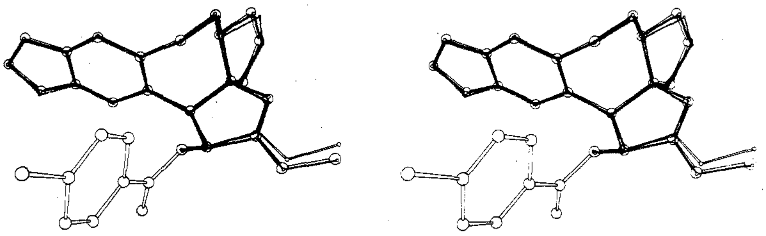

Figure 2. A stereoview comparing **1a**, **1b** (smallest atoms and bonds), and **3** (largest atoms and bonds) after least-squares fitting of the B rings.[5]

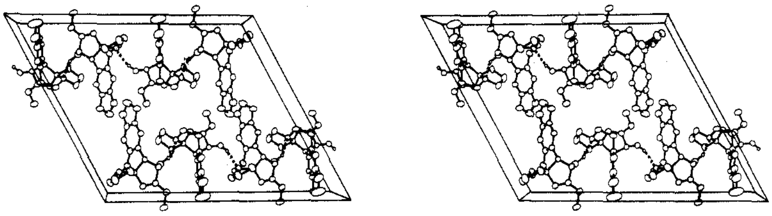

Figure 3. Stereoscopic view of a unit cell, *b* axis projection, with the *a* axis horizontal, the *c* axis approximately vertical, and dashed lines representing hydrogen bonds.

Experimental Section

Collection and Reduction of the Data. Oscillation and Weissenberg photographs of a 0.3 × 0.3 × 0.5 mm needle of 1 grown from ether indicated space group $C2$. The cell parameters were found by least-squares fitting of the settings for four angles of eight reflections on a Picker-FACS-I diffractometer (Cu Kα, λ = 1.54178 Å, graphite monochromator) to be a = 22.834 (5), b = 8.158 (3), c = 19.534 (4) Å, β = 117.7 (1)°, ρ_c = 1.298 g/ml (ρ_o = 1.291 g/ml), and Z = 8. Intensity data were collected using a scintillation counter with pulse-height analyzer, θ–2θ scan technique, 2°/min scan rate, 10-sec background counts, attenuators when the count rate exceeded 10^4 counts/sec, and 2° scan range with a dispersion factor allowing for α_1-α_2 splitting at large 2θ values. Of 2910 independent reflections measured, 2690 > $3\sigma(I)$ were considered observed. Three standard reflections were monitored every 50 measurements to check crystal alignment and the stability; no decrease in the intensity of standards was observed. Lorentz and polarization corrections were applied to the data, but no correction was made for absorption.

Solution and Refinement. The structure was solved by the vector search method using the coordinates of the cephalotaxine part of cephalotaxine *p*-bromobenzoate;[2] two minima were obtained, corresponding to the two molecules in the asymmetric unit. The initial calculations of structure factors gave an R value of 0.252. Two cycles of isotropic least-squares refinement of nonhydrogen atoms reduced R to 0.122 and two more cycles of anisotropic least-squares refinement of nonhydrogen atoms brought R to 0.077. A difference map at this stage revealed all the hydrogen atoms. One more cycle of least-squares refinement using anisotropic temperature factors for nonhydrogen atoms and isotropic temperature factors (of nonhydrogen atoms to which they were attached) for hydrogen atoms reduced R to 0.052. The refinement was terminated at this stage with the ratios of shifts in parameters to estimated standard deviations all less than 0.3. Refinement was based on F_o, the quantity minimized being $\Sigma\omega(F_o - F_c)^2$. Unit weights were used throughout the refinement. The scattering factors used were those of Hanson et al.[3] No correction was applied for extinction.

Results and Discussion

Table I gives the observed fractional coordinates in **1a** and **1b**, and Figure 1 shows ORTEP[4] drawings of both molecules. Table II gives bond lengths and Table III bond angles. In Figure 2, the conformations of cephalotaxine molecules **1a** and **1b** and cephalotaxine *p*-bromobenzoate (**3**)[2] are compared after least-squares fitting of the aromatic ring carbons.[5] *The extreme similarity of the conformations of the cephalotaxine portion of these three molecules provides strong support for the view that the antileukemic esters of cephalotaxine, e.g.,* **2**, *share this conformation.*[2] It should be noted that Dreiding models permit considerable flexibility for the seven-membered ring, and from these models, it is not obvious that the observed conformation should be preferred.

