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Communications

The Cause of Dispersion Phenomenon in Grunwald-Winstein Plots: Solvolyses of Cyclopentyl Tosylate in Aqueous Binary Mixtures

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Dispersion into sepatrate lines in the correlation of the specific rates of solvoysis of a substrate in various binary mixtures was documented[1~3] in early treatments using the Grunwald-Winstein equation [eqn. (1)].

$$\log(k/k_o)=mY+c \quad (1)$$

In equation (1), k and k_o are specific rates of solvolysis of a substrate in a given solvent, of solvent ionizing power Y, and in 80% ethanol respectively, m is the sensitivity to changes in Y values, and c is a residual (constant) term. Equation (1) is commonly written without the intercept (c), which is not required for typical interpretations, but c is often considered "hidden" adjustable parameter in the correlations.[4]

In general, dispersion effects in unimolecular solvoyses[5,6] make smaller contribution to the overall linear free energy relationship (LFER) than solvent nucleophilicity effects in bimolecular solvolyses. It was suggested[2] that a second term which is governed by the sensitivity l to solvent nucleophilicity N, should be added to equation (1) for bimolecular solvolyses. The resulting equation (2) is often referred to as the extended Grunwald-Winstein equation.

$$\log(k/k_o)=mY+lN \quad (2)$$

It was suggested that a Y scale based on 2-adamantyl tosylate solvolysis[7,8,9] (Y_{OTs}) would be the most appropriate, and N_{OTs} values can be obtained from equation (3).

$$N_{OTs}=\log(k/k_o)_{MeOTs}-0.3Y_{OTs} \quad (3)$$

The cause of dispersion in Grunwald-Winstein plots using equation (1) is when the leaving group in the solvoysis of a given substrate differs from the leaving group present in the standard substrate used to establish the Y scale being used in the correlation.[10]

Another cause of dispersion phenomenon due to not only the resonance stabilization within benzylic cabocations but also appreciable crowding in the vicinity of the reaction center.[11]

Rate constants for solvolyses of cyclopentyl tosylate are reported for aqueous binary mixtures with acetone, ethanol and methanol (Table 1). In order to eliminate dispersion phenomenon factor to variation of leaving group in Grunwald-Winstein plots, we tried to correlate log k with Y_{OTs} using k values obtained in this work. The Grunwald-Winstein plots of first-order rate constants for cyclopentyl tosylate with Y_{Cl} (based on 2-adamantyl chloride) show large dispersions (Figure 1). However, the plot of first-order rate constants for cyclopentyl tosylate with Y_{OTs} (based on 2-adamantyl tos-

Table 1. Rate Constants (k) Solvolyses of Cyclopentyl Tosylate in Aqueous Alcohol and Acetone Binary Mixtures at 25 ℃

v/v %	MeOH	EtOH	Acetone
		$k\times10^4$	
100	0.115	0.0325	
90	0.242	0.103	
80	0.515	0.254	0.0288
70	1.07	0.496	0.112
60	2.20	0.907	0.321
50	4.56	1.93	0.919
40	9.17	4.35	2.48
30	19.3	12.0	7.69
20	36.8	32.7	21.9
10	69.1	69.3	59.3
H_2O	101	101	101

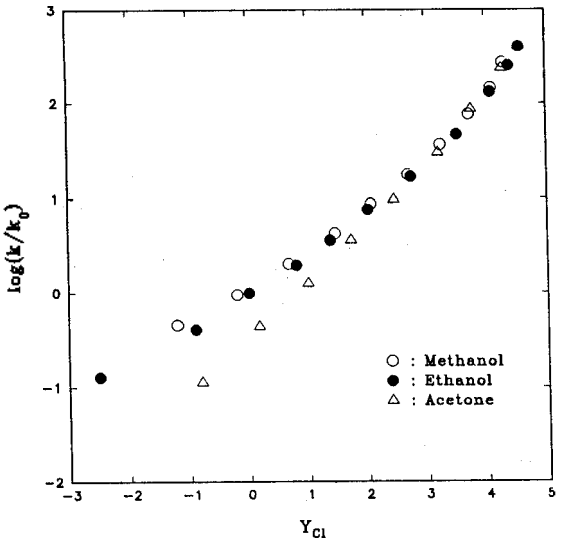

Figure 1. Logarithms of first-order rate constants for solvolyses of cyclopentyl tosylate at 25 ℃ *vs.* Y_{Cl}.

