[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

Orientation in Reactions of Nitryl Chloride and Acrylic Systems[1]

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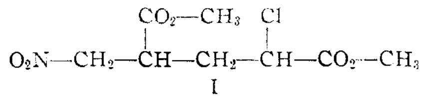
Reaction of nitryl chloride with methyl acrylate yields methyl 2-chloro-3-nitropropionate, methyl 2,3-dichloropropionate and dimethyl 2-chloro-4-nitromethylpentanedioate (and methyl 2,3-dinitropropionate:methyl 2-nitrito-3-nitropropionate). Methyl 2-chloro-3-nitropropionate was identified by conversion to methyl 3-nitroacrylate; the structure of dimethyl 2-chloro-4-nitromethylpentanedioate was established after hydrolysis and reduction to glutaric acid. Addition of nitryl chloride to acrylic acid and acrylonitrile gives 2-chloro-3-nitropropionic acid, and 2-chloro-3-nitropropionitrile and 2,3-dichloropropionitrile, respectively. The identity of 2-chloro-3-nitropropionic acid was confirmed by dehydrochlorination to 3-nitroacrylic acid and subsequent hydration to 2-hydroxy-3-nitropropionic acid. The structure of 2-chloro-3-nitropropionitrile was proven, after conversion into 3-nitroacrylonitrile, by hydrolysis to 3-nitroacrylamide and subsequent reaction with nitrous acid to give 3-nitroacrylic acid. The direction and modes of addition of nitryl chloride to unsaturated systems are discussed.

Pure nitryl chloride[3] may be prepared conveniently in 80–90% yield from anhydrous nitric and chlorosulfonic acids[3a] (Equation 1, see Experimental)

$$HNO_3 + ClSO_3H \longrightarrow NO_2Cl + H_2SO_4 \qquad (1)$$

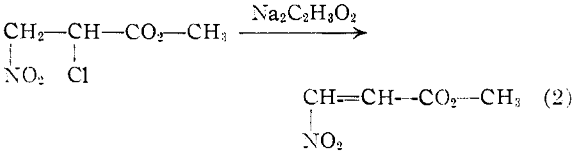
In order to obtain information concerning the direction and modes of addition of nitryl chloride to unsaturated systems, the reactions of nitryl chloride with methyl acrylate, acrylic acid and acrylonitrile have been investigated in various solvents. During this study it was reported[4] that reaction of nitryl chloride with methyl acrylate and acrylonitrile in the absence of a solvent yields methyl 2-chloro-3-nitropropionate and 2-chloro-3-nitropropionitrile, respectively; no physical nor chemical evidence other than analytical data was given for the structures proposed for these adducts. It is now reported that nitryl chloride and methyl acrylate react at 0° to give methyl 2,3-dichloropropionate (7%), methyl 2-chloro-3-nitropropionate[5] (75%) and dimethyl 2-chloro-4-nitromethylpentanedioate (I) (5–10%).



$$O_2N-CH_2-\underset{}{CH}(CO_2-CH_3)-CH_2-CH(Cl)-CO_2-CH_3$$

I

A product was also obtained (−10%) which is believed to be methyl 2-nitrito-3-nitropropionate and methyl 2,3-dinitropropionate[6]; these products were not separated completely because of the difficulties involved in their purification. Reaction of nitryl chloride and methyl acrylate occurred readily in chloroform, methanol and ethyl ether and the direction of addition was identical with that obtained in the absence of a solvent. Methyl 2-chloro-3-nitropropionate was identified upon being converted into methyl 3-nitroacrylate[6,7] by reaction either with pyridine, N,N-dimethylaniline (65%) or anhydrous sodium acetate (92%) (Equation 2).



$$\underset{NO_2}{CH_2}-\underset{Cl}{CH}-CO_2-CH_3 \xrightarrow{Na_2C_2H_3O_2} \underset{NO_2}{CH}=CH-CO_2-CH_3 \qquad (2)$$

The structure of dimethyl 2-chloro-4-nitromethylpentanedioate (I) was established, after hydrolysis and decarboxylation with 70% sulfuric acid at 110–115° and subsequent reduction with 57% hydriodic acid, by conversion into glutaric acid (Equations 3); similar treatment of the other probable isomeric adducts dimethyl 2-chloromethyl-4-nitropentanedioate and dimethyl 2-chloromethyl-3-nitromethylbutanedioate, would be expected to yield 2-methylsuccinic acid.[8] Glutaric acid was characterized as its di-*p*-bromophenacyl ester.

$$O_2NCH_2-CH(-CO_2CH_3)-CH_2-CHCl-CO_2-CH_3 \xrightarrow[115^\circ]{H_2SO_4,H_2O} [(HO_2C)_2-CH-CH_2-CHCl-CO_2H] \xrightarrow{-CO_2} [HO_2C-CH_2-CH_2-CHCl-CO_2H] \xrightarrow{HI} HO_2C-CH_2-CH_2-CH_2-CO_2H \qquad (3)$$

Reaction of nitryl chloride and glacial acrylic acid at 0° resulted principally in formation of 2-chloro-3-nitropropionic acid (65–71%) (Equation 4); the direction of addition of nitryl chloride to acrylic acid is identical to that with methyl acrylate. The structure of 2-chloro-3-nitropropionic acid was established (Equation 4), after thermal dehydrochlorination (65–70%) or reaction with sodium actate (98%) to give 3-nitroacrylic acid by con-

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[1] This research was supported by The General Tire and Rubber Company and the Office of Naval Research.

