Acta Cryst. (1970). B**26**, 1519

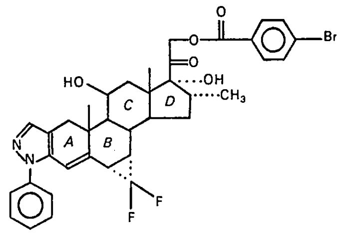
The Structure of 6α,7α-Difluoromethylene-16α-methyl-11β,17α,21-trihydroxypregn-4-en-20-one[3,2-*c*]-2′-phenylpyrazole 21-(*p*-Bromobenzoate)*

BY ARILD T. CHRISTENSEN

Syntex Research, Institute of Organic Chemistry, Palo Alto, California, U.S.A.

(*Received* 20 *June* 1969)

6α,7α-Difluoromethylene-16α-methyl-11β,17α,21-trihydroxypregn-4-en-20-one[3,2-*c*]-2′-phenylpyrazole 21-(*p*-bromobenzoate), $C_{37}H_{37}F_2N_2O_5Br$, crystallizes in space group $P2_12_12_1$ with $a=24{\cdot}107$ (0·020), $b=14{\cdot}451$ (0·008), $c=9{\cdot}942$ (0·007) Å, and four molecules in the unit cell. The structure, which was solved by application of the tangent formula to the heavy-atom phases, was refined by blockdiagonal least-squares to a final *R* value of 0·065. The refinement was based on 2650 reflections collected with an autcmatic diffractometer. The structure corresponds to the formula:



The *A* ring is puckered, the *B* ring is in the half-chair conformation and the *D* ring is a slightly distorted β-envelope. Bond distances and bond angles found in the cyclopropane moiety indicate significant contribution from double bond–no bond resonance.

Introduction

6α, 7α-Difluoromethylene-16α-methyl-11β, 17α,21-trihydroxypregn-4-en-20-one[3,2-*c*]-2′-phenylpyrazole is a potent topical antiinflammatory agent (Harrison, Beard, Kirkham, Lewis, Jamieson, Rooks & Fried, 1968); the present work was carried out as part of a program undertaken at this laboratory to investigate the correlation between biological activity and structure.

Experimental

The heavy-atom derivative was prepared by Dr Ian Harrison, who also supplied the crystals. The compound crystallizes from acetone in prismatic needles, elongated along the *c* axis. Preliminary precession photographs indicated orthorombic symmetry. The systematic extinctions, *h*00, 0*k*0 and 00*l* with *h*, *k* or *l* odd, are consistent with space group $P2_12_12_1$. Cell dimensions were determined on a Picker diffractometer with a full-circle goniostat, using Cu radiation. The cell parameters and direction cosines of the reciprocal axes relative to the instrument coordinate system were refined by least-squares.

The refinement, which was based on nine strong reflections in the 2θ range 37 to 88°, gave the following results (estimated standard deviations in parentheses): $a=24{\cdot}107$ (0·020), $b=14{\cdot}451$ (0·008), $c=9{\cdot}942$ (0·007) Å (λ Cu $K\alpha=1{\cdot}54051$ Å). These values give a calculated density of 1·33 g.cm^{-3} for $Z=4$. The density observed by flotation in an aqueous solution of KI was 1·33 g.cm^{-3}.

The crystal used for determination of cell parameters and collection of intensity data had dimensions of approximately $0{\cdot}35\times0{\cdot}18\times0{\cdot}18$ mm. The calculated linear absorption coefficient for copper radiation is 22 cm^{-1}. No correction for absorption was applied.

A total of 3366 unique reflections was scanned by use of the 2θ–θ technique; of these, 2650 which had an intensity greater than three times their e.s.d. were recorded as 'observed'. Two standard reflections, which were measured at regular intervals during the course of the data collection, tapered off to approximately 95% of the original intensity.

Determination and refinement of the structure

A sharpened three-dimensional Patterson function clearly revealed the position of the Br atom. However, a subsequent Fourier synthesis based on the phase angles due to the Br atom proved difficult to interpret. This is not surprising, as the Br atom does not represent more than about 39% of the scattering power of the molecule.

* Syntex contribution No. 361.

Recent studies (Karle, 1968) suggested that application of the tangent formula (Karle & Hauptman, 1956) would be the best approach to solving the structure. All reflections with E (the normalized structure factor) $\geq 1{\cdot}5$ were assigned phase angles computed from the Br atom parameters; weight factors giving a measure of the reliability of the phases were also computed (Sim, 1960). Using the weights and the E values as criteria, 260 reflections were selected ($E \geq 1{\cdot}6$). These phases were refined by three cycles of the tangent formula.

An E map calculated from the refined phases rendered the whole structure, with the exception of the atoms belonging to the phenyl group attached to the N atom. These atoms were located from a Fourier synthesis with phases determined by the atomic positions already found.

The positional parameters of the structure were refined by two cycles of block-diagonal least squares with isotropic temperature factors set at 4 Å^2. At this stage the R index was 0·20, and anisotropic temperature parameters were introduced. After seven more cycles the refinement was terminated. The last shifts were all well below the corresponding e.s.d.'s, and the final R value was 0·065 for all observed reflections. In the three last cycles the hydrogen atoms, except those on the methyl and hydroxyl groups, were included in the structure factor calculations with isotropic temperature factors of 4·5 Å^2. The hydrogen positions (Table 1) were calculated from the carbon atom positions, assuming a C–H distance of 1·07 Å.

The positional and thermal parameters for the final structure are given in Tables 2 and 3 respectively.

