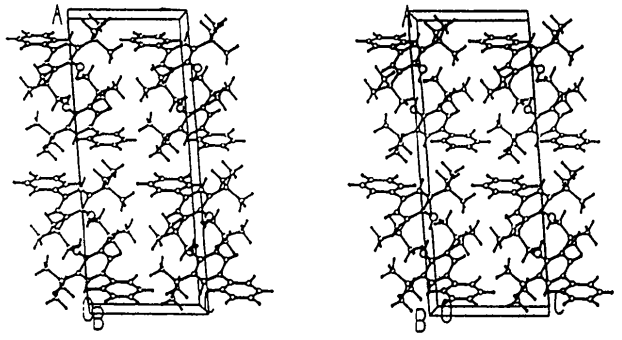

Fig. 2. Stereoscopic view of the structure seen along [010] drawn by *PLUTO*.

1·487 Å value calculated for a C(sp^2)—C(sp^2) bond by Dewar & Schmeisinger (1960). The phenyl ring is planar while the phenolic ring is distorted, probably due to the substituents, as found by Maze-Baudet (1973). The O atom is at 0·051 (2) Å from the ring plane and the H atom at 0·43 (4) Å from that plane. Comparisons with other phenols with one or two *tert*-butyl groups at *ortho* positions will be made in a later paper. The dihedral angle between the two ring planes has the value 37·7 (4)°; so the inter-ring torsion is large compared with the value of 2° found for 4-hydroxybiphenyl (Brock & Haller, 1984).

The packing is shown in Fig. 2. No close intermolecular contacts between the atoms were found in the crystal; so there are no hydrogen bonds because of the steric hindrance at *ortho* positions.

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Structure of Cholesterol *n*-Hexyl Carbonate

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Abstract. 5-Cholesten-3β-ol-3-*n*-hexyl carbonate, $C_{34}H_{58}O_3$, $M_r = 514{\cdot}6$, monoclinic, $P2_1$, $a = 12{\cdot}728$ (2), $b = 9{\cdot}184$ (1), $c = 13{\cdot}991$ (2) Å, $\beta = 92{\cdot}93$ (1)°, $V = 1633{\cdot}3$ (6) Å^3, $T = 298$ K, Mo $K\alpha$ graphite monochromator, $\lambda = 0{\cdot}71073$ Å, $Z = 2$, $D_m = 1{\cdot}05$, $D_x = 1{\cdot}046$ g cm^{-3}, $\mu = 0{\cdot}34$ cm^{-1}, $F(000) = 572$, $R = 0{\cdot}126$ for 1600 data having $I > 3\sigma(I)$. The bond lengths and valence angles in the structural unit of the cholesterol and carbonate groups are normal but the hexyl group has shortened bond lengths due to the high thermal vibration in this region, and the C(17) cholesterol side chain is almost fully extended. Adjacent

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molecules are related by the 2_1 screw symmetry along the *b* axis so that they are arranged in an antiparallel array, corresponding to type II packing mode.

Introduction. There is growing interest in the structural features of the fatty acid esters of cholesterol, because they undergo characteristic phase transitions (Gray, 1962) depending on the type of the fatty acid moiety, and because they are a storage form of cholesterol. The fatty acid esters are important constituents of plasma lipoproteins (Atkinson, Deckelbaum, Small & Shipley, 1977) and of some animal cell membranes, and they are involved in the development of arteriosclerosis (Steinberg, 1981). Moreover, cholesterol-containing liposomes have attracted attention as a potentially valuable system in various aspects of genetic engineering (Ostro, 1983).

Structural studies on cholesterol derivatives focused on the fatty acid esters (Kang, Chung & Park, 1985). In this series, homologous cholesteryl fatty-acid esters with different chain lengths or different degree of unsaturation and cholesterol halides were investigated. It is also conceivable that variation of the substituents attached at the C(3) hydroxyl group of the cholesterol molecule may lead to different intermolecular interactions and thus influence the molecular packing arrangements which are best studied by crystallographic methods. The packing modes may consequently be relevant for more complex biological systems of higher structural hierarchy such as plasma lipoproteins and cell membranes or fatty acid deposits involving this class of lipids.

