## Nitrosation of 9-Acylamidoxanthenes

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The title compounds (1a-g) react with nitrosating agents at  $-60^{\circ}$  to produce carboxylic acids and xanthone. The reaction is proposed as an alternate approach to carboxylic acid preparation when direct nitrosation of an amide fails. The reaction is shown not to proceed by the usual nitrosoamide decomposition mechanism from the fact that nitrosation of N-(9-xanthyl)benzamide-carbonyl-<sup>18</sup>O produced xanthone containing no oxygen-18 and benzoic acid containing all of the oxygen-18. Mechanism studies were hampered owing to xanthone formation from several substrates. Plausible reaction intermediates were prepared and were found to produce xanthone on nitrosation. Thus attempts to trap intermediates were not successful.

Thermal nitrosoamide decomposition holds an important position in both synthetic and theoretical organic chemistry. Reaction yields are generally good and the products are easily isolated in pure condition. Alkyl nitrosoamides produce esters, acids, diazoalkancs, and olefins as major products. The actual products obtained in a particular reaction depend mainly on the structure of the alkyl group and the solvent polarity.<sup>1</sup>

In attempting to prepare 9-diazothioxanthene, we found that nitrosation of 9-acetylamidothioxanthene at  $-60^{\circ}$  with dinitrogen tetroxide in tetrahydrofuran solution produced only acetic acid and thioxanthone. N-Nitroso-9-acetylamidothioxanthene was not observed. Also, we found that nitrosation of 9-acylamidoxanthenes (1) produced the corresponding carboxylic acid and xanthone (2) as the only products. Although nitrosation of N-unsubstituted amides is a useful method for converting carboxamides to carboxylic acid, the conversion of N-substituted amides into acids by nitrosation is not a generally useful reaction.<sup>1,2</sup> Thus we investigated the nitrosation of 9-acylamidoxanthenes for its synthetic utility. Also, we studied the reaction from a mechanistic point of view, since the facile conversion of 1 into a carboxylic acid and 2 without isolation or detection of a Nnitrosoamide indicated a deviation from the usual nitrosoamide decomposition mechanism.<sup>1</sup> These studies are the subject of this paper.



Nitrosation of the 9-acylamidoxanthenes<sup>3</sup> with nitrous acid, dinitrogen tetroxide, or nitrosyl chloride was successful only for the latter two reagents. Dinitrogen tetroxide was used extensively in the synthetic studies while both dinitrogen tetroxide and nitrosyl chloride were used in the mechanism studies. Reaction yields with nitrosyl chloride were comparable to the yields obtained using dinitrogen tetroxide,

(3) R. F. Phillips and B. M. Pitt, J. Amer. Chem. Soc., 65, 1355 (1943).

but a thorough comparison of the two reagents was not made. Product yields were best when the sodium salt of the 9-acylamidoxanthene was used. The results given in Table I show the yields of carboxylic

TABLE I



<sup>a</sup> Identified by comparison with authentic material. <sup>b</sup> Yields of isolated pure acid. <sup>c</sup> Identity and yield determined by nmr spectroscopy.

acids and xanthone obtained from nitrosation of the 9-acylamidoxanthene N-sodium salt with dinitrogen tetroxide at  $-60^{\circ}$  in tetrahydrofuran solution. We were unable to detect any N-nitroso compound by nmr spectroscopy at low temperatures.<sup>4</sup> We could observe that the carboxylic acid salt and xanthone were formed almost immediately after the addition of dinitrogen tetroxide. Nmr spectroscopy showed that the amount of carboxylic acid salt formed was equal to the amount of xanthone formed. We were able to isolate pure xanthone in good yield (75-99%), but the carboxylic acid was isolated in lower yields (40-62%) despite numerous attempts to improve the isolation procedure. We did not find any other products which would give a quantitative material balance.

Direct nitrosation of carboxamides is generally a good method for preparing carboxylic acids. However, in the event that direct nitrosation fails, the nitrosation of 9-acylamidoxanthenes should be considered as a potentially useful alternate route.

The usual intermediate in nitrosoamide decomposition is a diazo ester formed by the combination of a carboxylate anion and a carbonium ion.<sup>1a</sup> In

(4) R. A. Moss, Tetrahedron Lett., 611 (1961).

 <sup>(</sup>a) E. H. White and D. J. Woodcock, "Chemistry of the Amino Group," S. Patai, Ed., Wiley, New York, N. Y., 1968, Chapter 8; (b) T. J. Lobl, J. Chem. Educ., 49, 730 (1972).

