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The Simultaneous First- and Second-Order Esterifications of *l*-Menthol by Acyl Chlorides: Autocatalyses by Menthol in Acetonitrile and in Liquid Sulfur Dioxide*

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The propionylation and *p*-methoxybenzoylation of *l*-menthol in various solvents have been studied. In chloroform, benzene, ethyl methyl ketone and carbon tetrachloride, the reaction follows the second-order rate law. However, in acetonitrile or in liquid sulfur dioxide, the rate follows the second-order rate law only at the initial stage of the reaction; thereafter it gradually deviates from the second-order type to the first-order one. Moreover, the first-order rate equations both in acetonitrile and liquid sulfur dioxide are dependent on the initial concentration of the alcohol; the over-all rates being expressed as:

$$\text{Rate}=k_1{}^\circ(\text{AcCl})(\text{ROH})_0+k_2(\text{AcCl})(\text{ROH})$$

where $(\text{ROH})_0$, (ROH), (AcCl), $k_1{}^\circ$ and k_2 are the concentrations of the alcohol at time zero and t, that of the acyl chloride at time t, the first-order rate constant and the second-order rate constant respectively.

It has been reported in a preceding paper[1] that the initial rates of the esterifications between *l*-menthol and acetyl chloride in various solvents obey the second-order and the first-order rate laws with the alcohol and the acetyl chloride respectively and that the rates depend neither upon the dielectric constants nor upon the Z values[2] of the solvents. The rate constant in liquid sulfur dioxide is the largest, the reason for this has also been discussed.

However, the inspection of the conversion vs. time curve in liquid sulfur dioxide revealed that the order of the reaction varies gradually and that the reaction obeys the first-order rate law after the middle stage of the reaction has passed.

Since the reaction rate of acetyl chloride with menthol in liquid sulfur dioxide is so rapid, the rate constant has only been determined by an extrapolation method. In the present paper, a further investigation of the esterification has been undertaken on slower rate systems, the propionylation and *p*-methoxybenzoylation of *l*-menthol in various solvents, thus we hope to make an unambiguous scrutiny of the reaction mechanism.

The reaction processes in various solvents, from the initial stages through the completion of the reactions, have been examined and analyzed; we found that the first-and second-order esterifications take place simultaneously in some of the solvents used, such as acetonitrile, liquid sulfur dioxide and nitromethane. When nitromethane is used as the solvent, another phenomenon in addition to the simultaneous reactions has also been observed; this finding will be published elsewhere in the near future.

The simultaneous nucleophilic substitutions ($\text{S}_\text{N}1$ and $\text{S}_\text{N}2$), the so-called border-line cases, in liquid sulfur dioxide have already been reported by Ingold et al.[3], and the possibility of such a phenomenon has been discussed by Tokura and Kondo[4] in connection with the Menschutkin reaction in liquid sulfur dioxide. Moreover, the first-order reaction rates in acetonitrile and in liquid sulfur dioxide have been found to be enhanced by the initial concentration of the *l*-menthol

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* Substitution in Liquid Sulfur Dioxide, Part V. Part IV: Ref. 1)

[1] N. Tokura and F. Akiyama, This Bulletin, **37**, 1723 (1964).

[2] E. M. Kosower, *J. Am. Chem. Soc.*, **80**, 3253 (1958).

[3] M. L. Bird, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, **1954**, 634.

[4] N. Tokura and Y. Kondo, This Bulletin, **36**, 200 (1963).

employed. This means that the autocatalyses by the alcohol and/or the material produced from the alcohol are taking place in the esterification in these solvents.

Experimental

Solvents.—The following materials were purified by the methods described in the preceding paper[1] and were used as the solvents; liquid sulfur dioxide, chloroform, acetonitrile, benzene, ethyl methyl ketone, nitromethane and carbon tetrachloride.

