

The Reaction of Aroyl Alkyl Carbonates with Isocyanates

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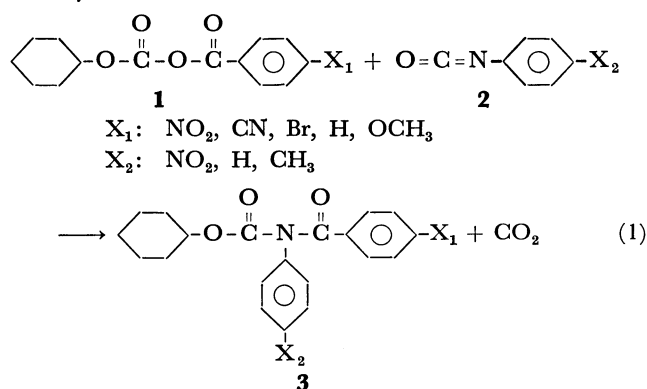
Aroyl alkyl carbonates were treated with isocyanates with or without addition of sodium methoxide and alkyl *N*-aroylcarbanilates were obtained as the major products. Based on ^{18}O tracer study and catalytic effect of alkoxide ion, a base catalyzed ionic reaction process was confirmed for the mechanism of the carbanilate formation.

Thermal decomposition of acyl alkyl carbonates giving esters has been known to proceed through two different mechanisms.¹⁾ The one is a cyclic unimolecular process and the second one is an ionic mechanism involving alkoxide ion as a chain carrying agent. The structure of the starting material and the nature of the solvent are considered to have important roles in making a choice between the two mechanisms. These results suggest that if the reaction carried out with a second reactant, such as isocyanate which reacts facilely with alkoxide ion, the formation of the product through alkoxide ion as an intermediate would be interrupted.

Acyl alkyl carbonates, on the other hand, are also known as acylating reagents.²⁾ Thus, alkoxy-acylation of isocyanates giving *N*-acylcarbanilates can be expected by the reaction with acyl alkyl carbonates. We have now tried the reaction and wish to report our results focusing our attention mainly to the synthesis of *N*-aroylcarbanilate and the formation mechanism.

Results and Discussion

Cyclohexyl benzoyl carbonate (**1**) was heated with phenyl isocyanate (**2**) in *o*-dichlorobenzene as a solvent at 150–160 °C. As expected, the product obtained was cyclohexyl *N*-benzoylcarbanilate (**3**), along with the products apparently formed by thermal decomposition of the carbonate³⁾ such as esters, acid anhydrides and symmetrical carbonates.



At the beginning of this study, the reaction was carried out without base. In the meantime, however, addition of a small amount of methoxide ion in the solution was found to complete the reaction much faster and with better result. Accordingly, the reaction was carried out with a small amount (*ca.* 15 mol%) of sodium methoxide. The results are given in Table 1.

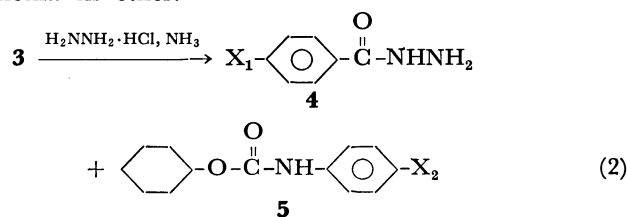
The structure of the product was determined by the following observations. Namely, aroyl hydrazides (**4**)

TABLE 1. REACTION OF AROYL ALKYL CARBONATE AND ISOCYANATE

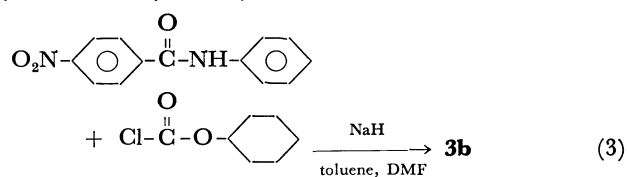
1	Reactant				Product	
	X ₁	2	X ₂	NaOCH ₃	3	Yield % ^{a)}
1a	CN	2a	H	none ^{b)}	3a	36
1b	NO ₂	2a	H	added ^{c)}	3b	68
1c	Br	2a	H	added	3c	59
1d	H	2a	H	added	3d	54
1e	CH ₃ O	2a	H	added	3e	52
1d	H	2b	NO ₂	added	3f	46
1d	H	2c	CH ₃	added	3g	56

a) Yields of **3** were calculated based on **1**. b), c) See Experimental.

