

The Crystal Structure of Cholesteryl Aniline

Young Ja Park*, Sangsoo Kim†, and Seung Bun Lee

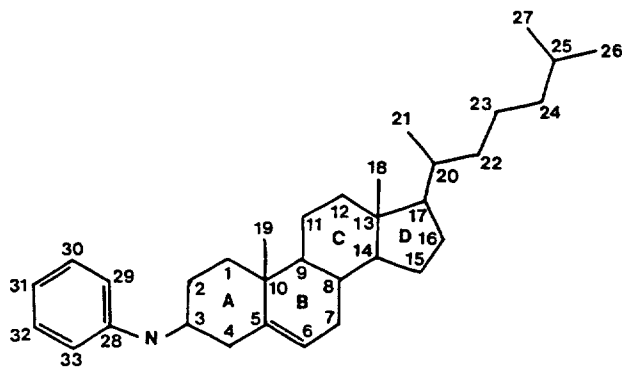
Department of Chemistry, Sook Myung Women's University, Seoul, Korea 140-742

†Lucky Central Research Institute, Taejon 305-343. Received May 24, 1990

Cholesteryl aniline ($C_{33}H_{51}N$) is monoclinic, space group $P2_1$, with $a = 9.020(3)$, $b = 6.000(1)$, $c = 27.130(9)$ Å, $\beta = 98.22(2)^\circ$, $Z = 2$, $D_c = 1.06$ g/cm³ and $D_m = 1.04$ g/cm³. A diffraction data set was collected with Mo- K_α radiation ($\lambda = 0.7107$ Å) on a diffractometer with a graphite monochromator to a maximum 2θ value of 50° , by the ω - 2θ scan technique. The coordinates of the non-hydrogen atoms and their anisotropic temperature factors were refined by full-matrix least-squares methods to final R of 0.058. In cholesteryl group, bond distances were normal except in tail part, where high thermal vibration resulted in apparent shortening of the C-C distances. The crystal structure consists of bilayers of thickness $d_{001} = 27.13$ Å, in each of which there is the tail to tail arrangement of molecules aligned in the unit cell with their long axes approximately parallel to the $[104]$ axis. The two halves of the double layer are related to each other by the screw axis.

Introduction

The crystal structure analysis of the cholesteryl aniline has been undertaken as one of a series of X-ray crystal structure determinations of cholesterol derivatives. Examination of the unit cell parameters of the cholesterol derivatives suggests that the majority of derivatives may have one of three common crystal packing arrangements, so called monolayers of type I and type II, and bilayers type.¹ However, the crystal data of cholesteryl aniline we obtained indicate that the cholesteryl aniline belongs to none of three crystal structure types. Therefore the primary aim in this study is to obtain structural informations concerning the conformation and the mode of the molecular interactions.



Cholesteryl Aniline

Experimental

Cholesteryl aniline, from Sigma Chemical Company Ltd., was recrystallized by slow evaporation of a mixture of acetone, ethanol and ether solution at 5°C . The resulting monoclinic, colorless, plate-like single crystals melted at 191.9°C .

Preliminary X-ray Weissenberg photographs showed that the crystal system is monoclinic with space group $P2_1$. Subsequent X-ray data were collected using a Nonius CAD-4 diffractometer with Mo- K_α graphite-monochromated radiation ($\lambda = 0.7107$ Å). And the accurate crystal lattice parameters were obtained by a least-squares fit of 23 reflections

Table 1. Summary of Crystal Data, Intensity Collection and Least-Squares Refinements Statistics

