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# The Chemistry of the Euphorbiaceae. A New Diterpene from *Croton californicus*

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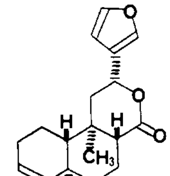
**Abstract:** The major diterpenic component of the medicinal plant *Croton californicus* has been isolated and the structure determined by a combination of spectral and x-ray crystallographic studies. Methyl barbascoate (**1**) crystallizes in the space group $P2_1$ (No. 4, $C_2^2$) with two molecules in the unit cell. Cell constants at −164 °C are $a$ = 9.224 (6), $b$ = 10.049 (7), $c$ = 10.390 (7) Å, and $\beta$ = 112.44 (4)°. The structure was refined to $R(F)$ = 0.048 and $R_w(F)$ = 0.058, with the goodness of fit 1.05. The absolute stereochemistry was determined by circular dicroism comparison with (−)-methyl hardwickiate. Methyl barbascoate is a member of the growing class of trans clerodanes.

The spurge family (Euphorbiaceae) includes some 8000 species which occur in tropical and temperate regions all over the world. The largest genus of the spurge family is that of *Croton*. Many of them are odorous and contain a milky juice which is more or less poisonous.[2] The commercially available Oil of Croton derives from an Asiatic species *Croton tiglium L.* and is the source of phorbol esters, whose cocarcinogenic properties have been the object of numerous research efforts.[3,4]

As a part of a general research program on the chemistry of terpenoids from the Euphorbiaceae, we have investigated an American species, *Croton californicus*.[5] This pale olive-green perennial herb is common in sandy areas of the Mohave Desert. Indians made a hot poultice of its powdered leaves as a pain reliever for rheumatism.

The constituents of the ethanol extract of *C. californicus* can be directly compared with commercial Croton Oil by high resolution gas chromatography[6] (Figure 1). The presence of a major diterpenic component in *C. californicus* which is absent in *C. tiglium* is clearly evident. The isolation and structure elucidation of this component is now described.



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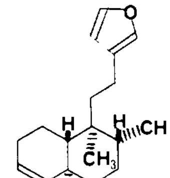
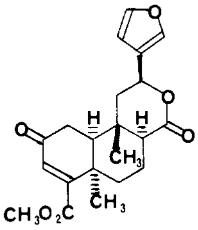


2a R,H
b R,CH3



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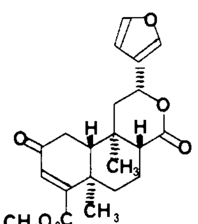

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The ethanol extract of *C. californicus* was chromatographed on silica gel yielding the substance in question (−)-methyl barbascoate[7] (**1**) as crystals, mp 152-153 °C. This compound analyzed for $C_{21}H_{26}O_5$ and was assigned the structure depicted in **1** (without stereochemistry) on the basis of the following spectral data. The infrared spectrum of **1** has carbonyl absorptions at 1715 and 1745 cm$^{-1}$ due to unsaturated ester and $\delta$-lactone. Bands at 1500 and 875 cm$^{-1}$ indicate a $\beta$-substituted furan ring which was confirmed by an ultraviolet maximum at 212 nm and NMR signals at $\delta$ 6.4 (1 H, m) and 7.4 (2 H, m). The NMR spectrum, in addition, showed the presence of two angular methyl groups at $\delta$ 1.02 and 1.27 and a methyl ester at $\delta$ 3.7. The vinyl proton appeared as a triplet ($J$ = 1.5

