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Rates and Alkyl Group Size in Solvolysis of Alkyl Derivatives

Mirko Orlović, Olga Kronja, Krešimir Humski, and Stanko Borčić*

Faculty of Pharmacy and Biochemistry, University of Zagreb, A. Kovačića 1, 41000 Zagreb, Croatia, Yugoslavia

Eugenio Polla*

INA-Research & Development, Proleterskih brigada 78, 41000 Zagreb, Croatia, Yugoslavia

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The logarithm of solvolysis rate constants in 80% aqueous ethanol of 1,1-dimethyl-1-alkyl chlorides **1** and 1-phenyl-1-alkyl chlorides **2** decrease monotonically with increasing number of carbon atoms in the alkyl group. The first member of both series deviates from the corresponding correlation lines which have the same slope. In contrast, solvolysis rates in 80% aqueous ethanol of 1-methyl-1-alkyl tosylates **3** do not depend upon the size of the alkyl group. The results are rationalized in terms of a mechanism that is very similar in reactions of series **1** and **2** but different from that of series **3**.

One of common criteria of neighboring group participation in solvolysis is an increased reaction rate relative to that of a reference compound. In the simplest case the (often titrimetrically) measured first-order rate constant of the participating system, k_t, is considered to be the sum of the rate constant of the nucleophilically unassisted process, k_c, and of that of the neighboring group assisted process,[1] k_Δ (eq 1).

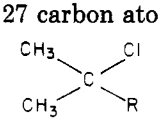
$$k_t = k_c + k_\Delta \qquad (1)$$

In order to estimate the magnitude of k_Δ it is therefore necessary to know k_t as well as k_c. Since the latter rate constant cannot be measured directly, a reference compound is used for that purpose. This approximation represents a limiting factor to the validity of the rate enhancement criterion. Thus only large observed rate ratios (>1000)[2] are considered to be indicative of participation. It is widely recognized that smaller rate acceleration are often ambiguous. Nevertheless, because of the form eq 1 even small observed rate effects (<100)[3,4] can conceal considerable participation and should not be ignored. This has been pointed out on several occasions.[5] In such cases the correct choice of a reference substrate becomes of utmost importance. The two substrates whose rates are to be compared should resemble each other as closely as possible.[3]

For the above reasons it was found necessary in the course of our work on simple and extended π-participation in solvolysis of 5-alkenyl[4] and 5,9-alkadienyl[6] derivatives to determine the rates of the corresponding saturated analogues. A number of alkyl chlorides and tosylates were therefore prepared and their solvolysis rates measured. The results show some interesting trends which are herewith reported.

Results

The series of tertiary chlorides **1** and secondary chlorides **2** were prepared by the reaction of the parent alcohols with thionyl chloride. The series of secondary tosylates **3** was prepared from the corresponding alcohols and *p*-toluenesulfonyl chloride in pyridine. All parent alcohols were prepared from the corresponding Grignard reagents (RMgBr) and acetone (**1**), benzaldehyde (**2**), and acetaldehyde (**3**), respectively. Alkyl group R contained from 1 to 27 carbon atoms



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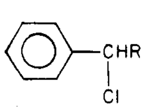
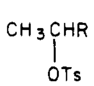


2



$\underset{\text{OTs}}{\mathrm{CH_3\underset{|}{C}HR}}$

3

Derivatives **1**–**3** were subjected to solvolysis in 80% aqueous ethanol at several temperatures and the reaction rates followed titrimetrically. The calculated first-order

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Table I. Solvolysis of 1,1-Dimethyl-1-alkyl Chlorides 1, 1-Phenyl-1-alkyl Chlorides 2, and 1-Methyl-1-alkyl Tosylates 3 in 80% Aqueous Ethanol. Rate Constants and Activation Parameters