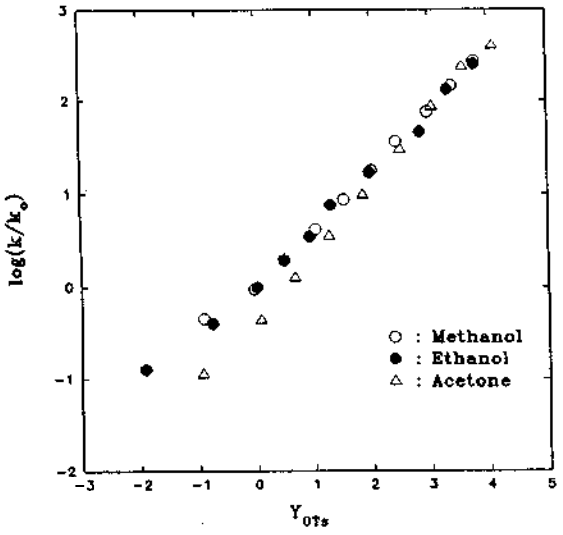

Figure 2. Logarithms of first-order rate constants for solvolyses of cyclopentyl tosylate at 25 ℃ *vs.* Y_{OTs}.

ylate) still shows dispersions (Figure 2).

Cyclopentyl tosylate is neither conjugated systems nor aromatic rings adjacent reaction center in the substrate. Therefore, it can not be explained by phenomenon of the dispersion cause by differential solvation effect on the stabilized reaction center by conjugation with adjacent conjugated system or aromatic rings. Therefore such phenomenon can be explained as dispersion effect caused by other specific solvent effect or change of reaction mechanisms according to the variation of solvent composition. In order to examine the cause of this dispersion phenomenon, we tried to correlate extended Grunwald-Winstein plots of the rate data in Table (1). The extended Grunwald-Winstein plot shows fairly good correlation ($m=0.70$, $l=0.91$, $r=0.996$) for cyclopentyl tosylate solvolysis (Figure 3).

The nucleophilicity parameter (N) has previously been

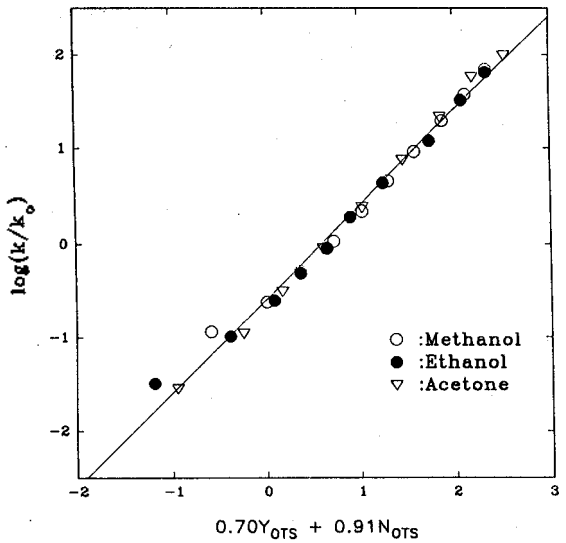

Figure 3. Plot of $\log(k/k_o)$ for cyclopentyl tosylate against $0.70\ Y_{OTS}+0.91N_{OTS}$ ($r=0.996$).

shown to give considerable improvement when it is added as an lN term to original Grunwald-Winstein correlations of the solvolyses of cyclopentyl tosylate. The m value is changed slightly after removal of dispersion, but the associated standard errors are substantially reduced. The correlaton coefficient of 0.989 in the absence of the lN term was improved to 0.996 with the lN term.

