Functionalized Hydrocarbons with Condensed Ring Skeletons. IV. A 2,7-Dimethyltricyclo[8.4.0.0^{2,7}]tetradec-8-ene

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Abstract. Tetramethyl 1,10-*trans*-1,2-*cisoid*-2,7-*cis*-2,7-dimethyltricyclo[8.4.0.0^{2,7}]tetradec-8-ene-5,5,12,12-tetracarboxylate, $C_{24}H_{34}O_8$, $M_r = 450 \cdot 53$, monoclinic, $P2_1/n$, $a = 7 \cdot 895$ (2), $b = 28 \cdot 103$ (6), $c = 10 \cdot 876$ (3) Å, $\beta = 92 \cdot 00$ (2)°, $V = 2411 \cdot 62$ Å^3, $Z = 4$, $D_x = 1 \cdot 241$ Mg m^{-3}, $\lambda(Cu\,K\bar{\alpha}) = 1 \cdot 5418$ Å, $\mu = 0 \cdot 728$ mm^{-1}, $F(000) = 968$, room temperature, final $R = 0 \cdot 048$ for 2717 observed reflections. The structure consists of three angularly fused six-membered rings A, B and C. The relative stereochemistry is *trans* for the AB ring junction, *syn* between the C(1) proton and C(2) methyl and *cis* for the BC ring junction (abbreviated to T–S–C). Ring A adopts a chair conformation. A double bond is contained within the half-chair conformation of ring B. The C(2) and C(7) methyl groups of the ring C chair conformation are borne axially and equatorially respectively.

Introduction. Steroid-like diterpene molecules are commonly seen in the realm of natural products. It is rare, however, that carbon skeletons similar to that of (3) (Fig. 1), with methyl groups at C(8) and C(9) (steroid numbering), are found (Cimino, Gavagnin, Sodano, Puliti, Mattia & Mazzarella, 1988). The transannular Diels–Alder reaction of macrocyclic trienes has already been demonstrated to be a simple method for producing three functionalized rings and four chiral centres in the resulting adducts (Lamothe, Ndibwami & Deslongchamps, 1988a; Marinier & Deslongchamps, 1988). The dimethyltetradecane skeleton of compound (3) was thus easily constructed by this method. In recent communications (Michel, Proulx & Michel-Dewez, 1988; Michel, Boulay & Marinier, 1989; Michel, Michel-Dewez & Roughton, 1988) the conformational properties and X-ray data of earlier studies in this series have been detailed.

A simple molecular model of macrocycle (2), the cyclization product of allylic chloride triene (1) (Fig. 1), suggests that the transannular Diels–Alder reaction could pass *via* a single boat-like transition state to yield a racemic tricycle with T–S–C relative ring-junction stereochemistry. Apart from the potential for natural-product synthesis, the methodology may indirectly offer insights into both the mechanism of the transannular Diels–Alder reaction and the conformational properties of resulting adducts. Precise determination of the stereochemistry and conformation of (3) was most practically achievable by the present crystallography study.

Experimental. Crystal: $0 \cdot 20 \times 0 \cdot 20 \times 0 \cdot 10$ mm; automatic four-circle diffractometer with Cu $K\bar{\alpha}$ radiation; lattice parameters determined from 25 medium-angle reflections ($30 \le \theta \le 50°$); $0 \le h \le 8$, $0 \le k \le 30$, $-11 \le l \le 11$; $2\theta_{max} = 144°$; one standard reflection monitored every 100 reflections without significant deviation; 3291 unique measured reflections, 2717
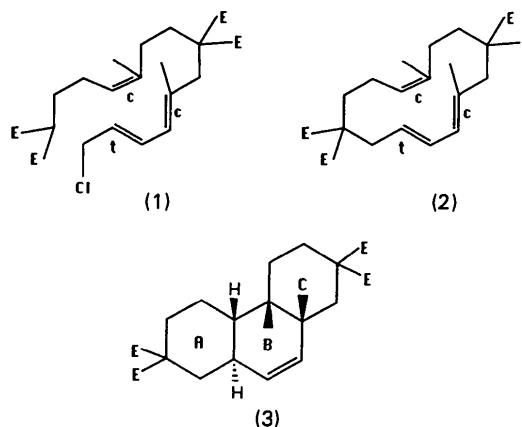

Fig. 1. Synthetic scheme ($E = COOCH_3$).

