The Nitrosation of N,O-Dibenzoylhydroxylamine

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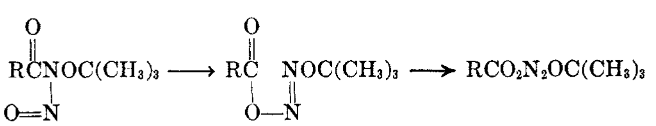
Treatment of N,O-dibenzoylhydroxylamine with alkyl nitrites or nitrosyl chloride gives rise to rapid gas formation and benzoic anhydride in essentially quantitative yield. With the alkyl nitrite reaction the single gaseous product is nitrous oxide. When nitrosyl chloride is used for the nitrosation, the gaseous products include nitrous oxide as well as nitric oxide and nitrogen. Nitrous oxide is rapidly converted into nitrogen and nitric oxide on exposure to solutions containing nitrosyl chloride. Oxygen-18-labeling studies indicate that no symmetrical intermediates intervene in these reactions. Additional oxygen-18-labeling studies indicate that the product arises from a process which allows oxygen atom randomization.

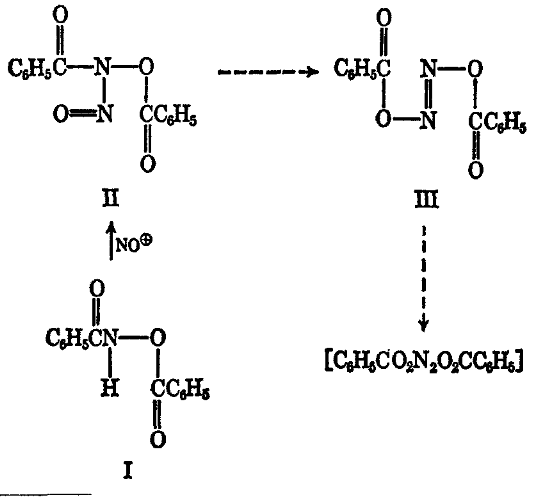
Recent studies[2,3] in these laboratories of the rearrangement and decompositions of N-nitroso-N-acyl-O-*t*-butylhydroxylamines have demonstrated this class of compounds can be used to generate acycloxy-*t*-butoxy radical pairs under mild conditions. The radical-forming step in this sequence is thought to be the concerted homolytic cleavage of the O-acyl-O′-*t*-butyl hyponitrite. Several[4] examples of such radical cleavage reactions are known for dialkyl hyponitrites. Also, it has been reported[5] that treatment of hyponitrous acid with acid chlorides and pyridine at −60° gives compounds, thought to be diacyl hyponitrites, which form radicals when warmed above −20°.



$$\mathrm{R\overset{O}{\overset{\|}{C}}\underset{O=N}{N}OC(CH_3)_3 \longrightarrow R\overset{O}{\overset{\|}{C}}\;\underset{O-N}{\overset{\|}{N}}OC(CH_3)_3 \longrightarrow RCO_2N_2OC(CH_3)_3}$$

We presently wish to report the results of our investigations of the nitrosation of N,O-dibenzoylhydroxylamine (I) which were initiated in the hope of generation benzoyloxy–benzoyloxy radical pairs by an analogous deaminative route (Scheme I).

Scheme I



Results and Discussion

When a suspension of I in chloroform or methylene chloride was treated with amyl nitrite or butyl nitrite, immediate gas evolution was evident and continued for about 2 hr. The yield of evolved gas was essentially quantitative and its mass spectrum identified it as nitrous oxide. Examination of the infrared spectra of the solutions at intermediate times showed no clear indication of any buildup of N-nitroso compound concentration. However, the presence of the alkyl nitrite would make its detection difficult in any case. The final product solution contained essentially a quantitative amount of benzoic anhydride as judged by infrared techniques.

The conversion into benzoic anhydride can also be carried out at 0° or below using nitrosyl chloride and pyridine as the nitrosation agent. Gas formation under these conditions occurred as rapidly as the nitrosyl chloride solution was added. The infrared spectrum of the final solution, after aqueous washing, was identical with that of authentic benzoic anhydride. The yield of this product was greater than 90%.