Materials.—Commercial extra-pure-grade *l*-menthol was used without further purification; m. p. 41.5—43°C, $[\alpha]_D^{25} -47.6°$ (benzene). Preliminary examinations in liquid sulfur dioxide and in other solvents verified that the optical rotations of the solutions of *l*-menthol were stable over all the reaction times employed. Propionyl chloride was distilled, and the fraction boiling from 76.6 to 78.2°C was used. *p*-Methoxybenzoic acid and thionyl chloride (1 : 1.5 molar ratio) were heated together on a water bath for a half hour; the chloride produced was then distilled, the fraction with a b. p. of 132—133°C/11 mmHg being used.

The Identification of the Esters Obtained.—The reaction mixture after the esterification was concentrated in vacuo, and the residual oil was fractionated. The yield was almost quantitative. *l*-Menthyl propionate: b. p. 116°C/8 mmHg, $[\alpha]_D^{25} -82.18°$, (benzene);

Found: C, 73.63; H, 11.64. Calcd. for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39%.

l-Menthyl *p*-methoxybenzoate: b. p. 197°C/7 mmHg $[\alpha]_D^{25} = -80.0°$ (benzene);

Found: C, 74.87; H, 8.83. Calcd. for $C_{18}H_{26}O_3$: C, 74.44; H, 9.02%.

The specific rotations of *l*-menthyl propionate in various solvents are listed in the following table.

TABLE I. THE SPECIFIC ROTATIONS OF *l*-MENTHYL PROPIONATE IN SOLVENTS

Solvent	$-[\alpha]_D^{25}$ degree·dm^{-1}·g^{-1}·ml.
Liq.SO_2	79.04
Chloroform	84.19
Acetonitrile	77.25
Ethyl methyl ketone	78.86
Benzene	82.18
Nitromethane	80.44

The Kinetic Procedure.—The polarimetric procedure used for the kinetic followings was described earlier,[1] a graphic representation of the apparatus (a polarimeter equipped with a pressure-cell for use in the reaction in liquid sulfur dioxide) will also be found therein. *l*-Menthol dissolved in a solvent was placed in the cell. An acyl chloride in an ampoule was deposited in a cell situated in a polarimeter before a menthol solution was introduced. After the temperature equilibration of the apparatus containing the menthol solution in the thermostat had been attained, the ampoule in the cell was broken by a vigorous shaking and the solution was mixed. Then the kinetic following by means of polarimetry was began.

The Estimation of the Rate Constant.—The second-order rate constant, k_2, may be obtained from the slope of the linear plot:

$$\log \frac{(\mathrm{ROH})_0\{l([\mathrm{R}]°_\mathrm{E}-[\mathrm{R}]°_\mathrm{A})(\mathrm{AcCl})_0-(\alpha-\alpha_0)\}}{(\mathrm{AcCl})_0(\alpha_\infty-\alpha)} \text{ vs. } t,$$

since

$$\frac{1}{(\mathrm{AcCl})-(\mathrm{ROH})_0} \times \ln \frac{(\mathrm{ROH})_0\{l([\mathrm{R}]°_\mathrm{E}-[\mathrm{R}]°_\mathrm{A})(\mathrm{AcCl})_0-(\alpha-\alpha_0)\}}{(\mathrm{AcCl})_0(\alpha_\infty-\alpha)} = k_2 \cdot t \qquad (1)$$

where $(\mathrm{ROH})_0$ and $(\mathrm{AcCl})_0$ are the initial concentrations of the alcohol and the acyl chloride and $(\mathrm{R})°_\mathrm{A}$ and $(\mathrm{R})°_\mathrm{E}$ are the specific rotations of the alcohol and the ester in the solvents in degree·dm^{-1}·mol^{-1}·l. respectively. l, α, α_0 and α_∞ are the length of the cell, dm., and the rotations of the solution at time t, zero and infinity.

When equimolar concentrations of menthol and acyl chloride were used, the rate constant, k_2, was given by the slope of the linear plot of :

$$\frac{1}{\alpha_\infty-\alpha} \text{ vs. the time, } t,$$

since:

$$\frac{1}{\alpha_\infty-\alpha} - \frac{1}{\alpha_\infty-\alpha_0} = \frac{k_2 \cdot t}{l[(\mathrm{R})°_\mathrm{E}-(\mathrm{R})°_\mathrm{A}]} \qquad (2)$$

First-order Rate Constant.—The first-order rate constant, k_1, will be expressed as;

$$\ln \frac{\alpha_\infty-\alpha_0}{\alpha_\infty-\alpha} = k_1 \cdot t \qquad (3)$$

Therefore, the $-\log(\alpha_\infty-\alpha)$ vs. t plot will give a straight line, whose slope will be the value of k_1.