Figure 3 shows the molecular packing, governed by hydrogen bonds between the alcohol proton in **1a** and the nitrogen in **1b** (2.92 Å between O4 and N) and the alcohol proton in **1b** and the nitrogen in **1a** (2.94 Å between O4 and N); these bonds form chains of molecules parallel to the diagonals of the *ab* face. Other short intermolecular distances between nonhydrogen atoms are O3–O2 (3.12 Å), O3–C3 (3.25 Å), O4–C16 (3.29 Å), and O3–C2 (3.21 Å).

Acknowledgments. We thank the Public Health Service (CA-10944) for financial aid and the University of Arizona Computer Center for computer time.

Registry No.—1, 24316-19-6.

Supplementary Material Available. Tables of temperature factors and torsion angles (4 pages). Ordering information is given on any current masthead page.

References and Notes

(1) R. G. Powell, D. Weisleder, and C. R. Smith, Jr., *J. Pharm Sci.*, **61**, 1227 (1972), and references cited therein.

(2) S. K. Arora, R. B. Bates, R. A. Grady, and R. G. Powell, *J. Org. Chem.*, **39**, 1269 (1974); an x-ray study has also been carried out on racemic cephalotaxine methiodide [D. J. Abraham, R. D. Rosenstein, and E. L. McGandy, *Tetrahedron Lett.*, 4085 (1969)].

(3) H. P. Hanson, F. Herman, J. D. Lea, and S. Skillman, *Acta Crystallogr., Sect. B.*, **17**, 1040 (1964).

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

(5) Obtained with the aid of the program BMFIT: S. C. Nyburg, *Acta Crystallogr., Sect. B*, **30**, 251 (1974).

Crystal Structure of 1-(*o*-Chlorophenyl)-1-(*p*-chlorophenyl)-2,2-dichloroethane

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1,1-Dichloro-2-(*o*-chlorophenyl)-2-(*p*-chlorophenyl)ethane (I, *o,p'*-DDD), strikingly close in structure to the insecticides *o,p'*- (II) and *p,p'*-DDT (III), is used in the treatment of tumors of the adrenal cortex.[1] However, the mech-

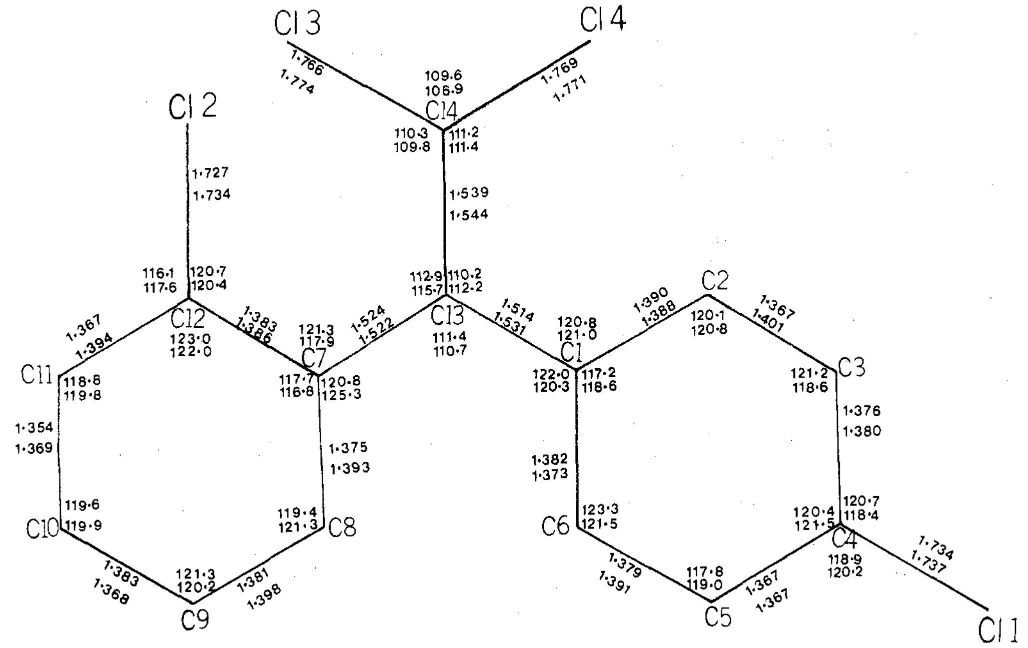


Figure 1. Bond distances (Å) and angles (°) in *o,p*′-DDD (I, above) and *o,p*′-DDT (II, below).[2]

