(14) E. Gabbay and S. M. Lee, unpublished results, 1973.
(15) E. J. Gabbay and A. DePaolis, *J. Amer. Chem. Soc.*, **93**, 562 (1971).
(16) E. J. Gabbay, R. Scofield, and C. S. Baxter, *J. Amer. Chem. Soc.*, **95**, 7850 (1973).
(17) (a) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, N.Y., 1959; (b) O. Jardetsky and C. D. Jardetsky, *Methods Biochem. Anal.*, **9**, 235 (1962).
(18) E. J. Gabbay, R. DeStefano, and C. S. Baxter, *Biochem. Biophys. Res. Commun.*, **51**, 1083 (1973).
(19) R. DeStefano, Ph.D. Thesis, University of Florida, 1973 (unpublished results).
(20) E. J. Gabbay, R. Glaser, and B. L. Gaffney, *Ann. N.Y. Acad. Sci.*, **171**, 810 (1970).
(21) G. Cohen and H. Eisenberg, *Biopolymers*, **35**, 251 (1969), and references therein.
(22) The intrinsic viscosity, $[\eta]$, by definition is equal to $(\eta_{sp}/C)_{C\to 0}$ where C is the DNA concentration.
(23) C. Tanford, "Physical Chemistry of Macromolecules," Wiley, New York, N.Y., 1961.

Crystal and Molecular Structure of 2,2,5-*endo*,6-*exo*,8,9,10-Heptachlorobornane, $C_{10}H_{11}Cl_7$, a Toxic Component of Toxaphene Insecticide

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Abstract: Toxaphene insecticide contains over 175 distinct C_{10}-chloro compounds. Two of the components, one a $C_{10}H_{10}Cl_8$ compound and the other a $C_{10}H_{11}Cl_7$ compound, appear to contribute more than any others to the acute toxicity of toxaphene to mice treated intraperitoneally. The structure of the $C_{10}H_{11}Cl_7$ component has been determined by X-ray methods. The crystals are orthorhombic, space group $P2_12_12_1$, $a = 8.603$ Å, $b = 21.384$ Å, $c = 7.608$ Å, and $Z = 4$. Data were collected with an automatic diffractometer, over one-quarter of the reflection sphere with Ni-filtered, Cu Kα radiation. The molecule is 2,2,5-*endo*,6-*exo*,8,9,10-heptachlorobornane; the bond angles and distances agree with published values for similar compounds. The 100-MHz proton magnetic resonance spectrum of this compound has been analyzed and is shown to be completely consistent with the X-ray deduced structure. Several spin-spin couplings are discussed in relation to this structure. No isomeric impurities were detected.

Although toxaphene has been in commercial use for about 25 years and approximately one billion pounds have been applied to crops and livestock for pest insect control, very little is known about the composition of this material. Toxaphene is produced by chlorination of camphene to *ca.* 67–69% chlorine by weight, yielding a reproducible but very complex mixture of compounds with an overall average elemental composition of $C_{10}H_{10}Cl_8$.[2] No individual component, toxic or otherwise, has been previously isolated in pure form.

Preliminary examination of fractions from silica gel column chromatography by combination gc-mass spectroscopy reveals that toxaphene is a complex mixture of more than 175 compounds, mostly $C_{10}H_{18-n}Cl_n$ derivatives where the chlorine number (n) is 6, 7, 8, or 9.[3a] By use of mouse intraperitoneal acute toxicity as the monitoring criterion, two components have been isolated in crystalline form with empirical formulas $C_{10}H_{11}Cl_7$ and $C_{10}H_{10}Cl_8$. These two components are 6- and 14-fold, respectively, more toxic to mice than technical toxaphene. Their toxicity to houseflies treated topically is also greater by twofold for the $C_{10}H_{11}Cl_7$ component and fourfold for the $C_{10}H_{10}Cl_8$ component. The $C_{10}H_{11}Cl_7$ component is pure based on a variety of spectral and chromatographic criteria.[3b]

The determination of the crystal and molecular structure of the $C_{10}H_{11}Cl_7$ component is described in this paper. This component is a heptachlorobornane and it is likely that the majority of the other $C_{10}H_{18-n}Cl_n$ compounds in technical toxaphene are also polychlorobornanes.[3a]

Experimental Section

The heptachlorobornane was isolated by use of a partition column with β-methoxypropionitrile and heptane, followed by a silica gel–hexane absorption column. A repetition of these two steps in sequence was followed by preparative gc; the component was further purified by crystallization.[3b]

A Varian HR-100 equipped with an internal field-frequency lock provided 100-MHz proton magnetic resonance (pmr) spectra.[4] To clearly resolve the weaker peaks of complex multiplets, it was necessary to average as many as 200 scans using a 1000-channel time-averaging computer. Overlapping peaks constituted a major problem which was minimized through the use of carbon tetrachloride as the solvent. However, the doublet-split triplet resonance of H(4) is almost completely obscured in this solvent while it is resolved clearly in acetone. No unassigned impurity resonances could be detected in the spectral range of 2.3–4.8 ppm. It is, therefore, estimated that the isomeric purity of this compound exceeded 98%. High field resonances arising from the gc column coating or the crystallization solvents appeared to varying extents in different preparations.