[2] Taken in part from a thesis to be submitted by Franklin Conrad and a thesis submitted by Ralph B. Kaplan, August, 1950, to the Graduate School of The Ohio State University in partial fulfillment of the requirements for the Ph.D. degree.

[3] (a) K. Dachlauer, German Patent 509,405, Aug. 30, 1929; (b) *cf.*, H. J. Schumacher and G. Sprenger, *Z. anorg. allgem. Chem.*, **182**, 139 (1929); *Z. Elektrochem.*, **35**, 653 (1929); *Z. physik. Chem.*, **B12**, 115 (1931); (c) N. Schmeisser and E. Gregor-Haschke, *Z. anorg. Chem.*, **255**, 33 (1947).

[4] H. Brintzinger and K. Pfannstiel, *ibid.*, **256**, 325 (1947).

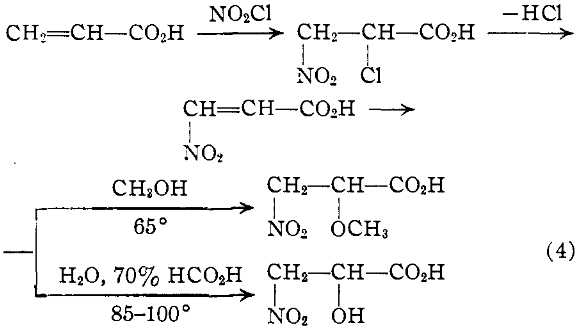
[5] The physical constants for methyl 2-chloro-3-nitropropionate obtained in this study differ significantly from that previously reported.[4]

[6] H. Shechter and F. Conrad, THIS JOURNAL, **74**, in press (1952).

[7] Methyl 3-nitroacrylate may exist in *cis* and *trans* modifications. The stereochemistry of this methyl 3-nitroacrylate (presumably *trans*) has not been established; however, this product is identical with that obtained from dinitrogen tetroxide and methyl acrylate or by dehydration of methyl 2-hydroxy-3-nitropropionate.[6]

[8] This proof of structure does not differentiate the other isomeric possibility dimethyl 2-chloro-5-nitrohexanedioate. This possible structure has been eliminated on the basis that (1) the dimer adduct does not give a pseudonitrole upon reaction with nitrous acid and (2) formation of the adduct would involve a series of unusual and unpredicted addition and dimerization processes.

version into 2-hydroxy-3-nitropropionic acid[6,9] with 70% formic acid. Attempts to esterify 3-nitroacrylic acid with methanol resulted, instead, in addition to the carbon–carbon double bond to produce 2-methoxy-3-nitropropionic acid (100%), (Equation 4).

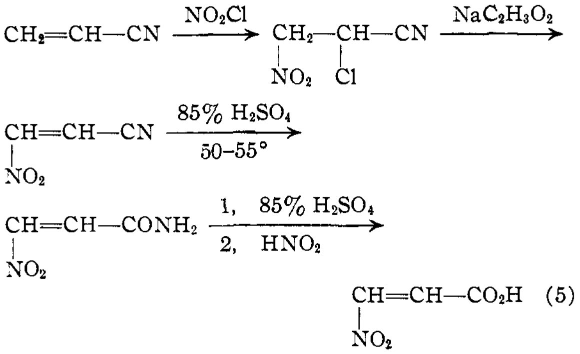


$$CH_2{=}CH{-}CO_2H \xrightarrow{NO_2Cl} \underset{NO_2}{CH_2}{-}\underset{Cl}{CH}{-}CO_2H \xrightarrow{-HCl} \underset{NO_2}{CH}{=}CH{-}CO_2H \longrightarrow$$

$$\xrightarrow[65^\circ]{CH_3OH} \underset{NO_2}{CH_2}{-}\underset{OCH_3}{CH}{-}CO_2H$$

$$\xrightarrow[85\text{–}100^\circ]{H_2O,\ 70\%\ HCO_2H} \underset{NO_2}{CH_2}{-}\underset{OH}{CH}{-}CO_2H \qquad (4)$$

Addition of nitryl chloride to acrylonitrile at 0° in the absence of a solvent gave 2,3-dichloropropionitrile (13.5%) and 2-chloro-3-nitropropionitrile (Equations 5) (76%); in ethyl ether at 0°, 3-nitroacrylonitrile (48%) and ammonium chloride were produced along with 2,3-dichloropropionitrile (16%) and 2-chloro-3-nitropropionitrile (25%). The identity of 2-chloro-3-nitropropionitrile was established upon being converted into 3-nitroacrylic acid by the following method (Equations 5): reaction of 2-chloro-3-nitropropionitrile with sodium acetate gave 3-nitroacrylonitrile (79%); hydrolysis of the nitronitrile with sulfuric acid yielded 3-nitroacrylamide (54%); acid hydrolysis of 3-nitroacrylonitrile and subsequent reaction with nitrous acid resulted in the formation of 3-nitroacrylic acid (68%).



$$CH_2{=}CH{-}CN \xrightarrow{NO_2Cl} \underset{NO_2}{CH_2}{-}\underset{Cl}{CH}{-}CN \xrightarrow{NaC_2H_3O_2}$$

$$\underset{NO_2}{CH}{=}CH{-}CN \xrightarrow[50\text{–}55^\circ]{85\%\ H_2SO_4}$$

$$\underset{NO_2}{CH}{=}CH{-}CONH_2 \xrightarrow[2,\ HNO_2]{1,\ 85\%\ H_2SO_4} \underset{NO_2}{CH}{=}CH{-}CO_2H \qquad (5)$$

