STRUCTURE ELUCIDATION OF POLYCHLOROTERPENES OBTAINED FROM OPTICALLY ACTIVE PINENES: 2-endo,5,5,8,8,9,9,10,10,10-DECACHLOROFENCHANE BY NMR AND (1*R*,3*S*,4*S*,5*S*,6*S*,7*R*)-2,2,3-*exo*,5-*endo*,6-*exo*,8,9,9,10,10-DECACHLOROBORNANE BY VCD

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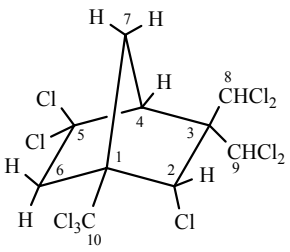
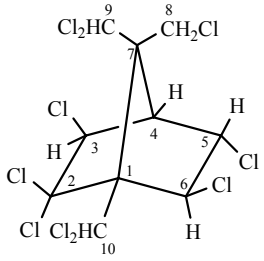
Introduction

A majority of Toxaphene congeners are chiral. Recently we have developed a method for synthesis of pure enantiomers of polychloroterpenes via hydrochlorination of optically active pinene followed by free-radical chlorination[1,2]. On the first stage pinene adds HCl with rearrangemet to a mixture of bornylchloride (major product) and fenchylchloride (minor product). On the second stage polychlorobornanes and, presumably, polychlorofenchanes are formed. The enantiomeric purity was confirmed by three independent methods – X-ray resolution, GC on chiral phase, measurement of optical activity. The next step would be exploration of additional methods for determination of absolute configuration and proof of existence of polychlorofenchanes.

In present work we report on the structure elucidation of the previously unknown 2-*endo*,5,5,8,8,9,9,10,10,10-Decachlorofenchane, Compound **A** by means of NMR, and determination of absolute configuration of optically active sample of already known 2,2,3-*exo*,5-*endo*,6-*exo*,8,9,9,10,10-Decachlorobornane, Compound **B**, using Vibrational Circular Dichroism(VCD). IR and VCD spectra were recorded and DFT calculations were performed in order to simulate IR and VCD spectra.



2-*endo*,5,5,8,8,9,9,10,10,10-Decachlorofenchane (DCF), Compound **A**



2,2,3-exo,5-endo,6-exo,8,9,9,10,10-Decachlorobornane (DCB), Compound **B**

Materials and Methods

Course of reactions, separation, purification and purities of products were controlled by GC/ECD. GC conditions were as follows : GC-Varian3700, inj. – Gerstel split/splitless at 250°C, column – DB-5(app. 50m), Det. – ECD(at 300°C), carrier gas – nitrogen, make-up – nitrogen. Pr.: 160 °C(2 min) - 20 °C/min - 280 °C(10 min) Purge 1.00-1.90 min. NMR spectra of ca 0.05M solutions in deuterochloroform were measured on Bruker DPX-300 or Bruker Avance DRX 500.

Racemic **A** was isolated from perchlorination products of Camphene. Optically active **A** and **B** were obtained by hydrochlorination of β-pinene in chloroform solution followed by free-radical perchlorination and separation of the mixture of nona- and decachloroterpenes on silicagel column with hexane as eluent. **B** was the first eluting major compound, while **A** – the second.

For the compound **B** geometry optimizations and the calculation of the dipole strengths and rotational strengths are performed using Gaussian03 revision B05.[1] The B3LYP hybrid functional is used, generally giving good results when calculating VCD intensities.[2,3] The conformational search is performed with the 6-31G* basis set, using a systematic search method.[4] This yielded 26 stationary points. Only the lowest energy geometry was considered as the other stationary points found were too high in energy. For this geometry the Hessian was calculated and it was found that this stationary point corresponds to a minimum in the potential energy surface.The 6-31G* basis set is regarded as an adequate basis set for the description of geometries, vibrational frequencies and IR/VCD intensities.[5,6] Atomic polar tensors (APT) and atomic axial tensors (AAT) are calculated using gauge-including/invariant atomic orbitals (GIAOs)[7,8], allowing the calculation of the dipole and rotational strengths. An appropriate scaling factor (0.967) is used to correct for the harmonic approximation.
The infrared (IR) and VCD spectra for **B** are measured using a Bruker Vector 22 and a Bruker IFS 66/S FTIR spectrometer coupled to a PMA37 module.[9] Spectra are recorded in a demountable cell with KBr windows and a 105 μm teflon spacer. The unpolarized IR absorbance spectra are recorded at a resolution of 4 cm^{-1}, the VCD spectra at a resolution of 6 cm^{-1}. To improve the VCD S/N ratio a long wavepass filter with an 1830 cm^{-1} cutoff is used. The collection time for the VCD spectrum is 90 min. **B** was dissolved in CS_2 at a concentration of 0.17M. In addition, to get a good estimate for baseline artifacts the VCD of the racemic mixture was measured.