formula	$C_{27}H_{45}NHC_6H_5$
M_w	461.8
space group	$P2_1$
a , Å	9.020 (3)
b , Å	6.000 (1)
c , Å	27.130 (9)
β , deg	98.22 (2)
Z	2
V , Å ³	1453.19
$\mu(\text{Mo-}K_\alpha)$, cm ⁻¹	0.64
density, g/cm ³	1.06(calc.) 1.04(measured by flotation in a $aq.$ KI solution)
radiation	Mo- K_α (graphite monochromator, $\lambda = 0.7107$ Å)
crystal size, mm	$0.4 \times 0.4 \times 0.1$
cell constant determination	23 reflections ($20^\circ < 2\theta < 28^\circ$)
reflection measured	$+h_{max}$. 10, $+k_{max}$. 7, $\pm l_{max}$. 32
2θ range, deg.	2-50
scan type	ω - 2θ
scan range, deg.	$0.7 + 0.35 \tan \theta$
No. of observed reflection	2296 $ F_o > 2\sigma(F_o)$
R	0.058
R_w	0.074
w	$k/(\sigma^2(F_o) + g(F_o)^2)$
diffractometer	Enraf-Nonius CAD-4

with $20^\circ < 2\theta < 28^\circ$. X-ray intensities were collected by ω - 2θ scan technique over a scan width of $(0.7 + 0.35 \tan \theta)^\circ$ in ω . Three standard reflections ($\bar{5}, 1, 2$), ($\bar{3}, \bar{2}, \bar{3}$), ($\bar{2}, \bar{1}, 12$) were monitored for intensity and orientation check every 135 reflections. There was no significant loss of intensities throughout data collection. The 3002 independent reflections measured, range of hkl ; $0 \leq h \leq 10$, $0 \leq k \leq 7$, $-32 \leq l \leq 32$, within $\sin \theta / \lambda = 0.59$ Å⁻¹. And the 2296 reflections with $|F_o| > 2\sigma|F_o|$ were used in structure determination. Data were corrected for Lorentz and polarization effects, but the absorp-

Table 2. Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Thermal Parameters for Non-hydrogen Atoms of Cholesteryl Aniline. The e.s.d.'s are in parentheses. $U_{eq} = 1/3 \sum_i \sum_j U_{ij} a_i^* a_j^* a_i a_j$ ($\text{\AA}^2 \times 10^3$)

Atom	x	y	z	Ueq.
C(1)	8109(5)	1112(0)	3601(1)	53(2)
C(2)	7168(4)	579(7)	4012(1)	59(2)
C(3)	5842(4)	-866(7)	3821(1)	54(2)
C(4)	6364(4)	-2981(7)	3589(1)	54(2)
C(5)	7368(3)	-2532(6)	3202(1)	47(2)
C(6)	7052(4)	-3420(7)	2753(1)	56(2)
C(7)	7982(4)	-3138(9)	2343(1)	59(2)
C(8)	9549(4)	-2197(7)	2532(1)	48(2)
C(9)	9418(3)	-261(6)	2898(1)	45(2)
C(10)	8690(3)	-1001(6)	3356(1)	47(2)
C(11)	10942(5)	928(8)	3039(1)	59(2)
C(12)	11742(5)	1547(7)	2604(1)	60(2)
C(13)	11920(4)	-484(6)	2268(1)	51(2)
C(14)	10323(4)	-1392(7)	2110(1)	50(2)
C(15)	10484(5)	-3002(9)	1680(1)	63(2)
C(16)	11732(5)	-1965(9)	1422(1)	70(2)
C(17)	12408(4)	-11(8)	1754(1)	58(2)
C(18)	12934(5)	-2227(9)	2549(2)	58(2)
C(19)	9826(5)	-2255(9)	3740(2)	60(2)
C(20)	14101(4)	313(7)	1723(1)	63(2)
C(21)	14827(6)	2078(11)	206(2)	86(3)
C(22)	14322(5)	783(12)	1184(2)	89(4)
C(23)	15950(5)	665(15)	1090(2)	100(4)
C(24)	16166(6)	1056(19)	563(2)	127(5)
C(25)	17737(8)	919(18)	442(2)	128(5)
C(26)	17744(13)	970(52)	-102(4)	249(17)
C(27)	18722(13)	2490(40)	706(5)	229(14)
C(28)	3943(3)	-69(6)	4385(1)	57(2)
C(29)	3546(4)	2007(7)	4174(1)	64(2)
C(30)	2456(5)	3290(9)	4362(2)	81(3)
C(31)	1752(4)	2516(11)	4748(2)	93(3)
C(32)	2147(4)	479(10)	4962(1)	84(3)
C(33)	3240(4)	-818(8)	4789(1)	64(2)
N	4926(3)	-1475(6)	4198(1)	64(2)

tions were ignored. All of the crystal data are summarized in Table 1.