Table 1. *Assumed hydrogen atom positions*

Hydrogen atom at	x	y	z
C(1)	1·0032	0·1927	0·6668
	1·0017	0·0793	0·7323
C(4)	0·1264	0·0378	0·5041
C(6)	0·0146	0·0043	0·2819
C(7)	1·0306	−0·0683	0·2855
C(8)	0·9161	0·0194	0·2986
C(9)	0·9533	−0·0484	0·5684
C(11)	0·8894	0·0383	0·6802
C(12)	0·8478	−0·1030	0·6197
	0·7971	−0·0182	0·5853
C(14)	0·9113	−0·1570	0·4403
C(15)	0·8821	−0·1245	0·1509
	0·9129	−0·2220	0·2271
C(16)	0·7978	−0·1924	0·1730
C(22)	0·7109	−0·2272	0·5686
	0·7274	−0·1091	0·5883
C(27)	0·5532	−0·1652	0·5490
C(28)	0·4549	−0·1308	0·5455
C(30)	0·4868	0·1357	0·3786
C(31)	0·5859	0·1071	0·3884
C(39)	0·0234	0·2835	0·8434
C(43)	0·1946	0·3234	0·6315
C(44)	0·2983	0·3126	0·6199
C(45)	0·3430	0·1629	0·6290
C(46)	0·2877	0·0216	0·7050
C(47)	0·1888	0·0347	0·7137

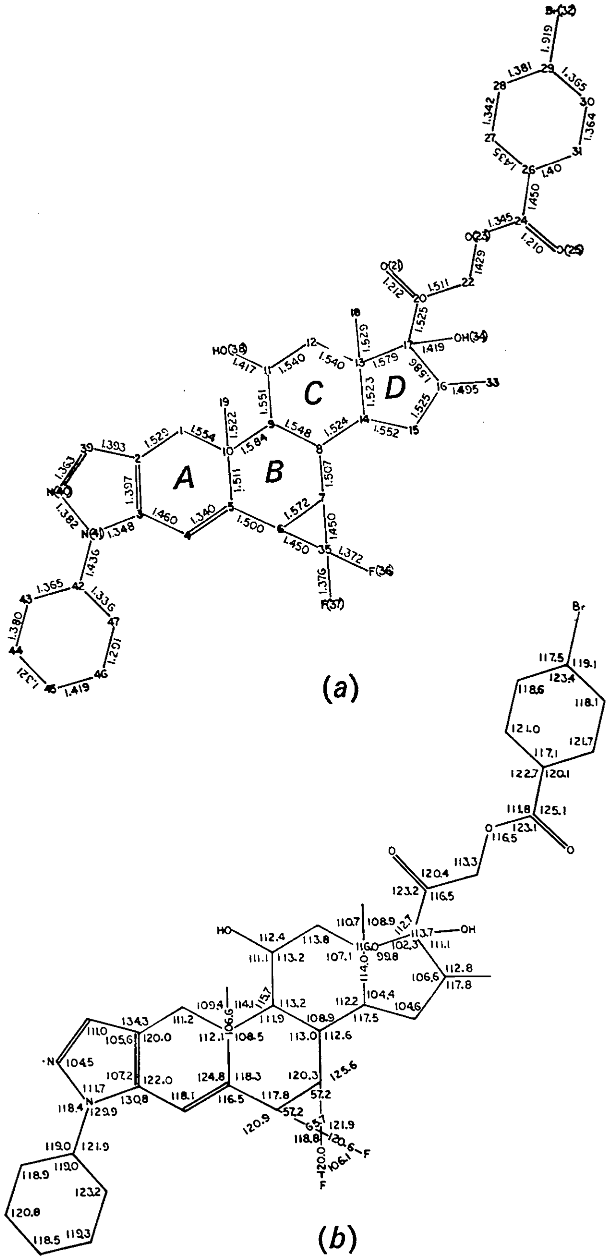


Fig. 1. (*a*) Bond lengths, (*b*) bond angles.

Table 2. *Final positional parameters and their standard deviations*

The e.s.d. (in parentheses) apply to the least significant digits.

	x	y	z
C(1)	0·98208 (27)	0·12513 (44)	0·65826 (57)
C(2)	1·03710 (26)	0·17140 (46)	0·69457 (68)
C(3)	1·08661 (29)	0·13829 (44)	0·63954 (69)
C(4)	1·08737 (27)	0·06803 (44)	0·53404 (68)
C(5)	1·03894 (28)	0·04335 (41)	0·47858 (64)
C(6)	1·04235 (28)	−0·01952 (45)	0·35882 (61)
C(7)	0·98677 (27)	−0·06219 (47)	0·30397 (71)
C(8)	0·93192 (25)	−0·03415 (43)	0·36425 (60)
C(9)	0·93765 (25)	0·00735 (40)	0·50712 (59)
C(10)	0·98344 (25)	0·08587 (40)	0·51280 (58)
C(11)	0·88111 (24)	0·03182 (42)	0·57254 (61)

