[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF PURDUE UNIVERSITY]

Nitration Studies. XI. Preparation of α-Nitroketones and Aldehydes. Nitration of Enol Acetates and Ethers[1]

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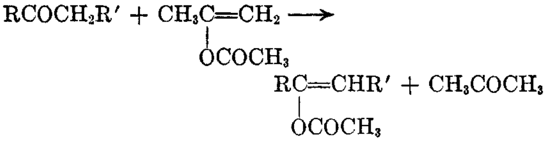
α-Nitroketones and aldehydes have been prepared in 12–36% yields by the nitration of enol acetates and ethers with nitryl chloride. Other nitrating agents gave lower yields.

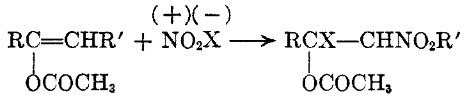
The nitration of ketones with nitric acid in both the liquid and vapor phases has been reported to give extensive oxidation and degradation with only very small amounts of α-nitroketones being isolated.[3] Nitration of ketones with alkyl nitrates in alkaline media has been reported as a good preparative method for α,α′-dinitroketones.[4] Although mononitroketones may be obtained in good yields from ketones containing only one α-methylene group,[5] mixtures of mono- and dinitroketones are obtained with ketones containing two α-methylene groups by this method.[6] The preparation of α-nitroaldehydes by nitration of aliphatic aldehydes seems not to have been reported.

The limitations of direct nitration methods may be ascribed in part to the low concentration of enol form normally present, since α-substitution reactions of carbonyl compounds have generally been postulated to proceed through such enol intermediates.[7] For this reason, it seemed probable that mononitration of ketones and aldehydes might be achieved more successfully if a derivative of the enol form were prepared and nitrated under mild conditions. In continuation of our studies on the preparation of α-nitrocarbonyl compounds,[8] we have investigated the action of various nitrating agents on a series of enol esters and ethers. The results of these experiments are shown in Table I.

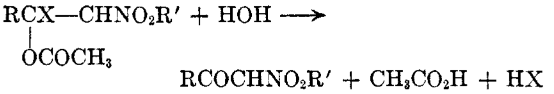
The over-all synthesis as applied to an enol acetate may be represented by the following equations:



$$\mathrm{RCOCH_2R' + CH_3\underset{\underset{\displaystyle OCOCH_3}{|}}{C}{=}CH_2 \longrightarrow \underset{\underset{\displaystyle OCOCH_3}{|}}{RC}{=}CHR' + CH_3COCH_3} \qquad (1)$$



$$\mathrm{\underset{\underset{\displaystyle OCOCH_3}{|}}{RC}{=}CHR' + \overset{(+)(-)}{NO_2X} \longrightarrow \underset{\underset{\displaystyle OCOCH_3}{|}}{RCX}{-}CHNO_2R'} \qquad (2)$$



$$\mathrm{\underset{\underset{\displaystyle OCOCH_3}{|}}{RCX}{-}CHNO_2R' + HOH \longrightarrow RCOCHNO_2R' + CH_3CO_2H + HX} \qquad (3)$$

Enol ethers react similarly but form an alcohol instead of acetic acid as by-product on hydrolysis. The reactions were run in ether, chloroform, or methylene chloride solvents at temperatures of −40° to 0°. The following nitrating agents were studied: nitryl chloride, acetyl nitrate, dinitrogen tetroxide, mixtures of dinitrogen tetroxide and halogens, butyl nitrate in acidic and alkaline media, and nitric acid. Successful mono-nitration of enol acetates and ethers was observed with nitryl chloride in 12–36% yields. Smaller yields (13–20%) of α-nitroketones were obtained through nitration with acetyl nitrate. The principal side reaction with this reagent seemed to be oxidation to 1,2-diketones and lower molecular weight acids. Dinitrogen tetroxide alone in ether solution gave a very low yield of ketone from the enol acetate of methyl ethyl ketone. The other nitrating agents gave little or none of the desired products.