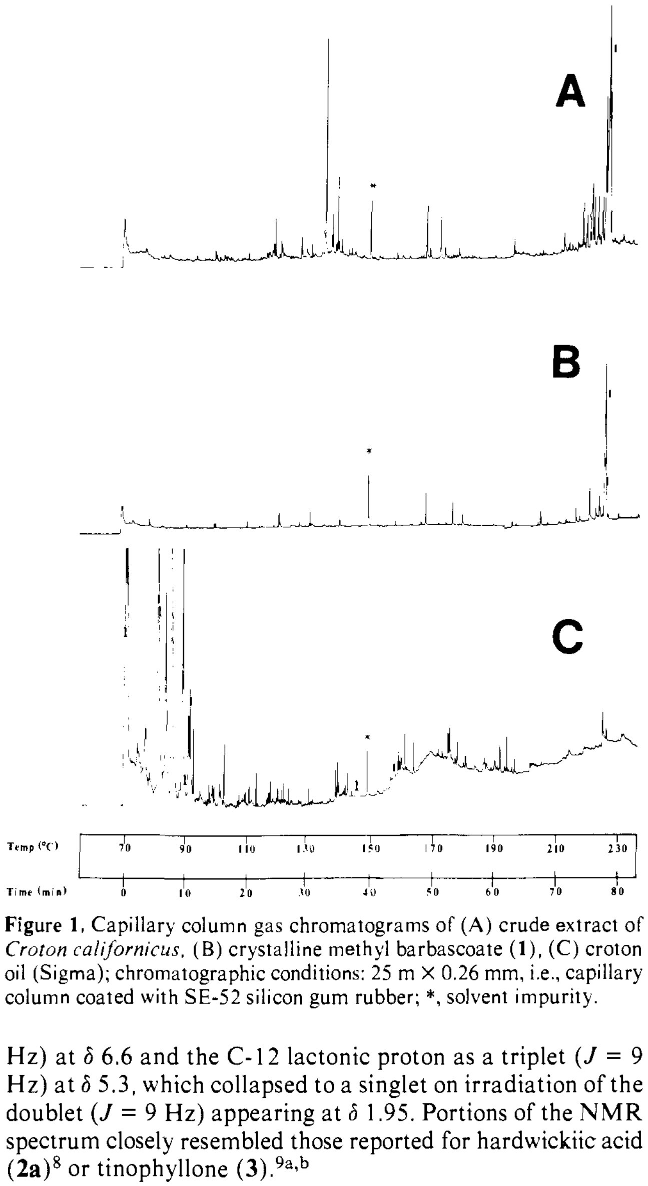


Figure 1. Capillary column gas chromatograms of (A) crude extract of *Croton californicus*, (B) crystalline methyl barbascoate (**1**), (C) croton oil (Sigma); chromatographic conditions: 25 m × 0.26 mm, i.e., capillary column coated with SE-52 silicon gum rubber; *, solvent impurity.

Hz) at $\delta$ 6.6 and the C-12 lactonic proton as a triplet ($J$ = 9 Hz) at $\delta$ 5.3, which collapsed to a singlet on irradiation of the doublet ($J$ = 9 Hz) appearing at $\delta$ 1.95. Portions of the NMR spectrum closely resembled those reported for hardwickiic acid (**2a**)[8] or tinophyllone (**3**).[9a,b]

The conversion of **1** to the closely related **3** was thus attempted. Oxidation of **1** with chromium trioxide in pyridine[10] led to the production of enone **4**, mp 193-195 °C. Direct comparison of **4** with an authentic sample of tinophyllone (**3**)[11] clearly showed they were not identical. On TLC (silica gel), for example, **3** had $R_f$ (ether) = 0.38 and **4** had $R_f$ (ether) = 0.31. The spectral data, however, were very similar for the two compounds.

Since tinophyllone (**3**) is a cis clerodane and both cis and trans series are known,[12] we surmised that (−)-methyl barbascoate (**1**) was a trans clerodane and thus compound **4** was a C-5 epimer of tinophyllone (**3**). This structural assignment was confirmed by a single crystal x-ray diffraction experiment, as depicted in Figure 2. The absolute configuration of **1** was determined to be that of the enantio series as shown in structure **1** by comparison of the circular dichroism spectra of **1** and authentic (−)-methyl hardwickiate (**2b**).[11]

## Experimental Section

Infra-red spectra were recorded on a Perkin-Elmer 237B spectrometer. Ultraviolet spectra were recorded on a Cary 14. Circular dichroism (CD) spectra were recorded with a Durrum-Jasco ORD/UV/CD-5 incorporating the SS-10 modification. CD data were represented as $\lambda_{max}$ ($\Delta\epsilon$) where $\Delta\epsilon = [\theta]/3300$. NMR spectra were taken on a Varian T-60 in $CDCl_3$ solution with internal $Me_4Si$ standard and 500 Hz sweep. Mass spectra were obtained on Varian MAT CH-7 and AEI MS-9 mass spectrometers.

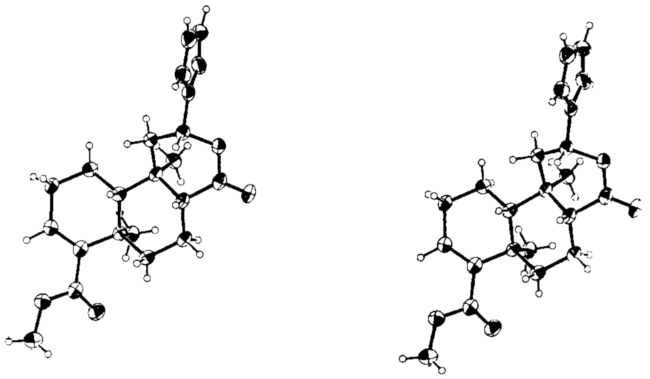


Figure 2. Stereodrawing of methyl barbascoate. Thermal ellipsoids are drawn at 50% probability with the exception of hydrogens which have been given an artificial $B$ of 0.5 for artistic purposes.

Microanalyses were obtained from Spang Microanalytical Laboratory, Ann Arbor, Mich. Melting points are uncorrected. Optical rotations were determined on a Rudolph Research automatic polarimeter. Thin-layer chromatography employed Brinkman precoated silica gel F-254 plates.

**Extraction of *Croton californicus*.** Leaves and terminal branches of *C. californicus* were collected in Los Angeles County (Antelope Valley), 3 miles east of 90th St. on Avenue N in Oct 1973. A sample of plant material has been deposited in the Indiana University Herbarium, Bloomington, Ind.

