fact, the $\bar{\nu}$ values of metal complexes were measured by elution with potassium sulfate solution as eluent. The results show that the $\bar{\nu}$ values of Co(III) complexes which have hydrophilic groups have smaller values than those of metal-phen complexes by elution with $0.25F$ $K_2SO_4$ solution (Table 2). Still more, $0.5F$ $KNO_3$ solution was used as an eluent to compare with the effect of sulfate. As a consequence, $\bar{\nu}$ values of metal-tn, en and $NH_3$ complexes by elution with $0.5$ $F$ $KNO_3$ solution were larger than those of metal-phen complexes. This phenomenon was the reverse compared with that with $0.25$ $F$ $K_2SO_4$. This results also show that hydrophilic groups interact more strongly with hydrophilic ions in eluent and hydrophobic group with hydrophobic ions.[13]

*Separation of Metal Complexes.* From the results obtained in this study some complexes were separated from the synthetic mixtures. Figure 3 shows the separation of synthetic mixture of $Co(gly)_3$, $[Ni(en)_3]^{2+}$, $[Fe(phen)_3]^{2+}$ or $[Co(phen)_3]^{3+}$, $[Co(en)_3]^{3+}$ and $[Co(NH_3)_6]^{3+}$.

## References


(1) H. Yoneda, C. E. Oh and S. Yamazaki, *Bull. Chem. Soc. Jpn.*, **53**, 2403 (1980).
(2) K. S. Lee and D. W. Lee, *Anal. Chem.*, **46**, 1903 (1974).
(3) K. S. Lee, D. W. Lee and W. Lee, *ibid.*, **47**, 2270 (1975).
(4) K. S. Lee, D. W. Lee and Y. S. Chung, *ibid.*, **45**, 396 (1973).
(5) R. M. Barnes and J. S. Genna, *ibid.*, **51**, 1065 (1979).
(6) R. Stock and C. B. F. Rice, "Chromatographic Methods", 3rd Ed., p. 16, Chapman and Hall, London, 1974.
(7) H. Yoneda, *Bull. Chem. Soc. Jpn.*, **40**, 2442 (1967).
(8) T. Baba, H. Yoneda and M. Muto, *ibid.*, **41**, 1965 (1968).
(9) T. Baba and H. Yoneda, *ibid.*, **43**, 2478 (1970).
(10) E. L. King and E. B. Dismukes, *J. Amer. Chem. Soc.*, **74**, 1674 (1952).
(11) E. L. King and R. R. Walters, *ibid.*, **74**, 4471 (1952).
(12) Y. Yoshikawa and K. Yamasaki, *Inorg. Nucl. Chem. Lett.*, **6**, 523 (1970).
(13) G. H. Searle, *Aut. J. Chem.*, **30**, 2625 (1977).
(14) L. F. Druding and G. B. Kauffman, *Coord. Chem. Rev.*, **5**, 409 (1968).
(15) H. Yoneda, S. Wakida, H. Nakazawa and U. Sakaguchi, *Bull. Chem. Soc. Jpn.*, **55**, 1073 (1982).
(16) B. G. Cox and A. J. Parker, *J. Amer. Chem. Soc.*, **94**, 3674 (1972).
(17) C. E. Oh, *J. Sci. Hiroshima Univ., Ser. A*, **44**, 145 (1980).
(18) A. D. Pethybrige and D. J. Spiers, *J. Chem. Soc., Faraday Trans. I*, **72**, 64 (1976).
(19) K. Miyoshi, T. Taura, C. Shimada and H. Yoneda, *Bull. Chem. Soc. Japan.*, **44**, 783 (1982).


# The Crystal and Molecular Structure of Thiamphenicol


**Whanchul Shin† and Sangsoo Kim**

*Department of Chemistry, College of Natural Sciences, Seoul National University, Seoul 151, Korea*

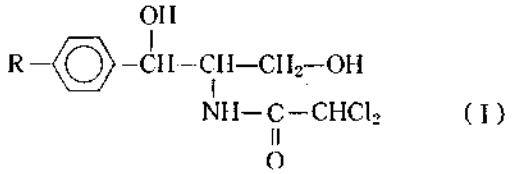

*(Received November 25, 1982)*



The structure of thiamphenicol, one of the congeners of chloramphenicol which is a well-known antibiotic, has been determined by single crystal x-ray diffraction techniques. The crystal structure was determined using diffractometer data obtained by the $2\theta$: $\omega$ scan technique with $MoK_\alpha$ radiation from a crystal having space group symmetry $P2_12_12_1$ and unit cell parameters $a=5.779$, $b=15.292$ and $c=17.322$ Å. The structure was solved by direct methods and refined by least squares to an $R=0.070$ for the 2116 reflections. The overall V-shaped conformation of thiamphenicol revealed in this study is consistent with those from the crystallographic studies and the proposed models from the theoretical and nmr studies of chloramphenicol. However there is no intramolecular hydrogen bond and the propanediol moiety is fully extended in the thiamphenicol molecule, while the crystal structures of chloramphenicol show the existence of the hydrogen bond between the two hydroxyl groups of the propanediol moiety forming an acyclic ring. All of the thiamphenicol molecules in the crystal are linked by a threedimensional hydrogen bonding network.