Table 2 (*cont.*)

	x	y	z
C(12)	0·83713 (25)	−0·04454 (44)	0·55482 (62)
C(13)	0·83275 (27)	−0·08172 (39)	0·41006 (61)
C(14)	0·89049 (28)	−0·11375 (45)	0·36885 (61)
C(15)	0·88097 (30)	−0·16927 (49)	0·23727 (69)
C(16)	0·82433 (31)	−0·21450 (50)	0·25584 (80)
C(17)	0·79971 (29)	−0·17526 (41)	0·39228 (66)
C(18)	0·80773 (33)	−0·00866 (45)	0·31677 (71)
C(19)	0·97421 (31)	0·16423 (44)	0·41294 (66)
C(20)	0·73708 (31)	−0·16077 (48)	0·38799 (81)
O(21)	0·71126 (20)	−0·15178 (37)	0·28420 (52)
C(22)	0·70737 (31)	−0·15994 (55)	0·52185 (83)
O(23)	0·64998 (19)	−0·13630 (33)	0·51128 (53)
C(24)	0·63835 (30)	−0·04778 (53)	0·48056 (71)
O(25)	0·67374 (22)	0·01014 (36)	0·46185 (58)
C(26)	0·57905 (28)	−0·03144 (48)	0·47379 (61)
C(27)	0·53893 (33)	−0·09863 (52)	0·51662 (74)
C(28)	0·48441 (31)	−0·08035 (59)	0·51145 (85)
C(29)	0·46738 (32)	0·00350 (66)	0·45910 (83)
C(30)	0·50323 (36)	0·07071 (60)	0·41716 (82)
C(31)	0·55873 (34)	0·05334 (51)	0·42597 (76)
Br(32)	0·38906 (4)	0·02597 (11)	0·44866 (14)
C(33)	0·82108 (42)	−0·31760 (54)	0·24694 (130)
O(34)	0·80768 (24)	−0·23873 (36)	0·49941 (192)
C(35)	1·02903 (20)	−0·11704 (31)	0·37049 (56)
F(36)	1·02034 (30)	−0·15644 (43)	0·49427 (69)
F(37)	1·05969 (18)	−0·17999 (25)	0·29808 (43)
O(38)	0·86198 (18)	0·11943 (28)	0·52843 (52)
C(39)	1·05260 (19)	0·24032 (29)	0·78502 (49)
N(40)	1·10884 (30)	0·24868 (47)	0·79115 (74)
N(41)	1·12837 (25)	0·18538 (38)	0·69839 (63)
C(42)	1·18723 (22)	0·17815 (37)	0·67873 (61)
C(43)	1·21682 (30)	0·25610 (48)	0·64924 (73)
C(44)	1·27382 (41)	0·25003 (60)	0·63922 (95)
C(45)	1·29917 (43)	0·16920 (73)	0·64720 (119)
C(46)	1·26713 (43)	0·08976 (75)	0·67885 (134)
C(47)	1·21400 (42)	0·09764 (85)	0·69070 (164)

Table 3. *Final thermal parameters, with E.S.D. in parentheses*

The temperature factor has the form $\exp[-\frac{1}{4}(B_{11}h^2a^{*2}\ldots+2B_{12}hka^*b^*\ldots)]$.

	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
C(1)	4·83 (29)	4·03 (26)	2·40 (21)	0·15 (24)	−0·26 (20)	−0·77 (20)
C(2)	4·00 (26)	4·43 (28)	3·38 (25)	0·16 (24)	0·02 (23)	−0·26 (24)
C(3)	5·17 (32)	3·41 (25)	3·44 (27)	0·05 (25)	0·07 (25)	−0·38 (24)
C(4)	4·26 (26)	3·85 (25)	3·70 (28)	−0·68 (23)	0·37 (24)	−0·61 (24)
C(5)	5·29 (30)	3·15 (23)	3·17 (25)	−0·37 (23)	0·61 (23)	0·01 (22)
C(6)	5·32 (30)	3·99 (26)	2·63 (23)	0·11 (24)	0·22 (22)	−0·57 (22)
C(7)	4·48 (28)	4·40 (29)	3·25 (26)	−0·27 (25)	0·54 (24)	−0·26 (25)
C(8)	4·27 (25)	3·80 (25)	2·97 (23)	−0·26 (23)	−0·16 (21)	0·29 (22)
C(9)	4·67 (27)	3·40 (23)	2·57 (21)	−0·04 (21)	−0·00 (19)	−0·28 (20)
C(10)	4·37 (26)	3·67 (24)	2·26 (21)	0·18 (21)	0·23 (20)	−0·19 (20)
C(11)	4·39 (26)	3·83 (25)	2·84 (23)	−0·06 (22)	0·42 (21)	0·31 (22)
C(12)	4·17 (25)	4·30 (26)	2·84 (24)	−0·05 (23)	0·37 (21)	−0·28 (23)
C(13)	4·59 (27)	3·09 (23)	2·67 (23)	0·00 (22)	−0·31 (21)	0·19 (20)
C(14)	4·90 (28)	3·83 (27)	2·59 (23)	0·00 (24)	−0·09 (23)	−0·05 (21)
C(15)	5·24 (33)	4·70 (30)	3·59 (27)	−0·07 (27)	0·03 (25)	−1·02 (25)
C(16)	5·42 (35)	4·81 (30)	4·58 (33)	−0·37 (28)	−0·39 (29)	−0·66 (28)
C(17)	5·11 (31)	3·25 (22)	3·14 (27)	−0·15 (23)	−0·21 (23)	−0·01 (22)
C(18)	6·68 (36)	3·72 (27)	3·57 (28)	0·20 (27)	−0·81 (27)	0·48 (25)
C(19)	6·56 (36)	3·47 (26)	3·16 (25)	−0·74 (27)	0·07 (26)	0·81 (22)
C(20)	4·91 (32)	3·92 (28)	4·93 (37)	−0·36 (26)	−0·66 (28)	0·40 (29)
O(21)	5·38 (22)	6·70 (25)	3·67 (21)	0·03 (20)	−1·20 (18)	−0·67 (21)
C(22)	4·94 (31)	5·82 (34)	4·52 (35)	0·39 (29)	−0·05 (28)	1·06 (32)
O(23)	4·87 (20)	5·14 (21)	4·84 (22)	0·17 (17)	0·51 (18)	0·56 (20)
C(24)	5·14 (33)	5·68 (35)	3·66 (28)	−0·87 (29)	0·07 (26)	−0·90 (28)
O(25)	6·06 (24)	5·50 (23)	5·63 (26)	−1·33 (20)	0·59 (21)	−0·71 (23)
C(26)	4·92 (30)	5·13 (30)	2·57 (24)	−0·43 (27)	0·10 (22)	−0·76 (25)
C(27)	6·15 (36)	5·31 (33)	3·49 (28)	−1·45 (30)	0·59 (28)	−0·54 (27)
C(28)	4·98 (32)	6·77 (39)	4·74 (35)	−1·11 (30)	0·55 (29)	−1·35 (34)
C(29)	5·55 (32)	7·60 (45)	4·84 (35)	0·64 (33)	−0·29 (30)	−1·85 (36)
C(30)	5·84 (38)	5·99 (39)	4·38 (34)	0·53 (33)	0·02 (31)	−0·44 (33)
C(31)	6·94 (39)	4·82 (32)	3·75 (30)	−0·76 (29)	0·24 (29)	−0·72 (27)
Br(32)	5·50 (4)	14·27 (10)	9·19 (6)	1·92 (5)	−0·26 (4)	−3·02 (7)
C(33)	8·64 (23)	4·10 (19)	10·47 (21)	−1·25 (18)	3·56 (19)	−2·10 (19)
O(34)	5·53 (33)	4·36 (25)	4·90 (28)	−0·48 (26)	−0·73 (27)	1·46 (23)
C(35)	5·73 (22)	3·60 (15)	3·32 (18)	0·35 (15)	1·24 (17)	−0·86 (15)
F(36)	6·91 (21)	4·25 (17)	4·83 (22)	0·56 (16)	1·30 (19)	1·00 (18)
F(37)	6·08 (21)	4·89 (17)	6·68 (21)	−0·14 (17)	1·79 (19)	−2·15 (17)
O(38)	5·56 (31)	3·65 (29)	4·40 (29)	0·75 (26)	−0·08 (26)	−0·37 (27)
C(39)	5·10 (27)	4·22 (25)	4·13 (26)	−0·06 (22)	0·21 (24)	−0·64 (23)
N(40)	5·35 (22)	4·38 (22)	4·39 (24)	0·08 (19)	−0·04 (21)	−1·17 (21)
N(41)	4·22 (32)	3·92 (29)	4·30 (30)	−0·18 (27)	0·17 (26)	−0·63 (26)
C(42)	5·17 (52)	4·47 (41)	4·04 (41)	−1·03 (40)	0·61 (40)	−0·81 (37)
C(43)	8·15 (57)	5·40 (58)	5·80 (60)	−2·15 (50)	2·14 (49)	−1·58 (53)
C(44)	8·20 (52)	8·07 (51)	8·23 (76)	−3·79 (43)	3·34 (53)	−3·19 (56)
C(45)	6·99 (43)	8·47 (65)	10·72 (92)	−1·84 (48)	2·88 (57)	−4·18 (75)
C(46)	6·05 (43)	8·93 (40)	11·84 (60)	0·88 (37)	0·59 (46)	−1·40 (46)
C(47)	6·22 (43)	5·90 (41)	8·69 (61)	−0·45 (37)	1·66 (46)	−0·00 (47)

