of (2-chloro-2-propyl)toluene. [A synthetic control mixture of ortho, meta, and para isomers of (2-chloro-2-propyl)toluene was shown to be clearly separable on the column.]

Registry No. Ia, 544-25-2; Ib, 4281-04-3; Ic, 1541-11-3; Id, 3479-89-8; $TeCl_4$, 10026-07-0; benzyl chloride, 100-44-7; 1-chloro-1-phenylethane, 672-65-1; benzhydryl chloride, 90-99-3; 3-(2-chloro-2-propyl)toluene, 13240-60-3; 7-methoxycycloheptatriene, 1714-38-1; methylmagnesium iodide, 917-64-6; tropylium tetrafluoroborate, 27081-10-3; phenylmagnesium bromide, 100-58-3; eucarvone, 503-93-5; eucarvol, 503-92-4; 3-methylacetophenone, 585-74-0; *p*-methylacetophenone, 122-00-9; 2-(2-chloro-2-propyl)toluene, 85681-40-9; 2-(2-hydroxy-2-propyl)toluene, 7572-79-4; 2-bromotoluene, 95-46-5; 4-(2-chloro-2-propyl)toluene, 7243-79-0.

π Participation and Stereoselectivity. Solvolysis Rates of (*E*)- and (*Z*)-1-Aryl-5-heptenyl Chlorides

Mirko Orlović, Eugenio Polla, and Stanko Borčić*

Faculty of Pharmacy and Biochemistry, University of Zagreb, 41001 Zagreb, Yugoslavia

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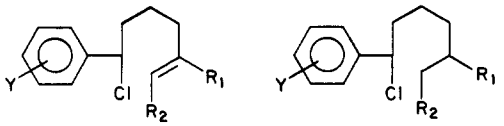
We have reported[1,2] that the solvolysis rates of most chlorides of the series U are enhanced relative to those of the corresponding series S.[3]



U S

1, $R_1 = R_2 = H$
2, $R_1 = CH_3$; $R_2 = H$
(*E*)-3, $R_1 = H$; $R_2 = CH_3$
4, $R_1 = R_2 = CH_3$

Y = *p*-OCH_3, *p*-CH_3, H, *p*-Br, *m*-Br

There is no rate acceleration in the following cases: (a) when the aliphatic double bond is substituted with only one alkyl group as in series **1U**, (b) when the terminal double bond in **1U** is replaced by a cyclopropane ring,[4] and (c) in all cases when the substituent on the phenyl ring is the very electron-donating *p*-methoxyl. All other chlorides of the U series react faster than the corresponding chlorides of the S series, and the k_U/k_S ratio increases as the electron-donating ability of the substituent Y decreases; i.e., the largest rate enhancements are observed when Y = *m*-Br.[2] The relevant k_U/k_S values given in Table I have a puzzling feature: rate enhancements observed with (*E*)-**3U** are somewhat *larger* than those of **2U**.

This observation is not consistent with a participation mechanism involving charge-localized carbenium-ion-like transition states. If such were the case, then **2U** and (*E*)-**3U** would react by way of a tertiary and a secondary

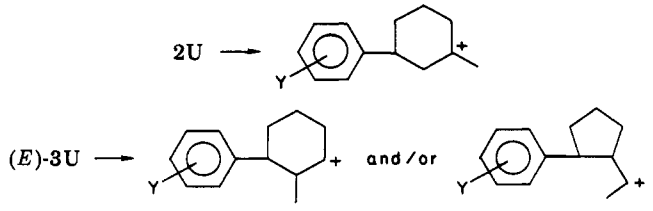


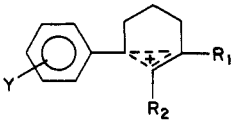
Table I. Solvolysis of 1-Arylalkyl Chlorides and 1-Aryl-5-alkenyl Chlorides: Relative Rates at 25 °C

		k_U/k_S			
Y[a]	solvent[b]	2	(*E*)-3	(*Z*)-3	4
p-OCH_3	95E	1.07	0.89	1.25	1.08
p-CH_3		1.50	2.42	0.95	3.22
	80E	1.13	1.43	1.52	2.23
H		2.57	5.93	2.75	16.1
	97T			3.95	
p-Br		3.05	6.18	5.17	18.9
m-Br		5.73	10.3	17.5	58.2

[a] Substituent on the phenyl ring. [b] 95E and 80E are 95 and 80 vol % aqueous ethanol, respectively; 97T is 97 wt % aqueous 2,2,2-trifluoroethanol.

carbenium ion, respectively, and since the former is more stable then the latter, rate enhancements with **2U** could be expected to be much more important than those with (*E*)-**3U**, which is contrary to observation.

