Conformational Studies. Part 8.[1] Crystal and Molecular Structure of 17β-Iodoacetoxy-4,4-dimethylandrostan-5-en-3-one

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Crystals of the title complex (2) are monoclinic, space group $P2_1$, $a = 6.394(2)$, $b = 11.303(4)$, $c = 15.566(4)$ Å, $\beta = 92.92(2)°$, $Z = 2$. The structure has been refined by full-matrix least-squares calculations to a final R of 0.046 for 1 065 observed reflections. The conformations of the rings are: A, skewed boat; B, half-chair; C, chair; and D, half-chair distorted towards a C(13) envelope.

THE conformation of ring A in 4,4-dimethyl-3-oxo-steroids has been the subject of much discussion,[2] and is of interest not only because of the widespread occurrence of such compounds in nature and their biological activity, but also because the high degree of substitution leads to a large number of steric interactions.

The crystal structures of the iodoacetates of 17β-hydroxy-4,4-dimethyl-5α-androstan-3-one (1a),[3] and of the 19-nor-analogue (1b) [3,4] have been reported, and compared [5] with those of the corresponding steroids (1c) and (1d) devoid of the 4,4-dimethyl substituents. The crystal structure determination of 17β-iodoacetoxy-4,4-dimethylandrost-5-en-3-one (2) was undertaken to establish the effect of the 5,6-unsaturation on the conformation

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[1] Part 7, G. Ferguson, D. F. Rendle, J. M. Midgley, and W. B. Whalley, preceding paper.

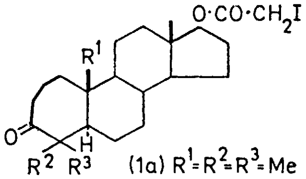
[2] N. L. Allinger and M. DaRooge, *J. Amer. Chem. Soc.*, 1962, **84**, 461; J. Lehn, J. Levisalles, and G. Ourisson, *Tetrahedron Letters*, 1962, 682; J. S. E. Holker and W. B. Whalley, *Proc. Chem. Soc.*, 1961, 464; M. J. T. Robinson and W. B. Whalley, *Tetrahedron*, 1963, **19**, 2123.

[3] G. Ferguson, E. W. Macaulay, J. M. Midgley, J. M. Robertson, and W. B. Whalley, *Chem. Comm.*, 1970, 945.

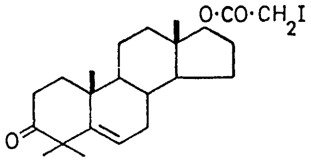
[4] E. W. Macaulay, Ph.D. Thesis, University of Glasgow, 1968.

[5] D. F. Rendle, Ph.D. Thesis, University of Guelph, 1972.

of the complete steroid molecule, and on ring A in particular.



(1a) $R^1 = R^2 = R^3 = Me$
(1b) $R^1 = H$, $R^2 = R^3 = Me$
(1c) $R^1 = Me$, $R^2 = R^3 = H$
(1d) $R^1 = R^2 = R^3 = H$



(2)