Typical Runs.—The second-order plots of the esterifications in chloroform, ethyl methyl ketone and benzene are visualized in Fig. 1. The second-order plots of the reactions in acetonitrile and in liquid sulfur dioxide are shown in Figs. 2 and 5, which show the deviations from linearity as the reactions proceed.

The first-order plots of the same esterifications are seen in Figs. 3 and 6, which again exhibit the deviations from linearity in the initial periods of the reactions.

Results

The Propionylation of *l*-Menthol.—In chloroform, ethyl methyl ketone, benzene and carbon tetrachloride, the esterification reactions strictly obey the second-order rate law throughout the reaction (Fig. 1). These results, together with the second-order rate constants in acetonitrile, in liquid sulfur dioxide and in nitromethane, are listed in Table II.

That the second-order rate law consists of the first order with both the alcohol and the acyl chloride has already been established[5]; evidence for this was also given in the previous paper.[1]

On the contrary, in acetonitrile, liquid sulfur dioxide or nitromethane, the apparent kinetic order of the reaction varies as the reaction proceeds.

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5) J. F. Norris and A. A. Ashdown, *J. Am. Chem. Soc.*, **47**, 873 (1925).

Table II. The second-order rate constants (k_2, $\mathrm{sec^{-1} \cdot mol^{-1} \cdot l.}$) of the propionylation of *l*-menthol in various solvents

Solvent	Reaction temp., °C				
	5	15	25	30	35
Liq.SO_2	2.11×10^{-2}	3.12×10^{-2}	4.70×10^{-2}		
Nitromethane			1.50×10^{-3}		
Chloroform		8.99×10^{-4}	1.35×10^{-3}		2.17×10^{-3}
Benzene		2.39×10^{-4}	4.40×10^{-4}	5.70×10^{-4}	
Carbon Tetrachloride			8.13×10^{-4}		
Acetonitrile		2.12×10^{-4}	3.33×10^{-4}		5.70×10^{-4}
Ethyl methyl ketone		4.21×10^{-5}	9.18×10^{-5}		2.29×10^{-4}

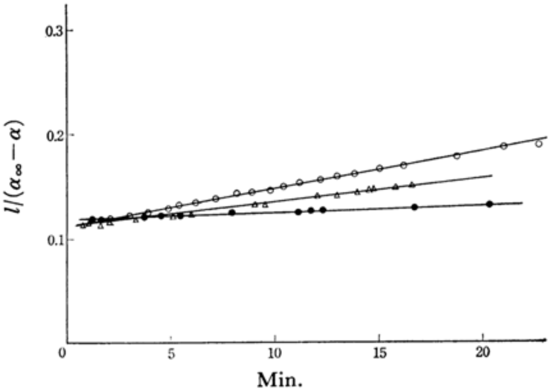

Fig. 1. Propionylation of *l*-menthol at 25°C.
-○- Chloroform
-△- Benzene
-●- Ethyl methyl ketone

