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Isokinetic Discrimination of Two Kinds of Quaternary Ammonium Salts formed by the Reactions of Tertiary Amines with Some Carboxylates

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A specific type of reaction should have a characteristic isokinetic temperature as long as the individual reactions are carried out in the same solvent and the reactions of substrates with bulky groups are excluded.

Two kinds of reactions of tertiary amine with carboxylates, quaternization and aminolysis reactions, were distinguished by isokinetic temperatures of 430 and 256, respectively.

Keywords——isokinetic discrimination; isokinetic temperature (β); methyl chlorobenzoates; methyl bromobenzoates; methyl nitrobenzoates; S_N2 type reaction; Menshutkin reaction; Finkelstein reaction; saponification; ammonolysis

It has long been known that esters react with tertiary amines to give ammonium salts.[1] Hammett and his coworkers[2] reported differences in alkylations of trimethylamine with methyl carboxylates and gave Eq. 1 for the formation of the tetramethylammonium ion.

$$(CH_3)_3N + RCO_2CH_3 \rightleftarrows \underset{\mathbf{1}}{RCO_2^-N^+(CH_3)_4} \qquad \text{(Eq. 1)}$$

In the reaction, the nitrogen of the pyramidal trimethylamine molecule approaches the methyl carbon on the side directly opposite to the oxygen atom.

On the other hand, formation of the quaternary ammonium salt as a quasi-stable intermediate in aminolysis by attack of the N-atom of a tertiary amine on the alkoxycarbonyl C-atom of the ester has been assumed to occur on the basis of the product of aminolysis and the rapid increase of the conductance of the reaction mixture.[3]

$$R_3N + R'CO_2CH_3 \rightleftarrows \underset{\mathbf{2}}{R'C(=O)-N^+(R_3)OCH_3^-} \xrightleftharpoons[\text{primary or } \textit{sec.} \text{ amine}]{} \text{amide} \qquad \text{(Eq. 2)}$$

It seems likely that there are two pathways in the reaction of tertiary amines with alkyl carboxylates, or two kinds of quaternary ammonium salts. In order to clarify this point, some S_N2 type reactions and reactions involving an attack of nucleophilic reagents on a carboxyl carbon, such as aminolysis and saponfication, were reinvestigated, because a characteristic isokinetic temperature should apply to a specific type of reaction, as long as the individual reactions are carried out in the same reaction medium and the reactions of substrates with bulky groups are excluded.

The reactions of trimethylamine with methyl benzoates were monitored by using potentiometric titration.

Experimental

Chemicals——All chemicals used for the preparation of methyl benzoates were of pure grade. Chloro- and bromobenzoates were prepared by esterification of the corresponding benzoic acids with methanol in the presence of a catalytic amount of sulfuric acid. Yields (%) of the methyl benzoates and saponification values were as follows; 81 and 330 (calcd 328.9) for *o*-Cl; 88 and 328.7 for *m*-Cl; 87 and 329.8 for *p*-Cl; 80 and 260.7 (calcd 260.9) for *o*-Br; 80 and 260.4 for *m*-Br; 63 and 258.4 for *p*-Br, respectively. Methyl nitrobenzoates (GR) were purchased from Nakarai Chemicals Co. Melting or boiling points were as follows: bp 275°C, mp 78°C and mp 96°C for *o*-, *m*- and *p*-NO_2; bp 243°C, mp 31°C and mp 80°C for *o*-, *m*- and *p*-Br; bp 230°C, bp 225°C and mp 43°C for *o*-, *m*- and *p*-Cl, respectively. Trimethylamine was vaporized by dropwise addition of 5% sodium hydroxide solution to a gently warmed 30% aqueous solution of the amine purchased from Nakarai Chemicals Co. The vapor was dried by passing it through a sodium hydroxide tube and then was absorbed in rectified methanol. Perchloric acid (70% aqueous solution) was of analytical grade (Nakarai Chemicals Co.).

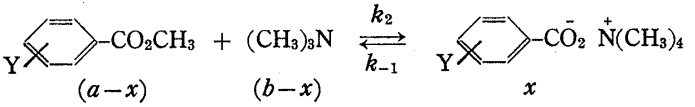
Instruments——A Hitachi-Horiba potentiometer, model M-5, and a Hitachi Perkin-Elmer UV-VIS spectrometer, model 139, were used at room temperature.

