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SYNTHESIS OF FLUORONITRO ALCOHOLS

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SUMMARY

The $S_{RN}1$ reaction of perfluoroalkyl iodides with the anhydrous lithium salt of 2-nitropropane-1,3-diol acetonide followed by hydrolysis provides a high yield route to polyfunctional fluoronitro alcohols.

INTRODUCTION

A variety of perfluoroalkylated organic compounds can be prepared from perfluoroalkyl iodides [1]. Although perfluoroalkyl iodides do not readily undergo S_N1 or S_N2 displacement, the iodides are replaced in a radical-chain nucleophilic substitution ($S_{RN}1$) reaction with salts of 2-nitropropane [2]. We have used this coupling reaction to produce fluoronitro alcohols[3] by starting with a functionalized secondary nitro compound.

RESULTS AND DISCUSSION

Tris(hydroxymethyl)nitromethane acetonide[4]** was deformylated with lithium hydroxide, using azeotropic removal of water by benzene, to give the anhydrous lithium salt of 2-nitropropane-1,3-diol acetonide (1) as a yellow crystalline solid. The salt 1, which was stable under nitrogen at -15°C for several months, gave 2-nitropropane-1,3-diol acetonide upon acidification in quantitative yield [5]. The nitronate salt was then reacted under nitrogen in DMF with 1-iodoperfluoroheptane, 1-iodoperfluorooctane, or 1-iodoperfluoro-

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** Correctly named as 5-nitro-2,2-dimethyl-1,3-dioxane. This material and its perfluoroalkylated derivatives will be named herein as fluoronitro alcohol acetone ketal (acetonide) derivatives.

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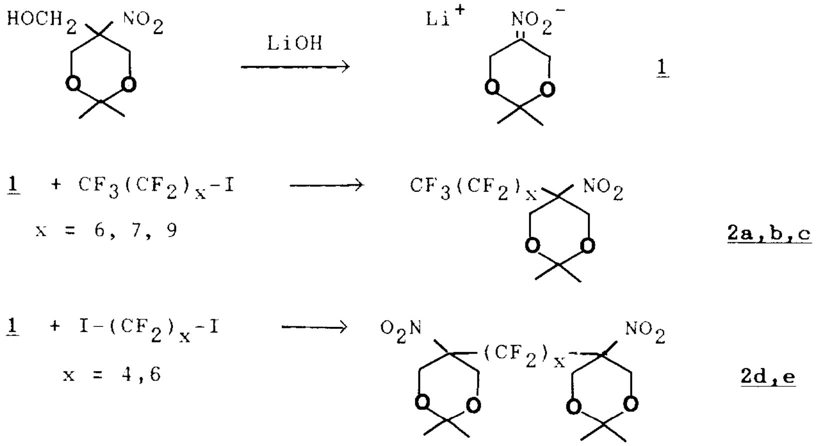
decane to give the corresponding perfluoroalkyl-substituted nitro compounds **2a–c** in 77%, 52% and 74% yields. Similarly, 1,4-diiodoperfluorobutane and 1,6-diiodoperfluorohexane were coupled with 1 to give the corresponding bis-adducts, **2d** and **2e**, in 87% and 90% yields, respectively. The reactions were complete in 2 to 24 hours as indicated by the disappearance of $-CF_2-I$ absorbance near δ -60 in the ^{19}F NMR spectrum.

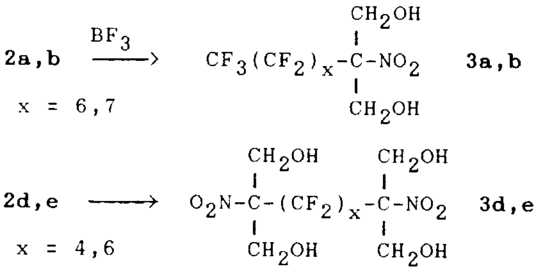


1

2a,b,c

2d,e

The perfluoroalkyl-substituted nitro acetonides **2a,b,d,e** were converted to the corresponding nitro diols (**3a,3b**) and dinitro tetrols (**3d,3e**) by transketalization with ethylene glycol and boron trifluoride etherate. Because of low solubility, the decyl derivative **2c** was unreactive under these conditions. Recrystallization of 3a,b or 3d,e from acetone regenerated the corresponding acetonides.



$$\mathbf{2a,b} \xrightarrow{BF_3} CF_3(CF_2)_x-\overset{\overset{\displaystyle CH_2OH}{|}}{\underset{\underset{\displaystyle CH_2OH}{|}}{C}}-NO_2 \quad \mathbf{3a,b}$$

x = 6,7

$$\mathbf{2d,e} \longrightarrow O_2N-\overset{\overset{\displaystyle CH_2OH}{|}}{\underset{\underset{\displaystyle CH_2OH}{|}}{C}}-(CF_2)_x-\overset{\overset{\displaystyle CH_2OH}{|}}{\underset{\underset{\displaystyle CH_2OH}{|}}{C}}-NO_2 \quad \mathbf{3d,e}$$

x = 4,6

EXPERIMENTAL

IR spectra were recorded in CH_2Cl_2 on a Perkin-Elmer 700 spectrometer. ^1H and ^{19}F NMR spectra were recorded in $CDCl_3$ on a Varian T-60 spectrometer and are reported in ppm relative to TMS and $FCCl_3$.