Leaves and small stems (210 g) of *C. californicus* were extracted with ethanol in a modified Soxhlet extractor for 3 days. The ethanol was evaporated on a rotary evaporator and the residue taken up in ether and filtered. The dark ether solution was extracted twice with 1 N NaOH and twice with water. Drying over $MgSO_4$ and evaporation gave 7.2 g of dark oil (3.4%).

**Isolation of Compound 1.** The dark *C. californicus* extract (7.2 g) was chromatographed on 200 g of silica gel (gradient elution with ether-petroleum ether), taking 20-ml fractions. From fractions no. 26-28 was isolated 182 mg (0.09%) of compound **1**. Recrystallization from ether gave the analytical sample as needles of mp 152-153 °C: TLC (60% ether-petroleum ether) $R_f$ 0.28; $[\alpha]_D$ −70°; uv (MeOH) $\lambda_{max}$ ($\epsilon$) 286 nm (500), 212 (16000); CD (MeOH) 286 nm (−0.38), 230 (−6.6) sh, 210 (−8.7); ir 1745, 1715, 1500, 875 cm$^{-1}$; NMR $\delta$ 1.02 (3 H, s), 1.27 (3 H, s), 1.95 (2 H, d, $J$ = 9 Hz), 3.7 (3 H, s), 5.3 (1 H, t, $J$ = 9 Hz), 6.4 (1 H, m), 6.6 (1 H, t, $J$ = 1.5 Hz), 7.4 (2 H, m); mass spectrum $m/e$ (% base) 358 (19), 205 (25), 159 (21), 133 (20), 121 (28), 107 (30), 105 (40), 96 (24), 95 (41), 94 (33), 93 (25), 91 (49), 81 (64), 79 (37), 77 (24), 69 (22), 67 (20), 55 (50), 45 (35), 44 (100). Anal. Calcd for $C_{21}H_{26}O_5$: mol wt, 358.1782; C, 70.37; H, 7.31. Found: mol wt, 358.1773; C, 70.64; H, 7.38.

**Preparation of Compound 4.** To a dry flask fitted with magnetic stirrer and argon inlet was added 300 mg of $CrO_3$ (3 mmol, dryed over $P_2O_5$) and 15 ml of dry $CH_2Cl_2$. To the rapidly stirring suspension was added 0.48 ml (6 mmol) of dry pyridine, yielding a deep burgundy solution. After 20 min, 75 mg (0.21 mmol) of compound **1** in $CH_2Cl_2$ was added, and the mixture was stirred at room temperature overnight. The reaction mixture was then filtered through 12 g of activity III neutral $Al_2O_3$ and the flask and $Al_2O_3$ were washed with 150 ml of $CH_2Cl_2$. The $CH_2Cl_2$ was evaporated and the residue purged twice with benzene to remove traces of pyridine. NMR and TLC indicated that a new compound was present at lower $R_f$. TLC (ether) showed starting **1** at $R_f$ 0.53 (61% by NMR) and a new compound **4** at $R_f$ 0.31 (39% by NMR). Preparative thin-layer chromatography gave an oil which deposited 16.2 mg (22%) of compound **2**; mp 193-195 °C; $[\alpha]_D$ −14°; ir 1745, 1725, 1675, 1500, 875 cm$^{-1}$; NMR $\delta$ 1.06 (3 H, s), 1.43 (3 H, s), 3.8 (3 H, s), 5.33 (1 H, t, $J$ = 9 Hz), 6.23 (1 H, s), 6.37 (1 H, m), 7.4 (2 H, m); mass spectrum $m/e$ (% base) 372 (17), 248 (8), 234 (7), 219 (11), 216 (3), 206 (5), 205 (7), 202 (2), 121 (19), 119 (11), 105 (18), 95 (32), 94 (100). Anal. Calcd for $C_{21}H_{24}O_6$: mol wt, 372.1574. Found: mol wt, 372.1564.

**Comparison of Compound 4 and Tinophyllone 3.** A small sample of authentic tinophyllone (**3**) was graciously provided by Professor Aguilar-Santos. This material showed the following properties: mp 170-173 °C (reported 175 °C); ir 1745, 1725, 1670, 1500, 875 cm$^{-1}$; NMR $\delta$ 0.9 (3 H, s), 1.54 (3 H, s), 2.0 (2 H, d, $J$ = 9 Hz), 3.9 (3 H, s), 5.4 (1 H, t, $J$ = 9 Hz) 6.32 (1 H, s), 6.46 (1 H, m), 7.5 (2 H, m); mass spectrum $m/e$ (% base) 372 (31), 248 (13), 234 (5), 219 (5), 216 (13), 206 (2), 205 (2), 202 (14), 121 (23), 119 (11), 105 (15), 95 (29), 94 (100). Compound **4** and **3** separated cleanly on TLC (ether) with $R_f$ (**4**) 0.31 and $R_f$ (**3**) 0.38. These materials also were shown to be not identical by high-pressure liquid chromatography (Ether/EM LiChrosorb SI 60) and VPC (5 ft × ⅛ in. OV101 at 250 °C).

