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Acta Cryst. (1981). **B37**, 1881–1884

New Methods and Reagents in Organic Synthesis.

XIII. Structure of 3 β -(1-Pyrrolidinyl)-5 α -cholestane-3 α -carbonitrile

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(Received 1 December 1980; accepted 23 March 1981)

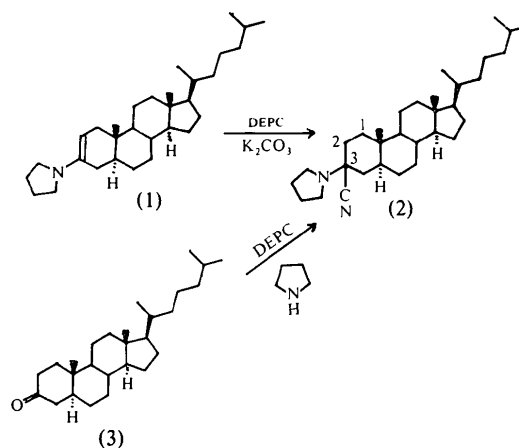
Abstract

The reaction of 3-(1-pyrrolidinyl)-5 α -cholest-2-ene with diethyl phosphorocyanidate or of 5 α -cholestan-3-one with diethyl phosphorocyanidate and pyrrolidine was found to afford the title compound by X-ray diffraction methods. $C_{32}H_{54}N_2$, $M_r = 466.8$, is monoclinic, space group $P2_1$ with $a = 10.589$ (2), $b = 10.335$ (2), $c = 13.516$ (2) Å, $\beta = 98.47$ (1)°, $V = 1462.9$ (5) Å³, $Z = 2$, $D_m = 1.032$ (1), $D_c = 1.059$ Mg m⁻³. Anisotropic least-squares refinement led to the residual value $R = 0.084$ for a total number of 2672 independent reflections. The cyclopentane ring is best represented by a half-chair conformation and the side chain attached to C(17) by a *trans* zigzag one. In the crystal structure, the molecules are held together by normal van der Waals contacts, and neither hydrogen bonding nor a short contact is observed.

Introduction

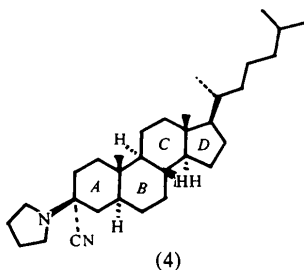
It was reported in our previous communication (Harusawa, Hamada & Shioiri, 1979*a*), that the

reaction of 3-(1-pyrrolidinyl)-5 α -cholest-2-ene (1) with diethyl phosphorocyanidate [DEPC, $(C_2H_5O)_2P(O)CN$] gave 3-(1-pyrrolidinyl)-5 α -cholestane-3-carbonitrile (2). (2) was also obtained by the reaction of 5 α -cholestan-3-one (3) with DEPC and pyrrolidine (Harusawa, Hamada & Shioiri, 1979*b*). The configuration at C(3) of (2) was tentatively assigned as 3 α -cyano and 3 β -(1-pyrrolidinyl), from the comparison of thermodynamic stabilities of (2) and its epimer, the former being much more stable.



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In order to confirm the structure and stereochemical assignment, we determined the crystal structure of (2) and established the structure to be 3 β -(1-pyrrolidiny)-5 α -cholestane-3 α -carbonitrile (4).



Experimental

Crystals suitable for X-ray analysis were obtained by recrystallization from ethyl acetate.

Preliminary cell dimensions and space group were determined from oscillation and Weissenberg photographs. The density of the crystal was measured by flotation using a mixture of methanol and ethylene glycol. A crystal of dimensions 0.5 \times 0.4 \times 0.2 mm was used for the intensity measurement. The intensity data were collected on a Rigaku automated four-circle diffractometer using Cu K α radiation monochromated by a graphite plate, the ω -2 θ scan mode being employed. 2672 independent reflections below 2 θ = 130 $^\circ$ were collected and used for the structure determination. Corrections were made for Lorentz and polarization effects, but not for absorption. No appreciable structural deterioration was detected during the run.

Structure determination and refinement

The structure was solved by the direct method with the program *MULTAN* 78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978) using 272 reflections with $|E| \geq 1.50$. When the set with the highest ψ_0 value was used to synthesize an *E* map, geometrically acceptable positions for 23 out of 34 nonhydrogen atoms were obtained. The remaining atoms were located by successive Fourier syntheses. Isotropic refinement using the full-matrix least-squares method converged to an *R* of 0.151. Anisotropic refinement was then performed by the block-diagonal least-squares method. All the H atoms were found from a difference Fourier synthesis at the stage *R* = 0.126. After inclusion of the H atoms with isotropic thermal parameters, further refinement was carried out. The final *R* value was 0.084. The atomic scattering factors for all atoms were taken from *International Tables for X-ray Crystallography* (1974).