<sup>(2) (</sup>a) C. A. Buehler and D. E. Pearson, "Survey of Organic Synthesis,"
Wiley-Interscience, New York, N. Y., 1970, p 752; (b) B. C. Challis and
J. A. Challis, "The Chemistry of Amides," J. Zabicky, Ed., Wiley, New York,
N. Y., 1970, Chapter 13.

our case the expected diazo ester structure from 1c would be that shown below (A). Diazo ester A could



decompose to the ester 3 and then oxidize to 2. We found, however, that nitrosation of N-(9-xanthyl)benzamide labeled with oxygen-18 in the carbonyl position produced xanthone and benzoic acid with all of the oxygen-18 being retained in the benzoic acid.

This result shows that the normal mechanism for diazo ester production in diazo amide decompositions is not operative in this system. Other methods for forming a diazo ester are possible, however; so we cannot say that a diazo ester is not an intermediate. Ester formation is possible even though we did not detect any ester product. Nitrosation of 9-xanthyl ptoluate (3) produced toluic acid and xanthone, thus showing that 9-xanthyl esters do not survive the reaction conditions.

Attempts to trap free radical diazo,<sup>5</sup> carbenic,<sup>6</sup> free radical,<sup>7</sup> and ionic intermediates<sup>8-10</sup> were unsuccessful, as all attempts produced only xanthone. Nitrosation of some preformed possible intermediates also produced xanthone. Reactions which produced xanthone are summarized in Table II. The main

## TABLE II · XANTHONE-PRODUCING REACTIONS Nitrosating agent Trapping agent Substrate LiClO<sub>4</sub>, NaN<sub>8</sub> 1a $N_2O_4$ (C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>SiH, ethane-1b $N_2O_4$ dithiol, cyclohexene, vinyl acetate, methyl vinyl ketone Xanthylium perchlorate N<sub>2</sub>O<sub>4</sub>, NOCl Xanthylium perchlorate NaN<sub>3</sub> $N_{2}O_{4}$ 9-Chloroxanthene NOCl, N<sub>2</sub>O<sub>1</sub> Xanthydrol $N_2O_4$

problem with these studies is that xanthone is formed easily and in high yield (>80%) from many different substrates and nitrosating agents regardless of the presence of a trapping agent. These reactions may proceed by different mechanisms and thus no firm mechanistic conclusions can be drawn. Further exemplifying this dilemma is the fact that the reaction of 9-chloroxanthene with silver nitrate solution also produced xanthone.

Thus our main mechanistic conclusion based on the oxygen-18 labeling results is that N-nitroso-9-acylamidoxanthenes decompose by a mechanism which

deviates from the usual nitrosomide decomposition mechanism. At present we prefer a mechanism which involves separate carboxylate ions and the stable xanthylium cation.8,11

## **Experimental Section**

All temperature readings are uncorrected. Nmr spectra were obtained on a Varian T-60 instrument. Mass spectral measurements were made on a Varian MAT-111 spectrometer at 70 eV.

Materials.-Pure xanthydrol (mp 122-124°) was obtained after several recrystallizations of commercial xanthydrol from ether-hexane. Urethane and benzamide were obtained from commercial sources. Phenylacetamide (mp 152-154°), ptoluamide (mp 158-159°), 1-naphthamide (mp 186-188°), and triphenylacetamide (mp 244-245°) were obtained from reaction of the corresponding acid chlorides with anhydrous ammonia in dry benzene. Di-*tert*-butylacetamide (mp 109–110°) was obtained by a reported procedure in 44% yield.<sup>15</sup>

9-Acylamidoxanthenes (1a-g) were prepared by the method of Phillips and Pitt.<sup>3</sup> A mixture of freshly recrystallized xanthydrol (0.015 mol) and an amide (0.007 mol) was heated at  $80^\circ$  in 125 ml of glacial acetic acid for 30 min. The mixture was then allowed to stand in a refrigerator overnight, during which the desired material crystallized. Pure material was obtained by recrystallization from 1:1 dioxane-water solution. The remaining filtrate was diluted with water (125 ml) and extracted with ether. Removal of the ether furnished any unreacted amide almost quantitatively. Yields of 1a-g ranged from 20 to 99% (1g, 20%). The nmr spectra (CDCl<sub>s</sub>) of these compounds exhibited complex signals at  $\tau$  2.4-2.6 for the aromatic protons, the amide proton, and the carbinyl proton. Infrared spectra (KBr) showed absorptions at 3300-3460 (NH) and 1640-1690 cm<sup>-1</sup> (C=O). Compounds 1b, 1d, 1f, and 1g are new compounds which gave satisfactory elemental analyses. Observed melting points follow: 1a, 226-228° (224-225°3); 1b, 164-166°; 1c, 224-226° (222-223°8); 1d, 244-245°; 1e, 197-198° (194-195°<sup>3</sup>); 1f, 89-92°; 1g, 83-85°