Observed and calculated structure factors are given in Table 4.

Computing procedures

The least-squares routine for calculating cell dimensions and diffractometer coordinates, the diffractometer setting program and the programs for calculating Fourier summations are referenced in a previous paper (Hope & Christensen, 1968).

The program for cyclic phase refinement by the tangent formula was that of Brenner & Gum (1968). The whole phase refinement took only 4 minutes on a CDC 3800 computer, and in many cases the method will represent a substantial saving in computer time compared with the more conventional method of successive Fourier summations. (This has proved to be the case for the analysis of two other structures, $C_{23}O_3Cl_2H_{30}Br$ and $C_{32}O_4F_4H_{33}Br$, recently completed in this laboratory.)

The least-squares program was a block-diagonal version of the full-matrix routine written by P. K. Gantzel, R. A. Sparks and K. N. Trueblood. The program, which

Table 4. *Observed and calculated structure factors and phase angles*

The columns are l, $10F_o$, $10F_c$ and the phase angle.

[illegible]			

Table 4 (*cont.*)

[illegible]

minimizes the weighted sum of $(KF_o - G|F_c|)^2$, originally had provision for applying partial shifts, the shifts being the shift called for multiplied by a constant. This version was revised by A. T. Christensen so the applied shifts were given by $\Delta' q_n = k_1 \Delta q_n + k_2 \Delta q_{n-1}$, where Δq_n is the shift called for in the nth cycle (Sparks, 1961, and references cited therein). The values used for k_1 and k_2 were 0·8 and 0·2 respectively, except

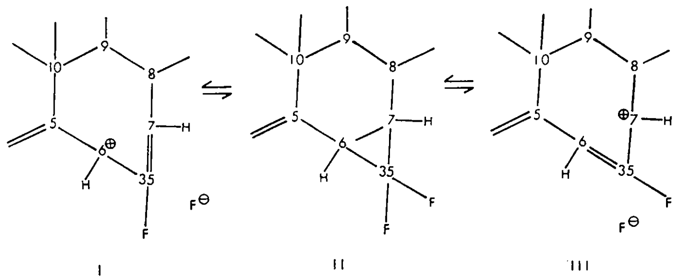


Fig. 2. Resonance structures.

for the two last cycles where the values 1·0 and 0·0 were used. The weighting scheme used was that of Hughes (1941).