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Table 1. Final coordinates and B_{iso} values $(\times 10^2)$ with e.s.d.'s in parentheses

$$B_{iso} = \tfrac{8}{3}\pi^2 \mathrm{trace}(U).$$

	x	y	z	$B_{iso}(\text{Å}^2)$
O1	0.5427 (2)	0.0711 (1)	0.9070 (2)	4.85
O2	0.7096 (2)	0.0787 (1)	1.0747 (2)	4.82
O3	0.9613 (2)	0.1694 (1)	1.0415 (2)	4.85
O4	0.9592 (2)	0.1165 (1)	0.8889 (1)	3.71
O5	0.7362 (3)	0.4456 (1)	0.6746 (2)	6.51
O6	0.6138 (2)	0.4784 (1)	0.8337 (2)	5.61
O7	0.6913 (3)	0.4019 (1)	1.0747 (2)	8.07
O8	0.9076 (3)	0.4286 (1)	0.9710 (2)	6.66
C1	0.5778 (3)	0.2949 (1)	0.8380 (2)	2.88
C2	0.5479 (3)	0.2418 (1)	0.8678 (2)	3.01
C3	0.6147 (3)	0.2302 (1)	0.9985 (2)	3.50
C4	0.6006 (3)	0.1781 (1)	1.0330 (2)	3.91
C5	0.6938 (3)	0.1453 (1)	0.9434 (2)	2.96
C6	0.6424 (3)	0.1578 (1)	0.8099 (2)	3.13
C7	0.6468 (3)	0.2111 (1)	0.7745 (2)	2.89
C8	0.8266 (3)	0.2290 (1)	0.7688 (2)	3.14
C9	0.8773 (3)	0.2721 (1)	0.7996 (2)	3.32
C10	0.7641 (3)	0.3093 (1)	0.8511 (2)	2.98
C11	0.7877 (3)	0.3583 (1)	0.7912 (2)	3.47
C12	0.6817 (3)	0.3968 (1)	0.8517 (2)	3.54
C13	0.4947 (3)	0.3810 (1)	0.8590 (2)	4.09
C14	0.4720 (3)	0.3306 (1)	0.9095 (2)	4.06
C15	0.3557 (3)	0.2315 (1)	0.8549 (3)	4.69
C16	0.5687 (3)	0.2128 (1)	0.6424 (2)	4.28
C17	0.6390 (3)	0.0939 (1)	0.9693 (2)	3.42
C18	0.6659 (4)	0.0310 (1)	1.1111 (3)	6.46
C19	0.8854 (3)	0.1461 (1)	0.9657 (2)	3.09
C20	1.1404 (3)	0.1104 (1)	0.9018 (3)	4.85
C21	0.6833 (3)	0.4423 (1)	0.7746 (2)	4.06
C22	0.6011 (4)	0.5229 (1)	0.7663 (3)	6.22
C23	0.7559 (4)	0.4089 (1)	0.9797 (2)	4.72
C24	0.9954 (6)	0.4422 (1)	1.0842 (3)	11.19

observed with $I > 3\sigma(I)$; structure solved by direct methods with *SHELXS*86 (Sheldrick, 1986); molecular illustration drawn using *ORTEP*II (Johnson, 1976); difference Fourier analysis and refinement using full-matrix least-squares techniques *SDP-Plus* (Okaya & Frenz, 1984); function $\sum w(|F_o| - |F_c|)^2$ with $w = 1/(\sigma F_o)^2$, minimized to give an unweighted residual of 0.048; $wR = 0.068$; $S = 2.687$; max. Δ/σ (for non-H atoms) = 0.23; max. density peak = 0.25 e Å⁻³; H atoms assigned isotropic temperature factors corresponding to their attached atoms, positional parameters refined. Atomic scattering factors from *SHELXS*86.

