

Aminolysis Reaction of Reactive Diesters with Amine

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ABSTRACT: Diesters having hydroxyl groups can react with diamines under mild conditions to form polyamides having pendant hydroxyl groups. The reactivity enhancement owing to the hydroxyl group was investigated in terms of the aminolysis reaction of aliphatic or heterocyclic hydroxyl diesters with butylamine. Apparent rate constants could be expressed in the following equation:

$$k_{\text{obs}} = k_1[\text{BuNH}_2] + k_2[\text{BuNH}_2]^2$$

The enhancement effect of the hydroxyl group on the aminolysis reaction was interpreted either as the polarity change of the ester carbonyl group, in the case of heterocyclic diesters, or as the intermolecular hydrogen bonding with amine, in the case of aliphatic diesters.

KEY WORDS Polyamide / Hydroxyl Diesters / Heterocyclic Diesters / Aminolysis / Hydrogen Bonding /

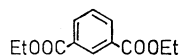
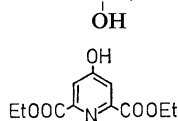
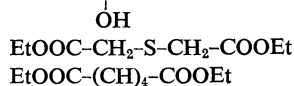
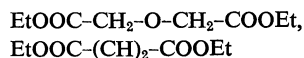
Polycondensation reactions of diesters with diamines are usually carried out in a molten state at elevated temperatures because the reactivity of ordinary diesters is not sufficiently high enough to carry out the polycondensation under mild conditions, unless one uses so-called active diesters, such as *p*-nitrophenyl ester. However, previous papers¹⁻³ revealed that the reactivity of ordinary diesters, such as methyl ester, is so greatly enhanced by introducing hetero atoms or heterocyclic groups that the polycondensation of these diesters can take place under mild conditions to produce the corresponding polyamides. For instance, tartarate or mucate, which have hydroxyl groups,² or diesters having γ -pyrone moiety³ can react with diamine even at room temperature to form polyamides.

This paper deals with the aminolysis reaction of these reactive diesters having hydroxyl groups in order to investigate the reactivity enhancement owing to the hydroxyl groups. Kinetic measurements of various hydroxyl diesters were carried out using butylamine and the reaction mechanism is discussed.

EXPERIMENTAL

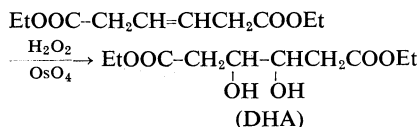
Materials

The following diesters were obtained by the esterification of the corresponding dicarboxylic acids according to a conventional method and were purified by distillation or recrystallization.

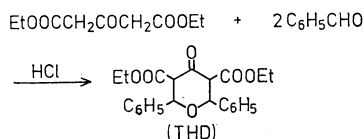


Commercially available diethyl succinate, oxalate, or acetone dicarboxylate were used after purification by distillation.

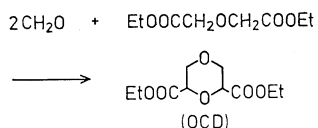
Diethyl 3,4-dihydroxyadipate⁴ (DHA) was synthesized by the oxidation of *trans*-2-butenedicarboxylate with hydrogen peroxide in 2-methyl-2-propanol at 0°C, in the presence of osmium tetroxide as a catalyst.



Diethyl 2,6-diphenyl-3,5-tetrahydropyronedicarboxylate (THD)⁵ was synthesized from diethyl acetonedicarboxylate and benzaldehyde, by bubbling hydrogen chloride under cooling with water.

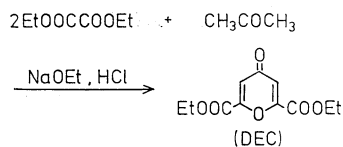


Diethyl 1,4-dioxo-2,6-cyclohexanedicarboxylate (OCD) was synthesized⁶ from trioxane and diethyl diglycolate in the presence of sulfuric acid.



Diethyl chelidonate (DEC) was prepared⁷ from diethyl oxalate and acetone in the presence of

sodium ethoxide.