The atomic form factors were those given by Hanson, Herman, Lea & Skillman (1964). The anisotropic temperature factors are of the form: exp $[-(h^2\beta_{11}+k^2\beta_{22}+l^2\beta_{33}+hk\beta_{12}+hl\beta_{13}+kl\beta_{23})]$. The R index defined by $R=\sum||F_o|-|F_c||/\sum|F_o|$ included observed reflections only.

The structure

Interatomic distances and angles calculated from the final positional parameters are given in Tables 5 and 6 respectively and are also shown in Fig. 1. Torsion angles and fold angles are given in Table 7.

Table 5. *Interatomic distances*

E.s.d. × 1000 are given in parentheses.
For identification of atoms see Fig. 1.

Atoms	Distance	Atoms	Distance
1—2	1·529 (9) Å	16–33	1·495 (11) Å
2—3	1·397 (10)	17–20	1·525 (11)
2–39	1·393 (10)	17–34	1·419 (8)
3—4	1·460 (10)	20–21	1·212 (10)
3–41	1·348 (9)	20–22	1·511 (12)

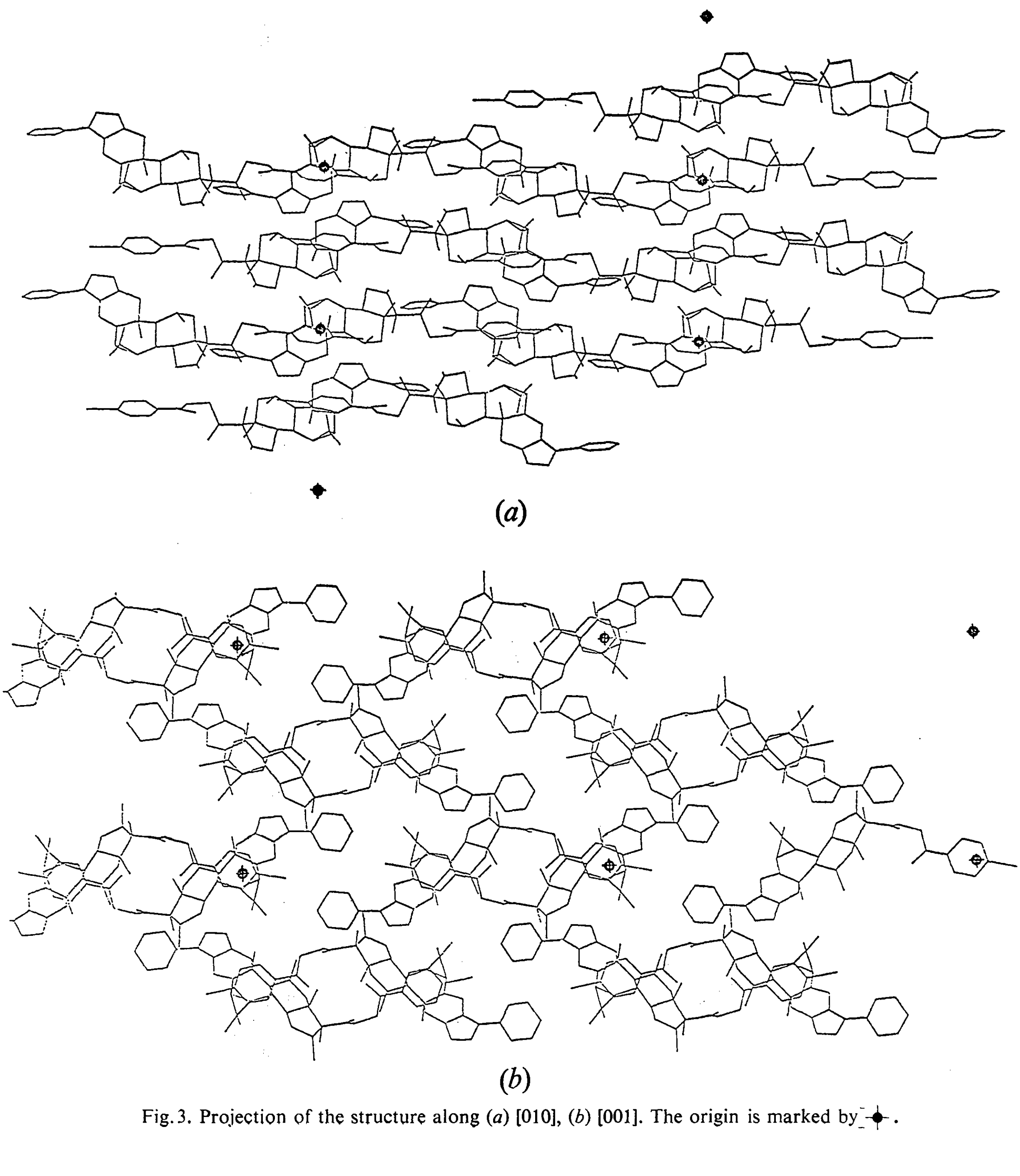


Fig. 3. Projection of the structure along (*a*) [010], (*b*) [001]. The origin is marked by ✦.