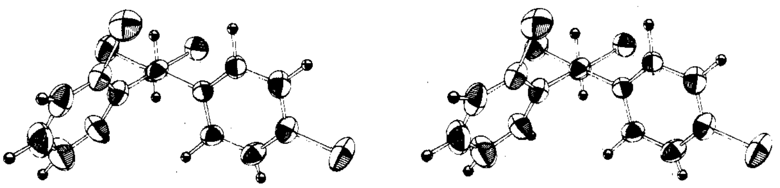
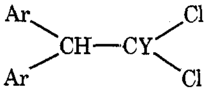


Figure 2. Stereoscopic view of an *o,p*′-DDD (I) molecule. Hydrogen atoms are depicted as spheres, and other atoms as 50% probability ellipsoids.

anism of its action and the reason why it acts so differently from the structurally related insecticides remain unknown. In the hope that a knowledge of the preferred conformation of *o,p*′-DDD (I) will aid in answering the above questions, an x-ray study was undertaken on the drug itself; similar studies had been carried out earlier on the insecticides II and III.[2]



	Ar	Ar′	Y
I	o-ClC_6H_4	p-ClC_6H_4	H
II	o-ClC_6H_4	p-ClC_6H_4	Cl
III	p-ClC_6H_4	p-ClC_6H_4	Cl

Experimental Section

Colorless crystals of *o,p*′-DDD (I, $C_{14}H_{10}Cl_4$) were grown from ethanol–water. A needle 0.2 × 0.2 × 0.3 mm was mounted with the *a* axis parallel to the goniostat ϕ axis. The space group was determined by film methods to be $P2_1/c$. The cell parameters were determined by least-squares fitting of the settings for the four angles of seven reflections on a Picker FACS-I diffractometer (Cu Kα, λ = 1.54178 Å, graphite monochromator) to be a = 6.136 (3), b = 9.712 (5), c = 23.603 (9) Å, β = 93.35 (3)°, and Z = 4. The crystal density was measured by flotation as 1.49 g/ml, agreeing well with a calculated density of 1.50 g/ml. Intensity data were collected using a scintillation counter with pulse-height analyzer, θ–2θ scan, 2°/min scan rate, 10-sec background counts, attenuators when the scan rate exceeded 10^4 counts/sec, and 2° scan range with a dispersion factor allowing for α_1–α_2 splitting at large 2θ values. Of 2474 independent reflections measured, 1881 > $3\sigma(I)$ were considered observed. Three standard reflections were monitored every 50 measurements; no decrease in the intensity of standards was observed. Lorentz and polarization corrections were applied, but no correction was made for absorption (μ = 70.9 cm^{-1}).

Phases for reflections with normalized structure factor E > 1.5 were generated using the direct method program MULTAN.[3] All nonhydrogen atoms were located on an E map using calculated phases as coefficients. Full matrix least-squares refinement in which positional and isotropic thermal parameters were varied reduced R to 0.166. Two more cycles of least-squares refinement using anisotropic thermal parameters reduced R to 0.105. A difference map at this stage revealed all the hydrogen atoms. Two more cycles of least-squares refinement using anisotropic temperature factors for nonhydrogen atoms and isotropic temperature factors (of nonhydrogen atoms to which they were attached) for hydrogen atoms brought R to 0.069. A difference map failed to show any unaccounted electron density, and refinement was terminated at this stage with the ratios of shifts in parameters to estimated standard deviations all less than 0.5. Refinements were based on F_0, the quantity minimized being $\Sigma w(F_0 - F_c)^2$. The weighting scheme used was based on counter statistics as defined by Corfield et al.,[4] the value of p being 0.04. The scattering factors used were those of Hanson et al.[5] (anomalous scattering factors for Cl). No correction was applied for extinction.