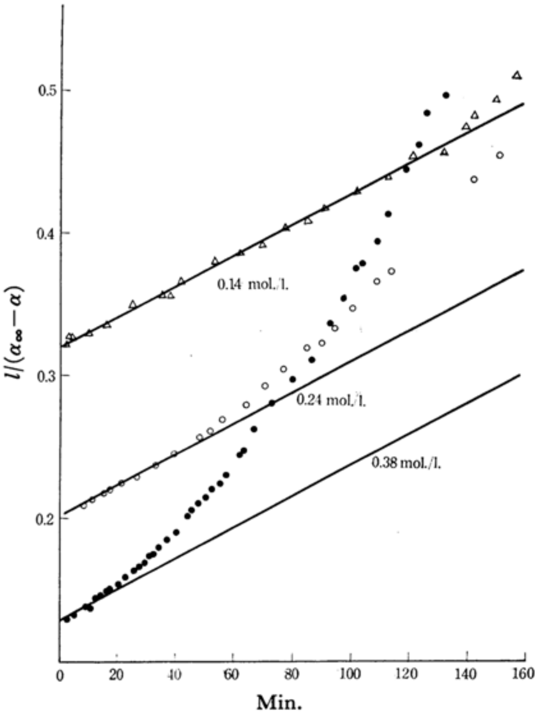

Fig. 2. Second-order plots in acetonitrile. 25°C

During the initial stage of the reaction, a second-order law was directive, this was followed by a gradual transition to an apparent first-order rate law, first order in acyl chloride and zero order in the alcohol. In the present paper, the findings and the discussion of the esterification in nitromethane are omitted, since another interesting feature has been found in nitromethane.

Propionylation in Acetonitrile.—As may be seen in Fig. 2, the second-order plot of the reaction deviates from linearity as the reaction proceeds. Figure 3 is the first-order plot of the esterification in the middle and the final periods of the reaction, following the first-order rate law.

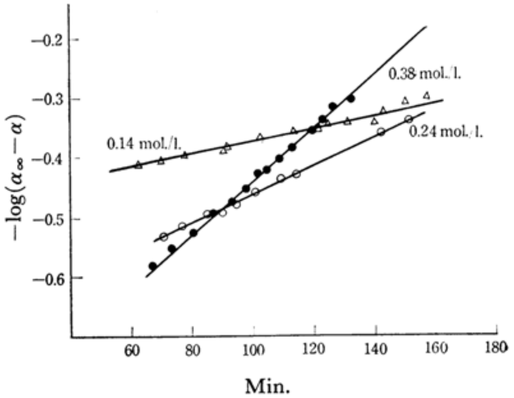

Fig. 3. First-order plots in acetonitrile. 25°C

The deviation from the second-order law is greatly affected by the initial concentration of the alcohol. Also, the rate constant of the first-order reaction is affected by the initial concentration of the alcohol, although the rate law is zero-th order in the alcohol concentration. The transition or the deviation points which are shown by the conversions from the second law, may be seen in Fig. 2 and are listed in Table III.

The larger the initial concentration, the earlier the transition point appears, as may be seen in Table III. The dependency of the rate constant, k_1 on the initial concentration is visualized in Fig. 4, which shows a linear correlation between k_1 and $(ROH)_0$.

TABLE III. FIRST-ORDER RATE CONSTANTS OF THE ESTERIFICATION IN ACETONITRILE, 25°C
THE DEPENDENCE OF THF RATE CONSTANTS ON THE INITIAL CONCENTRATIONS

$(ROH)_0$ mol./l.	$(AcCl)_0$ mol./l.	k_1, sec^{-1}	Conversion at the transition point, %
0.14	0.14	3.85×10^{-5}	35
0.24	0.24	9.19×10^{-5}	18
0.36	0.24	1.43×10^{-4}	
0.38	0.38	1.63×10^{-4}	11
0.38	0.19	1.53×10^{-4}	
0.48	0.24	2.28×10^{-4}	
0.67	0.38	3.11×10^{-4}	

The rate expression, then, will be

$$\text{Rate} = k_1{}^\circ(\text{ROH})_0(\text{AcCl}) \qquad (4)$$

since

$$k_1 = k_1{}^\circ(\text{ROH})_0 \qquad (5)$$

while $k_1{}^\circ$ is estimated to be $k_1{}^\circ=5.14+10^{-4}$ $sec^{-1}\cdot mol^{-1}\cdot l.$ at 25°C.