All numerical calculations were carried out on an ACOS-700 computer of the Computation Center of Osaka University using programs of *The Universal Crystallographic Computing System* (1979).

Results and discussion

The final positional parameters with their estimated standard deviations are listed in Tables 1 and 2.* Bond lengths and angles for nonhydrogen atoms, with the atomic numbering, are given in Fig. 1.

Fig. 2 shows configurational and conformational aspects of the molecule. The configuration at C(3) is, as was expected, 3 α -cyano and 3 β -(1-pyrrolidiny). Rings A, B and C all exist in the chair conformation and are

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36067 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Fractional coordinates* ($\times 10^4$) and *B_{eq}* values for nonhydrogen atoms

C(1) was fixed at an arbitrary position along the *y* axis to define the origin.

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B_{eq}</i> (Å^2)
C(1)	2065 (6)	1317	8482 (4)	4.6 (2)
C(2)	3271 (6)	1560 (8)	9254 (5)	4.9 (3)
C(3)	4454 (5)	1840 (7)	8765 (4)	4.1 (2)
C(4)	4159 (6)	2900 (7)	7950 (5)	4.7 (2)
C(5)	2934 (5)	2597 (7)	7203 (4)	4.6 (2)
C(6)	2769 (6)	3627 (9)	6384 (5)	5.5 (3)
C(7)	1619 (6)	3264 (9)	5598 (5)	5.7 (3)
C(8)	400 (6)	3089 (7)	6075 (5)	4.7 (3)
C(9)	603 (5)	2061 (6)	6923 (4)	3.8 (2)
C(10)	1754 (5)	2426 (7)	7737 (4)	3.8 (2)
C(11)	-644 (5)	1764 (8)	7326 (4)	4.2 (2)
C(12)	-1751 (5)	1396 (7)	6502 (4)	4.2 (2)
C(13)	-1994 (5)	2463 (6)	5692 (4)	3.9 (2)
C(14)	-698 (5)	2648 (7)	5280 (4)	4.5 (2)
C(15)	-1059 (6)	3554 (10)	4392 (6)	6.6 (4)
C(16)	-2408 (6)	3030 (9)	3915 (5)	5.7 (3)
C(17)	-2860 (6)	2079 (7)	4696 (4)	4.4 (2)
N(18)	5501 (5)	2301 (6)	9504 (4)	5.0 (2)
C(19)	5859 (6)	1456 (9)	10381 (5)	6.1 (3)
C(20)	7097 (7)	2086 (11)	10874 (6)	7.2 (4)
C(21)	7702 (7)	2695 (12)	10049 (6)	7.2 (4)
C(22)	6682 (6)	2663 (9)	9113 (6)	5.9 (3)
C(23)	4824 (6)	612 (8)	8303 (5)	4.9 (3)
N(24)	5124 (7)	-298 (8)	7980 (6)	7.9 (4)
C(25)	1427 (7)	3672 (9)	8293 (6)	5.9 (3)
C(26)	-2472 (7)	3704 (8)	6130 (6)	5.9 (3)
C(27)	-4325 (5)	2110 (7)	4660 (4)	4.4 (2)
C(28)	-4988 (6)	1768 (7)	3591 (4)	4.9 (3)
C(29)	-6391 (5)	2113 (8)	3406 (5)	5.0 (3)
C(30)	-6990 (6)	1689 (10)	2338 (5)	5.7 (3)
C(31)	-8458 (8)	1855 (15)	2131 (6)	8.0 (4)
C(32)	-4772 (6)	1173 (9)	5417 (5)	5.6 (3)
C(33)	-8966 (8)	1022 (15)	1202 (7)	9.4 (6)
C(34)	-8733 (13)	3250 (15)	2015 (13)	11.1 (6)

