(10) S. A. Heininger and J. Dazzi, *Chem. Eng. News*, **35**, 87 (1957).
(11) Except sodium 2-naphthalenesulfonate. See Table IV, footnote *k*.
(12) Z. Rappoport, Ed., "Handbook of Tables for Organic Compound Identification", 3d ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1967, pp 392–405.
(13) F. Challenger and M. I. Simpson, *J. Chem. Soc.*, 1593 (1948).
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(15) Bis(2-nitrophenyl) disulfide was notably resistant to oxidation, and these conditions somewhat pressed the stability limits of Me_2SO. Though distillation of DMS had slowed by 7 h, it was still continuing at more than the usual rate.

Reactions of Fluorodinitroethoxyacetyl Chloride and Fluorodinitroethoxyacetic Anhydride with Friedel–Crafts Catalysts[1]

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Simple aliphatic anhydrides have been reported to react with boron trifluoride to give the symmetrical ketones.[2,3] Simple acid halides and tertiary amines gave ketene dimers, which on hydrolysis gave the corresponding ketones.[4] On the other hand, tertiary carboxylic acids, acid halides, and anhydrides underwent decarbonylation with Friedel–Crafts catalysts;[5] pivalyl chloride and aluminum chloride gave HCl, CO, and isobutylene.[6]

These reactions of fluorodinitroethoxyacetic acid derivatives were investigated as a continuation of our earlier work on this class of compounds.[7,8]

Fluorodinitroethoxyacetic acid and fluorodinitroethoxyacetyl chloride needed for this work were prepared by reported[7] procedures. Fluorodinitroethoxyacetic anhydride, unknown prior to this work, was synthesized in 60% yield by dehydrating fluorodinitroethoxyacetic acid with acetic anhydride:

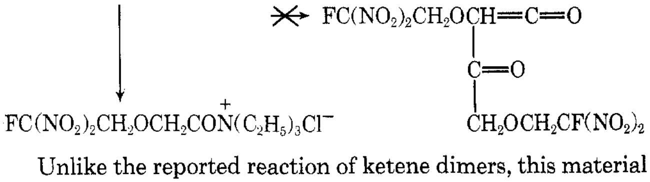
$$2FC(NO_2)_2CH_2OCH_2CO_2H + (CH_3CO)_2O \xrightarrow[\Delta]{} [FC(NO_2)_2CH_2OCH_2CO]_2O$$

Fluorodinitroacetic anhydride reacted with boron trifluoride under the reaction conditions employed by Man and Hauser.[3] The reaction product, however, was not the expected ketone, but fluorodinitroethoxymethyl fluorodinitroethoxyacetate:

$$[FC(NO_2)_2CH_2OCH_2CO]_2O \xrightarrow{BF_3} FC(NO_2)_2CH_2OCH_2COOCH_2OCH_2CF(NO_2)_2$$

A small amount of fluorodinitroethoxymethyl acetate was also obtained in this reaction.

Fluorodinitroethoxyacetyl chloride reacted readily with triethylamine in ethereal solution to give a white, crystalline solid. The stoichiometry of reaction and the solubility characteristics of this product indicated that instead of the expected ketene dimer, the reaction product was fluorodinitroethoxyacetyl triethylammonium chloride:



$$FC(NO_2)_2CH_2OCH_2COCl + N(C_2H_5)_3 \not\rightarrow \begin{array}{l} FC(NO_2)_2CH_2OCH{=}C{=}O \\ \quad\quad\quad\quad\quad\quad\quad | \\ \quad\quad\quad\quad\quad\quad\; C{=}O \\ \quad\quad\quad\quad\quad\quad\quad | \\ \quad\quad\quad\quad\quad\quad CH_2OCH_2CF(NO_2)_2 \end{array}$$

$$FC(NO_2)_2CH_2OCH_2COCl + N(C_2H_5)_3 \longrightarrow FC(NO_2)_2CH_2OCH_2CO\overset{+}{N}(C_2H_5)_3Cl^-$$

Unlike the reported reaction of ketene dimers, this material yielded dark, tarry product on treatment with water which did not contain any 1,3-bis(fluorodinitroethoxy)acetone.

