The Solvent Effects of Esterification: The Reaction of l-Menthol with Acetyl Chloride in Liquid Sulfur Dioxide[*1]

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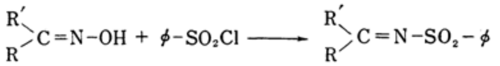
It has been reported in a previous paper[1)] that, in the rearrangement of cyclohexanone oxime *p*-toluenesulfonate in various solvents, there are no clearcut correlations between the log. of the rate constants versus the dielectric constants, the dipole moments or the *Z*-values of the solvents. Among the solvents used, liquid sulfur dioxide gave the largest rate constant for the rearrangement. It has been suggested that liquid sulfur dioxide, as an electrophilic solvent, favors the formation of a *bare* cation, without interfering with the formation of the aza-cyclopropenyl cation which is a requisite intermediate to carrying out the Beckmann rearrangement.

It has also been indicated in previous paper[2-4)] that the rate of the cationic polymerization of styrene in liquid sulfur dioxide is the fastest among the solvents used for the polymerization, giving a polymer of the highest degree of polymerization with a narrow molecular weight distribution.

On the other hand, it has already been shown that the reaction rate of the Wagner-Meerwein rearrangement[5)] is very fast in liquid sulfur dioxide and that the decomposition of an allylsulfinate is the fastest in liquid sulfur dioxide.[6)]

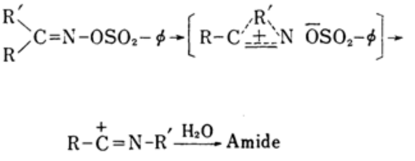
On the contrary, the rate of the Menschutkin reaction[7)] in liquid sulfur dioxide is the slowest among the solvents used. All of these results naturally lead to the conclusion that in liquid sulfur dioxide those reactions are advantageous in which cations or carbonium ions play the principal role, while the reactions of anions or carbanions are retarded or inhibited by strong interaction with liquid sulfur dioxide. In general, the reaction of $\rho<0$, (ρ is a constant in Hammett's relation, $\log k/k_0=\rho\sigma$[8)]), is very much favored in liquid sulfur dioxide, as is seen in the Beckmann rearrangement and in cationic polymerization.[2,3,9)]

The purpose of the present article on the esterification of *l*-menthol is to study the solvent effects on the esterification in connection with the elucidation of the solvent effects of the Beckmann rearrangement,[10)] since the latter rearrangement consists of two, consecutive steps, viz., the esterification of the oxime and the rearrangement of the oxime ester, as may be illustrated as follows:



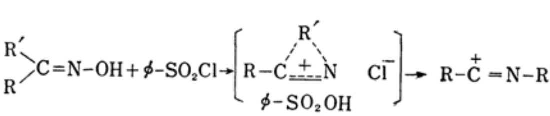
$$\begin{matrix}R'\\R\end{matrix}\!\!>\!C=N-OH+\phi-SO_2Cl\longrightarrow\begin{matrix}R'\\R\end{matrix}\!\!>\!C=N-SO_2-\phi$$

(1)



(2)

Alternately, a concerted one-step mechanism may also be considered:



(3)

When the rearrangement follows the consecutive processes 1 and 2, the solvent effects of the esterification may have an important bearing and influence if the rate-determining step is the esterification of the oxime. The solvent effects of the rearrangement step have already been discussed.[1)] It has been believed that, in liquid sulfur dioxide, an acyl halide such as acetyl chloride is partly ionized, such as:

[*1] Substitution in Liquid Sulfur Dioxide, Part IV. Part III; N. Tokura and Y. Kondo, This Bulletin, **36**, 200 (1963).

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1) N. Tokura, T. Kawahara and S. Ikeda, This Bulletin, **37**, 138 (1964).

2) R. Asami and N. Tokura, *J. Polymer Sci.*, **42**, 545 (1960).

3) N. Tokura, M. Matsuda and M. Iino, This Bulletin, **36**, 278 (1963).

4) M. Matsuda, *Kobunshi*, **13**, 88 (1964).

5) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill, New York (1940), p. 318.

6) S. H. Sharman, F. F. Caserio, R. F. Nystron, J. C. Leak and W. G. Young, *J. Am. Chem. Soc.*, **80**, 5965 (1958).

7) N. Tokura and Y. Kondo, This Bulletin, **36**, 200 (1963).

8) Cf. Ref. 5, p. 186.

9) N. Tokura, T. Kawahara and T. Watanabe, This Bulletin, **36**, 760 (1963).