Results and Discussion

Table I shows the observed atomic coordinates. Figure 1 gives the bonds lengths and angles in I and II;[2] average standard deviations in I are 0.004, 0.006, and 0.04 Å for C–Cl, C–C, and C–H bonds, respectively, and 0.2, 0.3, and 1.2° for Cl–C–C, C–C–C, and H–C–C angles, respectively.

Figure 2 gives the conformation and thermal ellipsoids[6] of I, and Figure 3 compares the conformations of the antitumor agent I and the insecticide II. These conformations can be largely described in terms of the torsion angles about the C13–C14, C13–C1, and C13–C7 bonds. About C13–C14, I possesses almost perfect staggering with the hydrogens anti; in II and III, the deviation from perfect staggering in somewhat greater.[2] In all three structures, one aromatic ring is within a few degrees (2, 4, and 4° for I, II, and III, respectively) of the "butterfly" angle;[2] in the first two of these substances, it is the *o*-chlorophenyl ring, and the chlorine on this ring takes the position *away* from the other chlorines. The largest conformational difference

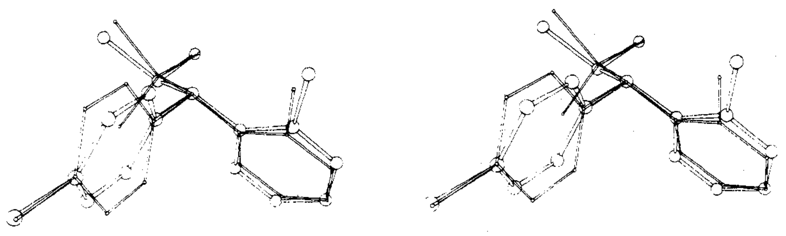


Figure 3. Stereoscopic view comparing I (larger atoms) and II,[2] with least-squares fitting of C1, C4, C7, C10, C13, and C11.[7]

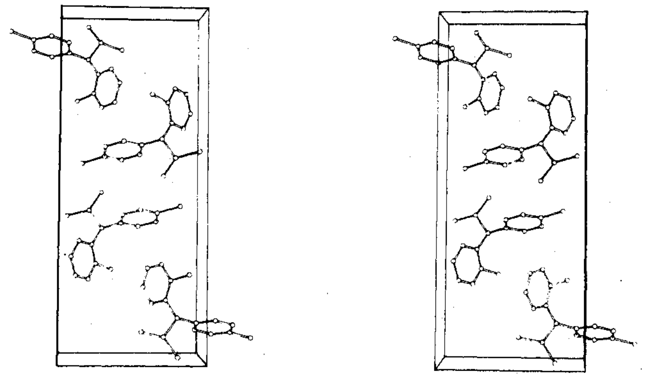


Figure 4. Stereoscopic view of a unit cell, *a* axis projection, *b* axis horizontal, *c* axis vertical.

Table I
Fractional Coordinates and Estimated Standard Deviations

Atom	*x*/*a*	*y*/*b*	*z*/*c*
Cl1	0.5464 (3)	0.1565 (2)	0.4397 (1)
Cl2	−0.0152 (3)	0.6226 (2)	0.2480 (1)
Cl3	−0.0429 (2)	0.6983 (2)	0.4756 (1)
Cl4	−0.0342 (3)	0.9429 (2)	0.4061 (1)
C1	0.2296 (8)	0.5599 (5)	0.3880 (2)
C2	0.4400 (8)	0.5569 (5)	0.4133 (2)
C3	0.5343 (9)	0.4340 (6)	0.4288 (2)
C4	0.4250 (9)	0.3116 (5)	0.4196 (2)
C5	0.2212 (9)	0.3101 (5)	0.3929 (2)
C6	0.1268 (8)	0.4348 (5)	0.3781 (2)
C7	0.2399 (8)	0.7666 (5)	0.3244 (2)
C8	0.4080 (10)	0.8569 (6)	0.3373 (2)
C9	0.5222 (12)	0.9122 (7)	0.2940 (3)
C10	0.4678 (12)	0.8810 (7)	0.2378 (3)
C11	0.3038 (11)	0.7910 (6)	0.2248 (2)
C12	0.1911 (9)	0.7367 (5)	0.2678 (2)
C13	0.1217 (8)	0.6952 (5)	0.3713 (2)
C14	0.1007 (8)	0.7865 (5)	0.4240 (2)
HC2	0.511 (6)	0.645 (4)	0.412 (2)
HC3	0.665 (6)	0.434 (4)	0.452 (2)
HC5	0.145 (6)	0.235 (4)	0.388 (2)
HC6	−0.047 (6)	0.442 (4)	0.366 (2)
HC8	0.438 (6)	0.899 (4)	0.383 (2)
HC9	0.604 (6)	1.005 (4)	0.304 (2)
HC10	0.548 (6)	0.927 (4)	0.205 (2)
HC11	0.286 (6)	0.769 (4)	0.183 (2)
HC13	−0.041 (6)	0.679 (4)	0.358 (2)
HC14	0.229 (6)	0.811 (4)	0.439 (2)