Kinetics——Methanol solutions of the methyl benzoates (0.0629 M) (100 ml) and trimethylamine (0.2 M) (25 ml) were mixed in an Erlenmeyer flask. Without delay, the mixture was divided into 10 ml portions and sealed in 12 ampoules. The ampoules were immersed in a bath thermostated at 150±0.3°C. At intervals, an ampoule was taken, cooled in an ice bath and opened. The reaction mixture was washed out with distilled water (60 ml) and subjected to potentiometric titration with 0.0508 N aqueous solution of perchloric acid. The reaction equilibrium point was obtained from 3 ampoules kept at the reaction temperature for more than 100 h.

Results and Discussion

Hammett *et al.*[2] have shown that the rate of reactions expressed by Eq. 1 is determined by the strength of the parent acids of the carboxylates and the steric factors of the alkyl groups should be excluded.

In the present experiments, relatively dilute solutions were employed in order to avoid solubility problems and the accuracy of the rate measurements was enhanced by utilizing potentiometry.



(Eq. 3)

In Eq. 3, substituents Y were NO_2, Cl and Br. The second-order reaction rate constants (k_2) of the reaction (Eq. 3) are calculated by the use of Eq. 4.

$$k_2t = \{z/(ab-z^2)\} \ln\{z(ab-zx)/ab(z-x)\} \quad \text{(Eq. 4)}$$

Table I. Rate Data for the Quaternization of Trimethylamine with Methyl *p*-Nitrobenzoate at 145°C

Time h	Conversion %	$\frac{z}{ab-z^2} \ln \frac{z(ab-zx)}{ab(z-x)}$
0	0	0
3	22.7	5.27
6	38.5	11.30
11	51.3	19.17
20	65.7	36.28
30	72.9	53.46
45	77.3	72.12
100	85.3	
110	85.3	

Initial Concn. of trimethylamine and methyl *p*-nitrobenzoate: 0.056 M each.
Conversion (%) at equilibrium stage: 85.3%

TABLE II. Rate Data and Activation Parameters for the Quaternization of Trimethylamine with Methyl Benzoates

Temp.	Nitrobenzoates			Bromobenzoates		
	o-NO_2	*m*-NO_2	*p*-NO_2	*o*-Br	*m*-Br	*p*-Br
	$10^4 k_2$	$10^4 k_2$	$10^4 k_2$	$10^4 k_2$	$10^4 k_2$	$10^4 k_2$
K	$M^{-1} s^{-1}$	$M^{-1} s^{-1}$	$M^{-1} s^{-1}$	$M^{-1} s^{-1}$	$M^{-1} s^{-1}$	$M^{-1} s^{-1}$
413	9.40	3.49	4.46	2.84		
418	11.82	4.57	4.67	3.80	2.00	
423	15.35	5.68	6.40	5.01	2.64	2.12
428					3.39	2.65
433						3.30
$\Delta H^{\neq}$ (kcal/mol)	16.6	16.3	21.6	19.2	17.9	15.1
$\Delta S^{\neq}$ (e.u.)	−32.8	−35.7	−22.8	−29.1	−33.7	−40.4

Temp.	Chlorobenzoates		
	o-Cl	*m*-Cl	*p*-Cl
	$10^5 k_2$	$10^5 k_2$	$10^5 k_2$
K	$M^{-1} s^{-1}$	$M^{-1} s^{-1}$	$M^{-1} s^{-1}$
373	2.20		
383	4.16	2.09	
393	7.31	4.46	3.29
403	15.34	9.22	6.50
408			9.23
$\Delta H^{\neq}$ (kcal/mol)	18.5	21.8	21.1
$\Delta S^{\neq}$ (e.u.)	−31.0	−23.4	−26.0

1 cal=4.184 J.

Here, a is the initial concentration of the methyl benzoates, while b is the initial concentration and x and z are the consumed concentrations of trimethylamine at time t and equilibrium stage, respectively.