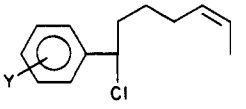
It was pointed out[2] that these results are not easily accommodated by a bridged, carbonium ion **5** like transition state. Although **5** is consistent with a small reactivity difference between **2U** and (*E*)-**3U**, nevertheless the expectation is again that the former should be more reactive than the latter.



5

A relevant analogy is the observation that while in acid-catalyzed hydration isobutene is about 10^4 times more reactive than *trans*-2-butene,[5,6] it is still 3 times more reactive in bromine addition,[7,8] a reaction proceeding by way of bridged bromonium ions.

It appears that there must be a factor, possibly steric in origin and not immediately obvious from formula **5**, which is responsible for an additional rate enhancement of (*E*)-**3U** and/or for a rate deceleration of **2U**. In this respect it seemed of interest to measure the solvolysis rates of the geometric isomers of (*E*)-**3U**, i.e., the series (*Z*)-**3U**.



(*Z*)-3U

The results of this investigation are summarized in Table II. Using previously[2] measured values for k_{3S}, the $k_{(Z)\text{-}3U}/k_{3S}$ ratios were calculated and are shown in column five of Table I. If the rate enhancements of the two geometrically isomeric series of structure **3U** are compared, it can be seen (Table I) that the stereochemistry of the participating double bond has very little influence on the reaction rates. Both series of chlorides **3U** react at very similar rates, and the rate enhancements tend to be of the same magnitude or larger than those measured with **2U** relative to **2S**. In fact, in the case of *m*-Br-substituted derivatives, where the participation is the most pro-

(1) Polla, E.; Borčić, S.; Sunko, D. E. *Tetrahedron Lett.* **1975**, 799.
(2) Mihel, I.; Orlović, M.; Polla, E.; Borčić, S. *J. Org. Chem.* **1979**, *44*, 4086.
(3) For a review article about cationic olefinic cyclizations see: Johnson, W. S. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 9.
(4) Ostović, D.; Kronja, O.; Borčić, S. *Croat. Chem. Acta* **1981**, *54*, 203.
(5) Knittel, P.; Tidwell, T. T. *J. Am. Chem. Soc.* **1977**, *99*, 3408.
(6) Lowry, T. H.; Richardson, K. S. "Mechanism and Theory in Organic Chemistry", 2nd ed.; Harper and Row: New York, 1981; p 512.
(7) Reference 6, p 524.
(8) Dubois, J. E.; Mouvier, G. *Bull. Soc. Chim. Fr.* **1968**, 1426.
(9) Exner, O. *Collect. Czech. Chem. Commun.* **1966**, *31*, 65, 3222.

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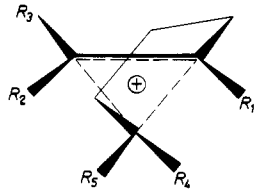
Table II. Rates and Activation Parameters for Solvolyses of (Z)-1-Aryl-5-heptenyl Chlorides ((Z)-3U)

Y[a]	solvent[b]	temp, °C	10^5k,[c] s^{-1}	$\Delta H^{\ddagger}$,[d] kJ mol^{-1}	$-\Delta S^{\ddagger}$,[d] J K^{-1} mol^{-1}
p-OCH_3	95E	5	355 (4)		
		15	1110 (5)		
		25	3192	75.4 ± 9.2	20.6 ± 32.3
p-CH_3		60	32.7 (5)		
		50	21.6 (8)		
		35	2.78 (1)		
		25	0.824	98.5 ± 18.6	12.0 ± 58.7
	80E	35	53.6 (20)		
		25	18.5 (10)	81.2 ± 13.0	44.1 ± 43.1
H		60	26.2 (11)		
		50	8.83 (9)		
		40	3.39 (20)		
		25	0.589	89.4 ± 6.2	45.2 ± 19.2
	97T	25	186 (1)		
p-Br		35	108 (3)		
		25	43.7 (6)	69.0 ± 6.0	77.7 ± 19.9
m-Br		50	36.0 (17)		
		40	14.2 (2)		
		25	3.10	78.6 ± 9.3	67.5 ± 29.4