10) N. Tokura, K. Shiina and T. Terashima, ibid., **35**, 1986 (1962).

$$\mathrm{CH_3COCl = CH_3CO^+ + Cl^-} \qquad (4)$$

as has been evidenced by the cationic polymerization of styrene with acetyl chloride as an initiator in liquid sulfur dioxide. Thus the esterification of an alcohol in liquid sulfur dioxide by acyl halide is expected to proceed with an unusual rapidity.

l-Menthol was chosen as the alcohol because of the convenience of its kinetic rate measurement by polarimetry. Acetyl chloride was used as the acylating agent. As was expected, the esterification rate in liquid sulfur dioxide was the largest among the solvents used.

Experimental

Materials. — The commercial *l*-menthol was used without further purification, m. p. 41.5∼43°C, $[\alpha]^{25}_{\mathrm{D}}$ in benzene=47.6°. Acetyl chloride was distilled, and a fraction with a b. p. of 52.0∼53.0°C was used. Liquid sulfur dioxide was dried with phosphorus pentoxide and distilled. The other solvents were purified by the authorized methods as indicated in a previous paper.[1]

Polarimetry.—A Shimadzu Lippich II-type polarimeter with a sodium lamp (D-line, 589.2 mμ) in a thermostat was used. A pressure cell about 2.2 dm. long and 10 mm. in diameter and equipped with a needle valve on its center was used for the measurement of the rate in liquid sulfur dioxide (Fig. 1). An ordinary polarimetry cell was used for the measurement in other solvents. As the initial concentration, 0.45 mole per liter each of *l*-menthol and acetyl chloride was used.

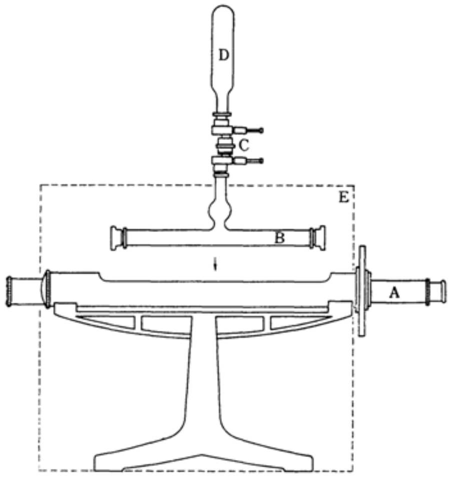


Fig. 1. A polarimeter equipped with a pressure cell.

A: Polarimeter
B: Measuring pressure cell
C: A joint-coupling with two kneedle valves
D: A pressure cell
E: A thermostat

Kinetic Procedure.—The rate of the esterification was followed conveniently by polarimetry. However, the specific rotations of *l*-menthol slightly differed from solvent to solvent.

The esterification is a reversible reaction and generally might be acid-catalyzed, so the reaction rate should be expressed as:

Rate = (Rate of the forward reaction)
− (Rate of the reverse reaction)
+ (Acid catalysis by HCl formed by the reaction)

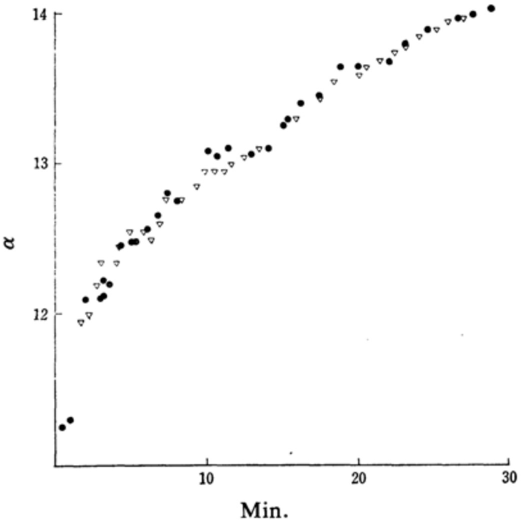


Fig. 2. Effect of HCl concentrations on the reaction rate.

● HCl 0.926 mol./l. ▽ HCl 0.501 mol./l.
liq. $\mathrm{SO_2}$ 38.38 mol. % $\mathrm{SO_2\text{-}CCl_4}$ system