Since α-nitroaldehydes of structure $\mathrm{RCHNO_2}$-CHO are readily capable of self-addition to form polymers, they cannot be isolated. For this reason, we have instead prepared the adducts only from the reactions of vinyl acetate and butyl vinyl ether with nitryl chloride and used them to prepare derivatives of the corresponding α-nitroacetaldehyde. With compounds of the structure $\mathrm{R_2CNO_2}$-CHO, such polymerizations do not occur and hence we have been able to prepare 2-nitro-2-methylpropanal as a constant-boiling fraction which gave an analytically pure 2,4-dinitrophenylhydrazone.

EXPERIMENTAL

The following experiments illustrate the procedures employed.

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[1] Abstracted from a thesis submitted to the faculty of the Graduate School of Purdue University in partial fulfillment of the requirements for the Ph.D. degree, August 1958.

[2] American Cyanamid Fellow, 1957–58.

[3] (a) R. Behrend and N. Tryller, *Ann.*, **283**, 244 (1894); (b) G. Ponzio and M. Fileti, *J. prakt. chem.*, **51**, 504 (1895); **55**, 192 (1897); (c) H. B. Hass and D. E. Hudgin, *J. Am. Chem. Soc.*, **76**, 2692 (1954); (d) C. D. Hurd and M. E. Nilson, *J. Org. Chem.*, **20**, 927 (1955).

[4] H. Feuer, J. W. Shepherd, and C. Savides, *J. Am. Chem. Soc.*, **78**, 4364 (1956).

[5] F. Strauss and W. Ekhard, *Ann.*, **444**, 146 (1925).

[6] R. Boschan, R. T. Merrow, and R. W. Van Dolah, *Chem. Revs.*, **55**, 485 (1955).

[7] J. Hine, *Physical Organic Chemistry*, McGraw-Hill Book Co., Inc., New York, 1956, p. 224.

[8] G. B. Bachman and T. Hokama, *J. Am. Chem. Soc.*, **81**, 4882 (1959).

TABLE I

NITRATION OF ENOL ESTERS AND ETHERS

Enol Ester or Ether	Nitrating Agent	Solvent	Time, Hr.	Temp., °C.	Product	Yield, %
(1) $CH_2{=}CHOCOCH_3$	NO_2Cl	$(C_2H_5)_2O$	4	0	$ClCH_2CHClOCOCH_3$ $O_2NCH_2CHClOCOCH_3$	10.8 36.0
(2) $CH_2{=}CHOC_4H_9$	NO_2Cl	$CHCl_3$	4	−20	$ClCH_2CHClOC_4H_9$ $O_2NCH_2CHClOC_4H_9$[a]	20.0 Trace
(3) $(CH_3)_2C{=}CHOCOCH_3$	NO_2Cl	CH_2Cl_2	4	−40	$(CH_3)_2CClCHO$ $(CH_3)_2CNO_2CHO$	21.0 12.0
(4) $CH_3CH{=}C(CH_3)OCOCH_3$	NO_2Cl	$(C_2H_5)_2O$	4	0	$CH_3COCHNO_2CH_3$[b]	36.0
(5) $CH_3CH{=}C(CH_3)OCOCH_3$	$CH_3CO_2NO_2$	CH_3CO_2H	4	25	$CH_3COCHNO_2CH_3$[b] $CH_3COCOCH_3$	13.0 17.0
(6) $CH_3CH{=}C(CH_3)OCOCH_3$	N_2O_4	$(C_2H_5)_2O$	2	0	$CH_3COCHNO_2CH_3$[b] $CH_3COCOCH_3$	5.0 40.0
(7) $CH_3CH{=}C(CH_3)OCOCH_3$	$N_2O_4 + Cl_2$	CCl_4	2	0	$CH_3COCHClCH_3$	58.0
(8) $CH_3CH{=}C(CH_3)OCOCH_3$	$N_2O_4 + Br_2$	CCl_4	2	0	$CH_3COCHBrCH_3$	50.0
(9) $CH_2{=}C(C_6H_5)OCOCH_3$	NO_2Cl	$(C_2H_5)_2O$	3	0	$C_6H_5COCH_2NO_2$[b] $C_6H_5COCH_2Cl$	36.0 14.0
(10) $CH_2{=}C(C_6H_5)OCOCH_3$	N_2O_4	$(C_2H_5)_2O$	4	0	$C_6H_5COCH_2NO_2$[b]	20.0
(11) $CH_3CH{=}C(C_6H_5)OCOCH_3$	NO_2Cl	$(C_2H_5)_2O$	2	0	$C_6H_5COCHNO_2CH_3$[b]	28.0
(12) $CH_3CH{=}C(C_6H_5)OCOCH_3$	$CH_3CO_2NO_2$	CH_3CO_2H	4	25	$C_6H_5COCHNO_2CH_3$[b]	21.0