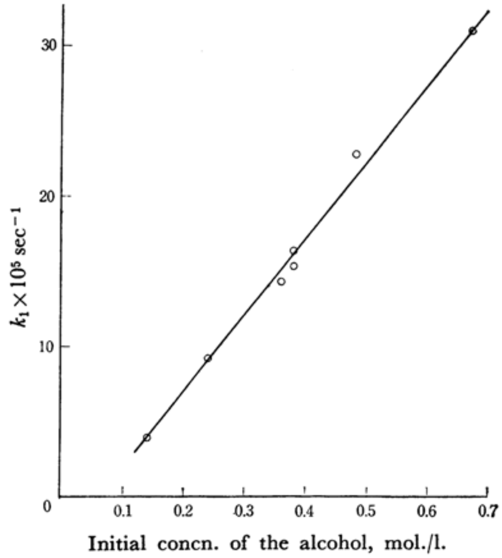

Fig. 4. Dependency of k_1 on $(ROH)_0$ in acetonitrile at 25°C.

Propionylation in Liquid Sulfur Dioxide.—The results resemble those in acetonitrile, but the transition to the first order occurs at a later period of the reaction, as may be seen in Fig. 5 and in Table IV. The first-order plots are also visualized in Fig. 6, which confirms a linear dependency on the initial concentration of menthol, as in the case of acetonitrile.

TABLE IV. THE TRANSITION FROM THE SECOND-ORDER LAW AT 25°C IN Liq.SO_2

Initial concn. mol./l.	Transition point conversion, %
0.27	76
0.13	78
0.11	81

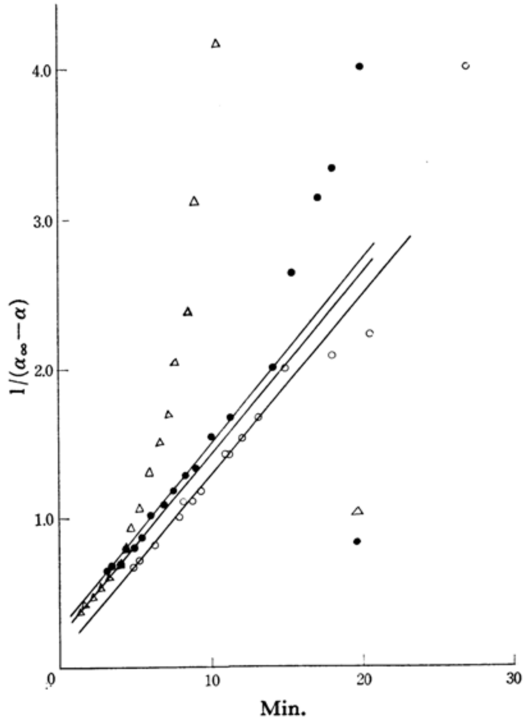

Fig. 5. Second-order plots in liquid sulfur dioxide. 25°C
△ 0.27 mol./l. ● 0.13 mol./l. ○ 0.11 mol./l.

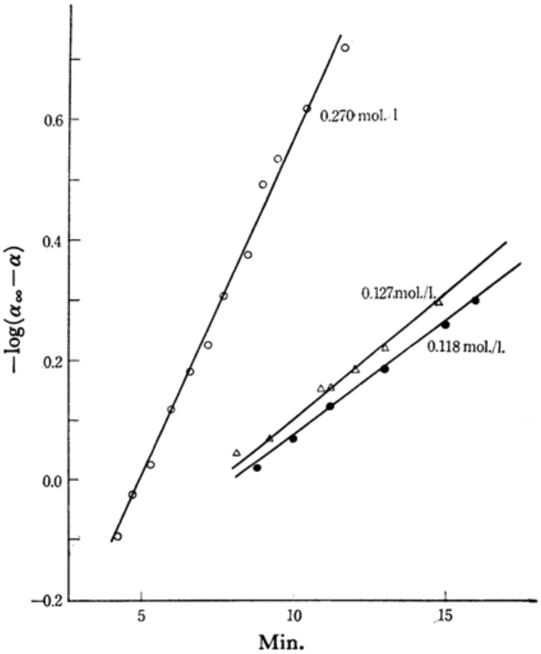

Fig. 6. First-order plots in liquid sulfur dioxide. 25°C

The higher the initial concentrations, the earlier the deviations from the second-order rate law; however, in liquid sulfur dioxide the deviation occurs at a later stage, at over a 76% conversion, as is shown in Fig. 5.

