The Mechanism of Decomposition of Some *p*-Nitrobenzoic Benzylcarbonic Anhydrides[1]

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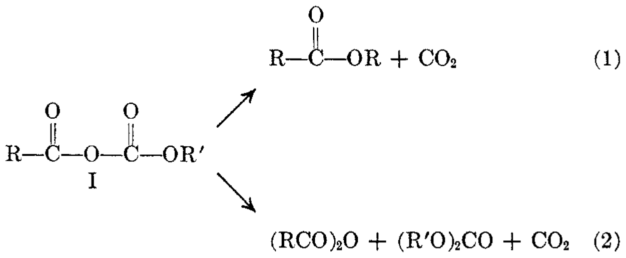
Benzylcarbonic *p*-nitrobenzoic anhydride (IV) and the following substituted benzyl compounds have been synthesized: *p*-nitro (V), *p*-methoxy (VI), and 2,4,6-trimethyl (VII). The *p*-methoxy compound was prepared by carbonation of sodium *p*-methoxybenzoxide, followed by treatment of the carbonate with *p*-nitrobenzoyl chloride. The anhydrides decompose with heat to yield principally the corresponding esters and carbon dioxide. The rates of decomposition of IV, VI, and VII have been measured in DMF and *o*-dichlorobenzene; the *p*-methoxy compound reacts most rapidly, and the activation parameters, which have been determined for all three anhydrides in at least one solvent, are characterized by large, negative entropies of activation (-19 to -33 eu). There is a rate increase for the *p*-methoxy compound of 40 (at 54°) in going from *o*-dichlorobenzene to DMF. The rate for VI is increased in DMF by several nucleophiles; DABCO and sodium benzoate are the most active catalysts, and the rate increases linearly with the concentration of the catalyst. The halides, $(CH_3)_4NX$, also are catalysts, the rate effect being in the order $Cl > Br > I$. Lithium chloride is a better catalyst than $(CH_3)_4NCl$. Oxygen-18 labeling experiments showed that the benzyl compound IV underwent no alkyl oxygen cleavage under any conditions examined; the *p*-methoxy compound, however, shows mainly alkyl oxygen cleavage in dichlorobenzene at 120°, but, in DMF, or in dichlorobenzene with Dabco as catalyst, acyl oxygen cleavage is the principal path.

It was shown earlier that carboxylic carbonic anhydrides decomposed to yield two types of products:[2,3] esters (path 1), and symmetrical anhydrides and carbonates (path 2). In general, the ratio of 1 to 2 was not greatly affected by changes in concentration, temperature, and presence of catalysts, although high concentrations of boron trifluoride were found to favor ester formation.[3c] Stereochemical[3] and O^{18} labeling studies[4] showed that, when R′ was a secondary alkyl group, there was no cleavage of the alkyl oxygen in the decomposition of the mixed anhydride I. Qualitative and quantitative observations[3] suggested that the decomposition of I occurred through a series of ionic chain reactions.



$$R{-}C(=O){-}O{-}C(=O){-}OR' \;\; (\mathrm{I}) \longrightarrow R{-}C(=O){-}OR + CO_2 \qquad (1)$$

$$\longrightarrow (RCO)_2O + (R'O)_2CO + CO_2 \qquad (2)$$

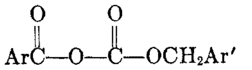
A study of *p*-nitrobenzoic *t*-butylcarbonic anhydride[5] (II) indicated that it decomposed by alkyl oxygen cleavage to give isobutene and other products formed from the *t*-butyl carbonium ion. However, III, the sulfur analog[6] of II, gave a quantitative yield of the thiol ester with no detectable alkyl sulfur cleavage, a result which emphasizes the slow rate of carbon–sulfur cleavage compared with carbon–oxygen cleavage in many reactions.

$$\underset{\mathrm{II}}{ArCOOCOOC(CH_3)_3} \longrightarrow ArCOOCOO^- + {}^+C[CH_3]_3$$

$$Ar = p\text{-}NO_2C_6H_4$$

$$\underset{\mathrm{III}}{ArCOOCOSC(CH_3)_3} \longrightarrow ArCOSC(CH_3)_3 + CO_2$$

The object of the present work was to examine the behavior of a series of benzylcarbonic anhydrides (IV–VII) which might be expected to show alkyl oxygen cleavage.



$$ArC(=O){-}O{-}C(=O){-}OCH_2Ar'$$

IV, Ar = p-$NO_2C_6H_4$; Ar′ = C_6H_5
V, Ar = p-$NO_2C_6H_4$; Ar′ = p-$NO_2C_6H_4$
VI, Ar = p-$NO_2C_6H_4$; Ar′ = p-$CH_3OC_6H_4$
VII, Ar = p-$NO_2C_6H_4$; Ar′ = 2,4,6-$(CH_3)_3C_6H_2$

The mixed anhydrides studied were derived from *p*-nitrobenzoic acid, because these could be purified by crystallization. Anhydrides IV and V were prepared by the usual chlorocarbonate procedure; this was not practical with VI because of the instability of *p*-methoxybenzyl chlorocarbonate.[7] The anhydrides IV, VI, and VII were readily obtained by the carbonation procedure previously used[5] to prepare the *t*-butyl derivative II.

$$HOCH_2Ar' \xrightarrow{NaH} NaOCH_2Ar' \xrightarrow[THF]{CO_2}$$

$$NaOCOCH_2Ar' \xrightarrow{ArCOCl} ArCOOCOOCH_2Ar'$$

The anhydrides IV, V, and VII decomposed mainly by path 1, based on the amount of carbon dioxide evolved and the amount of ester isolated; small amounts of *p*-nitrobenzoic anhydride were also formed. The data are in Table I. Anhydride V apparently yielded a mixture of ester and path 2 products, but pure materials could not be isolated.