Results and Discussion

1. Structure elucidation of **A.**

The following NMR spectra were recorded in order to determine number, positions and orientation of substituents in a polychlorofencane molecule:
^{1}H
^{13}C
^{13}C DEPT-135
PFG DQF ^{1}H, ^{1}H COSY
PFG ^{1}H, ^{13}C HMQC with BBI
PFG ^{1}H, ^{13}C HMBC with BBI (evol. Delay = 50 msec)
The structure that fits best the results is given below (Fig. 1):

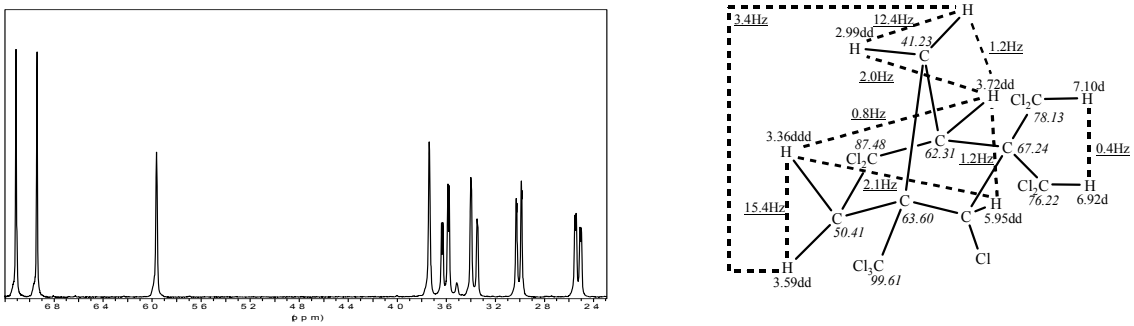


Figure 1. ^{1}H NMR spectrum (300MHz) and the structure of the compound **A** – 2-*endo*,5,5,8,8,9,9,10,10,10-Decachlorofenchane with ^{1}H, ^{13}C (*italics*) chemical shifts (δ, ppm) and ^{1}H-^{1}H coupling constants(underlined) J(Hz)

The preservation of the structure of fenchane (1,3,3-trimethylnorbornane) is confirmed by two key features of ^{1}H NMR spectrum. The first is a pair of doublets at 2.52ppm and 2.99ppm and J = 12.4Hz. This can only belong to a CH_2-group in a five-member ring. It is known for a long time that for CH_2Cl group δ > 3ppm, for CH_2 in a six-member ring J > 14Hz[12]. The second is presence of only one signal of a bridgehead proton at 3.72ppm. Other signals may not belong to a bridgehead proton because of either large chemical shifts or large coupling constants. As free-radical chlorination never yields substitution at a bridgehead, there must be a carbon substituent at one of bridgehead carbon atoms. A small coupling constant (0.4Hz) between the two signals of protons of two other carbon substituents - $CHCl_2$ groups confirms that they are at the same C in the ring. Primary

assignment in ^{13}C spectrum is based on HMQC and confirmed by DEPT. HMBC results are in a good agreement with the proposed structure too, taking into account the large variability of spin-spin interaction depending on dihedral angles between bonds in bicyclic structures. It is noteworthy that **A** bears a trichloromethyl group at the bridgehead. This structural feature has not been found before among the products of free radical chlorination of terpenes with Cl_2. Perhaps, in fenchane the bridgehead methyl group is not sterically hindered by two other methyl groups in β-position, while in bornane or camphene the two are in α-position. Unusual location of three Cl atoms at one C can also explain unusual chromatographic behavior – the lowest elution volume on silicagel and the shortest RRT for decachloroterpenes on GC (0.989 relative to Parlar no. 62). Nevertheless unequivocal structural assignment of **A** would require growing of crystals followed by X-ray analysis, which should also confirm absolute configuration.

1. Determination of absolute configuration of **B.**

A conformational analysis was performed on the (1*R*,3*S*,4*S*,5*S*,6*S*,7*R*)-2,2,3-*exo*,5-*endo*,6-*exo*,8,9,9,10,10-decachlorobornane which yielded 26 stationary point. Only the lowest energy geometry was considered as the other stationary points found were too high in energy. For this geometry(Fig. 2) the Haussian was calculated and it was found that this stationary point corresponds to a minimum in the potential energy surface. Further, the IR and VCD intensities were calculated. In this way IR and VCD spectra could be simulated.