The gaseous products from the nitrosyl chloride reaction included nitrous oxide, but as a relatively minor component of the product gas mixture. The major components were nitrogen and nitric oxide as indicated by the mass spectrum of the total gas mixture. When air was allowed to come in contact with this mixture, the brown color of nitrogen dioxide was immediately observed. In a separate control experiment, a sample of nitrous oxide containing 0.536 atom % oxygen-18 was condensed into a solution of nitrosyl chloride and pyridine. The evacuated sample tube was shaken for a few minutes and cooled to −80° and the residual gases were analyzed. The mass spectrum of this gas mixture was nearly identical with that observed for the product gases from the nitrosyl chloride reaction. The residual nitrous oxide contained at least 0.50 atom % oxygen-18. It thus appears that the nitrous oxide is formed in this reaction but is unstable in the presence of the nitrosation agent.

While we have no direct evidence that nitrosohydroxylamine II is produced in these reactions, we infer its presence from the formation of nitrous oxide (N–N bond formation) and the close analogy with N-acyl-O-*t*-butylhydroxylamine compounds[2,3] in which the nitroso compound is stable enough to be observed by spectral methods. With this assumption, several

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[1] National Science Foundation Undergraduate Research Participant, summer 1965.

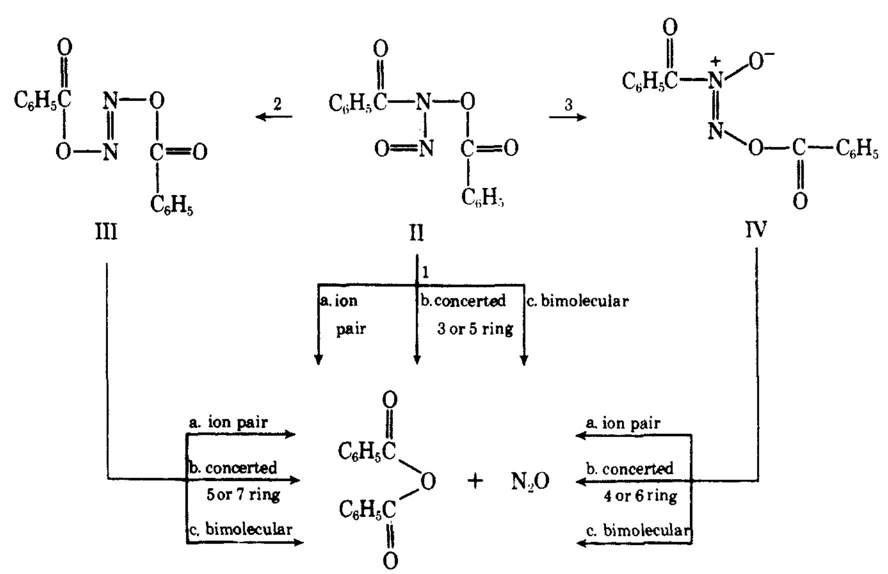
[2] T. Koenig and M. Deinzer, *J. Amer. Chem. Soc.*, **88**, 4518 (1966).

[3] T. Koenig and M. Deinzer, *ibid.*, **90**, 7014 (1968).

[4] T. G. Traylor and H. Kiefer, *ibid.*, **89**, 6667 (1967); S. K. Ho and J. B. de Sousa, *J. Chem. Soc.*, 1788 (1961); T. G. Traylor and H. Kiefer, *Tetrahedron Lett.*, 6163 (1966), and references therein.

[5] A. Mercer and D. A. Scott, British Patent 848,492 (1960); *Chem. Abstr.*, **55**, 5346 (1961).

SCHEME II



possible mechanisms for its conversion into the observed products occurred to us. The nitroso compound II could (1) go directly to product, (2) rearrange to the expected hyponitrite III, or (3) rearrange to azoxy compound IV by a 1,4 O-N acyl migration. Each of these intermediates (II, III, or IV) could be giving product formation by (a) acylium-acylate ion-pair formation, (b) two separate concerted processes involving cyclic transition states of different ring sizes, or (c) a bimolecular chain process involving attack by benzoate ion or benzoic acid. These possibilities are summarized in Scheme II.[6] The rates of these reactions are too fast for kinetic studies to be useful. A reduction in the number of possible mechanistic paths is possible using oxygen-18-labeling techniques. The expectations for the operation of the several mechanisms listed in Scheme II are summarized in Table I.

