Discussion. The final atomic parameters for the title compound are listed in Table 1.* A perspective view of the molecule and the atom-numbering scheme are given in Fig. 1. Fig. 2 shows the structural formula, labels of C—C bonds, and dimensions averaged according to idealized D_{2h} molecular symmetry.

The sets of atoms (I) [C(4), C(5), C(7) and C(8)], (II) [C(16), C(17), C(19) and C(20)], (III) [C(1), C(2), and C(21) to C(24)] and (IV) [C(9) to C(14)] all conform to strict planarity, the maximum deviations from the corresponding best planes being 0·002, 0·003, 0·009 and 0·009 Å, respectively. The molecule, however, appears to deviate very slightly but perceptibly from rigorous D_{2h} symmetry. The dihedral angles ($\sigma \sim 0{\cdot}3°$) between pairs of planes are: (I) and (II), 0·7°; (I) and (III), 87·7°; (II) and (III), 87·8°; (I) and (IV), 87·9°; (II) and (IV), 88·0°; (III) and (IV), 1·3°.

The considerable molecular strain is reflected by the fact that each *para*-fused benzenoid ring is boat-shaped, with its bow and stern C atoms displaced inward towards the other ring by 0·15 (1) Å. The transannular non-bonded distances *p* and *q* (see Fig. 2) agree closely with the corresponding values of 2·78 and 3·09 Å found in [2.2]paracyclophane (Hope, Bernstein & Trueblood, 1972). The inter-ring bridging bond *e* is normal (see data compiled by Keehn, 1983) and in excellent accord with the measured distance of 1·488 (2) Å in 1,2:3,4:11,12:13,14-tetrabenzo[4.4]-metacyclophane (Irngartinger, 1976). An unusual feature in the present structure is the significant lengthening of bond *d* in relation to other C—C bonds in the *ortho*-fused ring. A precedent of this type of distortion in highly strained hydrocarbons exists in 5,6,11,12-tetradehydrodibenzo[*a*,*e*]cyclooctene, in which the inner C_{sp^2}—C_{sp^2} bond has a length of 1·435 (2) Å at 290 K (Destro, Pilati & Simonetta, 1977).

* Lists of bond lengths and bond angles, anisotropic thermal parameters and H-atom coordinates have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42735 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

CHAN, C. W. & WONG, H. N. C. (1985). *J. Am. Chem. Soc.* **107**, 4790–4791.

DESTRO, R., PILATI, T. & SIMONETTA, M. (1977). *Acta Cryst.* B**33**, 447–456.

DETITTA, G. T., EDMONDS, J. W., LANGS, D. A. & HAUPTMAN, H. (1975). *Acta Cryst.* A**31**, 472–479.

HOPE, H., BERNSTEIN, J. & TRUEBLOOD, K. N. (1972). *Acta Cryst.* B**28**, 1733–1743.

International Tables for X-ray Crystallography (1974). Vol. IV, pp. 55, 99, 149. Birmingham: Kynoch Press. (Present distributor D. Reidel, Dordrecht.)

IRNGARTINGER, H. (1976). *Acta Cryst.* B**32**, 696–702.

JACOBSON, N. & BOEKELHEIDE, V. (1978). *Angew. Chem. Int. Ed. Engl.* **17**, 46–47.

KEEHN, P. M. (1983). *Cyclophanes*, Vol. I, edited by P. M. KEEHN & S. M. ROSENFELD, pp. 69–238. New York: Academic Press.

SCHILLING, J. W. (1970). *Crystallographic Computing*, edited by F. R. AHMED, pp. 201–204. Copenhagen: Munksgaard.

SHELDRICK, G. M. (1982). *Computational Crystallography*, edited by D. SAYRE, pp. 506–514. Oxford Univ. Press.

SPARKS, R. A. (1976). *Crystallographic Computing Techniques*, edited by F. R. AHMED, pp. 452–467. Copenhagen: Munksgaard.