[a] B.p. 76° (2 mm.); not analyzed but reacted with anthranilic acid to obtain the anil, m.p. 200°.[10] [b] *Cf.* reference 8.

α-Chloro-β-nitroethyl acetate. Reaction of vinyl acetate with nitryl chloride. Nitryl chloride,[9] 84 g. (1.0 mol.), was distilled in a current of nitrogen gas in 1 hr. into a stirred solution of vinyl acetate, 86 g. (1.0 mol.), in ether, 240 ml., at 0°, contained in a 500-ml., 3-necked flask equipped with a stirrer, gas inlet tube, and a reflux condenser fitted with a drying tube. After 2 hr. at 0°, the reaction mixture was allowed to warm to room temperature (2 hr.). The mixture was then concentrated under water aspiration, and distilled under nitrogen atmosphere at reduced pressure. α,β-Dichloroethyl acetate, b.p. 32° (10 mm.), n_D^{26} 1.4420, 17 g. (10.8% theory), and α-chloro-β-nitroethyl acetate, b.p. 66° (2 mm.), n_D^{26} 1.4446, 61 g. (36% theory), were obtained.

Anal. Calcd. for $C_4H_6NO_4Cl$: C, 78.67; H, 3.60; N, 8.36; Cl, 21.16. Found: C, 78.82; H, 3.67; N, 8.36; Cl, 21.01.

Hydrolysis of α-chloro-β-nitroethyl acetate in the presence of anthranilic acid gave the anil of nitroacetaldehyde, m.p. 200°. A mixture melting point with an authentic sample of the anil prepared from methazonic acid[10] showed no depression.

3-Nitro-2-butanone. Reaction of 2-buten-2-yl acetate with nitryl chloride. Nitryl chloride, 25 g. (0.3 mol.), was distilled in 1 hr. into a solution of 2-buten-2-yl acetate, 34 g. (0.3 mol.), in ether, 200 ml., at 0°, and the reaction mixture was stirred for 3 hr. Methanol, 30 ml., was added and the mixture was stirred for another 0.5 hr. The ether solution was washed twice with water, dried, and distilled. 3-Chlorobutanone, b.p. 40° (40–50 mm.), n_D^{26} 1.4168, 11 g. (30% theory), semicarbazone, m.p. 138°, lit.[11] m.p. 138–139°; and 3-nitro-2-butanone,[8] b.p. 56° (2 mm.), n_D^{26} 1.4360, 12.5 g. (36% theory), were obtained.

The aniline derivative, m.p. 102°, and the 2,4-dinitrophenylhydrazine derivative of 3-nitro-2-butanone, m.p. 124°, were prepared. Mixture melting points with authentic samples of these derivatives showed no depression. Lit.,[8,12] anil, m.p. 101–102°, 2,4-dinitrophenylhydrazone, m.p. 125°.

A similar experiment using dinitrogen tetroxide yielded only 5% of the nitroketone. Most of the product consisted of biacetyl (40% theory).

2-Nitro-2-methylpropanal. Reaction of 2-methyl-1-propen-1-yl acetate with nitryl chloride. 2-Methyl-1-propen-1-yl acetate, 61 g. (0.5 mol.), was added in 2 hr. to a solution of nitryl chloride, 37 g. (0.45 mol.), in dichloromethane, 200 ml., at −40°, and the mixture was stirred for another 2 hr. Methanol, 32 g., was added and the mixture was stirred for 1 hr., and then allowed to stand overnight at room temperature. Distillation gave: (a) 2-chloro-2-methylpropanal, b.p. 88–90°, 11 g. (21% theory); (b) 2-nitro-2-methylpropanal, b.p. 49° (3 mm.), n_D^{26} 1.4398, 5 g. (12% theory), the infrared spectrum showed absorption at 5.76 μ (carbonyl group) and at 6.34 and 7.25 μ (nitro group).