Structure Determination and Refinement

The phase problem was solved by direct method using the program SHELXS-86.² The direct method were applied to 589 reflections with $|E| > 1.3$. All the carbon and nitrogen atoms were located on the E map. The refinement was carried out with full-matrix least-square method, using the program SHELX-76.³ Four cycles of isotropic full-matrix least-squares refinements decreased R value to 0.14. And then anisotropic thermal parameters were introduced for the carbon and nitrogen atoms. After four cycles of anisotropic refinement, R reduced to 0.11. At this stage the 30 hydrogen atoms were found on the difference Fourier map and remain-

Table 3. Bond Distances ($\text{\AA}$) for Cholesteryl Aniline. The e.s.d.'s are in parentheses.

C(1)-C(2)	1.529(5)	C(1)-C(10)	1.557(4)
C(2)-C(3)	1.508(5)	C(3)-C(4)	1.520(6)
C(3)-N	1.451(4)	C(4)-C(5)	1.506(4)
C(5)-C(6)	1.324(4)	C(5)-C(10)	1.515(4)
C(6)-C(7)	1.495(4)	C(7)-C(8)	1.540(5)
C(8)-C(9)	1.542(5)	C(8)-C(14)	1.505(4)
C(9)-C(10)	1.552(4)	C(9)-C(11)	1.547(5)
C(10)-C(19)	1.547(6)	C(11)-C(12)	1.514(5)
C(12)-C(13)	1.544(5)	C(13)-C(14)	1.542(5)
C(13)-C(17)	1.547(4)	C(13)-C(18)	1.520(6)
C(14)-C(15)	1.536(5)	C(15)-C(16)	1.540(6)
C(16)-C(17)	1.549(6)	C(17)-C(20)	1.554(5)
C(20)-C(21)	1.503(7)	C(20)-C(22)	1.530(6)
C(22)-C(23)	1.527(6)	C(23)-C(24)	1.488(8)
C(24)-C(25)	1.502(9)	C(25)-C(26)	1.477(12)
C(25)-C(27)	1.418(12)	C(28)-C(29)	1.396(5)
C(28)-C(33)	1.415(4)	C(28)-N	1.373(4)
C(29)-C(30)	1.400(6)	C(30)-C(31)	1.381(7)
C(31)-C(32)	1.378(8)	C(32)-C(33)	1.389(6)

Table 4. Bond Angles ($^\circ$) for Cholesteryl Aniline. The e.s.d.'s are in parentheses