Discussion

It has been previously found that addition of nitryl chloride to vinyl bromide in carbon tetrachloride results in the formation of 1-bromo-1-chloro-2-nitroethane[10] (85%), and that unsymmetrical terminal olefins react with nitryl chloride in chloroform to yield 1-nitro-2-chloroalkanes (for example, 2-methyl-1-propene gives 2-chloro-2-methyl-1-nitropropane); there was no evidence for isomeric orientation in these reactions.[11] Since it has been established that the orientation in addition of nitryl chloride to acrylic systems is identical with that obtained with vinyl bromide and unsymmetrical alkenes, it appears that the direction of attack of nitryl chloride on olefinic centers is independent of the electronic demands of the group attached to the unsaturated system. It is also of interest that the direction of addition of dinitrogen tetroxide and nitryl chloride to unsymmetrical terminal olefins or methyl acrylate is identical in solvents of low dielectric constant in that a nitro group is always formed at the terminal position in preference to the isomeric nitrite.[6,12]

Although, as yet, not completely definitive, the collective results of this and previous investigations[10,11] allow certain considerations of the modes of addition of nitryl chloride in solvents of low dielectric constant. Reaction of nitryl chloride with unsaturated centers may be expected to involve direct bimolecular attack resulting in homolytic or heterolytic cleavage or (and) initial dissociation of nitryl chloride followed by a subsequent addition process. The resulting modes of cleavage during addition or of initial dissociation may be represented by at least three processes[13] (Equations 6, 7, 9)

$$NO_2Cl \rightleftarrows \cdot NO_2 + .Cl \qquad (6)$$

$$NO_2Cl \rightleftarrows \overset{+}{NO_2} + Cl^- \qquad (7)$$

$$NO_2Cl \rightleftarrows NO_2^- + Cl^+ \qquad (8)$$

Upon considering (1) the possible modes of cleavage of nitryl chloride, (2) the specific direction of addition and the absence of halonitrites[6] from reactions of nitryl chloride and acrylic compounds,[14] (3) the formation of dimethyl 2-chloro-4-nitromethylpentanedioate from methyl acrylate and nitryl chloride, and (4) the identical direction of addition of nitryl chloride to electronegatively or electropositively substituted olefins, it appears that reaction of nitryl chloride and acrylic systems in low dielectric media does not involve heterolytic polarization or heterolytic initial dissociation (Equations 7, 8) during addition. It is suggested that addition of nitryl chloride to acrylic systems (and possibly vinyl halides and unsymmetrical

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(9) H. B. Hill and O. F. Black, THIS JOURNAL, **32**, 231 (1904).

(10) W. Steinkopf and M. Kuhnel, *Ber.*, **75B**, 1323 (1942).

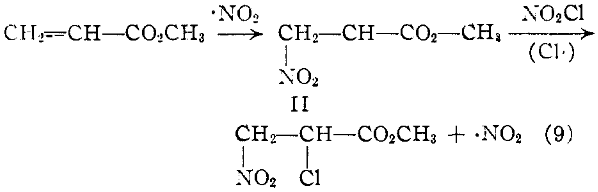
(11) (a) C. M. Himel, U. S. Patent 2,511,915, June 20, 1950; (b) C. A. Sears, Abst., 119th Meeting of the Am. Chem. Society, April 10, 1951, p. 77 M. Dichloroalkanes, nitronitrites and dinitroalkanes were also obtained in low yields in these experiments.

(12) N. Levy and C. W. Scaife, *J. Chem. Soc.*, 1093 (1946); *ibid.*, 1100 (1946); N. Levy, C. W. Scaife and A. E. Wilder-Smith, *ibid.*, 52 (1948).

(13) (a) Gaseous nitryl chloride has been reported[3b] to decompose into nitrogen dioxide and chlorine by a first order process; the equations postulated for this process are: (1) $NO_2Cl \rightarrow \cdot NO_2 + \cdot Cl$ (slow) and (2) $NO_2Cl + \cdot Cl \rightarrow \cdot NO_2 + Cl_2$ (fast). The recent studies by R. A. Ogg, Jr., and M. K. Wilson, *J. Chem. Phys.*, **18**, 900 (1940), however, cast grave doubts on the quasi-unimolecular decomposition of NO_2Cl. In the present investigation it has been observed that liquid nitryl chloride decomposes very slowly in storage at 0–5° into nitrogen dioxide and chlorine. (b) Sears, ref. 11b, p. 73 M, has postulated ionization of nitryl chloride in aluminum chloride as follows: $NO_2Cl + AlCl_3 \rightarrow \overset{+}{NO_2} + AlCl_4^-$. (c) H. H. Batey, Jr., private communication, and Schmeisser, *et al.*,[4c] have studied the "positive" character of chlorine in reactions of nitryl chloride.

(14) Reaction of methyl acrylate with $\overset{+\delta-\delta}{NO_2Cl}$ would be predicted to give methyl 3-chloro-2-nitropropionate; addition as $\overset{-\delta+\delta}{NO_2Cl}$ would be expected to result in formation of both methyl 2-chloro-3-nitropropionate and methyl 2-chloro-3-nitritopropionate.