Discussion. Table 1 gives the final atomic parameters with their B_{iso} values.* Fig. 2 shows the atom numbering and an *ORTEP* perspective view of the tricyclic compound. Bond lengths and angles are given in Tables 2(a) and (b) respectively. Selected torsion angles (°) in the tricycle skeleton are given in Table 2(c). The results of the structure determination indicate that (3) has T–S–C relative stereochemistry. Ring A adopts a chair conformation. The cis BC ring junction confers conformational mobility on the adduct. Presumably after the Diels–Alder reaction, which is

* Lists of structure factors, anisotropic thermal parameters, H-atom parameters and torsion angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51653 (18 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. Molecular geometry.

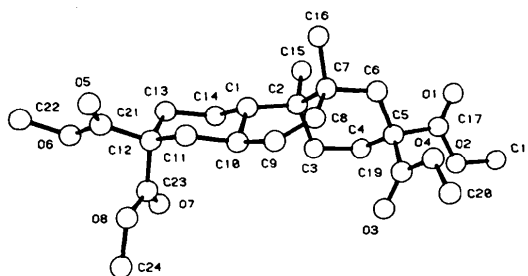(a) Intramolecular bond lengths (Å) with e.s.d.'s in parentheses

O(1)–C(17)	1.188 (3)	C(2)–C(15)	1.546 (3)
O(2)–C(17)	1.328 (3)	C(3)–C(4)	1.517 (4)
O(2)–C(18)	1.443 (4)	C(4)–C(5)	1.546 (4)
O(3)–C(19)	1.197 (3)	C(5)–C(6)	1.535 (3)
O(4)–C(19)	1.328 (3)	C(5)–C(17)	1.537 (4)
O(4)–C(20)	1.443 (3)	C(5)–C(19)	1.524 (3)
O(5)–C(21)	1.182 (3)	C(6)–C(7)	1.547 (4)
O(6)–C(21)	1.330 (4)	C(7)–C(8)	1.509 (3)
O(6)–C(22)	1.451 (4)	C(7)–C(16)	1.544 (3)
O(7)–C(23)	1.185 (3)	C(8)–C(9)	1.315 (4)
O(8)–C(23)	1.326 (4)	C(9)–C(10)	1.497 (4)
O(8)–C(24)	1.443 (4)	C(10)–C(11)	1.537 (4)
C(1)–C(2)	1.547 (4)	C(11)–C(12)	1.530 (4)
C(1)–C(10)	1.527 (3)	C(12)–C(13)	1.546 (3)
C(1)–C(14)	1.534 (4)	C(12)–C(21)	1.529 (4)
C(2)–C(3)	1.534 (3)	C(12)–C(23)	1.530 (3)
C(2)–C(7)	1.562 (3)	C(13)–C(14)	1.532 (4)