RESULTS AND DISCUSSION

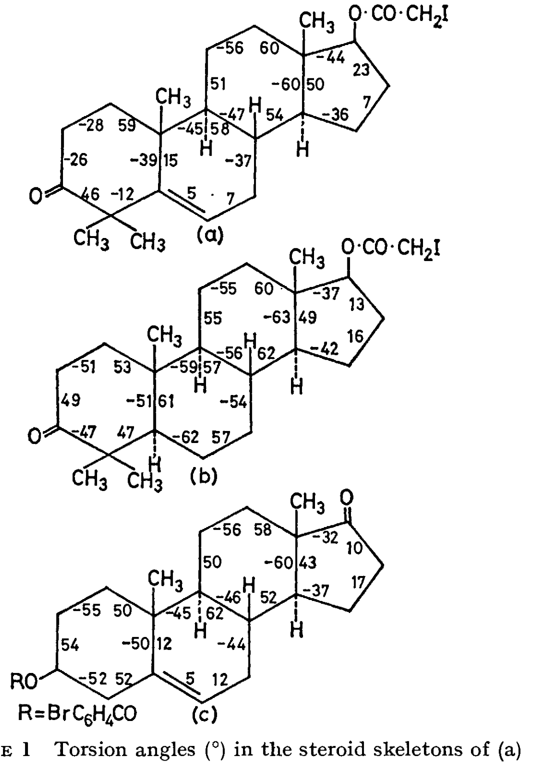


FIGURE 1 Torsion angles (°) in the steroid skeletons of (a) (2), (b) (1a), and (c) (3)

The torsion angles in the steroid skeletons of (2), of (1a), and of 3β-*p*-bromobenzoyloxyandrost-5-en-17-one (3),[6] a steroid with similar B and C rings, are given in Figure 1. The most striking feature in (2) is the conformation of ring A (Figure 2); C(3) and C(10) are above the C(1), C(2), C(4), C(5) plane by 0.43 and 0.55 Å, while the deviations of C(1), C(2), C(4), and C(5) from the least-squares plane through them are alternatively positive and negative (see Table 1). This arrangement, as well as the distribution of torsional angles, is characteristic of a skewed boat. The conformation of ring A in (1a) is a flattened chair and the adoption of this conformation has been attributed to a rotation about the C(4)–C(5) bond to relieve the transannular interaction between the C(21) and C(19) methyl groups.[3] The relief of the same interaction in (2), together with elimination of the very strong C(6)-methine hydrogen • • • C(4)-α-methyl interaction, which would be present were ring A to exist in a normal chair conformation, are removed by the conversion of ring A into a skewed boat conformation in

TABLE 1

Least-squares planes calculated through various atoms in the molecule. Equations of planes are in the form $Ax' + By' + Cz' + D = 0$ where $x' = ax + cz\cos\beta$, $y' = by$, $z' = cz\sin\beta$. Devations (Å) of relevant atoms from the planes are given in square brackets

Plane (1): C(1), C(2), C(4), C(5)

$$-0.647x' - 0.755y' - 0.108z' + 4.142 = 0$$

[C(1) 0.15, C(2) −0.14, C(3) −0.43, C(4) 0.13, C(5) −0.10, C(10) −0.55]

Plane (2): C(5), C(6), C(7), C(10)

$$-0.794x' - 0.538y' - 0.284z' + 6.595 = 0$$

[C(5) −0.02, C(6) 0.02, C(7) −0.01, C(8) −0.25, C(9) 0.44, C(10) 0.01]

Plane (3): C(8), C(9), C(11), C(12), C(13), C(14)

$$-0.623x' - 0.745y' - 0.238z' + 5.895 = 0$$

[C(8) −0.20, C(9) 0.15, C(11) −0.24, C(12) 0.26, C(13) −0.25, C(14) 0.26]

Plane (4): C(15), C(16), C(17)

$$-0.543x' - 0.834y' - 0.097z' + 4.345 = 0$$

[C(13) −0.59, C(14) 0.18, C(15) 0.0, C(16) 0.0, C(17) 0.0]

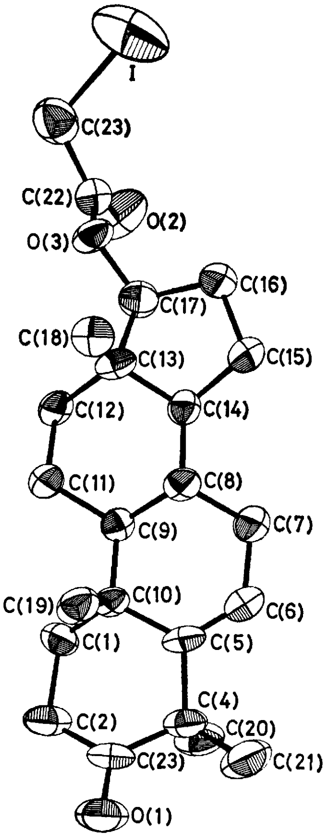


FIGURE 2 Diagram of the molecule of (2) showing the atom numbering scheme used in the analysis