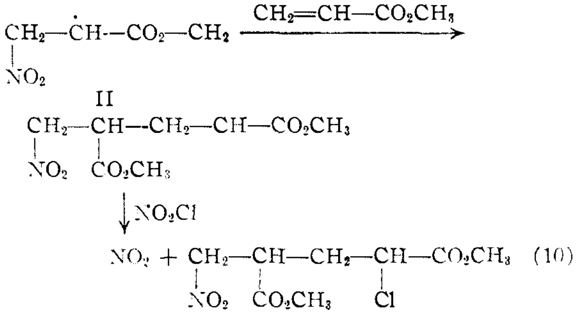
olefins[15]) involves essentially a homolytic process in which nitrogen dioxide (from Equation 6) or nitryl chloride attacks the terminal position of the double bond, resulting exclusively in C–N attachment[6] (II, Equation 9); completion of the reaction may occur by exchange of the intermediate radical with nitryl chloride to yield chloronitro compound and nitrogen dioxide (Equation 9)



$$\mathrm{CH_2{=}CH{-}CO_2CH_3} \xrightarrow{\cdot\mathrm{NO_2}} \underset{\substack{|\\ \mathrm{NO_2}\\ \mathrm{II}}}{\mathrm{CH_2}}\mathrm{{-}CH{-}CO_2{-}CH_3} \xrightarrow[(\mathrm{Cl}\cdot)]{\mathrm{NO_2Cl}}$$

$$\underset{\substack{|\\ \mathrm{NO_2}}}{\mathrm{CH_2}}{-}\underset{\substack{|\\ \mathrm{Cl}}}{\mathrm{CH}}\mathrm{{-}CO_2CH_3} + \cdot\mathrm{NO_2} \quad (9)$$

Similarly, dimethyl 2-chloro-4-nitromethylpentanedioate (I) from nitryl chloride and methyl acrylate may result from reaction of II with methyl acrylate and subsequent exchange with nitryl chloride.



$$\underset{\substack{|\\ \mathrm{NO_2}\\ \mathrm{II}}}{\mathrm{CH_2}}{-}\dot{\mathrm{C}}\mathrm{H{-}CO_2{-}CH_2} \xrightarrow{\mathrm{CH_2{=}CH{-}CO_2CH_3}}$$

$$\underset{\substack{|\\ \mathrm{NO_2}}}{\mathrm{CH_2}}{-}\underset{\substack{|\\ \mathrm{CO_2CH_3}}}{\mathrm{CH}}\mathrm{{-}CH_2{-}CH{-}CO_2CH_3}$$

$$\Big\downarrow \mathrm{NO_2Cl}$$

$$\mathrm{NO_2} + \underset{\substack{|\\ \mathrm{NO_2}}}{\mathrm{CH_2}}{-}\underset{\substack{|\\ \mathrm{CO_2CH_3}}}{\mathrm{CH}}\mathrm{{-}CH_2{-}}\underset{\substack{|\\ \mathrm{Cl}}}{\mathrm{CH}}\mathrm{{-}CO_2CH_3} \quad (10)$$

The 2,3-dichloro adducts (up to 16%) may arise from an analogous process in which addition of a chlorine atom occurs at the terminal position followed by reaction with nitryl chloride; however, no final conclusions can be drawn at present concerning the importance of this reaction since decomposition of nitryl chloride yields chlorine and nitrogen dioxide.

Experimental

Prepartion of Nitryl Chloride.—Nitryl chloride was prepared from nitric acid (100%) and chlorosulfonic acid (100%) at 0°; the procedure developed is a modification of the method of Dachlauer.[3a]

Reagents.—Technical chlorosulfonic acid (Eastman Kodak Co.) was distilled at atmospheric pressure[16] in a glass apparatus protected by drying tubes containing anhydrous calcium chloride; b.p. 149–151°. Nitric acid (100%), prepared by distillation of a mixture of concentrated nitric acid (70% HNO_3, C.P.) and excess sulfuric acid (96%, C.P.) at a pressure of 22 mm. in a glass apparatus, was used efficiently; however, it was more convenient to use fuming nitric acid (91.6%) to which was added sufficient fuming sulfuric acid to combine with the water present.[17]

Procedure.—All operations were performed in a hood. All connections in the apparatus were of ground glass; openings in the system were fitted with drying tubes containing calcium chloride.

Fuming sulfuric acid (123 g., 30% sulfur trioxide) was added dropwise to fuming nitric acid (100 g., 1.47 moles, sp. gr. 1.50, 91.6% acid content) at 0° in a 500-ml. three-necked, round bottom flask equipped with an equi-pressure dropping funnel, an efficient motor-driven glass stirrer sealed with sulfuric acid, and a condenser cooled by Dry Ice–acetone. A receiver (a test-tube of 125–150 ml. capacity) was connected to the condenser and then immersed in a cooling mixture of Dry Ice–acetone. The mixed acids were stirred vigorously at 0° while chlorosulfonic acid (170.5 g., 97.5 ml., 1.47 moles) was added slowly in 3–4 hours, or at a rate such that brown "nitrous fumes" did not appear above the reaction mixture. With the addition of each drop of chlorosulfonic acid, almost colorless gaseous nitryl chloride was evolved. After chlorosulfonic acid had been added, the cooling bath was removed and the mixture was studied for one-half hour.

The product was a dense pale-yellow liquid freezing at −145 ± 2°, lit.[3b] −145° and boiling from −17 to −15°, lit.[3b] −15°; yield 95–108 g. (80–90%). On the basis of analysis, the nitryl chloride is 98–99% pure[18] (98% based on Cl content, 99% on acidity).