Crystals suitable for X-ray analysis were grown from hexane-ether in the ratio of 5:1. The crystals were colorless prisms elongated along c. Weissenberg and precession photographs were used to determine the unit cell dimensions and space group. The unit cell is orthorhombic; the only systematic absences were $(h00)$, $(0k0)$, and $(00l)$ when h, k, and l were odd. The crystallographic data are summarized as follows: $C_{10}H_{11}Cl_7$, formula wt = 379.37, orthorhombic, space group $P2_12_12_1$, $a = 8.603 \pm 0.005$ Å, $b = 21.384 \pm 0.009$ Å, $c = 7.608 \pm 0.005$ Å, $Z = 4$, $F(000) = 760$, $\rho_c = 1.80$ g cm^{-3}, λ(Cu Kα) = 1.5418 Å, $\mu = 127$ cm^{-1} (for Cu Kα).

The density of the crystal could not be measured accurately because of their high solubility. The assumption of four molecules per unit cell, which gives a calculated density of 1.80 g cm^{-3}, was proven to be correct by the subsequent structure determination.

Dimensions of the crystal used for intensity measurements were 0.07 × 0.07 × 0.26 mm parallel to a, b, and c, respectively. Integrated intensities were obtained with a four-circle automatic diffractometer. The Ni-filtered Cu Kα radiation was detected by a scintillation counter coupled to a single-channel pulse-height analyzer. Data over one-quarter of the diffraction sphere were recorded out to a 2θ angle of 115° by means of the θ-2θ scanning technique. The scan rate was 1°/min (in 2θ). Backgrounds were counted for 20 sec at 0.5° below and above the lower and upper scan limits, respectively. A total of 2567 reflections were measured. Two standard reflections were measured after every 48 reflections; the first had an initial scan count of 240 and decreased by 30% and the second had an initial scan count of 1290 and decreased by 37%. The intensity data were corrected in step-wise fashion with a maximum correction of 34%. The data were also corrected for absorption by use of the program "AGNOST" as revised by Templeton and Templeton.[5] The average absorption correction was 2.189 with a minimum of 1.918 and a maximum of 3.320. In spite of the large linear absorption coefficient, the use of the data corrected for absorption led to only a small improvement in the R index (0.066–0.065) and did not help distinguish the correct absolute configuration as discussed below.

When the data were sorted by combining the Friedel pairs (centric sort) there were 1146 unique reflections of which 19 were measured as zero, and 60 additional reflections had an intensity less than $\sigma(I)$. When the Friedel pairs were not combined (acentric sort) 1923 reflections were unique, 56 reflections had zero intensity, and 115 additional reflections had an intensity less than $\sigma(I)$. The value of $\sigma(I)$ was calculated from the expression

$$\sigma(I) = [C + (T_c/2T_b)^2(B_1 + B_2)]^{1/2}$$

where C is the total counts in scan time T_c, and B_1 and B_2 are the two background counts taken for T_b = 20 sec. When a reflection was measured more than once, the intensities were averaged and the standard deviation was set equal to the greater of $(\Sigma\sigma_i^2)^{1/2}/n$ or $(\Sigma\Delta_i^2)^{1/2}/(n-1)$, where σ_i and Δ_i are the standard derivatives of the ith measurement and the deviation of the ith measurement from the average, respectively, and n is the number of measurements. To reduce the weight given to intense reflections, an additional term, $(0.05I)^2$, was included in the calculation of $\sigma^2(F^2)$

$$\sigma^2(F^2) = [\sigma^2(I) + (0.05I)^2]/(\mathrm{LP})^2$$

where L and P are the Lorentz and polarization factors.

A full-matrix least-squares program furnished by Zalkin[6] was used to refine the parameters. This program minimizes the function $\Sigma w(\Delta F)^2$ where $\Delta F = |F_o| - |F_c|$; F_o and F_c are the observed and calculated structure factors, and w is a weighting factor taken equal to $1/\sigma^2(F)$ when $I > \sigma(I)$; otherwise $w = 0$. Scattering factors for all atoms except hydrogen were taken from the tables published by Cromer and Waber;[7] for hydrogen the values published by Stewart, Davidson, and Simpson[8] were used. Anomalous dispersion terms were included for the chlorine atoms.

Determination of the Structure. Normalized structure factors $|E|$ were calculated by Wilson's method and are shown in Chart I.

Chart I

	Calcd	Centro-symmetric	Noncentro-symmetric
Av $\|E\|$	0.87	0.798	0.886
Av $\|E^2 - 1\|$	0.816	0.968	0.736
Av E^2	1.02	1.00	1.00

Calculated averages are in better agreement with those predicted for a noncentrosymmetric crystal than for a centrosymmetric one[9] in agreement with the deduced space group. A total of 140 reflections had $|E|$ values equal to, or greater than, 1.50. These values in conjunction with the program MULTAN[10] were used to solve the structure by direct methods. An $|E|$ map gave the parameters for the 17 heavy atoms. Three cycles of least-squares refinement with isotropic temperature factors resulted in a discrepancy index R_1, defined as $\Sigma||F_o| - |F_c||/\Sigma|F_o|$, of 0.23. Additional refinement with anisotropic temperature factors reduced R_1 to 0.068.

