for poly-γ-methyl-L-glutamate.[10] This product was soluble in water, dioxane, or alcohol. End group analysis by sodium methoxide titration in dimethylformamide[11] gave for one run an equivalent weight of 820. End group determination *via* the dinitrophenyl derivative[12] gave equivalent weights, for a second run, of about 1100.

Part of the product from one run was saponified with 2 *N* sodium hydroxide (25°, 18 hr.); the resulting solution was acidified and continuously extracted with methylene chloride. Concentration of the extract and recrystallization from acetone–ether yielded a small amount of 3,6-bis(carboxyethyl)-2,5 diketopiperazine, m.p. 154–157°.[13]

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(10) C. H. Bamford, A. Eliott, and W. E. Hanby, *Synthetic Polypeptides*, Academic Press, New York, 1956, p. 157.

(11) M. Sela and A. Berger, *J. Am. Chem. Soc.*, **77**, 1893 (1955).

(12) I. Leube, H. Restle, and M. Niedmann, *Z. Naturforsch.*, **9b**, 186 (1954).

(13) A. Blanchetiere, *Bull. soc. chim. France*, [4] **31**, 1046, 1051 (1922); **35**, 1317 (1924).

The Preparation of Polyfluoronitrosoalkanes from Nitrosyl Polyfluoroacylates

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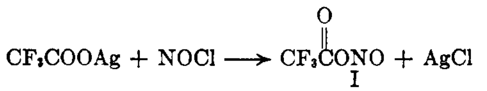
The recent publication of Banks, Haszeldine, and McCreath[1] on the preparation and properties of perfluoroacyl nitrites prompts us to report our work in this area.

The reaction of silver trifluoroacetate with nitrosyl chloride was initially described by J. Banus and R. N. Haszeldine.[2] In their experiments a mixture of silver trifluoroacetate and nitrosyl chloride was pyrolyzed after removing excess nitrosyl chloride. This treatment resulted in a low yield (13–16%) of trifluoronitrosomethane plus a considerable amount of chlorotrifluoromethane and some hexafluoroethane.

In the present investigation, dry, finely ground silver trifluoroacetate was treated with excess nitrosyl chloride. After removal of excess nitrosyl chloride the product mixture was distilled under vacuum taking care not to heat the residue above 90°. Under these conditions there was only one volatile product, a yellow, chlorine free liquid obtained in almost quantitative yield (Equation 1). The elemental analysis and infrared spectra of this material showed it to be nitrosyl trifluoroacetate (I).



$$CF_3COOAg + NOCl \longrightarrow \underset{I}{CF_3\overset{O}{\overset{\|}{C}}ONO} + AgCl \quad (1)$$

The silver salts of longer chain perfluorocarboxylic acids reacted in a similar manner giving good yields of the corresponding nitrosyl perfluoroacylates.

Other polyfluorocarboxylic acids and chlorofluorocarboxylic acids will also undergo this reaction—for example, the perfluoro(β-alkoxypropionic) acids $R_fOCF_2CF_2COOH$ and the acids $CF_2Cl_2(CF_2CFCl)_nCF_2COOH$. Examples of the use of these acids are contained in the Experimental.

The nitrosyl polyfluoroacylates are quite stable at room temperature and even at 100° for moderate periods of time, as distinguished from their hydrocarbon analogs,[3] which explode upon mild heating and decompose into N_2O_3 and the acid anhydride under the influence of light. At higher temperatures (above 140°) the nitrosyl polyfluoroacylates must also be handled with considerable care, as they can decompose with explosive violence if not diluted with a suitable inert solvent.