Nitrosation of 1a-g.—Into a 38  $\times$  150 mm test tube equipped with a drying tube and magnetic stirring bar were placed 50 ml of tetrahydrofuran (distilled from lithium aluminum hydride) and 0.20 g (0.0083 mol) of sodium hydride which had been washed free of mineral oil with anhydrous ether. The 9-acylamidoxanthene (0.006 mol) was added and the mixture was stirred at room temperature overnight, during which the white suspension changed to a yellow solution. A rubber stopper fitted with glass inlet and outlet tubes equipped with calcium chloride drying tubes was inserted into the mouth of the test tube and the mixture was cooled to  $-60^{\circ}$  in a Dry Ice-isopropyl alcohol bath. Dinitrogen tetroxide (0.05 mol) was bubbled into the mixture at  $-60^{\circ}$ . After standing at  $-60^{\circ}$  for 10-15 min, the mixture was poured into 15-20 ml of ice-water and made slightly acidic with dilute hydrochloric acid. The mixture was extracted thoroughly with ether. The dried  $(MgSO_4)$  ether solution was concentrated on a rotary evaporator to produce a mixture of acid and xanthone. The acid was separated by dissolving in sodium bicarbonate solution, acidification, and extraction into ether which after drying and evaporation furnished the pure acid (Table I). The products were identified by comparison with authentic material. Aqueous work-up did not change the outcome of the reaction and made the purification easier. A similar reaction of 1b with dinitrogen tetroxide in an nmr tube at  $-20^{\circ}$  failed to produce evidence for the presence of a N-nitroso function,<sup>4</sup> but showed that the reaction was essentially complete in 5-10 min and the yields were quantitative.

Preparation of 9-Xanthydryl p-Toluate (3).-To a mixture of 3.4 g (0.025 mol) of *p*-toluic acid was added 2 ml (0.028 mol) of thionyl chloride in 50 ml of benzene. The mixture was heated at reflux overnight (10 hr) and the benzene and excess thionyl chloride were removed on a rotary evaporator. The oily product was added to 5.0 g (0.025 mol) of freshly recrystallized xan-

<sup>(5)</sup> J. Hamer, "1,4-Cycloaddition Reactions," J. Hamer, Ed., Academic

<sup>Press, New York, N. Y., 1967, Chapter 1.
(6) W. Kirmse, "Carbene Chemistry," Academic Press, New York, N. Y.,</sup> 1971, Chapter 8.

<sup>(7)</sup> W. A. Pryor, "Free Radicals," McGraw-Hill, New York, N. Y., 1966, Chapter 21.

<sup>(8)</sup> D. Bethell and V. Gold, "Carbonium Ions an Introduction," Academic Press, New York, N. Y., 1967, Chapter 6. (9) F. A. Carey and H. S. Tremper, J. Amer. Chem. Soc., 90, 2578 (1968);

<sup>91, 2944 (1969).</sup> 

<sup>(10)</sup> C. G. Swain, C. B. Scott, and K. H. Lohmann, ibid., 75, 136 (1953).

<sup>(11)</sup> Deviation from the usual nitrosoamide decomposition mechanism is known to occur when a highly reactive carbonium ion is involved [see E. H. White, H. P. Tiwari, and M. J. Todd, ibid., 90, 4734 (1968)]. Our studies suggest deviation from the usual mechanism when an especially stable carbonium ion is involved.

<sup>(12)</sup> M. S. Newman, A. Arkell, and T. Fukunaga, ibid., 82, 2498 (1960).

thydrol in dry benzene solution. The benzene was removed on a rotary evaporator to produce an oil which furnished 1.5 g (19%) of pure 3, mp 84-85°, on addition of ethanol. The nmr spectrum (CDCl<sub>3</sub>) showed absorptions at  $\tau$  2.1 (complex, aromatic and carbinyl protons, 13 H) and 7.5 (3 H, methyl). Anal. Calcd for C<sub>21</sub>H<sub>16</sub>O<sub>3</sub>: C, 79.7; H, 5.1. Found: C, 79.7; H, 4.9.