Fluorodinitroethoxyacetyl chloride did not react with weak Friedel–Crafts catalysts such as stannic chloride or ferric chloride. The acid chloride, however, reacted rapidly with aluminum chloride with evolution of a gas. The product of this reaction was characterized as the previously reported[9] chloromethyl fluorodinitroethyl ether.

$$FC(NO_2)_2CH_2OCH_2COCl + AlCl_3 \longrightarrow FC(NO_2)_2CH_2OCH_2Cl + CO$$

These results are consistent with the initial reaction of fluorodinitroethoxyacetic anhydride and fluorodinitroethoxyacetyl chloride with Friedel–Crafts catalysts to give fluorodinitroethoxyacylium cation intermediate. Instead of losing the α proton and yielding fluorodinitroethoxyketene as is the case with simple carboxylic acid derivatives, this intermediate undergoes decarbonylation to give fluorodinitroethoxymethyl cation:

$$FC(NO_2)_2CH_2OCH_2COCl \xrightarrow{AlCl_3} [FC(NO_2)_2CH_2OCH_2CO]^+ + Cl^-$$

$$[FC(NO_2)_2CH_2OCH_2CO]_2O \xrightarrow{BF_3} [FC(NO_2)_2CH_2OCH_2CO]^+ + FC(NO_2)_2CH_2OCH_2COO^-$$

$$[FC(NO_2)_2CH_2OCH_2CO]^+ \xrightarrow{-CO} [FC(NO_2)_2CH_2OCH_2]^+$$

Thus, the fluorodinitroethoxy group appears to promote decarbonylation rather than ketene formation because of oxygen stabilization of the resulting cation, $FC(NO_2)_2CH_2OCH_2^+$.

Experimental Section

Fluorodinitroethoxyacetic Anhydride. A solution of 10 g (0.0472 mol) of fluorodinitroethoxyacetic acid[7] in 15 ml of acetic anhydride was refluxed for 8 h and the excess of acetic anhydride and acetic acid were removed under reduced pressure. The reaction product, 8.3 g, was contaminated with fluorodinitroethoxyacetic acid which was removed by distillation at 175–180 °C (0.1 mm). The degassed material amounting to 6.1 g (64% yield) solidified at room temperature and was crystallized from carbon tetrachloride to give 5.1 g of a white, crystalline solid: mp 54 °C; ^1H NMR ($CDCl_3$) δ 4.32 (d, J_{HF} = 16 Hz, 4 H, $2FCCH_2$–) and 4.69 ppm (s, 4 H, 2 –CH_2CO–).

Anal. Calcd for $C_8H_8F_2N_4O_{13}$: C, 23.66; H, 1.98. Found: C, 23.42; H, 2.03.

Fluorodinitroethoxymethyl Fluorodinitroethoxyacetate. A slow stream of boron trifluoride was passed at 0 °C for ca. 50 min into a stirred and cooled solution of 4 g (0.01 mol) of fluorodinitroethoxyacetic anhydride in 3 ml of chloroform. The resulting mixture was added to a solution of 4 g of sodium acetate in 9 ml of water and heated at 95–100 °C for 45 min. Chloroform was allowed to evaporate. The cooled mixture was extracted with 25 ml of methylene chloride and the methylene chloride solution was washed with 50 ml of saturated aqueous sodium bicarbonate solution followed by 50 ml of water. The methylene chloride solution was dried and stripped to give 2.2 g of oil. The crude material was distilled at 150 °C (0.1 mm) in a short-path micro distillation apparatus to give 1.9 g of fluorodinitroethoxymethyl fluorodinitroethoxyacetate, a colorless oil: ^1H NMR ($CDCl_3$) δ 5.25 (s, 2 H, –$COOCH_2O$–), 4.62 and 4.68 (two doublets, $J_{HF} \simeq$ 16 Hz, 4 H, 2 $FCCH_2$–), and 4.23 ppm (s, 2 H, –OCH_2COO–).

Anal. Calcd for $C_7H_8F_2N_4O_{12}$: C, 22.24; H, 2.13. Found: C, 22.36; H, 2.18.

A few drops of a colorless liquid obtained as a forerun in the above distillation was identified as fluorodinitroethoxymethyl acetate: ^1H NMR ($CDCl_3$) δ 5.17 (s, 2 H, –$COOCH_2$–), 4.66 (d, J_{HF} = 16 Hz, 2 H, $FCCH_2$–), and 2.10 ppm (s, 3 H, CH_3).

