Studies of the Isomerization of Unsaturated Carboxylic Acids. IV. Base-catalyzed Rearrangements of β,γ-Unsaturated Esters to α,β-Isomers

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Dimethyl methylenesuccinate, dimethyl citraconate, and dimethyl mesaconate mutually rearranged in the presence of triethylamine at room temperature. The rearrangement was found dependent on the polarity of the solvent and the basicity of the amine, and the rate was found to be first-order in both ester and amine. A mechanism has been proposed from a kinetic study.

In the preceding paper of this series, it was reported that such unsaturated dicarboxylic esters as dimethyl methylenesuccinate (**1**), dimethyl citraconate (**2**), and dimethyl mesaconate (**3**) mutually rearranged at high temperatures and that rearrangement would proceed by the mechanism involving carbanion intermediates formed under the general-base catalysis of methanol used as a solvent.[1] According to the above mechanism, the addition of a base, *e.g.*, tertiary amines, may accelerate the rearrangement. The base-catalyzed rearrangements of other unsaturated esters to their isomers have been reported in the literature.[2–5]

This paper deals with the interconversion between **1**, **2**, and **3** in the presence of a tertiary amine. The rearrangement of an unsaturated monocarboxylic ester, methyl 3-butenoate (**4**), has also been examined and compared with that of **1**.

Experimental

All the boiling points are uncorrected.

Materials. The organic solvents and amines were purified by ordinary methods. The following compounds were prepared by the methods described in the literature: dimethyl methylenesuccinate (dimethyl methylenebutanedioate) (**1**),[1] bp 111 °C/13 Torr; dimethyl citraconate (dimethyl (*Z*)-2-methyl-2-butenedioate) (**2**),[1] bp 116°C/15 Torr; dimethyl mesaconate (dimethyl (*E*)-2-methyl-2-butenedioate) (**3**),[1] bp 118 °C/16 Torr; methyl 3-butenoate (**4**),[6] bp 108 °C; methyl (*Z*)-2-butenoate (**5**),[7] bp 119 °C (contaminated with 23% of **6**); methyl (*E*)-2-butenoate (**6**),[6] bp 120 °C; dimethyl ethylidenesuccinate,[8] bp 112 °C/15 Torr; dimethyl isopropylidenesuccinate,[8] bp 115 °C/14 Torr.

Procedure. A mixture of the ester (12 mmol), tertiary amine (12 mmol), and solvent (15 ml) was placed in a test tube fitted with a stopcock and kept in a thermostated bath. The mixture was stirred with a magnetic stirrer. Aliquots (1 ml) of the mixture were taken at regular intervals, treated with aqueous hydrochloric acid (3 ml), and extracted with benzene (2 ml). The benzene extracts were washed with sodium hydrogencarbonate and subjected to GLC analysis.

Kinetics. The initial rate constants were calculated from the plot of $\ln[\text{ester}]_0/[\text{ester}]_t$ against time. The activation parameters were obtained from the Arrhenius plot for the rate of the disappearance of ester.

*Reaction in Methanol-*d. A mixture of **1** (12 mmol), triethylamine (12 mmol), and methanol-*d* (15 ml) was stirred and kept at 50 °C in a thermostated bath, and at appropriate intervals aliquots of the mixture were taken. The aliquots were treated with aqueous hydrochloric acid and extracted with carbon tetrachloride. The carbon tetrachloride extracts were subjected to GLC and NMR analyses. The NMR spectra were recorded on a Varian T-60A spectrometer.

Analysis. The extracts were analyzed by GLC using a 90 m BDS capillary column with Yanagimoto G-80 for the esters (**1**, **2**, and **3**), and a 4.5 m DNP column with Yanagimoto GCG-220 for the esters (**4**, **5**, and **6**). It was confirmed that no rearrangement took place in the course of the treatment and gas chromatographic analysis.

Results

It was observed that the β,γ-unsaturated esters, **1** and **4**, rearranged to the α,β-isomers in the presence of the tertiary amine at ambient temperature and that the α,β-esters, **2** and **3**, rearranged to the β,γ-isomer. The gas chromatogram of the reaction mixture revealed that the mixture contained only three isomers of each ester; no by-product was detected.

