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COPPER COUPLING REACTIONS OF 1,3-BIS(2-HYDROXYHEXAFLUORO-2-PROPYL)-5-IODOBENZENE AND ITS DERIVATIVES

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SUMMARY

Attempts to homocouple 1,3-bis(2-hydroxyhexafluoro-2-propyl)-5-iodobenzene (diol iodide) with copper fail to give the desired biphenyl tetrol. However, the dimethyl ether derivative of the diol iodide reacts smoothly with copper to give the biphenyl tetramethyl ether in good yields. The diacetate derivative of the diol iodide with copper gives only reduction of the aryl iodide. Heterocoupling of the diol iodide with 1,4-diiodoperfluorobutane gives a tetrol containing the -$(CF_2)_4$- bridge.

INTRODUCTION

The preparation of fluoro alcohols containing hexafluoro-2-hydroxypropyl groups has been of interest to us as these products give rise to polymeric materials with low critical surface tension [1-3]. A principal goal has been to build into the monomeric unit an ideal number of trifluoromethyl groups in order to maximize the hydrophobic and oliophobic properties of bulk polymer. Epoxy and acrylic materials based on these fluoro alcohols have a number of properties which may provide superior surface characteristic for dental and medical prosthetic devices and for barrier coating against corrosive liquids [4].

In this study we have attempted to prepare a tetra functional fluoro alcohol which would increase polymer cross-linking and thereby provide improved mechanical moduli and higher glass transition temperatures above those shown by similar polymers derived from difunctional fluoro alcohols.

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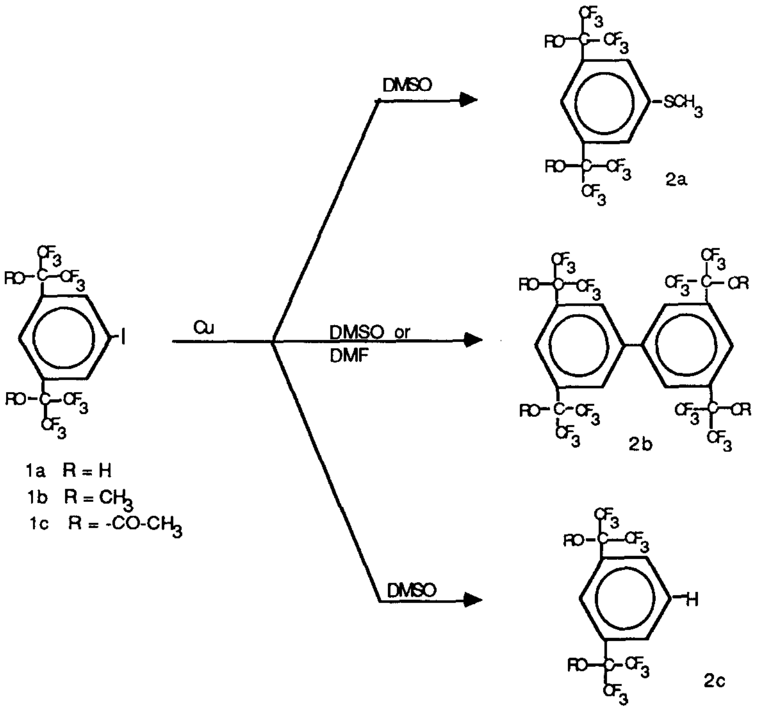
RESULTS AND DISCUSSION

In previous studies we have shown that copper coupling reactions of perfluoroalkyl iodides with 1,3-bis(2-hydroxyhexafluoro-2-propyl)-5-iodobenzene (1a) in DMSO proceed in high yield [1,3,5]. Others have similarly demonstrated the facile nature of copper coupling reactions of perfluoroalkyl iodides with variously substituted aryl iodides and further shown that functional groups did not lower yields nor alter the reaction pathway [6]. By contrast, the structure of the perfluoroalkyl iodide is a critical factor. Only primary iodides couple smoothly and in high yield. Secondary iodides, phenyl iodide and perfluorophenyl iodide heterocouple in low yield giving principally reduction products [1,6].

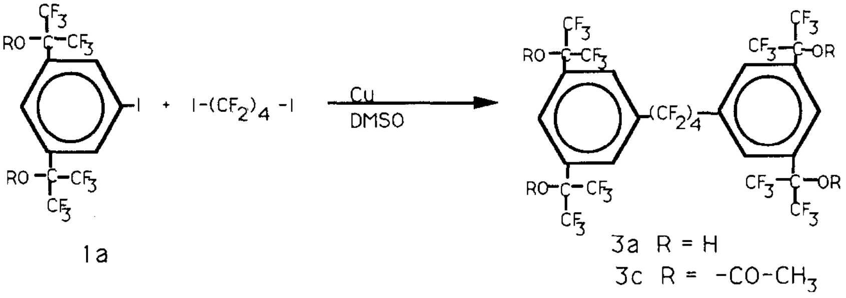
In Scheme 1 below we summarize the results of this study.