comes in the rotation of the remaining *p*-chlorophenyl ring of each compound: the deviations from the "butterfly" angle are 24, 47, and 33° for I, II, and III, respectively. In I, the 24° rotation decreases repulsion between (a) the C14 hydrogen and the nearby ortho hydrogen on the *p*-chlorophenyl ring, and (b) the chlorine on the *o*-chlorophenyl ring and the other ortho hydrogen on the *p*-chlorophenyl ring. In II and III, a chlorine replaces the hydrogen on C14, and further rotation is required to minimize the energy. Thus, the conformation of the antitumor agent I in this crystal differs somewhat from those of the crystalline insecticides II and III.[2] The slight differences observed may be responsible for the difference in activity, but unfortunately neither activity is as yet well understood.[2,8]

Figure 4 shows the packing diagram for I. The only intermolecular distances less than 3.5 Å are 3.353 (Cl3–Cl5) and 3.434 Å (Cl1–C14).

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Registry No.—*o,p'*-DDD, 53-19-0.

Supplementary Material Available. Tables of temperature factors, bond distances and angles involving hydrogens, and torsion angles (3 pages). Ordering information is given on any current masthead page.

References and Notes

(1) F. E. Knock, "Anticancer Agents", Charles C. Thomas, Springfield, Ill., 1967, pp 205–206.

(2) T. P. DeLacy and C. H. L. Kennard, *J. Chem. Soc., Perkin Trans. 2,* 2148 (1972).

(3) G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. B,* **26,** 274 (1970).

(4) P. W. R. Corfield, R. J. Deodens, and J. A. Ibers, *Inorg. Chem.,* **6,** 197 (1967).

(5) H. P. Hanson, F. Herman, J. D. Lea, and S. Skillman, *Acta Crystallogr., Sect. B,* **17,** 1040 (1964).

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

(7) Calculated with the aid of the program BMFT: S. C. Nyburg, *Acta Crystallogr., Sect. B,* **30,** 251 (1974).

(8) For conflicting views on the reason for the insecticidal activity of II and III, see E. F. Rogers, H. D. Brown, I. M. Rasmussen, and R. E. Neal, *J. Am. Chem. Soc.,* **75,** 2991 (1953); R. Reimschneider and H. D. Otto, *Z. Naturforsch.,* **96,** 95 (1954).

An Improved Synthesis of Dichloromethylenetriphenylphosphorane

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The phosphorus ylide, dichloromethylenetriphenylphosphorane (II), has been shown to be of good synthetic utility in the Wittig method of converting aldehydes,[1-3] ketones,[1,2] keto esters,[3] and acyl cyanides[4,5] to the corresponding 1,1-dichloroethylene derivatives.

Methods previously reported for the preparation of II include (a) the reaction of potassium *tert*-butoxide with chloroform in the presence of triphenylphosphine,[1] (b) the reaction of triphenylphosphine with $PhHgCCl_2X$, where X = Cl or Br,[6] and (c) the reaction of triphenylphosphine with carbon tetrachloride.[2] The last procedure offers several advantages, among which are simplicity and cost of the starting materials. It does have the disadvantage of being rather slow, i.e., several days at 0°. This time may be shortened by heating the reaction mixture to reflux; however, by-prod-