Anal. Calcd. for NO_2Cl: acidity in water, 24.55 milliequiv. g. %. Found: 24.72. Calcd. for NO_2Cl: Cl, 43.6. Found: Cl, 44.9.

Reaction of Nitryl Chloride and Methyl Acrylate.—Nitryl chloride (195.6 g., 2.4 moles, 20% excess) was distilled through a gas delivery tube in 2 hours into methyl acrylate (172 g., 2 moles, anhydrous, b.p. 43.5° (200 mm.)) at 0° in a three-necked flask equipped with a liquid sealed stirrer, and a series of drying tubes. The mixture, orange-red in color, was stirred for one hour at room temperature. Excess nitryl chloride (now containing chlorine and nitrogen dioxide) was removed by distillation at reduced pressure; the color of the mixture became light yellow-orange. The product was distilled under nitrogen at reduced pressure to yield: Fraction 1 (22.2 g., 7.1%), b.p. 43–82° (18–22 mm.); Fraction 2 (251 g., 75.1%), b.p. 68–110° (2–4 mm.), and Residue (43 g., 12.1%). Rectification of Fractions 1 and 2 at reduced pressure under nitrogen in a helix-packed column (24 × 2 cm.) yielded Fraction 1a (18.5 g., 5.9%), b.p. 72.5° (21 mm.), Fraction 2a (207.1 g., 62.1%), b.p. 88° (4 mm.), and higher boiling products.

Fraction 1a, after rerectification, was identified as methyl 2,3-dichloropropionate, a yellow liquid; b.p. 72.5° (21 mm.), lit.[19] 72–75° (21 mm.); d^{20}_{4} 1.329, lit.[17] d^{20}_{4} 1.3283, n^{20}_{D} 1.4543, lit.[17] n^{20}_{D} 1.4482 (this fraction contained traces of methyl 3-nitroacrylate).

Anal. Calcd. for $C_4H_6O_2Cl_2$: C, 30.59; H, 3.85. Found: C, 31.44; H, 4.02.

Rectification of Fraction 2a yielded **methyl 2-chloro-3-nitropropionate**, a yellow liquid, b.p. 88° (4 mm.), lit.[4] 91° (4 mm.), n^{20}_{D} 1.4573, d^{20}_{4} 1.389, lit.[4]D 1.43.

Anal. Calcd. for $C_4H_6O_4NCl$: C, 28.66; H, 3.58; N, 8.36; Cl, 21.2. Found: C, 28.87; H, 3.19; N, 8.69; Cl, 21.3.

Distillation of the residue, upon removal of the dinitro and the nitro–nitrite adducts, yielded **dimethyl 2-chloro-4-nitromethylpentanedioate** (5–10%), a yellow liquid, b.p. 131° (0.8 mm.), n^{20}_{D} 1.4715, d^{20}_{4} 1.3423, MR_D (calcd.) 52.94, MR_D (found) 52.84.

Anal. Calcd. for $C_8H_{12}O_6NCl$: C, 37.87; H, 4.73; N, 5.52; Cl, 14.00. Found: C, 38.31; H, 4.31; N, 5.59; Cl, 14.88.

Reaction of methyl acrylate and nitryl chloride in anhydrous ethyl ether at 0° yielded methyl 2,3-dichloropropionate (7.6%), methyl 2-chloro-3-nitropropionate (69.7%) and unidentified higher boiling products (methyl 2,3-dinitropropionate, dimethyl 2-chloro-4-nitromethylpentanedioate, etc.); in general, reaction in the absence of solvents (chloroform, methanol and ethyl ether) gave products which were more readily distillable. Methyl 2-chloro-3-nitropropionate dissolves in alkaline media to form deep red solutions. The pure chloronitro ester may be kept for months without appreciable decomposition.

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(15) Although the fact that the direction of addition of nitryl chloride to terminal olefins, vinyl bromide and acrylic systems is identical cannot be used as conclusive evidence that all three reactions proceed by the same mechanism, it is of interest that reaction of the same unsaturated compounds with hydrogen bromide in the presence of peroxides gives identical addition in which the bromine atom adds exclusively at the terminal position; *cf.* M. S. Kharasch, M. C. McNab and F. R. Mayo, THIS JOURNAL, **55**, 2521 (1933): *ibid.*, **55**, 2531 (1933), and M. S. Kharasch and M. C. McNab, unpublished work.

(16) C. Sanger and E. Riegel, *Z. anorg. Chem.*, **76**, 79 (1912); *Proc. Am. Acad.*, **47**, 673.

(17) Anhydrous nitric acid (100%) is now commercially available from The General Chemical Division, Allied Chemical and Dye Corporation, and may be used directly in this preparation.

(18) These analytical data were supplied by Castarina and Tomlinson, Chemical Research Section, Picatinny Arsenal, Dover, New Jersey.

(19) P. F. Franklin and A. Turnbull, *J. Chem. Soc.*, **105**, 459 (1914).

