Delta- and Epsilon-1,2,5,6,9,10-Hexabromocyclododecane

Arsenault G[a], Konstantinov A[a], McAlees A[a], McCrindle R[b,*], Riddell N[a] and Yeo B[a].
[a] Wellington Laboratories Inc., Research Division, Guelph, Ontario, N1G 3M5, Canada
[b] Chemistry Dept., University of Guelph, Guelph, Ontario, N1G 2W1, Canada

Abstract

Analysis of technical hexabromocyclododecane (HBCD) by other workers has revealed the presence of two additional HBCD compounds (δ- and ε-HBCD) in very low concentrations (<1%) along with α/β/γ-HBCD. Chiral LC chromatography indicated that these two compounds exist as meso compounds but their stereochemistries were not assigned. δ- and ε-HBCD were synthesized in our laboratory by bromination of trans,trans,trans-cyclododecatriene and isolated as pure compounds. The stereochemistries of δ- and ε-HBCD were assigned based on their ^{1}H NMR spectrum as 1*R*,2*S*,5*R*,6*S*,9*S*,10*R*-1,2,5,6,9,10-hexabromocyclododecane and 1*R*,2*S*,5*R*,6*S*,9*R*,10*S*-1,2,5,6,9,10-hexabromocyclododecane, respectively. We confirmed that these two isomers can be found in technical grade HBCD.

1.0 Introduction

Hexabromocyclododecane (HBCD) stands third in production volume of brominated flame retardants (BFRs) after the decabromodiphenyl ether mixture and tetrabromobisphenol A (TBBPA).[1] HBCD is mainly used (85% of volume) as the principal flame retardant in polystyrene foams, while secondary applications include its use in residential, commercial and transportation upholstery, draperies, and wall coverings.[2,3] In 2001, global production was approximately 16,700 tons of which about 60% were consumed[3,4] in Europe and 20% in North America (1999 numbers). With the implementation of mandatory (EU), or voluntary (Japan), restrictions on the production of some brominated flame retardants, the use of HBCD as a replacement product is expected to increase.[3,4]

Industrial production of HBCD involves the bromination of cis,trans,trans-cyclododecatriene (ctt-CDT).[5] Since bromination of a carbon-carbon double bond mainly occurs in a 1,2-diaxial manner, a cis-double bond preferentially leads to RR- and SS-stereoisomers (trans-configuration), whereas the RS- and SR-stereoisomers (cis-configuration) are predominantly formed upon bromination of a trans-double bond.[6,7] Therefore, three diastereomeric pairs of enantiomers are obtained via bromination of ctt-CDT [α-, β- and γ-HBCD]. Analysis of technical HBCD reveals the presence of two additional HBCD compounds in very low concentrations (<1%).[6] Chiral LC chromatography indicated that these two compounds exist as meso compounds, meaning that the structures of both compounds have no overall chirality. The stereochemistries of these two meso forms have not yet been assigned.[6,8] Analysis of technical ctt-CDT in our lab revealed the presence of a small amount of trans,trans,trans-cyclododecatriene (ttt-CDT). Therefore, it is probable that the two meso compounds are formed by the bromination of the ttt-CDT isomer. These isomers have been referred to as delta(δ)- and epsilon(ε)-HBCD.[6,9] In keeping with the naming of the α-, β- and γ-HBCD isomers, the designations δ and ε are given based on their order of elution from a C_{18} LC column.

There have been additional reports[4,10] involving the analysis of HBCD in which small additional peaks were detected, but the identity of these peaks could not be confirmed due to a lack of standards.

The objective of this work was to synthesize the compounds presumed to be δ- and ε-HBCD, confirm their structures by NMR spectroscopy, and determine if these HBCD isomers are present in technical HBCD.

2.0 Experimental

2.1 Synthesis of δ- and ε-HBCD

δ - and ε-HBCD were prepared by bromination of ttt-CDT (Sigma-Aldrich) using published procedures.[5]
δ–HBCD (**1**): Mp 178-181°C; δ_H (80°C, C_6D_5Br) 4.12 (br s, 1H), 3.99 (t, 1H), 3.93 (br m, 1H), 2.10 (br s, 2H), 2.07 (m, 1H), 1.94 (br m, 1H), 1.83 (m, 1H), 1.67 (m, 1H); δ_C (80°C, C_6D_5Br) 57.7 (CHBr), 54.5 (CHBr), 52.4 (CHBr), 34.7 (CH_2), 33.0 (CH_2), 32.5 (CH_2). 2D ^{1}H-^{1}H and 2D ^{1}H-^{13}C NMR experiments showed the following geminal hydrogen pairings: δ2.07 & 1.83; δ1.94 & 1.83; both protons at δ2.10.
ε-HBCD (**2**): Mp 107-109°C; δ_H (22°C, $CDCl_3$) 4.33 (s, 1H), 2.40 (m, 1H), 2.24 (m, 1H). A 2D ^{1}H-^{1}H NMR experiment showed the two signals at δ 2.40 & 2.24 are coupled; vicinal couplings were also observed for δ 4.33 & 2.40; δ 4.33 & 2.24.

