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PREPARATION OF 1,3,5-TRIS(2-HYDROXYHEXAFLUORO-2-PROPYL)BENZENE AND SOME OF ITS DERIVATIVES

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SUMMARY

Grignard and lithium exchange methods have been used to prepare the polyfluoro alcohol, 1,3,5-tris(2-hydroxyhexafluoro-2-propyl)benzene. Preparation of the tris glycidyl ether of this alcohol and other derivatives are reported.

INTRODUCTION

In the preceding paper we have mentioned some of the important applications of polyfunctional fluoro alcohols in polymeric material [1]. The principal compound of this study, namely 1,3,5-tris(2-hydroxyhexafluoro-2-propyl)benzene (4) is also of interest to us as a potential polymer cross-linking agent and because it possesses six trifluoromethyl groups. A single report in the patent literature [2] is the only previously described method of synthesis of 4. However, the severe conditions of this method, 20 Kilobar pressure and 150-300°C, preclude its synthesis in many laboratories.

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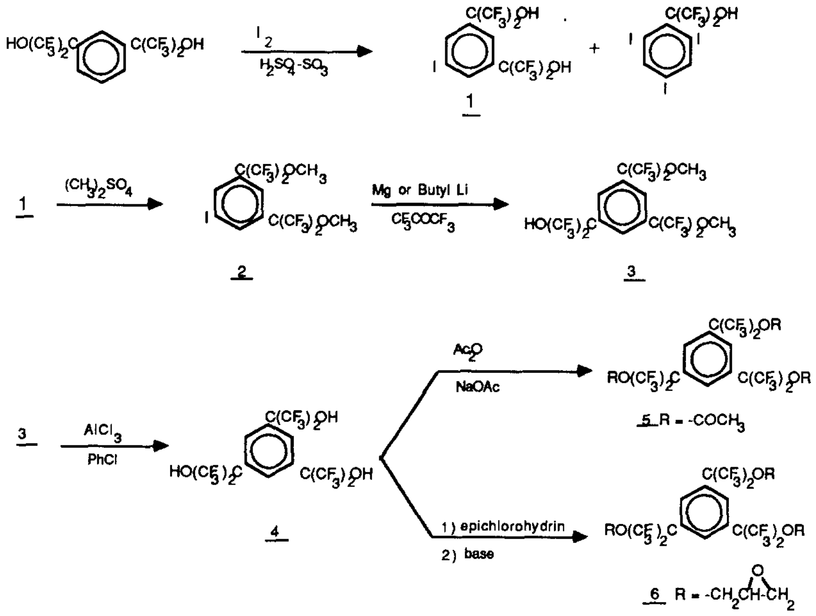
RESULTS AND DISCUSSION

In this paper we present a three step synthesis of 4 from a readily obtainable starting material that has been described previously [3]. The procedure is straight forward and, except for rigorous drying in the second step, does not require unusual laboratory conditions.

A rough distillation cut of 1,3-bis(2-hydroxyhexafluoro-2-propyl)benzene was used in the preparation of 1 (see Scheme below). A gas chromatograph analysis of the starting diol showed that it contained approximately three percent of (2-hydroxyhexafluoro-2-propyl)benzene and thirteen percent of 1,4-bis(2-hydroxyhexafluoro-2-propyl)benzene as impurities. The para diol isomer is very difficult to separate from the meta isomer by distillation or by fractional recrystallization. Fortunately, the para isomer does not react in the iodine-fuming sulfuric acid mixture and it is easily separated from the product 1. The minor impurity, (2-hydroxyhexafluoro-2-propyl)benzene, was converted in high yield to 1-(2-hydroxyhexafluoro-2-propyl)-2,4,6-triiodobenzene which was readily separated from 1 by fractional distillation.



Compound 1 was converted to the dimethyl ether (2) using dimethyl sulfate and aqueous base. The product isolated from this reaction by simple distillation is greater than 99 percent pure. It was used in the Grignard and lithiation reactions without further purification. Butyl lithium was the preferred reagent for the conversion of 2 to 3. The formation of the aryl lithium intermediate and the subsequent reaction with hexafluoroacetone were rapid and easy to control. Product yield by this method was also superior to the Grignard procedure.