Therefore, this shows the importance of solvent nucleophilicity compared to solvent ionizing power for the solvolysis of cyclopentyl tosylate. This study has showed that the magnitude of l and m values associated with a change of solvent composition is able to predict the transition state variation to more product like transition state (asymmetric TS, $[N^{\delta+}\cdots C\cdots L^{\delta-}]^{\ddagger}$), where bond breaking is much more progressed and bond formation is slightly more advanced, upon increasing solvent inonizing power or solvent nucleophilicity.

The S_N2 reaction via product like transision state has appears to cause the dispersions in the present Grunwald-Winstein correlations.

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A New Route to a Key Chiral Intermediate of Thienamycin from *trans*-Ethyl Crotonate

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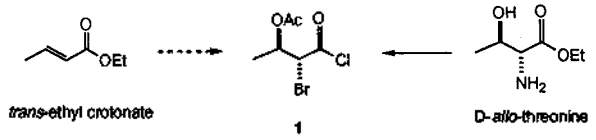
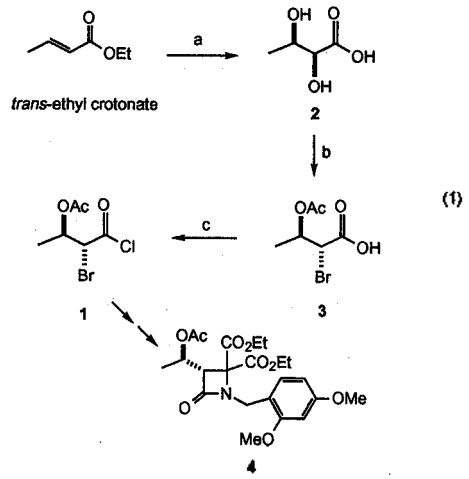
Thienamycin,[1] a β-lactam antibiotic exhibiting broad antibiotic activity, and its derivatives are continuing targets for research and development in the area of antibiotics.[2] Among various intermediates[2b,c] to those compounds, acid chloride **1** is unique in that the corresponding amides afford the β-lactam ring, azetidinones, *via* a complete intramolecular S_N2 type cyclization.[3] The intermediate **1** has been prepared as a chiral form from D-*allo*-threonine[4] or as a racemic form from *trans*-crotonic acid.[3] Considering the high cost of nonracemic threonine, we counted that any route to chiral intermediate **1** from cheap crotonates would be quite compatible.



Scheme 1.

In this brief communication, we describe a concise route to **1** from *trans*-ethyl crotonate employing asymmetric dihydroxylation (ADH).[5] Although structural transformations after ADH reactions from α,β-unsaturated esters to acetoxy bromo esters have been reported,[6] to our best knowledge, any route to **1** or to acetoxy bromo acyl chloride derivatives has not been developed. We followed a known procedure[6] using $(DHQD)_2PHAL$[7] to obtain *threo*-2,3-dihydroxy ester in 94% yield. And hydrolysis of the ester using LiOH in MeOH afforded the corresponding acid **2**[8] quantitatively. The dihydroxy acid **2** was transformed with HBr in acetic acid to provide *erythro*-β-acetoxy-α-bromo acid **3**[8] in 91% yield. Finally, the desired acyl chloride **1** was readily prepared by treating **3** with $SOCl_2$ in methylene chloride in a quantitative yield. With no necessity of purification, the four step sequence from the crotonate afforded the intermediate **1** in good yields. This reaction sequence would be applicable in general for the preparation of analogue acid chlorides. And the intermediate **1** was converted to a known azetidinone **4** for comparison using dimethoxybenzylaminomalonate.[9] The spectral data of **4** (^1H NMR, ^{13}C NMR) matched well with those in the literature,[9] though the optical purity is lower ($[\alpha]_D^{24}$ +30.9° (c=2.0, EtOH), lit.[9] $[\alpha]_D^{24}$ +39.5° (c=2.03, EtOH)).



Reagents: a. $(DHQD)_2PHAL$, $K_2OsO_2(OH)_4$, NMO, t-BuOH ; LiOH, MeOH
b. HBr, AcOH, 45°C c. SO_2Cl_2, CH_2Cl_2

In conclusion, this concise route employing practical procedures suggests a compatible pathway to the key intermediate, and the optimization for optical purity is left as further work.

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