C(1)-C(2)-C(3)	114.4(2)	C(1)-C(10)-C(5)	108.2(3)
C(1)-C(10)-C(9)	108.4(3)	C(1)-C(10)-C(19)	109.8(3)
C(2)-C(1)-C(10)	113.4(2)	C(2)-C(3)-C(4)	110.2(3)
C(2)-C(3)-N	113.9(2)	C(3)-C(4)-C(5)	113.1(3)
C(3)-N-C(28)	124.7(3)	C(4)-C(3)-N	108.8(3)
C(4)-C(5)-C(6)	119.9(3)	C(4)-C(5)-C(10)	116.4(2)
C(5)-C(6)-C(7)	124.7(3)	C(5)-C(10)-C(9)	111.1(2)
C(5)-C(10)-C(19)	108.1(3)	C(6)-C(5)-C(10)	123.7(3)
C(6)-C(7)-C(8)	112.3(2)	C(7)-C(8)-C(9)	109.8(3)
C(7)-C(8)-C(14)	111.6(2)	C(8)-C(9)-C(10)	112.3(3)
C(8)-C(9)-C(11)	111.1(3)	C(8)-C(14)-C(13)	114.8(2)
C(8)-C(14)-C(15)	118.7(4)	C(9)-C(8)-C(14)	109.5(3)
C(9)-C(10)-C(19)	111.3(3)	C(9)-C(11)-C(12)	115.2(3)
C(10)-C(9)-C(11)	113.3(2)	C(11)-C(12)-C(13)	111.5(3)
C(12)-C(13)-C(14)	105.8(3)	C(12)-C(13)-C(17)	117.0(3)
C(12)-C(13)-C(18)	110.7(3)	C(13)-C(14)-C(15)	104.4(3)
C(13)-C(17)-C(16)	104.3(3)	C(13)-C(17)-C(20)	118.8(3)
C(14)-C(13)-C(17)	100.8(2)	C(14)-C(13)-C(18)	111.6(3)
C(14)-C(15)-C(16)	104.2(4)	C(15)-C(16)-C(17)	107.1(3)
C(16)-C(17)-C(20)	111.7(3)	C(17)-C(13)-C(18)	110.4(3)
C(17)-C(20)-C(21)	113.4(3)	C(17)-C(20)-C(22)	109.9(3)
C(20)-C(22)-C(23)	114.2(4)	C(21)-C(20)-C(22)	111.3(4)
C(22)-C(23)-C(24)	114.5(4)	C(23)-C(24)-C(25)	117.3(5)
C(24)-C(25)-C(26)	110.9(6)	C(24)-C(25)-C(27)	113.3(9)
C(26)-C(25)-C(27)	113.6(12)	N-C(28)-C(29)	122.5(3)
N-C(28)-C(33)	118.4(3)	C(28)-C(29)-C(30)	119.6(3)
C(28)-C(33)-C(32)	120.1(4)	C(29)-C(28)-C(33)	118.9(3)
C(29)-C(30)-C(31)	120.9(5)	C(30)-C(31)-C(32)	120.0(4)
C(31)-C(32)-C(33)	120.5(3)		

ing hydrogen atomic positions were calculated from the carbon framework assuming standard geometry ($C-H = 1.08 \text{ \AA}$, $\angle H-C-H = 109^\circ$). The function $\sum w(|F_o| - |F_c|)^2$ was mini-

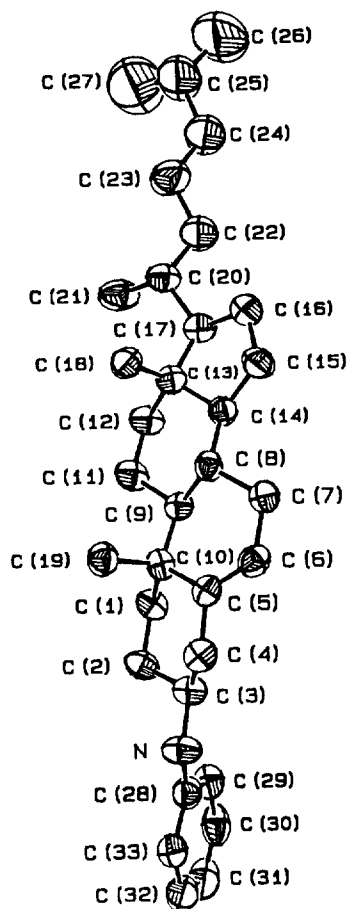


Figure 1. Molecular conformation with atomic numbering in Cholesteryl aniline.

mized in the refinements, where w is the weight of the reflection, defined by $w = 1.00/[\sigma^2(F_o) + 0.008(F_o)^2]$. In the final refinement, the positional parameters of all atoms, anisotropically for the carbon and nitrogen atoms, isotropic thermal parameters for the hydrogen atoms were refined. The final R and R_w values were 0.058 and 0.074, respectively for the 2296 observed reflections.

The final atomic coordinates and thermal parameters of the non-hydrogen atoms are given in Table 2.

