

A Three Dimensional View of the alpha- and gamma-1,2,5,6,9,10-Hexabromocyclododecane Conformers with the help of Nuclear Magnetic Resonance Spectral Characterization and Semi-Empirical Calculations

Gilles Arsenault¹, Brock Chittim¹, Alan McAlees¹ and Robert McCrindle².

¹ Wellington Laboratories Inc. Guelph, Ontario, N1G 3M5, Canada

² University of Guelph, Chemistry Dept., Guelph, Ontario, N1G 2W1, Canada

Introduction

The hexabromocyclododecanes (HBCDs) constitute one of the most important groups of flame retardants¹. Recently, there has been a growing interest among environmental laboratories in methods for determining the levels of the three HBCD isomers (alpha, beta and gamma) in the biota²⁻⁶. This has led to the interesting trend that the gamma (γ -) HBCD isomer is the predominant isomer in sediments and the alpha (α -) isomer is the predominant isomer in fish.

There are few literature references⁷ reporting any NMR data on the individual HBCD isomers. This study reports the full ¹H- and ¹³C-NMR spectral characterization of alpha (α -) and gamma (γ -) HBCD. 3-D models of the two structures are proposed based on the use of various NMR experimental techniques, an evaluation of coupling constant magnitudes and computer modeling of three dimensional structures. It is hoped that an understanding of the structural differences between isomers can shed some light into the different behavior of these isomers in the environment.

Materials and Methods

Chemicals. The α , β and γ -HBCD congeners were purified from a commercial technical mixture as described in the literature. The preparation of the deuterated (²H₁₈) and carbon-13 (¹³C₁₂) HBCD isomers is reported elsewhere⁷.

NMR Experiments. The NMR experiments were performed either on a Bruker 400MHz or 600MHz instrument.

Results and Discussions

Alpha-Hexabromocyclododecane

The NMR spectra of α -HBCD are expected to be greatly simplified because the structure has a C₂ axis of symmetry. As illustrated in figure 1a, the cyclic structure has 6 unique carbons and 9 unique protons. The labeling schemes for the alpha isomer used in our work are shown in figure 1.

The full characterization of α -HBCD was achieved by performing the following NMR experiments on the compounds indicated in brackets: $^1\text{H-NMR}$, 2D $^1\text{H-NMR}$ and 2D $^1\text{H}^{13}\text{C-NMR}$ (on α -HBCD), 2D $^{13}\text{C-}^{13}\text{C-NMR}$ (on $^{13}\text{C}_{12}$ - α -HBCD).

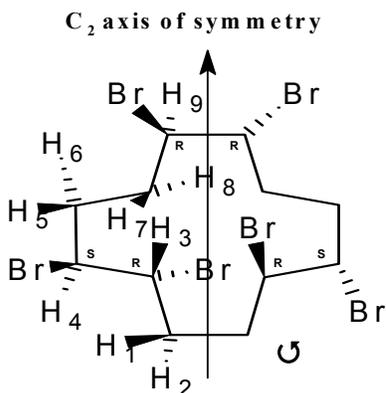


Figure 1a: Proton numbering scheme for α -HBCD

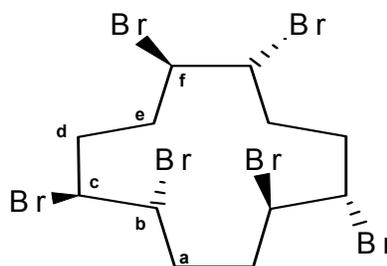


Figure 1b: Carbon numbering scheme for α -HBCD

Gamma-Hexabromocyclododecane

The NMR spectra of γ -HBCD are also expected to be greatly simplified because the structure has a C_2 axis of symmetry. As illustrated in figure 2a, the cyclic structure has 6 unique carbons and 9 unique protons. The labeling schemes used in our work are shown in figure 2.

The full characterization of γ -HBCD was achieved by performing the following NMR experiments on the compounds indicated in brackets: $^1\text{H-NMR}$, 2D $^1\text{H-NMR}$, 2D $^1\text{H-}^{13}\text{C-NMR}$ and 1H-NMR gradient TOSCY (on γ -HBCD), $^2\text{H-NMR}$ (on $^2\text{H}_{18}$ - γ -HBCD), 2D $^{13}\text{C-}^{13}\text{C-NMR}$ (on $^{13}\text{C}_{12}$ - γ -HBCD).