Demethylation of the diether alcohol (3) to the triol (4) was accomplished by using anhydrous aluminum chloride in hot chlorobenzene. Other standard methods of methyl ether cleavage were not successful. The triol 4 was hydroscopic and took up atmospheric moisture to give a soft, gummy solid. Anhydrous 4 was obtained by vacuum sublimation at 0.5 torr.

The triglycidyl ether of 4 was obtained in high yield by standard procedures. Amine and anhydride cured polymeric material based on 6 appeared to possess enhanced hydrophobic properties.

The fluorine NMR spectrum of (6) gave a signal with the expected chemical shift (-72.0 ppm) but appeared as a multiplet due to the chiral center in the glycidyl group and restricted rotations about the ether link. At 25°C, the F-19 NMR signal for the geminal trifluoromethyl groups appeared as a doublet of octets with the larger coupling constant equal to 119 Hertz. At 52°C, the F-19 spectrum appeared as a doublet of sextets with the larger coupling constant equal to 99 Hertz. In this molecule, the geminal trifluoromethyl groups serve as an asymetric probe and reflect the different environments due to the chiral center five bonds away at the second carbon of the glycidyl group. Since there are two asymetric centers in the molecule, each diastereomer presents a different set of field environment for the trifluoromethyl groups. The temperature effects noted above indicate that restricted rotations about the ether link further complicate the situation. The proton and carbon-13 spectra appeared as expected.

The acetate of 4 gave a normal proton and fluorine spectra and showed no signs of restricted rotation of the geminal trifluoromethyl groups.

EXPERIMENTAL

General

Reagent grade solvents hexane and THF were twice distilled from calcium hydride then stored over 5A molecular sieves and a nitrogen atmosphere. Other solvents were used as received. Proton and fluorine NMR spectra were obtained on a Varian EM-390L using tetramethylsilane (TMS) and trichlorofluoromethane (F-11) as internal standards. Infrared spectra were obtained on a Perkin Elmer 1430 spectrophotometer. Mass spectra were obtained on a Finnegan TSQ-70 instrument. Melting points are uncorrected. Carbon-13 NMR data were obtained on a Brucker MSL-300. The spectrum was proton decoupled with reported values related to tetramethylsilane as zero.

Preparation of 1,3-bis(2-hydroxyhexafluoro-2-propyl)-5-iodobenzene (1)

This compound was prepared by an improved procedure described previously [3] Starting with the 600 g of the meta diol, containing by GC analysis approximately 3 percent 2-hydroxyhexafluoro-2-propylbenzene and 13 percent of the para diol there was obtained: 74 g of the unreacted para diol as a white, easily sublimed solid; 578 g of the desired product 1; and 38 g of 2,4,6-triiodo-1-(2-hydroxyhexafluoro-2-propyl)benzene. (nc), mp 110-112°C (after recryst. $CHCl_3$/pet. ether and vac. sublimation), ^{1}H-NMR ($CDCl_3$) $\delta = 2.80$ (broad, 1H), 8.12 (s, 2H); MS (70 eV) 622 (mol. ion) 100%, 605 (M-OH) 20%, 553 (M-CF_3) 75%, 495 (M-I) 5%, 478 (M-HOI) 12%, 426 (M-CF_3I), 38%, 357 (M-C_2F_6I) 36%,, 241 (M-3I) 42%, 201 (M-$C_3HOF_6I_2$) 65%, 74 (C_6H_2) 75%; IR (KBr) 3600-3200 (br. OH), 3110, 1635, 1530, 1410, 1385, 1300-1190, 1165, 1125, 1115, 980, 885, 735, 715 cm^{-1}.

Preparation of 5-iodo-1,3-bis(methoxyhexafluoro-2-propyl) benzene (2)

The iodo diol (1) was methylated using the procedure described previously [1].

Preparation of 1,3-bis(2-methoxyhexafluoro-2-propyl)-5-(2-hydroxyhexafluoro-2-propyl)benzene (3)

(a) Grignard method

Rigorous exclusion of water is required to prepare the Grignard reagent. All glassware was oven baked overnight, assembled hot and protected with dry argon and drying tubes.