Anal. Calcd for $C_5H_7FN_2O_7$: C, 26.56; H, 3.12. Found: C, 27.3; H, 3.14.

Reaction of Fluorodinitroethoxyacetyl Chloride with Aluminum Chloride. Gas was evolved immediately when 0.3 g of anhydrous aluminum chloride was added to 1.0 g (0.047 mol) of fluorodinitroethoxyacetyl chloride. When evolution of gas ceased in ca. 10 min, the mixture was washed with 10 ml of ice water and extracted with 10 ml of methylene chloride. The methylene chloride solution was distilled to give 0.85 g of a colorless liquid, bp 40 °C (0.2 mm), identified as chloromethyl fluorodinitroethyl ether by comparing its physical properties and its ^1H NMR spectrum with those of an authentic sample of the ether.[9] There was no reaction when a 4:1 molar mixture of fluorodinitroethoxyacetyl chloride and stannic chloride was heated at 95–100 °C for a few hours. Similarly, no reaction occurred when the acid chloride saturated with boron fluoride was allowed to stand at ambient temperature for 4 days.

Reaction of Fluorodinitroethoxyacetyl Chloride with Triethylamine. To a stirred and cooled (0–5 °C) solution of 2.3 g (0.01 mol) of fluorodinitroethoxyacetyl chloride[7] in 70 ml of diethyl ether was added dropwise (15 min) a solution of 1.0 g (0.01 mol) of triethylamine in 15 ml of diethyl ether. A white, crystalline solid precipitated instantaneously. The mixture, protected from moisture by a calcium chloride drying tube, was refluxed for 24 h, cooled, and filtered. The filter cake, washed with ether, amounted to ca. 3 g. The filtrate and washings were combined and evaporated on a rotary evaporator, leaving no residue.

Registry No.—Fluorodinitroethoxyacetic anhydride, 58815-88-6; fluorodinitroethoxyacetic acid, 25172-22-9; fluorodinitroethoxymethyl fluorodinitroethoxyacetate, 58815-89-7; fluorodinitroethoxymethyl acetate, 50836-79-8; fluorodinitroethoxyacetyl chloride, 25172-23-0; aluminum chloride, 7446-70-0; triethylamine, 121-44-8.

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(1) This work was supported by Air Force Rocket Propulsion Laboratory, Director of Science and Technology, Air Force Systems Command, U.S. Air Force, Edwards, Calif. 93523.

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Bromination of 1-Alkyl-3-methyl-2-pyridones with *N*-Bromosuccinimide

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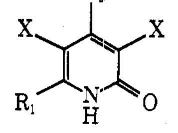
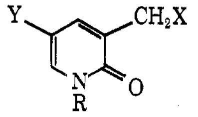
The functionalization of a β-methyl group attached to a pyridine or quinoline ring has proven to be an important step in several approaches to the synthesis of camptothecin[1,2,3] and bromination with *N*-bromosuccinimide (NBS) met with only limited success. With the pyridine derivatives no bromination of the ring or alkyl substituent occurred unless the basicity of the nitrogen was decreased by an electronegative, α substituent.[1,4] With 6-methyl- or 4,6-dimethyl-2-pyridone (**1** or **2**) NBS caused ring bromination to **3** and **4** rather than substitution of the methyl groups even using benzoyl peroxide as catalyst.[5,6] The earlier report[7] that 1,3-dimethyl-2-pyridone (**5**) gave bromination of the 3-methyl group with NBS to give **6** was recently questioned, for ring bromination to give **7** was confirmed as the product from this reaction.[3]



1, $R_1 = CH_3$; $R_2 = X = H$
2, $R_1 = R_2 = CH_3$; $X = H$
3, $R_1 = CH_3$; $R_2 = H$; $X = Br$
4, $R_1 = R_2 = CH_3$; $X = Br$



5, $R = CH_3$; $X = Y = H$
6, $R = CH_3$; $X = Br$; $Y = H$
7, $R = CH_3$; $X = H$; $Y = Br$
8, $R = PhCH_2$; $X = Y = H$
9, $R = PhCH_2$; $X = H$; $Y = Br$
10, $R = PhCH_2$; $X = Br$; $Y = H$