Diethyl 3,4-dihydroxy-2,5-furandicarboxylate (DHF) was synthesized⁸ from diethyl oxalate and diethyl diglycolate in the presence of sodium ethoxide. The same procedure afforded diethyl 3,4-dihydroxy-2,5-thiophenedicarboxylate (DHT), using diethyl dithioglycolate instead of diglycolate.

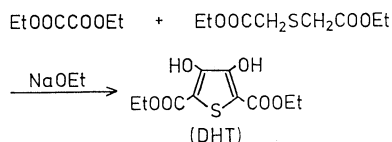
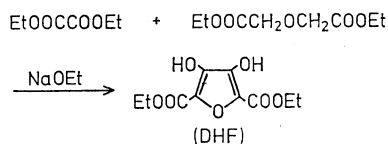


Table I. Characterization of diesters

Ester	mp [bp], °C	Elemental Analysis (calcd)		IR, cm ⁻¹	NMR, δ, ppm
		C%	H%		
$\text{CH}_3\text{CH}_2\text{OOC}-\underset{\text{OH}}{\text{CH}}_2-\underset{\text{OH}}{\text{CH}}-\text{CH}_2\text{COOCH}_2\text{CH}_3$	75—77	52.5 (51.3)	8.1 (7.8)	ν _{OH} 3370, 3460 ν _{C=O} 1710, 1732	a 1.4, c 2.7 e 3.45, b, d 4.3
$\text{CH}_3\text{CH}_2\text{OOC}-\underset{\text{H}_5\text{C}_6}{\text{C}}=\underset{\text{H}_5\text{C}_6}{\text{C}}-\text{COOCH}_2\text{CH}_3$	[215—216] (0.1 mm)	71.0 (69.7)	6.0 (6.1)	ν _{C=O} 1679, 1741 ν _{C=C} 1644	a, 1.1, b 4.0 c, d 5.0 e 7.2
$\text{CH}_3\text{CH}_2\text{OOC}-\text{C}_4\text{H}_4\text{O}_2-\text{COOCH}_2\text{CH}_3$	[71—72] (0.02 mm)	47.5 (51.7)	7.4 (6.9)	ν _{CH} 2960 ν _{C=O} 1750	a 1.3, d 2.63 b, c 4.1
$\text{CH}_3\text{CH}_2\text{OOC}-\text{C}(\text{O})=\text{C}(\text{O})-\text{COOCH}_2\text{CH}_3$	63	55.2 (55.0)	5.1 (5.0)	ν _{C=O} 1652, 1739	a 1.4, b 4.4 c 7.07
$\text{CH}_3\text{CH}_2\text{OOC}-\text{C}_4\text{H}_2\text{O}_2-\text{COOCH}_2\text{CH}_3$	198—199	50.9 (49.2)	5.3 (5.0)	ν _{C=O} 1683 ν _{C=C} 1580	a 1.3, b 4.3 c 10.0
$\text{CH}_3\text{CH}_2\text{OOC}-\text{C}_4\text{H}_2\text{S}-\text{COOCH}_2\text{CH}_3$	142—143	45.7 (46.2)	4.8 (4.6)	ν _{C=O} 1679	a 1.3, b 4.3 c 9.28

All of these synthesized diesters gave satisfactory results of elemental analyses and showed IR and NMR spectra compatible with their expected structures. Melting or boiling points and analytical data of these diesters are summarized in Table I.

All of reagents and solvents were purified before use.

Kinetic Measurement

A solution of diesters in dioxane was mixed with a given amount of butylamine in the presence or absence of a catalyst, and the solution was placed in a water bath kept at a constant temperature. Rates of the aminolysis reaction were followed by measuring the amount of liberated ethanol by means of a gaschromatographic analysis, which was carried out by using a flame-ionization type JEC-20KFP (Nippon Denshi Co.) with a column of triton X-100.

Spectrum Measurement

The IR spectrum was measured by a Hitachi model 215 infrared spectrophotometer either in solutions or in KBr disks. The NMR spectrum of diesters was measured by a Hitachi R-22 or R-24 nuclear magnetic resonance spectrometer in tetrachloromethane, chloroform-*d*, or dimethyl sulfoxide-*d*₆ solutions. ¹³C-NMR measurements were carried out in dioxane or dimethyl sulfoxide solutions by a Hitachi R-42 Fourier Transform NMR. Tetramethylsilane was used as a standard.