The nitrosyl polyfluoroacylates show the high volatility and ready hydrolysis typical of covalent nitrosyl compounds. Absorption in the visible region (yellow color) also indicates a covalently bonded nitrosyl group rather than the nitrosonium ion (NO^+) present in salts such as nitrosyl fluoroborate or perchlorate. Nitrosyl trifluoroacetate, the lowest member of the perfluoro acid series, boils at 99° at atmospheric pressure and the perfluorobutyrate and perfluorooctanoate have boiling points of 72° at 93 mm. and 55° at 1.5 mm., respectively. These compounds all show infrared absorption[4] at 5.06–5.08 μ (s,b) associated with the nitrosyl group and carbonyl absorption at 5.83–5.87 μ (s,b). The boiling points and the broadness of infrared bands suggests that these materials are associated. The fact that the ultraviolet spectrum, although diffuse, changes with concentration also supports this view.

Many metal chlorides, including the alkali and alkaline earth chlorides, aluminum chloride, ferric chloride, zinc chloride, and cadmium chloride release nitrosyl chloride rapidly when treated with a nitrosyl polyfluoroacylate. Therefore, preparation of nitrosyl polyfluoroacylates from nitrosyl chloride and the polyfluoro acid salt of these metals is generally unfavorable. However, when lead chloride is treated with a nitrosyl polyfluoroacylate, nitrosyl chloride is slowly liberated, and by heating or by removing nitrosyl chloride under vacuum the equilibrium expressed in Equation 2 can be driven completely to the left. On the other hand, if the lead salt is treated with excess liquid nitrosyl,

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(1) R. E. Banks, R. N. Haszeldine, and M. K. McCreath, *Proc. Chem. Soc.*, 64 (1961).

(2) J. Banus, *J. Chem. Soc.*, 3755 (1953). R. N. Haszeldine and J. Jander. *J. Chem. Soc.*, 4172 (1953).

(3) Francesconi and Cialdea, *Gazz. chim. ital.*, **34**, 1435 (1904).

(4) Nitrosyl polyfluoroacylates react rapidly with sodium chloride; hence silver chloride cells must be used.

$$(R_f\mathrm{COO})_2\mathrm{Pb} + 2\mathrm{NOCl} \rightleftarrows 2R_f\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{ONO} + \mathrm{PbCl_2} \quad (2)$$

chloride and the insoluble lead chloride filtered off, the corresponding nitrosyl polyfluoroacylate is obtained after removal of nitrosyl chloride from the filtrate. When employing the lead salts to prepare nitrosyl polyfluoroacylates, it is helpful to use a low boiling chlorofluoroalkane as a solvent— for example, $\mathrm{CCl_3F}$ (Freon 11)— and to recycle the solvent and nitrosyl chloride. In this manner yields of from 80-90% of the nitrosyl polyfluoroacylates may be realized.

Other nitrosating agents such as dinitrogen tetroxide and nitrosyl fluoroborate were generally not effective in the preparation of nitrosyl polyfluoroacylates, although a small yield of nitrosyl trifluoroacetate was obtained when calcium trifluoroacetate was heated under vacuum at 90° with $\mathrm{(NO)_2S_2O_7}$.

Nitrosyl trifluoroacetate reacts violently with water to form trifluoroacetic acid and nitrous acid. Alcohols yield the corresponding nitrite ester. Another property which indicates the highly reactive nature of these materials is their ability to oxidize metals. In this respect they are more reactive than nitrosyl chloride. In addition to reacting with active metals such as alkali and alkaline earth metals, iron, aluminum, zinc, and lead they react with mercury, copper, nickel, and silver with the formation of the corresponding salt of the polyfluorocarboxylic acid and the release of nitric oxide.