Effects of Solvent and Amine. The initial relative rates for the rearrangement of **1** with various solvents and amines were measured. An equimolecular amount of amine to **1** was employed in order to accelerate the reaction. The reaction rate was found sensitive to the dielectric constant of the solvent, as shown in Table 1. In a polar solvent such as dimethyl sulfoxide (DMSO), **1** rearranged rapidly to **3**. In the case of a nonpolar solvent, cyclohexane, however, the rearrangement was quite slow.

The effect of amine on the rate is shown in Table 2. Methanol was used as a solvent, since some amines were not soluble in DMSO and acetonitrile. Tertiary

TABLE 1. EFFECT OF SOLVENT ON THE REARRANGEMENT OF **1**[a)]

Solvent	Dielectric constant, D	Relative rate[b)]
DMSO	46.7	1.00
Sulfolane	44.0	1.04
Acetonitrile	37.5	0.349
Methanol	32.6	0.163
THF	7.6	0.0127
Cyclohexane	2.0	0.00319

a) Ester **1**, 12 mmol; triethylamine, 12 mmol; solvent, 15 ml; temp, 50 °C.
b) The rate for the disappearance of **1** in DMSO ($k=2.21\times10^{-4}$ $\text{l mol}^{-1}\,\text{s}^{-1}$) is taken as 1.00.

TABLE 2. EFFECT OF AMINE ON THE REARRANGEMENT OF **1**[a)]

Amine	pK_a	Relative rate[b)]
Tributylamine	10.9	0.700
N,N-Dimethylcyclohexylamine	10.7	1.93
Triethylamine	10.7	1.00
N-Ethylpiperidine	10.4	0.542
N-Methylpiperidine	10.1	0.810
N,N-Dimethylbenzylamine	8.9	0.129
Triallylamine	8.3	0.0136
Pyridine	5.2	0
N,N-Dimethylaniline	5.1	0

a) Ester **1**, 12 mmol; amine, 12 mmol; methanol, 15 ml; temp, 50 °C. b) The rate for the disappearance of **1** in the presence of triethylamine ($k=3.60\times 10^{-5}$ l mol^{-1} s^{-1}) is taken as 1.00.

amines were suitable bases for the test of the effect of amine on the rearrangement. When primary or secondary amines were used for the reaction in methanol, the aminolysis of **1** by diethylamine occurred. Tertiary amines appear to act as specific bases and general acids for the reaction. The reactivity of tertiary amines examined increased approximately with increase in basicity. The results listed in Table 2 indicate that a steric factor, in addition to an electronic one, participates in determining the reactivity of the amine with **1**.

Equilibria. The equilibria of the three isomers in DMSO containing triethylamine were examined. The results of the rearrangement are summarized in Table 3, and as may be seen, the equilibrium composition was found to be 34% for **1**, 4% for **2**, and 62% for **3**. Under identical conditions, the values in the rearrangement of methyl butenoate, attempted for a comparison, were 0% for **4**, 4% for **5**, and 96% for **6**. The esters, **4** and **5**, rearranged practically to **6**. The effect of the alkyl substituent on the rearrangement was also examined. γ-Substituted **1**, dimethyl ethylidenesuccinate and dimethyl isopropylidenesuccinate, did not rearrange to their isomers.

TABLE 3. EQUILIBRIUM BETWEEN **1**, **2**, AND **3**[a)]

Starting ester	Time, h	Composition, %		
		1	**2**	**3**
1	1	61.8	0.3	37.9
1	12	33.7	2.7	63.6
2	12	29.5	41.8	28.7
3	1	20.1	0.1	79.8
3	12	36.5	3.4	60.1
1	54	34.7	3.1	62.2
1 : **3**=2 : 1	54	34.5	4.1	61.4
1 : **3**=1 : 1	54	34.3	4.1	61.6
1 : **3**=1 : 2	54	34.1	3.9	62.0
3	54	32.5	4.1	63.4
2	54	33.5	7.5	59.0

a) Ester, 12 mmol; triethylamine, 12 mmol; DMSO, 15 ml; temp, 50 °C.