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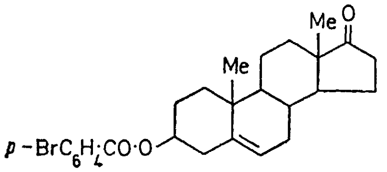
[6] J. C. Portheine, C. Romers, and E. W. M. Rutten *Acta Cryst.*, 1972, **B28**, 849.

which gunwale and stem–stern interactions are essentially minimised. In (3) ring A adopts the expected slightly distorted chair conformation.[6]



(3)

The conformation of ring B in (2) is a half-chair with C(8) 0.25 above and C(9) 0.44 Å below the least-squares plane through C(5), C(6), C(7), and C(10). The distribution of the torsional angles in ring B is also characteristic of a half-chair, and shows that the ring is slightly deformed in the region of the atoms C(5) and C(6) with respect to the half-chair conformation in cyclohexene.[7] Comparison of the torsional angles between (2) and (3)[6] reveals a large measure of similarity in the conformation of ring B in these two steroids. Such differences as do exist may be ascribed to the large differences in the conformations of ring A.

Ring C in (2) adopts a conformation similar to that of a normal chair, but with a slight flattening at the junction with ring B. This is reflected in the smaller value of the C(14)–C(8)–C(9)–C(11) torsion angle, −47°, compared with the value of −56° in (1a).[3] This slight distortion is most likely attributable to the double bond in ring B since the conformation of ring C is virtually identical with that found in (3),[6] there being no significant differences between corresponding torsion angles.

The conformation of ring D in (2) may be described qualitatively as being distorted away from a half-chair towards a C(13) envelope with C(13) 0.59 Å above and C(14) 0.18 Å below the C(15)—(17) plane (Table 1). Alternatively, the conformation may be characterised more quantitatively by the values of 49.6 for the 'puckering angle' ϕ_m, and 18.9° for the 'phase angle' δ.[8] These values are very similar to those for 17β-hydroxyandrostan-3-one (ϕ_m 46.5 and δ 16.1°),[9] but differ greatly from those for (1a) (ϕ_m 48.2 and δ −4.5°) where the conformation of ring D is much closer to a half-chair.[3] It therefore appears that the 5(6) double bond in ring B as well as methyl substituents at C(4) play important roles in determining the conformation of D ring. These results dramatically demonstrate the reality of 'conformational transmission'.[10]

The interatomic distances and angles, listed in Table 2, are for the most part in accord with accepted values[11] and require little comment. The mean $C(sp^3)$–$C(sp^3)$ distance is 1.538(7) with $C(sp^3)$–$C(sp^2)$ 1.52(1) Å. Two of the C–C bonds [C(1)–C(2) 1.60(2) and C(4)–C(5) 1.57(1) Å] appear longer than normal but when the standard deviations are taken into account they are probably not significantly different from the accepted values of 1.537(5) and 1.510(5) Å respectively.[11] The intermolecular contacts have the expected range of

TABLE 2

Molecular dimensions, with estimated standard deviations in parentheses

(*a*) Bond lengths (Å)