Nitrosyl trifluoroacetate can be pyrolyzed to trifluoronitrosomethane and carbon dioxide. This is a general and very useful means of preparing perfluoronitroso compounds (Equation 3). As

$$R_f\mathrm{COONO} \xrightarrow{\Delta} R_f\mathrm{NO} + \mathrm{CO_2} \quad (3)$$

there is no chlorine present, as in the one step preparation of nitroso compounds from silver salts and nitrosyl chloride, the formation of chloroperfluoro compounds is avoided. The pyrolysis is best performed by entraining the nitrosyl polyfluoroacylate in a stream of inert gas and then passing the gas mixture through a hot tube at 160–200°. Care must be exercised to maintain only a partial pressure of reactant (conveniently 300 mm.), as the pure vapors will explode under these conditions. When this precaution was taken the pyrolysis proceeded smoothly to give yields of trifluoronitrosomethane in the range of 55–65% so that the overall yield of trifluoronitrosomethane in the two-step synthesis was 50–60%. The major by-products of the pyrolysis, in addition to the carbon dioxide released, were carbonyl fluoride, oxides of nitrogen, and some trifluoronitromethane.

A calculation, based on bond strengths, of the energy released if nitrosyl trifluoroacetate were to decompose to the most stable products, namely carbon tetrafluoride, nitrogen, carbon dioxide, and oxygen, reveals an energy content of approximately 750 cal. per gram which would place nitrosyl trifluoroacetate in the same range as some commercial explosives. Although the products of such an explosive decomposition were never determined, a differential thermal analysis of nitrosyl trifluoroacetate in a sealed capsule revealed that above 110° the decomposition was exothermic.[5] However, when superheating was carefully avoided, pure nitrosyl trifluoroacetate was refluxed at atmospheric pressure under nitrogen for forty eight hours (99°) without appreciable decomposition. At room temperature the nitrosyl polyfluoroacylates appear to be relatively insensitive to shock, electrical spark, and local heating with a hot wire.

EXPERIMENTAL

Preparation of nitrosyl trifluoroacetate from silver trifluoroacetate. Nitrosyl chloride (65 g., 1.0 mole) was distilled from a gas transfer system into a 500 ml. round bottom flask containing 138 g. (0.623 mole) dry finely powdered silver trifluoroacetate. The mixture was allowed to warm to −20° and remain at that temperature for 2 hr. with occasional vigorous manual swirling of the slurry. The excess nitrosyl chloride was removed at room temperature and the product distilled under high vacuum and condensed in a receiver cooled in Dry Ice–acetone. Redistillation of this material gave 82.4 g. (92.5% yield) nitrosyl trifluoroacetate, b.p. 47° at 94 mm.

Anal. Calcd. for $\mathrm{C_2F_3NO_3}$: C, 16.8%; F, 39.8%; N, 9.78%. Found: C, 17.0%; F, 39.3%; N, 8.8%.

Its NMR peak was at $\mathrm{C_6H_5}\phi^{*6} = 74.68$ (10% by volume).

Preparation of nitrosyl perfluorooctanoate from silver perfluorooctanoate. Silver perfluorooctanoate (30 g., 0.058 mole) was treated with 35 g. nitrosyl chloride (0.54 mole) as described in the above example. Distillation of the liquid product obtained gave 23.2 g. (90% yield) nitrosyl perfluorooctanoate, b.p. 55–60° at 1.5 mm.

Preparation of trifluoronitrosomethane by pyrolysis of nitrosyl trifluoroacetate. A 100-ml. pear-shaped flask having a nitrogen inlet extending to the bottom was connected to a 2 × 28 cm. Pyrex pyrolysis tube by 1 mm. capillary tubing. The capillary tubing was wound with heating tape to prevent condensation of the entrained reactant. A thermocouple was taped to the outside of the pyrolysis tube which was in turn wrapped with aluminum foil and then heating tape. The exit gases from the pyrolysis tube were passed through a Dry Ice–acetone trap followed by two liquid air traps.