Table 2. Atomic positional parameters ($\times 10^3$) of the hydrogen atoms

	x	y	z		x	y	z
H(1a)	130 (6)	106 (7)	889 (5)	H(21a)	840 (7)	218 (8)	995 (5)
H(1b)	221 (6)	34 (7)	808 (5)	H(21b)	799 (7)	381 (8)	1022 (5)
H(2a)	341 (6)	66 (7)	974 (5)	H(22a)	692 (7)	196 (9)	853 (6)
H(2b)	309 (6)	233 (8)	973 (5)	H(22b)	661 (7)	367 (9)	870 (6)
H(4a)	498 (7)	304 (8)	753 (5)	H(25a)	127 (6)	444 (7)	770 (5)
H(4b)	405 (6)	399 (7)	837 (5)	H(25b)	216 (7)	404 (9)	886 (6)
H(5)	302 (6)	163 (8)	679 (5)	H(25c)	57 (7)	367 (9)	865 (6)
H(6a)	359 (6)	376 (8)	610 (5)	H(26a)	-264 (6)	440 (7)	560 (5)
H(6b)	265 (7)	464 (8)	668 (5)	H(26b)	-184 (7)	417 (8)	664 (5)
H(7a)	177 (7)	233 (9)	521 (5)	H(26c)	-330 (7)	373 (9)	649 (6)
H(7b)	147 (6)	398 (7)	502 (4)	H(27)	-463 (7)	308 (8)	487 (6)
H(8)	16 (7)	416 (8)	648 (5)	H(28a)	-487 (6)	67 (7)	348 (5)
H(9)	88 (6)	101 (8)	664 (5)	H(28b)	-452 (6)	223 (8)	311 (5)
H(11a)	-84 (7)	262 (8)	770 (5)	H(29a)	-650 (7)	322 (9)	354 (6)
H(11b)	-47 (6)	95 (7)	785 (5)	H(29b)	-695 (6)	156 (8)	399 (5)
H(12a)	-248 (6)	116 (8)	680 (5)	H(30a)	-682 (7)	48 (8)	224 (5)
H(12b)	-154 (6)	49 (7)	620 (5)	H(30b)	-658 (6)	221 (8)	182 (5)
H(14)	-38 (6)	165 (8)	500 (5)	H(31)	-933 (5)	161 (7)	271 (4)
H(15a)	-47 (7)	364 (9)	388 (6)	H(32a)	-413 (8)	34 (9)	574 (6)
H(15b)	-111 (7)	470 (8)	467 (5)	H(32b)	-554 (4)	66 (5)	507 (3)
H(16a)	-241 (7)	253 (8)	323 (5)	H(32c)	-496 (8)	156 (9)	600 (6)
H(16b)	-305 (6)	391 (8)	372 (5)	H(33a)	-1008 (9)	60 (11)	78 (7)
H(17)	-264 (7)	92 (8)	450 (5)	H(33b)	-847 (9)	-32 (11)	152 (7)
H(19a)	607 (7)	39 (9)	1010 (5)	H(33c)	-849 (8)	131 (10)	51 (6)
H(19b)	514 (6)	135 (8)	1088 (5)	H(34a)	-840 (7)	273 (9)	219 (6)
H(20a)	768 (7)	128 (8)	1134 (5)	H(34b)	-939 (9)	392 (11)	264 (7)
H(20b)	685 (7)	283 (8)	1136 (5)	H(34c)	-882 (8)	375 (10)	131 (6)

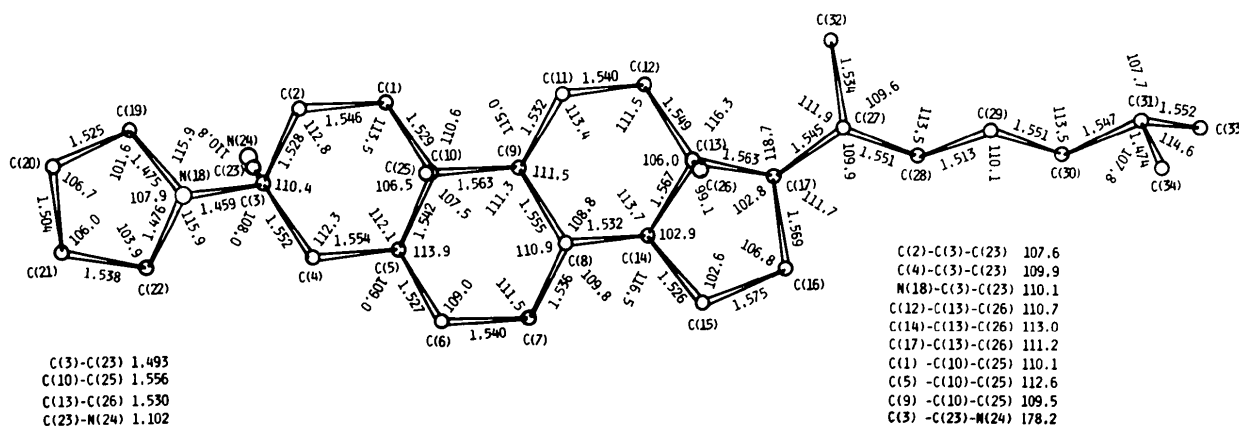


Fig. 1. Bond lengths (Å) and angles ($^{\circ}$). E.s.d.'s for bond lengths are in the range 0.008–0.011 Å. Bond angles have e.s.d.'s between 0.5 and 1.3 $^{\circ}$.