The rate measurement for methyl *p*-nitrobenzoate is shown in Table I, as an example.

The reactions of other methyl benzoates also satisfy Eq. 4. Rate constants for various methyl benzoates were obtained at three different temperatures. Rate data and activation parameters are summarized in Table II. From these activation parameters, the isokinetic temperature (β)[4] was calculated to be 429.

As shown in Fig. 1, the three substituents were aligned regardless of Hammett's σ value, although they are usually arranged in σ-value order. This is considered to result from the fortuitous measurement of the rates in the vicinity of the isokinetic temperature.

Related reactions were divided into two groups. One is a rear attack of the nitrogen atom of the amine on the methyl group (S_N2 type reaction) and the other is a nucleophilic attack of the nitrogen atom of the amine on the carboxylate carbon.

Isokinetic plots for related reactions have been tried using thermodynamic data collected from the literature. The Menshutkin reaction[5-7] also involves formation of a quaternary ammonium ion. Isokinetic plots of the reaction gave a value of 429 (Fig. 2). It has been shown that the tertiary amine attacks the back side of the alkyl group of alkyl halides in this reaction. A similar reaction mechanism was proposed for the Finkelstein reaction or Conant-Finkelstein reaction[8,9] and for the reaction of alkyl bromides with thiosulfate anion,[10] where iodide or thiosulfate anion attacks the back side of alkyl chlorides. These S_N2 type reactions gave β values of 431 and 430, respectively (Figs. 3 and 4).

From these three β values, it appears that the β value of the quaternization reaction involving attack by trimethylamine on the back side of the methyl group of the ester is 430.

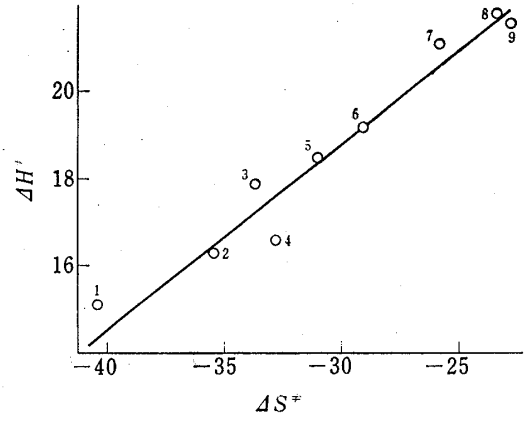


Fig. 1. Isokinetic Plot for the Quaternization of Trimethylamine with Methyl Benzoates in Methanol (9 Points, β= 429)

1, methyl *p*-bromobenzoate; 2, methyl *m*-nitrobenzoate; 3, methyl *m*-bromobenzoate; 4, methyl *o*-nitrobenzoate; 5, methyl *o*-chlorobenzoate; 6, methyl *o*-bromobenzoate; 7, methyl *p*-chlorobenzoate; 8, methyl *m*-chlorobenzoate; 9, methyl *p*-nitrobenzoate.

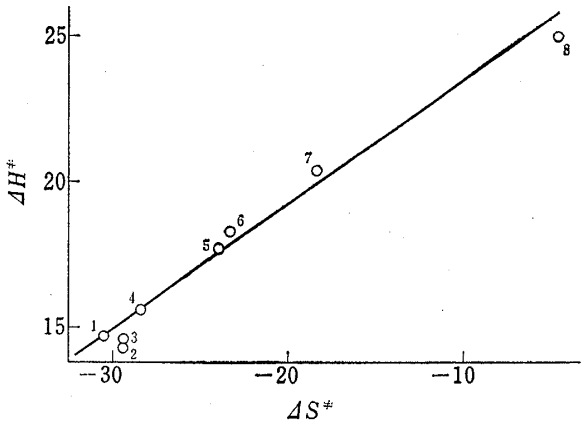


Fig. 2. Isokinetic Plot for the Menshutkin Reaction with Methyl Iodide in Methanol (8 Points, β=429)