**Circular Dichroism of 2b.** A small sample of (−)-hardwickiic acid methyl ester (**2b**) was kindly supplied by Professor Dev. This material showed the following properties: TLC (10% ether-petroleum ether) $R_f$ 0.5, $[\alpha]_D$ −115° (reported $[\alpha]_D$ −113.5°); CD (MeOH) 240 nm (−4.4), 210-215 (−0.8) sh; ir 1718 cm$^{-1}$; NMR $\delta$ 0.77 (3 H, s), 0.84 (3 H, d, $J$ = 6 Hz), 1.27 (3 H, s), 3.66 (3 H, s), 6.2 (1 H, s), 6.54 (1 H, m), 7.13 (1 H, s), 7.72 (1 H, s); mass spectrum $m/e$ (% base) 330 (11), 283 (13), 235 (42), 203 (58), 151 (26), 139 (100), 105 (28), 96 (59).

**Collection and Reduction of the X-Ray Data.** Crystals of **1**, obtained by evaporation from ether solution, occurred as needles elongated along $b$. A crystal of approximately 0.5 mm length was cut from a well-formed needle of approximately 0.3 × 0.3 mm cross section.

Precession photographs exhibit $2/m$ Laue symmetry, with systematic extinctions of $k$ odd for $0k0$, indicating the space group $P2_1$ (No. 4, $C_2{}^2$). The crystal was mounted on a glass fiber with silicone grease and cooled on the diffractometer to −164 ± 5 °C using a standard gas-flow cooling system,[13] and no evidence of a phase transition was apparent. Cell dimensions of $a$ = 9.224 (6), $b$ = 10.049 (7), $c$ = 10.390 (7) Å, and $\beta$ = 112.33 (4)° were obtained from a least-squares fit of angular data from ten reflections centered in $\pm 2\theta$ at −164 °C. The calculated density is 1.34 g cm$^{-3}$ for $Z$ = 2. $\omega$ scans of three nearly orthogonal reflections gave half-peak widths of 0.27° with no apparent abnormalities. Data were collected on a Picker FACS-1-diffractometer equipped with a highly oriented graphite monochromator (002 reflection), 2.3° takeoff angle, Mo K$\alpha$ radiation ($\lambda$ 0.71069), and a 4 × 4 mm receiving aperture. The source-monochromator-sample distance was 27 cm, and the sample-receiving aperture distance was 26 cm. Data were collected using fixed counting techniques for the region $1 > 2\theta < 50°$, and for $\pm h + k \pm l$. The triply redundant raw data were reduced to intensities ($I$) and $\sigma(I)$[14] and corrected for Lorentz and polarization terms. The final unique data consisted of 1671 reflections, of which 1650 had nonzero intensities.

The intensities of three reflections chosen as standards were monitored after every 200 measurements and held constant to within ±2% for the duration of data collection. Based on prior experience, an "ignorance factor" of 0.1 was used in the data reduction. Sixty-five reflections had standard deviations greater than the average $\sigma(F)$, the maximum being $4.5\sigma(I)$. These data were assigned $\sigma$ corresponding to the calculated standard deviation. No absorption correction was performed ($\mu$, Mo K$\alpha$ 1.02 cm$^{-1}$).

**Solution and Refinement of the X-Ray Structure.**[15] Normalized structure factors were calculated utilizing a K-curve, and statistics confirmed a noncentric space group. Initial attempts using MULTAN with two ambiguities (16 solutions) failed to find a suitable solution. When three ambiguities were introduced (64 solutions), the $E$ map based on the solution with the second lowest "residual" and third highest "figure of merit" located 12 peaks which could be assigned. Three successive Fourier synthesis were used to successfully locate all remaining nonhydrogen atoms.

Isotropic refinement rapidly converged to $R(F)$ = 0.183 and $R_w(F)$ = 0.142. Attempts to assign the furan oxygen atom at this point failed, since the thermal parameter of the atomic position assigned oxygen scattering terms was invariably larger than the corresponding carbon thermal parameter by a factor of 2. This, coupled with the obtained distances and angles, led to the conclusion that the furan ring is disordered. Anisotropic refinement was then initiated and the two para positions [CO(1) and CO(2), Figure 3a] of the furan ring were given 0.5 occupancies in both carbon and oxygen. After three cycles a difference Fourier synthesis was used to locate 18 of the hydrogen atoms, and the positions of the remaining nine were calculated assuming C-H = 0.95 Å, and either tetrahedral or planar angles. Four cycles of anisotropic refinement with these hydrogens fixed ($B_{iso}$ = 3.5) were continued in this manner, with a difference Fourier synthesis between each cycle to relocate the hydrogens. At this stage all hydrogens were apparent with the exception of those associated with the furan ring and H(021). The latter were placed in calculated positions and three final cycles completed allowing the occupancy of the furan disorder to vary. Hydrogens were also placed on the disordered furan atoms with an occupancy of 0.5.