Nitrosyl trifluoroacetate was placed in the pear-shaped flask and heated with an oil bath to 75–78°. Nitrogen bubbled through the hot liquid at 150 ml. per minute entrained the nitrosyl trifluoroacetate through the pyrolysis tube. The latter was heated to 190–192° and the pyrolysis was continued for 3.5 hr at which time 24.7 g. (0.173 mole) of nitrosyl trifluoroacetate had been pyrolyzed. The pyrolysis was then stopped and the Dry Ice trap warmed to −20° to allow gases dissolved in the less volatile products to distill into the liquid air traps. The product from the liquid air traps was bubbled through two washing towers containing 5% potassium hydroxide and finally a Drierite drying tube. Distillation of this material gave 9.6 g. (56% yield) of trifluoronitrosomethane. The infrared spectrum of this

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(5) We are indebted to Dr. R. D. Lowrey for the energy content calculations and to Dr. R. L. Bohon for the differential thermal analysis measurements.

(6) Filipovich and Tiers, *J. Phys. Chem.*, **63**, 761 (1959).

material was identical to the spectrum of a sample of CF_3NO prepared from CF_3I.[7]

Nitrosyl perfluorobutyrate from lead perfluorobutyrate. A 1-l. three neck flask was equipped with a stirrer, a Dry-Ice–acetone cold finger condenser, and a 250-ml. Erlenmeyer flask attached to the reaction flask via thin-walled rubber tubing so that solids could be added without exposure to atmospheric moisture. The reaction flask was cooled in Dry Ice–acetone, charged with nitrosyl chloride (176 g., 2.7 moles), and stirred while lead perfluorobutyrate (104 g., 0.164 mole) was added portionwise from the Erlenmeyer flask. After the addition was complete (approximately 10 min.) the addition assembly was replaced with a glass stopper and the reaction mixture was stirred at reflux for 4 hours. After being allowed to stand overnight in Dry Ice, the mixture was again brought to reflux and 200 ml. CCl_3F were added. The precipitate was allowed to settle and the mixture was filtered being careful to decant the bulk of the solution before the solids were poured into the funnel The filtration was performed in a sintered glass funnel under 2 to 3 lb. nitrogen pressure. The excess nitrosyl chloride and CCl_3F were removed at room temperature and the product remaining distilled under reduced pressure yielding 72 g. (90% yield) nitrosyl perfluorobutyrate, b.p. 72°/93 mm.

Anal. Calcd. for $C_4F_7NO_3$: C, 19.8; F, 54.7; N, 5.76. Found: C, 20.4; F, 55.1; N, 5.4.

The NMR $C_6H_5\phi^*$[6] values for CF_3, —CF_2—, and —CF_2— adjacent to the carbonyl were 80.71 triplet, 126.45 singlet, and 118.28 quartet, respectively, at 10% conc. by volume.

Preparation of nitrosyl trifluoroacetate from calcium trifluoroacetate and $(NO_2)S_2O_7$. Calcium trifluoroacetate (25.0 g., 0.094 mole) was triturated with $(NO)_2S_2O_7$ (25.0 g., 0.106 mole) under a stream of nitrogen. The mixture was then stirred and heated at 90° under vacuum. A yellow liquid (4 g.) was collected in a trap cooled in Dry Ice–acetone. The infrared spectrum of this material showed it to be nitrosyl trifluoroacetate plus some trifluoroacetic acid.

Preparation of Nitrosylperfluoro(β-ethoxy)propionate from silver perfluoro(β-ethoxy)propionate. A 500 ml. round bottom flask was equipped with an outlet protected by a drying tube, a magnetic stirrer, and a 125 ml. Erlenmeyer flask attached to the reaction flask via thin-walled rubber tubing so that solids could be added without exposure to atmospheric moisture. The reaction flask was flushed with dry nitrogen, cooled in Dry Ice–acetone, charged with 30 cc. (42.6 g., 0.65 mole) nitrosyl chloride and stirred while 34.5 g. (0.892 mole) silver perfluoro(β-ethoxy)propionate was added portionwise from the Erlenmeyer flask. After the addition was complete (approximately ten minutes), the addition assembly was replaced with a glass stopper and the reaction mixture was stirred at −20° to −40° for 2 hr. The mixture was then allowed to warm to room temperature while the excess nitrosyl chloride distilled into a Dry Ice trap. The residue was vacuum distilled giving 27 g. (97.7% yield) nitrosyl perfluoro(β-ethoxy)propionate, b.p. 44°C at 14 mm.