5-Cholesten-3β-ol-3-*n*-hexyl carbonate (CHC) is one of the cholesteryl *n*-alkyl carbonates the structures of which have been investigated by us in conjunction with the previously reported data on fatty acid esters. The present study was performed to obtain some insight concerning the effect of the tail part attached at the C(3) hydroxyl on the conformation of the cholesterol skeleton, and its influence on intermolecular interactions and crystal packing mode.

Experimental. The CHC sample was obtained from Tokyo Kasei Kogyo Co. Ltd and recrystallized from acetone at room temperature in the form of needles. The density was determined by the flotation method using a mixture of $KI/HgCl_2$ in aqueous solution. Space group and initial unit-cell constants were derived on the basis of X-ray photographs and accurate cell constants were obtained from measurements on a Stoe four-circle diffractometer (20 reflections in range $10 < \theta < 15°$) equipped with Mo tube and graphite monochromator, which also served to collect the X-ray intensity data [$(\sin\theta)/\lambda$(max.) = 0·526 Å^{-1}]. Because of the small size of the crystal used (0·5 mm), no corrections were made for extinction or absorption effects. 2581 unique data measured, index range h −14 to 13, k −10 to 0, l 0 to 15; 1600 [$I > 3\sigma(I)$] used in analysis; no drop in intensity of reference reflections.

Table 1. *Fractional atomic coordinates* (×10^4) *and equivalent isotropic thermal parameters*

$U_{eq} = \frac{1}{3}(U_{11} + U_{22} + U_{33})$ (×10^3).

	x	y	z	U_{eq}(Å^2)
O(3)	8398 (10)	3052	1645 (10)	133
O(28)	9743 (10)	3603 (21)	841 (11)	187
O(0)	8948 (14)	5394 (22)	1687 (16)	301
C(1)	5541 (14)	3656 (20)	2194 (11)	79
C(2)	6554 (20)	3406 (22)	1618 (14)	109
C(3)	7534 (14)	3480 (33)	2230 (15)	106
C(4)	7436 (13)	2281 (27)	2938 (14)	85
C(5)	6525 (10)	2473 (19)	3550 (10)	66
C(6)	6635 (11)	2463 (18)	4527 (10)	74
C(7)	5761 (12)	2629 (20)	5144 (12)	73
C(8)	4652 (11)	2422 (20)	4650 (11)	65
C(9)	4599 (11)	3207 (19)	3674 (11)	65
C(10)	5458 (11)	2554 (18)	2971 (10)	77
C(11)	3508 (12)	3176 (22)	3212 (11)	81
C(12)	2649 (12)	3673 (22)	3919 (12)	79
C(13)	2671 (11)	2767 (15)	4818 (9)	74
C(14)	3780 (9)	2949 (15)	5269 (9)	49
C(15)	3669 (12)	2361 (21)	6220 (11)	74
C(16)	2598 (11)	2826 (18)	6542 (11)	72
C(17)	2046 (11)	3408 (17)	5655 (11)	74
C(18)	2360 (12)	1208 (20)	4618 (11)	87
C(19)	5211 (11)	1113 (19)	2625 (12)	84
C(20)	820 (10)	3130 (20)	5647 (11)	72
C(21)	236 (13)	3620 (22)	4745 (15)	97
C(22)	367 (12)	3834 (23)	6522 (12)	96
C(23)	−729 (13)	3211 (21)	6763 (13)	103
C(24)	−1098 (14)	3892 (24)	7666 (13)	106
C(25)	−2127 (14)	3481 (33)	7982 (19)	252
C(26)	−2440 (21)	4182 (36)	8809 (16)	181
C(27)	−2715 (24)	2333 (46)	7618 (30)	352
C(28)	9053 (12)	4093 (27)	1451 (14)	194
C(29)	10462 (32)	4604 (44)	438 (48)	598
C(30)	11343 (33)	3818 (38)	63 (32)	313
C(31)	12161 (38)	4596 (77)	123 (18)	737
C(32)	12699 (59)	4066 (38)	−610 (21)	408
C(33)	13547 (32)	3112 (56)	−369 (23)	311
C(34)	14487 (16)	2532 (39)	−683 (17)	159