Table 5 (*cont.*)

Atoms	Distance	Atoms	Distance
4—5	1·340 (10) Å	22–23	1·429 (9) Å
5—6	1·500 (9)	23–24	1·345 (9)
5–10	1·511 (9)	24–25	1·210 (9)
6—7	1·572 (10)	24–26	1·450 (10)
6–35	1·450 (10)	26–27	1·435 (11)
7—8	1·507 (9)	27–28	1·342 (12)
7–35	1·450 (10)	28–29	1·381 (13)
8—9	1·548 (9)	29–30	1·365 (13)
8–14	1·524 (9)	29–32	1·919 (9)
9–10	1·584 (9)	30–31	1·364 (12)
9–11	1·551 (9)	31–26	1·403 (11)
10—1	1·554 (9)	35–36	1·372 (8)
10–19	1·522 (9)	35–37	1·376 (8)
11–12	1·540 (9)	39–40	1·363 (10)
11–38	1·417 (8)	40–41	1·382 (9)
12–13	1·540 (9)	41–42	1·436 (10)
13–14	1·523 (10)	42–43	1·365 (12)
13–17	1·579 (9)	43–44	1·380 (15)
13–18	1·529 (10)	44–45	1·321 (16)
14–15	1·552 (10)	45–46	1·419 (17)
15–16	1·525 (11)	46–47	1·291 (14)
16–17	1·586 (11)	47–42	1·336 (12)

Table 6. *Bond angles*

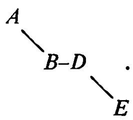
E.s.d.'s are given in parentheses.
For identification of atoms see Fig. 1.

Atoms	Angle	Atoms	Angle
1—2—3	120·0 (0·6)°	15–14–13	104·4 (0·5)°
1—2–39	134·3 (0·6)	15–16–33	117·8 (0·7)
1–10–19	109·4 (0·5)	16–15–14	104·6 (0·6)
2—3—4	122·0 (0·6)	16–17–34	111·1 (0·5)
2–39–40	111·0 (0·6)	17–16–15	106·6 (0·6)
3—2–39	105·6 (0·6)	17–16–33	112·8 (0·7)
3—4—5	118·1 (0·6)	17–20–21	123·2 (0·7)

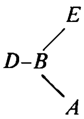
Table 0 (*cont.*)

Atoms	Angle	Atoms	Angle
3–41–42	129·9 (0·6)°	17–20–22	116·5 (0·7)°
4—5—6	116·1 (0·6)	18–13–14	114·0 (0·6)
4—5–10	124·8 (0·6)	18–13–17	108·9 (0·5)
5—6—7	117·8 (0·6)	20–17–13	112·7 (0·5)
5—6–35	120·9 (0·6)	20–17–34	104·1 (0·6)
5–10—1	112·1 (0·5)	20–17–34	104·1 (0·6)
5–10—9	108·5 (0·5)	20–22–23	113·3 (0·7)
5–10–19	106·6 (0·5)	21–20–22	120·4 (0·7)
6—7—8	120·3 (0·6)	22–23–24	116·5 (0·6)
6—7–35	57·2 (0·4)	23–24–25	123·1 (0·7)
6–35—7	65·7 (0·5)	23–24–26	111·8 (0·6)
6–35–36	120·6 (0·6)	24–26–27	122·7 (0·7)
6–35–37	118·8 (0·6)	24–26–31	120·1 (0·7)
7—6–35	57·2 (0·5)	25–24–26	125·1 (0·7)
7—8—9	113·0 (0·5)	26–27–28	121·0 (0·7)
7—8–14	112·6 (0·6)	27–26–31	117·1 (0·7)
7–35–36	121·9 (0·6)	27–28–29	118·6 (0·8)
7–35–37	120·0 (0·6)	28–29–30	123·4 (0·9)
8—7–35	125·6 (0·6)	29–30–31	118·1 (0·8)
8—9–10	111·9 (0·5)	30–31–26	121·7 (0·7)
8—9–11	113·2 (0·5)	32–29–28	117·5 (0·7)
8–14–15	117·5 (0·5)	32–29–30	119·1 (0·7)
9—8–14	108·9 (0·5)	34–17–13	113·7 (0·5)
9–10–19	114·1 (0·5)	36–35–37	106·1 (0·5)
9–11–12	113·2 (0·5)	39–40–41	104·5 (0·6)
9–11–38	111·1 (0·5)	40–41—3	111·7 (0·6)
10—1—2	111·2 (0·5)	40–41–42	118·4 (0·6)
10—5—6	118·3 (0·6)	41—3—2	107·2 (0·6)
10—9–11	115·7 (0·5)	41—3—4	130·8 (0·7)
11–12–13	113·8 (0·5)	41–42–43	119·0 (0·7)
12–11–38	112·4 (0·5)	41–42–47	121·9 (0·7)
12–13–14	107·1 (0·5)	42–43–44	118·9 (0·8)
12–13–17	116·0 (0·5)	43–44–45	120·8 (1·0)
12–13–18	110·7 (0·5)	44–45–46	118·5 (1·0)
13–14—8	112·2 (0·5)	45–46–47	119·3 (1·1)
13–17–16	102·3 (0·5)	46–47–42	123·2 (0·9)
14–13–17	99·8 (0·5)	47–42–43	119·0 (0·8)

Table 7. *Torsion and fold angles*

Torsion angle (*T*), 

. Viewed along *B–D* the angle is that through which *A–B* must be rotated to cover *D–E*, a positive rotation being clockwise.

Fold angle (*F*), 

. The fold is along *D–B* and the angle is positive for *B* below *ADE* when viewed as in the diagram