Scheme 1

Our initial goal was to homocouple the diol iodide (1a) to give a biphenyl tetrol (2b) (where R = H). Using conditions which gave good yields of heterocouple products, namely 120-140°C for 12-16 hours, the diol iodide (1a) in DMSO was unreactive. At higher temperatures using DMF or DMSO the reaction gave increasing amounts of intractable resins and few identifiable products. At 150°C for 16 hours in DMSO the major product was 1,3-bis(2-hydroxyhexafluoro-2-propyl)-5-methylmercaptobenzene (2a). The NMR spectrum of 2a could not exclude the possibility that the product was indeed the desired biphenyl tetrol (2b) (where R = H) complexed with one mole DMSO. In our previous work it had been shown that the DMSO complexes were extraordinarily stable and could be distilled under vacuum without decomposition [1]. However, conversion of 2a to the corresponding diacetate gave an unambiguous NMR and mass spectra.

As will be seen below, it was convenient to convert the very high boiling fluoro alcohols to the corresponding acetates to facilitate purification and NMR spectra interpretation. For example, solvent shifts and accurate integration of the NMR broad O<u>H</u> peak in the fluoro alcohols was particularly troublesome. Previous studies have shown that the alcohol proton absorption for hexafluoro-2-propanol shifted from 3.98 ppm in $CDCl_3$ to 7.96 ppm in DMSO [7].



Scheme 2

Homocoupling of 1b with copper in either DMF or DMSO proceeded smoothly to give an 80% yield of the expected biphenyl tetramethyl ether (2b). The methyl ether bonds in fluoro ethers of this kind are unusually resistant to cleavage. However, we have shown that aluminum chloride in hot chlorobenzene may serve as an effective reagent to cleave resistant ethers to the corresponding alcohols [8]. Unfortunately, in this case 2b was resistant to hydrolytic cleavage by boiling conc. HI, boiling conc. HBr in acetic acid and gave polymeric tars with aluminum chloride in chlorobenzene.

The diol iodide (1a) was converted to the diacetate (1c) in the hope that the ester protection would permit copper coupling to a biphenyl tetraacetate which then could be readily hydrolyzed to the desired tetrol. This plan also failed as the copper coupling reaction gave a complex mixture of products resulting from ester hydrolysis and reduction of the aryl iodide. After treating the complex product mixture with acetic anhydride, the principal product isolated was a 56% yield of 1,3-bis(2-acetoxyhexafluoro-2-propyl)benzene (2c).

Copper coupling of 1a with 1,4-diiodoperfluorobutane gave a 49 percent yield of the desired tetrol (3a) (Scheme II). In this case, product was isolated as a 1:2 complex of DMSO and the tetrol. This was unusual as all of the previously isolated DMSO-meta diol complexes were 1:1 ratio [1]. The proton NMR of 3a showed both free O$\underline{H}$ and bonded O$\underline{H}$ ·· DMSO absorption appearing at 3.37 ppm and 9.28 ppm respectively. As additional DMSO was added to the solvent mixture the peak at 3.37 ppm decreased in area with a corresponding increase at 9.28 ppm. In each case, the integrated total free and bonded OH was equal to four protons.

Again, the conversion of 3a to the tetraacetate (3c) permitted easy purification with the removal of the complexed DMSO. The NMR spectrum of 3c provided an unambiguous analysis and structure proof.

EXPERIMENTAL

Reagent grade solvents (DMSO, DMF) were distilled at reduced pressure then stored over 5A molecular sieves. The copper powder (Baker and Adamson - Code 1618) and 1,1,2-trichlorotrifluoro-ethane F-113 (Aldrich - 17,282-0) were used as received. Proton and fluorine spectra were obtained on a Varian 390L using tetramethylsilane and trichlorofluoromethane (F-11) as internal standards.

Infrared spectra were obtained on a Perkin-Elmer 1430 spectrophotometer. Melting points were obtained in capillary tubes and are uncorrected. The diol iodide (1a) was prepared by the procedure descibed in reference 1.