However, since the over-all yield of the ester after the reaction was over 80∼90 per cent and since the catalytic effect of HCl in such non-aqueous solvents was found to be negligibly small (Fig. 2), the rate expression may be simplified to the following equation, especially when the rate is estimated in the initial stage of the reaction. Then the rate is:

$$\text{Rate} = \mathrm{d}x/\mathrm{d}t = k(a-x)^2 \qquad (5)$$

where equimolar initial concentrations, a, of *l*-menthol and acetyl chloride were used, k is the second order rate constant, and x is the concentration of the ester at time t. Equation 5 is integrated to Eq. 6:

$$1/(a-x) - 1/a = k\cdot t \qquad (6)$$

We can assume, at $t=0$, $\alpha_0 = a\cdot[\mathrm{R}]^{\circ}_{\mathrm{A}}\cdot l$, and $t=t$, that $\alpha_t = (a-x)\cdot[\mathrm{R}]^{\circ}_{\mathrm{A}}\cdot l + x\cdot[\mathrm{R}]^{\circ}_{\mathrm{E}}\cdot l$, where l is the length of the cell of the polarimeter in dm., α_0 and α_t are rotations at the times 0 and t, $[\mathrm{R}]^{\circ}_{\mathrm{A}}$ is the molar rotation of *l*-menthol (degree·dm^{-1}·mol^{-1}·l.), and $[\mathrm{R}]^{\circ}_{\mathrm{E}}$ is that of the ester formed. After the completion of the reaction, α_t at the end or α_∞ may be written approximately as:

$$\alpha_\infty = a\cdot[\mathrm{R}]^{\circ}_{\mathrm{E}}\cdot l \qquad (7)$$

$$\alpha_\infty - \alpha_t = (a-x)\cdot l\cdot([\mathrm{R}]^{\circ}_{\mathrm{E}} - [\mathrm{R}]^{\circ}_{\mathrm{A}})$$

Then:

$$a-x=(\alpha_\infty-\alpha_t)/l\cdot([R]_E^\circ-[R]_A^\circ) \tag{8}$$

$$a=(\alpha_\infty-\alpha_0)/l\cdot([R]_E^\circ-[R]_A^\circ) \tag{9}$$

Substituting 8 and 9 in 6, we get:

$$1/(\alpha_\infty-\alpha_t)-1/(\alpha_\infty-\alpha_0)=k\cdot t/l\cdot([R]_E^\circ-[R]_A^\circ) \tag{10}$$

The second-order rate constant, k, may be obtained from the slope of a linear plot, $1/(\alpha_\infty-\alpha_t)$ vs. t. An example is shown in Fig. 3. The specific rotations of the alcohol and the ester, $[\alpha_A]_D^{25}$ and $[\alpha_E]_D^{25}$, are listed in Table I.

TABLE I. SPECIFIC ROTATIONS IN VARIOUS SOLVENTS AT 25°C

Solvent	$[\alpha_A]_D^{25}$	$[\alpha_E]_D^{25}$
Dimethylformamide	46.1	72.3
Nitromethane	42.0	76.4
Chloroform	45.1	80.2
Ethylenedichloride	45.5	72.7
Benzene	47.6	73.7
Toluene	46.3	70.2
Acetonitrile	50.7	74.3
Ethyl methyl ketone	44.5	71.8
Tetrahydrofuran	48.4	77.6
Liq. SO_2	53.5	84.8

$[\alpha_A]_D^{25}$: Specific rotation of *l*-menthol
$[\alpha_E]_D^{25}$: Specific rotation of *l*-menthyl acetate

Since the rate of the esterification in liquid sulfur dioxide was fast enough to allow the estimation of the rate constant by this procedure, the rate constant in liquid sulfur dioxide was obtained by the following extraporation. A variety of mixtures of liquid sulfur dioxide in carbon tetrachloride were prepared, and the rates in these mixtures were estimated. The log·k's vs. the molar per cents of sulfur dioxide concentrations-plots were strictly linear, and the line was extrapolated to the 100 per cent sulfur dioxide to obtain the rate constant, k, in liquid sulfur dioxide. The rates of the esterification in other solvents were directly measured by the above procedure; the results are listed in Table II, together with the values of liquid sulfur dioxide.