Attempts to solve the crystal structure by direct methods (Main, Lessinger, Woolfson, Germain & Declercq, 1976) failed. However, since the crystal data for CHC are similar to those of cholesteryl hexanoate (Park & Craven, 1981), the atomic positional parameters of the tetracyclic system of the latter were used as starting model in a series of Fourier syntheses which allowed the location of all the non-hydrogen atoms of the ester group and the cholesterol C(17) side chain. The positions of atoms C(28) to C(31) in the hexyl group are only poorly defined because these atoms display large thermal vibration amplitudes. In order to rule out possible disorder of these atoms, a new independent data set was collected using a CAD-4 diffractometer at Riken Institute, Saitama, Japan. The refinement converged at the same results, however, and attempts to interpret the electron density on the basis of side-chain disorder failed. H atoms were placed in positions calculated on the basis of the carbon–oxygen skeleton, with a C—H bond distance of 1·0 Å. They were used with isotropic temperature factors U_{11} = 0·05 Å^2 (Sheldrick, 1976) in full-matrix least-squares refinement on F values, in which the positional and anisotropic thermal parameters of C, O atoms were optimized; weights were assigned according to w

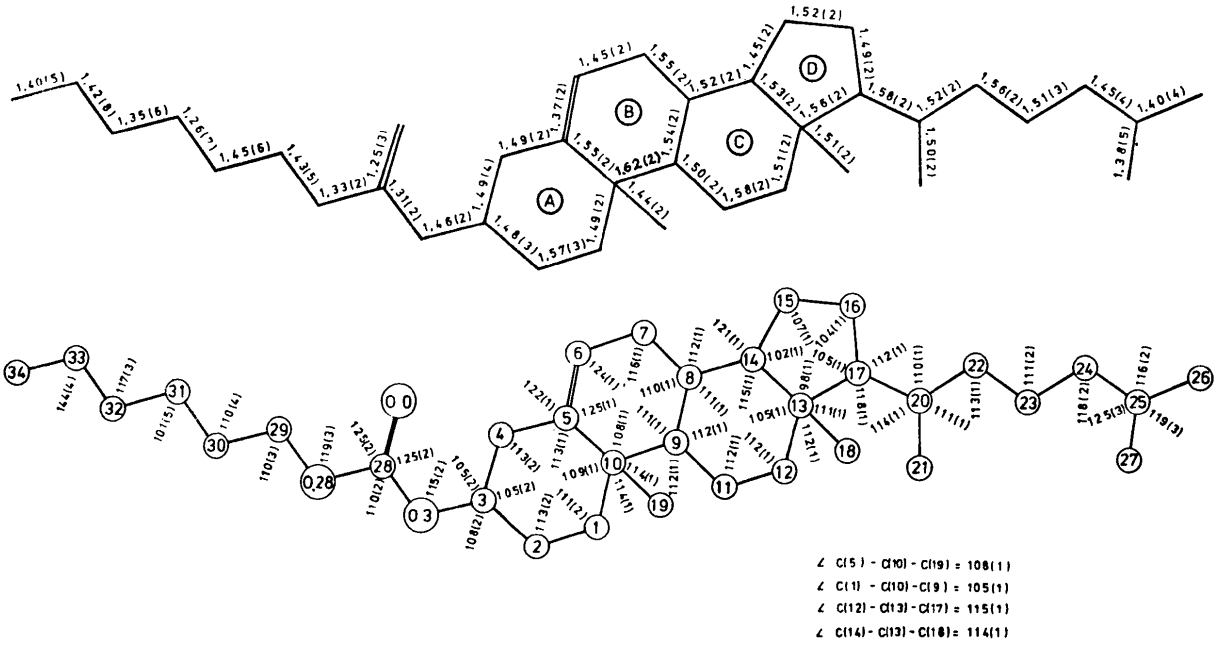

Fig. 1. Atomic numbering scheme and bond angles (°) and distances (Å). Standard deviations obtained from the least-squares correlation matrix are given in parentheses.