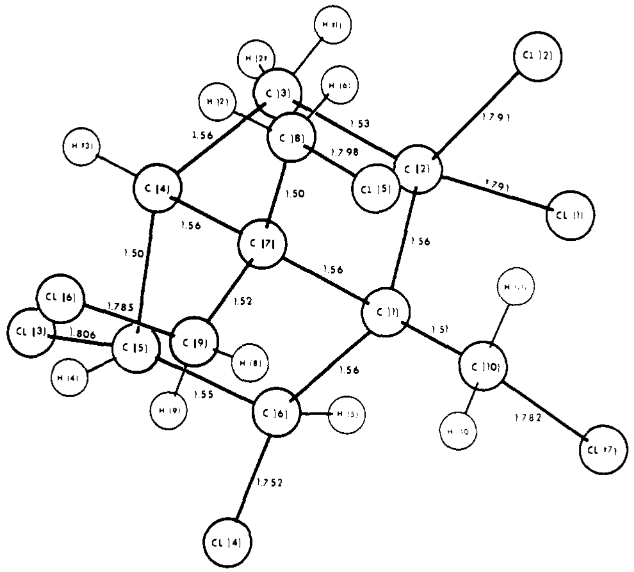

Figure 1. The atom numbering scheme used in this paper and the bond distances between heavy atoms. Estimated standard deviations are 0.009 Å for C–Cl distances and 0.01 Å for C–C distances. This view corresponds to that shown in Figure 2.

Positions of the 11 hydrogen atoms were calculated. They were included in three additional cycles of least-squares refinement of the positional parameters for all 28 atoms, anisotropic temperature factors for the heavy atoms, and the temperature factor of H(1). The temperature factors of the other 10 hydrogen atoms were set equal to that of H(1). This refinement reduced the discrepancy index to its final value of 0.065.[11] $R_2 = [\Sigma w(\Delta F)^2/\Sigma wF_o^2]^{1/2}$ was 0.064 and the standard deviation of an observation of unit weight was 1.52. Good agreement between observed and calculated structure factors for the intense reflections indicated that a correction for secondary extinction was not necessary.

Results

The atomic numbering scheme used in this paper and the bond distances between the heavy atoms are shown in Figure 1. The orientation in this drawing corresponds to the stereoscopic view of the molecule shown in Figure 2. The positional and thermal parameters and their estimated standard deviations for all atoms are given in Table I.

Thermal parameters of the heavy atoms are within the normal range, including those for the atoms bonded to the methyl carbon atoms. The thermal parameters of the hydrogen atoms were tied to that of H(1) because, when refined independently, the temperature factor for H(4) went slightly negative.

Bond angles for the heavy atoms are given in Table II; bond distances and angles involving hydrogen are listed in Table III.

The pmr spectrum of the heptachlorobornane preparation in the region from δ 2.3 to 5.4 ppm was analyzed on the basis of X-ray deduced structure and the observed spin-spin couplings. Table IV summarizes the spectral data. Electronic integration confirmed the presence of 11 protons. The resonance of H(1) can be identified from expected geminal and vicinal couplings and from a long range, 1.8 Hz coupling to H(4) which arises because of their planar W configuration. Vicinal coupling between H(2) and H(3) would be expected to be very small because of the 77° (X-ray determined) dihedral angle. There is no detectable splitting of the "AB" doublet to which H(1) is geminally coupled, but the extra width of these lines indicates a vicinal

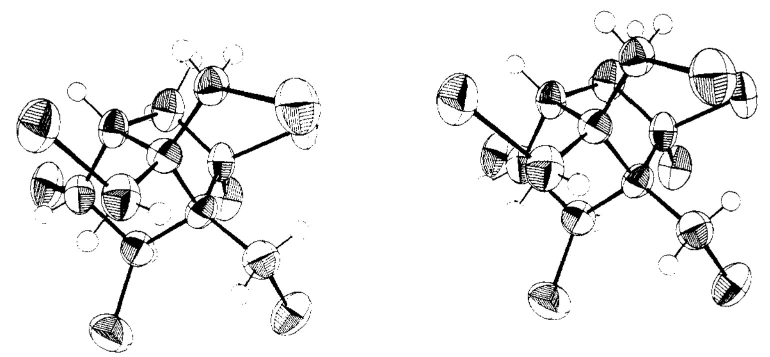

Figure 2. Stereoscopic view of the molecule. The ellipsoids are drawn at the 50% probability level.

Table I. Positional and Thermal Parameters (Å^2) for 2,2,5-*endo*-6-*exo*-8,9,10-Heptachlorobornane[a]