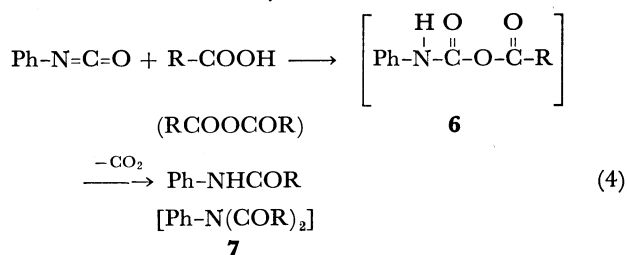
and cyclohexyl carbanilates (**5**) were obtained on treating **3** with hydrazine hydrochloride and ammonia in ether.



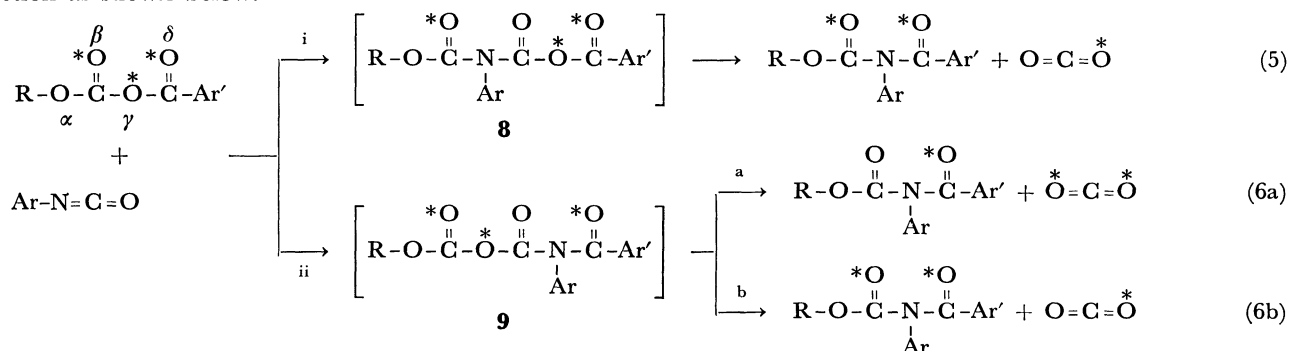
Spectroscopic evidences and elemental analysis also confirmed this structure. The carbanilate **3b** was also prepared by the reaction of *p*-nitrobenzanilide, sodium hydride and cyclohexyl chloroformate.



The reaction of phenyl isocyanate with a carboxylic acid or anhydride, which appears to be an analogous reaction to the present reaction, was studied by Ötvös *et al.*⁴⁾ An unstable mixed anhydride **6** was suggested as an intermediate which led to an amide or imide **7** on decarboxylation.

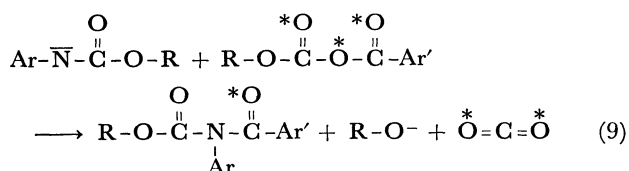
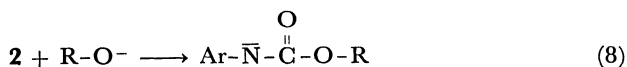


By analogy with this mechanism, there are two possible processes that can be shown for the present reaction as shown below.



Nucleophilic attack of the aryloxy group on the isocyanate results in formation of **8**. Attack of the γ -oxygen atom on the isocyanate with acyl-oxygen bond fission forms **9** as an intermediate. Decarboxylation of those intermediates lead to the product **3**.

The other possible process to give **3** is a base catalyzed reaction involving alkoxide ion as a catalyst. These processes can be distinguished by using ^{18}O labeled **1** at β , γ and δ oxygens as shown as asterisk in the equations, although the processes (6a) and (9) give the same results.



^{18}O Labeled **1a'** was prepared as follows:⁵⁾ The reaction of *p*-cyanobenzoic acid- ^{18}O (0.826 excess atom%) with cyclohexyl chloroformate gave the carbonate **1a** which was then allowed to scramble ^{18}O by heating at 70 °C in CCl_4 for 12 hr. The ^{18}O distribution in **1a'** after heating was analyzed obtaining nearly complete ^{18}O scramblings among β , γ and δ oxygens. The reaction of the labeled **1a'** with phenyl isocyanate (**2a**) was carried out in *o*-dichlorobenzene without addition of sodium methoxide. After heating for 16 hr at 160 °C, **3a** was obtained in 36% yield. ^{18}O Content and distribution in **3a** were measured after the cleavage re-

action shown in Eq. (2). The result is given in Scheme 1.

