Marked Difference between 1,1,3,3-Tetramethyl-2-oxobutyl and 1,3,3-Trimethyl-2-oxocyclopentyl Systems in the Grunwald–Winstein Relationships in Solvolysis

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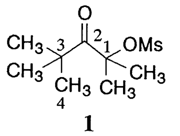
The solvolysis rates of 1,1,3,3-tetramethyl-2-oxobutyl methanesulfonate (**1**) have been reported to give a nicely linear Grunwald–Winstein relation, whereas those of structurally similar 1,3,3-trimethyl-2-oxocyclopentyl methanesulfonate (**2**) exhibit a scattered plot and well correlated by $\log(k/k_0) = (0.57 \pm 0.07)N_{\mathrm{OTs}} + (0.55 \pm 0.05)Y_{\mathrm{OTs}} + (0.03 \pm 0.09)$. These results indicate the difference in the direction of departure of the leaving group in the transition state.

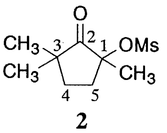
The dependency of solvolysis rates on the solvent ionizing power (Y_X) is referred to as the Grunwald–Winstein or the mY_X relationship (Eq. 1), and has been utilized to diagnose solvolysis mechanisms, in particular the presence or absence of solvent nucleophilic assistance to ionization.[1]

$$\log(k/k_0) = mY_X + c \qquad (1)$$

We herein report markedly different responses of 1,1,3,3-tetramethyl-2-oxobutyl methanesulfonate (mesylate) (**1**) and 1,3,3-trimethyl-2-oxocyclopentyl mesylate (**2**) in mY_{OTs} relations. The contrast suggests a possibility that the Grunwald–Winstein relations may be used in specifying the direction of departure of a leaving group during ionization of some particular compounds.

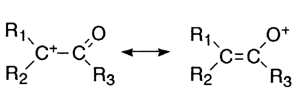


1



2

The solvolysis of **1** was extensively studied by Creary more than a decade ago,[2] and the unexpectedly fast rate in 97% 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), which was 55 times greater than that of isopropyl mesylate at 25 °C, was interpreted to suggest the stabilization of the intermediate carbocation by delocalization of positive charge to the carbonyl oxygen (Eq. 2).[2,3]



(2)

In order that an effective overlap of the developing cationic p orbital and the π system occurs, all the p orbitals should be coplanar. Although **1** was assumed to satisfy this requirement,[2] we wished to examine mesylate **2** that definitely warrants the prerequisite.

Mesylate **2** was synthesized from corresponding alcohol **3** that was derived from 1,3,3-trimethyl-2-(trimethylsiloxy)cyclopentene[4] via epoxidation with *m*-chloroperoxybenzoic acid accompanying a rearrangement[5] to the trimethylsilyl ether of **3** followed by desilylation.[6] The rates of solvolysis of **2** were measured in various solvents, and the rate constants at 25 °C are shown in Table 1 with some activation parameters.

Table 1. The first-order rate constants and some activation parameters for the solvolysis of **2** at 25 °C

Solvent[a]	k[b]	$\Delta H^{\ddagger}_{298}$	$\Delta S^{\ddagger}_{298}$
	$\mathrm{s^{-1}}$	kcal mol^{-1}[c]	cal K^{-1}mol^{-1}[c]
EtOH	4.47×10^{-7}	21.9	−14.0
80% EtOH	4.00×10^{-6}	20.6	−14.2
60% EtOH	1.01×10^{-5}		
40% EtOH	3.25×10^{-5}		
MeOH	1.35×10^{-6}	21.6	−12.8
CF_3CH_2OH	3.84×10^{-7}[d]	22.1	−13.7
AcOH[e]	8.18×10^{-8}[d]	25.2	−6.5
HCO_2H[f]	1.98×10^{-5}	20.8	−10.2

[a]Buffered with 0.025 M 2,6-lutidine except for AcOH and HCO_2H (M = mol dm^{-3}). Percent EtOH refers to percent ethanol/water (v/v). [b]Determined titrimetrically. [c]1 cal mol^{-1} = 4.184 J mol^{-1}. [d]Extrapolated from data at higher temperatures. [e]Buffered with 0.025 M NaOAc. [f]Buffered with 0.025 M NaOCHO.