[a] Substituent on the phenyl ring. [b] 95E and 80E are 95 and 80 vol % aqueous ethanol, respectively; 97T is 97 wt % aqueous 2,2,2-trifluoroethanol. [c] Numbers in parentheses are uncertainties of the last reported figure; i.e., 355 (4) = 355 ± 4; uncertainties are standard deviations of the mean. Rate constants reported without uncertainty are calculated values from other temperatures. [d] Uncertainties are standard deviations of the mean.

nounced, it is the (Z)-3U chloride which shows the largest rate enhancement. It is interesting to note that in the latter case the $k_{(Z)\text{-}3U}/k_{(E)\text{-}3U}$ ratio is 1.7 which is very near the reactivity ratio (1.5) for (Z)- vs. (E)-2-butene in bromine addition.[7,8]

The importance of steric hindrance to participation can be evaluated by examination of molecular models. There are two conformations of the substrates which involve very little angle strain and are favorable for the formation of **5**. One of them leads to the configuration of the carbonium ion **5** as depicted in **6a** and the other as in **6b**.



6

a R_4=Y-C_6H_4; R_5=H

b R_4=H; R_5=Y-C_6H_4

2U R_1=CH_3; R_2=R_3=H

E-3U R_1=R_3=H; R_2=CH_3

Z-3U R_1=R_2=H; R_3=CH_3

With **2U** and (E)-3U the aryl and the methyl group are on the same side of the three-membered ring produced by bridging, with the consequence that in one of the possible configurations (**6a** with **2U** and **6b** with (E)-3U) the free rotation of the two groups is hindered. No such interference exists, with (Z)-3U where the two groups are placed on the opposite sides of the three-membered ring, allowing for their free rotation both in **6a** and **6b**. On the other hand, some crowding can be expected with (Z)-3U since the methyl group in **5** is then in a pseudoaxial position. Thus, steric factors do not seem to be responsible for the anomalous reactivity of both (E)- and (Z)-3U relative to **2U**.

We have noted[2] that the rate enhancements observed with series U relative to series S seem to be due to a favorable $\Delta\Delta H^{\ddagger}$ overcompensating an unfavorable $\Delta\Delta S^{\ddagger}$. However, it was stated that this criterion of participation should be used with some caution because the activation parameters were all calculated from rates at only two closely spaced temperatures. Indeed, the calculated uncertainties of the enthalpies and entropies of activation given in Table II are rather large.

Table III. Free Energy Correlation in 97 wt % Aqueous 2,2,2-Trifluoroethanol at 25 °C

chlorides	n[a]	ρ^+	r[b]	s[c]	ψ[d]
3S[e]	5	−6.40	0.998	0.23	0.082
(Z)-3U	4	−4.56	0.999	0.054	0.063
	5	−5.76	0.989	0.44	0.209
4U[e]	4	−3.94	0.998	0.10	0.089
	5	−4.83	0.992	0.31	0.163

[a] Number of data points with (n = 5) or without (n = 4) the rate of p-anisyl derivative. [b] Correlation coefficient. [c] Standard deviation of the regression line. [d] Statistical test $\psi = [n(n-r^2)/n-2]^{1/2}$. A correlation is considered good if $\psi \leq 0.1$.[9] [e] Data from ref 2.

Linear Free Energy Relationships

It was shown[2] that in solvolyses of α-arylalkyl chlorides ρ^+ values are not solvent dependent. Therefore, the rates in Table II were extrapolated to 97 wt % of 2,2,2-trifluoroethanol solvent and 25 °C. The calculated free energy correlation is shown in Table III. An excellent fit is obtained if the rate for the p-anisyl derivative is excluded. If the latter point is included, the correlation is much worse. This observation and the lower ρ^+ value relative to the S series is consistent with an increasing amount of participation as the electron-donating power of the phenyl ring substituent decreases. The same observation was previously reported for series **4U**.[2]

Experimental Section

The chlorides were prepared in 85–95% yields by treating the corresponding carbinol in anhydrous ether in presence of pyridine with thionyl chloride at −15 °C under stirring for 1 h. After being stirred, the reaction mixture was brought to room temperature. Pyridinium hydrochloride was then filtered off, and the solvent and unreacted reagents were removed in vacuo. In all cases the NMR and IR spectra were consistent with the expected structure of the product. Parent carbinols were prepared from the Grignard reagent of (Z)-1-bromo-4-hexene and substituted benzaldehydes. The yields were, after chromatography on alumina, from 55% to 65%. All parent carbinols gave the expected NMR and IR spectra. Anal. Calcd for $C_{14}H_{20}O_2$ [(Z)-1-(4-methoxyphenyl)-5-hepten-1-ol]: C, 76.32; H, 9.15. Found: C, 76.58; H, 9.31. Calcd