The oxime of 2-chloro-2-methylpropanal melted at 104°. Lit.,[13] m.p. 104–105°.

The 2,4-dinitrophenylhydrazone of 2-nitro-2-methylpropanal, m.p. 150°, was prepared and analyzed.

Anal. Calcd. for $C_{10}H_{11}N_5O_6$: C, 40.41; H, 3.73; N, 23.56. Found: C, 40.52; H, 4.00; N, 23.56.

α-Nitropropiophenone. Reaction of 1-phenyl-1-propen-1-yl acetate with acetyl nitrate. Acetic anhydride, 12.0 g. (0.12 mol.), was added in 0.25 hr. to a cooled solution of 100% nitric acid, 6.3 g. (0.1 mol.). 1-Phenyl-1-propen-1-yl acetate, 12 g. (0.068 mol.), was added in 0.5 hr. to the cooled solution of acetyl nitrate, and the mixture was stirred at room temperature for 4 hr. The reaction mixture was hydrolyzed with 10% urea solution, 200 ml., and the aqueous solution was extracted 3 times with ether. The ether layers were combined, dried, and distilled. α-Nitropropiophenone, b.p. 120–124° (1 mm.), n_D^{26} 1.5434, 2.5 g. (21% theory), was obtained.

The 2,4-dinitrophenylhydrazine derivative, m.p. 177–178°, was prepared. A mixture melting point with an authentic sample of the derivative showed no depression. Lit.,[8] m.p. 178°.

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(9) Prepared by the procedure of H. Shechter, F. Conrad, A. L. Daulton, and R. B. Kaplan, *J. Am. Chem. Soc.*, **74**, 3052 (1952).

(10) German Patent **347,375** (to Badische Anilin-and-Soda Fabrik), Jan. 17, 1922.

(11) F. H. Curd and A. Robertson, *J. Chem. Soc.*, 717 (1933).

(12) C. D. Hurd and M. E. Nilson, *J. Org. Chem.*, **20**, 926 (1955).

(13) H. D. K. Drew and F. S. H. Head, *J. Chem. Soc.*, 49 (1934).

Attempted nitration of 2-buten-2-yl acetate with dinitrogen tetroxide–chlorine mixture. 2-Buten-2-yl acetate, 23 g. (0.2 mol.), was added in 1 hr. to a cooled solution of dinitrogen tetroxide, 9.2 g. (0.1 mol.), and chlorine, 7.1 g. (0.1 mol.), in carbon tetrachloride, 100 ml., and the reaction mixture was allowed to warm to room temperature (1 hr.). The carbon tetrachloride solution was washed with water, dried, and distilled. Only 3-chlorobutanone, b.p. 36° (40 mm.), n_D^{26} 1.4168, 12 g. (58% theory), and no 3-nitrobutanone was isolated.

LAFAYETTE, IND.

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Fluoroalkanethiolcarboxylic Acids

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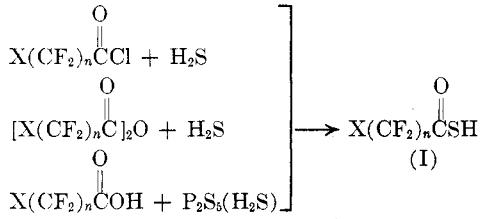
Fluoroalkanethiolcarboxylic acids (I) have been prepared by the reaction of the corresponding acid anhydride or halide with hydrogen sulfide or by reaction of the acid with phosphorus pentasulfide. The properties and reactions of these thioacids are described.