A plot of log k values for **2** against Y_{OTs} values[1a,7] is shown in Figure 1 together with a reproduced similar plot for **1**.[2] In contrast to the nicely linear correlation ($m = 0.63 \pm 0.04$, $r = 0.993$)[8] for **1**,[9] the considerable downward deviations of the AcOH, TFE, and HCO_2H points from the MeOH–EtOH–aq. EtOH line ($m = 0.47 \pm 0.01$, $r = 1.000$) are evident for **2**. Similar scattered mY_X relations are general in the solvolyses of primary and simple secondary alkyl tosylates.[1d,10] The enhanced rates in nucleophilic solvents such as MeOH, EtOH, and aq. EtOH have been interpreted to involve nucleophilic participation by solvent molecules from the rear side in the transition state of ionization.[1,10] We treated the rate data of Table 1 by using Eq. 3 including the nucleophilic parameter N_{OTs}.[1a,1d] Figure 2 shows the best fit plot with $l = 0.57 \pm 0.07$, $m = 0.55 \pm 0.05$, and $c = 0.03 \pm 0.09$ ($r = 0.982$).[11] The l value of 0.57 ± 0.07 is even greater than that for isopropyl tosylate ($l = 0.4$, $m = 0.58$)[1d] despite the tertiary structure of **2**.

$$\log(k/k_0) = lN_{\mathrm{OTs}} + mY_{\mathrm{OTs}} + c \qquad (3)$$

The success of applying Eq. 1 and Eq. 3 to the solvolyses of **1** and **2**, respectively, suggests that **1** most probably follows a k_c (limiting S_N1) mechanism whereas the solvolysis of **2** is nucleophilically assisted.[12] It is generally accepted that the nucleophilic assistance is increased by the introduction of an electron withdrawing group.[1] Then, how can one rationalize the essential absence of nucleophilic assistance in **1**? A plausible explanation involves the postulation of the transition state in which the mesylate group leaves along the C=O axis in such a

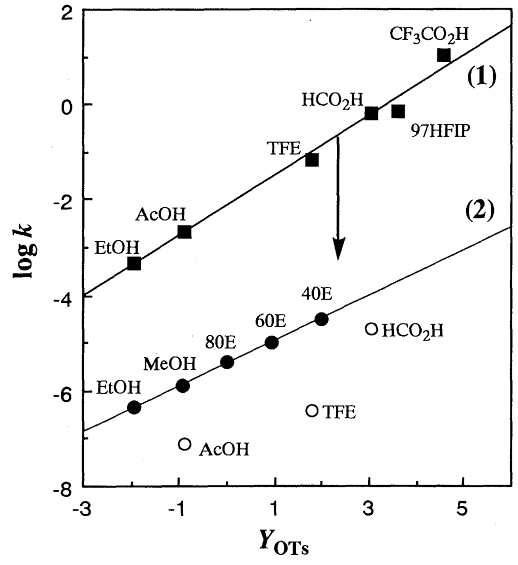
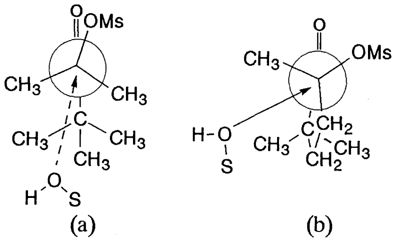


Figure 1. Plots of log k for solvolyses of **1** and **2** at 25 °C vs. Y_{OTs}. Solid squares are for **1** whose data were taken from Ref. 2, and shifted upward by 4 units. Solid circles are the methanol, ethanol, and aqueous ethanol points for **2**. The points for **2** in AcOH, TFE, and HCO$_2$H are excluded from the regression analysis and given by open circles.

manner that the B-strain between the *t*-butyl and the two methyl groups on C(1) is efficiently relieved [Scheme 1 (a)].[13] Investigation of molecular models indicates that the rear side of the C(1) position of the transition state of **1** is effectively blocked from nucleophilic solvent participation, whereas **2** is susceptible to the attack by solvent from the rear side [Scheme 1 (b)].[14]



Scheme 1.