Atom	X	Y	Z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
Cl1	0.2921 (2)	0.6226 (1)	−0.0729 (3)	3.4 (1)	8.4 (2)	4.5 (1)	0.5 (1)	0.83 (9)	0.2 (1)
Cl2	0.0230 (3)	0.5544 (1)	−0.1600 (3)	4.7 (1)	6.7 (1)	2.94 (9)	0.8 (1)	−0.7 (1)	−1.21 (9)
Cl3	0.3383 (3)	0.6291 (1)	0.4442 (3)	4.0 (1)	8.8 (2)	4.1 (1)	−1.1 (1)	−1.5 (1)	0.4 (1)
Cl4	0.0549 (3)	0.7587 (1)	0.2843 (3)	7.6 (2)	3.7 (1)	5.5 (1)	−1.1 (1)	0.4 (1)	−0.7 (1)
Cl5	−0.3584 (3)	0.5713 (1)	0.0561 (3)	3.6 (1)	6.3 (1)	5.4 (1)	−0.3 (1)	−1.3 (1)	−0.2 (1)
Cl6	−0.2632 (3)	0.6053 (1)	0.5438 (3)	4.6 (1)	5.3 (1)	3.17 (9)	0.41 (9)	0.70 (9)	0.25 (9)
Cl7	0.0190 (3)	0.7301 (1)	−0.1723 (3)	5.8 (1)	6.3 (1)	4.5 (1)	−0.2 (1)	0.3 (1)	2.0 (1)
C1	0.0067 (9)	0.6451 (3)	0.1010 (9)	2.9 (4)	3.8 (4)	3.3 (4)	0.4 (3)	−0.1 (3)	0.4 (3)
C2	0.1148 (9)	0.5937 (4)	0.020 (1)	2.7 (4)	5.4 (5)	3.1 (4)	0.1 (3)	−0.6 (3)	−0.4 (4)
C3	0.146 (1)	0.5488 (5)	0.173 (1)	3.4 (4)	5.9 (5)	4.0 (4)	1.6 (4)	−0.8 (4)	0.7 (4)
C4	0.0593 (9)	0.5795 (4)	0.331 (1)	3.0 (4)	4.4 (4)	3.1 (4)	0.4 (3)	−0.3 (4)	−0.2 (3)
C5	0.137 (1)	0.6397 (4)	0.385 (1)	3.8 (4)	5.2 (5)	3.1 (4)	−0.6 (4)	−0.4 (3)	−0.0 (4)
C6	0.116 (1)	0.6835 (4)	0.224 (1)	3.7 (4)	4.2 (4)	3.6 (4)	−1.4 (3)	−0.5 (4)	0.2 (3)
C7	−0.0907 (9)	0.6048 (4)	0.2394 (9)	3.1 (4)	3.2 (3)	3.1 (4)	0.0 (3)	0.1 (3)	0.1 (3)
C8	−0.1863 (9)	0.5504 (4)	0.177 (1)	3.0 (4)	3.4 (4)	3.2 (4)	0.4 (3)	−1.0 (3)	−0.4 (4)
C9	−0.195 (1)	0.6458 (4)	0.354 (1)	3.8 (4)	4.9 (5)	2.7 (4)	−0.1 (4)	0.8 (3)	−0.0 (4)
C10	−0.091 (1)	0.6831 (5)	−0.024 (1)	4.4 (5)	4.3 (5)	3.2 (4)	0.6 (4)	0.2 (4)	0.3 (4)
H1	0.132 (9)	0.497 (4)	0.122 (9)	3.5 (6)					
H2	0.23 (1)	0.547 (4)	0.20 (1)	3.5 (6)					
H3	0.049 (8)	0.553 (3)	0.43 (1)	3.5 (6)					
H4	0.11 (1)	0.661 (3)	0.47 (1)	3.5 (6)					
H5	0.23 (1)	0.688 (3)	0.16 (1)	3.5 (6)					
H6	−0.118 (9)	0.514 (3)	0.107 (9)	3.5 (6)					
H7	−0.213 (9)	0.529 (4)	0.26 (1)	3.5 (6)					
H8	−0.28 (1)	0.658 (4)	0.28 (1)	3.5 (6)					
H9	−0.149 (9)	0.684 (4)	0.41 (1)	3.5 (6)					
H10	−0.159 (9)	0.711 (3)	0.05 (1)	3.5 (6)					
H11	−0.147 (9)	0.655 (4)	−0.09 (1)	3.5 (6)					

[a] Calculated standard deviations are in parentheses. The anisotropic temperature factor has the form $T = \exp[-\Sigma\Sigma(B_{ij}h_ih_jb_ib_j/4)]$ where b_i is the *i*th reciprocal axis length, and *i* and *j* are cycled 1 through 3. The isotropic temperature factor has the form $T = \exp[-B(\sin\theta/2)^2]$.

Table II. Bond Angles (deg) Involving Heavy Atoms[a]

C(2)-C(1)-C(6)	104.3	C(4)-C(5)-C(6)	104.7
C(2)-C(1)-C(7)	101.1	C(4)-C(5)-Cl(3)	112.7
C(2)-C(1)-C(10)	117.4	C(6)-C(5)-Cl(3)	112.5
C(6)-C(1)-C(7)	101.7	C(1)-C(6)-C(5)	103.0
C(6)-C(1)-C(10)	115.7	C(1)-C(6)-Cl(4)	117.2
C(7)-C(1)-C(10)	114.5	C(5)-C(6)-Cl(4)	112.6
C(1)-C(2)-C(3)	104.2	C(1)-C(7)-C(4)	92.8
C(1)-C(2)-Cl(1)	114.8	C(1)-C(7)-C(8)	119.7
C(1)-C(2)-Cl(2)	112.6	C(1)-C(7)-C(9)	112.0
C(3)-C(2)-Cl(1)	111.4	C(4)-C(7)-C(8)	109.0
C(3)-C(2)-Cl(2)	111.3	C(4)-C(7)-C(9)	115.3
Cl(1)-C(2)-Cl(2)	103.6	C(8)-C(7)-C(9)	107.7
C(2)-C(3)-C(4)	103.8	C(7)-C(8)-Cl(5)	114.8
C(3)-C(4)-C(5)	110.8	C(7)-C(9)-Cl(6)	112.1
C(3)-C(4)-C(7)	101.2	C(1)-C(10)-Cl(7)	114.0
C(5)-C(4)-C(7)	100.9		

[a] Esd's are 0.5° for C-C-Cl angles and 0.7° for C-C-C angles.

coupling to H(3) of 0.6 Hz. Spin decoupling confirmed the assignment of all ring resonances.