for $C_{14}H_{20}O$ [(*Z*)-1-(4-methylphenyl)-5-hepten-1-ol]: C, 82.30; H, 9.87. Found: C, 82.19; H, 10.03. Calcd for $C_{13}H_{18}O$ [(*Z*)-1-phenyl-5-hepten-1-ol]]: C, 82.06; H, 9.54. Found: C, 81.87; H, 9.79. Calcd for $C_{13}H_{17}OBr$ [(*Z*)-1-(4-bromophenyl)-5-hepten-1-ol]: C, 58.00; H, 6.37. Found: C, 58.26; H, 6.05. Calcd for $C_{13}H_{17}OBr$ [(*Z*)-1-(3-bromophenyl)-5-hepten-1-ol]: C, 58.00; H, 6.37. Found: C, 57.83; H, 6.26.

Solvolysis rates were followed as described previously.[2] The reported values are the mean of three to five independent measurements. In all cases the first-order rate law was obeyed up to at least 80% reaction completion. Rate constants were calculated by means of a nonlinear least-squares program.

Acknowledgment. We thank Drs. Mihailo Mihailovič and Alan F. Thomas and Firmenich SA, Geneva, Switzerland, for gifts of (*Z*)-4-hexen-1-ol.

Registry No. **2U** (Y = *p*-OCH_3), 71434-71-4; **2U** (Y = *p*-CH_3), 71434-72-5; **2U** (Y = H), 71434-73-6; **2U** (Y = *p*-Br), 71434-74-7; **2U** (Y = *m*-Br), 71434-75-8; (*E*)-**3U** (Y = *p*-OCH_3), 85662-56-2; (*E*)-**3U** (Y = *p*-CH_3), 85662-57-3; (*E*)-**3U** (Y = H), 85662-58-4; (*E*)-**3U** (Y = *p*-Br), 85662-59-5; (*E*)-**3U** (Y = *m*-Br), 85662-60-8; (*Z*)-**3U** (Y = *p*-OCH_3), 85662-61-9; (*Z*)-**3U** (Y = *p*-CH_3), 85662-62-0; (*Z*)-**3U** (Y = H), 85662-63-1; (*Z*)-**3U** (Y = *p*-Br), 85662-64-2; (*Z*)-**3U** (Y = *m*-Br), 85662-65-3; **4U** (Y = *p*-OCH_3), 71434-50-9; **4U** (Y = *p*-CH_3), 71434-51-0; **4U** (Y = H), 71434-52-1; **4U** (Y = *p*-Br), 71434-53-2; **4U** (Y = *m*-Br), 71434-54-3; (*Z*)-1-(4-methoxyphenyl)-5-hepten-1-ol, 85662-66-4; (*Z*)-1-(4-methylphenyl)-5-hepten-1-ol, 85662-67-5; (*Z*)-1-phenyl-5-hepten-1-ol, 85662-68-6; (*Z*)-1-(4-bromophenyl)-5-hepten-1-ol, 85662-69-7; (*Z*)-1-(3-bromophenyl)-5-hepten-1-ol, 85662-70-0.

Solvent Isotope Effects on Equilibria of Mono- and Dihydration of Neutral Pteridine

Kenneth R. Davis and Richard Wolfenden*

Department of Biochemistry, University of North Carolina, Chapel Hill, North Carolina 27514

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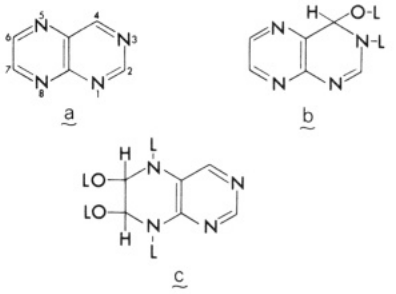
Reversible covalent hydration of C=N bonds has been observed in a number of heterocyclic compounds, of which unsubstituted pteridine is a prototype.[1] In a process that may resemble a partial reaction in substrate hydrolysis, adenosine deaminase catalyzes the stereospecific hydration of pteridine (Chart I, a) at the 3,4-position.[2] The product (Chart I, b) is a strong inhibitor.[3] Addition of D_2O to carbonyl compounds is known to proceed with an equilibrium constant substantially more favorable than that for addition of water,[4] and it seemed possible that fractionation factors might be useful in investigating interactions of pteridine with enzymes. In a thorough kinetic study of the nonenzymatic hydration of pteridine, Pocker et al.[5] reported results in which no substantial solvent isotope effect on the equilibrium of monohydration of pteridine was evident at pH values at and above neutrality. Reinvestigating this reaction, we have confirmed that the solvent isotope effect on the monohydration of pteridine is close to unity. We find in addition that pteridine *di*hydrate[6] (Chart I, c) is formed in neutral solution more slowly than the monohydrate. The dihydrate had been believed to be formed only as the cation in acid solution.[6]

