Supporting Information (see also the footnote on the first page of this article): $\log S$ vs. E plots for X,Y-substituted benzhydryl phenyl and methyl carbonates in 60%, 70%, 80% and 90% aq. ethanol with $\log S$ for X,Y-substituted benzhydryl chlorides *p*-nitrobenzoates.

Acknowledgments

We gratefully acknowledge the financial support of this research by the Ministry of Science, Education and Sport of the Republic of Croatia (Grant No. 006-0982933-2963).

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Received: November 18, 2009