Preparation of 1,3-bis(2-hydroxyhexafluoro-2-propyl)-5-methylmercaptobenzene (2a) nc

A mixture of 23.1 g (0.0431 mol) of (1a) [1], 15.0 g (0.236 mol) copper powder and 75 ml of freshly distilled DMSO was heated under a nitrogen atmosphere to 150°C for 16 hr. An unidentified foul smelling white solid (2.6 g) sublimed out of the reaction mixture to the condenser. The reaction mixture was poured into water and the apparatus washed with ether. The combined ether water mixture was filtered to give 20.24 g of copper-copper iodide residues. Evaporation of the ether layer gave a light brown viscous oil (22.3 g) which indicated 33% unreacted diol iodide (1a) and 67% compound 2a (79% yield) by GC analysis. Separation of 2a from the mixture was achieved by slow distillation through a 20 cm spinning band microstill. Pure 1,3-bis(2-hydroxyhexafluoro-2-propyl)-5-methylmercaptobenzene was obtained as a very viscous clear liquid: b.p. 43-45°C/0.02 mm; n_D^{24} 1.4395; IR (neat) 3590, 3460 br, 3100, 2910, 1580, 1425,1355,1290-1100,1000,965 865, 778, 730, 715, 695 cm^{-1}; ^1H-NMR ($CDCl_3$) δ = 2.50 (s, 3H, CH_3S-), 5.68 (bs, 2H, OH), 7.73 (s, $2H_{arom}$), 7.88 ppm (s, $1H_{arom}$); ^{19}F-NMR ($CDCl_3$) ø * = -76.1 ppm singlet.

Preparation of the Diacetate of 2a nc

Acetic anhydride (39.6 g), anhyd. sodium acetate (0.5 g) and 10.82 g of 2a were refluxed for 3 hours then poured into warm water and stirred rapidly. After cooling to room temperature the heavy oil solidified to a white solid. Recrystallization from ethanol and vacuum sublimation gave 10.18 g (80.0% yield) of 1,3-bis(2-acetoxyhexafluoro-2-propyl)5-methylmercaptobenzene nc: m.p. 71-72°C; MS (70eV) 540 (mol. ion), 497 (M-C_2H_3O), 493 (M-CH_3S), 385 (M-$C_5H_6O_2F_3$), 368 (M-$C_5H_7O_3F_3$), 316 (M-$C_6H_6O_2F_6$) and 288 (M-$C_6H_4O_2F_6S$); IR (KBr pellet) 3095, 2940, 1800, 1750, 1595, 1440, 1380, 1300-1180, 1165, 1155, 1090, 1115, 1085, 1040, 1025, 990, 900, 790, 745, 740, 730 cm^{-1}; ^1H-NMR

($CDCl_3$) $\delta = 2.27$ (s, 6H, CH_3CO-), 2.47 (s, 3H, CH_3S-), 7.17 (2, 1 H_{arom}), 7.32 ppm (2 H_{arom}); ^{19}F-NMR ($CDCl_3$) ø* = -71.0 ppm.

Preparation of 1c

In a manner similar to that described above, the diol iodide 1a was converted to 1c and carefully purified to a product showing a single peak by GC analysis, m.p. 95-96°C.

Reaction of 1c with Copper Powder

A mixture of 24.88 g (0.0401 mol) of 1c, 19.97 g (0.3143 mol) of powdered copper and 65.3 g of dry DMSO was heated to 123°C for 18 hrs under a nitrogen atmosphere. GC analysis of the resulting clear lower layer and the greenish upper layer showed that starting material (1c) was absent. Further heating to 153°C for 1.5 hr gave a lustrous ppt of free copper metal. The hot reaction mixture was filtered and the copper residues washed with warm DMSO. The combined filtrates were poured into water and the organic layer removed by extraction with $CHCl_3$. After removal of the $CHCl_3$, the heavy oil was heated with excess acetic anhydride and sodium acetate to give after work-up 11.0 g (56% yield) of 1,3-bis(2-acetoxy-hexafluoro-2-propyl)benzene: m.p. 80-82°C; ^1H NMR = 2.25 (s, 6H), 7.45 (s, 1H_{arom}) 7.53 ppm (s, 3H_{arom}).

A mixture of the product above with a sample of pure diacetate prepared from known 1,3-bis(2-hydroxyhexafluoro-2-propyl)benzene showed no depression in the melting point.

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

The diol iodide (1a) (53.62 g, 0.10 mol) and 100.9 g (0.80 mol) of dimethyl sulfate were mixed under a nitrogen atmosphere then an aqueous solution of sodium hydroxide (32.92 g NaOH in 128 ml H_2O) was added dropwise to the rapidly stirred reaction mixture. An ice bath was used to keep the reaction temperature below 35°C during the addition of the base (45 min). The ice bath was removed and the mixture stirred at room temperature for 1.5 hr. The heavy organic layer was removed and the aqueous layer extracted twice with ether (60 ml). The organic layer and the ether extracts were combined, dried over anhydrous calcium chloride, concentrated then distilled to give a forerun of 2.23 g (bp 25-30°C at 0.2 mm Hg) then 53.05 g (94.0% yield) of the desired product: b.p. 78-85°C at 0.10 mm Hg, n_D^{25} = 1.4375 (lit., [8] b.p. 126°C at 10 mm Hg, n_D^{20} = 1.4385). Analysis by GC showed that the product was better than 99% pure. An infrared spectrum matched an authentic sample and showed the absence of OH stretching frequencies.