Acta Cryst. (1986). C**42**, 705–708

Structure of 4β,10β-Dimethyleudesma-5,11(13)-diene-7β-lactone (Alantolactone)*

BY HELMUT W. SCHMALLE

Mineralogisch-Petrographisches Institut der Universität Hamburg, Grindelallee 48, *D*-2000 *Hamburg* 13, *Federal Republic of Germany*

(*Received* 22 *October* 1985; *accepted* 24 *December* 1985)

Abstract. $C_{15}H_{20}O_2$, $M_r = 232{\cdot}32$, orthorhombic, $P2_12_12_1$, $a = 6{\cdot}258$ (1), $b = 8{\cdot}156$ (1), $c = 25{\cdot}338$ (1) Å, $V = 1293{\cdot}3$ (2) Å^3, $Z = 4$, $D_x = 1{\cdot}193$ Mg m^{-3}, Cu $K\alpha$ radiation, $\lambda = 1{\cdot}5418$ Å, $\mu = 0{\cdot}53$ mm^{-1}, $F(000) = 504$, $T = 296$ K, final $R = 0{\cdot}042$ for 663 observed reflections. The naturally occurring sensitizing sesquiterpene lactone exhibits a distorted chair-shaped cyclohexane ring which is connected with a cyclohexane ring showing a deformed boat conformation. The 7,8-*cis*-fused lactone ring has a flattened envelope form. C(8) deviates −0·12 (1) Å, the *a*-methylene C(13) 0·11 (1) Å and the carbonyl oxygen O(2) −0·01 (1) Å from the best plane. Bond distances and angles are normal. The structure consists of discrete molecules.

* IUPAC name: 3aα,5,6,7,8,8a,9,9aα-octahydro-5β,8aβ-dimethyl-3-methylenenaphtho[2,3-*b*]furan-2(3*H*)-one.

0108-2701/86/060705-04$01.50

Introduction. High allergy-inducing activity of helenin – a mixture of the sesquiterpene lactones alantolactone and isoalantolactone, isolated from *Inula helenium* L. (Family Asteraceae) – has been observed by Hjorth (1970). Stampf, Benezra, Klecak, Geleick, Schulz & Hausen (1982) confirmed this finding in their investigation of helenin and its separated constituents. Stampf, Schlewer, Ducombs, Foussereau & Benezra (1978) reported that alantolactone and isoalantolactone were sensitizers on human volunteers and on guinea pigs, as well. Bleumink, Mitchell, Geissman & Towers (1976) observed that patients suffering from chrysanthemum contact allergy show positive allergic skin reactions to alantolactone. Similar observations have been made on guinea pigs sensitized with chrysanthemum extract (Schulz, Hausen, Wallhöfer & Schmidt-Löffler, 1975). Since cross reactivities were observed between alantolactone – which is used as a standard allergenic test compound – and different sesquiterpene lactone containing plant extracts, X-ray structure determinations of the title compound, isoalantolactone (Schmalle, Schoppe, Jarchow, Hausen & Schulz, 1986), and diepoxy-yomogin (Schmalle, Klupsch, Jarchow, Hausen & Schulz, 1986) have been performed in order to compare their conformations with those of other sesquiterpene lactones causing contact allergy.

Experimental. Naturally occurring alantolactone and isoalantolactone from *Inula helenium* L., separated by thin-layer chromatography; transparent needle-shaped crystals grown by slow evaporation from *n*-hexane and ethyl acetate; space-group determination from Weissenberg photographs; crystal dimensions 0·06 × 0·11 × 0·24 mm, Enraf–Nonius CAD-4 diffractometer; cell dimensions measured by least-squares refinement of 19 reflections in the interval $11° < \theta < 26°$; graphite-monochromatized Cu $K\alpha$ radiation; max. $\sin\theta/\lambda = 0{\cdot}518$ Å^{-1}, θ–2θ scan, zigzag mode, variable scan rate 0·3° to 20·0° min^{-1}, $-6 \le h \le 0$, $-8 \le k \le 8$, $0 \le l \le 26$; 10% loss of intensities in standard reflections $02\bar{6}$ and $0,0,\bar{10}$ monitored at the beginning and every 2 h (24 times) during data collection; 1654 reflections measured; data reduction with program of CAD-4 structure-determination package; Lorentz–polarization correction, no absorption correction; $R_{int} = 0{\cdot}031$; 944 unique reflections, 663 with $I > 3\sigma(I)$, 281 unobserved. Structure solved by direct methods with *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980) and refined on F_{hkl} by full-matrix least-squares technique; all H-atom positions subsequently determined from $\Delta\rho$ and refined with fixed $B_{iso} = 3{\cdot}16$ Å^2; number of reflections in final least-squares cycle $m = 663$, parameters refined, $n = 214$, unit weight, $R = 0{\cdot}042$; $(\Delta/\sigma)_{max} = 0{\cdot}65$ (0·24 for non-H atoms) in final refinement cycle; max. and min. heights in final $\Delta\rho$ 0·14 and −0·15 e Å^{-3}; computer programs used: *MULTAN*80 (Main *et al.*, 1980), *SHELX*76 (Sheldrick, 1976), *XANADU* (Roberts & Sheldrick, 1975), *ORTEP* (Johnson, 1971), *ORFFE* (Busing, Martin, Levy, Brown, Johnson & Thiessen, 1971); atomic scattering factors from *SHELX*76. The final atomic parameters are given in Table 1.*

