

Synthesis of some ^{14}C -labelled brominated flame retardants

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Introduction

The use of brominated flame retardant (BFR) in different synthetic polymers has increased over the last few decades. A large number of different BFR are used in different applications as in plastic details in cars, plastic cover of electronic equipment, computers etc (1). There is a risk for distribution of these substances in the environment and/or for exposure to humans, wildlife and fish during the whole life cycle of the flame retarded equipment. The knowledge about toxicity and metabolism of these substances is still limited. To promote studies on the toxicity and/or metabolism radiolabelled BFR may be used. Syntheses of ^{14}C -labelled 3,3',5,5'-tetrabromobisphenol A (TBBP-A), 2,2',4,4'-tetrabromodiphenyl ether (BDE-47) and 2,2',4,4',5-pentabromodiphenyl ether (BDE-99) are described in the present work.

Materials and methods

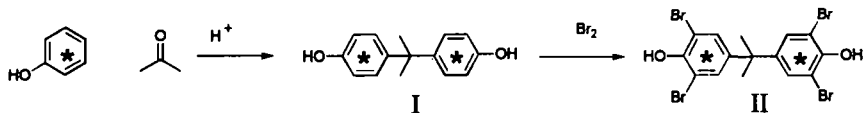
Chemicals: [^{14}C]Phenol with specific activity of 128 mCi/mmol was purchased from Amersham Life Science (UK). The phenol was diluted with unlabelled phenol that had been recrystallised from hexane before it was used. Solvents were all of pesticide grade from Fison, silica gel plates (DC Fertigplatten, Kieselgel 60 F₂₅₄) from Merck and scintillation measurements were made with the cocktail OptiScint HiSafe from Fison.

Instruments: Gas chromatography-mass spectrometry (GC-MS) was performed on a Finnigan ITS40 instrument, connected to a Varian 3400 GC with a split-splitless injector kept at 260 °C and used in the splitless mode. The GC was equipped with a fused silica DB-5 capillary column (30 m x 0.25 mm i.d., 0.25 µm film thickness, Restec Ltd, Bellefont, Pennsylvania, USA) and helium was used as the carrier gas. The oven temperature was programmed starting from 80 °C (2 min) increasing linearly at 10 °C/min up to 280 °C where the temperature was held for 10 min. The ITS40 was operated with an EI energy of 70 eV and an ion source temperature of 220 °C.

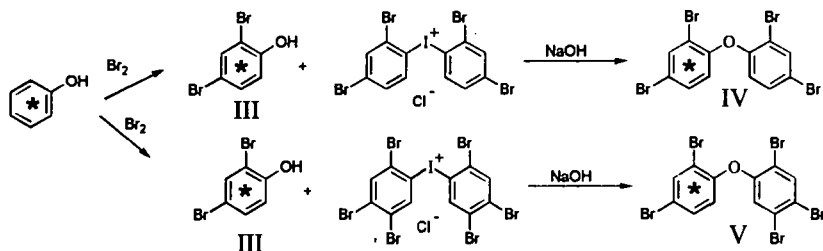
Radioactivity measurements were performed on a Wallac 1409 Emulsifier scintillator 299 (Wallac Oy, Turku, Finland).

Reaction schemes:

A



B



* = [U-14C]

Bisphenol A (I, Scheme A): [U-14C]Phenol (2.5 mCi, 24.2 mCi/mmol, 0.103 mmol) was dissolved in concentrated hydrochloric acid (50 μ l) and acetone (4 μ l, 0.054 mmol). The reaction mixture was stirred in a tightly sealed GC-vial (1 ml) at 50 $^{\circ}$ C for five days. After attending room temperature diethyl ether (0.5 ml) was added and the mixture transferred to a pyrex tube containing water (1 ml). The reaction vial was washed with small portions of diethyl ether. The pooled diethyl ether was washed with water and dried with sodium sulphate. The volume was adjusted to about 50 μ l by a gentle N₂ stream and the sample was purified on two silica gel plates using a mixture of chloroform and methanol (97/3) as the mobile phase. Two TLC bands containing radioactive material were removed by vacuum into small glass containers narrowed at both ends and supplied with a glass-wool plug. The substances were eluted from the gel with diethyl ether. The amount bisphenol A isolated was 1.03 mCi (48.4 mCi/mmol, 0.021 mmol, 41.2 %) and the other substance isolated was unreacted phenol (0.60 mCi, 24.2 mCi/mmol, 0.025, 24.0 %).