## Introduction

Thiamphenicol(TPL), 2, 2-dichloro-N-[2-hydroxy-1-(hydroxymethyl)-2-[4-(methylsulfonyl) phenyl] ethyl] acetamide (I), is one of the hundreds of chloramphenicol congeners and shows much weaker antibiotic activity than chloramphenicol. Chloramphenicol (CPL) is one of the simplest antibiotics known and the first one synthesized by the organic-chemical method.[1]



(I)

Thiamphenicol: $R=-SO_2CH_3$. Chloramphenciol: $R=-NO_2$

It is generally accepted that CPL inhibits protein synthesis by blocking the peptide bond formation in the 50 S subunit of the procaryotic ribosome, probably through an inhibition of the ribosomal peptidyl transferase.[2] However there have been controversies over the detailed mechanism of drug action at the molecular level. For example it is not yet known whether the CPL receptor site is in the aminoacyl (A) site or in the peptidyl (P) site of the 50 S subunit.[1,3,4] In the A site model, it has been postulated that drug activity of CPL comes from the ability to form an acyclic ring from the propanediol moiety of CPL through an intramolecular hydrogen bond between the two hydroxyl groups and from its structural resemblance to the intermediate in the catalytic reaction of peptidyl transferase.[3]

In an effort to relate the structure with the functional properties, many studies on the conformations of CPL and its congeners have been done. Crystal structure analysis of bromamphenicol, an isomorphous derivative of CPL, provided the first picture of the overall conformation in the crystalline state.[5] Subsequent theoretical calculations[6,8], nmr studies[7,8] and crystallographic studies[9,10] of CPL have shown that CPL assumes a relatively rigid V-shaped conformation despite the presence of many rotatable single bonds. However there have been conflicting results about the existence of the intramolecular hydrogen bond between the two hydroxyl oxygen atoms of the propanediol moiety. The crystal structures of CPL showed its presence, but the structural models predicted from the theoretical and nmr studies did not.

The crystal structure analysis of TPL has been undertaken in order to determine whether there is any consistency in the stable conformations among the congeners of CPL when the para substituent is different from that of CPL and whether the formation of an intramolecular hydrogen bond is required for the intrinsically stable conformation or is simply a result of crystal packing.

## Experimental

Transparent, prismatic crystals of TPL (Sigma) were obtained by slow evaporation of an ethanol solution at room temperature. The crystals were orthorhombic as determined from oscillation and Weissenberg photographs. The space group $P2_12_12_1$ was determined uniquely from the systematic absences. The unit cell parameters were determined by a least-squares fit of $2\theta$ angles for 25 centered reflections measured with $MoK_\alpha$ radiation on an automated Rigaku-Denki AFC diffractometer. Crystal data are as follows:

$C_{12}H_{15}NO_5SCl_2$; Mol. Wt. 356.2, F(000)=736
$a=5.779(1)$, $b=15.292(2)$, $c=17.322$ (1) Å
$V=1530.9$ Å$^3$, Space group $P2_12_12_1$, $Z=4$, $\mu=5.16$ cm$^{-1}$
$d_m=1.55$ gcm$^{-3}$ by flotation in $CCl_4$-$CH_2Cl_2$,
$d_c=1.545$gcm$^{-3}$

The reflection data from a crystal with dimensions of $0.2\times0.3\times0.4$ mm were collected with graphite-monochromated Mo $K_\alpha$ radiation using $2\theta$-$\omega$ scan technique over a range of 0.8° in $\omega$ plus a variable increment for spectral dispersion at a scan rate of 4°/min.[11] The background was counted for 10 sec at each end of the scan range. Three standard reflections were monitored after each 50 reflections. The intensities were corrected for Lorentz and polarization effects and then converted to structure factors. Of the 2578 independent reflections measured within the range of $2\theta\leq60.0°$, 462 were considered unobserved as defined by $F\leq6\sigma(F)$. No correction for the absorption and extinction effects was made.

## Structure Determination and Refinement

The structure was solved using the program MULTAN.[12] From the initial E map with the highest combined figure of merit it was possible to identify the positions of 16 atoms among 21 nonhydrogen atoms. One cycle of isotropic full-matrix least-squares refinement reduced the conventional R value ($R=\Sigma||F_0|-k|F_c||/\Sigma|F_6|$ where k is a single scale factor) from 0.39 to 0.28 and a subsequent difference Fourier map gave the positions of the remaining nonhydrogen atoms. After two cycles of isotropic and one cycle of anisotropic refinements with all nonhydrogen atoms, which lowered the R value to 0.13, all of the hydrogen atoms except two of the methyl group were located in a difference Fourier map. With all of the atoms including the two geometrically calculated methyl hydrogens two cycles of anisotropic refinement led the R value to 0.071. However the refined hydrogen positions were unacceptable and the temperature factors of the two chlorine atoms, especially $U_{22}$ component of Cl (1), were unreasonably large for the ordered structure. From an inspection of a difference map a disordered model of two chlorine atoms could be made and the refinements for the site occupancy factors for the two chlorine atoms showed 90 and 80 % occupancy for the major sites. However the R value became large (0.083) for the disordered model and the original minor sites from a map gradually moved to the major sites upon refinements. Therefore the refinement was terminated with the ordered model assuming a dynamic disordering effect.[13] Positions of the hydrogen atoms which were either calculated geometrically with the idealized bond lengths (1.08Å) and angles or located in a difference map were used in the final structure factor calculation. The final R value was 0.070 for 2116 observed reflections. All of the calculations were done using the program SHELX76.[14] The function minimized in the least-squares refinement was $\Sigma\omega(|F_0|-k|F_c|)^2$ and unit weight ($\omega$) was used throughout the analysis. All of the atomic scattering factors were from International Tables for X-ray Crystallography.[15] The final atomic parameters are listed in Table 1 and the final structure factor table is given in Table 2 (available as supplementary material from the author upon request).