A	*B*	*D*	*E*	Angle	*A*	*B*	*D*	*E*	Angle
1	2	3	4	8·25 (*T*)	13	14	8	9	62·45 (*T*)
2	3	4	5	7·84 (*T*)	17	13	14	15	46·73 (*T*)
3	4	5	10	2·88 (*T*)	13	14	15	16	−33·31 (*T*)
4	5	10	1	−27·15 (*T*)	14	15	16	17	5·76 (*T*)
5	10	1	2	38·79 (*T*)	15	16	17	13	22·37 (*T*)
5	6	7	8	4·65 (*T*)	16	17	13	14	−41·83 (*T*)
5	6	35	36	−8·89 (*T*)	39	2	3	41	1·04 (*T*)
5	6	35	37	−142·69 (*T*)	2	3	41	40	0·24 (*T*)
6	7	8	9	−20·80 (*T*)	3	41	40	39	−1·43 (*T*)
8	7	35	36	6·08 (*T*)	41	40	39	2	2·10 (*T*)
8	7	35	37	143·51 (*T*)	40	39	2	3	−2·00 (*T*)
7	8	9	10	49·91 (*T*)	35	7	6	5	−69·49 (*F*)
8	9	10	5	−62·71 (*T*)	35	7	6	8	−64·84 (*F*)
9	10	5	6	46·54 (*T*)	9	8	11	12	−40·41 (*F*)
14	8	9	11	−51·26 (*T*)	9	8	11	14	−47·67 (*F*)
8	9	11	12	44·82 (*T*)	13	12	14	8	56·27 (*F*)
9	11	12	13	−47·32 (*T*)	13	12	14	11	48·65 (*F*)
11	12	13	14	55·14 (*T*)	15	17	14	13	46·70 (*F*)
12	13	14	8	−63·73 (*T*)	16	17	14	13	43·00 (*F*)

Inspection of Table 3 shows that the majority of the B_{ii} are in the range commonly encountered. The rather large values for atoms C(43) to C(47), however, suggest a slight degree of disorder, perhaps also explaining the somewhat abnormal C–C distances found in this phenyl group [(*e.g.* C(44)−C(45) and C(46)−C(47)]. Other atoms with large B_{ii} are C(29) and Br(32). As the structure was refined by the block-diagonal approximation, the large values of B_{22} and B_{33} for the Br atom could be due to the correlation with the scale factor. (In the course of data collection index *h* was changed least rapidly, always increasing; so the small systematic change in the intensity scale should have manifested itself in B_{11} rather than in B_{22} and B_{33}.)

The conformation of the *A* ring is puckered with C(1) and C(10) displaced in opposite directions (about 0·33 and 0·20-Å respectively) from the plane through the 2,4-diene system. The pyrazole moiety is planar within experimental accuracy. Comparison with bond distances found in pyrazole (Ehrlich, 1960) and tetrakispyrazole-nickel chloride (Reimann, Mighell & Mauer, 1967) shows that the increased conjugation from the phenyl group and *A*-ring system has led to more uniform bond distances in the pyrazole ring.

The *B* ring is in the half-chair conformation with atoms C(9) and C(10) displaced 0·426 and 0·345 Å respectively from the least-squares plane through C(5), C(6), C(7) and C(8) (Table 8); these latter four atoms are coplanar to within 0·019 Å. The torsion angle C(5)–C(6)–C(7)–C(8) is 4°. The fold angle between the above plane and the cyclopropane ring is 67°.

The bond distances in the cyclopropane moiety deviate significantly from expected values. The distances C(35)–C(6) and C(35)–C(7) average 1·45 Å, significantly shorter than the value 1·51 Å reported by Bastiansen, Fritsch & Hedberg (1964) in the electron diffraction study of cyclopropane. In 6*β*,7*β*-methylene-17*β*-hydroxyandrost-4-en-3-one (Christensen, to be published) the C(6)–C(7) distance was found to be 1·55; the other two distances in the cyclopropane moiety averaged 1·52 Å. The two C–F distances C(35)–F(36) and C(35)–F(37) of 1·375 Å are about 0·04 Å longer than expected (accepted values are 1·38 Å for C–mono-F and 1·33 Å for C–poly-F bond lengths).

The angle F(36)–C(35)–F(37) is 106° while the H–C–H angle in cyclopropane is reported to be 115° (Bastiansen *et al.*, 1964).

The above observations are consistent with a significant contribution from the double bond–no bond resonance form illustrated in Fig. 2, the two resonance structures I and III being stabilized by delocalization of the positive charge [indicated at C(6) and C(7)] over the unsaturated part of the molecule. A review of double bond–no bond resonance is given by Hine (1963).

The *C* ring has the chair conformation, and, as reported by Cooper & Norton (1968) in their paper on 12*α*-bromo-11*β*-hydroxyprogesterone, the 11*β*-hydroxyl group is forced 'outward' by the 18*β*- and 19*β*-methyl groups. This causes an additional flattening of the

Table 8. *Least-squares planes*

Atom number	2*	3*	4*	5*	1	10					
Plane-to-atom distances (in Å)	0·017	−0·033	0·033	−0·017	0·332	−0·199					
Equation of plane	$-0.9601x-10.8308y+6.5698z=1.6942$										
Atom number	5*	6*	7*	8*	9	10					
Plane-to-atom distances (in Å)	0·011	−0·022	0·022	−0·011	0·421	−0·348					
Equation of plane	$1.7004x-11.2291y+6.2185z=4.2447$										
Atom number	6*	7*	35*	36	37						
Plane-to-atom distances (in Å)	0·000	0·000	0·000	−1·079	1·116						
Equation of plane	$10.5682x-2.4932y-8.7695z=7.9178$										
Atom number	14*	15*	16*	17*	13						
Plane-to-atom distances (in Å)	0·022	−0·035	0·034	−0·022	−0·702						
Equation of plane	$9.4605x-11.4896y+4.597z=11.4050$										
Atom number	2*	3*	39*	40*	41*	42*	4*	5*	1	10	
Plane-to-atom distances (in Å)	0·056	0·057	−0·028	−0·035	0·000	−0·019	0·063	−0·095	0·251	−0·341	
Equation of plane	$0.6920x-10.4206y+6.8822z=3.6554$										
Atom number	2*	3*	39*	40*	41*						
Plane-to-atom distances (in Å)	0·008	−0·002	−0·011	0·009	−0·005						
Equation of plane	$1.0823x-9.9670y+7.1850z=4.3959$										
Atom number	24*	26*	27*	28*	29*	30*	31*	32*	25	22	23
Plane-to-atom distances (in Å)	−0·007	−0·008	−0·006	0·021	−0·003	0·002	0·013	−0·012	0·159	−0·216	−0·210
Equation of plane	$0.4832x+5.5411y+9.1799z=4.4627$										

* Denotes atoms defining the plane.