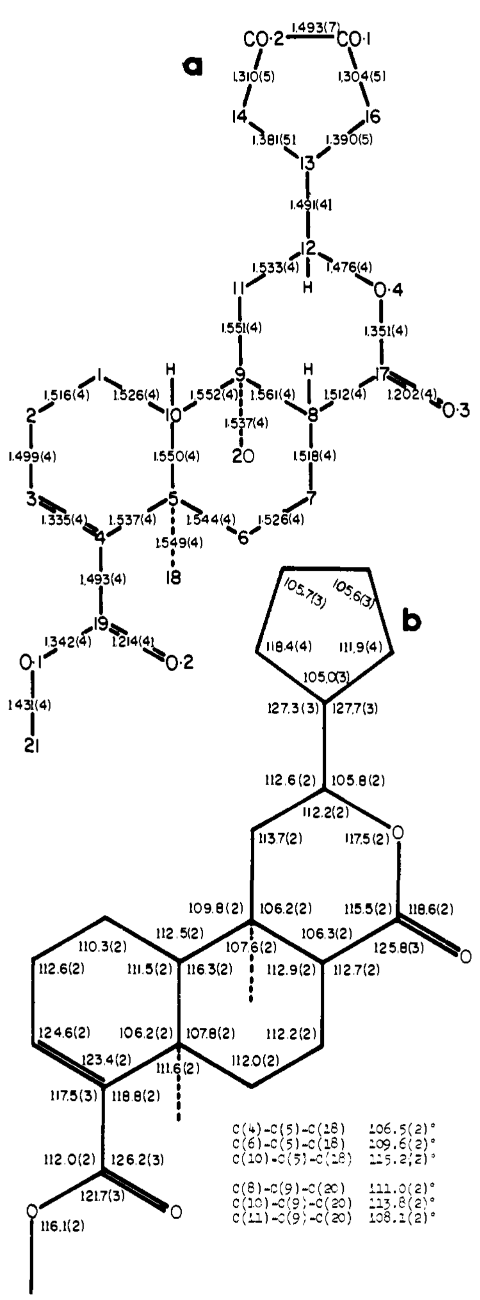


**Figure 3.** (a) Numbering scheme used and distances; (b) angles.

Final residuals are $R(F)$ = 0.048 and $R_w(F)$ = 0.058, and the largest $\Delta/\sigma$ for the last cycle was 0.015. The goodness of fit of the last cycle was 1.05, indicating the errors had been correctly estimated. In all, 238 parameters were refined with 1650 observations for a ratio of 7:1. The final occupancies (based on oxygen) were 0.51 (3) and 0.49 (3) for CO(1) and CO(2), respectively. A tabulation of the calculated structure factors is given in Table I[16] and the atomic coordinates and isotropic thermal parameters are given in Table II. Anisotropic thermal parameters are given in Table III.[16]

## Discussion

Structural parameters are shown in Figure 3 for nonhydrogen atoms, and complete distances and angles, including hydrogens, are given in Tables IV and V.[16] Torsion angles are listed in Table VI.[16] The average errors based on the variance-convariance matrix are 0.004 Å for distances and 0.02° for angles. Methyl barbascoate (**1**) possesses an A/B trans fusion with ring B in a chair and ring C in a boat conformation. The furan ring lies in an equatorial position on ring C and is nearly perpendicular to the molecular skeleton. The furan

Table II. Fractional Coordinates and Isotropic Thermal Parameters for $C_{21}H_{26}O_5$

