Synthesis of two nonabrominated diphenyl ethers (BDE-207 and BDE-208) via phenoxyanilines

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Introduction

Of the three technical mixtures of polybrominated diphenyl ethers used today i.e. the PentaBDE, OctaBDE and DecaBDE, the latter two products contain nonabrominated diphenyl ethers (nonaBDEs) as minor components [1-3]. NonaBDEs have also been shown to be formed from decaBDE (BDE-209), both via biotic and abiotic processes. NonaBDEs were one type of metabolites found in rats[4] and in rainbow trout [5] exposed to BDE-209. Photochemical degradation of BDE-209 generated nonaBDEs among other transformation products[6,7]. In environmental samples nonaBDEs have been reported from e.g. sediment and sewage sludge [8] as well as in human blood from occupationally exposed workers [9-11]. All three nonaBDEs have recently become commercially available, but they are still rarely reported in literature, and this even as nonaBDEs with unknown bromine substitution. No toxicology studies have been reported from single nonaBDE congeners.

The aim of the present work was to develop a synthetic method for the preparation of pure single nonaBDEs in order to provide net material for analytical standards, toxicological studies and for studies on physical/chemical properties and reactivity.

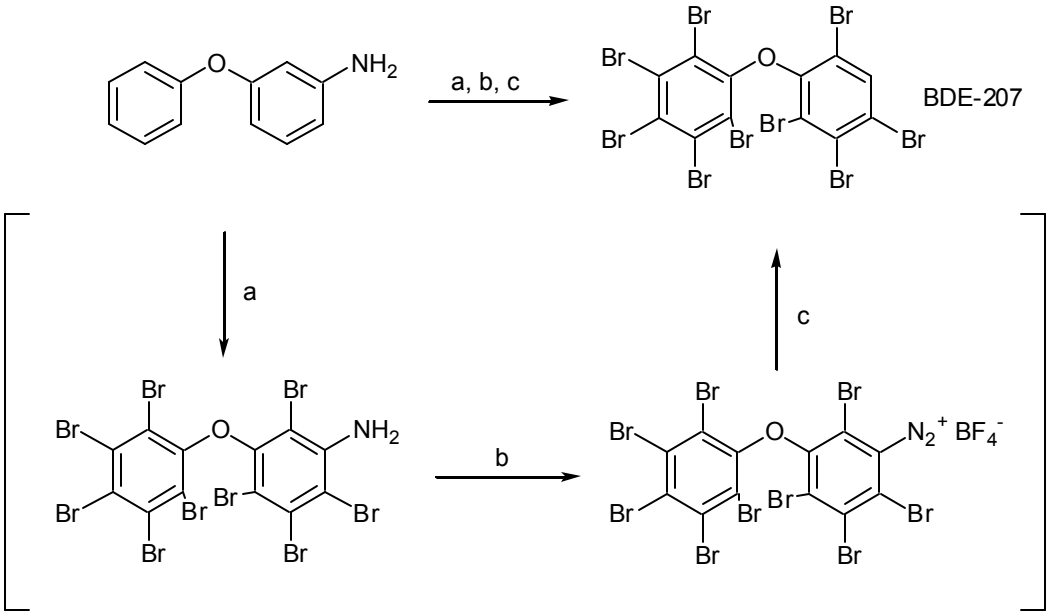
Materials and Methods

Chemicals: The starting materials; 3-phenoxyaniline, 4-phenoxyaniline, aluminium bromide, bortrifluorid-diethyl etherat, 3-methylbutylnitrit and iron (II) sulfate heptahydrate were purchased from Aldrich. Bromine was purchased from Acros Organics. All solvents used were of pro analysis quality.

Instruments: Gas chromatography-mass spectrometry (GC-MS) was performed on an ion trap GCQ Finnigan Mat instrument. The gas chromatograph was equipped with a fused silica capillary column (DB-5, 15 m × 0.25 mm, 0.025-mm film thickness, J&W Scientific, Folsom, USA). The temperature program was 80°C for 2 min, raised at 15°C min^{-1} to 300°C which was held for 15 min. The injections were made in the splitless mode using an injection temperature of 260°C. Helium was used as carrier gas. Mass spectra were recorded in electron ionization mode at an ion source temperature of 150°C and an electron energy of 70 eV. Mass spectra was scanned from 150 to 1000 *m/z*. High-performance liquid chromatography (HPLC) was performed on

a Shimadzu LC-9A (Kyoto, Japan) equipped with an UV detector UV100 from spectra-physics (Fremont, USA) and a preparative C_{18} reversed-phase column (Ace 5 C_{18}, 250 × 21 mm, 5 μm particles) from Advanced Chromatography Technologies (Aberdeen, Scotland) and the flow rate was 18 mL min^{-1} the eluent was 8% water and 92% acetonitrile and the wavelength was 310 nm.

Synthesis: BDE-207 and BDE-208 were prepared from 3-phenoxyaniline and 4-phenoxyaniline, respectively. The synthetic pathway is illustrated in Scheme 1 with the preparation of BDE-207 as the example. The two products between starting material and final nonaBDE product were cleaned up to some extent, but not isolated. Thus, the phenoxyaniline is perbrominated with bromine with aluminium bromide as Lewis acid catalyst similar as described elsewhere[12]. The crude product of the perbrominated phenoxyaniline was diazotisated following the method of Doyle and Bryker[13] in a THF/boron trifluoride etherate solution using 3-methylbutyl nitrit (IAN) and the following reduction was carried out in *N,N*-dimethylformamide (DMF) with iron (II) sulfate heptahydrate as catalyst, previously reported by Wassmundt and Kiesman[14]. The nonaBDE was isolated by preparative HPLC and recrystallized in acetonitrile/THF or recrystallized in acetonitrile/THF.



Scheme 1. a) Br_2, $AlBr_3$ b) IAN, BF_3 THF c) $FeSO_4 \times 7H_2O$, DMF. Compounds within the square bracket were not pure isolated.

Besides the synthesis pathway, the identity of the prepared BDE-207 and BDE-208 were determined by the comparison of their relative retention times on GC-MS with

standards of ditto unambiguously determined by X-ray crystallography[15,16]. GC-MS full scan spectra of the synthesized nonaBDEs were also in agreement with the standards.

Results and Discussion

The nonaBDEs BDE-207 and BDE-208 were prepared in three steps starting with 3-phenoxyaniline and 4-phenoxyaniline, respectively. Both these nonaBDEs were isolated in an over all yield of 10-15% 179,7-276,7g, starting from 2 mmol).
The reduction of decaBDE using sodium borohydride[16] or sodium thiolate[17] is up till today the only reported method for the synthesis of nonaBDEs. The major nonaBDE congener obtained from these procedures is BDE-206. Eriksson and coworkers isolated BDE-206 from the other two nonaBDEs formed as well as other PBDE congeners including the remaining decaBDE on a preparative HPLC[16]. From the same study it was reported that BDE-207 and BDE-208 coeluted on the HPLC column used, but could be separated when taking the first (BDE-207) and the last (BDE-208) part of the eluting peak. However, this procedure is both time and solvent consuming and an alternative synthetic pathway that only yields one of the three nonaBDE congeners is preferable for the preparation of BDE-207 and BDE-208. In the present study only one nonaBDE congener was formed by the synthetic pathway described, which consequently facilitated the isolation.
If 2-phenoxyaniline may be a precursor for the synthesis of BDE-206 using the method described above is under investigation. The perbromination of all three theoretical phenoxybenzoic acids with following decarboxylation is an additionally work for the synthesis of nonaBDEs, which is in progress.

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