**Reaction of 3 with Dinitrogen Tetroxide.**—A solution of 0.48 g (0.0015 mol) of **3** in 50 ml of dry tetrahydrofuran was treated at  $-60^{\circ}$  with 3.0 g (0.032 mol) of dinitrogen tetroxide. After 15 min, the tetrahydrofuran was removed on a rotary evaporator. The remaining mixture was identified as xanthone and p-toluic acid by nmr. Separation by extraction with sodium bicarbonate solution followed by acidification furnished pure p-toluic acid and xanthone, each in 67% yield. **Preparation of** N-(9-Xanthy1)benzamide-carbonyl-<sup>18</sup>O.—

Preparation of N-(9-Xanthyl)benzamide-carbonyl-<sup>18</sup>O.— Water (2.0 g, 0.10 mol) containing 3.15% oxygen-18 enrichment (Prochem) was added in a nitrogen atmosphere to 14.0 g (0.10 mol) of benzyl chloride. The mixture was stoppered and left standing for several days. Dry benzene was added and the mixture was dried by azeotropic distillation of any water present. Thionyl chloride (14.3 g, 0.12 mol) was added and the mixture was heated at reflux for several hours. Excess benzene and thionyl chloride were removed on a rotary evaporator and more dry benzene was then added. Dry ammonia was bubbled through the benzene solution. Benzamide (12.0 g, 99%) precipitated. Mass spectral analysis showed a 1.3 atom % oxygen-18 enrichment in the carbonyl oxygen. Reaction of 1.5 g (0.015 mol) of benzamide-<sup>18</sup>O with xanthydrol according to the procedure given previously for the formation of 9-acylamidoxanthenes produced 2.2 g (61%) of N-(9-xanthyl)benzamide-carbonyl-<sup>18</sup>O with an <sup>18</sup>O enrichment of 1.3% as determined by mass spectrometry.

Nitrosation of N-(9-Xanthyl)benzamide-<sup>18</sup>O.—N-(9-Xanthyl)benzamide-<sup>18</sup>O (1.50 g, 0.0052 mol) and 0.20 g (0.0083 mol) of mineral oil free sodium hydride in dry tetrahydrofuran were stirred in a nitrogen atmosphere overnight. Dinitrogen tetroxide (4.0 g, 0.043 mol) was added at  $-60^{\circ}$  during 15 min. The mixture was poured into water and worked up as described above to give xanthone in 100% yield and benzoic acid in 63% yield. Analysis by mass spectrometry showed that no oxygen-18 was present in the xanthone, but the benzoic acid contained a 1.3 atom % enrichment of the oxygen-18. The m/e 122 (parent) and 124 (P + 2) peaks were used in this analysis. Identical results were obtained in three separate runs.

Trapping Experiments Using N-(9-Xanthyl)urethane (1b).— Sodium hydride (0.20 g, 0.0083 mol) washed free of mineral oil was added to a solution of 1.2 g (0.0047 mol) of N-(9-xanthyl)urethane (1b) in 50 ml of dry ether and the mixture was stirred overnight. Dinitrogen tetroxide (4.0 g, 0.042 mol) was added at -60° during 15 min. Methyl vinyl ketone (2.3 g, 0.033 mol) was then added and the mixture was allowed to warm to 0°. The mixture was extracted with ether and the organic phase was separated, dried (MgSO<sub>4</sub>), and concentrated at 0° on a rotary evaporator. The product consisted of 93% xanthone and an unidentified red oil which appeared to be a mixture of polymeric methyl vinyl ketone or a product from the reaction of methyl vinyl ketone with dinitrogen tetroxide as determined by nmr and ir spectroscopy.

Spectral evidence was not found for any reaction between methyl vinyl ketone and a product derived from 1b. Similar experiments using cyclohexene or vinyl acetate as trapping agents produced xanthone without evidence for any participation of the trapping agent in the decomposition reaction of 1b. No observable change occurred when either chloroform or tetrahydrofuran were used as solvents. Ethanedithiol (excess) did not alter the course of the reaction.

Trapping Experiments Using N-(9-Xanthyl)-p-toluamide (1a). —Sodium hydride (0.20 g, 0.0083 mol) was added to a mixture of 1.20 g (0.0038 mol) of N-(9-xanthyl)-p-toluamide (1a) in 50 ml of dry tetrahydrofuran and the mixture was stirred overnight. Sodium azide (1.54 g, 0.024 mol) was added and the mixture was cooled to  $-60^{\circ}$ . Dinitrogen tetroxide (2.0 g, 0.22 mol) was added at  $-60^{\circ}$  and the mixture was allowed to warm to  $0^{\circ}$ . Tetrahydrofuran was removed at 0° on a rotary evaporator. Examination of the crude mixture by ir and nmr spectroscopy failed to show evidence for the presence for the presence of 9-azidoxanthene. Separation and purification of the components showed that the mixture consisted of 1a, xanthone, and *p*-toluic acid in 20, 73, and 43% yields, respectively.