Oxygen-18 Labeling Studies.—*p*-Methoxybenzyl alcohol was labeled with O^{18} by acid-catalyzed exchange[8] with water containing excess O^{18}. The O^{18} content in the alcohol was checked by conversion to the unstable chlorocarbonate, followed by decomposition[4,9] and analysis of the liberated carbon dioxide by mass spectrometry.

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[1] Supported by Grant GP-4961 from the National Science Foundation.

[2] D. S. Tarbell and N. A. Leister, *J. Org. Chem.*, **23**, 1149 (1958).

[3] (a) D. S. Tarbell and E. J. Longosz, *ibid.*, **24**, 774 (1959); (b) *ibid.*, **26**, 2161 (1961); (c) T. B. Windholz, *ibid.*, **25**, 1703 (1960).

[4] C. J. Michejda, D. S. Tarbell, and W. H. Saunders, Jr., *J. Am. Chem. Soc.*, **84**, 4113 (1962).

[5] C. J. Michejda and D. S. Tarbell, *J. Org. Chem.*, **29**, 1168 (1964).

[6] D. S. Tarbell and T. Parasaran, *ibid.*, **29**, 2471 (1964).

[7] *Cf.* K. B. Wiberg and T. M. Shryne, *J. Am. Chem. Soc.*, **77**, 2774 (1955).

[8] A. G. Davies, *J. Chem. Soc.*, 3474 (1958).

[9] P. Carré, *Bull. Soc. Chim. France*, [5] **3**, 1064 (1936).

TABLE I

DECOMPOSITION OF *p*-NITROBENZOIC BENZYLCARBONIC ANHYDRIDES (p-$NO_2C_6H_4CO_2CO_2Ar'$) WITHOUT SOLVENT

Compd (no.)	Temp, °C	% CO_2	% path 1 predicted	% ester isolated	% $(ArCO)_2O$ found
$C_6H_5CH_2$ (IV)	160 ± 5	89 ± 6	78	87	6–10
p-$CH_3OC_6H_4CH_2$ (VI)	140 ± 0.5	94 ± 6	88	95	Trace
p-$CH_3OC_6H_4CH_2$	110 ± 5	95 ± 3	90	76	4
2,4,6-$(CH_3)_3C_6H_2CH_2$ (VII)	100 ± 3	90 ± 5	80	79	3
p-$NO_2C_6H_4CH_2$ (V)	120 ± 5	75 ± 3	50	. .	. . .

TABLE II

OXYGEN-18 ANALYSES OF CARBON DIOXIDE FROM LABELED *p*-NITROBENZOIC BENZYLCARBONIC ANHYDRIDES

Compd (no.)	Source of CO_2 reaction	Procedure	100 (mass 46/ mass 44)	% excess oxygen-18
Natural abundance (calcd[a])			0.4018	
Dry Ice		Obsd	(Av) 0.401	0.0
p-$CH_3OC_6H_4CH_2O^*COCl$	Neat, room temp	*b*	1.154	
			1.151	
			(Av) 1.153	100
$ArCOOCOO^*CH_2C_6H_4OCH_3$-$p$ (VI)	Neat, 100–125°	*b*	0.910	68
			0.928	70
			0.908	67
VI*	In *o*-dichlorobenzene at 88°	*c*	1.000	80
			1.000	80
			1.000[d]	80
			0.994[d]	79
VI*	In *o*-dichlorobenzene at 120°	*c*	1.014	82
			1.030	82
VI*	In *o*-dichlorobenzene + DABCO[d] at room temp	*c*	0.417	2.1
			0.419	2.4
			0.429	3.7
VI*	In DMF[e] at room temp	*b*	0.490	11.8
			0.499	13.0
			0.498	12.9
VI*	In DMF + DABCO at room temp	*b*	0.434	4.4
			0.439	5.1
$C_6H_5CH_2O^*COCl$	Neat, 140°	*c*	1.610	
	Neat, 110°	*c*	1.643	
			1.597	
			1.594	
			(Av) 1.611	100.0
$ArCOOCOO^*CH_2C_6H_5$ (IV)	Neat, 140–150°	*b*	0.424	1.9
			0.425	2.0
IV*	In DMF at 80°	*c*	0.417	1.3
			0.417	1.3
IV*	In *o*-dichlorobenzene at 140°	*c*	0.440	3.2
			0.434	2.7
IV*	In *o*-dichlorobenzene + $C_6H_5COOC_6H_5$ at 150°	*c*	0.433	2.6
			0.434	2.7

[a] J. H. Beynon, "Mass Spectrometry and its Applications to Organic Chemistry," Elsevier Publishing Co., New York, N. Y., 1962. [b] Procedure is described in the Experimental Section (a). [c] Procedure is described in the Experimental Section (b). [d] The reaction was stopped at 25% completion. [d] 1,4-Diazobicyclo[2.2.2]octane. [e] N,N-Dimethylformamide.

Benzyl alcohol did not exchange readily with O^{18}-labeled water and was therefore prepared by exchanging benzaldehyde[4,10] with isotopic water, followed by hydride reduction. The labeled alcohol was converted to the chlorocarbonate, and the carbon dioxide obtained by decomposition was analyzed for isotopic composition. The remainder of the labeled alcohol was converted to the mixed anhydride *via* the carbonation of the alkoxide.

The possibility that there was oxygen scrambling during the carbonation of the sodium benzyl oxide was disproved by the very low percentage of excess O^{18} found in the carbon dioxide evolved when the labeled mixed anhydride IV was decomposed (Table II). If there had been appreciable scrambling during carbonation, the species $ArCOO^*CO^*OCH_2Ar'$ would have had excess O^{18} in the asterisked positions, and the carbon dioxide liberated would have had an excess of O^{18}.