2.2 High Resolution Gas Chromatography/Low Resolution Mass Spectrometry (HRGC/LRMS)

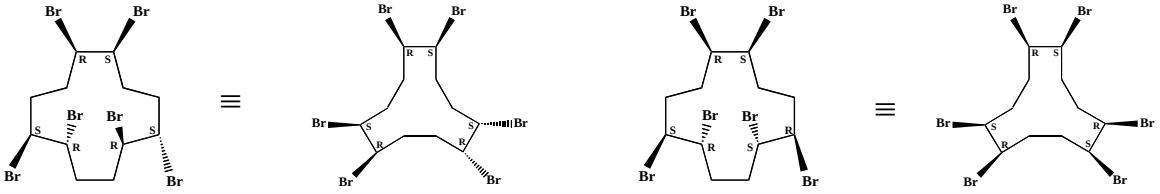
HRGC/HRMS was performed on a Shimadzu GC/MS-QP2010 using a J&W 30m DB-5 column (0.25 mm ID, 0.25 μm film). All injections were done in splitless mode. All analyses were done with the following GC conditions: helium carrier gas flow at 1.0 ml/minute, injector temperature at 200°C, temperature program set to the following parameters: initial oven temperature at 140°C, hold for 1 minute, ramp at 40°C/minute to 200°C, hold for 5.5 minutes, ramp at 10°C/minute to 325°C, hold for 20 minutes. Spectra (50 to 1000 u) were obtained in positive ion, electron impact mode (EI+).

2.3 LC/MS

LC/MS experiments were conducted on a Waters Acquity Ultra Performance LC interfaced to a Micromass Quattro micro API (triple quad mass spectrometer). Separations were performed on an Acquity UPLC BEH C_{18} column (1.7 um, 2.1 x 100 mm). A typical LC method started at 65% (80:20 MeOH: ACN) and 35% water (both with 10 mM NH_4OAc) at a flow rate of 350 μL/minute. The program was then ramped to 100% (80:20 MeOH: ACN) over 15 minutes and held for 2 minutes before returning to initial conditions.

2.4 ^{1}H-NMR Experiments

^{1}H-NMR analyses were performed on a 400 MHz Bruker instrument using either deuterochloroform or deuterated bromobenzene (CDN Isotopes) as the solvent and TMS as an internal standard.



δ-HBCD (**1**) ε-HBCD (**2**)

Figure 1. Structures for δ- and ε-HBCD

3.0 Results and Discussion

3.1 Analysis of technical cis-trans-trans-1,5,9-cyclododecatriene (ctt-CDT)

GC-MS analysis of a technical sample of ctt-CDT (Aldrich) indicates the presence of approximately 3% of a second CDT isomer. ^{1}H-NMR spectra of this technical sample confirm the presence of ttt-CDT in ctt-CDT. This is not surprising as the synthesis of ctt-CDT typically results in the formation of ttt-CDT as an impurity.[11,12] Bromination of ttt-CDT should only produce two possible isomers, **1** and **2**. Therefore, bromination of technical ctt-CDT containing small amounts of ttt-CDT will produce HBCD containing **1** and **2** as minor components.

3.2 Bromination of ttt-CDT and product characterization

Technical ttt-CDT was brominated using published methods. The products, δ- and ε-HBCD, were isolated by a combination of crystallization and HPLC separation techniques and characterized by NMR spectroscopy, GC/MS and LC/MS analyses. The assignment, δ and ε, were based on their order of elution from a C18 LC column, δ eluting before ε. Their NMR spectra confirm that δ- and ε-HBCD have structures **1** and **2**, respectively. ε-HBCD (**2**) has a very simple NMR spectrum due to the three planes of symmetry present in the structure. All CHBr and CH_2 moieties within the structure are equivalent. However, the geminal protons in the CH_2 groups are non-equivalent due to different magnetic environments above and below the ring. δ-HBCD (**1**) also shows a simplified NMR spectrum due to the single plane of symmetry present in the structure. This creates six non-equivalent carbons within the ring structure.