TABLE V. FIRST-ORDER RATE CONSTANTS, k_1 IN VARIOUS INITIAL CONCENTRATIONS OF $(ROH)_0$ AT 25°C

$(ROH)_0$, mol./l.	k_1, sec^{-1}
0.27	4.15×10^{-3}
0.133	1.72×10^{-3}
0.127	1.63×10^{-3}
0.120	1.46×10^{-3}

As is illustrated in Fig. 7 and Table V, the dependency of k_1 on $(ROH)_0$ in liquid sulfur dioxide is linear and the $k_1°$ value is given as;

$$\text{Rate}=k_1(\text{AcCl})$$

$$=k_1°(\text{ROH})_0(\text{AcCl}) \qquad (6)$$

since $k_1=k_1°(\text{ROH})_0 \qquad (7)$

$$k_1°=1.77\times10^{-2}\,\text{sec}^{-1}\cdot\text{mol}^{-1}\cdot\text{l. at } 25°\text{C}$$

The Kinetic Parameter of the Second-order Reaction.—The activation parameters for the second-order reaction in various solvents as estimated from the results in Table II are listed in Tables VI and VII.

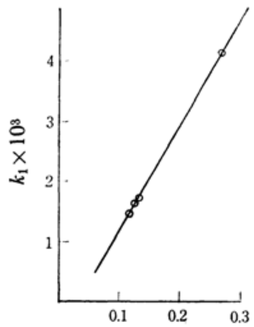

Fig. 7. Dependency of k_1 on $(ROH)_0$ in liquid sulfur dioxide at 25°C.

TABLE VI. THE ACTIVATION PARAMETERS OF THE ESTERIFICATION OF *l*-MENTHOL WITH PROPIONLY CHLORIDE IN SOLVENTS

Solvent	$\varDelta E^{\neq}$ kcal./mol.	$\varDelta H^{\neq}$ kcal./mol.	$\varDelta S^{\neq}$, e. u.
Liq. SO_2	6.57	5.98	−44.55
Chloroform	7.75	7.16	−47.6
Acetonitrile	8.53	7.94	−47.7
Benzene	11.40	10.81	−37.6
Ethyl methyl ketone	15.00	14.41	−28.52

TABLE VII. THE ACTIVATION PARAMETERS OF THE ESTERIFICATION OF *l*-MENTHOL WITH *p*-METHOXYBENZOYL CHLORIDE IN Liq. SO_2 AND $CHCl_3$

Solvent	$\varDelta E^{\neq}$	$\varDelta H^{\neq}$	$\varDelta S^{\neq}$
liq. SO_2	10.07	9.48	−35.3
$CHCl_3$	17.96	17.37	−23.4

Discussion

The results may be summarized as follows. The reactions, the propionylations and the *p*-methoxybenzoylations of *l*-menthol follow the second-order rate law in chloroform, benzene, ethyl methyl ketone and carbon tetrachloride at 25°C, as they do in the acetylations of *l*-menthol, which were reported on earlier.1)

However, in acetonitrile or in liquid sulfur dioxide, the rate obeys the second-order rate law at the initial stage of the reaction, the second-order plot, deviates from linearity as the reaction proceeds, and gradually changes into a first-order rate reaction. The apparent transition or the deviation from the second-order rate law is prompted when the initial concentration of the alcohol is increased and acetonitrile is used as the solvent.

The inversion of the rate laws during an acylation in a solvent has not hitherto been reported, although the change in the rate orders in the acylation of an alcohol by solvents has been reported by Brown and Hudson.6) The change in the reaction orders during a reaction course in a solvent, as is reported in the present paper, may be plausibly explained as the results of simultaneous reactions consisting of a first-order type and a second-order type reaction, such as have been frequently encountered and discussed in nucleophilic substitutions in various solvents7) including liquid sulfur dioxide.3) Thus, it may be shown by the following expression:

$$\text{Rate}=k_1(\text{AcCl})+k_2(\text{AcCl})(\text{ROH}) \qquad (8)$$

or, for equimolar initial concentrations of the alcohol and the acyl chloride:

$$\text{Rate}=\mathrm{d}x/\mathrm{d}t=k_1(a-x)+k_2(a-x)^2 \qquad (9)$$

where a and x are the concentrations of the alcohol initially added and of the ester formed respectively.