Lithium Salt of 2-Nitropropane-1,3-diol Acetonide (1).

A mixture of 2-hydroxymethyl-2-nitropropane-1,3-diol monoacetonide[4] (9.5 g, 50 mmol) and lithium hydroxide monohydrate (2.1 g, 50 mmol) was suspended in 50 mL of benzene and refluxed under nitrogen. Water was removed azeotropically by the use of a Dean-Stark trap and after 1 h, when no more water azeotrope formed, the solvent was removed under reduced pressure. The resultant yellow solid (1) was dissolved in 20 mL of DMF and used immediately.

Coupling Reaction of 1 with Perfluoroalkyl Iodides.

(a) 2-Nitro-2-(1-perfluorodecyl)propane-1,3-diol Acetonide (2c).

A solution of 1 (50 mmol in 20 mL DMF) was added to 1-iodoperfluorodecane (6.5 g, 10 mmol) in DMF (30 mL) under nitrogen and the mixture was stirred at 25°C in laboratory light. After 24 h, the reaction was complete on the basis of ^{19}F NMR analysis. The mixture was diluted with water (200 mL) and filtered. The precipitate was washed with water, dried *in vacuo,* and sublimed to give 5.1 g (74%) of **2c**, mp 65-68°C; IR 3000, 1570 cm^{-1}; ^1H NMR δ 1.3 (s, 3 H), 1.4 (s, 3 H), 4.25 and 4.7 (AB d, J = 13 Hz, 4 H); ^{19}F NMR δ -81.2 (m, 3 F), -118.4 (m, 16 F), -122.8 (m, 2 F). Anal. Calcd for $C_{16}H_{10}NF_{21}O_4$: C, 27.72; H, 1.40; N, 2.00. Found: C, 27.84; H, 1.54; N, 2.05.

(b) 2-Nitro-2-(1-perfluoroheptyl)propane-1,3-diol Acetonide (2a).

By the same procedure, 1-iodoperfluoroheptane (5.0 g, 10 mmol) was reacted with the nitronate salt 1 (50 mmol in DMF, 100 mL) to give 4.1 g (77%) of **2a**, mp 53-54 °C: IR 3000, 1565, 1210, 1150 cm^{-1}; ^1H NMR δ 1.25 (s, 3 H), 1.35 (s, 3 H), 4.3 and 4.7 (AB, J = 13 Hz, 4 H); ^{19}F NMR δ -80 (m, 3 F), -111.6 (m, 2 F), -118.0 (m, 8 F), -122.0 (m, 2 F). **Anal.** Calcd for $C_{13}H_{10}F_{15}NO_4$: C, 29.50; H, 1.9; N, 2.64. Found: C, 29.79; H, 2.11; N, 2.63.

(c) 2-Nitro-2-(1-perfluorooctyl)propane-1,3-diol Acetonide (2b).

By the same procedure, 1-iodoperfluorooctane (14.2 g, 25 mmol) was reacted with the nitronate salt 1 (0.1 mol in DMF, 200 mL) to give 7.5 g (52%) of **2b**, mp 67-68 °C; IR 3000, 1570 cm^{-1}; ^{1}H NMR δ 1.25 (s, 3 H), 1.35 (s, 3 H), 4.3 and 4.7 (AB, J = 13 Hz, 4 H); ^{19}F NMR δ -80 (m, 3 F), -112.46 (m, 2 F), -118.0 (m, 10 F), -122.0 (m, 2 F). **Anal.** Calcd for $C_{14}H_{10}F_{17}NO_4$: C, 29.03; H, 1.74; F, 55.76; N, 2.41. Found: C, 29.08; H, 1.65; F, 55.76; N, 2.34.

(d) 2,7-Bis(hydroxymethyl)-2,7-dinitro-3,3,4,4,5,5,6,6- octafluorooctane-1,8-diol Diacetonide (2d).

By the same procedure, 1,4-diiodoperfluorobutane (13.7 g, 0.03 mol) was reacted with the nitronate salt 1 (0.1 mol in DMF, 150 mL) to give 13.8 g (87%) of **2d**, mp 139-141 °C; ^{1}H NMR δ 1.35 (s, 6 H), 1.50 (s, 6 H), 4.40 and 4.75 (AB, J = 13 Hz, 8 H); ^{19}F NMR δ -107.6 (4 F), -113.6 (4 F). **Anal.** Calcd for $C_{16}H_{20}F_8N_2O_8$: C, 36.93; H, 3.87; N, 5.38. Found: C, 36.99; H, 3.80; N, 5.17.