(b) Valence angles (°) with e.s.d.'s in parentheses

C(17)–O(2)–C(18)	116.01 (23)	C(8)–C(7)–C(16)	107.28 (19)
C(19)–O(4)–C(20)	117.95 (20)	C(7)–C(8)–C(9)	125.08 (24)
C(21)–O(6)–C(22)	115.83 (22)	C(8)–C(9)–C(10)	123.92 (23)
C(23)–O(8)–C(24)	117.3 (3)	C(1)–C(10)–C(9)	111.45 (22)
C(2)–C(1)–C(10)	112.93 (21)	C(1)–C(10)–C(11)	109.17 (20)
C(2)–C(1)–C(14)	115.77 (20)	C(9)–C(10)–C(11)	112.60 (20)
C(10)–C(1)–C(14)	108.60 (21)	C(10)–C(11)–C(12)	112.01 (19)
C(1)–C(2)–C(3)	110.43 (20)	C(11)–C(12)–C(13)	110.88 (21)
C(1)–C(2)–C(7)	108.26 (19)	C(11)–C(12)–C(21)	109.89 (19)
C(1)–C(2)–C(15)	108.54 (21)	C(11)–C(12)–C(23)	110.53 (20)
C(3)–C(2)–C(7)	108.74 (20)	C(13)–C(12)–C(21)	107.12 (20)
C(3)–C(2)–C(15)	110.42 (21)	C(13)–C(12)–C(23)	110.68 (20)
C(7)–C(2)–C(15)	110.42 (21)	C(21)–C(12)–C(23)	107.63 (21)
C(2)–C(3)–C(4)	114.12 (21)	C(12)–C(13)–C(14)	114.06 (21)
C(3)–C(4)–C(5)	112.27 (20)	C(1)–C(14)–C(13)	110.50 (19)
C(4)–C(5)–C(6)	110.11 (20)	O(1)–C(17)–O(2)	124.0 (3)
C(4)–C(5)–C(17)	107.56 (19)	O(1)–C(17)–C(5)	125.52 (23)
C(4)–C(5)–C(19)	112.49 (20)	O(2)–C(17)–C(5)	110.38 (21)
C(6)–C(5)–C(17)	108.77 (20)	O(3)–C(19)–O(4)	123.77 (22)
C(6)–C(5)–C(19)	112.05 (19)	O(3)–C(19)–C(5)	126.01 (23)
C(17)–C(5)–C(19)	105.60 (21)	O(4)–C(19)–C(5)	110.22 (20)
C(5)–C(6)–C(7)	116.71 (21)	O(5)–C(21)–O(6)	123.4 (3)
C(2)–C(7)–C(6)	110.92 (19)	O(5)–C(21)–C(12)	125.4 (3)
C(2)–C(7)–C(8)	109.56 (21)	O(6)–C(21)–C(12)	111.19 (20)
C(2)–C(7)–C(16)	113.26 (20)	O(7)–C(23)–O(8)	123.31 (25)
C(6)–C(7)–C(8)	111.23 (21)	O(7)–C(23)–C(12)	126.4 (3)
C(6)–C(7)–C(16)	104.46 (20)	O(8)–C(23)–C(12)	110.25 (21)

(c) Selected torsional angles (°) with e.s.d.'s in parentheses

C(10)–C(1)–C(2)–C(3)	57.4 (2)	C(10)–C(1)–C(2)–C(7)	−61.5 (2)
C(14)–C(1)–C(2)–C(3)	−68.7 (2)	C(14)–C(1)–C(2)–C(7)	172.4 (3)
C(2)–C(1)–C(10)–C(9)	41.7 (2)	C(2)–C(1)–C(10)–C(11)	166.7 (3)
C(14)–C(1)–C(10)–C(9)	171.5 (3)	C(14)–C(1)–C(10)–C(11)	−63.5 (2)
C(2)–C(1)–C(14)–C(13)	−172.0 (3)	C(10)–C(1)–C(14)–C(13)	59.7 (2)
C(1)–C(2)–C(3)–C(4)	−176.4 (3)	C(7)–C(2)–C(3)–C(4)	−57.8 (2)
C(1)–C(2)–C(7)–C(6)	172.3 (3)	C(1)–C(2)–C(7)–C(8)	49.1 (2)
C(3)–C(2)–C(7)–C(6)	52.3 (2)	C(3)–C(2)–C(7)–C(8)	−70.9 (2)
C(2)–C(3)–C(4)–C(5)	57.3 (2)	C(3)–C(4)–C(5)–C(6)	−49.3 (2)
C(4)–C(5)–C(6)–C(7)	48.2 (2)	C(5)–C(6)–C(7)–C(2)	−50.2 (2)
C(5)–C(6)–C(7)–C(8)	71.4 (2)	C(6)–C(7)–C(8)–C(9)	−145.6 (3)
C(2)–C(7)–C(8)–C(9)	−22.6 (2)	C(7)–C(8)–C(9)–C(10)	3.1 (1)
C(8)–C(9)–C(10)–C(11)	−135.1 (3)	C(8)–C(9)–C(10)–C(1)	−12.0 (1)
C(1)–C(10)–C(11)–C(12)	60.2 (2)	C(9)–C(10)–C(11)–C(12)	−175.4 (3)
C(10)–C(11)–C(12)–C(13)	−51.2 (2)	C(11)–C(12)–C(13)–C(14)	47.9 (2)
C(12)–C(13)–C(14)–C(1)	−52.7 (2)		