compd	C_m,[a]	T, °C	k,[b,c] s^{-1}	$\Delta H^{\ddagger}$,[c] kJ mol^{-1}	$-\Delta S^{\ddagger}$,[c] J mol^{-1} K^{-1}
1a	1	25	$9.17 \times 10^{-6\,d}$		
1b	2	25	$1.53 \times 10^{-5\,d}$		
1c	3	25	$1.44 \times 10^{-5\,d}$		
1d	4	25	$1.31 \times 10^{-5\,d}$		
1e	5	60	$(7.40 \pm 0.26) \times 10^{-4}$		
		50	$(2.68 \pm 0.04) \times 10^{-4}$		
		40	$(8.80 \pm 0.23) \times 10^{-5}$		
		25	1.44×10^{-5}	91.38 ± 4.06	31.34 ± 12.64
1f	6[e]	60	$(6.52 \pm 0.04) \times 10^{-4}$		
		50	$(2.32 \pm 0.02) \times 10^{-4}$		
		40	$(7.71 \pm 0.13) \times 10^{-5}$		
		25	1.29×10^{-5}	90.29 ± 1.59	35.82 ± 4.94
1g	6	60	$(6.95 \pm 0.10) \times 10^{-4}$		
		50	$(2.57 \pm 0.04) \times 10^{-4}$		
		40	$(7.68 \pm 0.09) \times 10^{-5}$		
		25	1.25×10^{-5}	93.22 ± 4.02	26.28 ± 12.43
1h	7[f]	60	$(4.95 \pm 0.12) \times 10^{-4}$		
		50	$(1.75 \pm 0.04) \times 10^{-4}$		
		40	$(5.94 \pm 0.18) \times 10^{-5}$		
		25	1.01×10^{-5}	89.54 ± 3.94	40.41 ± 12.26
1i	8	70	$(1.75 \pm 0.03) \times 10^{-3}$		
		60	$(6.74 \pm 0.08) \times 10^{-4}$		
		50	$(2.38 \pm 0.03) \times 10^{-4}$		
		25	1.38×10^{-5}	88.91 ± 1.86	39.75 ± 5.57
1l	10	70	$(1.62 \pm 0.01) \times 10^{-3}$		
		60	$(6.04 \pm 0.08) \times 10^{-4}$		
		50	$(2.05 \pm 0.03) \times 10^{-4}$		
		25	1.08×10^{-5}	92.31 ± 1.75	30.48 ± 5.25
1m	12	70	$(1.65 \pm 0.02) \times 10^{-3}$		
		60	$(6.24 \pm 0.13) \times 10^{-4}$		
		50	$(2.19 \pm 0.01) \times 10^{-4}$		
		25	1.23×10^{-5}	89.98 ± 1.93	37.15 ± 5.79
1n	16	70	$(1.64 \pm 0.05) \times 10^{-3}$		
		60	$(6.08 \pm 0.24) \times 10^{-4}$		
		50	$(2.03 \pm 0.10) \times 10^{-4}$		
		40	$(6.07 \pm 0.22) \times 10^{-5}$		
		25	9.31×10^{-6}	94.80 ± 3.03	23.04 ± 9.14
1o	27[g]	70	$(1.12 \pm 0.04) \times 10^{-3}$		
		60	$(4.10 \pm 0.11) \times 10^{-4}$		
		50	$(1.37 \pm 0.05) \times 10^{-4}$		
		25	6.67×10^{-6}	93.97 ± 2.26	28.70 ± 6.74
2a	1	25	$1.00 \times 10^{-5\,h}$		
2b	2	70	$(2.52 \pm 0.07) \times 10^{-4}$		
		60	$(1.00 \pm 0.05) \times 10^{-4}$		
		50	$(3.71 \pm 0.16) \times 10^{-5}$		
		25	2.41×10^{-6}	85.30 ± 3.97	66.43 ± 11.88
2c	3	70	$(3.27 \pm 0.02) \times 10^{-4}$		
		60	$(1.28 \pm 0.05) \times 10^{-4}$		
		50	$(4.32 \pm 0.05) \times 10^{-5}$		
		25	2.43×10^{-6}	90.27 ± 3.04	49.67 ± 9.13
2d	5	60	$(8.76 \pm 0.46) \times 10^{-5}$		
		50	$(3.11 \pm 0.29) \times 10^{-5}$		
		25	1.72×10^{-6}	90.26 ± 0.98	52.58 ± 3.08
2e	6[e]	25	$2.14 \times 10^{-6\,i,l}$	86.65 ± 1.54[i]	62.85 ± 4.96[i]
2f	6	25	$2.14 \times 10^{-6\,i,l}$	87.57 ± 2.09[i]	59.79 ± 6.70[i]
2g	7[f]	25	$1.45 \times 10^{-6\,i,l}$	103.69 ± 6.45[i]	8.97 ± 20.76[i]
2h	8	60	$(1.30 \pm 0.03) \times 10^{-4}$		
		50	$(4.41 \pm 0.11) \times 10^{-5}$		
		40	$(1.37 \pm 0.03) \times 10^{-5}$		
		25	2.09×10^{-6}	95.46 ± 8.30	33.63 ± 2.57
2i	12	60	$(1.29 \pm 0.01) \times 10^{-4}$		
		50	$(3.90 \pm 0.03) \times 10^{-5}$		
		40	$(1.11 \pm 0.01) \times 10^{-5}$		
		25	1.44×10^{-6}	103.82 ± 0.74	8.69 ± 2.33
2l	16	70	$(3.27 \pm 0.08) \times 10^{-4}$		
		60	$(1.12 \pm 0.02) \times 10^{-4}$		
		50	$(3.52 \pm 0.04) \times 10^{-5}$		
		25	1.46×10^{-6}	99.55 ± 2.04	22.71 ± 6.12
3a	1	25	$2.99 \times 10^{-6\,l,m}$	90.54 ± 6.59[l]	47.09 ± 20.54[l]
3b	2	25	$3.81 \times 10^{-6\,l,m}$	90.45 ± 1.27[l]	45.34 ± 4.01[l]
3c	3	25	$3.12 \times 10^{-6\,l,m}$	90.87 ± 1.55[l]	45.54 ± 4.90[l]
3d	5	70	$(4.15 \pm 0.07) \times 10^{-4}$		
		60	$(1.58 \pm 0.04) \times 10^{-4}$		
		50	$(5.94 \pm 0.17) \times 10^{-5}$		
		25	3.66×10^{-6}	86.73 ± 1.72	58.18 ± 5.14