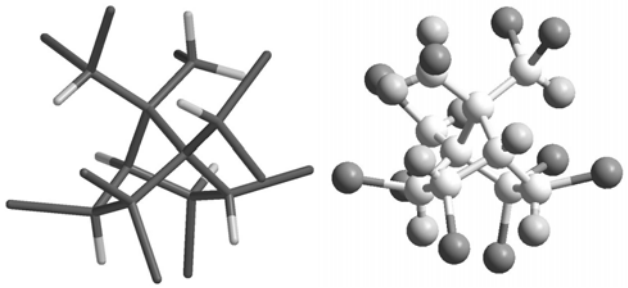


Figure 2. The optimized 3D structure of (1R,3S,4S,5S,6S,7R)-2,2,3-exo,5-endo,6-exo,8,9,9,10,10-decachlorobornane (2 images from opposite sides)

In figures 3 and 4 the simulated and experimental spectra are compared. For the IR a very good agreement is seen. As an harmonic approximation is applied in the theory, the calculated frequencies are overestimated, for which was partially (over) corrected with a frequency scaling factor (0.967).
Thus correctness of quantum-chemical calculation was confirmed.

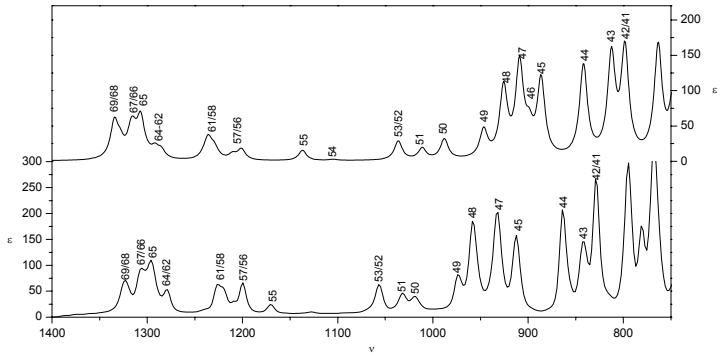


Figure 3. Experimental IR spectrum (bottom) for **B** and B3LYP/6-31G* (top) simulated IR spectrum for (1*R*,3*S*,4*S*,5*S*,6*S*,7*R*)-2,2,3-*exo*,5-*endo*,6-*exo*,8,9,9,10,10-decachlorobornane.

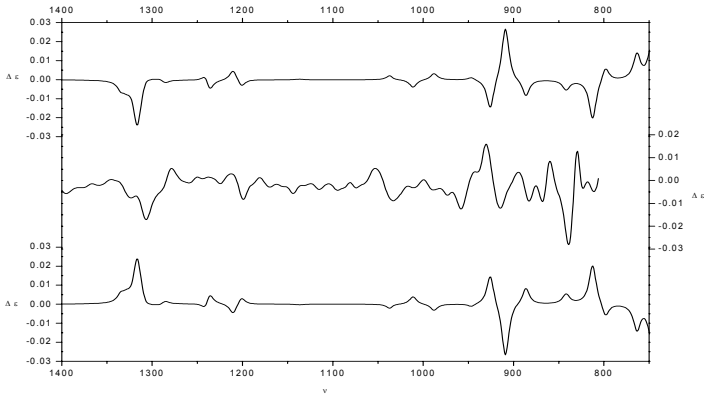


Figure 4. Experimental VCD spectrum (middle) for **B**, the B3LYP/6-31G* (top) simulated VCD spectrum for (1*R*,3*S*,4*S*,5*S*,6*S*,7*R*)-2,2,3-*exo*,5-*endo*,6-*exo*,8,9,9,10,10-decachlorobornane and the B3LYP/6-31G* (bottom) simulated VCD spectrum for another enantiomer, (1*S*,3*R*,4*R*,5*R*,6*R*,7*S*)-2,2,3-*exo*,5-*endo*,6-*exo*,8,9,9,10,10-decachlorobornane.

Comparing the VCD, also a good agreement is seen. As the VCD bands are positioned at the IR transition frequencies, a detailed analysis can be performed in which each VCD band can be identified and compared.
As the modeled spectra are calculated for the (1*R*,3*S*,4*S*,5*S*,6*S*,7*R*)-2,2,3-*exo*,5-*endo*,6-*exo*,8,9,9,10,10-decachlorobornane, it can be concluded that based on the detailed analysis, the absolute configuration of the measured enantiomer agrees with the modeled absolute configuration.

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