* Lists of structure factors, anisotropic thermal parameters of the C and O atoms, H-atom coordinates and bond lengths and angles concerning the H atoms have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42733 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Final atomic coordinates and U_{eq} values for alantolactone with e.s.d.'s in parentheses*

U_{eq} values are given in the form $\frac{1}{3}\sum_i\sum_k U_{ik}a_i^*a_k^*(\mathbf{a}_i.\mathbf{a}_k)$.

	x	y	z	U_{eq}(Å^2)
O(1)	0·8200 (9)	0·5005 (6)	0·5131 (2)	0·054 (3)
O(2)	1·1423 (9)	0·3956 (6)	0·4984 (2)	0·067 (4)
C(1)	0·534 (1)	0·8841 (9)	0·6271 (3)	0·053 (5)
C(2)	0·608 (2)	0·960 (1)	0·6787 (3)	0·065 (6)
C(3)	0·608 (2)	0·835 (1)	0·7230 (3)	0·060 (5)
C(4)	0·755 (1)	0·6897 (9)	0·7100 (3)	0·051 (5)
C(5)	0·717 (1)	0·6194 (8)	0·6556 (2)	0·039 (4)
C(6)	0·729 (1)	0·4605 (9)	0·6477 (2)	0·050 (5)
C(7)	0·728 (1)	0·3733 (8)	0·5957 (3)	0·048 (5)
C(8)	0·643 (1)	0·4802 (9)	0·5499 (3)	0·049 (5)
C(9)	0·553 (1)	0·645 (1)	0·5665 (3)	0·050 (5)
C(10)	0·678 (1)	0·7363 (7)	0·6096 (2)	0·040 (4)
C(11)	0·943 (1)	0·3241 (8)	0·5767 (3)	0·043 (4)
C(12)	0·987 (2)	0·4059 (9)	0·5255 (3)	0·052 (5)
C(13)	1·093 (2)	0·233 (1)	0·6003 (3)	0·070 (6)
C(14)	0·888 (2)	0·8019 (9)	0·5881 (3)	0·050 (5)
C(15)	0·990 (2)	0·730 (1)	0·7194 (3)	0·074 (7)

Table 2. *Bond lengths* (Å) *and angles* (°) *of alantolactone*

E.s.d.'s are given in parentheses.

O(1)–C(8)	1·457 (8)	C(5)–C(10)	1·525 (8)
O(1)–C(12)	1·336 (9)	C(6)–C(7)	1·497 (9)
O(2)–C(12)	1·193 (8)	C(7)–C(8)	1·55 (1)
C(1)–C(2)	1·52 (1)	C(7)–C(11)	1·48 (1)
C(1)–C(10)	1·569 (9)	C(8)–C(9)	1·52 (1)
C(2)–C(3)	1·52 (1)	C(9)–C(10)	1·536 (9)
C(3)–C(4)	1·54 (1)	C(10)–C(14)	1·52 (1)
C(4)–C(5)	1·512 (9)	C(11)–C(12)	1·485 (9)
C(4)–C(15)	1·53 (1)	C(11)–C(13)	1·34 (1)
C(5)–C(6)	1·314 (9)		
C(2)–C(1)–C(10)	112·4 (7)	C(7)–C(8)–O(1)	106·4 (6)
C(1)–C(2)–C(3)	111·3 (7)	C(9)–C(8)–O(1)	111·0 (6)
C(2)–C(3)–C(4)	111·1 (6)	C(8)–C(9)–C(10)	116·0 (6)
C(3)–C(4)–C(5)	113·2 (7)	C(1)–C(10)–C(5)	110·9 (5)
C(3)–C(4)–C(15)	112·2 (8)	C(1)–C(10)–C(9)	106·3 (6)
C(5)–C(4)–C(15)	112·1 (7)	C(5)–C(10)–C(9)	108·8 (5)
C(4)–C(5)–C(6)	120·3 (6)	C(1)–C(10)–C(14)	109·1 (6)
C(4)–C(5)–C(10)	119·0 (6)	C(5)–C(10)–C(14)	110·8 (6)
C(6)–C(5)–C(10)	120·6 (6)	C(9)–C(10)–C(14)	110·9 (6)
C(5)–C(6)–C(7)	127·1 (6)	C(7)–C(11)–C(12)	109·3 (7)
C(6)–C(7)–C(8)	113·2 (6)	C(7)–C(11)–C(13)	129·9 (7)
C(6)–C(7)–C(11)	114·2 (7)	C(12)–C(11)–C(13)	120·7 (8)
C(8)–C(7)–C(11)	102·8 (6)	C(11)–C(12)–O(1)	108·7 (7)
C(7)–C(8)–C(9)	114·8 (6)	C(11)–C(12)–O(2)	128·5 (8)
O(1)–C(12)–O(2)	122·9 (7)	C(8)–O(1)–C(12)	112·2 (5)

