

Synthesis and Characterization of Twenty-eight Brominated Diphenyl Ethers

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1. Introduction

Polybrominated diphenyl ethers (PBDE) are used in large quantities as additive flame retardants in polymers especially in electric devices, TV sets, computers, building materials and textiles (1). The PBDE are ubiquitous environmental contaminants that were first reported in pike from the river Viskan on the west coast of Sweden in 1981 (2) and later also in other wildlife species (1,3-7) and human adipose tissue (8) and plasma (E. Klasson Wehler, pers. comm.). PBDE are commercially produced via direct bromination of diphenyl ether (1). The technical products are generally mixtures of isomers and homologues (congeners) which, to our experience, are difficult to separate on a preparative scale.

Hitherto, primarily three routes have been used for the synthesis of BDE: (*i*) direct bromination of diphenyl ether (9), (*ii*) coupling of a bromophenolate with a bromobenzene according to the Ullman diphenyl ether synthesis (9) and (*iii*) coupling of a diphenyliodonium salt with a bromophenolate (10-12). The latter method has previously been used to synthesize a large number of chlorinated diphenyl ethers and also a few BDE (12-17).

The aim of the present study was to synthesize a number of low to medium brominated diphenyl ethers and to characterize them by ¹H NMR, UV, MS and melting points. The relative retention times in gas chromatography (GC) of the compounds were also determined. Two of the compounds, 2,2',4,6'-tetraBDE and 2,3,4,4',5,6-hexaBDE, were studied by X-ray crystallography.

2. Experimental

Chemicals. Bromobenzene was purchased from BDH (England). All bromophenol used were obtained from Aldrich (Germany). Iodine, benzene, fuming sulfuric acid (65% and 30%), concentrated sulfuric acid, hydrochloric acid, acetic anhydride, magnesium sulfate and all solvents used were from Merck (Germany). Potassium iodate was obtained from J.T. Baker (U.S.A). Fuming nitric acid, charcoal and celite were obtained from Kebo (Sweden) and sodium hydroxide from Eka Nobel (Sweden). Thin-layer chromatography was performed on silica gel plates (Merck, DC Fertigplatten, Kieselgel 60 F₂₅₄) and open silica gel chromatography on Kieselgel 60 (Merck, 40-63 μm particles).

Instruments. Gas chromatography-mass spectrometry (GC-MS) was performed on a quadrupole TSQ 700 Finnigan MAT instrument. The gas chromatograph was a Varian 3400 equipped with a DB-5 fused silica capillary column, 30 m × 0.25 mm, 0.025 mm film thickness (J&W Scientific) and the temperature program was 80 °C (2 min); 30 °C /min (4 min); 5 °C/min (24 min); 320 °C (10 min). Helium was used as the carrier gas and the temperature of the injector was 260 °C.

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Electron ionization (EI) was used as the ionization method at an ion source temperature of 140 °C and an electron energy of 70 eV. The relative retention times of the BDE synthesized were determined on a Varian 3400 gas chromatograph equipped with a XT1-5 fused silica capillary column, 30 m × 0.25 mm, 0.25 µm film thickness (Restek) and the temperature program was 100 °C (1 min); 10 °C/min (22 min); 320 °C (22 min). Helium was used as the carrier gas and the temperature of the injector was 280 °C. Crystals of 2,2',4,6'-tetraBDE and 2,3,4,4',5,6-hexaBDE were formed by recrystallization from n-hexane. The crystals were measured at room temperature on a Siemens STOE/AED2 diffractometer.

Synthesis

Diphenyliodonium bromide (1). The compound was synthesized according to Ziegler et al. (11). Potassium iodate (4.3 g, 20 mmol) was dissolved in conc. sulfuric acid (20 ml). Iodine (1.8 g, 7 mmol) was added at 15-20 °C. After stirring for 15 hrs, the iodylsulfate was collected and then suspended in concentrated sulfuric acid (25 ml) at 5-10 °C. Acetic anhydride (15 ml) and benzene (20 ml, 225 mmol) were added and the mixture was stirred at room temperature for two hours. Water (200 ml) was added and the mixture filtered. The filtrate was extracted three times with ethyl acetate (3×30 ml) and three times with ethyl ether (3×30 ml). Then the product was precipitated from the filtrate by the addition of sodium bromide (100 mmol, 10 g) in water (10 ml). Yield 7.0 g (19 mmol, 16.9 %).