| | $10^4X/a$ | $10^4Y/b$ | $10^4Z/c$ | $10B^a$ |
|---|---|---|---|---|
| C(1) | 3815 (4)[b] | 7641 (11) | 6102 (3) | 26 |
| C(2) | 3497 (3) | 6890 (11) | 7232 (3) | 26 |
| C(3) | 1995 (4) | 7309 (12) | 7357 (3) | 25 |
| C(4) | 923 (4) | 8095 (11) | 6452 (3) | 24 |
| C(5) | 1128 (3) | 8735 (12) | 5188 (3) | 22 |
| C(6) | −428 (4) | 8755 (11) | 3904 (3) | 25 |
| C(7) | −190 (4) | 9178 (11) | 2588 (3) | 25 |
| C(8) | 963 (3) | 8286 (11) | 2277 (3) | 23 |
| C(9) | 2592 (3) | 8207 (12) | 3507 (3) | 22 |
| C(10) | 2295 (3) | 7839 (11) | 4838 (3) | 23 |
| C(11) | 3504 (3) | 7070 (12) | 3140 (3) | 25 |
| C(12) | 2994 (4) | 6825 (11) | 1572 (3) | 25 |
| C(13) | 4303 (4) | 6359 (12) | 1183 (3) | 28 |
| C(14) | 4472 (5) | 5122 (12) | 677 (4) | 39 |
| C(16) | 5660 (4) | 7048 (12) | 1309 (4) | 37 |
| C(17) | 1280 (3) | 8742 (12) | 1022 (3) | 25 |
| C(18) | 1688 (4) | 10180 (12) | 5616 (3) | 28 |
| C(19) | −469 (4) | 8469 (12) | 6776 (3) | 27 |
| C(20) | 3519 (4) | 9504 (12) | 3637 (3) | 27 |
| C(21) | −1996 (4) | 7890 (11) | 8061 (4) | 33 |
| CO(1) | 6592 (4) | 6333 (13) | 909 (3) | 55 |
| CO(2) | 5791 (5) | 5022 (12) | 485 (4) | 57 |
| O(1) | −789 (3) | 7554 (11) | 7571 (2) | 28 |
| O(2) | −1237 (3) | 9479 (11) | 6411 (3) | 38 |
| O(3) | 700 (3) | 9691 (11) | 309 (2) | 29 |
| O(4) | 2383 (2) | 8042 (11) | 749 (2) | 26 |
| H(011) | 4328 | 8450 | 6429 | 35 |
| H(012) | 4562 | 7163 | 5905 | 35 |
| H(021) | 3440 | 5955 | 7023 | 35 |
| H(022) | 4294 | 6950 | 8135 | 35 |
| H(031) | 1739 | 6911 | 8113 | 35 |
| H(061) | −1038 | 9201 | 4105 | 35 |
| H(062) | −922 | 7962 | 3793 | 35 |
| H(071) | 11 | 10079 | 2592 | 35 |
| H(072) | −1170 | 9138 | 1820 | 35 |
| H(081) | 440 | 7454 | 1993 | 35 |
| H(101) | 1962 | 6977 | 4650 | 35 |
| H(111) | 4572 | 7218 | 3526 | 35 |
| H(112) | 3273 | 6127 | 3533 | 35 |
| H(121) | 2143 | 6157 | 1376 | 35 |
| H(141) | 3711 | 4414 | 485 | 35 |
| H(161) | 5886 | 7922 | 1656 | 35 |
| H(161) | 1030 | 10552 | 6046 | 35 |
| H(182) | 2815 | 10200 | 6264 | 35 |
| H(183) | 1680 | 10721 | 4963 | 35 |
| H(203) | 2853 | 10126 | 3647 | 35 |
| H(201) | 3906 | 9539 | 3122 | 35 |
| H(202) | 4539 | 9549 | 4497 | 35 |
| H(211) | −1763 | 8665 | 8616 | 35 |
| H(212) | −2811 | 8041 | 7441 | 35 |
| H(213) | −1975 | 7159 | 8654 | 35 |
| HO(1) | 7573 | 6577 | 890 | 35 |
| HO(2) | 6157 | 4259 | 141 | 35 |

[a] Isotropic parameters for nonhydrogen atoms are the equivalent of the anisotropic form given in Table III. Hydrogen isotropic thermal parameters were fixed at 3.5. [b] Figures in parenthesis in this and all succeeding tables refer to the estimated error in the last significant figure.

oxygen is disordered between the two para positions [CO(1) and CO(2), Figure 3a]. This disorder is nearly complete as evidenced by equivalent distances and angles and the occupancies determined from the least-squares treatment.

All distances and angles are normal, the principal distortion being in the vicinity of the 1,3-diaxial interaction between the C(18) and C(20) methyl groups. The C(18)-C(5)/C(20)-C(9) vectors are 20.8° out of parallel. Most of this distortion is located in the C(18)-C(5)-C(10) and C(20)-C(9)-C(10) angles, 115.3 and 113.8°, respectively, although some distortion occurs in the ring skeleton. The closest nonbonded, nonadjacent intramolecular contact is between C(18)H(3) and C(20)H(3). The 2.13 Å distance for the latter is somewhat smaller than that normally associated with van der Waals contacts.

The plane of the ester group is rotated 24.9° from the plane of the ethylene group of ring A, the rotation presumably due to intermolecular packing. Hydrogen distances and angles appear normal, the average C-H distance being 0.93 ± 0.07 Å. There are no particularly short intermolecular contacts, as seen in the packing diagram Figure 4. The shortest intermolecular H···H distance is 2.37 Å for C(3)H(1)···C(7)H(1)($-x$, $y - \frac{1}{2}$, $1 - z$), and there are seven other H···H distances less than 2.5 Å. There is also a short 2.26 Å distance between the hydrogen in a calculated position for CO(2) and O(4) at ($1 - x$, $\frac{1}{2} + y$, $-z$). The reliability of this distance is questionable, however, due to the disorder of the furan ring.

The smaller thermal parameters and estimated errors are typical of low-temperature structural studies.