The possibility of O^{18} scrambling in the labeled *p*-methoxybenzyl compound IV by a dissociation–recombination process[11] was ruled out by an experiment in which the labeled mixed anhydride VI was allowed to decompose to 25% completion in *o*-dichlorobenzene at 88°. The unreacted mixed anhydride, recovered from the incomplete reaction, was then decomposed in the presence of DABCO; it gave carbon dioxide which contained 3% excess of O^{18}. Thus the O^{18} was not in a position where it could form carbon

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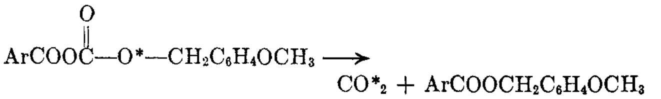
(10) C. A. Bunton, A. Konasiewicz, and D. R. Llewellyn, *J. Chem. Soc.*, 604 (1955).

(11) *Cf.* H. L. Goering, M. M. Pombo, and K. D. McMichael, *J. Am. Chem. Soc.*, **85**, 965 (1963), and earlier papers.

dioxide, and hence there had been no equilibration to form ArCOO*CO*OAr′.

Table II shows that in *o*-dichlorobenzene solution, or neat, VI decomposes mainly by alkyl oxygen cleavage. In *o*-dichlorobenzene at room temperature with



$$\mathrm{ArCOO\overset{O}{\overset{\|}{C}}{-}O^{*}{-}CH_2C_6H_4OCH_3 \longrightarrow CO^{*}_2 + ArCOOCH_2C_6H_4OCH_3}$$

DABCO as catalyst, and similarly with DABCO in DMF solution at room temperature, acyl oxygen cleavage is the main reaction path. The reaction thus takes an entirely different course in dichlorobenzene without catalyst; the more polar solvent DMF and the basic catalyst DABCO give mainly acyl oxygen cleavage.

The benzylcarbonic anhydride IV gives almost no alkyl oxygen cleavage under any conditions investigated; acyl oxygen cleavage is the only important reaction course.

Mass spectrometric examination of the benzyl *p*-nitrobenzoate from the O^{18}-labeled anhydride IV* showed that the ester contained excess O^{18} (see the Experimental Section).

Kinetic Studies.—The kinetics of decomposition of the benzylcarbonic anhydrides IV, VI, and VII were investigated, the *p*-methoxybenzyl compound VI being studied in most detail.

Data for VI in DMF are given in Table III; these runs gave linear first-order plots over 50–75% of the reaction course, the rate increasing toward the end of the reaction. The yield of carbon dioxide in DMF was similar to that in the absence of solvent (90 ± 5%). When a solution in which one decomposition had been run was used as solvent for a second run, the rate of the second decomposition was about twice that of the first (*cf.* ref 3b). The ester, *p*-methoxybenzyl *p*-nitrobenzoate, exhibited a slight catalytic effect on the decomposition of VI, but not enough to account for the rate increase in the reused solution.

TABLE III

RATES OF THE DECOMPOSITION OF *p*-NITROBENZOIC *p*-METHOXYBENZYLCARBONIC ANHYDRIDE

Temp, °C	Concn, mole/l.	10^4k_1, sec^{-1}
	In DMF	
32.0 ± 0.1	0.05	1.68
	0.05	1.79
	0.11	1.64
	0.11	1.62
	Av	1.68 ± 0.08
40.0 ± 0.1	0.05	2.92
	0.05	3.05
	Av	2.99 ± 0.09
47.5 ± 0.2	0.08	5.50
	0.08	5.60
	0.05	5.66
	0.07	5.78
	Av	5.64 ± 0.11
54.0 ± 0.2	0.06	8.80
	0.06	8.61
	Av	8.71 ± 0.13
	In *o*-Dichlorobenzene	
80.0 ± 0.3	0.08	1.86
	0.045	1.90
	Av	1.88 ± 0.03
87.0 ± 0.3	0.04	2.98
	0.043	2.93
	Av	2.96 ± 0.04
97.0 ± 0.3	0.054	6.22
	0.053	6.50
	Av	6.36 ± 0.20
54.0 (extrapolated)		0.220

It is apparent from Table III that the rate was reasonably reproducible and that the first-order rate constant was not changed by a twofold change in concentration. The Arrhenius plot gave a good straight line; the activation parameters are collected in Table IV.

TABLE IV

ACTIVATION PARAMETERS FOR DECOMPOSITION OF $p\text{-}O_2NC_6H_4COOCOOCH_2Ar$

Ar	Solvent	$\Delta E^{\ddagger}$, kcal/mole	$\Delta S^{\ddagger}$, (at 25°), eu
C_6H_5	DMF	15.1 ± 1.0	−32.8 ± 2.8
$p\text{-}CH_3OC_6H_4$	DMF	15.0 ± 0.3	−28.7 ± 0.8
$p\text{-}CH_3OC_6H_4$	DCB[a]	18.7 ± 0.6	−24.7 ± 1.7
$2,4,6\text{-}(CH_3)_3C_6H_2$	DCB	21.0 ± 0.6	−19.4 ± 1.5

[a] DCB is *o*-dichlorobenzene.

The rate of decomposition of VI in *o*-dichlorobenzene (Table III) was slower than in DMF by a factor of about 40 at 54°. The carbon dioxide evolution was 85 ± 11%.