3.3 Analysis of δ- and ε –HBCD by GC/MS and LC/MS

α-, β- and γ-HBCD can not be separated by gas chromatography (GC) because the isomers isomerize at temperatures > 160°C[13,14] and give a single broad peak. The same issue arises when one attempts to analyze δ- and ε-HBCD by GC. Significantly, the signal seen for δ/ε-HBCD has a different retention time than that for α/β/γ-HBCD (see Figure 2) indicating that there is no interconversion between these two groups. Integration of the signals in Figure 2 showed that the responses are equivalent (although the γ-HBCD signal is broader).

The interconversion of isomers is not a problem during LC analysis of HBCD. Under careful LC conditions, all five isomers (α-, β-, γ-, δ- and ε-HBCD) can be cleanly separated on a C_{18} column (see Figure 3). The response factors vary significantly among the five isomers (see peak areas in parentheses in Figure 3) which are present in equi-molar amounts. It should be noted that the LC elution order of δ- and ε-HBCD relative to α/β/γ-HBCD is very similar to that of the unknown HBCD signals observed in previous studies.[4,6]

3.4 Analysis of technical grade HBCD

LC/MS analysis of a technical grade HBCD sample shows the presence of three strong signals corresponding to the α/β/γ-HBCD isomers along with two much smaller signals assigned as δ- and ε-HBCD (see Figure 4). Notably, the chromatogram revealed the presence of at least three other HBCD isomers. GC/MS analysis of the HBCD technical mixture showed a small peak attributable to δ/ε-HBCD (see Figure 5). Therefore, this supports the presence of δ- and ε-HBCD in the technical mixture as having structures **1** and **2**. This, in turn, would indicate that the minor HBCD contaminants observed in the environment[4,10] are the same isomers.

4. Conclusions

The two minor HBCD components (δ- and ε-isomers) found in technical grade HBCD have been identified as having the structures **1** and **2**. These components originate from the bromination of residual amounts of ttt-CDT present in technical ctt-CDT.

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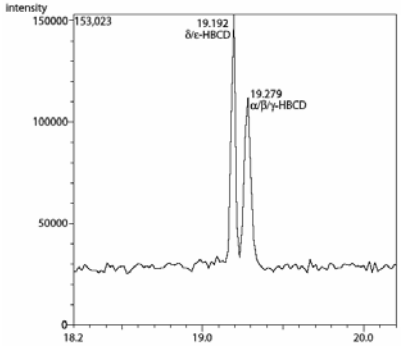

Figure 2. GC chromatogram when δ- and γ-HBCD were injected in equi-molar amounts

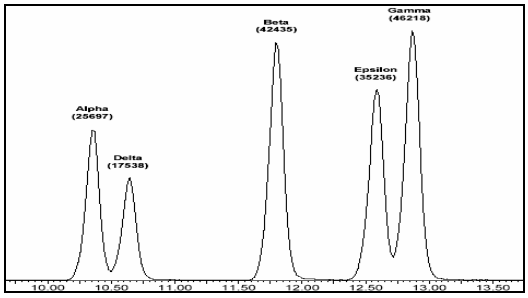

Figure 3. LC chromatogram of the 5 HBCD isomers in equi-molar amounts

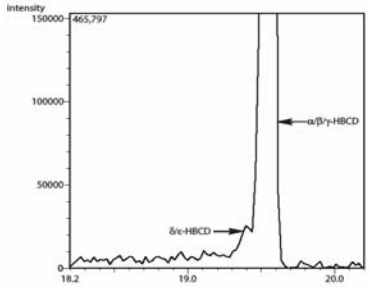

Figure 4. GC chromatogram of technical HBCD

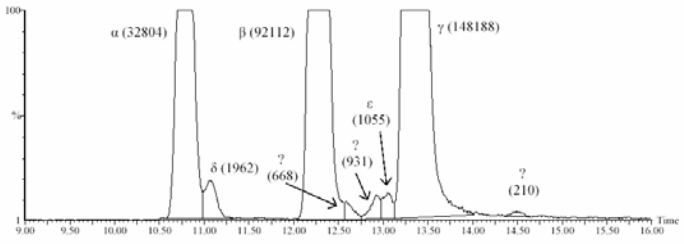

Figure 5. LC chromatogram of technical HBCD