Since 1-substituted 3-bromomethyl-2-pyridone would be a convenient intermediate the NBS reaction with 1-alkyl-3-methyl-2-pyridones (**5** and **8**) was reinvestigated. A dilute solution of 1-benzyl-3-methyl-2-pyridone (**8**) was treated with NBS and dibenzoyl peroxide in refluxing carbon tetrachloride for 50 min and a solid product remained after filtration and evaporation of the solvent. The NMR spectrum of the product showed the triplet at 6.17 ppm due to the aromatic 5 proton, but the singlet at 2.16 ppm due to the signal for the *C*-methyl was missing. A new singlet was evident at 4.47 ppm due to a bromomethylene group. The elemental analyses confirmed that bromination of the methyl group had occurred to give **10**. A careful analysis of the NMR spectrum showed the presence of a trace of starting compound **8** but there were no signals which could be assigned to **9**. The reaction was repeated using the concentration of reagents previously reported to give ring bromination of **5**[3] and again the major product was the bromomethyl derivative **10** with only 20–30% of the ring brominated product **9** detectable by NMR. Indeed a reasonable yield of ring bromination of **8** could be obtained only by a reaction with NBS in the *absence* of dibenzoyl peroxide. In benzene or carbon tetrachloride the NMR of the crude product showed the presence of only about 10% of the bromomethyl derivative **10**.

The reactions were repeated with 1,3-dimethyl-2-pyridone (**5**) and NBS, in the absence of dibenzoyl peroxide or with this catalyst in a concentrated reaction mixture, and gave **7** as the major product by ring bromination. The crude products contained about 10% unreacted **5** and 10% of the 3-bromomethyl-1-methyl-2-pyridine (**6**) detected by NMR analysis. The reaction of **5** with NBS and dibenzoyl peroxide after an eightfold dilution gave mainly side-chain bromination to form **6** contaminated with only a few percent of starting material or product of ring bromination, **7**.

The ring or chain bromination of 1-alkyl-3-methyl-2-pyridones with NBS can be controlled in two examples to give either ring or side chain substitution. In the absence of dibenzoyl peroxide as a catalyst, NBS gave bromination of the ring in the same manner as would be expected with molecular bromine. In the presence of dibenzoyl peroxide, dilute reaction conditions gave side chain bromination with NBS. In concentrated reaction mixtures significant yields of ring bromination occurred even in the presence of dibenzoyl peroxide. The 1-methyl derivative, **5**, was more sensitive to this concentration effect than was the 1-benzyl-3-methyl-2-pyridone (**8**). By a proper choice of reaction conditions selectivity could be controlled to give crude products which crystallized and whose NMR analyses showed less than 10% contamination by the isomeric bromination product.

Experimental Section

1-Benzyl-3-methyl-2-pyridone (8). To a solution of 6.44 g of 87% KOH in 150 ml of absolute ethanol at 50 °C was added 3-methyl-2-pyridone.[8] The resulting solution was stirred for 20 min before the dropwise addition of benzyl chloride. The mixture was stirred at 50 °C for 3 h, concentrated under reduced pressure, poured into 180 ml of water, and extracted with chloroform (3 × 50 ml). The organic phase was washed with water and saturated salt solution, dried ($MgSO_4$), filtered, and concentrated to yield a light yellow oil which crystallized under pentane with cooling. The solid was collected and dried to give 15.75 g (86%) of **8** as white crystals, mp 69–71 °C. The product was recrystallized twice from petroleum ether (bp 30–60 °C)–methylene chloride to afford an analytical sample of **8**: mp 70.5–71.5 °C; NMR ($CDCl_3$) δ 7.12–7.48 (m, including s at 7.36, 7 H total), 6.06 (t, 1 H), 5.15 (s, 2 H), 2.16 (s, 3 H); ir (KBr) 1645 cm^{-1}.

Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.34; H, 6.78; N, 7.11.

1,3-Dimethyl-2-pyridone (5). Using the procedure above, 6.94 g (63.6 mmol) of 3-methyl-2-pyridone and 13.0 g (91.6 mmol) of methyl iodide gave after vacuum distillation 6.63 g (85%) of **1** as a clear oil: bp 63 °C (0.05 mm) [lit.[8] bp 83–84 °C (1.3 mm)]; NMR ($CDCl_3$) δ 7.24–7.50 (m, 2 H), 6.16 (t, 1 H), 3.60 (s, 3 H), 2.16 (s, 3 H); ir (neat) 1650 cm^{-1}.