Anal. Calcd. for $C_5F_9NO_4$: C, 19.4%; N, 4.52%. Found: C, 19.3%; N, 4.5%.

Preparation of nitrosyl 3,4-dichloropentafluorobutyrate from silver 3,4-dichloropentafluorobutyrate. Silver 3,4-dichloropentafluorobutyrate (44.9 g., 0.127 mole) was allowed to react with 40 ml. (57 g., 0.87 mole) nitrosyl chloride in the same manner as described above for perfluoro (β-ethoxy)propionate. Distillation of the product gave 31 g. (88.5% yield) nitrosyl 3,4-dichloropentafluorobutyrate, b.p. 63° at 5.5 mm.

Anal. Calcd. for $C_4F_5Cl_2NO_3$: C, 17.4; F, 34.4; N, 5.1. Found: C, 17.7; F, 34.1; N, 4.5.

Preparation of nitrosyl 3,5,6-trichlorooctafluorocaproate from silver 3,5,6-trichlorooctafluorocaproate. Silver 3,5,6-trichlorooctafluorocaproate (26.8 g., 0.0570 mole) was allowed to react with 40 ml. (57 g., 0.87 mole) nitrosyl chloride in the same manner as described above for perfluoro(β-ethoxy)propionate. Distillation of the product gave 20.0 g. (89.4% yield) nitrosyl 3,5,6-trichlorooctafluorocaproate, b.p. 73° at 0.5 mm.

Anal. Calcd. for $C_6F_8Cl_3NO_3$: C, 18.4; F, 38.7; N, 3.56. Found: C, 18.6; F, 38.4; N, 3.4.

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[7] R. N. Haszeldine, *J. Chem. Soc.*, 2075 (1953).

The Amidomethylation of 2-Chlorobenzoic Acid[1]

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The amidomethylation of 2-chlorobenzoic acid was undertaken in order to study the effect of the chlorine and carboxy substituents on the orientation of the entering amidomethyl group and to utilize the product in preparing derivatives to be tested for physiological activity.

The use of *N*-hydroxymethylchloroacetamide in concentrated sulfuric acid as reported by Tscherniac[3] and other workers[4–7] to amidomethylate benzoic acid was utilized in this work. It was noted in our study that if the ratio of sulfuric acid to 2-chlorobenzoic acid was doubled, the yield of product was increased from 40 to 65%. This product was shown to be 2-chloro-5-(chloroacetylaminomethyl)benzoic acid (I).

Hydrolysis of I by means of concentrated hydrochloric acid gave 3-carboxy-4-chlorobenzylamine hydrochloride (II).

The action of formaldehyde and sodium bicarbonate on II followed by hydrogenation with a palladium-charcoal catalyst gave *m*-toluic acid (III), which was identified by melting point and infrared spectra.

3-Carboxy-4-chlorobenzylamine hydrochloride was decarboxylated with soda-lime to yield 4-chlorobenzylamine, which was identified as the benzoyl derivative.

Vigorous oxidation of III with potassium dichromate and sulfuric acid gave 4-chloroisophthalic acid (IV).

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[2] Undergraduate research project.

[3] J. Tscherniac, German Patent **134,979** (1902); P. Friedlander, *Fortsch. Teerfarb.*, 6, 143 (1900–1902).

[4] A. Einhorn and T. Mauermayer, *Ann.*, **343**, 295 (1905).

[5] A. Einhorn and M. Gottler, *Ber.*, **42**, 4837 (1909).

[6] H. E. Zaugg and B. H. Horrom, *J. Am. Chem. Soc.*, **80**, 4317 (1958).

[7] H. Hellman, *Angew. Chem.*, **69**, 463 (1957).