The effect of various catalysts on the rate of decomposition of the *p*-methoxybenzyl compound in DMF is shown in Table V. The effect of the most active catalysts, DABCO and sodium benzoate, is proportional to their concentration, except at high concentrations of DABCO. The greater activity of the latter compared to that of triethylamine is presumably due to greater accessibility of basic nitrogens in DABCO. Pyrazine and imidazole show negligible and negative catalytic activity, respectively. The lack of catalytic effect of hydrogen chloride, which was a strong catalyst in dibutylcarbitol solution with benzoic butylcarbonic

TABLE V

EFFECT OF ADDITIVES ON THE DECOMPOSITION OF *p*-NITROBENZOIC *p*-METHOXYBENZYLCARBONIC ANHYDRIDE (VI) IN DMF AT 32.0°

Additive	Mole %	Relative rate
None[a]		1.0
DABCO	0.4	2.5
	1.0	4.2
	2.0	9.0
	5.0	28.3
C_6H_5COONa	0.1	1.9
	0.5	3.5
	2.5	13.8
NEt_3	9.7	2.3
	15.4	3.8
Pyrazine	7	1.3
SbF_3	43	1.0
HCl	21	0.7
Imidazole	10	0.7
NMe_4Cl	1.5	1.5
	10	3.2
NMe_4Br	10	2.6
NMe_4I	10	2.2
LiCl	10	3.7

[a] Initial concentration of mixed anhydride was 0.07 mole/l.

anhydride,[3b] is probably due to the basic nature of DMF which binds hydrogen chloride so firmly that it does not affect the anhydride.[12] The same explanation accounts for the lack of activity of antimony trifluoride. The differences in catalytic activity between the tetramethylammonium halides are not large, but are in the order expected for nucleophilic activity in aprotic solvents[13] (chloride > bromide > iodide). The greater effectiveness of lithium chloride compared to that of tetramethylammonium chloride is due doubtless to the more effective solvation of the lithium ion by DMF.[14]

The decomposition of the anhydride was slightly retarded by tosyl chloride and was unaffected by lithium perchlorate.

The reactions in Table V showed good first-order kinetics for 35–60% of the reaction.

It may be concluded that the decomposition of the anhydride to the ester in DMF is catalyzed by nucleophiles such as halide ions, amines, and carboxylate ions, and that the variations in catalytic activity can be reasonably explained.

The decomposition of p-nitrobenzoic 2,4,6-trimethylbenzylcarbonic anhydride (VII) in o-dichlorobenzene gave the ester and 90 ± 3% of the theoretical amount of carbon dioxide. The reaction gave excellent first-order plots, over 80–90% of the reaction. The (extrapolated) first-order rate constant at 54.0° is 0.082×10^{-4} sec^{-1}, compared to 0.220×10^{-4} for the p-methoxy compound, in the same solvent.

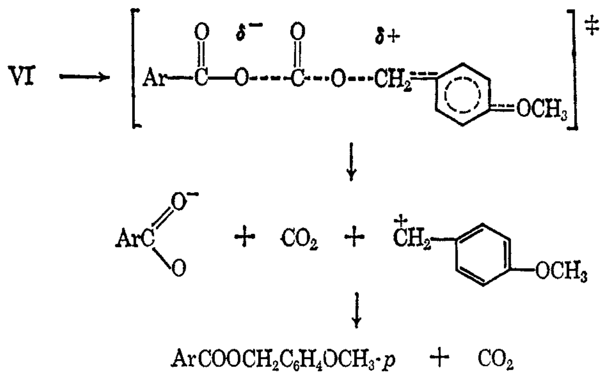
The decomposition of p-nitrobenzoic benzylcarbonic anhydride (IV) in DMF was slower than that of the p-methoxy analog by a factor of about 8 at 54°, and the rate constants were erratic from one run to another, even though care was taken to purify the solvent and to clean the glass reaction flask. Hence the activation parameters in Table IV for the benzyl compound are not so reliable as those for the other compounds.

In o-dichlorobenzene, the benzyl compound decomposed slowly at 140°, with an induction period of about 50 min, during which about 10% of the total amount of carbon dioxide was evolved; the initial first-order rate constant was 3×10^{-5} sec^{-1}, and the rate increased two- to fourfold during the course of the reaction. The reaction was 95% complete in about 240 min. The presence of 5% of benzoyl peroxide retarded the reaction so much that no accurate rate measurement was possible at 140°, and there was little change after 5 hr. Phenyl benzoate had a similar retarding effect. Clearly, the decomposition reaction of the benzylcarbonic anhydride in o-dichlorobenzene was different in character from the other reactions studied. At 100° the decomposition of the benzyl compound IV in o-dichlorobenzene was too slow to measure, but, in the presence of 0.064% DABCO, the reaction was accelerated so much that 95% of the carbon dioxide was collected in 18 min.

In DMF the benzyl compound IV also showed a 22–28-fold rate increase in the presence of 10 mole % of lithium chloride; the corresponding figure for the p-methoxy compound (Table V) was 3.7.

Discussion

It is well established that the introduction of a p-methoxyl group in a benzyl ester promotes heterolysis of the benzyl oxygen bond.[15] In o-dichlorobenzene solution or without solvent, the p-methoxybenzylcarbonic anhydride was shown by the O^{18} experiments to undergo mainly alkyl oxygen cleavage. This suggests a transition state as below; the large, negative entropy of activation must mean a high degree of solvation of the transition state, or the loss of considerable rotational freedom. This concerted mechanism is in agreement with the observation that O^{18} did not become scrambled in the unreacted anhydride, when the labeled VI was allowed to decompose to 25% of completion in o-dichlorobenzene.[16]



The acyl oxygen cleavage reactions of the p-methoxy compound in DMF, and the nucleophile-catalyzed reactions may be provisionally regarded as going through the set of ionic chain reactions postulated previously.[3b]

Experimental Section[17]