I–C(23)	2.068(14)	C(6)–C(7)	1.501(16)
		C(7)–C(8)	1.514(15)
O(1)–C(3)	1.215(13)	C(8)–C(9)	1.499(16)
O(2)–C(22)	1.184(16)	C(8)–C(14)	1.560(14)
O(3)–C(17)	1.443(13)	C(9)–C(10)	1.539(12)
O(3)–C(22)	1.310(13)	C(9)–C(11)	1.562(15)
		C(10)–C(19)	1.574(17)
C(1)–C(2)	1.602(15)	C(11)–C(12)	1.539(14)
C(1)–C(10)	1.512(15)	C(12)–C(13)	1.548(15)
C(2)–C(3)	1.495(16)	C(13)–C(14)	1.501(14)
C(3)–C(4)	1.525(18)	C(13)–C(17)	1.547(14)
C(4)–C(5)	1.570(14)	C(13)–C(18)	1.525(15)
C(4)–C(20)	1.543(19)	C(14)–C(15)	1.495(17)
C(4)–C(21)	1.497(18)	C(15)–C(16)	1.573(15)
C(5)–C(6)	1.298(16)	C(16)–C(17)	1.558(18)
C(5)–C(10)	1.508(15)	C(22)–C(23)	1.541(17)

(*b*) Valency angles (°)

C(17)–O(3)–C(22)	114.4(9)	C(1)–C(10)–C(19)	106.9(10)
C(2)–C(1)–C(10)	112.3(8)	C(5)–C(10)–C(9)	111.3(9)
C(1)–C(2)–C(3)	113.6(9)	C(5)–C(10)–C(19)	109.0(8)
C(2)–C(3)–C(4)	118.3(9)	C(9)–C(10)–C(19)	109.8(8)
C(2)–C(3)–O(1)	119.2(12)	C(9)–C(11)–C(12)	112.5(9)
C(4)–C(3)–O(1)	122.4(9)	C(11)–C(12)–C(13)	109.6(8)
C(13)–C(4)–C(5)	111.1(9)	C(12)–C(13)–C(14)	108.2(8)
C(3)–C(4)–C(20)	106.3(10)	C(12)–C(13)–C(17)	113.1(8)
C(3)–C(4)–C(21)	109.9(9)	C(12)–C(13)–C(18)	110.5(9)
C(5)–C(4)–C(20)	109.7(9)	C(14)–C(13)–C(17)	98.4(8)
C(5)–C(4)–C(21)	111.1(10)	C(14)–C(13)–C(18)	115.3(8)
C(20)–C(4)–C(21)	108.8(10)	C(17)–C(13)–C(18)	110.9(8)
C(4)–C(5)–C(6)	119.1(9)	C(8)–C(14)–C(13)	113.9(8)
C(4)–C(5)–C(10)	118.5(9)	C(8)–C(14)–C(15)	118.9(9)
C(6)–C(5)–C(10)	122.2(9)	C(13)–C(14)–C(15)	105.2(9)
C(5)–C(6)–C(7)	125.4(10)	C(14)–C(15)–C(16)	103.5(9)
C(6)–C(7)–C(8)	112.9(9)	C(15)–C(16)–C(17)	104.1(9)
C(7)–C(8)–C(9)	111.8(9)	C(13)–C(17)–O(3)	112.1(9)
C(7)–C(8)–C(14)	110.8(8)	C(16)–C(17)–O(3)	110.9(9)
C(9)–C(8)–C(14)	110.8(8)	C(13)–C(17)–C(16)	103.6(8)
C(8)–C(9)–C(10)	112.2(8)	O(2)–C(22)–O(3)	125.4(11)
C(8)–C(9)–C(11)	113.2(8)	O(2)–C(22)–C(23)	124.4(10)
C(10)–C(9)–C(11)	114.1(9)	O(3)–C(22)–C(23)	110.2(9)
C(1)–C(10)–C(5)	110.3(9)	C(22)–C(23)–I	109.8(9)
C(1)–C(10)–C(9)	109.4(7)		

(*c*) Intermolecular contacts <4.0 Å

C(6) ··· O(1^{I})	3.523	C(19) ··· O(2^{IV})	3.412
C(6) ··· C(23^{II})	3.658	C(20) ··· O(1^{I})	3.675
C(7) ··· C(23^{II})	3.880	C(20) ··· C(23^{II})	3.987
C(7) ··· $\mathrm{I}^{\mathrm{III}}$	3.936	C(21) ··· O(1^{I})	3.626
C(11) ··· O(2^{IV})	3.768	C(21) ··· C(23^{V})	3.963
C(11) ··· C(16^{IV})	3.815	C(23) ··· O(1^{VI})	3.647
C(12) ··· C(16^{IV})	3.979	O(1) ··· $\mathrm{I}^{\mathrm{VII}}$	3.403
C(15) ··· C(18^{III})	3.892	O(2) ··· $\mathrm{I}^{\mathrm{VIII}}$	3.893
C(16) ··· C(18^{III})	3.722		