$= 3{\cdot}77/[\sigma^2(F) + 0{\cdot}000541F^2]$. The refinement converged (maximum shift/e.s.d. 0·78) with atomic parameters given in Table 1 at a relatively high conventional $R = 12{\cdot}6\%$ ($wR = 12{\cdot}0\%$),* probably because a part of the molecule is not well defined, and the crystal structure is stabilized only by van der Waals forces. A final difference electron density map showed residual density in the range 0·33 to $-0{\cdot}26$ e Å^{-3}. Atomic scattering factors as programmed in *SHELX*76 (Sheldrick, 1976).

Discussion. *Molecular structure of CHC.* A schematic representation of CHC showing the numbering system and the intramolecular bond lengths and angles with e.s.d.'s calculated from the least-squares correlation matrix is given in Fig. 1, and an *ORTEP* (Johnson, 1971) stereoview of the CHC molecule is shown in Fig. 2. In view of the relatively large e.s.d.'s in atomic parameters, especially of the side chains, we cannot discuss individual bond lengths and angles in detail. In the *n*-hexyl side chain, bond distances are, in general, shortened due to high thermal vibration, with C(30)–C(31), 1·26 (7) Å, suffering most. For the tetracyclic system the bonding geometry is not significantly different from that in cholesteryl acetate (Sawzik & Craven, 1979*a*) and in cholesteryl hexanoate (Park & Craven, 1981) which served as search model in the present structure determination. The C(5)–C(6) bond length of 1·37 (2) Å indicates double-bond character as anticipated, and only C(9)–C(10), 1·62 (2) Å, is longer than the expected sp^3–sp^3 bond length of 1·54 Å.

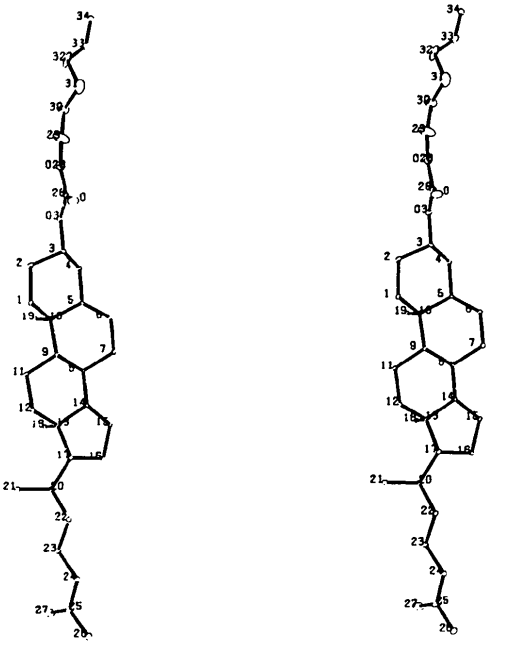

Fig. 2. Stereo diagram of the molecule, with anisotropic thermal ellipsoids drawn at their 20% probability level (Johnson, 1971).

* Lists of structure amplitudes, anisotropic temperature factors and H-atom coordinates have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51200 (10 pp.). Copies may be obtained through The Executive Secretary, Internaional Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Selected torsion angles* (°) *in cholesterol n-hexyl carbonate*

C(13)–C(17)–C(20)–C(21)	−55 (2)	C(2)–C(3)–O(3)–C(28)	111 (2)
C(13)–C(17)–C(20)–C(22)	180 (1)	C(3)–O(3)–C(28)–O(28)	−174 (2)
C(16)–C(17)–C(20)–C(21)	−176 (1)	C(4)–C(3)–O(3)–C(28)	−137 (2)
C(16)–C(17)–C(20)–C(22)	58 (2)	O(3)–C(28)–O(28)–C(29)	173 (3)
C(17)–C(20)–C(22)–C(23)	−161 (1)	C(28)–O(28)–C(29)–C(30)	161 (3)
C(21)–C(20)–C(22)–C(23)	72 (2)	O(28)–C(29)–C(30)–C(31)	−150 (4)
C(20)–C(22)–C(23)–C(24)	177 (1)	C(29)–C(30)–C(31)–C(32)	−52 (4)
C(22)–C(23)–C(24)–C(25)	178 (2)	C(30)–C(31)–C(32)–C(33)	−103 (5)
C(23)–C(24)–C(25)–C(26)	−178 (2)	C(31)–C(32)–C(33)–C(34)	−158 (6)