Discussion. The atom-numbering scheme is shown in the *ORTEP* drawing of Fig. 1. Bond lengths and angles concerning the non-hydrogen atoms are given in Table 2. The *bc* projection of the unit cell is shown in Fig. 2, and Fig. 3 shows the endocyclic torsion angles of the structure.

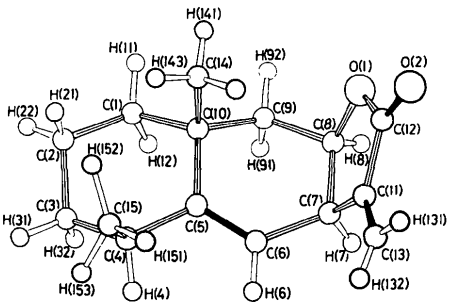

Fig. 1. *ORTEP* drawing of alantolactone. Blackened bond lines indicate C=C and C=O double bonds.

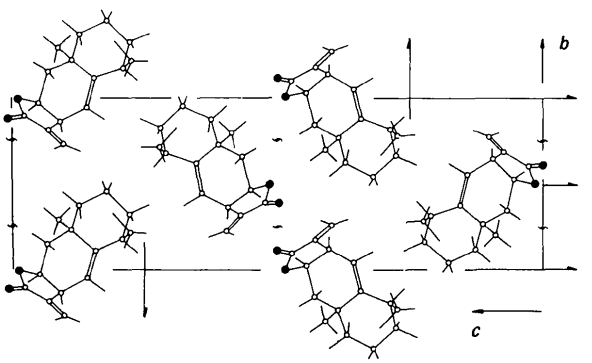

Fig. 2. The *bc* projection of the structure of alantolactone. Filled circles of the molecular models show O atoms and open circles C atoms.

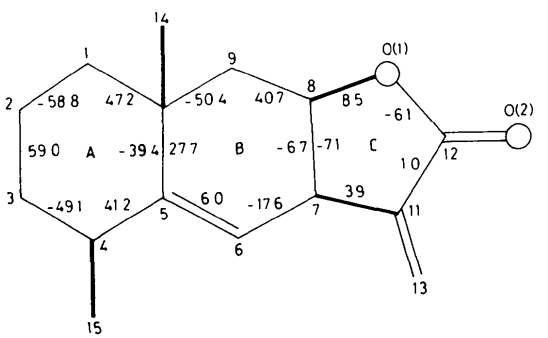

Fig. 3. Endocyclic torsion angles (°) for alantolactone. The e.s.d.'s range from 0·8 to 1·0°.