Preparation of p-Nitrobenzoic Benzylcarbonic Anhydrides by the Chlorocarbonate Method.[3a] A. p-Nitrobenzoic Benzylcarbonic Anhydride (IV).—In a flash equipped with a stirrer and an addition funnel was placed 200 ml of anhydrous ether, 3.4 g (0.02 mole) of p-nitrobenzoic acid, and 3.4 g (0.02 mole) of benzyl chlorocarbonate (Columbia Organic Chemicals). The mixture was chilled at −78° with a Dry Ice-acetone bath, and was stirred vigorously. Freshly distilled triethylamine (2 g, 0.02 mole) in 10 ml of ether was added dropwise over a period of *ca.* 1 hr. After 2 additional hr at −10°, the mixture was filtered to remove the amine hydrochloride, which was obtained in 96% yield. The ether solution was thoroughly washed with 0.5 N hydrochloric acid, 2% sodium bicarbonate, and ice water and dried. Approximately half of the ether was evaporated at 0°, and petroleum ether (bp 30–60°) was added to yield 3.8 g (63%) of solid material which melted at 60–65°. After several recrystallizations from chloroform and petroleum ether, it melted at 64.5–66°. The ultraviolet spectrum in ethanol showed λ_{max} 256 mμ (ϵ 1.41×10^4). The infrared spectrum had the following characteristic peaks (cm^{-1}, in chloroform): 1812 s, 1747 s, 1610 w, 1530 m, 1460 w, 1350 m, 1322 w, 1285 w, 1170 s, 1070 s, 965 s, 872 m, 855 m.

Anal. Calcd for $C_{15}H_{11}NO_6$: C, 59.80; H, 3.68. Found: C, 59.83; H, 3.95.

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[12] Hydrogen chloride has a dissociation constant of 2.83×10^{-4} in DMF: A. B. Thomas and E. G. Rochow, *J. Am. Chem. Soc.*, **79**, 1843 (1957).

[13] *Cf.* A. J. Parker, *J. Chem. Soc.*, 1328 (1961); S. Winstein, L. G. Savedoff, S. Smith, I. D. R. Stevens, and J. S. Gall, *Tetrahedron Letters*, No. 9, 24 (1960).

[14] H. E. Zaugg, B. W. Horrom, and S. Borgwardt, *J. Am. Chem. Soc.*, **82**, 2895 (1960).

[15] A. G. Davies and J. Kenyon, *Quart. Rev.* (London), **9**, 203 (1955). M. P. Balfe, *et al.*, *J. Chem. Soc.*, 797 (1946); 605 (1942).

[16] For somewhat analogous decomposition reactions, see S. J. Rhoads and R. E. Michel, *J. Am. Chem. Soc.*, **85**, 585 (1963), for alkyl chloroglyoxalates; W. L. Olivier and W. G. Young, *ibid.*, **81**, 5811 (1959) for butenyl chloroformates; and J. L. Kice, R. A. Bartsch, M. A. Dankleff, and S. L. Schwartz, *ibid.*, **87**, 1734 (1965) for aralkyl thiocarbonates.

[17] Melting points are uncorrected. Analyses were by A. G. Revilla of this laboratory and Micro-Tech Laboratories, Skokie, Ill. Infrared spectra were taken on a Perkin-Elmer Model 421 recording spectrophotometer. Ultraviolet spectra were taken on a Cary recording spectrophotometer, Model 11 MS. We are indebted to Dr. L. D. Colebrook for the nmr spectra.

B. *p*-Nitrobenzoic *p*-Nitrobenzylcarbonic Anhydride (V).—This was prepared by the same procedure, except that 150 ml of ethyl acetate was added to dissolve the anhydride prior to the filtration; the product was obtained in 65% yield. After repeatedly dissolving in *o*-dichlorobenzene and reprecipitating by the addition of petroleum ether, it melted at 101–104° dec in a vacuum-sealed capillary tube. Its infrared spectrum exhibited the following absorptions (cm^{-1}, in chloroform): 1815 s, 1752 s, 1610 s, 1528 s, 1458 w, 1350 s, 1320 m, 1270 m, 1181 s, 1167 s, 1070 s, 990 s, 850 m. The ultraviolet spectrum in ethanol gave $\lambda_{\max}$ 262 mμ (ϵ 2.21 × 10^4).

Anal. Calcd for $C_{15}H_{10}N_2O_8$: C, 52.03; H, 2.91; N, 8.09. Found: C, 52.30; H, 2.95; N, 8.35.

Preparation of Mixed Anhydrides by the Carbonate Procedure. A. *p*-Nitrobenzoic *p*-Methoxybenzylcarbonic Anhydride (VI).—A mixture of 27 g (0.2 mole) of distilled anisyl alcohol and 11 g of sodium hydride (51% purity) in 120 ml of tetrahydrofuran (THF)[18] was refluxed on a steam bath for 3–4 hr. The mixture was then chilled in an ice–salt bath, and dry carbon dioxide was passed into the mixture. After a few minutes, the mixture began to gel. The addition of carbon dioxide continued for *ca.* 30 min. Tetrahydrofuran (90 ml) was added to dilute the gel, and 37 g (0.2 moles) of *p*-nitrobenzoyl chloride in 100 ml of chloroform was added dropwise. The mixture was stirred vigorously for 3 hr at −10 to 0° and was then filtered with the aid of a filter aid (Celite). The filtrate was washed more than ten times with ice water and dried thoroughly over magnesium sulfate. The addition of petroleum ether yielded a yellow solid (40.8 g, 62%), which melted at 86–88°. After several recrystallizations from chloroform and petroleum ether, it melted at 89–90°. The infrared spectrum in chloroform showed the following peaks (cm^{-1}): 1807 s, 1745 s, 1610 m, 1585 w, 1530 s, 1515 m, 1462 m, 1350 m, 1320 m, 1304 w, 1285 w, 1252 m, 1182 s, 1164 s, 1110 w, 1070 s, 1032 w, 1012 w, 960 m, 870 w, 850 m. Its ultraviolet absorption was at $\lambda_{\max}$ 259 mμ (ϵ 1.24 × 10^4) (in ethanol) and $\lambda_{\max}$ 260 mμ (ϵ 1.56 × 10^4) (in chloroform). The nmr spectrum had signals at τ 6.20 (3 H), 4.69 (2 H), 3.17–2.52 (multiplet, 4 H), and 1.72 (4 H).