* Roman numerals as superscripts refer to the following equivalent positions relative to the reference molecule at x,y,z:

I	$1 - x, -\frac{1}{2} + y, 2 - z$	V	$x, y, 1 + z$
II	$1 - x, -\frac{1}{2} + y, 1 - z$	VI	$x, y, -1 + z$
III	$2 - x, -\frac{1}{2} + y, 1 - z$	VII	$-1 + x, y, 1 + z$
IV	$1 - x, \frac{1}{2} + y, 1 - z$	VIII	$-1 + x, y, z$

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[7] J. F. Chiang and S. H. Bauer, *J. Amer. Chem. Soc.*, 1969, **91**, 1898.

[8] C. Altona, H. J. Geise, and C. Romers, *Tetrahedron*, 1968, **24**, 13.

[9] B. Busetta, C. Courseille, J. M. Fornies-Marquina, and M. Hospital, *Cryst. Structure Comm.*, 1972, **1**, 43.

[10] D. H. R. Barton, A. J. Head, and P. J. May, *J. Chem. Soc.*, 1957, 935.

[11] *Chem. Soc. Special Publ.*, No. 18, 1965.

values and the crystal structure (Figure 3) contains discrete molecules separated by normal van der Waals contacts.

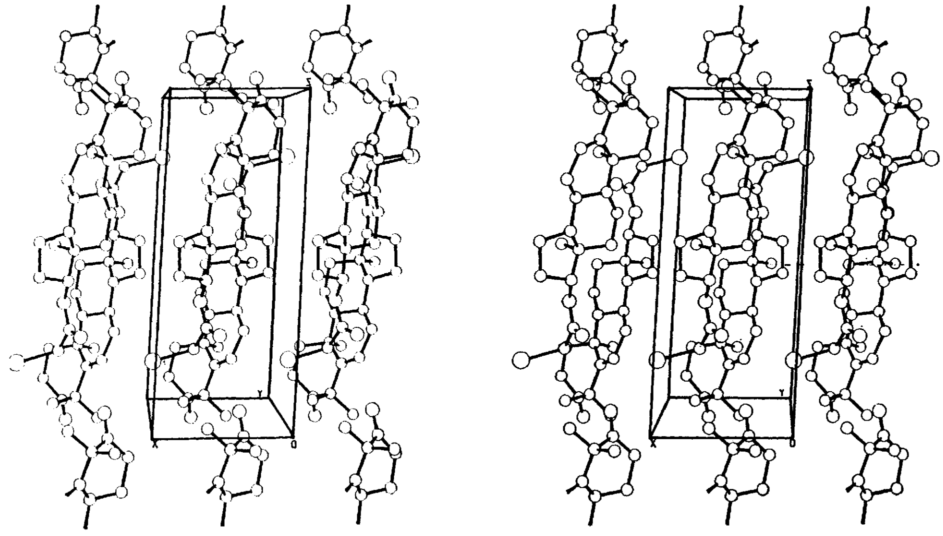

FIGURE 3 Stereodiagram of the crystal structure of (2)