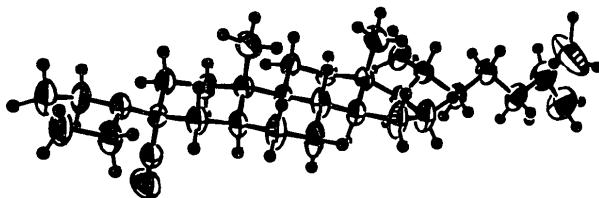


Fig. 2. Perspective view of the molecular structure.

trans connected: torsion angles C(1)–C(10)–C(5)–C(6), C(4)–C(5)–C(10)–C(9), C(10)–C(9)–C(8)–C(14) and C(7)–C(8)–C(9)–C(11) are 176.9 (6), 182.7 (6), 177.5 (5) and 186.4 (6) $^{\circ}$, respectively.

The cyano group on the atom C(3) is axial and the pyrrolidine group is equatorial. The latter is almost fully extended in the plane of the cholestane skeleton [mean dihedral angle of both rings = 6.3 (4) $^{\circ}$]. The side chain attached to C(17) has a *trans* zigzag conformation: torsion angles C(13)–C(17)–C(27)–C(28), C(17)–C(27)–C(28)–C(29), C(27)–C(28)–C(29)–C(30), C(28)–C(29)–C(30)–C(31) and C(29)–C(30)–C(31)–C(33) are 177.0 (6), –164.7 (6), –177.7 (7), 173.0 (9) and –163 (1) $^{\circ}$, respectively. There seem to be no significant deviations from the accepted values with respect to the bond distances. All C–C bonds are in the range 1.493 to

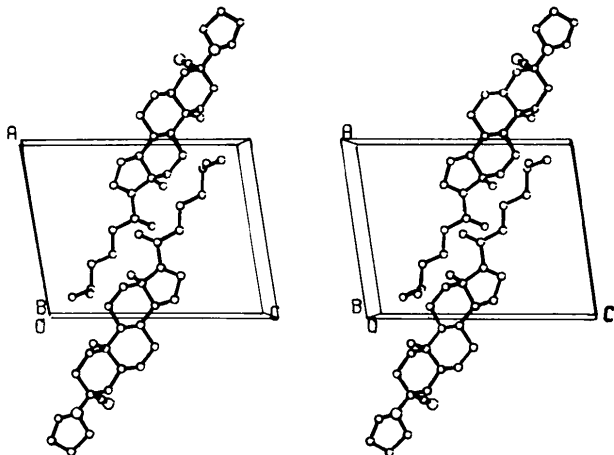


Fig. 3. Stereoscopic view of the molecular packing in the unit cell viewed down the b axis.

1.575 Å with a mean value of 1.541 Å, and the C(23)–N(24) bond (1.02 Å) is of triple-bond length (Kennard, 1968). The bond length C(31)–C(34), 1.474 Å, is significantly shorter than the average, probably due to the large temperature factor of C(34). The average value of the angles within the three cyclohexane rings (110.9°) is larger than the ideal tetrahedral angle (109.5°). This implies that the perhydrophenanthrene skeleton is flattened with respect to the ideal model, as was found in $2\beta,3\alpha$ -dichloro- 5α -cholestane (Geise, Romers & Rutten, 1966), and $2\alpha,3\beta$ -dichloro- and $2\alpha,3\beta$ -dibromo- 5α -cholestanes (Geise & Romers, 1966). The angles in the cyclopentane ring, D , are considerably smaller than 109.5° . This may be due to the strain inherent in the C/D ring junction [C(12)–C(13)–C(17) = 116.3 , C(8)–C(14)–C(15) = 116.5°]. The sum of the torsion angles C(12)–C(13)–C(14)–C(8) and C(17)–C(13)–C(14)–C(15) [112.3 (7°)] conforms to an empirical value of 109 (3°) for C/D junctions with an axial methyl at C(13) and a β -substituent at C(17) (Geise, Altona & Romers, 1967).

The conformation of a cyclopentane ring may be described by the parameters Δ and φ_m (Altona, Geise & Romers, 1968; Duax & Norton, 1975). The D ring can be described as a half-chair with $\Delta = -5.7^\circ$ and $\varphi_m = 51.3^\circ$.

In the crystal structure, the molecules are packed approximately parallel to the plane (112). This accounts for the high value of the structure factor of this reflection. Fig. 3 shows a stereoscopic drawing of the crystal structure viewed along [010]. No interactions shorter than the sum of the van der Waals radii occur. The molecules are held together by van der Waals contacts with neighbouring molecules translated by a diad screw axis and form head-to-tail parallel sheets perpendicular to the b axis.

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