Anal. Calcd for $C_{16}H_{13}NO_7$: C, 58.01; H, 3.96; N, 4.23. Found: C, 57.74; H, 3.92; N, 4.43.

B. *p*-Nitrobenzoic 2,4,6-Trimethylbenzylcarbonic Anhydride (VII).—This was obtained in 25% yield by the carbonate method. Since it was very soluble in chloroform, ether was used to replace chloroform in the procedure described earlier. It melted at 81.5–83°, and its ultraviolet spectrum in ethanol showed $\lambda_{\max}$ 258 mμ (ϵ 1.27 × 10^4). The nmr spectrum had the following signals: τ 7.72 and 7.58 (9 H), 4.50 (2 H), 3.08 (2 H), and 1.72 (4 H). The infrared spectrum exhibited the following characteristic absorptions (cm^{-1}, in chloroform): 1809 s, 1747 s, 1610 m, 1530 s, 1460 w, 1350 m, 1320 w, 1230 w, 1182 s, 1168 s, 1070 s, 1015 m, 965 m, 870 w, 850 m.

Anal. Calcd for $C_{18}H_{17}NO_6$: C, 62.97; H, 4.99; N, 4.08. Found: C, 62.83; H, 5.19; N, 4.31.

C. *p*-Nitrobenzoic Benzylcarbonic Anhydride (IV).—This mixed anhyride was obtained in 52% yield by the carbonate method. This material had a melting point of 64.5–66°, and infrared absorptions at 1812 and 1747 cm^{-1}, identical with those of the sample prepared by the chlorocarbonate method.

Thermal Decomposition of Benzylcarbonic *p*-Nitrobenzoic Anhydrides.—These were carried out by heating the anhydride and collecting the carbon dioxide evolved in ascarite, as previously described.[3a]

The products of decomposition were isolated by chromatography and crystallization and were identified by comparison with known samples.[19]

Preparation of 2,4,6-Trimethylbenzyl *p*-Nitrobenzoate.—A mixture of 1.5 g of mesitylcarbinol and 0.7 g of sodium hydride in 20 ml of THF was heated at reflux for 2 hr. The mixture was cooled and was treated with 1.7 g of *p*-nitrobenzoyl chloride. After 1–2 hr at room temperature, the mixture was filtered, and the solvent was removed under reduced pressure. After recrystallization from ethanol, it yielded 0.0685 g (21%) of the ester, mp 89–90°, whose infrared spectrum in KBr showed the following absorptions (cm^{-1}): 1720 s, 1610 m, 1525 s, 1350 m, 1320 w, 1300 w, 1270 s, 1110 m, 1100 m, 1012 w, 870 w, 850 w, 716 m. The ultraviolet spectrum in ethanol exhibited absorption at $\lambda_{\max}$ 250 mμ (ϵ 1.39 × 10^4). The nmr spectrum had signals at τ 7.72, 7.58 (9 H), 4.51 (2 H), 3.05 (2 H), and 1.82 (4 H).

Anal. Calcd for $C_{17}H_{17}NO_4$: C, 68.21; H, 5.73; N, 4.68. Found: C, 68.32; H, 5.97; N, 4.81.

Preparation of N-*p*-Tolyl *p*-Methoxybenzyl Carbamate.—A carbon tetrachloride solution of approximately equimolar quantities of anisyl alcohol and *p*-tolyl isocyanate was heated on a steam bath for *ca.* 15 min. Addition of petroleum ether to the cold solution yielded the crystalline solid, which after recrystallizations from carbon tetrachloride melted at 87–88°. The analytical sample in KBr showed the following peaks (cm^{-1}): 3340 w, 1730 (shoulder), 1695 s, 1615, 1610 (doublet), 1470 w, 1410 w, 1320 m, 1300 w, 1250 s, 1210 (shoulder), 1180 m, 1060, 1035 (doublet), 820 m, 790 w.

Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.81; H, 6.31; N, 5.30.

Reaction of *p*-Nitrobenzoic *p*-Methoxybenzylcarbonic Anhydride with *p*-Toluidine.—*p*-Toluidine (0.2146 g) in 10 ml of chloroform was added at room temperature to another chloroform solution (10 ml) of 0.6585 g of *p*-nitrobenzoic *p*-methoxybenzylcarbonic anhydride (VI). The reaction was allowed to continue for 0.5 to 1 hr. Solid material, collected by filtration, weighed 0.2979 g, mp 197–203°. The infrared spectrum in KBr exhibited the characteristic amide absorptions at 3320 and 1645 cm^{-1}. The filtrate was extracted with 50 ml of sodium bicarbonate solution and washed with water. The chloroform solution was dried, chromatographed on neutral alumina, and eluted with petroleum ether–ether. There was obtained 0.632 g (12%) of N-*p*-tolyl *p*-methoxybenzoyl carbamate, which melted at 85–88°. Its infrared spectrum was superimposable on that of the authentic sample made above. Another fraction which came off later was identified as the amide and weighed 0.0859 g, which, combined with the amide obtained earlier, gave 0.3838 g (71%) of N-*p*-nitrobenzoyl-*p*-toluidine. Upon recrystallizations from benzene and petroleum ether, it melted[20] at 203.5–204°. The sodium bicarboate extract was neutralized with concentrated hydrochloric acid to yield crude *p*-nitrobenzoic acid melting at 230–240°, which accounted for *ca.* 10%. Similar results were obtained when the reaction was carried out in anhydrous ether instead of chloroform.