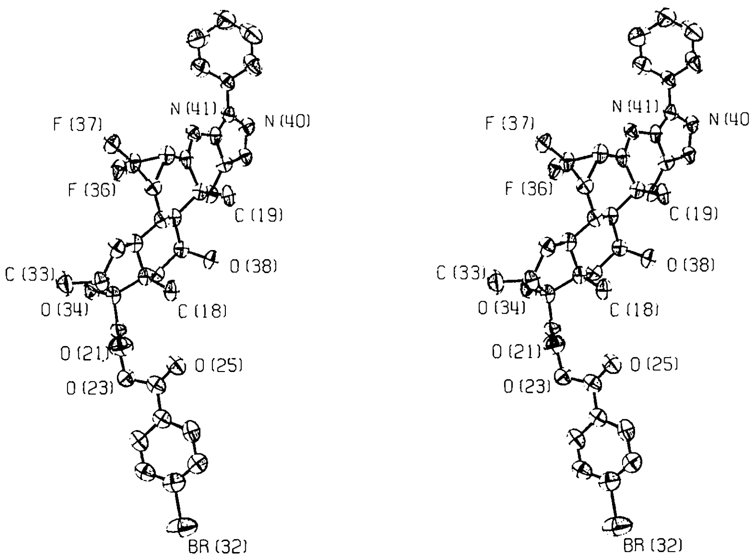


Fig. 4. A stereoscopic representation of the molecule, drawn with *ORTEP* (Johnson, 1965).

C ring [additional to the overall flattening observed in both simple six-membered rings (Davis & Hassel, 1963) and in steroids, *e.g.* Norton (1965) and High & Kraut (1966)]. The average C–C–C angle in the C ring is 111·4°. The short intramolecular distances C(19)–O(38) and C(18)–O(38) of 3·10 and 3·01 Å respectively are 0·3 to 0·4 Å shorter than the sum of van der Waals radii (CH_3, 2·0 and O, 1·4 Å), and indicate the strong steric forces present.

The torsion angle C(14)–C(15)–C(16)–C(17) is 5·5°, indicating that the *D* ring is a slightly distorted *β*-envelope (Brutcher & Leopold, 1966); C(13) is displaced 0·707 Å from the least-squares plane through C(14), C(15), C(16) and C(17). The fold angle about C(14)–C(17) is near 45°.

The absolute configuration of the molecule was assigned from the geometry around C(13).

All intermolecular distances are normal; the shortest distances involving the hydroxy groups are O(34)–N(40) of 2·90 Å, which corresponds to the sum of van der Waals radii, and O(38)–O(21) of 3·13 Å which is too large for hydrogen bonding. The packing is illustrated in Fig. 3.

A stereoscopic representation of the molecule is presented in Fig. 4.

The author wishes to thank Drs J. Fried, I. Harrison, P. Nelson & K. Untch of this Institute for helpful discussion on the chemical aspects of the molecule, and Dr R. E. Marsh of California Institute of Technology for preparing the *ORTEP* stereo drawing.

References

Bastiansen, O., Fritsch, F. N. & Hedberg, K. (1964). *Acta Cryst.* **17**, 538.
Brenner, S. A. & Gum, P. H. (1968). *The Tangent Formula Program for the X-ray Analysis of Noncentrosymmetric Crystals.* NRL Report 6697.
Brutcher, F. V. & Leopold, E. J. (1966). *J. Amer. Chem. Soc.* **88**, 3156.
Cooper, A. & Norton, D. A. (1968). *Acta Cryst.* B**24**, 811.
Davis, M. & Hassel, O. (1963). *Acta Chem. Scand.* **17**, 1181.
Ehrlich, H. W. W. (1960). *Acta Cryst.* **13**, 946.
Hanson, H. P., Herman, F., Lea, J. D. & Skillman, S. (1964). *Acta Cryst.* **17**, 1040.
Harrison, I. T., Beard, C., Kirkham, L., Lewis, B., Jamieson, I. M., Rooks, W. & Fried, J. H. (1968). *J. Medicinal Chemistry,* **11** (4), 868.
High, D. F. & Kraut, J. (1966). *Acta Cryst.* **21**, 88.
Hine, J. (1963). *J. Amer. Chem. Soc.* **85**, 3239.
Hope, H. & Christensen, A. T. (1968). *Acta Cryst.* B**24**, 375.
Hughes, E. W. (1941). *J. Amer. Chem. Soc.* **63**, 1737.
Johnson, C. K. (1965). *ORTEP, A FORTRAN Thermal Ellipsoid Plot Program for Crystal Structure Illustrations.* ORNL-2794, Oak Ridge National Laboratory, Oak Ridge, Tennessee.
Karle, J. (1968). *Acta Cryst.* B**24**, 182.
Karle, J. & Hauptman, H. (1956). *Acta Cryst.* **9**, 635.
Norton, D. A. (1965). *Biophys. J.* **5**, 425.
Reimann, C. W., Mighell, A. D. & Mauer, F. A. (1967). *Acta Cryst.* **23**, 135.
Sim, G. A. (1960). *Acta Cryst.* **13**, 511.
Sparks, R. A. (1961). In *Computing Methods and the Phase Problem in X-ray Crystal Analysis.* p. 170, paper 17. Oxford: Pergamon Press.