Table I (Continued)

compd	C_m,[a]	T, °C	k,[b,c] s^{-1}	$\Delta H^{\ddagger}$,[c] kJ mol^{-1}	$-\Delta S^{\ddagger}$,[c] J mol^{-1} K^{-1}
3e	6[e]	70	$(4.29 \pm 0.02) \times 10^{-4}$		
		60	$(1.61 \pm 0.03) \times 10^{-4}$		
		50	$(5.96 \pm 0.16) \times 10^{-5}$		
		25	3.54×10^{-6}	88.54 ± 1.49	52.54 ± 4.47
3f	6	70	$(3.58 \pm 0.02) \times 10^{-4}$		
		60	$(1.39 \pm 0.01) \times 10^{-4}$		
		50	$(5.05 \pm 0.01) \times 10^{-5}$		
		25	3.09×10^{-6}	87.41 ± 1.64	57.33 ± 4.93
3g	8	70	$(3.88 \pm 0.14) \times 10^{-4}$		
		60	$(1.59 \pm 0.04) \times 10^{-4}$		
		50	$(5.48 \pm 0.12) \times 10^{-5}$		
		25	3.40×10^{-6}	86.92 ± 3.28	58.03 ± 9.83
3h	10	70	$(3.46 \pm 0.03) \times 10^{-4}$		
		60	$(1.24 \pm 0.02) \times 10^{-4}$		
		50	$(4.82 \pm 0.11) \times 10^{-5}$		
		25	2.82×10^{-6}	88.93 ± 6.16	53.41 ± 18.41
3i	12	70	$(3.42 \pm 0.07) \times 10^{-4}$		
		60	$(1.24 \pm 0.05) \times 10^{-4}$		
		50	$(5.09 \pm 0.19) \times 10^{-5}$		
		25	3.27×10^{-6}	85.36 ± 6.13	63.97 ± 18.36

[a] C_m indicates the number of carbon atoms in the alkyl moiety. [b] Average rate constant for three to six independent measurements. [c] Uncertainties are standard deviations of the mean. [d] From ref 15. [e] 4-Methylpentyl. [f] 4-Methylhexyl. [g] 4,8,13,17,21-Pentamethyldocosanyl. [h] From ref 10. [i] From ref 4a. [l] Calculated from kinetic data in ref 14. [m] Calculated from rates at higher temperatures.

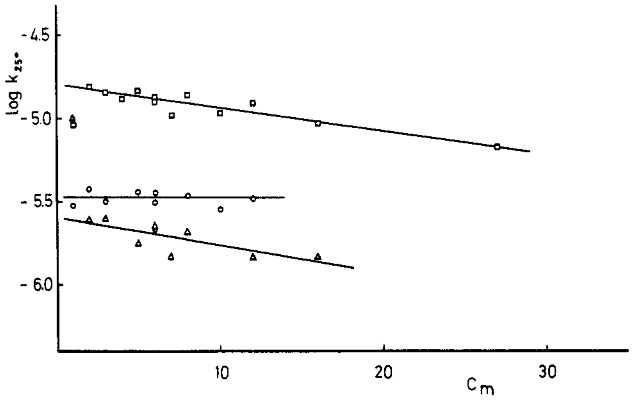

Figure 1. Plot of the log $k_{25\,°C}$ vs. C_m for the solvolysis of 1,1-dimethyl-1-alkyl chlorides **1** (□), 1-phenyl-1-alkyl chlorides **2** (▲), and 1-methyl-1-alkyl tosylates **3** (○) in 80% aqueous ethanol.

rate constants are given in Table I together with those obtained from the literature. Table I also shows the number of carbon atoms in the alkyl group and chain-branching (if any) as well as the calculated activation parameters. The observed trends are illustrated in Figure 1 by a plot of the log of the rate constant at 25 °C against the number of carbon atoms (C_m) in the alkyl group R.