1, *N*,*N*-methylpropylaniline;[5] 2, *N*,*N*-dimethyl-*m*-toluidine;[6] 3, *N*,*N*-dimethylaniline;[7] 4, *N*,*N*-dimethyl-*p*-chloroaniline;[6] 5, *N*,*N*-dimethylaniline+ethyl iodide;[7] 6, *N*,*N*-dibutylaniline;[5] 7, *N*-methyl tetrahydro-homoquinoline;[7] 8, 1-dimethylamino-2,6-dimethylbenzene.[7]

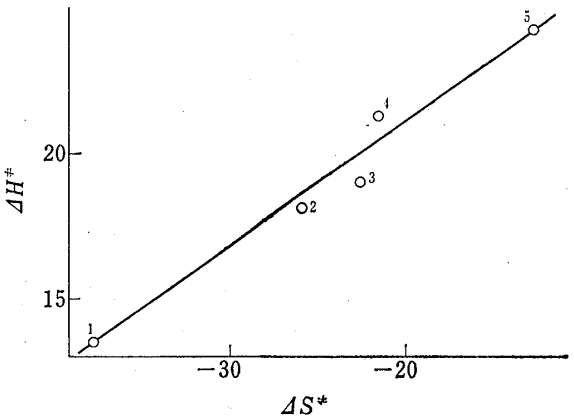


Fig. 3. Isokinetic Plot for the Finkelstein Reaction of Alkyl Chloride with Iodide Anion in Acetone (S_N2 Type) (5 Points, β= 431)

1, ethyl chloride;[8] 2, propyl chloride;[8] 3, butyl chloride;[8] 4, 1,1,2-trichloroethane;[9] 5, isopropyl chloride.[9]

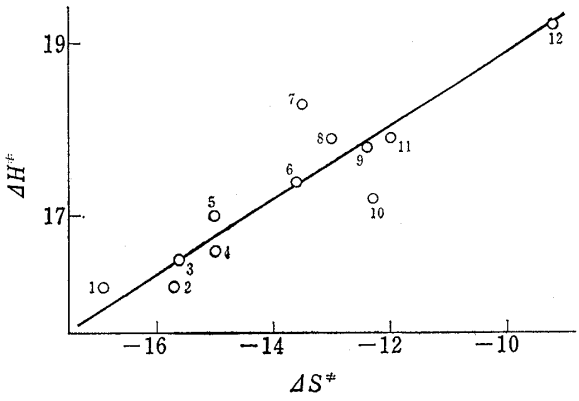


Fig. 4. Isokinetic Plot for the Reaction of Alkyl Bromides with Thiosulfate Anion in 50% Ethanol[10] (S_N2 Type) (12 Points, β= 430)

1, propyl; 2, ethyl; 3, δ-ethoxybutyl; 4, δ-chlorobutyl; 5, γ-ethoxypropyl; 6, γ-chloropropyl; 7, β-chloroethyl; 8, β-phenylethyl; 9, δ-phenylbutyl; 10, γ-ethylsulfonylpropyl; 11, γ-phenylpropyl; 12, β-ethylsulfonylethyl.

This is consistent with the known Walden inversion on the alkyl carbon.[11]

On the other hand, an attack of the N-atom of the tertiary amine on the carboxylate carbon as a reactive site gave quite different β values. For examples, isokinetic plots of the ammonolysis of alkyl carboxylates with ammonia[12,13] or aniline[3] (Fig. 5) and saponification of some acetates and thiolacetates[14,15] with sodium hydroxide (Fig. 6) resulted in β values of 256 and 259, respectively.

It may be said in this connection that the β values of saponifications were reported to be 400[4] both for saponification of ethyl benzoate in various media[16,17] and for saponification of ethyl *m*-nitrobenzoate in some solvents.[16] These β values do not reflect the reaction mechanism, but represent the solvent effect. In fact, the β value of alkyl acetate and thiolacetate in only one solvent (62% acetone) has been found to be 270.[4] According to our