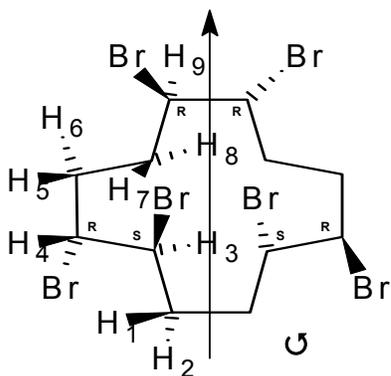


Figure 2a: Proton numbering scheme for γ -HBCD

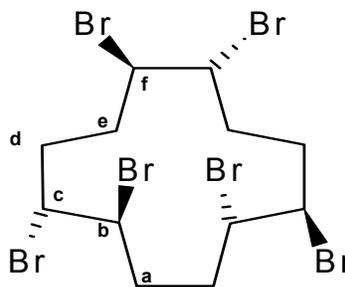


Figure 2b: Carbon numbering scheme for γ -HBCD

Structure Assignment

It was not possible to assign all non-equivalent protons for either diastereomer using only the data generated from the NMR experiments. To help in the full assignment of the ^1H -NMR signals, 3D structures for both α - and γ -HBCD were calculated for the equilibrium conformers using the semi-empirical method available in the Spartan program⁸ (Spartan'02 Windows version). The generated 3D structures are shown in figure 3. These calculations would be expected to provide a good first approximation of the lowest energy conformer for the HBCD. There was good agreement between the expected coupling constants estimated from the calculated structure using the Karplus equation with the measured dihedral angle between vicinal protons and the measurable $J_3(^1\text{H}-^1\text{H})$ coupling constants from the NMR experiments. This correlation strongly suggests that the calculated structures shown in Figure 3 closely resemble the actual molecules in solution as seen by NMR.

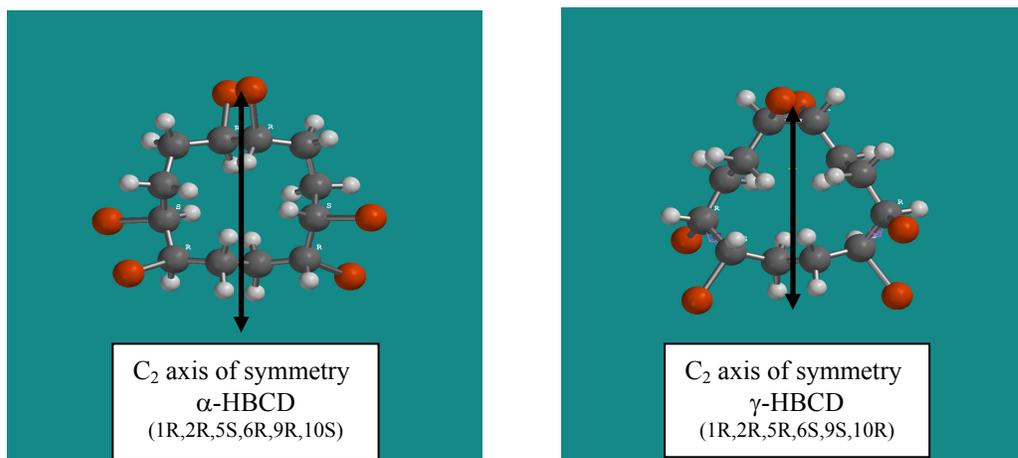


Figure 3: 3-D structure of α - and γ -HBCD

The solid state structure reported⁹ for α -HBCD closely matches the 3D structure generated in this study. This similarity adds weight to the belief that semi-empirical calculations can approximate the lowest energy structure as seen in solution by NMR. However, the crystal structure reported for γ -HBCD is different from the 3D structure generated in this study. One possible explanation for the difference is that the γ -HBCD adopts different preferred conformations in solution and the solid state.

Due to the complexity of the spectra and the fluxional behavior of the molecule, we did not attempt to elucidate the three dimensional structure of β -HBCD using NMR data.

Structure Differences

It is clearly seen from figure 3 that the structures of α - and γ -HBCD are visually quite different. These distinctions in structure will probably result in differences in properties such as polarity, dipole moment, solubility and rates of biological uptake or metabolism. Calculated dipole moments from the semi-empirical calculations gave values of 1.29 and 2.23 Debye, respectively. Not surprisingly, we and others⁹ have observed significant differences in solubility in various organic solvents between the three diastereomers (α , β and γ). It is thus a mistake to assume that these compounds would behave in a similar fashion in the environment. This information should provide useful insight for other researchers into the possible different behavior of the alpha and gamma-HBCD diastereomers in the environment. This work also shows that more work needs to be done with the individual diastereomers in determining their physico-chemical properties and how this relates to the differences observed so far in their distribution in sediments and fish samples. Indeed, differing water solubilities for the three isomers may be key factors in these differences.

Summary

The use of various NMR experiments along with the analysis of the magnitude of the NMR chemical shifts and coupling constants, and computer modeling has enabled the visualization of the dimensional structures for both the alpha (α) and gamma (γ) diastereomers. This information may provide useful insight into the different behavior of the α - and γ -HBCD diastereomers in the environment.

References

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