Concerning the conformation of the steroid system, rings *A* and *C* assume a chair conformation, ring *B* is in a half-chair form and ring *D* adopts the expected 13α, 14β half chair (Fig. 2). The atoms defining the ethylene group, C(4) to C(7) and C(10) are coplanar within experimental error, as are the atoms of the ester linkage, C(28), O(28), C(29), O(0), O(3). The intramolecular distance C(3)···C(16), which is a useful measure for comparing the overall length of the tetracyclic system, is 8·95 (3) Å, within the range of 8·86 to 9·01 Å observed in related molecules (Park & Craven, 1981). Among the selected torsion angles given in Table 2, C(2)–C(3)–O(3)–C(28), 111 (2)°, is important for determining the overall structure of the molecule. The corresponding torsion angles are 114·3° in cholesteryl hexanoate (Park & Craven, 1981), 137° in cholesteryl oleate (Craven & Guerina, 1979*a*), and 121° in cholesteryl octanoate (Craven & Guerina, 1979*b*). Another parameter which serves to define the overall twist of the cholesteryl skeleton is the torsion angle comprising the two methyl groups, C(19)–C(10)··· C(13)–C(18); this is 6 (2)° and on the low side if compared with related molecules where values of 7·9 to 15° were observed (Pattabhi & Craven, 1979).

The C(17) side chain has an all-*trans* conformation with torsion angles, from C(13)–C(17)–C(20)–C(22) to C(23)–C(24)–C(25)–C(26) of 180 (1), −161 (1), 177 (1), 178 (2), −178 (2)° (Table 2). In contrast, the conformation of the *n*-hexyl group deviates considerably from the expected all-*trans* and the e.s.d.'s are larger, with torsion angles from O(3)–C(28)–O(28)–C(29) to C(31)–C(32)–C(33)–C(34) being 173 (3), 161 (3), −150 (4), −152 (4), −103 (5), −158 (6)°. Because the conformation of *n*-alkyl chains is, in general, all-*trans*, we assume that the deviation from this scheme is caused by packing effects.

Molecular packing. The stereoscopic packing diagram in Fig. 3 (Johnson, 1971) indicates that the cholesteryl group is oriented parallel to the *ac* plane with the long molecular axis parallel to the [20$\bar{1}$] direction, so that the two screw-axis-related molecules displayed in Fig. 3 are nearly antiparallel to each other. They stack with an overlap of rings *B, C, D,* a scheme that was observed previously in cholesteryl chloroformate and called type II monolayer (Chandross & Bordner, 1978). It contrasts with the type I monolayer found in cholesteryl laurate (Sawzik & Craven, 1979*b*),

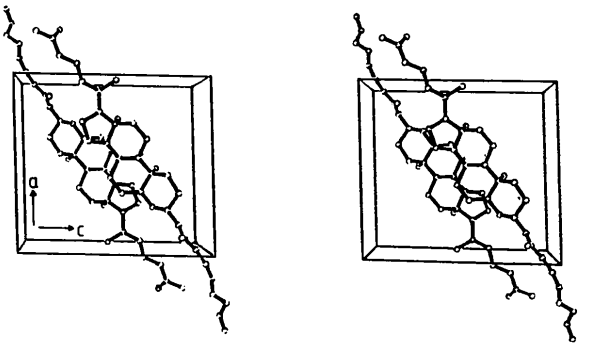

Fig. 3. Packing diagram (Johnson, 1971). Note overlap of cholesterol systems and antiparallel alignment of *n*-alkyl chains due to type II packing mode.

decanoate (Pattabhi & Craven, 1979) and nonanoate (Guerina & Craven, 1979) where adjacent molecules are not related by crystallographic symmetry and have their tetracyclic systems almost perpendicular to each other.

In directions nearly parallel to the crystallographic *b* axis there are several intermolecular close contacts less than 4·0 Å, with C(6)–C(18), 3·84 (2) Å, being the shortest (Table 3).* The crystal structure is stabilized only by van der Waals forces, which explains the relatively high thermal motion expecially of the aliphatic chains.

