

Molecular modelling: an interesting tool to explain persistence and lability of compounds of technical toxaphene

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Introduction

Toxaphene is a complex mixture of several hundreds of bicyclic hydrocarbons [1]. More than 30,000 congeners and enantiomers exist alone of polychlorinated bornanes, the major substance class of toxaphene [2]. However, the number of compounds detected in the environment is much lower. Depending on the matrix and the trophic level of a species, degradation leads to CTT patterns different to the technical mixture (Table 1).

Table 1: Major CTT compounds in different matrices (for structures see Table 2)

Technical Mixtures [3][4]	Marine Mammals [5][6]	Lake Sediment [7]
B7-515*	B8-1413	B6-923
B8-806/B8-809	B9-1679	B7-1001

* systematic codes according to ref. [8]

The major compounds in industrial CTT mixtures, B7-515 and B8-806/B8-809, were not detected in the blubber of Weddell seals [9] which points to the fact that these compounds are metabolized on high trophic level biota. On the other hand, the major persistent CTT congeners in marine mammals were only low abundant in sediment samples from Canadian lakes [7]. Two questions arise among others: why are only several hundred (and which) out of 30,000 present in technical mixtures? Why are only few CTTs persistent in the environment? Recently, we found some plausible explanations by application of semiempirical methods [10]. Here we add some details to these observations.

Experimental Methods

Semiempirical calculations were applied with the semiempirical Austin Model 1 (AM1) method [11] as implemented in the MOPAC package version 6.0 [12]. Details on the calculation mode were earlier presented in detail [10][13][14].

Results and Discussion

The "bridge and *exo*" rule

Exclusively alternating *endo-exo-endo-exo* conformation of the chloro-substituents on the six-membered ring was regarded as a determining factor leading to stability of polychlorinated bornanes. The "bridge and *exo*" rule says that requirement for a dichloromethyl group on C-8 is a 6-*exo*-chlorine atom, requirement for a dichloromethyl group on C-9 is a 2-*exo*-chlorine atom. Compounds with both 2-*exo* and 6-*exo* chlorine atoms on the six-membered ring may exist as pairs of isomers with one having a 8,8,9- and the other a 8,9,9-substitution on C-8 and C-9. An example for this are B8-806 (2-*endo*,2-*exo*,5-*endo*,6-*exo*,8,8,9,10,10-octachlorobornane) and B8-809 (2-*endo*,2-*exo*,5-*endo*,6-*exo*,8,9,9,10,10-octachlorobornane). On the other hand, the "bridge and *exo*" rule explains why a compound such as 2-*endo*,3-*exo*,5-*endo*,6-*exo*,9,9,10,10-octachlorobornane (B8-1928), which is obtained by exchange of B8-1413's substituents on C-8 with those on C-9, is not likely to exist [10]. Although we have no definite explanation for this rule, all polychlorinated bornanes elucidated so far fulfill this requirement.

The "energetic favored conformation" rule

Figure 1 shows the nomenclature of bornane including conformations.

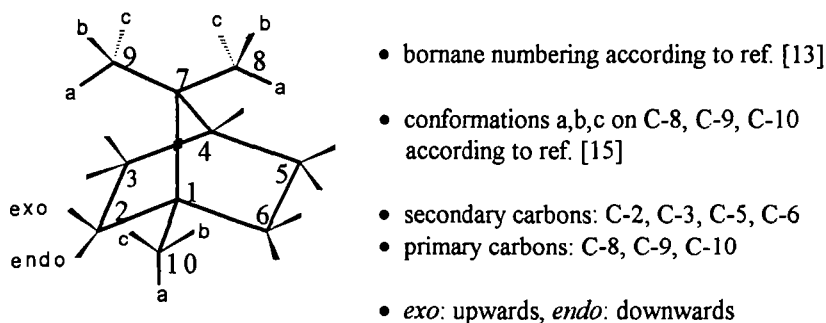
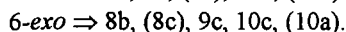
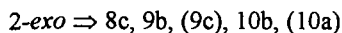


Figure 1 Structure and systematic numbering of the bornane backbone

Experimental data point to the fact that rotations about the C-7→C-8, C-7→C-9, and C-1→C-10 bondings are not restricted at physiological temperatures (no atropisomers exist for the investigated CTTs). On the other hand, chlorine atoms on the primary methyl groups C-8, C-9, and C-10 are preferably located in energetically favored conformations. These energetically favored conformations are most likely directed by *exo*-chlorine atom on C-2 and C-6 in the following manner:



The conformers in parantheses refer to a second chlorine atom in the case of a dichloromethyl group while those without parantheses refer to the energetically favored conformer in the case of a chloromethyl group. The reason for the energetically favored conformations is steric hindrance of bulky chlorine substituents (see Figure 2, left). B9-1679 has a 6-*exo* chlorine atom which is close in space with position 10b. For this reason the two chlorine atoms on C-10 of B9-1679 are in 10a, 10c position. In this conformation the 6-*exo* chlorine atom is close in space with the hydrogen on 10b and the 2-*exo* hydrogen close in space with the chlorine atom on 10c. Rotation of the dichloromethyl group on C-10 into 10a, 10b conformation requires approx. 20 kJ/mol energy (Figure 2, right).