The integration of Eq. 9 gives this relation:

$$\log\frac{a-x}{a-x+k_1/k_2}=\frac{-k_1}{2.303}t+\log\frac{a}{a+k_1/k_2} \qquad (10)$$

By substituting the values, k_1 and k_2, obtained experimentally into the left term of Eq. 10, the plots of $\log\frac{a-x}{a-x+k_1/k_2}$ vs. time t are linear, as is shown in Figs. 8 and 9, in both acetonitrile and liquid sulfur dioxide. The slopes of the respective plots are fairly coincident with the experimentally-attained values of k_1's in the range of experimental error.

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6) D. A. Brown and R. F. Hudson, *J. Chem. Soc.*, **1953**, 883, 3352.

7) a) W. G. Young and L. J. Keefer, *J. Am. Chem. Soc.*, **66**, 421 (1944). b) V. Gold, ibid., **78**, 4633 (1956). c) Y. Pocker, *J. Chem. Soc.*, **1954**, 3939, 3943. d) P. Casapieri and R. E. Swart, ibid., **1961**, 4342.

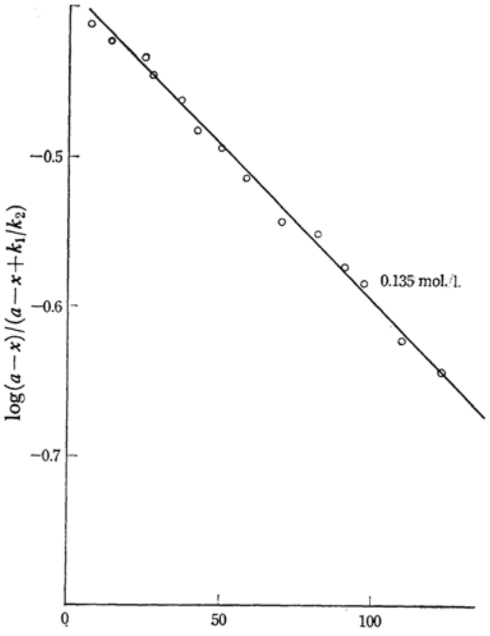

Fig. 8. Plots of the simultaneous reactions in acetonitrile at 35°C.

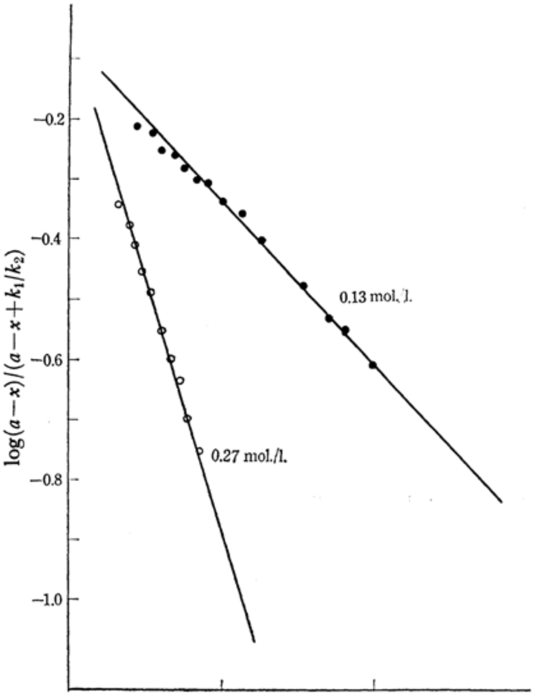

Fig. 9. Plots of the simultaneous reactions in liquid sulfur dioxide at 25°C.

These results satisfactorily confirm the assumption of the simultaneous nature of the reaction in two solvents.