Equilibration of Anisyl Alcohol with O^{18}-Enriched Water.[8]—Redistilled anisyl alcohol (5 g) and 20 ml of O^{18}-enriched water (Isomet Corp., 1.6% 0^{18}) were mixed with 50 ml of THF, concentrated sulfuric acid (0.2 ml) was added, and the mixture was heated at reflux for 2 hr. The mixture was allowed to cool to room temperature and solid sodium bicarbonate was added to neutralize the acid. The alcohol was taken up in 150 ml of ether, which was then washed three times with water and dried. The ether solution of labeled anisyl alcohol had a volume of 120 ml.

Preparation of O^{18}-Labeled *p*-Nitrobenzoic *p*-Methoxybenzylcarbonic Anhydride.—One-half (60 ml) of the ether solution of the labeled alcohol was used for the preparation of the mixed anhydride by the carbonate method as above. Pure, crystalline material was obtained in 45% yield based on anisyl alcohol. It melted at 89–90°, and had strong infrared absorptions at 1745 and 1807 cm^{-1}.

Preparation of Labeled *p*-Methoxybenzyl Chlorocarbonate.—In a 50-ml, three-necked flask was placed 30 ml of the ether solution of the labeled alcohol. Ether was distilled off at 0° *in vacuo*. A gas inlet and a Dry Ice condenser protected by a drying tube were fitted onto the flask, which was chilled in a Dry Ice–acetone bath. About 3 ml of phosgene was condensed at −78°, and distilled into the reaction flask. The mixture was stirred vigorously and the temperature was allowed to rise to −30° to −20° by gradually adding water to the Dry Ice–acetone mixture. Stirring was continued for about 1 hr at this temperature, then hydrogen chloride and excess phosgene were removed through a trap containing dilute, aqueous sodium hydroxide solution *in vacuo* at *ca.* −20°. The crude material showed characteristic carbonyl absorption at 1750 cm^{-1} in the infrared spectrum.

Equilibration of Benzaldehyde with O^{18}-Enriched Water.[4]—Benzaldehyde (20.8 g) was mixed with 25 ml of O^{18}-enriched water (Isomet Corp., 1.6% O^{18}), concentrated sulfuric acid (0.2 ml) was added, and the mixture was stirred and heated at 100° for 4 hr. The mixture was then cooled in an ice bath, and solid sodium bicarbonate was added to neutralize the sulfuric acid.

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[18] Purified over potassium hydroxide and lithium aluminum hydride: L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass, 1955, p 292.

[19] Particulars in the Ph.D. Thesis of R. C. L. Chow, University of Rochester, 1966.

[20] The reported value is 203°: P. Grammaticakis, *Bull. Soc. Chim. France*, 1956 (1960).

The aqueous layer was saturated with sodium chloride. Upon separation, it yielded the labeled aldehyde, which was then taken up in 150 ml ether and dried.

The labeled **benzyl alcohol** was obtained by reducing the above labeled aldehyde with lithium aluminum hydride in ether.

Preparation of Labeled *p*-Nitrobenzoic Benzylcarbonic Anhydride and Labeled Benzyl Chlorocarbonate.—The labeled mixed anhydride was prepared by tne carbonate method, starting with the labeled alcohol, in 25% yield based on the benzaldehyde. Its melting point and infrared spectrum were identical with those of the authentic sample.

The labeled benzyl chlorocarbonate was prepared in the usual manner with phosgene, starting with about one quarter of the ether solution of the labeled benzyl alcohol. The ether was removed *in vacuo* before the preparation.

Decomposition of Labeled Chlorocarbonates and Labeled Mixed Anhydrides.—All the decompositons were carried out in the same manner, following one of the two procedures described in this section.

A.—A sample of the labeled compound was weighed and placed in a 10 ml reaction tube fitted with a standard-taper inner joint (12/30), which was connected to a high-vacuum manifold of conventional design. It was degassed to *ca.* 10^{-6} mm. The main valve opening to the mercury diffusion pump was closed, and the reaction was started at a desired temperature. The carbon dioxide evolved was condensed in a liquid nitrogen trap. After the reaction was complete, the carbon dioxide was redistilled at −78° to a sample tube equipped with a high-vacuum stopcock and an inner joint (12/30). The sample was then analyzed for O^{18} on a mass spectrometer.

B.—When the labeled compound was decomposed in a solution and/or at elevated temperature, it was necessary to carry out the reaction in sealed tubes. The reaction vessel was a cylindrical flask (5 × 1.25 in.) equipped with a break seal and a standard-taper inner joint (12/30) in the center outlet, and a section of constriction followed by another inner joint (12/30) on the side arm. In a typical run, 5 ml of the reaction solution was injected into the reaction vessel, which was then attached to the vacuum system. It was degassed several times and sealed at the constriction. The sealed tube was immersed in a constant-temperature bath. When the reaction was complete, the carbon dioxide evolved from the reaction was transferred to the high-vacuum manifold by opening the break seal. The carbon dioxide was redistilled at −78°, and trapped in one of the sample tubes and analyzed on a mass spectrometer.