The stereochemistry of alantolactone and related compounds has been reviewed by Cocker & McMurry (1960). The configuration shown in Fig. 1 has been chosen because the corresponding absolute stereochemistry at C(7), C(8) and C(10) has been found in most of the eudesmanolide structures and has been determined by NMR spectra for alantolactone, isoalantolactone and their dihydro derivatives (Marshall & Cohen, 1964). Ring *A* of the title compound is a distorted cyclohexane ring. The best plane has been calculated among three groups of four atoms with C(1), C(10), C(3), and C(4). Their mean deviation is 0·005 Å; C(2) and C(5) deviate 0·68 (1) and −0·46 (1) Å from this plane. The mirror-plane asymmetry parameter (Duax & Norton, 1975) $\Delta C_s(2)$ of the best chair form is 1·5 (2)°. Ring *B* has a distorted boat conformation, which was found by a least-squares fit through the atoms C(5), C(10), C(7), and C(8) with a mean deviation of 0·073 Å. C(6) and C(9) deviate −0·12 (1) and −0·54 (1) Å. The corresponding asymmetry parameter $\Delta C_s(6)$ is 14·9 (1)°. On the other hand, ring *B* may be considered as having a distorted half-chair conformation. In this case, C(5), C(6), C(7), and C(10) belong to a best plane with mean deviation of 0·019 Å; C(8) and C(9) deviate −0·32 (1) and −0·77 (1) Å from the plane. The 7,8-*cis*-fused α-methylene-γ-lactone ring forms a flattened envelope with its best least-squares plane passing through C(7), C(11), C(12), and O(1); mean deviation 0·005 Å; atom C(8) deviates −0·12 (1) Å from the plane. The asymmetry parameter $\Delta C_s(8)$ is 1·8 (4)°.

The ring systems of the synthetic 7,8-*trans*-fused epialantolactone show similar conformations (Schultz, Godfrey, Arnold & Clardy, 1979). The relative stereochemistry at C(10), C(7) and C(8) in the title compound is identical with the conformations observed in isoalantolactone (Schmalle, Schoppe *et al.*, 1986) and in diepoxy-yomogin (Schmalle, Klupsch *et al.*, 1986), which is in accordance with the findings of Marshall, Cohen & Hochstetler (1966). The steric arrangement of the *A*-ring methyl groups of alantolactone is also observed in the tricyclic diterpene levopimaric acid, the main sensitizer of colophony (Karle, 1972), in many steroid structures [one of the strongest contact allergens from *Chrysanthemum indicum* L. has a steroid skeleton (Schmalle, 1986)], and in the pentacyclic triterpene 9(11)-fernene, a constituent found in the allergenic leatherleaf fern *Arachnoides adiantiformis* (Schmalle, Jarchow & Hausen, 1980). The stereochemistry of the *A* rings of allergenic compounds may play a role concerning cross-allergic reactivities in sensitized patients.

However, the contact allergen alantolactone most probably binds covalently to amino acid side chains of the receptor protein in the skin. Nucleophilic addition at the α-methylene group of alantolactone with the sulfhydryl group of cysteine, the imidazole group of histidine

and the ε-amino group of lysine has been demonstrated by Dupuis, Mitchell & Towers (1974). Dupuis, Benezra, Schlewer & Stampf (1980) successfully reacted alantolactone with model proteins and with guinea pig skin protein extract.

Intermolecular distances were calculated up to 3·6 Å with *ORFFE* (Busing *et al.*, 1971). There are no C—H···O interactions between neighbouring molecules; the structure consists of discrete molecules.

This investigation was supported by a grant from the Deutsche Forschungsgemeinschaft, Bonn, Federal Republic of Germany. The author thanks Dr Gunadi Adiwidjaja for the collection of the intensity data.

References

BLEUMINK, E., MITCHELL, J. C., GEISSMAN, T. A. & TOWERS, G. H. N. (1976). *Contact Dermatitis*, **2**, 81–88.

BUSING, W. R., MARTIN, K. O., LEVY, H. A., BROWN, G. M., JOHNSON, C. K. & THIESSEN, W. E. (1971). *ORFFE*. Oak Ridge National Laboratory, Tennessee.

COCKER, W. & MCMURRY, T. B. H. (1960). *Tetrahedron*, **8**, 181–204.

DUAX, W. L. & NORTON, D. A. (1975). In *Atlas of Steroid Structure*. New York, Washington, London: Plenum.

DUPUIS, G., BENEZRA, C., SCHLEWER, G. & STAMPF, J.-L. (1980). *Mol. Immunol.* **17**, 1045–1051.

DUPUIS, G., MITCHELL, J. C. & TOWERS, G. H. N. (1974). *Can. J. Biochem.* **52**, 575–581.

HJORTH, N. (1970). *Contact Dermatitis Newslett.* **8**, 180.

JOHNSON, C. K. (1971). *ORTEP*. Report ORNL-3794, revised. Oak Ridge National Laboratory, Tennessee.

KARLE, I. L. (1972). *Acta Cryst.* B**28**, 2000–2007.

MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1980). *MULTAN80. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

MARSHALL, J. A. & COHEN, N. (1964). *J. Org. Chem.* **29**, 3727–3729.