Magnesium (0.88 g, 36 mmol), a magnetic stirring bar and 50 ml of THF were placed in a three necked flask fitted with condenser, additional funnel, thermometer, and argon inlet tube. About 15 ml of a mixture containing 2 (20.00 g, 35.5 mmol) and 50 ml of THF was added from the additional funnel and the reaction mixture heated to reflux. After 0.5 hr the reaction mixture turned cloudy and the remainder of the 2/THF mixture was added at reflux temperature during 1 hr. The reaction mixture was refluxed for an additional 1.5 hr, then cooled to 20°C and hexafluoroacetone (11.8 g, 71 mmol) was added at 0.5 g per min rate. The mixture spontaneously heated to 50°C, then was allowed to stir and vent unreacted HFA overnight.

The reaction mixture was hydrolyzed with 70 ml of 1.7 N hydrochloric acid then extracted with a total of 200 ml of ether. The ether extracts were washed with sat. NaCl solution, dried, then concentrated to a heavy oil (22 g). Distillation removed lower boiling by-products (mainly THF/hexafluoroisopropyl alcohol 1:1 complex) then gave a 10 g fraction (bp 105-107°C at 10 mm) which contained 95% of the desired product 3. Purification of 3 by recrystallization from petroleum ether (38-50°C) and slurrying with warm conc. sulfuric acid gave 17.3 g (17.4% yield) of 3 as white crystals, mp 72-73°C.

(b) Butyl lithium procedure

All glassware and inlet TFE tubing was dried in an oven and stored in a desiccator prior to assembling.

A three necked flask fitted with a thermometer, dry-ice condenser, nitrogen inlet, rubber septum and oil bubbler outlet was charged with 30.93 g (54.8 mmol) of 2, 150 ml of dry hexane and a magnetic stirring bar. The solution was cooled by a dry-ice bath to -65°C where 22.3 ml (10% excess) of a 2.7 molar solution of butyl lithium in hexane was added (0.5 hr). The mixture was allowed to slowly warm to 13°C (1.3 hr) then recooled to -35°C. Hexafluoroacetone (10.0 g, 60.2 mmol) from a weighed cylinder was introduced via a long needle through the septum to a point about 2.5 cm above the stirred liquid level. The addition of HFA took 0.8 hr and was quite exothermic at the start. The reaction mixture was allowed to warm to 20°C, hydrolyzed with 66 ml of 4 N hydrochloric acid then extracted with a total of 200 ml ether. The ether extracts were washed with sat. NaCl solution, aqueous 5% sodium bisulfite solution, dried over anhyd. magnesium sulfate then concentrated under water aspirator vacuum. Distillation of the viscous oil gave 1.2 g forerun then 27.3 g of crude 3, bp 73-76°C at 0.2 mm. Pure 3 was separated from unreacted 2 and 1,3-bis(2-methoxyhexafluoro-2-propyl)benzene by repeated vacuum sublimation to give 20.5 g (62% yield) of a hard white crystal: mp 73-74°C; ^{1}H-NMR ($CDCl_3$) δ = 3.50 (s, 6H), 3.95 (s, 1H), 7.98 (s, 1H), 8.13 ppm (s, 2H); IR (KBr) 3522 br, 3118, 3019, 2980, 2875, 1458, 1300-1100, 1051, 1031, 1009, 1000, 985, 979, 898, 740, 732, 715, 709 cm^{-1}; ^{19}F-NMR (CCl_4) ø* = -77.0 (s, 12F), -83.5 ppm (s, 6F).

Preparation of 1,3,5-tris(2-hydroxyhexafluoro-2-propyl)benzene (4)

