Reaction of 2-(Diethylamino)ethanol with Benzoyl Chloride

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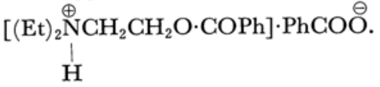
In the benzoylation of 2-(diethylamino)ethanol (I) by the Schotten-Baumann method using an excess amount of benzoyl chloride (II), the expected product could not be isolated; two kinds of viscous products were obtained in good yields instead. The product A with the lower boiling point was different from 2-(diethylamino)ethyl benzoate (III) in physical constants and viscosity. A had the following properties: 1) A gave a positive nitrogen test. 2) A gave a negative chlorine test. 3) An ethanol solution of A gave a picrate of yellow needles, mp 135°C, which was identical with the picrate of III. 4) When an equimolecular amount of I was added to a benzene solution of benzoic acid, an exothermic reaction took place and, on distillation, the mixture gave half the original amount of I unchanged and a viscous product which was identical with A. 5) Similarly, when an equimolecular amount III was added to a benzene solution of benzoic acid, the mixture gave A on distillation. 6) The results of elemental analysis nearly concurred with the calculated values for a 1 : 1 adduct of III and benzoic acid. These facts suggest that A is a benzoic acid salt of III,  $[(Et)_2\underset{H}{\overset{\oplus}{N}}CH_2CH_2O\cdot COPh]\cdot PhCO\overset{\ominus}{O}$. The other product B, with a higher boiling point, was found to be identical with benzoic anhydride.

Furthermore, when an equimolecular amount of II was reacted with I, A and unchanged I were obtained, but B was not formed. When III was used in place of I, A and B were obtained in good yields. Accordingly, it seems that A is formed faster than B. When alkali carbonates were used in place of sodium hydroxide, A and B were obtained, but III was not formed. (See Table 1.) When ether was previously added to the solution and the reaction was carried out in a non-aqueous system, neither A nor B was observed; only III was obtained.

In the benzoylation of I by the Claisen acylating method¹⁾ using an equimolecular amount of II, only III was obtained in high yield; when an excess amount of II was used, however, A and B were obtained, but III was not formed. The use of sodium hydroxide gave similar results, as did potassium carbonate.

Table 1. Benzoylation of I by the Schotten-Baumann method

Carbonates	Products, g	
	A	B
NaOH	8.5	11.1
Na_2CO_3	5.3	22.6
K_2CO_3	6.6	19.2
$CaCO_3$	1.8*	19.3*
$BaCO_3$	3.4*	8.5*

* The values are not accurate because of the low solubility of bases in water.
I (5.9 g, 0.05 mol) and II (35.2 g, 0.25 mol) were used.

Table 2. Benzoylation of I by the Claisen method and the Spassow method

	Products, g		
	III	A	B
The Claisen method	15.2*	—	—
	—	18.6**	33.1**
The Spassow method	17.0*	—	—
	—	22.7**	33.4**

* I (11.7 g, 0.1 mol) and II (14.1 g, 0.1 mol) were used.
** I (11.7 g, 0.1 mol) and II (70.3 g, 0.5 mol) were used.

Table 3. Reaction of II in the presence of *t*-amines

t-Amines	Benzoic Anhydride(g)
Pyridine	15.6 (0.069 mel, 28%)
Triethylamine	25.1 (0.111 mol, 44%)
Dimethylaniline	32.6 (0.144 mol, 58%)

t-Amine (0.1 mol) and II (70.2 g, 0.5 mol) were used.

The benzoylation of I by the Spassow method²⁾ gave similar results to those obtained by the Claisen method. These results are shown in Table 2.

Under the same conditions as in the Schotten-Baumann method, several tertiary amines converted II into B in a good yield. These results are shown in Table 3.

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1) L. Claisen, *Ber.*, **27**, 3182 (1894).

2) A. Spassow, *ibid.*, **70**, 1926 (1937).

On the basis of these results, the following conclusions may be deduced: i) The formation of B must be due to the presence of a diethylamino group in I, because B is not formed in the benzoylation of ethanol by the Schotten-Baumann method. ii) As has been mentioned in a previous paper,[3] a hydroxyl group in I seems to be activated by a diethylamino group. Therefore, it seems that III is produced more easily than ethyl benzoate. iii) A is formed faster than B. iv) The kinds of bases do not affect the experimental results essentially. v) Both A and B are formed in an aqueous alkaline solution, while neither A nor B is observed in a non-aqueous solution. This last fact seems to justify the following postulation: A is formed from III and the benzoic acid is produced by the hydrolysis of II, and then B is formed by the reaction of A with II; that is, A may be considered as an intermediate of the formation of B. The reaction sequence of I in the Schotten-Baumann method is schematically summarized in Fig. 1.

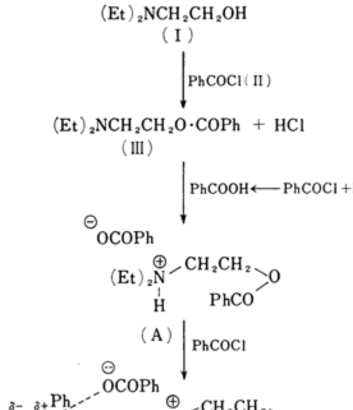

Fig. 1.

Experimental

Materials. I was purified by distillation. bp 161°C, n_D^{14} 1.4445. Commercially avaiable II was used.