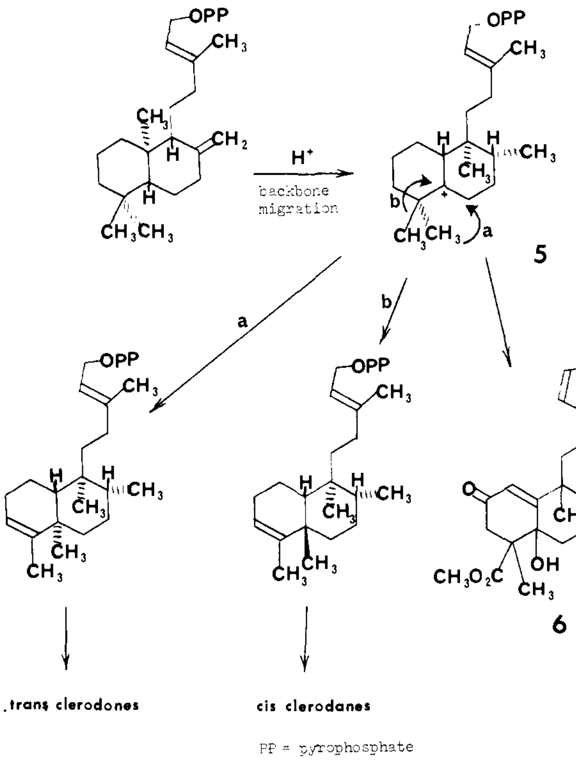
The circular dichroism (CD) spectrum of **1** (Figure 5) is composed of contributions from the $\alpha,\beta$-unsaturated carboxylate ester, the $\delta$-lactone, and the furan chromophores. The CD spectrum of (−)-methyl hardwickiiate (**2b**) (absolute configuration[8] as shown) closely approximates the contribution of the $\alpha,\beta$-unsaturated carboxylate ester in (−)-methyl barbascoate (**1**) and establishes the absolute configuration of **1** to be as represented.

Subtraction of the spectrum of **2b** from **1** leaves a strong negative band at 210 nm (Figure 5) attributed to the $n \rightarrow \pi^*$ $\delta$-lactone and the $\pi \rightarrow \pi^*$ furan electronic transitions. The $\delta$-lactone $n \rightarrow \pi^*$ Cotton effect for **1** having the absolute configuration indicated and the boat conformation is predicted to be negative by Wolf's rule for $\delta$-lactones[17] in agreement with the observed sign of the 210-nm band. The $n \rightarrow \pi^*$ $\delta$-lactone contribution to the 210-nm band must be negative unless the $\pi \rightarrow \pi^*$ furan Cotton effect is larger (more negative) than the observed $\Delta\epsilon$ of −8. Although the chiroptical properties of the furan chromophore do not appear to have received extensive study,[18] a $\Delta\epsilon$ of −8 seems somewhat large for either the furan or the lactone,[17,19] suggesting that both chromophores have negative Cotton effects in the 210–220-nm region. If the negative band at 240 nm is assigned to the $\alpha,\beta$-unsaturated ester $n \rightarrow \pi^*$ transition[20] then the very weak band at 286 nm in the spectrum of **1** should result from a furan electronic transition.[21]

It is noteworthy that (−)-methyl barbascoate (**1**) is a member of the enantio series and thus surprisingly antipodal to tinophyllone (**3**). Both normal and enantio clerodanes have been observed before.[22]

The number of known[12] cleordanes has been steadily increasing. Two distinct series, cis and trans A/B ring fusion, are apparent. These compounds are thought to arise by successive methyl migrations from a labdane precurser (Scheme I).

Scheme I



**trans clerodanes** **cis clerodanes**

PP = pyrophosphate

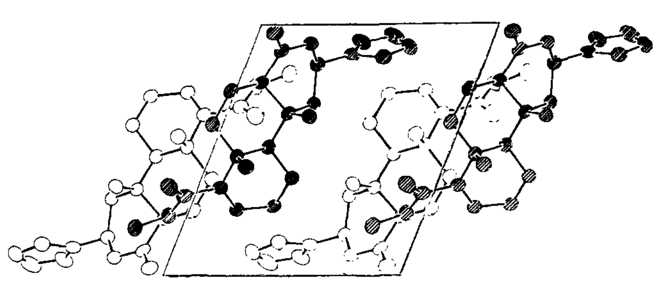


**Figure 4.** Unit cell packing with hydrogen atoms removed for clarity. View is down the *b* axis, and shaded molecules are above unshaded molecules. Coordinates of Table II are for the shaded molecule to the left.