RESULTS AND DISCUSSION

Various diesters were allowed to react with an excess amount of butylamine in dioxane at 60°C. The apparent rate constants of the aminolysis reaction, which were obtained as a first order reaction, are summarized in Tables II and III.

Tables II and III indicate that apparent rate constants k_{obs} for the reaction of such hydroxyl diesters as tartarate or mucate, and for the reaction of diesters having furan or γ -pyrone nuclei, are 10^3 to 10^4 times as large as those of ordinary diesters which do not have hetero atom groups. The aminolysis reaction of ester with amine has been extensively studied by Menger,⁹ who found

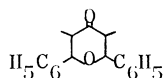
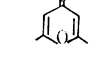
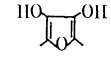
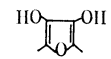
Table II. Observed rate constants for the condensation of various aliphatic diesters with butylamine^a in dioxane at 60°C

EtOOC-R-COOEt R	$C_{Eo}^b \times 10^3, M$	k_{obs}, sec^{-1}
Diethyl oxalate	6.44	1.8×10^{-3}
-CH ₂ -	10.05	$< 10^{-8}$
-(CH ₂) ₂ -	9.89	$< 10^{-8}$
-CH ₂ COCH ₂ -	10.33	8.5×10^{-8}
-CH ₂ OCH ₂ -	10.84	6.5×10^{-7}
-CH ₂ SCH ₂ -	10.84	1.5×10^{-7}
-(CH) ₂ - OH	10.87	1.1×10^{-6}
-CH ₂ (CH) ₂ CH ₂ - OH	8.70	1.2×10^{-5}
-(CH) ₄ - OH	9.98	2.3×10^{-4}

^a Concn of Bu-NH₂, $5.00 \times 10^{-1} M$.

^b Initial concentration of ester group.

Table III. Observed rate constants for the condensation of various heterocyclic diesters with butylamine^a in dioxane at 60°C

EtOOC-R-COOEt R	$C_{Eo}^c \times 10^3, M$	k_{obs}, sec^{-1}
	12.29	1.8×10^{-7}
	9.90	8.4×10^{-7}
	10.61	1.8×10^{-6}
	5.13	1.1×10^{-4}
	10.06	1.2×10^{-4}
	5.21	1.2×10^{-4}
	10.04	1.8×10^{-4}
	5.20	2.2×10^{-6}
	11.55	0 ^b

^a Concn of Bu-NH₂, $5.00 \times 10^{-1} M$.

^b Too slow to detect.

^c Initial concentration of ester group.

that the apparent rate constants of the aminolysis reaction can be expressed as a function of amine when the amount of amine is used in excess. When the values of $k_{\text{obs}}/[\text{BuNH}_2]$ are plotted as a function of $[\text{BuNH}_2]$, a good linear relation-

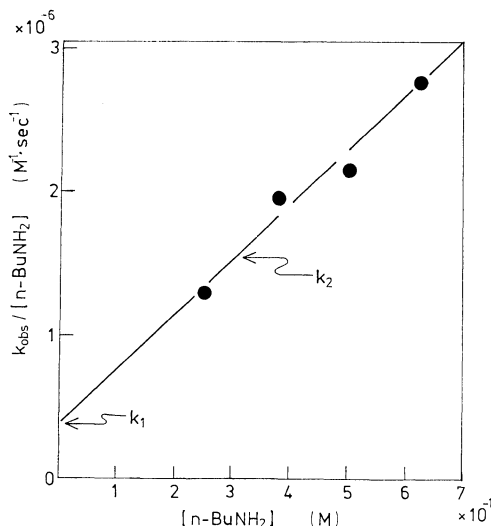


Figure 1. Plot of observed rate constants for butylaminolysis of diethyl tartarate in dioxane at 60°C vs. $[\text{butylamine}]$; initial ester concn, $1.087 \times 10^{-2} M$.

ship is observed, as shown in Figure 1, and k_{obs} can be expressed in the following equation, as Menger found for the aminolysis reaction of ordinary esters.

$$k_{\text{obs}} = k_1[\text{BuNH}_2] + k_2[\text{BuNH}_2]^2 \quad (1)$$

The apparent rate constants k_1 and k_2 can be determined from the intercepts and slopes of the straight lines, as shown in Figure 1.