Because of the appreciable nonequivalence to be expected from protons on a carbon adjacent to an asymmetric center,

Table III. Distances (Å) and Angles (deg) Involving Hydrogen Atoms[a]

H(1)-C(3)	1.2	H(4)-C(5)-C(6)	106
H(2)-C(3)	0.8	H(4)-C(5)-Cl(3)	96
H(3)-C(4)	1.0	H(5)-C(6)-C(1)	108
H(4)-C(5)	0.8	H(5)-C(6)-C(5)	108
H(5)-C(6)	1.1	H(5)-C(6)-Cl(4)	108
H(6)-C(8)	1.1	H(6)-C(8)-H(7)	99
H(7)-C(8)	0.8	H(6)-C(8)-C(7)	114
H(8)-C(9)	0.9	H(6)-C(8)-Cl(5)	112
H(9)-C(9)	1.0	H(7)-C(8)-C(7)	109
H(10)-C(10)	1.0	H(7)-C(8)-Cl(5)	108
H(11)-C(10)	0.9	H(8)-C(9)-H(9)	107
H(1)-C(3)-H(2)	98	H(8)-C(9)-C(7)	106
H(1)-C(3)-C(2)	109	H(8)-C(9)-Cl(6)	111
H(1)-C(3)-C(4)	127	H(9)-C(9)-C(7)	118
H(2)-C(3)-C(2)	113	H(9)-C(9)-Cl(6)	102
H(2)-C(3)-C(4)	106	H(10)-C(10)-H(11)	112
H(3)-C(4)-C(3)	114	H(10)-C(10)-C(1)	108
H(3)-C(4)-C(5)	110	H(10)-C(10)-Cl(7)	109
H(3)-C(4)-C(7)	119	H(11)-C(10)-C(1)	106
H(4)-C(5)-C(4)	124	H(11)-C(10)-Cl(7)	109

[a] Esd's 0.1 Å for the distances, 5° for angles involving one hydrogen and 10° for angles involving two hydrogens.

Table IV. Pmr Shielding Values and Spin-Spin Coupling Constants for 2,2,5-*endo*-6-*exo*-8,9,10-Heptachlorobornane[a]

Hydrogen	(1)	(2)	(3)	(4)	(5)	(6)[e]	(7)[e]	(8)[e]	(9)[e]	(10)[f]	(11)[f]
δ[b]	3.01	3.36	2.59	4.68	5.33	4.35	4.18	4.61	4.18	4.53	3.83
Splitting[c]	ad, d, d	ad	t	t, d	d	ad, d	ad, d	ad, d	ad, d	ad	ad
Interaction	1,2	1,3	1,4	2,3	3,4	4,5	6,7	6,8	7,9	8,9	10,11
J[d]	16.2	4.5	1.8	0.6	4.5	4.6	12.4	1.8	1.8	12.5	12.5

[a] In CCl_4 at 100 MHz and 31°. [b] In ppm downfield from TMS; doublet centers are reported. [c] Key: ad, asymmetric doublet (half of "AB" quartet); d, doublet; t, triplet. Listed in order of decreasing coupling. [d] Derived from first-order analysis, in Hz. [e] Proton assignments for C(8) and C(9) may be exchanged or interchanged. [f] These assignments may be interchanged..

Table V. Deviation from Atoms of Least-Squares Plane and Dihedral Angle between Them[a]

Plane forming atoms	d (Å)	Plane forming atoms	d (Å)
plane (1)		plane (3)	
C(1)	−0.028	C(2)	−0.025
C(4)	0.029	C(3)	0.025
C(5)	−0.043	C(5)	−0.025
C(6)	0.041	C(6)	0.025
plane (2)		plane (4)	
C(1)	−0.008	C(4)	0.011
C(2)	0.012	C(7)	−0.006
C(3)	−0.012	C(1)	−0.016
C(4)	0.008	C(10)	0.012
	Angle (deg) between Plane Normals		
(1)-(2)	67.54	(2)-(3)	33.38
(1)-(3)	34.24	(2)-(4)	56.55
(1)-(4)	124.06	(3)-(4)	89.83

	Coefficients of the Equation of the Plane (Å)			
Plane	A	B	C	D
(1)	0.823	−0.341	−0.453	−4.986
(2)	0.812	0.537	0.229	7.632
(3)	0.989	0.104	−0.105	2.302
(4)	−0.010	0.771	0.636	11.157

[a] The plane is of the form $Ax + By + Cz = D$ where x, y, z and D are in Å units relative to the axes a, b and c.

the hydrogens on C(10) are assigned to an "AB" quartet whose doublets are centered at 4.53 and 3.83 ppm. The resonance of the methylene hydrogens on C(8) and C(9) consist of two partially overlapping doublet-split "AB" quartets in the region from 4.10 to 4.70 ppm. One "AB" double doublet is centered at 4.61 ppm, somewhat downfield from the other three but is obscured partially by the resonance of H(4) and H(10). Irradiation of this region produces a partial collapse of the other "AB" systems in the region from 4.10 to 4.45 ppm. However, because of the small separation of the irradiation and observing frequencies, it was impossible to analyze the double resonance spectra. The 1.8-Hz doublet splitting of the "AB" lines must arise from four-bond couplings between pairs of protons on C(8) and C(9). As indicated in Table IV, the assignment of the "AB" pairs to particular protons is quite arbitrary.