4,4'-Dibromodiphenyliodonium chloride (2). This synthesis is slightly modified compared to the method described by Nilsson et al. (12). A mixture of conc. sulfuric acid (15 ml) and 30% fuming sulfuric acid (30 ml) was added to iodine (12.7 g, 50 mmol) under stirring. Then a mixture of conc. sulfuric acid (4 ml), 65% fuming sulfuric acid (2 ml) and fuming nitric acid (6.5 ml) was slowly added. The reaction mixture was stirred at 70-80 °C for 1.5 hrs during which time yellow crystals of iodylsulfate precipitated. The iodylsulfate was chilled to 0 °C and then bromobenzene (40 g, 250 mmol) was then slowly added under stirring for 0.5 hr during which yellow colour partly disappeared. The mixture was stirred at 45 °C for 2 hrs, chilled to 0 °C and then water (100 ml) was added. **WARNING! Violent reaction.** The product precipitated as a brown oil. The product was collected, dissolved in methanol and crystallized as the chloride by the dropwise addition of conc. hydrochloric acid (5 ml). Yield 10.7 g (23 mmol, 18.4 %).

2,2',4,4'-tetrabromodiphenyliodonium chloride (3). A mixture of concentrated sulfuric acid (6.4 ml) and 30% fuming sulfuric acid (13 ml) was added to iodine (21 mmol, 5.4 g) under stirring according to Nilsson et al. (12). Then a mixture of conc. sulfuric acid (1.7 ml), 65% fuming sulfuric acid (0.8 ml) and fuming nitric acid (3.0 ml) was slowly added. The synthesis was performed as described above for the synthesis of **2** but with the addition of 1,3-dibromobenzene (25g, 106 mmol). Yield 16.6 g (26 mmol, 49.1%).

3,3',4,4'-tetrabromodiphenyliodonium chloride (4). The synthesis was performed as described above for the synthesis of **2**, with concentrated sulfuric acid (15 ml), 30 % fuming sulfuric acid (15 ml), iodine (50 mmol, 12.7 g), second addition of concentrated sulfuric acid (4 ml), 65 % fuming sulfuric acid (2 ml) and fuming nitric acid (6.5 ml), and 1,2-dibromobenzene (250 mmol). Yield 25.3 g (47 mmol, 38 %).

General procedure for the syntheses of BDE. This synthesis is based on the method described by Nilsson et al. (12). The bromophenol (2.5 mmol) was dissolved in an aqueous solution (20 ml) of NaOH (0.1 g, 2.5 mmol). The appropriate diphenyliodonium salt (2.5 mmol) was added and the mixture was refluxed during which time the product precipitated. The time needed to complete the reaction varied from 20 min to 1.5 h. The reaction mixture was extracted with diethyl ether (2×30 ml). The etheral layer was washed with water and dried over magnesium sulfate. The solvent was

evaporated and the product was purified on an open silica gel column with n-hexane as the eluent. The product was finally purified on a mixture of activated charcoal and celite (2g+8g) put in a column and the product was eluted with n-hexane.

3. Results and discussion

Twenty-eight BDE (Table 1) were synthesized by the reaction of various brominated phenols and four diphenyliodonium salts: diphenyliodonium bromide (1), 4,4'-dibromodiphenyliodonium chloride (2), 2,2',4,4'-tetrabromodiphenyliodonium chloride (3), and 3,3',4,4'-tetrabromodiphenyliodonium chloride (4), cf. Figure 1. The four diphenyliodonium salts were prepared according to two methods, only slightly modified compared to published methods (10,11,12). Both methods had to be used as the method described by Nilsson and coworkers (12) was not successful for the synthesis of diphenyliodonium chloride. The BDE synthesized were characterized by their melting points, UV, MS, ^1H NMR and relative retention times in GC.

Table 1. Brominated diphenyl ethers synthesized in the present study.

<i>Monobromodiphenyl ethers</i>	<i>Tetrabromodiphenyl ethers</i>
2-BDE	2,2',4,4'-tetraBDE
3-BDE	2,2',4,6'-tetraBDE
4-BDE	2,3',4,4'-tetraBDE
	2,3',4',6-tetraBDE
	2,4,4',6-tetraBDE
<i>Dibromodiphenyl ethers</i>	<i>Pentabromodiphenyl ethers</i>
2,4-diBDE	2,2',4,4',6-pentaBDE
2,4'-diBDE	2,3,4,5,6-pentaBDE
2,6-diBDE	2,3',4,4',6-pentaBDE
3,4-diBDE	
3,4'-diBDE	
4,4'-diBDE	
<i>Tribromodiphenyl ethers</i>	<i>Hexabromodiphenyl ether</i>
2,2',4-triBDE	2,3,4,4',5,6-hexaBDE
2,3',4-triBDE	
2,4,4'-triBDE	<i>Heptabromodiphenyl ethers</i>
2,4,6-triBDE	2,2',3,4,4',5,6-heptaBDE
2,4',6-triBDE	2,3,3',4,4',5,6-heptaBDE
2,3',4'-triBDE	
3,3',4-triBDE	
3,4,4'-triBDE	

