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PALLADIUM(II)ACETATE PROMOTED CYCLIZATION OF POLYCHLORINATED DIPHENYL ETHERS TO THE CORRESPONDING DIBENZOFURANS

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Introduction

Polychlorinated dibenzofurans (PCDFs) are found as contaminants in certain PCBs[1-4] and in technical formulations of chlorophenols[5-6] and compounds derived from them. Certain isomers of PCDFs-like their close structure analogues, the polychlorinated dibenzodioxins-have been shown to be extremely toxic[7-8] and their possible contamination of the environment has caused much concern.[9] There is therefore an urgent need for the further investiation of the chemical and toxicological properties of these compounds.

The syntheses of a few individual PCDFs have recently been described, where the products are obtained by a substitution in the dibenzofuran ring system.[10-12] These syntheses often comprise several steps, and the final separation may be tedious. We have previously published a simple photochemical synthesis of a dichlorinated dibenzofuran involving ring closure of the easily available trichlorodiphenyl ether.[13] In this paper we report a similar general one-step method for the synthesis of PCDFs from polychlorinated diphenyl ethers using palladium-promoted cyclization, see Fig 1. This cyclization reaction has previously been studied by Åkermark *et al.*[14] and Shiotani *et al.*[15] for alkyl- and nitro-substituted diphenyl ethers, and this report is an extension of their work to include the chlorinated derivatives.

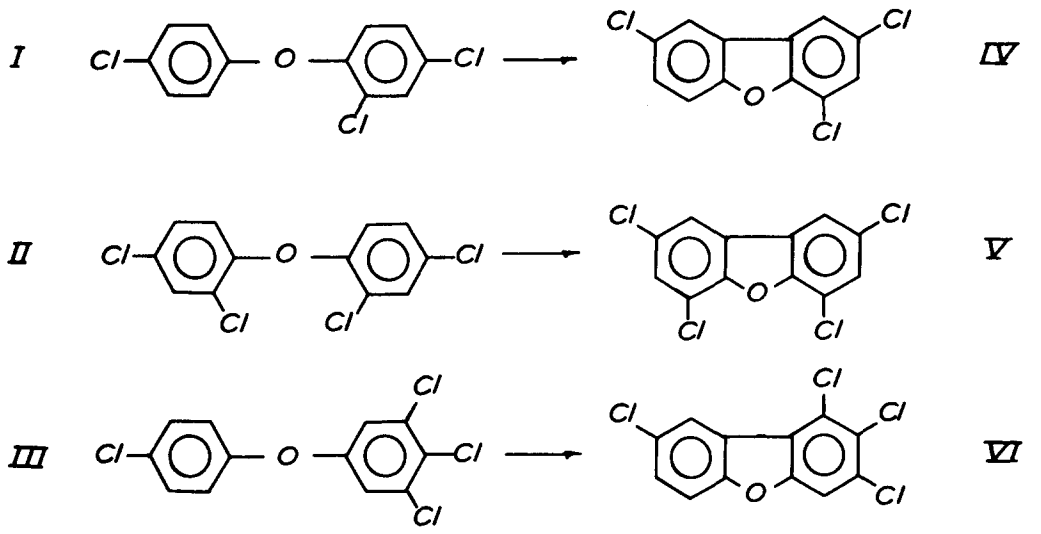

fig 1

Experimental

Caution: Some of these compounds have been found to be highly toxic and should be handled with extreme care. Work should be performed in glove boxes in an isolated toxic laboratory facility. Exhaust air should be filtered. All wastes should be incinerated. Contact with these compounds can cause chloracne and irreversible liver damage.

Mass spectra were recorded using a LKB 9000 instrument equipped with a Pye Unicam Model 84 GC. All chemicals were of synthetic grade unless otherwise specified. The yields were determined by comparing injections of starting material on GC with corresponding injections of the reaction mixtures and assuming the same response factors. In general, longer reaction times gave cleaner products but the total yield decreased.

2,4,4'-trichlorodiphenyl ether I and 2,2',4,4'-tetrachlorodiphenyl ether II were synthesized as previously described.[13]

2,3',4',5'-tetrachlorodiphenyl ether III was synthesized in an analogous manner to 2,4,4'-trichlorodiphenyl ether I but using 3,4,5-trichlorophenol instead of 2,4-dichlorophenol. Destillation of the crude product in vacuo for removal of the

p-chloroiodobenzene and one recrystallization of the residue from ethanol yielded 1.20 g (39 %), m.p. 65-7°C. GC analysis of this product on 2 % APM, 110° for 2 min - 40°/min - 210° gave only one component. The mass spectrum gave a molecular ion at m/e=306 and the typical cluster for four chlorine atoms.

2,4,8-trichlorodibenzofuran IV. 0.14 g (0.5 mmol) 2,4,4'-trichlorodiphenyl ether and 0.22 g (1.0 mmol) palladium(II)acetate were added to a mixture of 10 ml acetic acid and 1.12 g methanesulphonic acid (molar ratio = 15:1). After refluxing for 2 hours the mixture was diluted with water, made alkaline with $NaOH_{(s)}$ and extracted twice with ether. The combined ethereal extracts were washed with two portions of water, dried over $MgSO_4$, evaporated to dryness, and the residue redissolved in CCl_4 p.a. This solution was analysed on GC, 2 % APM, 210°. Yield 36 % of a 99 % pure product. The mass spectrum gave a molecular ion at m/e=270 and the typical cluster for three chlorine atoms.

1,2,3,8-tetrachlorodibenzofuran V. 0.15 g (0.5 mmol) 2,3',4',5'-tetrachlorodiphenyl ether and 0.22 g (1.0 mmol) palladium(II)acetate were added to a mixture of 10 ml acetic acid and 1.12 g methanesulphonic acid (molar ratio 15:1). After refluxing for 1 hour the mixture was worked up as previously described for 2,4,8-trichlorodibenzofuran IV. GC analysis showed a 98 % pure product in 32 % yield. The mass spectrum gave a molecular ion at m/e=304 and the typical cluster for four chlorine atoms.

2,4,6,8-tetrachlorodibenzofuran VI. Synthesized in the same manner as 1,2,3,8--tetrachlorodibenzofuran but with 2,2',4,4'-tetrachlorodiphenyl ether as starting material. This tetrachlorodibenzofuran could not be obtained in a pure state A longer reaction time resulted in a diminished residue of starting material but also in faster decrease of desired product. A reaction time of 4 hours gave 43 % product and 7 % starting material. An attempt to separate the mixture on a 1.6 x 100 cm column packed with Sephadex LH-20 and using 1,2-dichloroethane as eluant gave a purer product but no definitive separation could be obtained between starting material and the desired product. However, GC-MC gave a mass spectrum with a molecular ion at m/e=304 and the typical cluster for four chlorine atoms.

Discussion

Åkermark et al.[14] suggest a reaction mechanism where palladium makes an electrophilic attack on both o-carbons. This supports the suggested structures of the obtained PCDFs. In view of the very high toxicity of certain isomers of PCDFs, no attempts were made at further purification of the products obtained and only a limited number of isomers were prepared.

As previously shown by us,[13] it is possible to synthesize a DBF from the corresponding diphenyl ether by a photochemical ringclosure involving loss of an ortho chlorine atom. We can now use the same diphenyl ether to synthesize another dibenzofuran with the same number of chlorine atoms as the starting material. These investigations will continue, using other polychlorinated diphenyl ethers previously synthesized in this laboratory.[16]

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