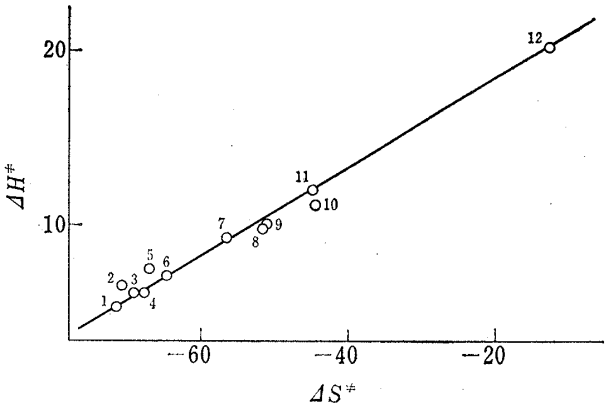


Fig. 5. Isokinetic Plot for Ammonolyses of Alkyl Carboxylates in Dioxane (12 Points, $\beta=256$)

1, ethyl acetate catalyzed by 5 M ethylene glycol;[12] 2, methyl acetate catalyzed by 10 M methanol;[12] 3, propyl acetate catalyzed by 5 M ethylene glycol;[12] 4, methyl acetate catalyzed by 5 M ethylene glycol;[12] 5, isopropyl acetate catalyzed by 5 M ethylene glycol;[12] 6, methyl acetate catalyzed by 10M water;[12] 7, isopropylpropyl lactate;[13] 8, propyl lactate;[13] 9, ethyl lactate;[13] 10, methyl lactate;[13] 11, methyl acetate;[13] 12, (phenyl *N*-phenylcarbamete+aniline) catalyzed by 0.02 M triethylenediamine.[3]

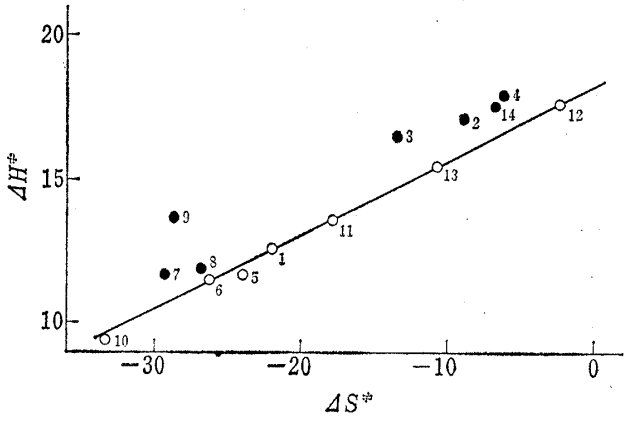


Fig. 6. Isokinetic Plot for Saponification of Some Acetates and Thiolacetates in 62% Acetone (7 Points, $\beta=259$)

●: Excluded on account of steric factors (isopropyl, isobutyl, *tert*-butyl and trityl groups).

1, methyl thiolacetate;[14] 2, isopropyl thiolacetate;[14] 3, *tert*-butyl thiolacetate;[14] 4, iso-butyl thiolacetate;[14] 5, methyl acetate;[14] 6, ethyl acetate;[14] 7, isopropyl acetate;[14] 8, isobutyl acetate;[14] 9, *tert*-butyl acetate;[14] 10, allyl acetate;[15] 11, benzyl acetate;[15] 12, allyl thiolacetate;[15] 13, benzyl thiolacetate;[15] 14, trityl thiolacetate.[15]

reexamination, the value should be corrected to 259 by excluding the substrates carrying a bulky group.

In this way, the analysis of isokinetic temperatures has proved that the quaternization proceeds by attack of trimethylamine on the methyl group (Chart 1), not on the carboxylate carbon of methyl benzoates.

On the other hand, the intermediate in the tertiary amine-catalyzed ammonolysis would be a quaternary ammonium salt formed by attack of the N-atom of the tertiary amine on the carboxyl C-atom of the carboxylate (Chart 2), because its isokinetic plot is on the extension line of the ammonolyses, and the line has a slope of 256 as its β-value, which is equal to that of nucleophilic attack on the C-atom of carboxylates.

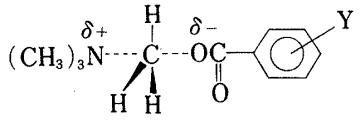


Chart 1

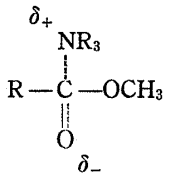


Chart 2

It should be emphasized that the solvent and steric effects have to be compensated for in order to obtain β-values which can be used to discriminate the reaction mechanism.

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