Mass Spectra Data.—The instrument used for the O^{18} analysis was an Atlas mass spectrometer, Model CH 4. The gas sample was analyzed at a 70-ev ionization potential, 20-μa ionization current, and *ca.* 50-μ sample pressure. Each sample was scanned 20–21 times. Each of the numbers listed in Table II was the average of the ratios measured by the peak height. Generally, the standard deviation between different scans of the same sample was less than 0.5%.[21]

A Controlled Experiment of the Equilibration of the O^{18} Label in the Thermal Decomposition of Labeled *p*-Nitrobenzoic *p*-Methoxybenzylcarbonic Anhydride (VI).—O^{18} labeled *p*-nitrobenzoic *p*-methoxybenzylcarbonic anhydride (0.1667 g) in 5 ml of *o*-dichlorobenzene was allowed to decompose at 88° for 15 min, corresponding to *ca.* 25% reaction. The reaction was arrested by cooling at −78°. The solution, which contained the unreacted mixed anhydride, was degassed thoroughly to remove the carbon dioxide evolved from the thermal decomposition.

To this solution, 0.064 g of DABCO was then added; it was again degassed, and was allowed to decompose in a high-vacuum manifold at room temperature. The carbon dioxide, which was generated in the catalytic decomposition, was analyzed in the usual fashion; it was found to contain 3.8% of the excess O^{18}. This result indicated that there was no equlibration of the label in the thermal decomposition.

Isolation and Analysis of the Product of the Decomposition of Labeled *p*-Nitrobenzoic Benzylcarbonic Anhydride.—Labeled *p*-nitrobenzoic benzylcarbonic anhydride (0.20 g, 0.67 × 10^{-3} mole) was decomposed at 140–150° in the absence of solvent. The residue was fractionally recrystallized from absolute ethanol several times. There was obtained a crystalline material, mp 82–84°, identified as benzyl *p*-nitrobenzoate. This material was evacuated to remove the last trace of solvent in the high-vacuum system for 4–5 hr. It was then analyzed by the mass spectrometer, with an ionization potential of 14 ev and less than 10-μ sample pressures. Results are given in Table VI.

TABLE VI

OXYGEN-18 ANALYSIS OF BENZYL *p*-NITROBENZOATE

Source of the ester	(Mass 259/mass 257) × 100[a]
Natural source	2.07 ± 0.01
	2.04 ± 0.03
Decomposition of IV*	2.97 ± 0.16
	3.11 ± 0.18

[a] The theoretical calculation of the ratio of mass 259 to mass 257 for $C_{14}H_{11}NO_4$ is 1.9566%. Calculated as in footnote *a*, Table III.

Purification of Materials Used in Kinetic Runs. Dimethylformamide (DMF).[12,22]—N,N-Dimethylformamide (Eastman Spectro Grade, 1500 ml) was refluxed with 50 g of barium oxide for *ca.* 5 hr. At the end of the period, it was distilled at 150° (750 mm) into a flask containing 50 g of phosphorus pentoxide. The mixture was stirred vigorously at room temperature overnight. It was then twice distilled *in vacuo* through a glass-helix-packed column (12 × 1 in.), bp 25° (0.8 mm), n^{23}D 1.4274 (lit.[23] n^{25}D 1.4279).

***o*-Dichlorobenzene** (Eastman White Label) was vacuum distilled at 35° (1 mm), $n^{22.5}$D 1.5489 (lit.[24] n^{25}D 1.5491).

Triethylamine was distilled from sodium, bp 89°, n^{29}D 1.3976.[25]

1,4-Diazabicyclo[2.2.2]octane (DABCO) (Aldrich Chemical Co.) was further purified by sublimation *in vacuo*. It melted at 160–161°.[26]

Hydrogen chloride gas was dried by passing it through concentrated sulfuric acid.

Pyrazine was distilled *in vacuo* and melted at 52–52.5°.

Imidazole was recrystallized from benzene and melted at 89.5–90°.

Kinetic Runs.—These were carried out by measuring the rate of carbon dioxide evolution, essentially as described earlier.[3b]

The activation parameters were calculated by the least-squares method on an IBM 650 computer by Mr. C. A. Whiteman.

Isolation of Products of Decomposition of Mixed Anhydride VI in DMF.—In an isolation run, 3.1285 g of *p*-nitrobenzoic *p*-methoxybenzylcarbonic anhydride was heated in 10 ml of DMF at *ca.* 55° for 3 hr; 150 ml of chloroform was then added, and the mixture was washed three times with water and extracted three times with sodium bicarbonate solution. The basic extract was neutralized with concentrated hydrochloric acid to yield 0.3533 g of crude *p*-nitrobenzoic acid. Recrystallization from ethanol-water, and then from methanol, gave 0.1312 g (8.5%) of the pure acid, mp and mmp 240–242° dec. The chloroform extract was washed thoroughly with water and dried; the chloroform was evaporated on the steam bath and 50 ml of petroleum ether was added to the residue. The solution was chilled in an ice bath, giving 1.9252 g (71%) of pure crystalline *p*-methoxybenzyl *p*-nitrobenzoate, mp and mmp 94–95°.

Registry No.—IV, 13137-24-1; labeled IV, 13169-20-5; V, 13144-35-9; VI, 13144-36-0; labeled VI, 13131-55-0; VII, 13131-56-1; 2,4,6-dimethylbenzyl *p*-nitrobenzoate, 13144-37-1; N-*p*-tolyl *p*-methoxybenzyl carbamate, 13144-38-2.

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[21] We are indebted to Mr. C. A. Whiteman for help with the mass spectrometric determinations.

[22] H. E. Zaugg and A. D. Schaefer, *Anal. Chem.*, **36**, 2121 (1964).

[23] R. L. Adelman, *J. Org. Chem.*, **29**, 1837 (1964).

[24] D. R. Dreisback and R. A. Martin, *Ind. Eng. Chem.*, **41**, 2875 (1949).

[25] A. I. Vogel [*J. Chem. Soc.*, 1832 (1948)] reported n^{20}D 1.4010.

[26] The reported melting point [A. Farkas, *et al.*, *J. Chem. Eng. Data*, **4**, 334 (1959)] is 158°.