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* This table has been deposited (see previous footnote).

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Structure d'un Photoproduit Psoralène–Thymine: Modèle pour l'Interaction avec l'ADN sur le Cycle Pyrone du Psoralène

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Abstract. Photoadduct 4-ethoxypsoralen–thymine (4a-methyl-11,1-epoxyethanofuro[3'',2'':6',7']chromeno-[2',3':1,2]cyclobuta[4,3-*d*]pyrimidine-2,4,5-trione), $C_{18}H_{14}N_2O_6$, $M_r = 354{\cdot}1$, monoclinic, $P2_1/c$, $a = 9{\cdot}021$ (3), $b = 11{\cdot}504$ (1), $c = 16{\cdot}397$ (3) Å, $\beta = 110{\cdot}45$ (1)°, $V = 1594{\cdot}4$ Å^3, $Z = 4$, $D_m = 1{\cdot}46$, $D_x = 1{\cdot}475$ Mg m^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 0{\cdot}072$ mm^{-1}, $F(000) = 736$, $T = 298$ K, $R = 0{\cdot}032$ for 1442 observed reflections. This original structure of an intramolecular photoproduct obtained photochemically gives structural information about the cycloaddition of the thymine base on the pyrone ring of the psoralen. The crystal structure displays deformations of the planes of the two rings which form a dihedral angle of 40·5° and a *cis–anti* conformation relative to the cyclobutane bridging component.

Introduction. L'une des caractéristiques importantes de la double hélice des acides nucléiques est leur aptitude à accepter des molécules possédant un chromophore plan aromatique qui peut s'intercaler entre les paires de bases de la double hélice. Ces molécules appelées intercalants possèdent pour la plupart des propriétés biologiques significatives. Ainsi, les isomères linéaires des furocoumarines ou psoralènes font partie de cette catégorie de molécules. Ce sont des composés hétérocycliques oxygénés que l'on rencontre principalement dans deux familles de plantes: les ombellifères et les rutacées.

Les psoralènes (furocoumarines) sont des agents photosensibilisants utilisés dans le traitement de certaines maladies de la peau: le vitiligo et le psoriasis (Parrish, Fitzpatrick, Tanenbaum & Pathak, 1974; Parrish, 1981). Les propriétés biologiques observées ont été reliées aux modes de réactions des psoralènes avec l'ADN. En effet, les furocoumarines sont capables de s'insérer entre deux couples de bases de l'ADN pour former un complexe d'intercalation (Musajo, Rodighiero & Dall'acqua, 1965; Cole, 1970, 1971). Ensuite, sous irradiation UV, il peut se produire une photoréaction entre la furocoumarine complexée et les bases pyrimidiques de l'ADN (Musajo, Bordin & Bevilacqua, 1967). La double liaison 5,6 de la thymine (ou de la cytosine) peut s'additionner sur la double liaison 3,4 (et) ou 4',5' de la furocoumarine pour former un pont cyclobutane 3,4 et 4',5', ce qui entraîne la formation d'un lien covalent entre les deux brins de l'ADN (réticulation ou 'cross linking').

Bien que de nombreuses recherches aient été effectuées sur ce problème (Kanne, Straub, Hearst & Rapoport, 1982), de nombreux points restent obscurs, en particulier ceux concernant la géométrie du complexe d'intercalation, la sélectivité de la réaction et les propriétés des photoproduits.

La synthèse de composés modèles dans lesquels un psoralène (méthoxy-5 psoralène) est relié à la molécule de thymine par une chaîne polyméthylénique conduit par irradiation à 365 nm à une photoaddition très sélective entre la double liaison 5,6 de la thymine et la double liaison 3,4 de la furocoumarine (Decout, Huart, Lhomme, Courseille & Hospital, 1984). La photoréaction du composé modèle dans lequel le noyau psoralène est relié à la thymine par une chaîne éthoxy conduit à un photoproduit intramoléculaire unique (Fig. 1) que nous avons étudié par diffraction des rayons X.

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