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Synthesis of 2,4,4′,5,5′-Pentachloro-2′-hydroxydiphenyl Ether, a Potential Precursor to 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin

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The toxicity of certain chlorinated dibenzo-*p*-dioxins has initiated intensified research on their formation in the production and use of chlorinated phenols and compounds derived therefrom.[1] In certain cases intermediates have been observed, *e.g.* nonachloro-2-hydroxydiphenyl ether, which undergoes ring closure to octachlorodibenzo-*p*-dioxin under different conditions.[2–5] This paper describes the synthesis of 2,4,4′,5,5′-pentachloro-2′-hydroxydiphenyl ether, an analogue precursor to the particularily toxic 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and therefore of obvious interest for chemical and toxicological investigations. The compound is prepared by demethylation of the corresponding methyl ether, which is obtained from the potassium salt of 3,4-dichloro-6-methoxyphenol on reaction with 1,2,4,5-tetrachlorobenzene in dimethyl sulfoxide. A similar procedure has been used in the direct synthesis of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin from 4,5-dichlorocatechol.[6] The present method seems more suitable than the alternative Ullmann ether synthesis which gave somewhat complicated product mixtures containing, *e.g.*, dechlorination products.

Experimental. 2,4,4′,5,5′-Pentachloro-2′-methoxydiphenyl ether. The potassium salt of 3,4-dichloro-6-methoxyphenol[7] (0.25 g; 1.3 mmol) and 1,2,4,5-tetrachlorobenzene (0.5 g; 2.3 mmol) in DMSO (13 ml) were heated to 100 °C for 60 h. The mixture was cooled to 20 °C and unreacted tetrachlorobenzene was partly removed by filtration. Sodium hydroxide (0.5 M, 50 ml) was added to the solution. The neutral components were isolated after extraction with hexane (3 × 10 ml; 0.24 g). 2,4,4′,5,5′-Pentachloro-2′-methoxydiphenyl ether was isolated by preparative TLC (Silica gel HF, ethyl ether – hexane, 35 – 65, R_F 0.7) and was crystallized from ethanol, m.p. 111 – 112 °C. Anal. $C_{13}H_7Cl_5O_2$: C, H. MS (IP 70 eV; *m/e*): pertinent peaks: 370 (M) and 320 (M – CH_3Cl).[2,4] ^{1}H NMR (100 MHz, $CDCl_3$): δ 3.81 (3 H, s), 6.76 (1 H, s), 7.04 (2 H, two singlets 1.5 Hz apart.), 7.50 (1 H, s). UV [abs. ethanol (log ε)]: 289 (4.10), 296 (sh, 4.05) nm.

2,4,4′,5,5′-Pentachloro-2′-hydroxydiphenyl ether. The crude product mixture mentioned above (100 mg), was dissolved in dichloromethane (2 ml). The solution was cooled in a dry ice-acetone mixture, and boron tribromide (100 mg) in dichloromethane (0.2 ml) was added. The mixture was allowed to reach 20 °C and was kept overnight. Hexane (4 ml) was added and 2,4,4′,5,5′-pentachloro-2′-hydroxydiphenyl ether was isolated by means of sodium hydroxide extraction (2 M, 2 × 10 ml) and acidification. Yield 30 mg, needles from hexane, m.p. 125 – 127 °C, MS [IP 10 eV; *m/e*; (% rel. int.)]: 356 (90, M), 321 (5, M – Cl), 320 (5, M – HCl), 286 (42, M – 2Cl), 180 (100, ether cleavage) 177 (20, ether cleavage). ^{1}H NMR (100 MHz, CCl_4): δ 5.40 (1 H, s), 6.70 (1 H, s), 8.00 (1 H, s), 8.05 (1 H, s), 8.48 (1 H, s) UV [abs. ethanol (log ε)]: 290 (4.04), 297 (sh. 4.00) nm.

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