Into a 300 ml flask was added 3 (53.0 g, 87.7 mmol), aluminum chloride (24.6 g, 88.0 mmol) and 220 ml of chlorobenzene. This mixture was stirred and heated at 70-75°C for 1 hr then cooled and the resulting black slurry poured slowly into 500 ml water. A crystalline solid was separated from a liquid phase by vacuum filtration. The solid and chlorobenzene layer of the filtrate were separately extracted with 10 percent sodium hydroxide solution (600 ml). The combined aqueous base extracts were washed with ether (500 ml) then acidified with 125 ml of conc. hydrochloric acid. The acidic mixture was extracted with ether (400 ml) and the ether extract washed with saturated salt solution then dried over anhyd. magnesium sulfate. The ether was filtered, concentrated under reduced pressure and the heavy oil distilled to give 27.8 g (55% yield) of 4, bp 101-102°C at 12 mm Hg, mp 95-101°C. Vacuum sublimation (50°C, 0.08 mm Hg) of the hygroscopic solid gave 4 as a hard crystalline product: mp 105-106°C; IR (KBr) 3620, 3599, 3518 br, 3132, 1468, 1300-1100, 1013, 982, 891, 776, 731, 709 cm^{-1}; ^{1}H-NMR (CDCl$_3$), δ = 3.43 (s, 3H) 8.27 ppm (s, 3H); ^{19}F (CDCl$_3$) ø* = -76.5 ppm (singlet).

Preparation of the triacetate of 4

A mixture of the triol (4) (0.33 g, 0,57 mmol), 0.3 g anhydrous sodium acetate and 35 ml of acetic anhydride was refluxed then slowly distilled removing about half the volume of acetic anhydride. The hot undistilled residue was poured into water, stirred rapidly then filtered. Recrystallization from ethanol gave 0.37 g (92%) of 1,3,5-tris(2-acetoxyhexafluoro-2-propyl)benzene: mp 105-106°C; ^{1}H NMR (CDCl$_3$) δ - 2.27 (s, 9H), 7.52 (s, 3H); ^{19}F NMR (CDCl$_3$) ø* = -71.2 ppm (singlet).

Preparation of the triglycidyl ether of 4

A mixture of 4 (16.0 g, 27.8 mmol), epichlorohydrin (38.5 g, 417 mmol) and tetramethylammonium bromide (0.62 g) was heated and stirred in a nitrogen blanketed closed system at 60°C for 100 hrs. The reaction mixture was concentrated by flash evaporation at 90°C/5 mm leaving 23.4 g of crude chlorhydrin. The crude chlorhydrin dissolved in 60 ml of a 3:1 mixture of toluene: ethanol was dehydrohalogenated by five successive one hr treatments with 3N aqueous sodium hydroxide at 50-55°C. The ethanol lost to the aqueous phase was replaced after each treatment. After the final base treatment the organic layer was removed by ether extraction and dried. Removal of volatile components at 80°C/5 mm gave a clear viscous liquid (18.6 g, 90% yield) which crystallized on standing to a white solid (mp 47-50°C). GC analysis indicated that this product was 99% pure. Recrystallization from heptane and vacuum sublimation gave an analytically pure sample of the triglycidyl ether of 4: mp 56-58°C, IR (KBr) 3090, 3020, 2957, 1300-1130, 1083, 1058, 1018, 920, 865, 848, 740, 711 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ = 2.70 (mult., 1H), 2.88 (mult., 1H), 3.30 (mult., 1H), 3.65-3.87 (mult., 2H), 8.09 ppm (s, 3H), ^{29}F NMR ø* = -72.0 ppm (mult.); $_{13}$C NMR (CDCl$_3$) δ = 44.1 (-CH-$\underline{C}$H$_2$), 49.3 (-$\underline{C}$H-CH$_2$), 67.7 (-O-$\underline{C}$H$_2$-), 82.3 (mult., $\underline{C}$(CF$_3$)$_2$), 121.9 (quart., $\underline{C}$F$_3$), 130.2 ppm (arom $\underline{C}$-H); MS (70 eV) 744 (mol. ion) 30%, 727 (M-OH) 28%, 714 (M-CH$_2$O)

5%, 701 (M-$CH_3H_6O_2$) 8%, 697 (M-CH_3O_2) 14%, 671 (M-) 50%, 670 (M-$C_3H_6O_2$) 50%, 597 (M-$C_6H_{11}O_4$) 50%, 417 ($C_{10}H_{13}O_5F_6$) 20%, 404 (M-$C_{11}H_{14}O_5F_6$) 55%, 73 ($C_3H_5O_2$) 91%, 57 ($C_3H_5O_2$) 100%, 43 (C_2H_3O) 84%.

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