Dehydrochlorination of Methyl 2-Chloro-3-nitropropionate; Methyl 3-Nitroacrylate.—Methyl 2-chloro-3-nitropropionate (167 g., 1 mole) was added dropwise to a stirred suspension of anhydrous sodium acetate (90 g., 1.1 moles) in ethyl ether (200 ml., anhydrous) at 5°. After addition was completed, stirring was stopped and the sodium chloride and sodium acetate were filtered. The solution was concentrated at reduced pressure until ether and most of the acetic acid had been removed. The dark red concentrate was distilled in nitrogen at reduced pressure to yield, after removal of acetic acid: (1) volatile product (116.9 g.), b.p. 72–76° (9–10 mm.), and (2) residue (15.8 g.). Redistillation of the volatile product under nitrogen gave **methyl 3-nitroacrylate** (115.6 g), b.p. 72° (11 mm.), a yellow solid, m.p. 38°, no depression by a sample obtained from methyl acrylate and dinitrogen tetroxide.[6] The residue from the initial distillation was washed with water and extracted with ethyl ether. The ether extract was dried over calcium sulfate and then distilled to give, after removal of ether, methyl 3-nitroacrylate (4.8 g.), b.p. 73° (10 mm.), m.p. 36–38°, and methyl 2-chloro-3-nitropropionate (7.2 g.), b.p. 80–90° (1–2 mm.). The combined methyl 3-nitroacrylate totaled 120.4 g. (91.9% yield).

Anal. Calcd. for $C_4H_5NO_4$: C, 36.64; H, 3.82; N, 10.69. Found: C, 36.48; H, 3.82; N, 10.56.

The yield of methyl 3-nitroacrylate, a lachrymatory solid, is lowered when hydrated sodium acetate is used. The quality and yield of product are greatly improved if the reaction mixture is worked up immediately and is not exposed to air. Methyl 3-nitroacrylate may be recrystallized from methanol–water; however, a purer product is obtained by vacuum distillation. Dehydrohalogenation of methyl 2-chloro-3-nitropropionate with N,N-dimethylaniline in anhydrous ethyl ether at 25° gave methyl 3-nitroacrylate in 64.7% yield. Similar results were obtained by reaction of anhydrous pyridine with the chloronitro ester; however, the product was much more difficult to purify. Methyl 3-nitroacrylate is insoluble in water but dissolves readily in aqueous acids or bases, and organic solvents. The nitroacrylate is rapidly oxidized by dilute potassium permanganate, but does not add bromine readily in carbon tetrachloride.

Proof of Structure of 2-Chloro-4-nitromethylpentanedioate; Glutaric Acid.—A mixture of dimethyl 2-chloro-4-nitromethylpentanedioate (2.4 g., 0.0094 mole) and 70% sulfuric acid (20 ml.) was heated at 110–115° for 6 hours and then cooled. After the mixture had been diluted with water and then continuously extracted with ethyl ether, its ether extract was concentrated at reduced pressure to give a clear yellow acidic oil (1.15 g.).

The hydrolysate (1.0-g. aliquot) was dissolved in 57% hydriodic acid (20 ml.) and refluxed for 48 hours. The cooled mixture was diluted with water and continuously extracted with ethyl ether. After removal of ether, crude glutaric acid remained. The dibasic acid, after neutralization with sodium carbonate and reaction with *p*-bromophenacyl bromide, was converted into **di-*p*-bromophenacyl glutarate**; m.p. 133–134° after recrystallization from ethanol–water; m.p. of authentic sample, 137–138°; lit. 136.8°[20]; mixed m.p. 136–137°. X-Ray diffraction patterns of the derivative and authentic di-*p*-bromophenacyl glutarate were identical.

Reaction of Nitryl Chloride and Acrylic Acid.—Nitryl chloride (85 g., 1.05 moles, 20% excess) was distilled into glacial acrylic acid (64 g., 0.89 mole) at 0°. After the orange-red mixture was stirred at room temperature for one hour, excess nitryl chloride was removed at reduced pressure. The sirupy product crystallized slowly at 0–5° into a white solid (109.3 g., 71.2% yield).

(**a**).—The white solid (20-g. aliquot, 18.3%) was dissolved in benzene (a gummy product (1.5 g.) remained which was not identified; the residue decomposed when left exposed to the atmosphere); the solution was concentrated at reduced pressure until precipitation occurred. Filtration of the mixture yielded a white solid (11.4 g., 40.5%); m.p. 72–74°, which when recrystallized from benzene yielded **2-chloro-3-nitropropionic acid**; m.p. 78–80°; neut. equiv. (calcd.) 153.5, neut. equiv. (found) 157.4. The acid is soluble in ethyl ether, acetone, hot benzene, alkaline media and mineral acids.

Anal. Calcd. for $C_3H_4NO_4Cl$: C, 23.45; H, 2.61; Cl, 23.13; N, 9.12. Found: C, 23.66; H, 2.70; Cl, 22.55; N, 9.03.

The benzene solutions were concentrated at reduced pressures, but no further crystallization occurred. Distillation of the liquid residue at 6 mm. gave a yellow solid (m.p. 134°); recrystallization of the product from hot benzene gave **3-nitroacrylic acid**, m.p. 136°, no depression by an authentic sample (see following Experimental).

(**b**).—Distillation of the crude reaction product at reduced pressures (0.7 mm.) resulted in dehydrochlorination of 2-chloro-3-nitropropionic acid into 3-nitroacrylic acid (65–70% yield), a yellow needle-like solid, m.p. 136°; neut. equiv. (calcd.) 117, neut. equiv. (found) 118. The product is identical with that isolated in procedure (a). 3-Nitroacrylic acid is soluble in ethyl ether, hot benzene, mineral acids and aqueous alkali.

Anal. Calcd. for $C_3H_3NO_4$: C, 30.77; H, 2.56; N, 11.96. Found: C, 30.70; H, 2.73; N, 12.04.