Moreover, in both solvents the first-order rate constants, the k_1 values, are dependent upon the initial concentrations of the alcohol; the higher the initial concentration, the larger the first-order rate constant, as is shown in Figs. 4 and 7. This suggests that the alcohol and/or a compound produced from the alcohol (perhaps the ester or HCl) might be responsible for the apparent autocatalysis in the propionylation of the alcohol, and that the over-all kinetics of the reaction may be expressed as;

$$\text{Rate}=k_1{}^{\circ}(\text{AcCl})(\text{ROH})_0+k_2(\text{AcCl})(\text{ROH}) \quad (11)$$

	$k_1{}^{\circ}$, $\text{sec}^{-1}\cdot\text{mol}^{-1}\cdot\text{l.}$	k_2, $\text{sec}^{-1}\cdot\text{mol}^{-1}\cdot\text{l.}$ at 25°C
Acetonitrile	5.14×10^{-4}	3.33×10^{-4}
Liq. SO_2	1.77×10^{-2}	4.70×10^{-2}

The multimolecularity of alcohol in the rate law of the esterification was first recognized by Ashdown[8] as early as in 1930 in his study of the ethanolysis of *p*-nitrobenzoyl chloride, where the reaction followed a third-order rate law, while it followed a second order in ethanol and a first order in the acyl chloride.

Ingold et al.[9] have also observed, in a nucleophilic substitution by ethanol in nitromethane, that the first-order rate constant is dependent on the initial concentration of the alcohol. The dependency of k_1 on the initial concentration of menthol $(\text{ROH})_0$ can be most adequately elucidated in terms of the solvation of the alcohol to enhance the rate-determining ionization of the acyl chloride.

The rate constants, both k_1 and k_2, are largest in liquid sulfur dioxide, as may be seen in Tables II, III and IV.

One might suspect that the expression 11 could be replaced by a simpler equation, such as;

$$\text{Rate} = k(\text{AcCl})(\text{ROH})_0 \quad (12)$$

since Eq. 12 is also consistent with the experimental fact that the reaction is second-order at the initial stage but soon changes to a first-order rate law. However, this rate equation is not adequate to explain the reaction in liquid sulfur dioxide where the second-order rate law predominates until a 80% conversion or so.

$(\text{ROH})_0$ can be explained in terms of the alcohol present in the reaction mixture and/or the compound produced as the result of the reaction of the alcohol in an equivalent molarity, such as that of the ester or of HCl.

An inspection of Table II will reveal that the second-order esterifications are more reactive in the electrophilic solvent than in the electrodonative solvent, suggesting that the rate-determining step is the formation of an ionic compound such as:

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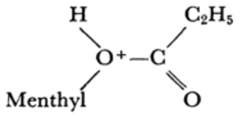
[8] A. A. Ashdown, *J. Am. Chem. Soc.*, **52**, 269 (1930).

[9] E. Gilles, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, **1954**, 2918.



It is interesting to note that, in both acetonitrile and liquid sulfur dioxide, which are the two extreme solvents (viz., a Lewis base and a Lewis acid), the reactions are simultaneous. One explanation for this is that acylium ions (RCO^+) are formed in an appreciable amount in these dipolar aprotic solvents with large polarities:

$$RCOCl \rightleftarrows RC^+O + Cl^-$$

Summary

The propionylation and *p*-methoxybenzoylation of *l*-menthol in various solvents have been studied. In chloroform, benzene, ethyl methyl ketone and carbon tetrachloride, and at the initial stages of the reaction courses in acetonitrile and in liquid sulfur dioxide, the reactions follow the second-order rate law. However, in acetonitrile or liquid sulfur dioxide, the rate gradually varies from the second-order type to the first-order type apparently as the reaction proceeds.

The phenomena in both solvents have been elucidated as resulting from simultaneous unimolecular and bimolecular reactions. Moreover, the first-order rate constants in both acetonitrile and liquid sulfur dioxide, are dependent on the initial concentration of the alcohol.

The over-all rates in the two solvents are expressed as:

$$\text{Rate} = k_1{}^{\circ}(\text{AcCl})(\text{ROH})_0 + k_2(\text{AcCl})(\text{ROH})$$

The rate constants in liquid sulfur dioxide, both k_1 and k_2, are the largest among those in the solvents used.

The authors are indebted to the Seitetsu Kagaku Co., Ltd., for its donation of liquid sulfur dioxide.