Description of the Structure. The crystal structure determination established that the compound under investigation is a heptachlorobornane. The arrangement of the hydrogen and chlorine atoms on the carbon skeleton is shown in Figure 2. This stereoscopic view[12] of the molecule also illustrates the conformation of the molecule and the thermal motion of the atoms. The thermal ellipsoids are drawn at the 50% probability level.

The chlorine atom on C(6) is cis to the C-$(CH_2Cl)_2$ bridge, in agreement with the orientation of the halogen atom in (−)-2-bromo-2-nitrobornane and (+)-10-bromo-2-chloro-2-nitrobornane.[13] The chlorine atom C(5) is trans to the C-$(CH_2Cl)_2$ bridge as is the chlorine atom on C(10). The two C-Cl bonds, C(9)-Cl(6) and C(8)-Cl(5), are directed in opposite directions and, in the crystal, the three CH_2-Cl bonds are nearly parallel. This arrangement appears to provide minimum intramolecular interaction between the chlorine atoms and also results in a compact molecule which allows efficient molecular packing in the crystal.

The C-C bond distances vary considerably from the single bond value of 1.533 Å[14] but are consistent with those reported for other bornane derivatives.[13] The C-Cl bond distances are all longer than the single bond value of 1.767 Å[15] except for C(6)-Cl(4). The C-Cl bond distances vary by 5σ and have an average value of 1.786 Å.

The average endocylic angle in the two cyclopentane rings, C(1) C(2) C(3) C(4) C(7) and C(1) C(7) C(4) C(5) C(6) is the same for both rings and has a value of 102.6°. The bridge angle of 92.8° is in excellent agreement with the values summarized by Allen and Rogers[16] for six similar compounds. If the bornane skeleton is regarded as a bridged cyclohexane ring in the boat conformation, it then has four four-atom planes. The description of these planes, the out-of-plane distances of the atoms making up the plane, and the dihedral angle between the planes is summarized in Table V. The dihedral angles are in good agreement with those reported for (+)-3-bromocamphor.[16] The packing of the molecules in the crystal is illustrated in Figure 3. The intermolecular contacts less than 3.5 Å are listed in Table VI. The contacts are compatible with the sum of the van der Waals radii and indicate that the only attractive force between molecules in the crystal are van der Waals interactions.

Nmr Discussion. The 12.4-Hz geminal couplings for the chloromethyl hydrogens are not significantly larger (in absolute magnitude) than the 10.8-Hz coupling in methyl chloride or the 11.1-Hz coupling in 1,2-dichloropropane,[17] and the H-C-H angles in the heptachlorobornane are approximately tetrahedral (Table III). On the other hand the corresponding angle for the ring methylene group is 11° smaller while the coupling magnitude is larger by almost 4 Hz. This value is larger than any listed in an extensive tabulation[17] of geminal couplings in the absence of α-unsaturation. In strain-free systems electron-withdrawing β-substituents in an eclipsed configuration are known to increase the magnitude of geminal couplings.[17] However, even with three eclipsing oxygens, the magnitude is increased by only 2.5 Hz, and in 5-*endo*-chlorobicycloheptene the geminal coupling of the hydrogens of C(6) is only 12.0 Hz.[18] It does not seem reasonable, therefore, to ascribe the 4 Hz coupling increase of the heptachlorobornane to the presence of two eclipsing β-chlorine substituents. No satisfactory theory now exists which relates geminal coupling to the H-C-H angles although much work has been done in this area.

The four-bond, 1.8 Hz coupling between H(1) and H(4) which arises as a result of the planar W pathway connecting them does not differ significantly from the corresponding coupling of 1.0 Hz reported for 2-*endo*-3-*endo*-dihydroxybornane where the same pathway exists.[19] In the 2-exo-3-exo isomer this pathway is not available and no coupling

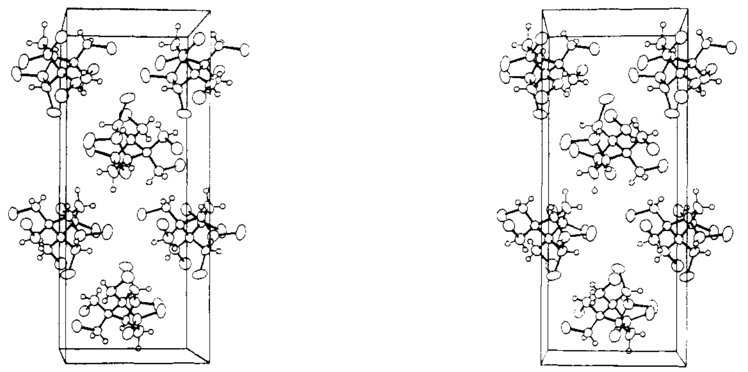

Figure 3. A stereoscopic view of the molecular packing in the unit cell. The structure is viewed parallel to z.