TABLE I

PREDICTED[a] OXYGEN-18-LABELING PATTERNS

Mechanism	N_2O[b]	Carbonyl[c]	Alkyl[d]	Amide[e]	Acid[f]
1a	0.00	0.25	0.50	25	75
1b (5 ring)	0.00	0.00	1.00	0	100
1b (3 ring)	0.00	0.50	0.00	50	50
1c	0.00	0.25	0.50	25	75
2a	0.50	0.375	0.250	37.5	62.5
2b (7 ring)	0.50	0.250	0.500	25	75
2b (5 ring)	0.50	0.500	0.000	50	50
2c	0.50	0.375	0.250	37.5	62.5
3a	1.00	0.250	0.500	25	75
3b (6 ring)	1.00	0.000	1.000	0	100
3b (4 ring)	1.00	0.500	0.000	50	50
3c	1.00	0.250	0.500	25	75

[a] Assuming no reversible preequilibria and with symmetry scrambling in the anhydride considered. [b] Fraction of oxygen-18 in the original hydroxylamine oxygen atom. [c] Fraction of oxygen-18 label, originally in the carbonyl position of the O-benzoyl group, expected in each carbonyl group of the anhydride. [d] Fraction of the oxygen-18 label, originally in the carbonyl position of the O-benzoyl group, expected in the alkyl position of the anhydride product. [e] Per cent of the total label expected in benzamide after ammonolysis of the anhydride. [f] Per cent of the total label expected in the benzoic acid after ammonolysis of the anhydride.

The two different types of labeling experiments considered are given in Table I. The nitrous oxide predictions are made for starting material which is labeled in the hydroxylamine oxygen atom. The small amount of excess label which finally remained in the synthetic sample of that compound is due to the exchange of the nitrite during the reduction with bisulfite. The predictions which are made for the labeling pattern in the anhydride are based on starting material which was labeled in the carbonyl position of the O-benzoyl group. The sensitivity of the experiments is increased with the larger fraction of excess oxygen-18 which could be incorporated into this compound.

The results of the reaction of labeled I, obtained from oxygen-18-enriched hydroxylamine, are summarized in Table II. The interpretation of the oxygen-18 content of the nitrous oxide from the nitrosyl chloride reaction is complicated by the secondary reaction of the product with the nitrosation agent. However, the control experiment with oxygen-18-enriched nitrous oxide, which was recovered after exposure to the nitrosation conditions (during which it was largely converted into nitrogen and nitric oxide), indicates that little oxygen-18 is lost during this process. The results with both reactions are thus suggestive of a direct mechanism (1a, 1b, or 1c) which does not involve either III or IV.

TABLE II

OXYGEN-18 RESULTS[a] FROM $C_6H_5CONH^{18}OCOC_6H_5$

Starting material[b]	Nitrous oxide[c]	Nitrous oxide[d]
0.306	0.000	0.005
0.303	0.003	0.000

[a] Atom per cent excess oxygen-18 per molecule, from corrected 46/44 mass spectral peak intensity ratios. [b] As carbon dioxide after combustion. [c] Amyl nitrite reaction. [d] Nitrosyl chloride reaction. A large amount of nitric oxide was present.

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[6] We do not include the formal possibility of radical pair formation and efficient cage recombination which would give the same oxygen-18 results as a in each case since no trace of carbon dioxide is produced in these reactions.

In order to distinguish between the concerted modes (1b) and ion pair (1a) or bimolecular (1c) modes of product formation, the reactions were carried out with oxygen-18-enriched I which was obtained from benzhydroxamic acid and benzyl-^{18}O chloride. The product solutions containing the anhydride were divided into two portions. One was quickly evaporated and added to refluxing anhydrous ammonia.[7] The resulting benzoic acid and benzamide were isolated, purified, and subjected to oxygen-18 analysis. Benzoic anhydride was isolated from the second portion of the original solution, purified, and its oxygen-18 content determined. These results are summarized in Table III (and Table IV).

TABLE III

OXYGEN-18 RESULTS[a] USING $C_6H_5CONHOC^{18}OC_6H_5$

Labeled I	Anhydride	Acid (%)[b]	Amide (%)[b]
	A. *n*-Butyl Nitrite Reaction		
1.22	1.19	0.84 (72)	0.33 (28)
1.19		0.82	0.33
	B. Nitrosyl Chloride Reaction		
1.19	1.19	0.89 (72)	0.33 (28)
1.18		0.88	0.35

[a] Atom per cent excess oxygen-18 per molecule. [b] Average per cent of the sum of the excess oxygen-18 contents of the amide and the acid.