In the case of diethyl mucate, which is 2,3,4,5-tetrahydroxyadipate, DHF or DHT, a simple relation between k_{obs} and $[\text{BuNH}_2]$ was observed, as shown in the following equation (2).

$$k_{\text{obs}} = k_1[\text{BuNH}_2] \quad (2)$$

The apparent rate constants k_1 and k_2 for the aminolysis reaction of various diesters are summarized in Table IV.

It is known¹⁰ that the aminolysis reaction of ester is accelerated by tertiary amines such as triethylenediamine (Dabco). Therefore, various tertiary amines or quaternary ammonium salts were added to the mixed solution of diesters and butylamine, and the rates of the aminolysis reaction were measured; these are summarized in Table V. Table V indicates that quaternary ammonium salts or trialkyl amines accelerate the

Table IV. Values of k_1 and k_2 for the condensation of various diesters with butylamine^a in dioxane

$\text{EtOOC}-\text{R}-\text{COOEt}$ R	$C_{\text{Eo}}^b \times 10^3, M$	Temp, °C	$k_1, M^{-1} \text{sec}^{-1}$	$k_2, M^{-2} \text{sec}^{-1}$
Diethyl oxalate	6.44	30	—	4.7×10^{-8}
$-(\text{CH})_2-$ OH	10.87	60	2.7×10^{-7}	3.9×10^{-6}
$-\text{CH}_2(\text{CH})_2\text{CH}_2-$ OH	4.35	30	3.0×10^{-6}	4.0×10^{-6}
$-(\text{CH})_4-$ OH	9.98	60	4.7×10^{-4}	—
	10.61	60	9.4×10^{-7}	5.9×10^{-6}
	5.21	60	2.3×10^{-4}	—
	5.20	60	4.3×10^{-6}	—
	5.13	20	—	2.7×10^{-4}
	10.06	60	2.6×10^{-5}	4.5×10^{-4}

^a Concn of Bu-NH_2 , $2.50-6.20 \times 10^{-1} M$.

^b Initial concentration of ester group.

Table V. Effects of various basic catalysts on the condensation of diethyl esters with butylamine^a in dioxane at 30°C

Ester	Catalyst	k_{obs} , sec ⁻¹	k_{obs} , relative
DHF ^b	None	2.9×10^{-5}	1
	Pyridine	2.9×10^{-5}	1.0
	<i>N,N</i> -Dimethyl-aniline	4.6×10^{-5}	1.6
	Bu ₃ N	6.1×10^{-5}	2.1
	Dabco	1.2×10^{-4}	4.3
	Bu ₄ NBr	1.5×10^{-4}	5.1
Mucate ^c	None	9.9×10^{-5}	1
	Pyridine	1.1×10^{-4}	1.1
	<i>N,N</i> -Dimethyl-aniline	1.1×10^{-4}	1.1
	Bu ₄ NClO ₄ ^d	3.3×10^{-4}	3.4
	Bu ₄ NBr ^d	3.9×10^{-4}	3.9
	Bu ₃ N	5.0×10^{-4}	5.1

^a Concn of BuNH₂, 5.00×10^{-1} M.

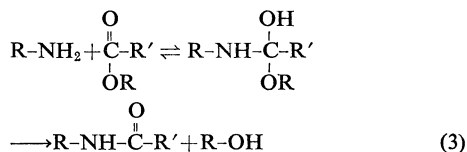
^b Concn of ester groups (C_{Eo}), 5.21×10^{-3} M; concn of catalyst, 2.50×10^{-1} M.

^c C_{Eo}, 5.48×10^{-3} M; concn of catalyst, 2.50×10^{-1} M.

^d Concn of catalyst, 2.0×10^{-1} M.

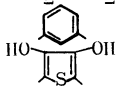
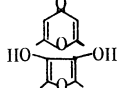
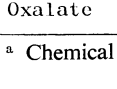
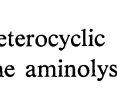
aminolysis reaction, while *N,N*-dimethylaniline or pyridine does not.