Table VI. Intermolecular Contacts (Å) to 3.5 Å[a]

Cl(1)-Cl(5^{x})	3.348	Cl(6)-H(6^{vi})	2.8
Cl(3)-H(1^{v})	3.0	Cl(6)-H(7^{vi})	3.3
Cl(3)-H(8^{x})	3.5	Cl(5)-H(3^{vii})	3.3
Cl(2)-H(2^{iv})	3.3	Cl(5)-H(7^{vii})	3.2
Cl(2)-H(7^{vii})	3.3	C(10)-H(5^{ix})	3.3
Cl(2)-H(3^{i})	3.1	H(5)-H(10^{viii})	2.8
Cl(7)-H(5^{ix})	3.8	H(3)-H(1^{v})	3.3
Cl(7)-H(4^{ii})	3.2	H(3)-H(2^{v})	3.5
Cl(7)-H(10^{viii})	3.2	H(1)-H(2^{iv})	3.4
Cl(7)-H(8^{viii})	3.1	H(6)-H(7^{vii})	3.1
Cl(6)-H(11^{iii})	3.2		

Symmetry Code

i	x	y	$1 - z$	vi	$-\frac{1}{2} - x$	$1 - y$	$\frac{1}{2} + z$
ii	x	y	$-1 + z$	vii	$-\frac{1}{2} - x$	$1 - y$	$-\frac{1}{2} + z$
iii	x	y	$1 + z$	viii	$\frac{1}{2} + x$	$\frac{1}{2} - y$	$-z$
iv	$\frac{1}{2} - x$	$1 - y$	$-\frac{1}{2} + z$	ix	$-\frac{1}{2} + x$	$\frac{1}{2} - y$	$-z$
v	$\frac{1}{2} - x$	$1 - y$	$\frac{1}{2} + z$	x	$1 + x$	y	z

[a] The estimated standard deviations for the Cl-Cl distance is 0.004 Å; for all other distances 0.1 Å.

was observed. The presence of this long range coupling in the hexachlorobornane thus confirms the exo configuration of H(4). Likewise, the 4.5-Hz vicinal coupling between H(4) and H(5) confirms its endo (trans) configuration. A value of 3.2 Hz has been reported[20] for the corresponding trans coupling in 1,2,3,4,6-*endo*,7,7-heptachlorobicyclo-[2.2.1]heptene while the cis coupling is 8.0 Hz. The absence of a 5-*exo*-chlorine should not vitiate the usefulness of this compound as a model.

The method used to manufacture toxaphene and to purify the sample used for this investigation should produce a racemic mixture. This was verified by optical rotatory dispersion and circular dichroism[21] on the heptachlorobornane sample used to grow crystals for this study. The observed noncentrosymmetric space group, as well as the results of the Wilson calculation tabulated above, indicate that the enantiomers must separate during crystallization. Although resolution of enantiomers by crystallization is rare, it does occur occasionally.[22] An attempt to determine the absolute configuration of the enantiomer in the crystal used to collect the X-ray intensity data proved inconclusive. The parameters of both enantiomers were least-squares refined, using the acentrically sorted data. The final R_1 index was essentially the same for both structures (0.0649 and 0.0652). The sign of $[F_c^2(hkl) - F_c^2(\bar{h}\bar{k}\bar{l})]$ for 18 Friedel pairs were compared with the observed values; 11 pairs favored one enantiomer and seven the other. this result is not surprising since the calculated difference for the Friedel pairs is small and within the experimental error of observation. An attempt to find left- and right-handed crystals by observation of a batch of crystals under the microscope failed to reveal any faces which would allow such a distinction to be made. Although resolution apparently occurs during crystallization, it cannot be demonstrated with the present X-ray data.

At least 28 other $C_{10}H_{11}Cl_7$ compounds are present in technical toxaphene.[23] Since toxic activity was the criterion used to isolate 2,2,5-*endo*,6-*exo*,8,9,10-heptachlorobornane from the other heptachlorides, it is concluded that either this heptachloride has greater toxic potency than the other heptachlorides, or the method used to manufacture technical toxaphene produces a larger yield of the heptachloride investigated in this paper.

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Supplementary Material Available. A listing of structure factor amplitudes, standard deviations, and the difference ($|F_o| - |F_c|$) for this structure will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JACS-75-408.

References and Notes

(1) (a) Western Regional Research Laboratory. (b) Division of Entomology and Parasitology.

(2) G. A. Buntin, U.S. Patent No. 2,565,471 (1951).

(3) (a) J. E. Casida, R. L. Holmstead, S. Khalifa, J. R. Knox, T. Ohsawa, K. J. Palmer, and R. Y. Wong, *Science*, **183**, 520 (1974); (b) S. Khalifa, T. R. Mon, J. L. Engel, and J. E. Casida, *J. Agr. Food Chem.*, submitted for publication.

(4) R. E. Lundin, R. H. Elsken, R. A. Flath, and R. Teranishi, *Applied Spectrosc. Rev.*, **1**, 131 (1967).

(5) L. K. Templeton and D. H. Templeton, *Amer. Cryst. Assoc. Abstract E10*, Storrs, Conn., Meeting, June 1973.

(6) A. Zalkin, Berkeley Lawrence Laboratory, private communications.

(7) D. T. Cromer and J. T. Waber, *Acta Crystallogr.*, **18**, 104 (1965).

(8) R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, **42**, 3175 (1965).

(9) G. H. Stout and L. H. Jensen, "X-Ray Structure Determination," Macmillan, New York, N.Y., 1968, p 321.

(10) G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. A*, **27**, 368 (1971).

(11) See paragraph at end of paper regarding supplementary material.

(12) C. K. Johnson, ORTEP: Report ORNL-3794, Oak Ridge National Laboratory, Oak Ridge, Tenn., 1965.

(13) G. Ferguson, C. J. Fritchie, J. M. Robertson, and G. A. Sim, *J. Chem. Soc.*, 1976 (1961).