Results and Discussion

The molecular conformation is depicted in Figure 1. The bond distances in the tail show the apparent shortening which is characteristic of cholesteryl compounds, and is caused by the high thermal vibrations in this region. In this case, it is especially pronounced in the C(25)–C(27) bond of 1.418 Å. In the cholesterol rings, the C–C bond distances range from 1.495 (4) to 1.557 (5) Å and the C(5) = C(6) distance is 1.324 (4) Å. In aniline group, the C–C bond distances range from 1.378 (8) to 1.415 (4) Å, respectively. The intramolecular distance C(3)–C(16) which is useful for comparing the length of the tetracyclic system has a value of 8.99 Å, which is close to the limits of range of 8.86 to 9.01 Å observed in related molecules.¹ A measure of the twist of the ring systems about its long axis, is given by the C(19)–C(10)–

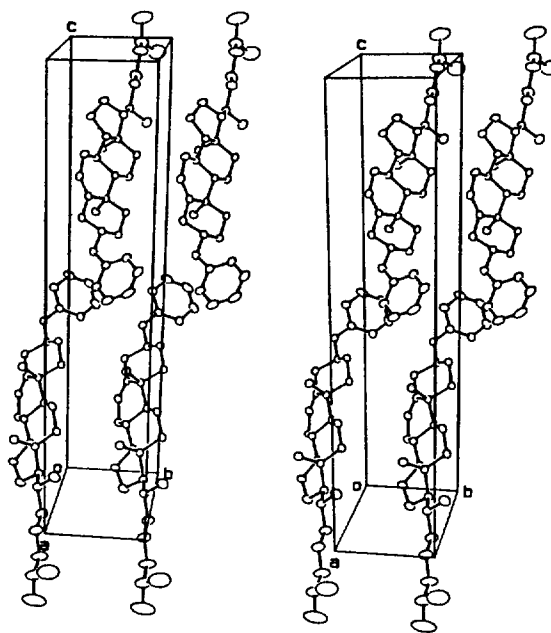


Figure 2. Molecular packing in Cholesteryl aniline viewed down the a -axis. Atoms are shown as 20% probability ellipsoids.

C(13)–C(18) pseudo torsion angle, which has a value of 14.8 (3)°. This torsion angle ranges between 7.9° and 18.0° in other related structures. Ring A and C assume the chair conformations; for ring A, $\langle \Delta C_s^A \rangle^* = 3.94$ and $\langle \Delta C_2 \rangle = 4.91$; for ring C, $\langle \Delta C_s \rangle = 6.64$ and $\langle \Delta C_2 \rangle = 8.07$. Ring B assumes a half chair and ring D the expected 13 β , 14 α -half chair conformations. The torsion angles, C(2)–C(3)–N–C(28) and C(4)–C(3)–N–C(28) which are important for determining the overall structure of the molecule are 75° and –161° respectively.

The C(17)–C(25) distance of 6.40 Å is taken as a measure of the extension of tail, this structure is almost fully extended. The seven atoms, C(17), C(20), C(22), C(23), C(24), C(25) and C(26), are in a zigzag planar chain and C(21) and C(27) are out of the plane.

The crystal structure is shown in Figures 2 and 3. The crystal structure consists of bilayers of thickness $d_{001} = 27.13$ Å, in each of which there is the tail to tail arrangement of molecules aligned in the unit cell with their long axes approximately parallel to the [104] axis. The two halves of the double layer are related to each other by the screw axis symmetry. Such bilayers are similar to those of sodium cholesteryl sulfate dihydrate.⁵

* ΔC_s : mirror plane asymmetry parameter

$$\Delta C_s = \left[\frac{\sum_{i=1}^m (\psi_i + \psi'_i)}{m} \right]^{1/2}$$

ΔC_2 : two-fold asymmetry parameter

$$\Delta C_2 = \left[\frac{\sum_{i=1}^m (\psi_i - \psi'_i)}{m} \right]^{1/2}$$

where $\Delta C_s(n)$ is measure of the deviations from mirror symmetry about a plane passing through atom n and the diametrically opposed atom o , and $\Delta C_2(n-o)$ is a measure of the deviations from two-fold symmetry about an axis bisecting bond ($n-o$). The symmetry related torsion angles are ψ and ψ' , and m is the number of such pairs.