Using triethylsilane (0.018 g) instead of sodium azide resulted in the precipitation of a white, high-melting, nonflammable material assumed to be the product of a reaction between dinitrogen tetroxide and triethylsilane. The remaining reaction mixture was poured into water and extracted with ether. An 80% recovery of starting material was obtained.

Addition of lithium perchlorate (0.013 mol) did not affect the reaction, as xanthone and *p*-toluic acid were obtained in 70 and 50% pure yield, respectively.

Reaction of N-(9-Xanthyl)-p-toluamide (1a) with Nitrosyl Chloride.—The sodium salt of 1a (0.0032 mol) was prepared as described above. Nitrosyl chloride (3.0 g, 0.46 mol) was added at -60° and the mixture was allowed to warm to 0°. Removal of the tetrahydrofuran on a rotary evaporator followed by the usual work-up gave a mixture of xanthone (80%) and p-toluic acid (80%).

Reactions of 9-Xanthyl Perchlorate.<sup>13</sup> A. Dinitrogen Tetroxide.—9-Xanthyl perchlorate (0.55 g, 0.0020 mol) and 0.25 g (0.0039 mol) of sodium hydride in 50 ml of dry tetrahydrofuran were treated at  $-60^{\circ}$  with 5.4 g (0.060 mol) of dinitrogen tetroxide. After 15 min, the mixture was concentrated on a rotary evaporator. Xanthone was the only product observed (quantitative yield).

**B.** Nitrosyl Chloride.—The same procedure described in A above was used except that 3.0 g (0.046 mol) of nitrosyl chloride was used in place of dinitrogen tetroxide. Xanthone was the only product obtained.

C. Dinitrogen Tetroxide and Sodium Azide.—9-Xanthyl perchlorate (1.0 g, 0.0035 mol) and 0.25 g (0.0039 mol) of sodium azide in 50 ml of dry tetrahydrofuran were treated at  $-60^{\circ}$  with 5.4 g (0.06 mol) of dinitrogen tetroxide. After 15 min the mixture was concentrated on a rotary evaporator, leaving a red oil which gave ir and nmr spectra identical with those of xanthone. Addition of 1 ml of hexane followed by cooling overnight at  $-5^{\circ}$  produced 0.10 g (14%) of pure xanthone.

Reactions of 9-Chloroxanthene.<sup>14</sup> A. Dinitrogen Tetroxide or Nitrosyl Chloride.—9-Chloroxanthene (1.1 g, 0.0050 mol) in dry tetrahydrofuran was treated at  $-60^{\circ}$  with 3.0 g (0.032 mol) of dinitrogen tetroxide or 3.0 g (0.046 mol) of nitrosyl chloride. The mixture was concentrated to produce xanthone quantitatively (crude). Pure xanthone was obtained in 80% yield.

**B.** Silver Nitrate.—9-Chloroxanthene (2.16 g, 0.010 mol) was added to 50 ml of 4% ethanolic silver nitrate solution. A white precipitate of silver chloride formed immediately. After filtration of the silver chloride, the mixture was concentrated to produce pure xanthone in 86% yield. Evidence for the presence of 9-xanthyl nitrate was not found.

**Reaction of Xanthydrol with Dinitrogen Tetroxide.**—The same procedure as that described above for the reaction of 9-chloroxanthene with dinitrogen tetroxide was followed. Pure xanthone was obtained in 90% yield.

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**Registry No.**—1a, 6319-64-8; 1b, 6319-53-5; 1c, 6319-60-4; 1d, 40429-09-2; 1e, 6319-63-7; 1f, 40429-11-6; 1g, 40429-12-7; 3, 40429-13-8;  $N_2O_4$ , 10544-72-6; NOCl, 2696-92-6; *p*-toluic acid, 99-94-5; xanthydrol, 90-46-0; 9-xanthyl perchlorate, 40429-14-9; 9-chloroxanthene, 28447-91-8.

<sup>(13)</sup> K. A. Hofmann, R. Roth, K. Hobold, and A. Metzler, Chem. Ber., 43, 2624 (1910).

<sup>(14)</sup> F. G. Eny-Jones and A. M. Ward, J. Chem. Soc., 535 (1930).