(14) M. J. S. Dewar and H. N. Schmeising, *Tetrahedron*, **11**, 96 (1960).

(15) L. E. Sutton, *et al.*, "Tables of Interatomic Distances and Configuration in Molecules and Ions," *Chem. Soc., Spec. Publ.*, **No. 18** (1965).

(16) F. H. Allen and D. Rogers, *J. Chem. Soc. B*, 632 (1971).

(17) A. A. Bothnerby, *Advan. Magn. Resonance*, **1**, 195 (1965).

(18) P. Laszlo and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **85**, 2709 (1963).

(19) F. A. L. Anct, *Can. J. Chem.*, **39**, 789 (1961).

(20) K. L. Williamson, *J. Amer. Chem. Soc.*, **85**, 516 (1963).

(21) We wish to thank Dr. W. Gaffield, Western Regional Research Center, for these observations.

(22) R. M. Secor, *Chem. Rev.*, **63**, 297 (1963).

(23) R. L. Holmstead, S. Khalifa, and J. Casida, *J. Agr. Food Chem.*, accepted for publication.

Crystal and Molecular Structure of the Orthorhombic Form of Prostaglandin A_1[1]

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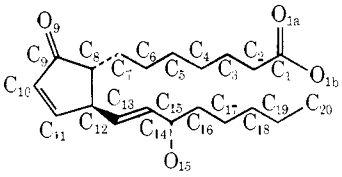
Abstract: The crystal and molecular structure of the orthorhombic polymorph of the renal antihypertensive prostaglandin A_1 [15(S)-hydroxy-10,13-dien-9-ketoprostanoic acid, structure A], $C_{20}H_{32}O_4$, has been determined by X-ray diffraction techniques. The compound crystallizes in the orthorhombic space group $P2_12_12_1$, with cell constants $a = 18.106$ (3), $b = 21.091$ (4), and $c = 5.420$ (1) Å; $Z = 4$, $d_{\text{calcd}} = 1.086$ g cm^{-3}. The structure was solved by direct methods employing calculated values for the cosines of the seminvariant Σ_2 triples. The refinement by F^2-based full-matrix least squares led to final agreement factors of $R(F) = 0.098$ [$R_w = 0.109$; $S = 1.14$, $\Sigma w(F_o - sF_c) = 1312$] for 1002 intensities measured on a G.E. XRD-5 single-crystal orienter using the stationary counter–stationary crystal technique. The molecular structure is characterized by extensions of the two side chains in the same direction away from the cyclopentenone ring. The crystal structure is stabilized by an infinite helical hydrogen-bonding network paralleling c, which does not involve the cyclopentenone moiety.

The prostaglandins are a ubiquitous class of compounds commonly found in mammals at levels approximating 1 ng/ml of plasma. They are implicated in a wide range of bodily functions, ranging from maintenance of normal tension to participation in the inflammation response and secretion of gastric acid. Current interest in prostaglandins as drugs is based upon their ability to maintain menstrual regulation, induce abortion at midtrimester, and induce labor at term. Their potential use in the treatment of asthma, hypertension, and duodenal ulcers is also under investigation. The chemical differences among the natural prostaglandins result in many of these intense biofunctional variations.[3,4]

The availability of a good single crystal of orthorhombic prostaglandin A_1 [PGA_1(o)][5] permitted a study of the molecular conformation of an unsubstituted prostaglandin and a comparison with the molecular structure of the prostaglandin $F_{1\beta}$ tribromobenzoate ($PGF_{1\beta}$) previously reported.[6] Although the structure of $PGF_{1\beta}$ confirmed the relative configuration of the prostaglandins, there remained some doubt concerning the influence of the bromobenzoate substituents upon the basic prostaglandin molecular conformation as observed in the crystal structure. To resolve this question, and to increase the molecular data base for further comparative studies, we have undertaken the crystal structure analysis of a series of prostaglandins beginning with PGA_1.



A

Experimental Section

Crystal Data. A clear columnar crystal extended along c was selected from a sample as received and analyzed under a polarizing microscope. The crystal, with dimensions 0.2 × 0.2 × 0.4 mm, was mounted with the c axis along the diffractometer ϕ axis, and the reciprocal cell orientation was determined by the stereographic projection method. The assigned cell was checked for errors by doubling all cell lengths and scanning low-angle reciprocal space for missed reflections. Centering 40 reflections in the range $55° \leq 2\theta \leq 65°$ with Cu $K\alpha_1$ radiation ($\lambda = 1.54051$ Å) and fitting these *via* least squares yielded these final cell dimensions: $a = 18.106$ (3), $b = 21.091$ (4), and $c = 5.420$ (1) Å. Systematic absences for $h00$, $h = 2n + 1$, $0k0$, $k = 2n + 1$, and $00l$, $l = 2n + 1$, imply space group $P2_12_12_1$. Scarcity of sample precluded a density measurement. The calculated density for $Z = 4$ (four molecules per unit cell) is 1.086 g cm^{-3}.

Intensity Measurement. The intensity data were collected on a General Electric XRD-5 manual diffractometer operated in the stationary crystal–stationary counter mode. Cu $K\alpha_1$ radiation was used with a 10-sec count for each reflection. A 0.0004 in. nickel foil was used as a filter, positioned in the shutter in front of the detector aperture. Background was collected for 10 sec at the same