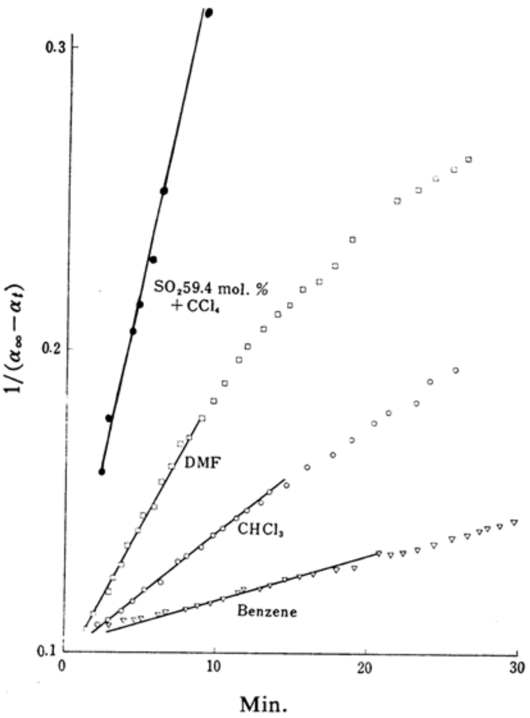


Fig. 3. Typical runs in various solvents.
DMF: Dimethylformamide

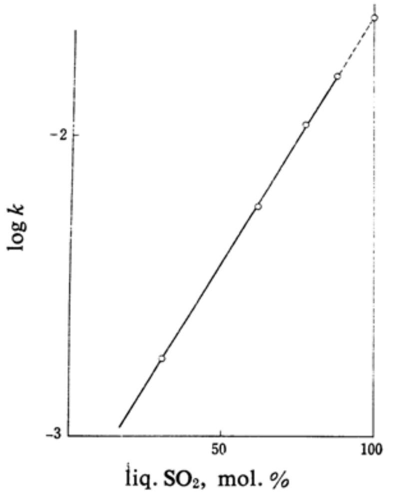


Fig. 4. Log k vs. liq. SO_2 mol. % in liq. SO_2-CCl_4 mixtures.

liq. SO_2 100 mol. % $k=6.95\times10^{-2}$ l./mol. sec.

TABLE II. THE SECOND-ORDER RATE CONSTANTS OF THE ESTERIFICATION AT 25°C *l*-MENTHOL AND ACETYL CHLORIDE

Solvent	k, l. mol^{-1} sec^{-1}
Dimethylformamide	2.66×10^{-3}
Nitromethane	2.17×10^{-3}
Chloroform	1.26×10^{-3}
Ethylenedichloride	8.61×10^{-4}
Benzene	3.56×10^{-4}
Toluene	3.47×10^{-4}
Acetonitrile	2.85×10^{-4}
Ethyl methyl ketone	6.27×10^{-5}
Tetrahydrofuran	5.05×10^{-5}
Liq. SO_2	6.95×10^{-2}
Carbon tetrachloride	0

Results and Discussion

The solvent effects of the esterification of *l*-menthol with acetyl chloride have been shown in Table II. The rate was the largest in liquid sulfur dioxide. Moreover, the order of the specific rates in the respective solvents is similar to that in the case of the Beckmann rearrangement. The orders are:

Esterification:

Liq. SO_2 > Dimethylformamide >
Nitromethane > $CHCl_3$ >
Ethylenedichloride > Benzene > Toluene >
Ethyl methyl ketone > Tetrahydrofuran >
CCl_4

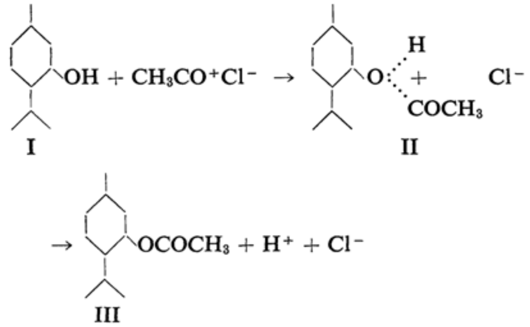
Rearrangement:[9]

Liq. SO_2 > CH_3OH > CH_3COOH >
Nitromethane > Ethanol > CH_3CN >
Pyridine > $CHCl_3$ > Acetone >
Ethylenedichloride > Ethyl methyl ketone >
CCl_4

As a control experiment, the optical stabilities of *l*-menthol and *l*-menthyl acetate in each solvent have also been examined. These materials were both optically stable in any solvent used for the experiment at 25°C.

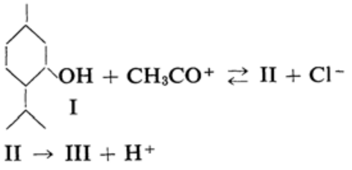
No catalytic effect of hydrochloric acid on the reaction rate was observed (Fig. 2). The lack of acid catalysis may be accounted for by the observation that the dissociation of hydrochloric acid in liquid sulfur dioxide and in a non-aqueous solvent is very small as compared to that in water and may be presumed to result in triplet- or multiplet-ion formation.[10] Although the esterifications obey a strictly second-order rate law within the experimental limitations, the mechanism of the reaction may differ somewhat according to the nature of the solvent.