Reaction of 2-Chloro-3-nitropropionic Acid and Sodium Acetate; 3-Nitroacrylic Acid.—Anhydrous sodium acetate (0.43 g., 0.005 mole) was added slowly to a stirred solution of 2-chloro-3-nitropropionic acid (0.7 g., 0.0046 mole) in anhydrous ethyl ether (50 ml.). The yellow-orange mixture was refluxed for one hour and then filtered. The filtrate was concentrated under reduced pressure until yellow crystals began to form; the semi-liquid was allowed to stand for one hour. Upon filtration, 3-nitroacrylic acid (0.53 g., 98.1% yield) was obtained; m.p. 136°; neut. equiv. (calcd.) 117, neut. equiv. (found) 118.

Anal. Calcd. for $C_3H_3O_4N$: C, 30.77; H, 2.56; N, 11.96. Found: C, 30.54; H, 2.44; N, 11.86.

Reaction of 3-Nitroacrylic Acid and Methanol; 2-Methoxy-3-nitropropionic Acid.—A mixture of 3-nitroacrylic acid (2.0 g., 0.017 mole) and methanol (75 ml., anhydrous) was refluxed for 3 hours. The solution was concentrated until most of the methanol had been removed. Solidification of the residue gave a white product which, when recrystallized twice from benzene, yielded **2-methoxy-3-nitropropionic acid** (2.53 g., yield 100%); m.p. 76–78°; neut. equiv. (calcd.) 149; neut. equiv. (found) 147.2. (The neutralization equivalent was determined at 0–2°; at higher temperatures, decomposition of the product occurred and lower values were obtained).

Anal. Calcd. for $C_4H_7NO_5$: C, 32.22; H, 4.69; N, 9.38. Found: C, 32.56; H, 4.44; N, 9.38.

Hydration of 3-Nitroacrylic Acid; 2-Hydroxy-3-nitropropionic Acid.—3-Nitroacrylic acid (0.25 g., 0.0017 mole) dissolved in 70% formic acid (10 ml.) was heated for 3 hours at 85–100°. The mixture was diluted with distilled water (20 ml.) and then concentrated at reduced pressures until a yellow oil remained. The product was dissolved in ethyl ether, decolorized with charcoal, and filtered. Benzene was added to the filtrate and the mixture was evaporated until a white crystalline solid precipitated. The solid was identical as 2-hydroxy-3-nitropropionic acid (0.24 g., 83% yield); m.p. 76–77°, lit.[6,9] 76–77°, no depression by an authentic sample.

Reaction of Nitryl Chloride and Acrylonitrile; 2-Chloro-3-nitropropionitrile.—Nitryl chloride (91.8 g., 1.2 moles, 20% excess) was distilled through a gas delivery tube in 2 hours into acrylonitrile (53 g., 1 mole, freshly distilled) at 0° in a flask equipped with a sealed stirrer, a condenser, and a drying tube. The dark red mixture was stirred at room temperature for one hour. Excess nitryl chloride (now containing dinitrogen tetroxide) was distilled from the mixture at reduced pressure; precaution was taken to prevent warming up of the product during this operation. The green-yellow product was distilled under nitrogen to yield: (1) 2,3-dichloropropionitrile (16.7 g., 13.5%), b.p. 61–67° (14–15 mm.), (2) nitrated product (103 g., 0.76 mole, 76.1%), b.p. 88–91° (1–1.5 mm.), and (3) residue (16.7 g., unidentified). Rectification of the nitrated product at reduced pressure in a helix-packed column (24 × 2 cm.) gave **2-chloro-3-nitropropionitrile**, a yellow liquid, b.p. 83° (1 mm.), lit.[4] b.p. 82° (1.5 mm.), $n^{20}\text{D}$ 1.4743, d^{25}_4 1.417, lit.[4] D 1.421.

Anal. Calcd. for $C_3H_3N_2O_2Cl$: C, 27.76; H, 2.23; Cl, 26.40. Found: C, 27.16; H, 2.27; Cl, 26.84.

Reaction of nitryl chloride and acrylonitrile in ethyl ether at 0° yields ammonium chloride, 2,3-dichloropropionitrile

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(20) T. L. Kelley and P. A. Kleff, THIS JOURNAL, **54**, 4444 (1932).

and 3-nitroacrylonitrile (48.2%) as well as 2-chloro-3-nitropropionitrile. The products from reaction in ethyl ether are very unstable and violent decomposition may occur when they are distilled. 2-Chloro-3-nitropropionitrile prepared from nitryl chloride and acrylonitrile must be distilled carefully several times at reduced pressure before it reaches maximum stability. The chloronitronitrile is very corrosive and blisters skin rapidly. It forms dark red solutions rapidly in dilute alkaline media.

Reaction of 2-Chloro-3-nitropropionitrile and Sodium Acetate; 3-Nitroacrylonitrile.—2-Chloro-3-nitropropionitrile (402 g., 3 moles) was added dropwise in one hour to a stirred suspension of anhydrous sodium acetate (297 g., 3.3 moles) in absolute ethyl ether (500 ml.) at 0°. Immediately after addition was completed, the red suspension was filtered free of sodium acetate and sodium chloride. Ethyl ether and acetic acid were removed at reduced pressure; the residue was distilled under nitrogen to yield: (1) volatile product (265.5 g., 93%), b.p. 59–87° (3–4 mm.) and (2) residue (31.9 g.). Refractionation of the volatile product under nitrogen in a glass-packed column (24 × 2 cm.) gave: **3-nitroacrylonitrile**, a yellow oil (231 g., 2.35 moles, 78.9%), b.p. 53–54° (3.3–3.4 mm.), n^{20}_D 1.4929, d^{20}_4 1.268, and residue (26 g.). The residue is composed principally of unreacted 2-chloro-3-nitropropionitrile.