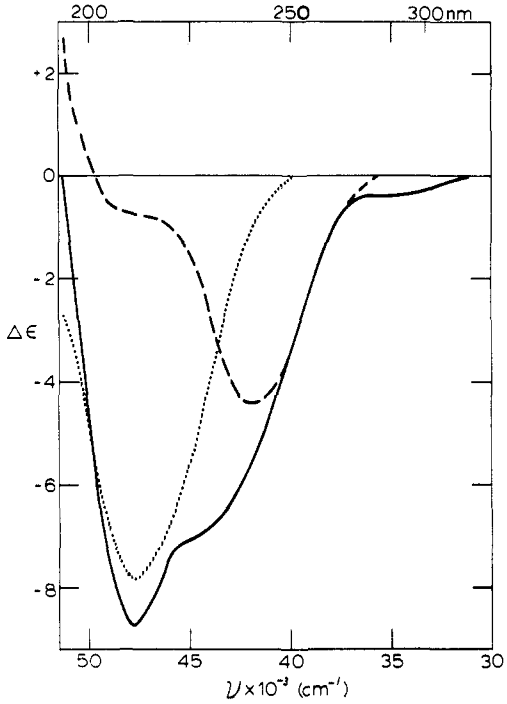


**Figure 5.** Circular dichroism spectra of methyl barbascoate (**1**, —) and methyl hardwickiate (**2b**, - - - -) in methanol. The spectrum of **1** minus **2b** (·····).

A concerted sequence of methyl migrations is possible for the production of trans clerodanes such as **1**, however, a "pause" at ion **5** is necessary to generate the cis A/B ring fusion present in **3**. Chettaphanin-1 (**6**)[26] has been isolated from another Euphorbiaceae and represents the partially rearranged skeleton corresponding to hypothetical ion **5**. A recent report describes the isolation[27] of both cis and trans clerodanes from the same tissue.

**Acknowledgments.** We wish to acknowledge the generous support of the Indiana University Department of Chemistry. We would also like to thank M. L. Lee for the capillary gas chromatographic analysis, and the Marshal H. Wrubel Computing Center for computer time.

**Supplementary Material Available:** A listing of structure factors (Table I), anisotropic thermal parameters (Table III), complete distances and angles (Tables IV and V), and torsion angles (Table VI) (20 pages). Ordering information is given on any current masthead page.

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(15) All computations were performed on a CDC6600 computer using an interactive program library based on the following programs: Germain, Main, and Woolfson's MULTAN, Larson's GENLES, DISAGL, and FOURIER, Johnson's ORTEP and various local programs. Scattering factors and anomalous dispersion terms were those compiled by D. T. Cromer and J. T. Waber, "International Tables for X-Ray Crystallography", Vol. IV, 149, 1975, pp 99–101.

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# The Triplet State of Chlorophylls[1]

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*Received August 25, 1975*

**Abstract:** The triplet state zero-field splittings and rates of intersystem crossing for the individual triplet spin sublevels in chlorophyll a, chlorophyll b, and zinc-substituted chlorophylls are presented. Whereas there are only small differences in zero-field splitting parameters among the chlorophylls, their kinetics show significant differences. The general trends in the chlorophyll intersystem crossing rate constants of the triplet spin sublevels may be explained qualitatively by a consideration of the one-center spin-orbit and spin-vibronic coupling activity of the chlorophyll ring system and the effect of side-chain substituents on these coupling mechanisms.

## I. Introduction

An understanding of the properties of the triplet state of chlorophylls as revealed by EPR studies is of importance from several points of view. First, since chlorophyll molecules contain large conjugated units, the mechanisms of intersystem crossing active in these molecules and their derivatives provide new tests for existing models of radiationless transitions in multi-ring organic systems. For studies of triplet state intersystem crossing in organic molecules, magnetic resonance spectroscopy has proven to be a most useful tool.[2-5] Second, in recent low-temperature EPR experiments on both the intact cells of photosynthetic bacteria and the reaction centers extracted from the cells, photoexcited triplet state EPR signals have been observed under conditions where electron-transfer processes have been blocked by chemical reduction of the electron acceptors.[6-8] These experiments have renewed interest in the possible role of the excited triplet state of chlorophylls in the initial photophysical processes of photosynthesis, although further work is necessary to clearly identify the function of the triplet state in photosynthetic mechanisms.[9] Finally, since triplet states are paramagnetic, an understanding of their magnetic properties and the changes which can occur in these properties would allow the use of the triplet state as a magnetic probe into chlorophyll-containing systems, providing information concerning the structure and molecular interactions within such systems. As has been shown in previous work from our laboratories,[10,11] the population and decay of chlorophyll (and derivatives) triplet states are sensitive to relatively small changes in molecular structure and surrounding environment. A characterization of the factors influencing chlorophyll triplet dynamics in isolated molecules is useful in understanding the changes in triplet properties which occur in more complex chlorophyll systems.

In the present work we attempt to detail the general features of chlorophyll triplet state intersystem crossing as revealed through EPR measurements over a range of temperatures, in varied solvent systems, and with metal center and substituent changes in the chlorophyll molecule. The methods used to obtain the data presented for discussion are high-field EPR on chlorophyll systems showing spin polarization[11] and zero-field optically detected EPR,[10,12] both of which have been detailed in previous publications from our laboratories. The discussion presented in this paper attempts to provide a description of the mechanisms active in the intersystem crossing of chlorophyll molecules and the effect of intra- and intermolecular interactions on these mechanisms.

## II. Results and Discussion

**A. The Zero-Field Splittings.** Table I contains the triplet state spin Hamiltonian parameters $|D|$ and $|E|$ for the mole-