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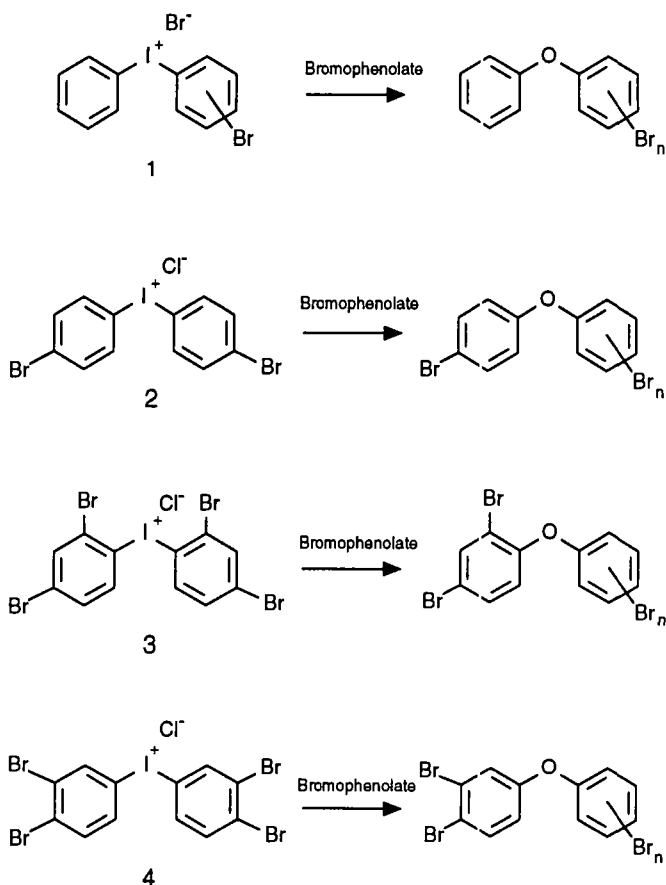


Figure 1. Pathways for the synthesis of the brominated diphenyl ethers.

NMR. ^1H NMR spectra were recorded for the 28 BDE. The protons were assigned by comparison with previously published spectra of polychlorinated diphenyl ethers (16-20). The ^1H chemical shifts for the protons in the non-brominated ring of 2-bromodiphenyl ether are all smaller than the corresponding shifts for that ring of 3- and 4-bromodiphenyl ether. Similarly, the protons in the *para*-brominated ring of 2,4'-dibromodiphenyl ether are all more upfield compared to the corresponding protons in 3,4'- and 4,4'-dibromodiphenyl ether due to the more efficient conjugation of the ether oxygen with the phenyl ring closest to the C-O-C plane. This conformational effect may be used in the assignment of ^1H or ^{13}C NMR spectra of halogenated diphenyl ethers (17,19,20).

Mass spectrometry. Electron ionization (EI) mass spectra were recorded for all the BDE synthesized. The molecular ion (M^+) and $(M-2Br)^+$ ions were found to be the most abundant ions. The non-*ortho*-BDE had M^+ as the base peak, while the *ortho*-BDE generally had $(M-2Br)^+$ ion as the base peak.

UV spectra. The UV spectra of BDE showed maximum absorbance at 203-220 nm ($\log \epsilon$ 4.2-5.2). Highly brominated diphenyl ethers seem to have larger absorbance coefficients and absorb at longer wavelengths.

Crystallography. The conformations of various diphenyl ethers have been studied for decades by different theoretical and experimental methods including X-ray crystallography. The conformations may be described by the two torsion angles between the C-O-C central plane and the phenyl rings. The conformations the diphenyl ethers adopt are always a compromise of two competing forces, (i) the conjugation of the ether oxygen with the phenyl rings and (ii) the steric hindrance between the *ortho*-substituents on the neighbouring rings (21-23).

In the present study, the crystal structures of 2,2',4,6'-tetraBDE and 2,3,4,4',5,6-hexaBDE were determined by single crystal X-ray diffraction. In the crystal conformation of 2,2',4,6'-tetraBDE, the 2-bromine substituent was found to be pointing out from the molecule. The two rings are at an angle of $90(1)^\circ$ of each other and the C-O-C angle is $120(2)^\circ$. Ring A is at an angle of $-106(3)^\circ$ to the C-O-C central plane while ring B is at an angle of $28(4)^\circ$ to that plane. No significant intermolecular interactions was found.

For 2,3,4,4',5,6-hexaBDE, the two rings are at an angle of $89.7(4)^\circ$ of each other. The C-O-C angle was found to be $116(1)^\circ$, which is among the smallest values reported for various kinds of diphenyl ethers (22-26). Ring B runs $85(2)^\circ$ out of the C-O-C central plane while the dihedral angle between ring A and that central plane is $16(2)^\circ$.

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5. References

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