Discussion

Solvolysis rate constants in 80% aqueous ethanol of 1,1-dimethyl-1-alkyl chlorides **1** decrease slowly and monotonically as the alkyl group C_m is changed from $m = 2$ to 27 (Table I and Figure 1). A regression analysis between the log of the solvolysis rate constant at 25 °C and m in C_m produced the linear relationship in eq 2, with n

$$\log k_{25\,°C} = -(1.35 \pm 0.18) \times 10^{-2} \times m - (4.81 \pm 0.02) \quad (2)$$

$= 12$, $r = 0.917$ (95.0), and $F = 53.1$ (95.0) [the values in parentheses are confidence levels, in percent, of the correlation coefficient r and the F value]. They indicate a reasonably good correlation. Similarly, in solvolysis of 1-phenyl-1-alkyl chlorides **2** the calculated rate constants in the same solvent yield practically the same linear relationship (from $m = 2$ to 16) (eq 3). with $n = 9$, $r = 0.762$

$$\log k_{25\,°C} = -(1.65 \pm 0.53) \times 10^{-2} \times m - (5.60 \pm 0.04) \quad (3)$$

(95.0), and $F = 9.72$ (95.0). The rate constants of the first member in both series deviate significantly from the corresponding correlations, the rate of *tert*-butyl chloride being too slow and that of 1-phenylethyl chloride too fast[7] (Figure 1). The solvolysis of simple tertiary alkyl chlorides such as **1** is considered to proceed by a limiting mechanism. Thus the solvolysis rate of *tert*-butyl chloride in 80% aqueous ethanol has been used as a reference for establishing Y values of solvents in the well-known Grunwald–Winstein equation.[8] It has however been suggested that the solvolysis of even *tert*-butyl chloride in the particular solvent might be slightly nucleophylically assisted.[9] Nevertheless, we consider that the decrease of the rate with the increase in the number of carbon atoms of the alkyl group in solvolysis of **1** must be due to a decreasing ease of the rate determining formation of the carbenium ion intermediate.

The solvolysis mechanism of 1-phenyl-1-alkyl chlorides **2** seems to be very similar to that of tertiary chlorides **1**. Thus the solvolysis of 1-phenylethyl chloride in 80% aqueous ethanol proceeds with practically the maximum secondary α-deuterium kinetic isotope effect for chloride as the leaving group ($k_H/k_D = 1.146$).[10] These large effects are thought to be indicative of a reaction mechanism in which the rate-determining step is the transformation of an internal ion pair into a solvent separated ion pair (or free carbocation).[10] It has been a rule of thumb that a phenyl group stabilizes an adjacent carbenium ion center approximately as well as two methyl groups.

The similarity of the reaction mechanisms of the series **1** and **2** is reflected in the practically identical response of their solvolysis rates to an increase in the bulk of the alkyl group R. It should be noted that the observed trends are in the opposite direction from those reported for the gas phase.[11] There, it has been shown that the heterolytic bond-dissociation energy $D(R^+-H^-)$ for the same type of carbenium ions is a *decreasing* linear function of the log of the number of carbon atoms in R^+. We therefore ascribe

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[7] If the first members of the series are included in the correlations the following values are obtained (95% confidence level): for **1** $r = 0.737$ and $F = 13.1$; for **2**, $r = 0.650$ and $F = 5.8$.

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our observations to a change in solvation requirements of the substrates and/or carbenium ion like transition states with the increasing bulk of the alkyl group R. Further rationalization would seem fruitless because the observed rate changes are quite small. It should, however, be mentioned that in this respect the deviation from the correlation of the first members of the series with both **1** and **2** is not surprising. The change in other effects besides solvation, such as hyperconjugative electron release and inductive electron donation would be expected to be the largest between the first two members of a series.