Fig. 2. *ORTEP* perspective view and atom numbering of (3).

expected to pass *via* a ring *B* boat conformation (Lamothe, Ndibwami & Deslongchamps, 1988*b*), an energetically preferred half-chair conformation is adopted by ring *B*. While the C(2) and C(7) methyl groups of ring *C* remain *gauche* to one another regardless of ring *B* conformation, a sterically more favourable interaction between the appropriate ring *A* and ring *C* protons is established when ring *B* adopts a half-chair conformation. As a result, the chair conformation of ring *C* carries the C(2) methyl group in an axial position, while the C(7) methyl group becomes equatorial.

The bond between C(7) and C(8) can be considered as an axial substituent on the chair conformation of ring *C*. Consequently, it would appear from Fig. 2 that the axial ester group on ring *C*, *i.e.* the bond between C(5) and C(19), is extended slightly outwards to minimize as much as possible the pseudo-1,3-diaxial interaction. No abnormally short intermolecular contacts were noted.

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Structure of Metformin Hydrochloride*†

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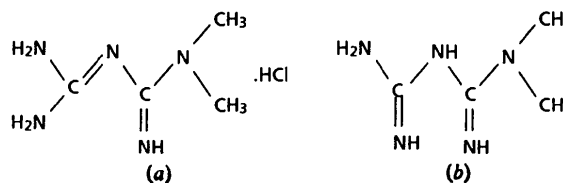
Abstract. *N,N*-Dimethylbiguanide hydrochloride, $C_4H_{12}N_5^+.Cl^-$, $M_r = 165.6$, monoclinic, $P2_1/a$, $a = 7.991$ (3), $b = 13.950$ (5), $c = 8.020$ (2) Å, $\beta = 114.98$ (3)°, $V = 810.4$ (5) Å^3, $Z = 4$, $D_m = 1.35$ (1), $D_x = 1.357$ Mg m^{-3}, Mo $K\alpha$, $\lambda = 0.7107$ Å, $\mu = 0.41$ mm^{-1}, $T = 295$ K, $F(000) = 352.0$, $R = 0.038$, $wR = 0.032$ for 980 observed reflections with $I > 3\sigma(I)$. The protonation occurs at one of the imino groups and the molecules are stabilized by means of N–H···Cl and N–H···N types of hydrogen bond.

Introduction. The title compound, a dimethyl-biguanide, is an oral hypoglycaemic drug and is found to have fewer side effects when compared to the other biguanides, *e.g.* phenformin (Herrnstadt, Mootz, Wunderlich & Mohrle, 1979). The sample compound was obtained from Franco Indian Pharmaceuticals Pvt. Ltd., Bombay, India. The structural analysis was undertaken to establish the structure–activity relation-

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† Alternative name: *N,N*-dimethylimidodicarbonimidic diamide hydrochloride.
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ship of the biguanides. Of the two tautomeric forms shown below (Ray, 1961), the compound takes the form (*a*).

Experimental. White needle of dimensions 0.55 × 0.50 × 0.18 mm from methanol. D_m by flotation. Three-dimensional intensity data on an Enraf–Nonius CAD-4 diffractometer at the Indian Institute of Technology, Madras. $\omega/2\theta$ scan technique. 25 accurately centred reflections with $16 \le 2\theta \le 38°$ for cell refinement. 2101 unique reflections in the range $4 < 2\theta < 50°$ with $0 < h \le 10$, $0 \le k \le 18$, $-10 \le l < 10$; 980 reflections with $I \ge 3\sigma(I)$. Two standard reflections (3̄40, 091) monitored for every 100 reflections. Maximum variation in intensity 6.4%. Intensity data corrected for Lorentz and polarization effects but not for absorption. Structure solution by Patterson and