MARSHALL, J. A., COHEN, N. & HOCHSTETLER, A. R. (1966). *J. Am. Chem. Soc.* **88**, 3408–3417.

ROBERTS, P. & SHELDRICK, G. M. (1975). *XANADU*. Program for crystallographic calculations. Univ. of Cambridge, England.

SCHMALLE, H. W. (1986). *Acta Cryst.* In preparation.

SCHMALLE, H. W., JARCHOW, O. H. & HAUSEN, B. M. (1980). *Acta Cryst.* B**36**, 2450–2453.

SCHMALLE, H. W., KLUPSCH, S., JARCHOW, O. H., HAUSEN, B. M. & SCHULZ, K.-H. (1986). *Acta Cryst.* In preparation.

SCHMALLE, H. W., SCHOPPE, I., JARCHOW, O. H., HAUSEN, B. M. & SCHULZ, K.-H. (1986). *Acta Cryst.* In preparation.

SCHULTZ, A. G., GODFREY, J. D., ARNOLD, E. V. & CLARDY, J. (1979). *J. Am. Chem. Soc.* **101**, 1276–1277.

SCHULZ, K. H., HAUSEN, B. M., WALLHÖFER, L. & SCHMIDT-LÖFFLER, P. (1975). *Arch. Derm. Forsch.* **251**, 235–244.

SHELDRICK, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.

STAMPF, J.-L., BENEZRA, C., KLECAK, G., GELEICK, H., SCHULZ, K.-H. & HAUSEN, B. M. (1982). *Contact Dermatitis*, **8**, 16–24.

STAMPF, J.-L., SCHLEWER, G., DUCOMBS, G., FOUSSEREAU, J. & BENEZRA, C. (1978). *Br. J. Dermatol.* **99**, 163–169.

Acta Cryst. (1986). C**42**, 708–711

The Stereochemistry of the Major Epimer Formed on Reaction of Methyl 1-Methyl-6-oxo-2,4-cyclohexadiene-1-carboxylate with Dimethyl Acetylenedicarboxylate: Trimethyl *endo*-5-Methyl-6-oxobicyclo[2.2.2]octa-2,7-diene-2,3,*exo*-5-tricarboxylate

BY JEFFERY F. SAWYER, ANABELA GOMES AND PETER YATES

Lash Miller Chemical Laboratories, University of Toronto, Toronto, Ontario, Canada M5S 1A1

(*Received* 19 *August* 1985; *accepted* 3 *December* 1985)

Abstract. $C_{15}H_{16}O_7$, $M_r = 308{\cdot}3$, monoclinic, $I2/a$, $a = 19{\cdot}534\ (5)$, $b = 7{\cdot}213\ (5)$, $c = 21{\cdot}371\ (6)$ Å, $\beta = 101{\cdot}53\ (2)°$, $U = 2950\ (4)$ Å^3, $Z = 8$, $D_x = 1{\cdot}39$ g cm^{-3}, Mo $K\bar{\alpha}$ radiation, $\lambda = 0{\cdot}71069$ Å, μ(Mo $K\bar{\alpha}$) $= 1{\cdot}04$ cm^{-1}, $F(000) = 1296$, $T = 298$ K, $R = 0{\cdot}058$ for 1155 reflections with $I \geq 3\sigma(I)$. X-ray analysis indicates that dimethyl acetylenedicarboxylate reacts preferentially on the methyl face of methyl 1-methyl-6-oxo-2,4-cyclohexadiene-1-carboxylate to give trimethyl *endo*-5-methyl-6-oxobicyclo[2.2.2]octa-2,7-diene-2,3,*exo*-5-tricarboxylate. In the bicyclo[2.2.2]octadiene system, opposite bonds are very slightly twisted away from being eclipsed, with torsion angles about the C(2)=C(3) and C(7)=C(8) double bonds and bond C(5)—C(6) of −2·3 (5), 1·2 (6) and −1·7 (3)°, respectively. The two methoxycarbonyl groups are canted by 12·4 (7) and 79·7 (7)° with respect to the plane of the C(2)=C(3) double bond.

Introduction. A key step in the syntheses of cedranoid sesquiterpenes that are being pursued in these laboratories is the photosensitized isomerization of bicyclo[2.2.2]octenones of type (4) to tricyclo[3.2.1.0^{2,8}]octanones (5); compounds (4) were prepared

0108-2701/86/060708-04$01.50