Kinetics. Kinetic measurements for the rearrangement of **1** and **4** were undertaken in the temperature range from 30 to 50 °C and in the concentration range of triethylamine from 0.12 to 12 mmol. The total esters were recovered quantitatively without any side reactions even after a prolonged reaction time. The rate of the rearrangement was found to be first-order in both ester and amine,

$$\text{rate} = k[\text{ester}][\text{amine}].$$

A good first-order plot for the disappearance of ester was obtained over a conversion of 20% in all cases of the esters, **1**, **2**, **3**, and **4**. The rate of the disappearance of **1** may be regarded as the rate from **1** to **3**, because the rate from **1** to **2** is much slower than that from **1** to **3** and because the rate of the reverse reaction[9)] from **3** to **1** is neglected at the initial stage of the reaction. The rates of the disappearance of **2** and **3** may be taken as the rate from **2** to **1** and that from **3** to **1**, respectively, because the direct interconversion between **2** and **3** may be negligible (*vide infra*). The activation parameters, $\Delta H^{\neq}$ and $\Delta S^{\neq}$, were 53.6 kJ mol^{-1} and -150 J K^{-1} mol^{-1} for **1**, 50.2 kJ mol^{-1} and -154 J K^{-1} mol^{-1} for **4**, respectively. In Table 4, these parameters are compared with those reported.[1,3)] There are distinct differences between the values in the base-catalyzed and thermal rearrangements, the addition of a tertiary amine

TABLE 4. KINETIC DATA FOR THE REARRANGEMENT[a)]

Ester	Temp, °C	$k\times 10^4$, l mol^{-1} s^{-1}
1	30±0.1	0.530
1	40	1.04
1	50	2.21 (2.30)[b)]
2	50	0.415
3	50	1.19 (1.19)[b)]
$E_a=56.2$ kJ mol^{-1}, $\Delta H^{\neq}=53.6$ kJ mol^{-1}, $\Delta S^{\neq}=-150$ J K^{-1} mol^{-1}.		
Thermal rearrangement of **1** to **3**[1)]		
$E_a=82.1$ kJ mol^{-1}, $\Delta H^{\neq}=77.8$ kJ mol^{-1}, $\Delta S^{\neq}=-184$ J K^{-1} mol^{-1}.		
4	30	1.27
4	40	2.05
4	50	4.65
$E_a=52.8$ kJ mol^{-1}, $\Delta H^{\neq}=50.2$ kJ mol^{-1}, $\Delta S^{\neq}=-154$ J K^{-1} mol^{-1}.		
Reported[3)] (ethyl ester, diethylamine, acetonitrile)		
$E_a=43.9$ kJ mol^{-1}, $\Delta H^{\neq}=36.8$ kJ mol^{-1}, $\Delta S^{\neq}=-171$ J K^{-1} mol^{-1}.		

a) Ester, 12 mmol; triethylamine, 12 mmol; DMSO, 15 ml. b) The value of k_f. See Ref. 9.

TABLE 5. THE REARRANGEMENT OF **2**[a)]

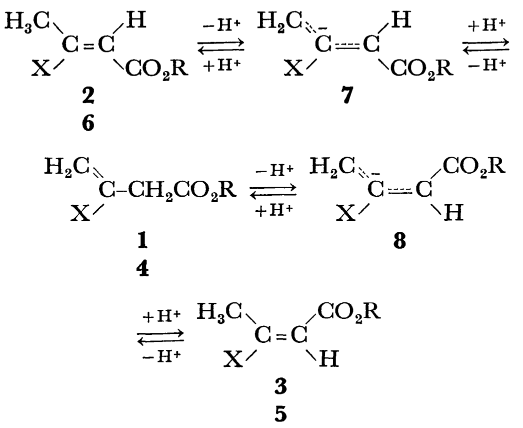
Time, min	Composition, %		
	1	**2**	**3**
40	6.0	93.1	0.9
60	7.8	90.3	1.9
80	9.5	87.6	2.9
100	10.4	85.7	3.9
120	12.5	82.4	5.1

a) Ester **2**, 12 mmol; triethylamine, 12 mmol; DMSO, 15 ml; temp, 50 °C.

accelerating the rearrangement significantly.