3,3',5,5'-Tetrabromobisphenol A (II, Scheme A): [U-14C]Bisphenol (600 μ Ci, 48.4 μ Ci/ μ mol, 12.4 μ mol) was dissolved in a mixture of methanol and water (3/1, 50 μ l) and bromine (2.8 μ l, 54.4 μ mol) was added with a 10 μ l GC-syringe. The mixture was stirred for 15 min at room temperature. After adding diethyl ether (0.5 ml) the mixture was washed several times with small portions of sodium hydrogen carbonate (1 M) and dried with sodium sulphate followed by clean-up on silica gel plates as described above. The TLC plates were developed in a mixture of hexane and acetone (4/1). The TLC band corresponding to tetrabromobisphenol A was removed as described above. Yield 518 μ Ci (48.4 μ Ci/ μ mol, 10.7 μ mol, 86.3 %) with > 99 % purity according to GC-MS.

2,4-Dibromophenol (III, Scheme B): A solution of bromine (7.3 μ l, 0.14 mmol) in carbon tetrachloride (1 ml) was slowly added to a mixture of [14 C]phenol (5.0 mCi, 73.8 mCi/mmol, 0.068 mmol) in carbon tetrachloride (100 μ l) containing catalytic amounts of *ferrum reductum*. The reaction mixture was stirred for two hours at room temperature. The extract was filtered through a small glass wool plug and the collected *ferrum reductum* was washed with diethyl ether. The volume of the solvent was reduced to ca 200 μ l and was then transferred to silica gel plates developed in a mixture of hexane and dichloromethane (1/1) for separation of the products. Two TLC bands containing 14 C was isolated as described above, the major product 2,4-dibromophenol (2.9 mCi, 73.8 mCi/mmol, 0.039 mmol, 58.0 %) and 4-bromophenol (1.36 mCi, 73.8 mCi/mmol, 0.018 mmol, 27.2 %).

2,2',4,4'-Tetrabromodiphenyl ether (IV, Scheme B): 2,4-Dibromo[14 C]phenol (2.9 mCi, 73.8 mCi/mmol, 0.039 mmol) was dissolved in an aqueous solution of sodium hydroxide (1.77 mg, 0.044 mmol, 1 ml) and 2,2',4,4'-tetrabromodiphenyl iodonium chloride (30 mg, 0.047 mmol), prepared as described elsewhere (2) was added and the reaction mixture was refluxed and stirred for two hours. After adjusted to room temperature the reaction mixture was extracted with diethyl ether (5x2 ml) and the diethyl ether was washed several times with small portions of water and finally the ether was dried by sodium sulphate. After reducing the volume of the extract it was applied on silica gel TLC plates that were developed in hexane. The product (2.0 mCi, 36.9 mCi/mmol, 0.054 mmol, 69.0 %) was isolated as described above.

2,2',4,4',5-Pentabromodiphenyl ether (V, Scheme B): 2,4-Dibromo[14 C]phenol (2.3 mCi, 49.0 mCi/mmol, 0.046 mmol), prepared from [14 C]phenol as described above, was coupled with 2,2',4,4',5,5'-hexabromodiphenyl iodonium chloride (44.2 mg, 0.056 mmol) under the same reaction conditions as in the synthesis of 2,2',4,4'-tetrabromo[14 C]diphenyl ether. The product (1.83 mCi, 24.5 mCi/mmol, 0.075 mmol, 79.6 %) was isolated after clean-up as described above.

Results and discussion

The synthesis of three radiolabelled PBDE congeners, BDE-47, 2,2',3,4,4'-pentabromodiphenyl ether (BDE-85) and BDE-99 were described some time ago (3). In the present work an alternative route for the synthesis of BDE-47 and BDE-99 is described that give significantly better yields. This is highly valuable since both PBDE congeners are of interest for toxicological and kinetic studies. The method also indicates the possibility for synthesis of a large number of other radiolabelled PBDEs via the reaction between a 14 C-labelled brominated phenol and a brominated diphenyl iodonium salt (2).

TBBP A has previously been synthesised labelled with 14 C (4) but not at a specific activity as high as we use in the present work. The previous method was modified for the use of small-scale synthesis without problem.

Acknowledgements

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References

1. WHO, Brominated diphenyl ethers, IPCS, Environmental Health Criteria, 162 1994.
2. Hu, J. (Licentiate thesis), Polybrominated diphenyl ethers (PBDE) - synthesis and characterization, Stockholm University, 1996.
3. Örn U., Eriksson L., Jakobsson E. and Bergman Å.; *Acta Chem. Scand.* 1996, 50, 802.
4. Susán A.B., Ebert D.A. and Duncan W.P.; *J. Labelled Comp. and Pharm.* 1979, XVI, 579.