(e) 2,9-bis(hydroxymethyl)-2,9-dinitro-3,3,4,4,5,5,6,6,7,7,8,8-dodecafluorodecane-1,10-diol diacetonide (2e).

By the same procedure 1,6-diiodoperfluorohexane (5.6 g, 0.01 mol) was reacted with the nitronate salt 1 (50 mmol in DMF, 100 mL) to give 5.0 g (90%) of **2e**, mp 138-139°C: IR 3000, 1565, 1350, 1210, 900 cm^{-1}; ^{1}H NMR δ 1.3 (s, 3 H), 1.4 (s, 3 H), 4.25 and 4.7 (assym AB, J 13 Hz, 4 H); ^{19}F NMR δ -113.2 (m, 4 F), -117.2 (m, 4 F), -118.8 (m, 4 F). **Anal.** Calcd for $C_{18}H_{20}F_{12}N_2O_8$: C, 34.85; H, 3.24; N, 4.51. Found: C, 34.54; H, 3.20; N, 4.41.

Hydrolysis of Acetonides

(a) 2,9-Bis(hydroxymethyl)-2,9-dinitro-3,3,4,4,5,5,6,6,7,7,8,8-dodecafluorodecane-1,10-diol (3e).

A solution of **2e** (19.0 g, 0.03 mol) and boron trifluoride etherate (10 mL) in ethylene glycol (500 mL) was heated at 85 °C for 16 h, cooled to ambient temperature and poured into water. The solids which formed were filtered, washed with water and recrystallized from ethyl acetate to give 11.8 g (72%) of **3e**, mp 186-189°C; ^{1}H NMR (DMSO-d_6) δ 5.8 (s, 4 H) (exchanges with D_2O), 3.3 (s, 8 H), ^{19}F NMR (DMSO-d_6) δ -107.6 (4 F), -114 (4 F), -117.2 (4 F). **Anal.** Calcd for $C_{12}H_{12}F_{12}N_2O_8$: C, 26.68; H, 2.23; F, 42.20; N, 5.18. Found: C, 26.78; H, 2.14; F, 42.23; N, 4.80.

(b) 2,7-Bis(hydroxymethyl)-2,7-dinitro-3,3,4,4,5,5,6,6-octafluorooctane-1,8-diol (3d).

Similar hydrolysis of **2d** (1.1 g, 2.1 mmol) using boron trifluoride etherate (0.5 mL) in ethylene glycol (50 mL) gave 0.55 g (57%) of **3d**, (as a monohydrate): mp 133-138°C; ^{1}H NMR (DMSO-d_6) δ 5.8 (s, 4 H) (exchanges with D_2O), 3.3 (s, 8 H), ^{19}F NMR (DMSO-d_6) δ -106.0 (4 F), -114 (4 F). **Anal.** Calcd for $C_{10}H_{14}F_8N_2O_9$: C, 26.21; H, 3.07; F, 33.17; N, 6.11. Found: C, 26.15; H, 3.09; F, 33.10; N, 5.83.

(c) 2-Nitro-2-(1-perfluoroheptyl)propane-1,3-diol (3a).

Similar hydrolysis of **2a** (4.0 g, 7.5 mmol) using boron trifluoroide etherate (3 mL) in ethylene glycol (60 mL) gave 4.0 g (58%) of **3a**, mp 137-138°C. An analytical sample was prepared by sublimation at 80°C (0.1 mm): ^{1}H NMR (DMSO-d_6) δ 4.3 (s, 2 H) (exchanges with D_2O), 3.3 (s, 4 H), ^{19}F NMR (DMSO-d_6) δ -80.0 (m, 3 F), -115.6 (m, 2 F), -118.4 (m, 8 F), -122.4 (m, 2 F). **Anal.** Calcd for $C_{10}H_6F_{15}NO_4$: C, 24.55; H, 1.23; N, 2.86. Found: C, 24.89; H, 1.39; N, 2.53.

(d) 2-Nitro-2-(1-perfluorooctyl)propane-1,3-diol (3b).

Similar hydrolysis of **2b** (5.0 g, 8.6 mmol) using boron trifluoride etherate (3 mL) in ethylene glycol (60 mL) gave 4.0 g (83%) of **3b**, mp 164-165°C; IR 3600, 1575, 1200 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 5.8 (s, 2 H, exchanges with D_2O), 3.3 (s, 4 H), ^{19}F NMR (DMSO-d_6) δ -80.0 (m, 3 F), -112.4 (m, 2 F), -117.6 (m, 10 F), -122.0 (m, 2 F). **Anal.** Calcd for $C_{11}H_6F_{17}NO_4$: C, 24.50; H, 1.12; N, 2.59. Found: C, 24.39; H, 1.01; N, 2.53.

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