Preparation of 3,3',5,5'-tetrakis(2-methoxyhexafluoro-2-propyl) biphenyl (2b) nc

A mixture of 25.0 g (0.0444 mol) of 1b, 20.2 g (0,318 mol) of copper powder and 2.0 ml of DMF was heated to 165°C for 1.5 hr, then to 230°C for 3.5 hrs. Additional copper powder (5.00 g) was added and the reaction again heated to 230°C for 2 hrs. The reaction mixture was diluted with ether then filtered and the copper residues washed with F-113. The combined filtrates were washed with 5% aqueous HCl, saturated NaCl solution, then dried over $MgSO_4$. Evaporation of the solvents and tituration of the semi solid residues with ligroin (35-60°C) gave 12.75 g (66%) white crystals of 2b: m.p. 109-111°C (from ethanol); IR (KBr pellet) 3020, 2995, 2890, 1615, 1320-1115, 1065, 1010, 950, 895, 750, 730, 725, 715, 675.cm^{-1}; ^{1}H NMR δ = 3.60 (s, 6H -OCH_3), 7.85 (s, 2H_{arom}), 7.95 ppm (s, 1H_{arom}); ^{19}F NMR ($CDCl_3$) $ø^*$ = -71.5 ppm.

Various attempts to demethylate the ether (2b) were unsuccessful. Either there was no reaction (refluxing conc. HI or acetic acid - HBr) or an intractable material was obtained (chlorobenzene - $AlCl_3$).

Reaction of 1a and 1,4-Diiodoperfluorobutane with Copper

A mixture of 11.14 g (0.0208 mol) of 1a, 4.55 g (0.010 mol) of 1,4-diiodoperfluorobutane, 6.35 g (0.100 mol) of copper powder and 11.0 g of DMSO was heated under a nitrogen atmosphere to 130°C for 18 hrs then cooled and filtered. The copper-copper iodide residues were washed repeatedly with ether and F-113. The combined filtrates were concentrated then distilled through a microstill. The fractions that distilled between 83-155°C at 0.15-0.25 mm Hg were dissolved in hot chloroform which, on cooling, gave 4.94 g (49%) of a white crystalline solid. Further purification by vacuum sublimation gave the 2:1 white solid complex DMSO: [1,4-bis(3',5'-bis(2-hydroxyhexafluoro-2-propyl)phenyl) perfluorobutane] (3a): m.p. 114.5-115.5°C; IR (KBr pellet) 3040, 1420, 1365, 1310-1115, 1055, 1030, 1000, 975, 948, 908, 890 cm^{-1}; ^{1}H-NMR (d_6 DMSO) δ = 2.57 (s, 3H), 3.37 and 9.28 (s, 4H), 8.08 (s, 4H), 8.44 ppm (s, 2H); ^{19}F-NMR (d_6 DMSO) ø* = -74.6 (s, 12F CF_3), -111.3 (t, 2F, Ar<u>CF</u>$_2$ -CF_2-), -121.9 ppm (t, 2F, Ar-CF_2-<u>CF</u>$_2$-).

A proton NMR spectrum of 3a in $CDCl_3$ showed a 4 to 3 integration ratio of the O<u>H</u> signal at 3.37 and 9.28 ppm. An addition of d_6 DMSO dropwise to the NMR tube caused an increase in the signal at 9.28 ppm and a decrease in the signal at 3.37 ppm. In pure d_6 DMSO, the integration ratio of the 9.28 ppm/3.37 ppm signals was 6 to 1.

Conversion of 3a to the Tetraacetate (3c)

The tetrol DMSO complex (3a) was converted to the tetraacetate by a procedure similar to that described above for the preparation of the acetate 1c. Recrystallization of the acetate from ethanol gave fine white needles: m.p. 128.5-129.5°C, ^1H-NMR ($CDCl_3$) $\delta = 2.28$ (s, 6H, <u>CH</u>$_3$CO-), 7.68 ppm (s, $3H_{arom}$); F^{19} NMR ø* = -71.0 (s, 12F), -111.5 (t, 2, F, Ar<u>CF</u>$_2$-), -122.3 ppm (s, 2F Ar-CF_2-<u>CF</u>$_2$-).

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