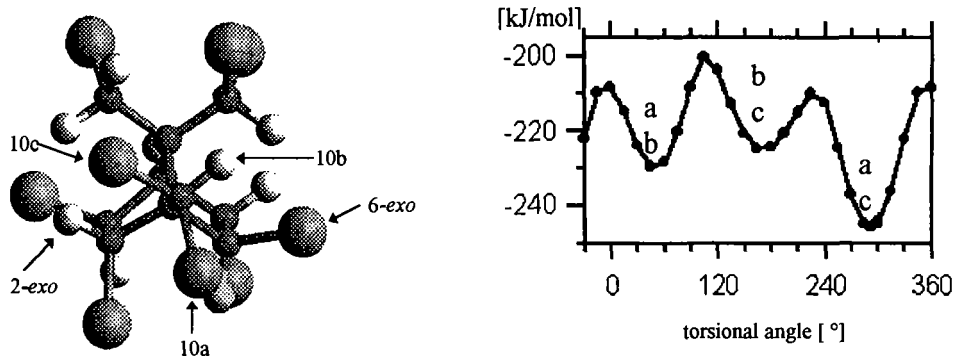


Figure 2: left: Molecular model of B9-1679 showing the 6-*exo* chlorine atom close in space with the hydrogen on 10b and the 2-*exo* hydrogen close in space with the chlorine atom on 10c.
 right: Heat of formation [kJ/mol] of the conformers of the rotation about the C-1→C-10 bonding of B9-1679. The energetically favored conformation is a,c which avoids bulky chlorine atoms in position close to the 6-*exo* chlorine atom

Consequently, CTTs with two *exo*-chlorine atoms vicinal to C-1 (2-*exo* and 6-*exo*) are energetically unfavorable. This explains why B7-515 and B8-806/B8-809 are not persistent in marine mammals. The “energetic favored conformation” rule is also useful to assign optimal conformations to CTTs. Stern et al. left the question open whether the substituents on C-8 and C-9 are in 8b,9c or in 8c,9b conformation [7]. The data above clearly demonstrates preferable conformers:

- 2-*endo*,3-*exo*,5-*endo*,6-*exo*,8b,9c,10c (IUPAC name and first enantiomer)
- 2-*exo*,3-*endo*,5-*exo*,6-*endo*,8c,9b,10b (second enantiomer)

Exclusive alternating *endo-exo-endo-exo* conformation of the chlorine atoms on the six-membered ring (C-1 to C-6) was considered as a requirement for stability of CTTs. Due to the “bridge-and-*exo*” rule, only the following seven CTTs may exist:

- 2-*endo*,3-*exo*,5-*endo*,6-*exo*,8,8,9,10,10-nonachlorobornane (B9-1679): detected [5][6]
- 2-*endo*,3-*exo*,5-*endo*,6-*exo*,8,8,9,10-octachlorobornane (B8-1412): detected [14]
- 2-*endo*,3-*exo*,5-*endo*,6-*exo*,8,8,10,10-octachlorobornane (B8-1413): detected [5][6]
- 2-*endo*,3-*exo*,5-*endo*,6-*exo*,8,9,10,10-octachlorobornane (B8-1414): detected [9]
- 2-*endo*,3-*exo*,5-*endo*,6-*exo*,8,8,10-heptachlorobornane (B7-1000): so far not detected
- 2-*endo*,3-*exo*,5-*endo*,6-*exo*,8,9,10-heptachlorobornane (B7-1001): detected [7]
- 2-*endo*,3-*exo*,5-*endo*,6-*exo*,8,10,10-heptachlorobornane (B7-1002): so far not detected

According to that B7-1000 and B7-1001 may be persistent CTTs in biological samples. In a earlier publication presence of an abundant heptachlorobornane was described [9] which may be either B7-1000 or B7-1002. Furthermore, this also explains why high-trophic level biota such as seal blubber is dominated by only one nonachlorobornane, i. e. B9-1679.

AM1 calculated heat of formations of CTTs

After optimization of the structures with the AM1 method, heat of formations were obtained (see Table 2).

Table 2: Structure and heat of formation (ΔE°) of CTTs

CTT	structure	ΔE° [kJ/mol] most stable conformer
B7-515	2,2,5-endo,6-exo,8,9,10	-215.78 (8b,9c,10a)
B7-1453	2-exo,3-endo,5-exo,9,9,10,10	-224.29 (9b,9c,10a,10b)
B8-831	2,2,5,5,9,9,10,10	-187.80 (9b,9c,10a,10b)
B8-806	2,2,5-endo,6-exo,8,8,9,10	-209.84 (8b,8c,9c,10a)
B8-809	2,2,5-endo,6-exo,8,9,9,10	-216.45 (8c,9b,9c,10a)
B8-1412	2-endo,3-exo,5-endo,6-exo,8,8,9,10	-244.38 (8b,8c,9c,10c)
B8-1413	2-endo,3-exo,5-endo,6-exo,8,8,10,10	-230.64 (8b,8c,10a,10c)
B8-1414	2-endo,3-exo,5-endo,6-exo,8,9,10,10	-245.91 (8b,9c,10a,10c)
B8-1945	2-exo,3-endo,5-exo,8,9,9,10,10	-237.70 (8c,9b,9c,10a,10b)
B8-2229	2-exo,5,5,8,9,9,10,10	-206.78 (9b,9c,10a,10b)
B9-1025	2,2,5,5,8,9,9,10,10	-187.69 (8c,9b,9c,10a,10b)
B9-1679	2-endo,3-exo,5-endo,6-exo,8,8,9,10,10	-245.68 (8b,8c,9c,10a,10c)

The following results can be extracted from Table 2:

- (i) high heat of formations are found for CTTs exclusive *endo-exo-endo-exo* substitution on the six-membered ring (B8-1412, B8-1413, B8-1414, B9-1679)
- (ii) geminal chlorine atoms significantly reduce the heat of formation
- (iii) all those identified as stable congeners had high heat of formation except B8-2229.

The data confirms our experimental findings except the low low heat of formation of B8-2229. One explanation may be the fact that B8-2229 is formed during dechlorination of B9-1025 which compensates for the degraded B8-2229 which was approx. 20 kJ/mol more stable than B9-1025.

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