The ^{18}O in **3a** was found only at the benzoyl oxygen and the incorporation (0.545 excess atom%) concurred well to that of mean value of β , γ and δ oxygens of the starting **1a** (0.551 excess atom%). The result indicates that the starting **1a** scrambled ^{18}O completely among the three oxygens before reacting with the isocyanate. This was quite reasonable since the reaction with the isocyanate required a higher temperature (160 °C) than the oxygen scrambling reaction of the carbonate (70 °C).⁵⁾

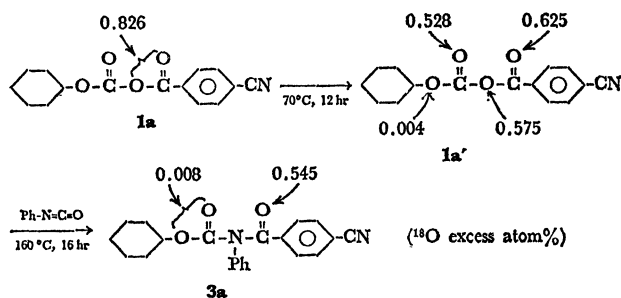
These results clearly ruled out the processes shown in Eqs. (5) and (6b) because only a negligible amount of ^{18}O was found in the carbanilate moiety in **3a**. The very small amount of ^{18}O seems to have originated from the ^{18}O in the alkoxide oxygen (α) of the starting material.

The base catalyzed reaction process shown in Eqs. (7)–(9) is the most probable mechanism between the two remaining possibilities because the reaction was catalyzed markedly by the addition of alkoxide ion.⁶⁾

Experimental

Preparation of Aryl Alkyl Carbonates. ^{18}O Labeled **1a** and **1d** were prepared in a similar manner reported in the previous paper. **1a**: mp 54.5–55.0 °C (lit.⁵⁾ mp 54.5–55.0 °C). **1d**: mp 21.0–22.0 °C (lit.⁵⁾ mp 21.0–21.5 °C). Carbonate **1b** was prepared as follows: An ether (50 ml) solution of triethylamine (15.0 g) was added dropwise into an ether (500 ml) suspension of *p*-nitrobenzoic acid (24.7 g) and cyclohexyl chloroformate (25.5 g) cooled in an ice bath. After stirring the mixture for additional 4 hr, water (200 ml) was added. The ether layer separated, was washed with dil. HCl, dil. aqueous $NaHCO_3$ and water then dried over Na_2SO_4 . The solvent was evaporated under reduced pressure to give **1b** in 57% yield. mp 49.0–50.0 °C (from ether). Found: C, 57.31; H, 5.11; N, 4.77%. Calcd for $C_{14}H_{15}O_6N$: C, 57.33; H, 5.16; N, 4.78%. Carbonates **1c** and **1e** were obtained similarly in 79 and 87% yields, respectively. **1c**: mp 19.5–20.5 °C. Found: C, 51.41; H, 4.50%. Calcd for $C_{14}H_{15}O_4Br$: C, 51.39; H, 4.62%. **1e**: mp 59.5–60.5 °C. Found: C, 65.03; H, 6.34%. Calcd for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52%.

Reaction of Aryl Alkyl Carbonates with Isocyanates. A typical run was as follows: A mixture of **1b** (5.96 g), phenyl isocyanate (3.10 g) and sodium methoxide (0.15 g) in *o*-dichlorobenzene (25 ml) was heated at 160 °C for 1.5 hr. After evaporation of the solvent under reduced pressure, the residual



Scheme 1.

oily material was dissolved in ether (50 ml) and washed with water, dil. HCl, dil. aqueous NaHCO₃ and water then dried over Na₂SO₄. The crude product was purified through a column chromatography on silica gel with benzene as an eluent then recrystallized from methanol obtaining **3b** (4.60 g). mp 103–104 °C. IR: 1735 and 1690 cm⁻¹ ($\nu_{C=O}$). Found: C, 65.34; H, 5.48; N, 7.53%. Calcd for C₂₀H₂₀O₃N₂: C, 65.21; H, 5.47; N, 7.61%. Physical properties and analytical results of other carbonates are as follows: **3a**: mp 105.0–105.5 °C. Found: C, 72.69; H, 5.66; N, 7.98%. Calcd for C₂₁H₂₀O₃N₂: C, 72.39; H, 5.79; N, 8.04%. **3c**: mp 90–91 °C. Found: C, 60.05; H, 4.93; N, 3.41%. Calcd for C₂₀H₂₀O₃NBr: C, 59.71; H, 5.01; N, 3.48%. **3d**: mp 77–78 °C. Found: C, 74.54; H, 6.59; N, 4.31%. Calcd for C₂₀H₂₁O₃N: C, 74.28; H, 6.55; N, 4.33%. **3e**: bp 228–233 °C/3 mmHg. **3f**: mp 97–98 °C. Found: C, 65.23; H, 5.42; N, 7.54%. Calcd for C₂₀H₂₀O₅N₂: C, 65.21; H, 5.47; N, 7.61%. **3g**: mp 81.5–82.5 °C. Found: C, 75.84; H, 6.96; N, 4.14%. Calcd for C₂₁H₂₃O₃N: C, 74.75; H, 6.87; N, 4.15%.