EXPERIMENTAL

17β-Iodoacetoxy-4,4-dimethylandrost-5-en-3-one (2).—17β-Hydroxy-4,4-dimethylandrost-5-en-3-one and chloroacetic anhydride gave *17β-chloroacetoxy-4,4-dimethylandrost-5-en-3-one* as needles, m.p. 125—126 °C from light petroleum (b.p. 60—80 °C) (Found: C, 70.3; H, 8.5; Cl, 9.0. $C_{23}H_{33}ClO_3$ requires C, 70.4; H, 8.5; Cl, 9.0%). A solution of this chloroacetate in acetone containing an excess of potassium bromide was heated under reflux for 3 h and the product purified by chromatography on silica from light petroleum (b.p. 60—80 °C), followed by crystallisation from the same solvent to give *17β-bromoacetoxy-4,4-dimethylandrost-5-en-3-one* as needles m.p. 120—122 °C (Found: C, 63.9; H, 7.6; Br, 16.5. $C_{23}H_{33}O_3Br$ requires C, 63.2; H, 7.6; Br, 18.3%).

17β-Iodoacetoxy-4,4-dimethylandrost-5-en-3-one (2) was prepared similarly as needles, m.p. 99—100 °C from light petroleum (b.p. 60—80 °C) (Found: C, 57.5; H, 6.6; I, 25.2. $C_{23}H_{33}IO_3$ requires C, 57.0; H, 6.9; I, 26.2%).

Crystals of (2) are colourless prisms elongated along *c*, with {100}, {010}, and {001} well developed. Unit-cell and space-group data were obtained from various rotation, Weissenberg, and precession photographs; accurate unit-cell parameters were obtained by a least-squares procedure applied to 2θ values for 12 general reflections measured on a Hilger and Watts diffractometer.

Crystal for Data (2).—$C_{23}H_{33}IO_3$, $M = 484.4$. Monoclinic, $a = 6.394(2)$, $b = 11.303(4)$, $c = 15.566(4)$ Å, $\beta = 92.92(2)°$, $U = 1\,123.5$ Å^3, $D_m = 1.42$ (flotation), $Z = 2$, $D_c = 1.43$, $F(000) = 496$. $\lambda(\text{Cu-}K_\alpha) = 1.5418$ Å, $\mu(\text{Cu-}K_\alpha)$ 115.6 cm^{-1}. Space group $P2_1$ (C_2^2) or $P2_1/m$ (C_{2h}^2), from systematic absences: $0k0$ when k is odd. $P2_1$ from structure analysis.

The intensities of all reflections with $2\theta(\text{Cu-}K_\alpha) < 100°$ (minimum interplanar spacing 1.0 Å) were measured on our PDP 8I controlled Hilger and Watts four-circle diffractometer, with experimental conditions as outlined previously.[1] A crystal of dimensions $0.40 \times 0.10 \times 0.06$ mm was used for data collection. Of 1 211 possible reflections with $2\theta < 100°$, 1 065 had $I > 3\sigma(I)$ and were considered observed; the other reflections were excluded from all refinement calculations. Data were corrected for Lorentz polarization and absorption effects.[12]

Structure Analysis.—Although there are two possible space groups from a consideration of systematic absences, the fact that the crystals were optically active eliminated $P2_1/m$. A three-dimensional electron-density map phased on the iodine atom alone (with the y co-ordinate set at $\frac{1}{4}$ to fix the origin) exhibited the usual pseudosymmetry. The phasing from the iodine alone was sufficient to reveal the co-ordinates of all the remaining non-hydrogen atoms of both anantiomorphs. A set of co-ordinates corresponding to a molecule with the known absolute configuration was chosen. Refinement by full-matrix least-squares calculations of the non-hydrogen atoms with anisotropic thermal parameters reduces R to 0.067. The function minimised was $\Sigma w(F_o - F_c)^2$ with $w = 0$ for the unobserved reflections, and to the reciprocal of the variance in F_o as determined from counting statistics for observed reflections. Scattering factors were from ref. 13 with allowance being made for the anomalous dispersion of iodine. A three-dimensional difference synthesis at this stage revealed all 33 hydrogen atoms in positions close to those expected on geometrical grounds. Two final cycles of refinement, with the hydrogens included in the structure-factor calculations (in calculated positions assuming C–H 1.08 Å and U 0.075 Å^2) but excluded from the refinement, gave a final R of 0.046 for the 1 065 observed reflections and 0.073 for all 1 211 reflections. The final value of R' $\{=\Sigma w(F_o - F_c)^2/\Sigma wF_o^2\}$ was 0.041. The maximum ratio of shift to estimated standard deviation on the final cycle was 0.8.