Chart I



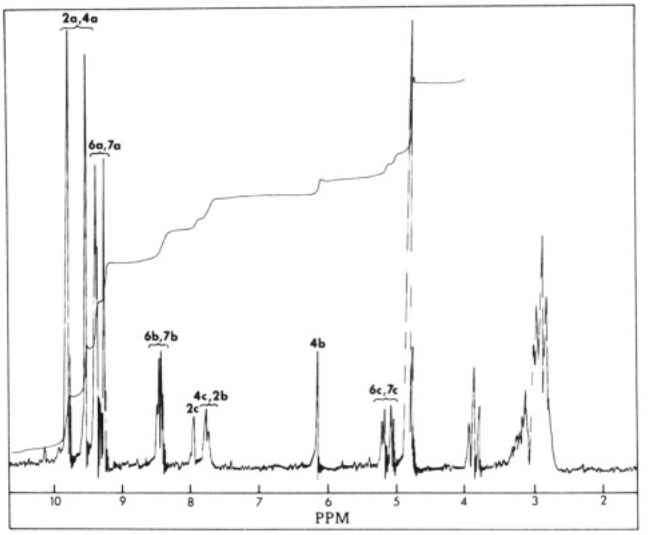


Figure 1. NMR spectrum of pteridine incubated in D_2O (0.17 M Hepes, pD = 8.2) at 34.2 °C for 8 h. The numbers indicate assignments of protons to the ring positions indicated Chart I, a–c. L refers to protium or deuterium.

Like monohydration, the equilibrium of dihydration appears to be almost completely insensitive to the replacement of water by D_2O.

Results and Discussion

The 90-MHz proton NMR spectrum of pteridine in buffered D_2O, after having been allowed to stand at 34.2 °C for 8 h, is shown in Figure 1. A similar spectrum was generated when pteridine (0.07 M) was allowed to act as its own buffer and incubated in D_2O, in which case the pD (pH meter reading + 0.4) was 7.7 immediately after the pteridine was dissolved, and gradually rose during the course of the experiment to 8.3. Thus the buffer (and relatively highly concentration of pteridine) is not responsible for the differences between the NMR spectrum in Figure 1 and those reported by Albert et al.[6] The earlier observations were evidently made at lower temperatures and/or shorter times than the present ones, as only resonances for the monohydrate and free pteridine appeared. A relatively high concentration of pteridine was used to obtain the data in Figure 1, because it was found that similar measurements could be made in H_2O with some precision at 0.7 M, allowing the determination of an approximate solvent isotope effect on the equilibrium constant for formation of the dihydrate. All of the resonances observed in D_2O were also observed in H_2O except for the dihydrate pair of doublets at 5.1–5.3 ppm. After incubation of pteridine for about 12 h in H_2O (or 30 h in D_2O) at 34.2 °C, more signals began to appear in the NMR spectrum. We were unable to assign these late resonances, as they overlapped considerably with the dihydrate and monohydrate ones; however, they appeared at such a rate as to require only minor corrections of the integrated in-

(1) Albert, A. *Adv. Heterocycl. Chem.* **1976**, *20*, 117.
(2) Evans, B. E.; Wolfenden, R. *J. Am. Chem. Soc.* **1972**, *94*, 5902.
(3) Evans, B. E.; Wolfenden, R. *Biochemistry* **1973**, *12*, 392.
(4) Mata-Segreda, J. F.; Wint, S.; Schowen, R. L. *J. Am. Chem. Soc.* **1974**, *96*, 5608.
(5) Pocker, Y.; Bjorkquist, D.; Schaffer, W.; Henderson, D. *J. Am. Chem. Soc.* **1975**, *97*, 5540.
(6) Albert, A.; Batterham, T. J.; McCormack, J. J. *J. Chem. Soc. B* **1966**, 1105.

0022-3263/83/1948-2280$01.50/0