¹⁸O Tracer Experiment. A solution of ¹⁸O labeled **1a** (6.0 g) in CCl₄ (50 ml) was heated at 70 °C for 12 hr. The solvent was removed under reduced pressure and the residue was used for the reaction with **2a**. The same procedure described in the previous paper⁵⁾ was used for the determination of ¹⁸O distribution in **1a** and **1a'**.

Reaction of **3** with Hydrazine. Anhydrous ammonia was bubbled into a mixture of **3a** (0.80 g) and hydrazine hydrochloride (0.80 g) in dry ether (50 ml) for 20 min with stirring at room temperature. The mixture was stirred for additional 7 hr. Cyclohexyl carbanilate (**5**) (0.50 g) was obtained from the ether solution by filtration. mp 83.5–84.5 °C (from CHCl₃-pet. ether) (lit.⁷⁾ mp 81–82 °C). The residue of the filtration gave *p*-cyanobenzhydrazide (0.20 g) on recrystallization. mp 197–198 °C (from methanol-CCl₄) (lit.⁸⁾ mp 198–199 °C).

¹⁸O-Analysis was done by the same way as reported previously.⁵⁾

Preparation of Cyclohexyl N-(*p*-Nitrobenzoyl)carbanilate (**3b**). A mixture of *p*-nitrobenzanilide (6.7 g) and NaH (1.5 g as 50% paste) in dry toluene (100 ml) was refluxed for 1 hr with

stirring. Into the mixture, cyclohexyl chloroformate (4.5 g) in DMF (20 ml) was added with stirring at 70 °C. After stirring for additional 30 min, the mixture was then washed with dil. HCl, dil. aqueous NaHCO₃ and water then dried over Na₂SO₄. Removal of the solvent gave crude **3b** (7.2 g) which was recrystallized from methanol. mp 103–104 °C.

References

- 1) T. B. Windholz, *J. Org. Chem.*, **25**, 1703 (1960); E. J. Longosz and D. S. Tarbell, *ibid.*, **26**, 2161 (1961); C. J. Michejda, D. S. Tarbell and W. H. Saunders Jr., *J. Amer. Chem. Soc.*, **84**, 4113 (1962); C. J. Michejda and D. S. Tarbell, *J. Org. Chem.*, **29**, 1168 (1964); T. Kashiwagi, S. Kozuka, and S. Oae, *Tetrahedron*, **26**, 3619 (1970); C. J. Michejda and D. V. Riesen, *J. Org. Chem.*, **37**, 3021 (1972).
- 2) D. S. Tarbell and J. A. Price, *J. Org. Chem.*, **22**, 245 (1957); N. A. Leister and D. S. Tarbell, *ibid.*, **23**, 1152 (1958); D. S. Tarbell and J. R. Price, *ibid.*, **21**, 144 (1956); B. R. Baker, J. P. Joseph, R. E. Schab, and H. Williams, *ibid.*, **19**, 1786 (1954); J. R. Vaughan Jr. and R. L. Osato, *J. Amer. Chem. Soc.*, **73**, 5553 (1951).
- 3) D. S. Tarbell and E. L. Longosz, *J. Org. Chem.*, **24**, 774 (1959); T. B. Windholz, *ibid.*, **25**, 1703 (1960); R. C. L. Chow and D. S. Tarbell, *ibid.*, **32**, 2188 (1967).
- 4) L. Ötvös, J. Marton, and J. M. Agoston, *Tetrahedron Lett.*, **1960**, No. 2, 15.
- 5) S. Oae, K. Fujinori and Y. Uchida, *Tetrahedron*, **26**, 3169 (1970); S. Oae, Y. Uchida, K. Fujimori, and S. Kozuka, *This Bulletin*, **46**, 1741 (1973).
- 6) The reaction without sodium methoxide required about 15 hr to complete. With sodium methoxide (ca. 15 mol%), on the other hand, the reaction was completed within 1.5 hr. These were observed by following the change of IR spectra of the reaction mixtures.
- 7) C. W. Whitehead and J. J. Traverso, *J. Amer. Chem. Soc.*, **77**, 5872 (1955).
- 8) G. M. Filho and J. G. da Cosa, *Anais escola super. quim. Univ. Recife*, **1**, No. 1, 41 (1959); *Chem. Abstr.*, **55**, 3601 (1961).