By contrast to series **1** and **2** the solvolysis rate in 80% aqueous ethanol of simple secondary 1-methyl-1-alkyl tosylates **3** does not change when the number of carbon atoms in the alkyl group is increased from 1 to 12 (Table I and Figure 1). The magnitude of the rate constant for any size of alkyl group R is given simply by eq 4. Also

$$\log k_{25\,^\circ\mathrm{C}} = -(5.468 \pm 0.071) \qquad (4)$$

by contrast, the first member of the series does not deviate from the correlation. The reaction mechanism of tosylates **3** in the particular solvent is different from that of chlorides **1** and **2**. Thus the solvolysis in 80% aqueous ethanol of isopropyl brosylate proceeds with a considerably reduced secondary α-deuterium kinetic isotope effect (k_H/k_D = 1.098 as compared to the maximum of 1.22).[12] Such effects are typical for reactions in which the formation of an internal ion pair is rate determining. Similarly, the work of Sneen[13] on solvolysis rates and products of 2-octyl mesylate indicates a rate-determining formation of an intimate ion pair followed by a fast attack of the nucleophile on the ion pair. On the other hand, there is evidence[14] suggesting considerable nucleophylic participation by the solvent in most solvolyses of simple secondary substrates.

Thus the transition states in solvolyses of **3** have much less carbenium ion character than those in reactions of **1** and **2** and therefore also different solvation requirements. Also, hyperconjugative and inductive stabilization of the transition states should be less pronounced, which eliminates the exceptional behavior of the first member in the series.

The different response of the solvolyses rates to an increase in the size of the group R between the series **1** and **2** on the one hand and series **3** on the other might thus well be due to different reaction mechanisms.

It should finally be mentioned that the calculated activation parameters are not accurate enough in order to observe any possible trends or correlations.

Experimental Section

Materials. 1,1-Dimethyl-1-alkyl chlorides and 1-phenyl-1-alkyl chlorides were prepared from the corresponding carbinols and thionyl chloride in the usual way. They gave IR and ^{1}H NMR spectra consistent with their structure and were shown to contain up to 10% of elimination product. Further purification proved to be unnecessary since the solvolysis rates were found to be independent of the contamination. Parent alcohols were prepared from the corresponding alkylmagnesium bromides and acetone or benzaldehyde in ether. They were purified by column chromatography on alumina using chloroform as eluent and gave IR and ^{1}H NMR spectra consistent with their structure.[4,8,15] 21-Pentamethyldocosanol (2-squalanyl alcohol) was prepared from 2,3-oxidosqualene[16] through epoxide ring opening by lithium aluminum hydride, hydrogenation of the resulting carbinol with Pd on carbon (1.05 equiv of H_2 absorbed), and purification by chromatography on silica gel. 1-Methyl-1-alkyl tosylates were prepared in the usual way[17] from the corresponding alcohols and tosyl chloride in pyridine. The parent alcohols were prepared from the corresponding alkyl magnesium bromides and acetaldehyde in ether.

Kinetic Measurements. The rates of solvolysis in 80% aqueous ethanol were followed titrimetrically by means of a pH-stat. Typically, 0.05 mmol of the substrate was dissolved in 25 mL of the solvent thermostated to 0.05 °C and the liberated acid titrated by using a 0.008 M solution of sodium in 80% aqueous ethanol. Each individual measurement followed strictly first-order kinetics up to at least 85% reaction and was repeated three to five times. First-order rate constants were calculated with a nonlinear least-square program.

Acknowledgment. We are grateful to the Yugoslav-American Joint Board (Croatian Council for Research and National Science Foundation) for the financial support of this research.

Registry No. **1a**, 507-20-0; **1b**, 594-36-5; **1c**, 4325-48-8; **1d**, 4398-65-6; **1e**, 4325-49-9; **1f**, 14093-16-4; **1g**, 928-60-9; **1h**, 102736-13-0; **1i**, 4325-51-3; **1l**, 4325-53-5; **1m**, 4325-54-6; **1n**, 102744-99-0; **1o**, 102736-14-1; **2a**, 672-65-1; **2b**, 934-11-2; **2c**, 27059-40-1; **2d**, 71434-68-9; **2e**, 71434-78-1; **2f**, 71434-47-4; **2g**, 56040-10-9; **2h**, 102736-15-2; **2i**, 102736-16-3; **2l**, 102736-17-4; **3a**, 2307-69-9; **3b**, 715-11-7; **3c**, 3813-69-2; **3d**, 5011-57-4; **3e**, 102736-18-5; **3f**, 1028-12-2; **3g**, 64154-07-0; **3h**, 102736-19-6; **3i**, 36297-27-5.

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