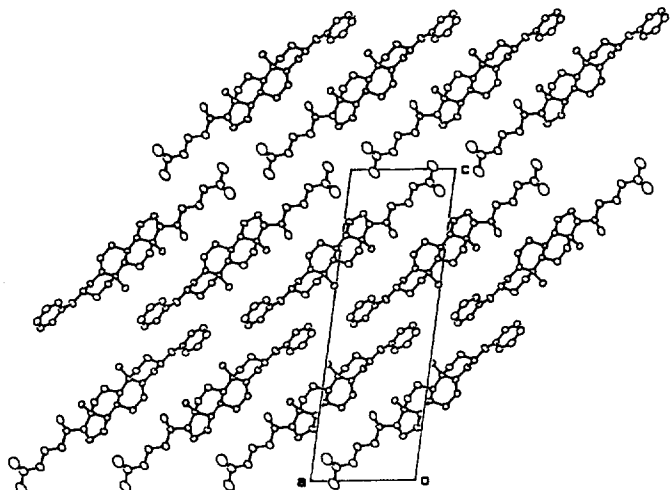


Figure 3. The structure of Cholesteryl aniline in projection down the *b*-axis. Atoms are shown as 30% probability ellipsoids.

The aniline groups, the rigid steroid skeleta and the branched hydrocarbon side chains form three regions with different packing character within the bilayer.

The lateral packing of the steroid skeleta is different from that found in other cholesteryl derivatives. In cholesteryl esters,⁶⁻¹⁵ the skeleta pack laterally in a double row arrangement in which the projecting methyl groups face each other and can interdigitate due to a displacement of the steroid skeleta in the direction of their maximum extension. In cholesteryl aniline the skeleta packed in single rows only. The methyl groups project into the space between two skeleta of the adjacent row.

The aniline groups are aligned so that their rings are stacked parallel in columns in the *a* direction and packed with its screw axis related neighbor. The closest approach between these two groups is 3.712 Å (C(32)...N contact) and the interplanar angle between two symmetry related benzene rings is 52.0°.

The packing of the bulky steroid and aniline groups provides the tail chain with unusually large space. This may explain the observed large thermal vibrations in the chain packing region.

There are several intermolecular contacts less than 4.0 Å, of which the shortest is C(11)...C(29) of 3.654 Å.

Acknowledgement. This work was supported by a research grant (901-0303-019-2) from the Korea Science and Engineering Foundation.

References

1. B. M. Craven, "The Physical Chemistry of Lipids", "Handbook of Lipid Research", Vol. 4, Chapter 6 Edit., D. M. Small, Plenum Press, New York (1986).
2. G. M. Sheldrick, SHELXS-86; Program for Crystal Structure Determination, Institute für Anorganische Chemie der Universität Göttingen, FRG (1986).
3. G. M. Sheldrick, SHELX-76; Program for Crystal Structure Determination, Univ. of Cambridge, England (1976).
4. W. L. Duax, and D. A. Norton, "Atlas of Steroid Structure", Vol. 1, p.18, Plenum Press, New York, U.S.A. (1975).
5. I. Pascher and S. Sundell, *Acta Chemica Scandinavica*, **A31**, 767 (1977).
6. B. M. Craven and P. Sawzik, *J. Lipid Res.*, **25**, 851 (1984).
7. B. M. Craven and N. G. Guerina, *Chem. Phys. Lipids*, **29**, 91 (1979).
8. I. H. Suh, T. S. Ko, Y. J. Park, Y. K. Yoon and W. Saenger, *Acta Cryst.*, **C44**, 2163 (1988).
9. Young Ja Park and B. M. Craven, *J. Korean Chemical Soc.*, **25**, 131 (1981).
10. B. K. Kang, M. J. Chung and Y. J. Park, *Bulletin of the Korean Chem. Soc.*, **6**, 333 (1985).
11. M. H. Kim, Y. J. Park, and C. T. Ahn, *Bulletin of the Korean Chem. Soc.*, **10**, 177 (1989).
12. R. J. Chandross and J. Border, *Acta Cryst.*, **B34**, 2872 (1978).
13. R. J. Chandross and J. Border, *Acta Cryst.*, **B33**, 2934 (1977).
14. S. Abrahamsson and B. Dahlen, *J. Chem. Soc. Chem. Comm.*, 117 (1976).
15. B. M. Craven and G. T. Detitta, *J. Chem. Soc. Perkin Trans. II*, 814 (1976).