Supporting this postulate, the solvolyses of **2** give greater amounts of substitution product than **1**, both without any rearrangements; the substitution/elimination ratios in ethanolysis at 75 °C are 33/67 and 5/95[2] for **2** and **1**, respectively. It is also inferred that **1** may not be a good model to examine the carbonyl π conjugation in α-carbonyl carbenium ions since the developing cationic p orbital may be almost perpendicular to the π system.

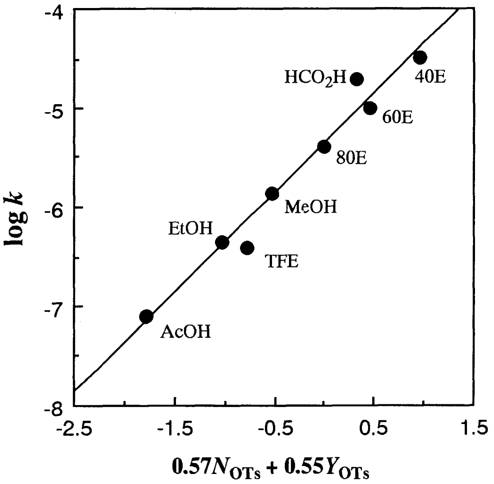


Figure 2. Plot of log k for solvolysis of **2** at 25 °C vs. $0.57N_{\mathrm{OTs}}$ + $0.55Y_{\mathrm{OTs}}$.

References and Notes

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2 X. Creary, *J. Am. Chem. Soc.*, **106**, 5568 (1984).

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6 1,3,3-Trimethyl-2-oxocyclopentyl mesylate (**2**): mp 28.1–29.1 °C; ^{13}C NMR (22.5 MHz, CDCl$_3$) δ 22.7, 25.6, 26.0, 33.2, 33.6, 41.0, 43.1, 90.6, and 217.0. Found: C, 48.94; H, 7.58%. Calcd for C$_9$H$_{16}$O$_4$S: C, 49.07; H, 7.32%. 2-Hydroxy-2,5,5-trimethylcyclopentanone (**3**): bp 84 °C/13 mmHg (1 mmHg = 133.322 Pa); ^{13}C NMR (22.5 MHz, CDCl$_3$) δ 23.5, 24.9 (2C), 33.5, 33.9, 43.1, 76.9, and 223.9. Found: C, 67.18; H, 9.99%. Calcd for C$_8$H$_{14}$O$_2$: C, 67.57; H, 9.92%.

7 The Y_{OTs} values are known to be applicable to mesylates.[1a]

8 In this communication the errors are given by standard errors.

9 A reported m value based on original Y_{OTs}[1d] was 0.66.[2]

10 D. J. Raber, W. C. Neal, Jr., M. D. Dukes, J. M. Harris, and D. L. Mount, *J. Am. Chem. Soc.*, **100**, 8137 (1978).

11 The use of Kevill's N_{T} parameters much improves the linearity (l = 0.58 ± 0.02, m = 0.67 ± 0.02, c = 0.04 ± 0.03, r = 0.998): D. N. Kevill and S. W. Anderson, *J. Org. Chem.*, **56**, 1845 (1991).

12 However, nucleophilic solvent involvement has been assumed to explain the small m value for **1**.[2]

13 The large solvolysis rate ratio of 22 in 80% ethanol at 25 °C between 2-chloro-2,4,4-trimethylpentane and 2-chloro-2-methylpropane has been attributed to relief of B-strain in the former: see, H. C. Brown and R. S. Fletcher, *J. Am. Chem. Soc.*, **71**, 1845 (1949); H. C. Brown, "The Nonclassical Ion Problem," with comments by P. v. R. Schleyer, Plenum Press, New York (1977), p. 22.

14 We have found that the nucleophilic solvent assistance is negligible in the solvolysis of a homologous compound 2-chloro-2,4,4-trimethylpentane: the result will be reported elsewhere.