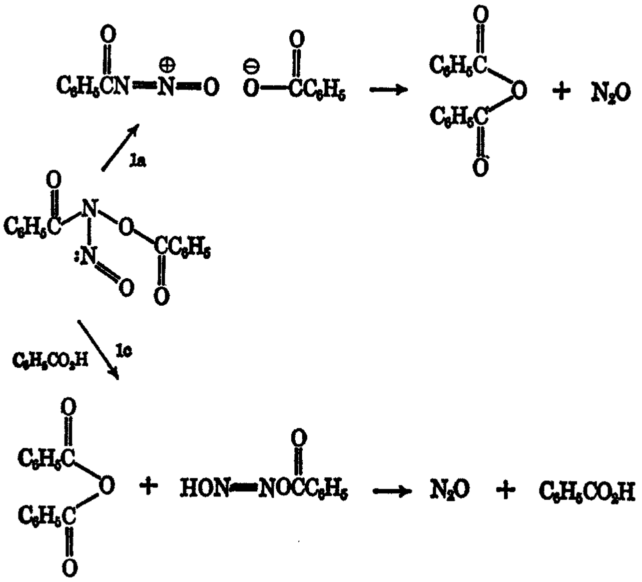
TABLE IV

ANALYTICAL DATA FOR OXYGEN-18 EXPERIMENTS

Compound	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N	Oxygen-18[a]
$C_6H_5CONH^{18}OCOC_6H_5$[b,c]	69.75	4.56	5.81	69.59	4.29	5.69	0.514, 0.504
$C_6H_5CONHOC^{18}OC_6H_5$[b]				69.51	4.68	6.05	0.807, 0.803
$C_6H_5CONHOC^{18}OC_6H_5$[c]				69.66	4.68	5.86	0.815, 0.807, 0.815
$C_6H_5CO_2COC_6H_5$[b]	74.33	4.46		74.19	4.50		0.807
$C_6H_5CO_2COC_6H_5$[c]				74.22	4.47		0.802
$C_6H_5CO_2H$[b,d]	68.85	4.95		68.66	5.08		0.856, 0.846
$C_6H_5CO_2H$[c,d]				68.76	5.01		0.829, 0.820
$C_6H_5CONH_2$[b,d]	69.41	5.82	11.56	69.29	5.98	11.44	0.755, 0.737
$C_6H_5CONH_2$[c,d]				69.41	5.92	11.69	0.738, 0.732

[a] Uncorrected 46:44 mass spectral peak intensity ratio. [b] Nitrosyl chloride reaction. [c] Alkyl nitrite reaction. [d] After ammonolysis.

The column of Table III labeled per cent is the per cent of the sum of the excess oxygen-18 in the acid and the amide. Since the anhydride is symmetrical, a problem exists with the interpretation of these numbers. If the product anhydride were formed with complete randomization of the oxygen atoms of the benzoate group in the starting material, and no postreaction equilibration of the oxygen atom of the N-benzoyl group of the starting compound occurs, then 75% of the total label would be expected in the acid and 25% of the total label would be expected in benzamide. If complete randomization of the oxygen atoms of the anhydride occurs by any mechanism, then the statistical 33% in the amide and 67% in the acid would result. The observed results are closest to the 75:25 prediction and indicate that there is extensive equilibration of the two oxygen atoms of the benzoate group. Thus mechanisms 1a (ion pair formation) or 1c (bimolecular of benzoic acid or benzoate ion) are suggested when the nitrous oxide results are considered.



The present data do not allow a clear distinction between these two possibilities. We presently favor the ion pair process because of the high yields of anhydride product and because no buildup in concentration of N-nitroso compound II could be detected.[8] Some buildup in concentration of II is necessary for the operation of path 1c. Also, the alcohol formed by the alkyl nitrite nitrosation could give esters by a process formally identical with 1c. The infrared spectra of the final product solutions indicated that there was very little if any ester formed during the reaction.

The deviation of the observed oxygen-18 distribution from exact adherance to the 75:25 prediction could be rationalized as resulting from postreaction equilibration of the oxygen atoms of the anhydride. It is also possible to interpret it in terms of some retention of the identity of carbonyl oxygen atom. This

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[7] D. B. Denney and M. Greenbaum, *J. Amer. Chem. Soc.*, **79**, 3701 (1957).

[8] E. M. White and D. W. Grisley, *ibid.*, **83**, 1141 (1961). These authors report, in a footnote, the decomposition products of N-nitroso-N,O-diacetylhydroxylamine.

type of retention has been observed in other deaminative carbonium–acylate ion-pair combinations.[9]

The absence of any radical formation can be simply rationalized by the ionic cleavage of II which is much more rapid than the nitrosoamide rearrangement when acylate is the leaving group. There are acid-catalyzed versions of path 1c which could be operative particularly with the nitrosyl chloride reaction. It should also be noted that the fragmentation could actually be occurring at some intermediate stage in the conversion of I to II, *i.e.*, before the nitrosation step is complete.

We hope to continue investigations of this type with the aim of removing some of the remaining ambiguities associated with the modes of reaction of these compounds.