Anal. Calcd. for $C_3H_2N_2O_2$: C, 36.73; H, 2.04; N, 28.57. Found: C, 36.43; H, 2.04; N, 28.12.

3-Nitroacrylonitrile is a powerful vesicant and lachrymator. It is oxidized by permanganate but absorbs bromine slowly. The nitronitrile can be stored for long periods at 0–5° without serious decomposition.

Reaction of 3-Nitroacrylonitrile and Sulfuric Acid; 3-Nitroacrylamide.—A mixture of 3-nitroacrylonitrile (3.0 g., 0.030 mole) and 85% sulfuric acid (25 ml.) was heated at 50–55° for 7 hours and then poured on ice. A yellow solid precipitated (1.23 g.), m.p. 165° (dec.); continuous extraction of the aqueous filtrate yielded additional solid (0.64 g.), m.p. 155–160°, m.p. 165° after recrystallization from benzene, and an oil (1.1 g., unidentified) that did not crystallize. An infrared spectrogram of the solid contained definite absorption bands for α-nitrounsaturated (6.45–6.50 microns), carbonyl (5.85–5.90 microns), amide (2.85–3.05 microns), and olefinic groups (6.0–6.05 microns); no bands characteristic of hydroxyl or nitrile groups were present. (A possible product of this reaction is 2-hydroxy-3-nitropropionitrile.) On the basis of the spectrographic and analytical data, the product is assigned the structure, **3-nitroacrylamide** (54% yield).

Anal. Calcd. for $C_3H_4N_2O_3$: C, 31.04; H, 3.45; N, 24.14. Found: C, 31.25; H, 3.46; N, 24.53.

Conversion of 3-Nitroacrylonitrile to 3-Nitroacrylic Acid by Hydrolysis and Deamination.—A mixture of 3-nitroacrylonitrile (2.5 g., 0.025 mole) and 85% sulfuric acid (20 ml.) was heated at 70–80° for 2.5 hours. The mixture was cooled, and a concentrated solution of sodium nitrite (3.5 g., 0.05 mole) in water was added slowly. After the mixture stopped foaming, it was heated to 80° for 10 minutes. The solution was cooled, diluted with water, and continuously extracted with ethyl ether. After the ether had been evaporated, a yellow solid remained which, after recrystallization from chloroform, was identified as 3-nitroacrylic acid (2.0 g., 0.0171 mole, 69.4%); m.p. 134.5°, no depression by an authentic sample; neut. equiv. (calcd.) 117, neut. equiv. (found) 116.7.

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Microbiological Synthesis of C^{14}-Labeled Streptomycin

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Radioactive streptomycin was prepared by microbiological synthesis using *S. griseus* as the active microörganism. Glucose and starch, uniformly labeled with C^{14}, were added to the medium as precursors in separate experiments. Glucose was the superior substrate since it appeared to be preferentially utilized for streptomycin formation. Radiostreptomycin was isolated as the crystalline helianthate. The specific activity of the product was ≃0.01–0.025 μc./mg. streptomycin base.

Streptomycin is a metabolism product of *Streptomyces griseus*.[1] The problem of labeling streptomycin with carbon-14 by microbiological synthesis can be solved, in principle, by adding to the fermentation medium a C^{14}-labeled compound utilized by the organism. This presupposes, of course, a knowledge of streptomycin precursors, and of the extent of incorporation of these substrates into the desired product.

One potential difficulty encountered in this approach is the rather large quantity of carbon present initially in the usual medium in the form of broth ingredients. Unless the radioactive precursor is of such a nature as to be used by the organism in preference to the normal broth components, the net effect will be a considerable diminution in specific activity of the carbon in the precursor with resultant formation of low specific activity product.

A logical substrate for labeling is glucose which is a common component of many fermentation media. Glucose uniformly labeled with C^{14} was employed in two of the experiments to be reported. Experiments were also performed with uniformly labeled starch and with a crude starch hydrolysate. Nutrient medium in shake flasks was inoculated with a *S. griseus* culture and the microörganism allowed to grow for about 24 hr., at which time the C^{14} substrate was added. The broth was harvested 1–3 days later. After filtration of the mycelium, the streptomycin in the filtrate was removed by adsorption on IRC 50 resin column and subsequent elution with 1 *N* HCl.

In all cases, evidence for the synthesis of radioactive streptomycin was obtained from concomitant measurements of the radioactivity and microbial activity of the column eluates, as shown in Table I. The carbon content of the broth, necessary for computing the item "broth carbon c.p.m./mg.," was determined by microanalysis of broth components. Allowance was also made for the carbon content of precursors, which was determined in the case of the starch hydrolysate. The quantity of carbon lost from the broth as carbon dioxide during the 28-hr. period prior to addition of precursor was found from blank experiments to amount to ≃10% of the initial total carbon content (≃1.2 g.) of the medium. This correction was made so that the specific activity of broth carbon recorded in the table refers to that prevailing at the time of addition of the substrate. Succeeding items show the total radioactivity (column eluate c.p.m.)

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[1] A. Schatz, E. Bugie and S. A. Waksman, *Proc. Soc. Exp. Biol. & Med.*, **55**, 66, (1944).