The steric effect of the ester group in methylenesuccinate on the rate was observed. The relative rate of diethyl and diisopropyl esters for **1** (1.0) were 0.75 and 0.36, respectively.

Deuterium Isotope Effect. When **1** was treated with triethylamine in methanol-*d* for 30 min, 50% of the hydrogen atoms in the α-methylene groups of the recovered **1** were replaced by deuterium atoms, whereas only 4% of **1** rearranged to **3**. The initial rate constant for the disappearance of **1** in methanol-*d*, k_{MeOD}, was measured and the ratio of $k_{\mathrm{MeOH}}/k_{\mathrm{MeOD}}$ was found to be 2.5.



1, **2**, **3** (X: $-CO_2CH_3$, R: $-CH_3$)
4, **5**, **6** (X: -H, R: $-CH_3$)

Scheme 1.

Discussion

Tertiary amines accelerated the rearrangement remarkably as expected. In view of the kinetic study, the same mechanism as described in the thermal rearrangement[1)] is proposed for the base-catalyzed rearrangements of the unsaturated esters, **1**, **2**, **3**, and **4**, as shown in Scheme 1. The formation of **3** from the carbanion (**8**) is the rate-determining step for the rearrangement of **1** supported by the following results; the second-order reaction dependent on ester and amine, the rate dependence on the polarity of the solvent and the basicity of the amine, a facile hydrogen-deuterium exchange of the hydrogen atoms in the α-methylene group of the recovered **1**, and the deuterium isotope effect observed on the reaction. The last two observations especially support the following equation,

$$\mathbf{1} + NR_3 \overset{\text{fast}}{\rightleftarrows} \mathbf{8} + HN^+R_3 \xrightarrow{\text{slow}} \mathbf{3} + NR_3.$$

The rate for the formation of **2** is slower than that of **3**, since the carbanion **8** may be more stable than **7**. In the carbanion **7** (X=$-CO_2CH_3$), there is a mutual repulsion between the two *cis*-oxygen atoms of the methoxycarbonyl groups. However, for the rearrangement of methyl butenoate, **8** (X=-H) is less stable than **7**, which can thus produce a *trans*-isomer. The equilibrium between **5** and **6** lies entirely to the left under the conditions, consequently, the thermodynamically stable esters, **3** and **6**, are the most favored products in the equilibria. The equilibrium composition in the base-catalyzed rearrangements of **1**, **2**, and **3** agrees very closely with that reported in the thermal rearrangement.[1)] A large negative value of entropy appears to indicate that the carbanion exists in a stabilized planar structure. However, carbanions from γ-alkylsubstituted methylenesuccinates may be unstable and/or return to starting esters, judging from the fact that the γ-alkylsubstituted methylenesuccinates do not rearrange to their isomers.

The direct *cis-trans* isomerization between **2** and **3**, another route in the rearrangement, may be negligible, because **1** predominated over **2** and **3** at the initial stage of the rearrangement of **3** and **2**, as shown in Tables 3 and 5, respectively. The *cis*-ester, **2**, rearranged consecutively to the *trans*-isomer, **3**, *via* **1**.

Thus, the mechanism reported in the thermal rearrangement using methanol as a solvent is strongly supported by the above description.

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9) The values of the rate constant for the forward reaction, k_f, were obtained by means of the equation for the reversible first-order reaction, $A \underset{k_r}{\overset{k_f}{\rightleftarrows}} B$, and

$$([B]_e/[A]_0) \ln \{[B]_e/([B]_e-[B]_t)\} = k_f t\,[\text{amine}],$$

where $[B]_e$ is the concentration of B when equilibrium is reached; K. J. Laidler, "Chemical Kinetics," McGraw-Hill Book Company, New York, N. Y. (1965), p. 19.

The values of k do not differ from those of k_f, as shown in Table 4. Here, k is the sum of k_f and k_r.