Esters of fluoroalkanethiolcarboxylic acids have been prepared by the reaction of fluoroacyl chlorides with mercaptans,[1] and by the oxidation of the bis(alkyl- and arylthio)-tetrafluorocyclobutenes.[2] However, parent fluoroalkanethiolcarboxylic acids (I) are an unknown class of compounds[3] and attempts to prepare these acids by hydrolysis of the corresponding thioesters yielded only the acids and thiols.[1] We have found that the fluoroalkanethiolcarboxylic acids (I) are readily prepared by heating the corresponding fluoroacyl chlorides or anhydrides with hydrogen sulfide at 200° in an autoclave. They can also be obtained by heating fluoroalkanecarboxylic acids with phosphorus pentasulfide under the same conditions.

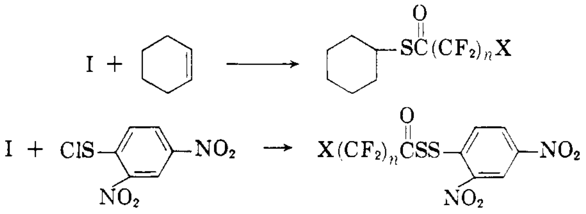


$$\left.\begin{array}{l} X(CF_2)_n\overset{\overset{O}{\|}}{C}Cl + H_2S \\ {[X(CF_2)_n\overset{\overset{O}{\|}}{C}]_2O} + H_2S \\ X(CF_2)_n\overset{\overset{O}{\|}}{C}OH + P_2S_5(H_2S) \end{array}\right] \longrightarrow \underset{(I)}{X(CF_2)_n\overset{\overset{O}{\|}}{C}SH}$$

where X = F or H

These conditions are more drastic than needed for the preparation of the hydrocarbon analogs.[4] It was noted in preliminary exploratory experiments that no reaction occurred between the fluoroacyl halide and hydrogen sulfide below a temperature of 100° and that heptafluorobutyric acid was unaffected by being heated at 120° with phosphorus pentasulfide. Heptafluorobutyryl chloride reacted with a solution of hydrogen sulfide in pyridine but no free thiol acid could be isolated. The strongly acidic character of this fluoroalkanethiolcarboxylic acid (see below) may cause formation of very stable salts with pyridine.

The fluoroalkanethiolcarboxylic acids are pale yellow liquids with the characteristic overpowering thioacid odor. They appear to react in a manner analogous to the alkane–thiocarboxylic acids[4] as shown by the following equations:



The ionization constants of fluoroalkanethiolcarboxylic acids are in the region of 0.6; only approximate values of these constants could be determined by conductivity measurement[5] because of apparent instability of the aqueous solutions. These thiol acids are much stronger acids than the hydrocarbon analogs[6] and are of strength comparable to the fluoroalkanecarboxylic acids. The large increase in the acidity of fluoroalkanecarboxylic acids compared to the hydrocarbon analogs has

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(1) M. Hauptschein, C. S. Stokes, and E. A. Nodiff, *J. Am. Chem. Soc.*, **74**, 4005 (1952).

(2) K. E. Rapp, J. T. Barr, R. L. Pruett, C. T. Bahner, J. D. Gibson, and R. H. Lafferty, Jr., *J. Am. Chem. Soc.*, **74**, 749 (1952).

(3) For a recent review of fluoroalkanecarboxylic acids and derivatives, see A. M. Lovelace, O. A. Rausch, and W. Postelnek, "Aliphatic Fluorine Compounds," Reinhold Publishing Corporation, New York, 1958, Chapters VII and XIII.

(4) E. H. Rodd, "Chemistry of Carbon Compounds," Elsevier, New York, 1951, Volume IA, pp. 593–595. Thiolacetic acid is prepared by passing hydrogen sulfide into a mixture of acetic anhydride and acetyl chloride at room temperature, by the reaction of excess hydrogen sulfide on acetyl chloride and pyridine, or by the distillation of the carboxylic acid from phosphorus pentasulfide.

(5) A. L. Henne and C. J. Fox, *J. Am. Chem. Soc.*, **73**, 2323 (1951) reported the ionization constants of trifluoroacetic acid and heptafluorobutyric acid as 0.59 and 0.68, respectively, at 25° in water.

(6) The ionization constant of thiolacetic acid is 4.7 × 10^{-4} compared to the value of 1.7 × 10^{-5} for acetic acid.