In a solvent such as liquid sulfur dioxide, acetyl chloride may ionize to acetylium cation and chloride anion as in Eq. 4, though the degree of the dissociation may not be very large. A *bare* (unsolvated) acetylium ion is to be expected in this case, while chloride anion may be strongly solvated by liquid sulfur dioxide. Thus, the rate-determining attack of the acylium ion on the oxygen atom of the alcohol is facile and effective. In Scheme 1, if the rate-determining step is the formation of intermediate II, the step of expelling a proton from II being very fast, the reaction rate must be determined by the effective concentration of the acylium cations. In liquid sulfur dioxide, the reaction rate is very large since a *bare* cation, viz., a free cation not solvated by the solvent, is thought to be available and the effective concentration of the cations is assumed to be the largest.



Scheme 1

On the other hand, ethyl methyl ketone and tetrahydrofuran are solvents in which the cations or the carbonium ions are strongly solvated by the solvents; thus the effective concentration of the cations is rather depressed. Nitromethane, chloroform, ethylenedichloride, benzene and toluene rank midway between these two kinds of solvents. It is interesting that, in dimethylformamide, the reaction is also rapid in spite of the nucleophilicity of this solvent. A different reaction mechanism may be considered, though a second-order rate law still holds. One possibility is that a rate-determining proton abstraction, preceded by an equilibrium of the formation of II (Scheme 2), is very easy in dimethylformamide.



Scheme 2

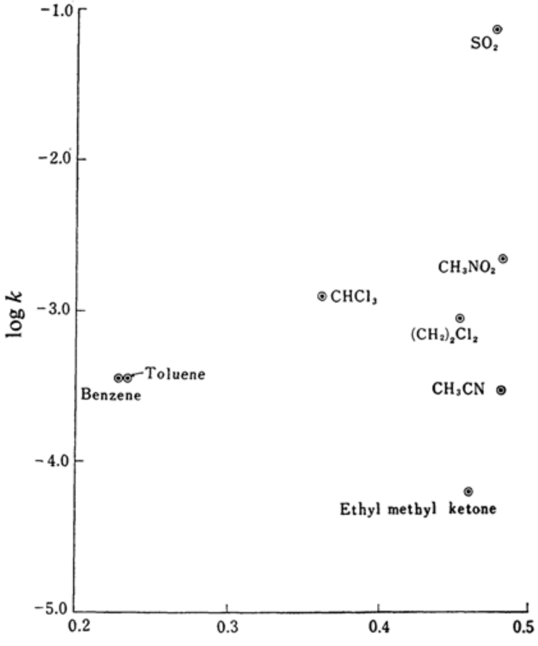


Fig. 5. Log *k* vs. $(D-1)/(2D+1)$ plots.

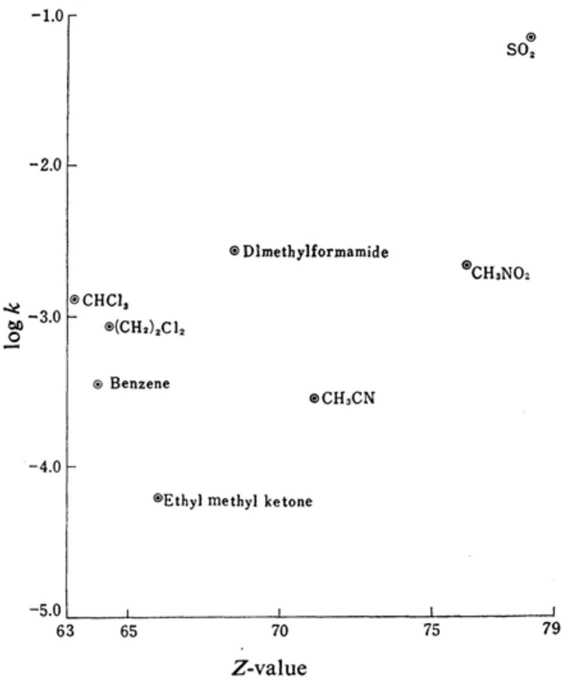


Fig. 6. Relationship between log k and Z-value.

The rate constants in various solvents vs. the ionizing powers (such as the dielectric constants and Z-values) of the solvents-relations, were further examined, as is illustrated in Figs. 5 and 6. The plots of $\log \cdot k$ vs. $(D-1)/(2D+1)$ or Z-value[11] resulted in complete randomness, without any linear correlation.

Summary

The solvent effects of the esterification of *l*-menthol with acetyl chloride in various solvents have been examined polarimetrically. In liquid sulfur dioxide, the rate of the esterification was the fastest among the solvents used. A *bare* carbonium ion formation in liquid sulfur dioxide may be the reason for this. The comparably large rate in dimethylformamide has also been discussed, along with the solvent effects in various other solvents.

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[11] E. M. Kosower, *J. Am. Chem. Soc.*, **80**, 3235 (1958).