Benzoylation of I by the Schotten-Baumann Method. The general procedure followed that described by Skraup.[4] I (5.9 g, 0.05 mol) was dissolved in 210 g of a 10% aqueous solution of sodium hydroxide (0.525 mol) and the mixture was cooled to below 5°C. II (35.2 g, 0.25 mol) was dropped in slowly with stirring for 2 hr, and then agitation was continued for a further 2 hr. The oil part was extracted with ether and distilled *in vacuo* to give two kinds of colorless viscous liquids, A (bp 138—139°C/4 mmHg, $n_D^{18.5}$ 1.5481, 8.5 g) and B (bp 181—182°C/4 mmHg, $n_D^{16.5}$ 1.5830, 11.1 g).

Found for A: C, 70.43; H, 7.31; N, 3.59%. Calcd for $C_{20}H_{25}O_4N$: C, 69.97; H, 7.29; N, 4.08%.

The picrate of A: yellow needles, mp 135°C (undepressed by admixture with the picrate of III.[5]

The structure of B was confirmed by hydrolysis to benzoic acid. The infrared spectrum of B was identical with that of benzoic anhydride prepared by another method.[6] Unchanged I (1 g) and benzoic acid (10.5 g) were obtained from the water part.

On the other hand, I (11.7 g, 0.1 mol) reacted with and equimolecular amount of II (14.1 g, 0.1 mol) to give A (9.9 g) and unchanged I (6 g).

Modified Method. Ether (100 m*l*) was previously added to a mixture of I (5.9 g, 0.05 mol) and a 10% aqueous solution of sodium hydroxide (210 g), and then II (35.2 g, 0.25 mol) was dropped in. The subsequent procedure was the same as the general procedure described above. A colorless liquid (bp 173—174°C/25.5 mmHg, $n_D^{21.5}$ 1.5002, 9.9 g (90%)) was obtained from the ether part. The infrared spectrum of this product was identical with that of III. Unchanged I (0.3 g) and benzoic acid (25.2 g) were obtained from the water part.

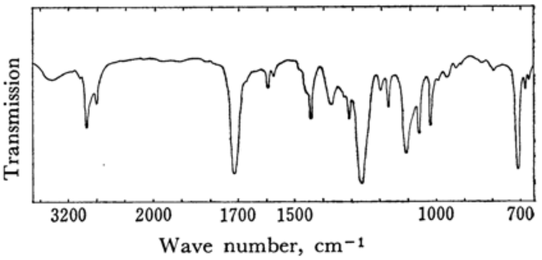

Fig. 2. Infrared spectrum of 2-(diethylamino) ethyl benzoate (III) in KBr disk.

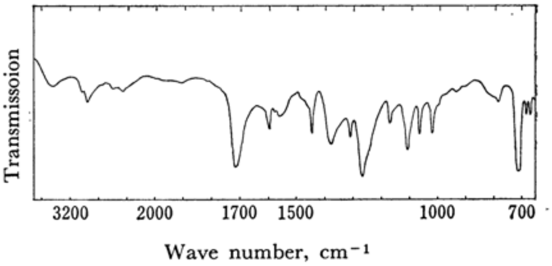

Fig. 3. Infrared spectrum of A in KBr disk.

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[3] T. Ogata, This Bulletin, **37**, 1117 (1964).

[4] Z. H. Skraup, *Monatsh.*, **10**, 390 (1891).

[5] T. Ogata and R. Goto, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **84**, 653 (1963).

[6] "Organic Syntheses," Coll. Vol. I, p. 91 (1941).

Reaction of Benzoic Acid with I. When I (11.7 g, 0.1 mol) was added slowly to a solution of benzoic acid (12.2 g, 0.1 mol) in 100m*l* of benzene, an exothermic reaction took place. The mixture was then distilled to give unchanged I (4.5 g (39%)) and A (14.4 g (42%)).

Reaction of Benzoic Acid with II. III (22.1 g, 0.1 mol) was added to a solution of benzoic acid (12.2 g, 0.1 mol) in 100 m*l* of benzene. This mixture was then distilled to give A (30.3 g (88.3%)).

Reaction of III with Benzoyl Chloride. Under the same conditions as in the Schotten-Beaumann method described above, III (11 g, 0.05 mol) was reacted with II (35.2 g, 0.25 mol). A (15.4 g (90%)) and B (16.5 g) were obtained from the oil part, while benzoic acid (4.6 g) was obtained from the water part.

Benzoylation of I by the Clasien Acylating Method.1) The general procedure: II (14.1 g, 0.1 mol) was added slowly to a mixture of I (11.7 g, 0.1 mol), potassium carbonate (22 g, 0.16 mol), and 150 m*l* of anhydrous ether at 40°C. Then the whole mixture was kept at this temperature for about 7 hr. After the addition of 50 m*l* of water, the ether layer was separated and distilled to give a colorless liquid of III 15.2 g (68%)). Benzoic acid (2.1 g) was obtained from the water part.

Benzoylation of I by the Spassow Method.2) The general procedure: II (14.1 g, 0.1 mol) was added slowly to a mixture of I (11.7 g, 0.1 mol), magnesium turnings (2.4 g, 0.1 g atom), and 150 m*l* of anhydrous ether at 40°C. Then the mixture was kept at this temperature for 3 hr. After the addition of 50 m*l* of water, the ether layer was separated and distilled to give III (17 g (77%)).

Reaction of Tertiary Amines with II. The procedure followed the Schotten-Baumann method described above, except that tertiary amines were used in place of I. The results are shown in Table 3.