Experimental Section

Microanalytical data were obtained from Berkeley Microanalytical Laboratoris, Berkeley, Calif. Mass spectra were obtained using a modified Consolidated Electrodynamic Corp. 26-614 residual gas analyzer. Infrared spectra were obtained using a Beckman IR-5 spectrophotometer. The combustion train used in the oxygen-18 analysis of solid samples was modeled after that described by Oliver.[10] Solvents were dried by distillation and stored over molecular sieves. Benzoyl chloride-^{18}O was obtained by hydrolysis of benzotrichloride in oxygen-18-enriched water.[11] Dibenzhydroxamic acid and oxygen-18-enriched dibenzhydroxamic acid were prepared by the method of Hauser.[12]

Hydroxylamine-^{18}O.—Nitrosyl chloride was hydrolyzed in oxygen-18-enriched water containing potassium hydroxide. The resulting potassium nitrite solution was converted into hydroxylamine hydrochloride by reduction with sulfur dioxide and hydrolysis of the disulfonate.[13]

Alkyl Nitrite Nitrosation.—A weighed amount of the hydroxamic acid was suspended in chloroform or methylene chloride at room temperature. The flask was flushed with nitrogen and attached to a gas buret. The system was allowed to equilibrate while stirring for about 0.5 hr. Amyl nitrite or *n*-butyl nitrite was then added rapidly from a pressure-equalizing addition funnel. Gas evolution was immediately apparent and continued for 2–4 hr. The rates of gas evolution were not very reproducible and seemed to depend on the purity of the nitrite used.

The infrared spectra of the final product solutions showed benzoic anhydride was present in essentially quantitative yield by comparison with those of authentic material of known concentration. The isolated yields of crystalline material (mp 43.5–44°) were less than 50%.

Nitrosyl Chloride Reactions.—The procedure in this case was the same except that the dibenzhydroxamic acid suspension was cooled to 0° or below before the gas buret was attached. The nitrosyl chloride was added as a chloroform or methylene chloride solution. The final product solution was washed with cold dilute acid and cold dilute bicarbonate and dried over calcium chloride. The infrared spectra of the resulting solutions were identical with those of authentic benzoic anhydride. The yields in these cases were above 90%.

Gaseous Products.—The gaseous products were identified in separate experiments. For the amyl nitrite reaction, the dibenzhydroxamic acid suspension was added to a flash fitted with a break-seal side arm and cooled to 0°. The amyl nitrite was added and the flask and contents were quickly attached to a vacuum line, cooled to −80° and degassed and sealed under high vacuum. The flask was then warmed to 80° for 1 hr, cooled to −80° and the gaseous product collected on the vacuum train.

For the nitrosyl chloride reaction, a flask with two break-seal chambers was charged first with nitrosyl chloride in chloroform, frozen, evacuated and sealed under high vacuum. Some air probably remained since this solution could not be degassed. The other chamber was charged with the starting material, degassed, and sealed. The seal separating the two was broken and the two reagents were mixed. The material was cooled to −80° and the gaseous products collected on the vacuum line and transferred to a mass spectrometer tube.

Oxygen-18 Experiments.—The procedures for the oxygen-18 labeled compounds were identical with the above. The benzoic anhydride solutions were divided into two fractions. One was evaporated and the residual oil added to refluxing liquid ammonia.[7] The benzoic acid and benzamide which resulted were purified by sublimation. The benzoic anhydride from the second fraction of the original product solution was isolated by recrystallization from petroleum ether (bp 30–60°). The analytical data for these compounds are described in Table IV.

Registry No.—I, 959-32-0; $C_6H_5CONH^{18}OCOC_6H_5$, 18542-85-3; $C_6H_5CONHOC^{18}OC_6H_5$, 18542-86-4; amyl nitrite, 463-04-7; *n*-butyl nitrite, 3681-80-9; nitrosyl chloride, 2696-92-6.

Acknowledgment.—We are grateful to the National Science Foundation for financial support of this work.

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(9) E. M. White and C. A. Aufdermarch, *J. Amer. Chem. Soc.*, **83**, 1179 (1961).

(10) F. H. Oliver, *Analyst*, **80**, 593 (1955).

(11) L. Ponticoryo and D. R. Henberg, *J. Amer. Chem. Soc.*, **76**, 1075 (1954).

(12) C. R. Hauser and W. B. Renfrow, *ibid.*, **59**, 2308 (1937).

(13) G. K. Rollefson and C. F. Oldershaw, *ibid.*, **54**, 977 (1932).