Interatomic distances are in Table 2 and the co-ordinates of the atoms are in Table 3. Measured and calculated

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[12] P. Coppens, 'Crystallographic Computing,' ed. F. R. Ahmed, Munksgaard, Copenhagen, 1970.

[13] 'International Tables for *X*-Ray Crystallography,' Kynoch Press, Birmingham, 1962.

TABLE 3

Fractional co-ordinates ($\times 10^5$ for I, $\times 10^4$ for C and O, $\times 10^3$ for H), with estimates standard deviations in parentheses

Atom	x/a	y/b	z/c
I	1 035(17)	25 000 *	19 722(7)
O(1)	3 467(16)	3 032(7)	391(4)
O(2)	5 456(19)	1 199(9)	2 819(5)
O(3)	6 832(11)	2 519(8)	3 737(3)
C(1)	1 900(18)	2 651(13)	8 099(6)
C(2)	1 536(19)	3 030(12)	9 072(6)
C(3)	3 118(16)	2 525(13)	9 710(5)
C(4)	4 204(20)	1 374(10)	9 486(6)
C(5)	4 957(18)	1 406(9)	8 542(5)
C(6)	6 112(19)	549(10)	8 277(6)
C(7)	6 944(20)	453(10)	7 395(7)
C(8)	6 518(18)	1 547(9)	6 853(6)
C(9)	4 412(16)	2 069(8)	7 004(6)
C(10)	4 172(14)	2 389(11)	7 955(5)
C(11)	3 779(18)	3 084(10)	6 361(6)
C(12)	4 019(16)	2 725(10)	5 418(5)
C(13)	6 292(15)	2 308(9)	5 298(5)
C(14)	6 728(17)	1 268(9)	5 879(6)
C(15)	8 733(19)	753(10)	5 596(6)
C(16)	8 577(20)	924(10)	4 592(7)
C(17)	6 565(18)	1 685(10)	4 425(6)
C(18)	7 814(17)	3 341(9)	5 418(6)
C(19)	5 444(20)	3 550(10)	8 183(6)
C(20)	2 563(24)	385(11)	9 568(8)
C(21)	6 000(25)	1 144(13)	119(7)
C(22)	6 327(20)	2 106(10)	2 968(7)
C(23)	7 096(21)	2 953(12)	2 276(7)
H(11) †	140	337	766
H(12)	99	190	792
H(21)	162	398	912
H(22)	3	276	924
H(61)	654	−12	872
H(71)	861	32	745
H(72)	625	−30	707
H(81)	760	221	705
H(91)	329	140	686
H(111)	471	384	649
H(112)	216	331	643
H(121)	369	345	500
H(122)	293	203	524
H(141)	560	61	582
H(151)	9	123	590
H(152)	891	−15	579
H(161)	993	139	438
H(162)	848	10	428
H(171)	525	118	422
H(181)	763	375	602
H(182)	942	304	541
H(183)	755	396	492
H(191)	515	375	885
H(192)	703	339	813
H(193)	489	424	780
H(201)	122	53	913
H(202)	320	−47	940
H(203)	203	32	19
H(211)	715	179	12
H(212)	545	105	76
H(213)	674	29	998
H(231)	704	381	250
H(232)	607	283	172

* Held invariant to fix the origin. † The first number(s) in the label corresponds to that of the carbon atom to which the hydrogen is bonded.

structure amplitudes and thermal parameters have been deposited as Supplementary Publication SUP 22165 (6 pp.).*

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* See Notice to Authors No. 7 in *J.C.S. Perkin II*, 1977, Index issue.