Menger⁹ has proposed as the mechanism of the aminolysis reaction that a tetrahedron intermediate is formed by a quick attack of amine on an ester carbonyl group, which is accompanied by an equilibrium, and this intermediate product yields amide and alcohol as a rate-determining step:



In order to investigate the quick attack of amine on an ester carbonyl group, the electron density of the ester carbonyl group should be determined. ¹³C-chemical shifts of the acyl carbon are known¹¹ to reflect electron densities of the acyl carbon atom. Therefore, ¹³C-chemical shifts of the acyl carbons of various diesters were compared with k_{obs} values of the aminolysis reaction. Diethyl succinate or diethyl isophthalate was taken as a standard in aliphatic or heterocyclic series, respectively. As shown in Table VI,

Table VI. ¹³C-NMR Chemical shifts of acyl of various diethyl esters

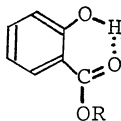
EtOOC-R-COOEt R	log k_{obs} (60°C)	δ_c , ppm ^a
$-(\text{CH}_2)_4-$	-3.63	173.49
$-(\text{CH}_2)_2-$	-5.97	172.41
$-\text{CH}_2-$	≤ -7	172.41
$-\text{CH}_2\text{OCH}_2-$	-6.19	170.49
$-\text{CH}_2\text{COCH}_2-$	-7.07	167.40
	—	165.24
	-5.65	162.08
	-3.92	160.16
	-3.76	158.38
Oxalate	-2.75	158.69

^a Chemical shifts from TMS.

heterocyclic diesters which are reactive toward the aminolysis reaction show a great shift of the peaks connected with the acyl carbon atoms. Therefore, the electron density of these heterocyclic diesters must be sufficiently low to be subjected to an easy attack of amine. On the other hand, hydroxyl diesters which are also reactive toward the aminolysis reaction did not exhibit a significant shift of the acyl carbon peak. IR spectra of these aliphatic hydroxyl diesters also did not exhibit any systematic shift of the absorption owing to the carbonyl group of the esters. These results suggest that the high reactivity of aliphatic hydroxyl diesters must be due to another reason which is not primarily related with the electron density of the carbonyl group of the esters.

The reactivity enhancement owing to the hydroxyl group for the aminolysis reaction of aromatic hydroxyl diesters has been studied by Menger.⁹ Menger and coworkers reported that the aminolysis reaction of aromatic esters is greatly enhanced by substituting with a hydroxyl group at the ortho position of an aromatic nucleus. A strong intramolecular hydrogen bonding between the hydroxyl and ester carbonyl groups may reduce the electron density to such an extent that an easy attack of amine may take place. Thus, *o*-hydroxyl salicylate can react with

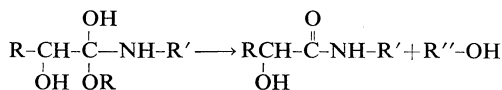
amine with a much faster rate than that for benzoate.



The same reason as the ortho effect would explain the high reactivity of the heterocyclic diesters having hydroxyl groups, because IR and ^{13}C -NMR spectra indicate a change in the electron density of the carbonyl group for these heterocyclic diesters.



On the other hand, no systematic change in electron density of the ester carbonyl group was observed in the case of aliphatic hydroxyl diesters. The reactivity enhancement of aliphatic hydroxyl diesters may be ascribed either to the hydrogen-bonding of the hydroxyl group with the approaching amine or to a rapid transformation of a tetrahedron intermediate, which is formed by an attack of amine on an ester carbonyl group at the intermediate stage, into amide and alcohol.



The apparent rates of the aminolysis reaction of aliphatic hydroxyl diesters are greatly influenced by the polarity of solvents, as reported in a previous paper.² The solvent effect may relate either to the hydrogen bonding or to the rapid transformation of the tetrahedron intermediate.

As described before, the rates of the aminolysis reaction of mucate, DHF or DHT, can be expressed in the simple form of eq 2 without having a second term of k_2 . This would be explained by the reason that the transformation of the tetrahedron intermediate into amide, which is the ratedetermining step, may be very fast.

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