## Results and Discussion

The atomic numbering scheme, the bond distances and angles are presented in Figure 1. The dimensions of the methylsulfonyl group agree well with those found in methyl 2, 2-diphenylvinyl sulfone.[16] Most of the bond distances and angles are normal and agree within $2\sigma$ with those found in

**TABLE 1: Fractional Coordinates and Temperature Factors for Thiamphenicol**

A. Nonhydrogen atoms[a]

| Atom | $x$ | $y$ | $z$ | $U11$ | $U22$ | $U33$ | $U23$ | $U13$ | $U12$ |
|---|---|---|---|---|---|---|---|---|---|
| S | 3535(4) | 7776(2) | 3540(1) | 26(1) | 24(1) | 33(1) | 1(1) | 2(1) | −5(1) |
| C(1) | 3177(16) | 6643(5) | 3425( ) | 28(5) | 20(4) | 24(4) | −2(3) | 3(4) | −4(3) |
| C(2) | 1180(17) | 6355(6) | 3052(5) | 27(4) | 25(4) | 26(4) | 5(3) | −6(4) | −4(4) |
| C(3) | 816(18) | 5450(6) | 2994(5) | 28(5) | 28(4) | 23(4) | 7(4) | −7(4) | −3(4) |
| C(4) | 2395(17) | 4867(5) | 3319(5) | 26(4) | 23(4) | 22(4) | 0(3) | 3(4) | −2(4) |
| C(5) | 4375(17) | 5175(6) | 3693(6) | 27(5) | 26(4) | 37(5) | 5(4) | −5(4) | 3(4) |
| C(6) | 4772(17) | 6081(6) | 3751(6) | 26(5) | 24(4) | 34(5) | −3(4) | −7(4) | −4(4) |
| C(7) | 1864(17) | 3900(6) | 3303(5) | 27(4) | 22(4) | 24(4) | 1(3) | 5(3) | 1(4) |
| C(8) | 58(17) | 3697(5) | 3951(5) | 27(4) | 19(3) | 21(4) | 1(3) | 1(4) | −3(3) |
| C(9) | −633(19) | 2728(6) | 3945(6) | 35(5) | 18(3) | 30(4) | 3(3) | 3(4) | −4(4) |
| C(10) | 221(17) | 4668(6) | 5062(5) | 30(5) | 24(4) | 20(4) | 0(3) | −4(4) | 2(4) |
| C(11) | 1143(20) | 4819(7) | 5873(6) | 37(6) | 35(5) | 32(5) | −8(4) | −9(5) | 14(5) |
| C(12) | 1654(22) | 8095(7) | 4273(7) | 42(6) | 38(5) | 34(5) | −13(4) | 9(5) | −2(5) |
| N | 924(14) | 3942(5) | 4715(4) | 27(4) | 20(3) | 20(3) | −1(3) | −2(3) | 5(3) |
| O(1) | 5965(14) | 7909(5) | 3830(5) | 27(4) | 36(4) | 80(6) | −1(4) | −10(4) | −11(3) |
| O(2) | 2994(15) | 8214(5) | 2826(4) | 56(6) | 33(4) | 32(3) | 12(3) | 0(4) | −6(4) |
| O(3) | 3862(13) | 3368(4) | 3439(4) | 32(4) | 27(3) | 36(3) | 0(3) | 10(3) | 8(3) |
| O(4) | −2510(15) | 2588(5) | 4464(5) | 38(4) | 30(3) | 45(4) | 9(3) | 10(4) | −8(3) |
| O(5) | −1084(15) | 5211(4) | 4813(4) | 52(5) | 31(3) | 34(3) | −8(3) | −10(4) | 21(4) |
| Cl(1) | −365(6) | 4104(3) | 6541(2) | 36(2) | 121(3) | 29(1) | 10(2) | 2(1) | −2(2) |
| Cl(2) | 4160(5) | 4627(2) | 5956(2) | 30(1) | 57(2) | 44(1) | −1(1) | −9(1) | −7(1) |

B. Hydrogen atoms[b]

| Atom | $x$ | $y$ | $z$ | $U$ | Atom | $x$ | $y$ | $z$ | $U$ |
|---|---|---|---|---|---|---|---|---|---|
| H(C2) | 4 | 678 | 283 | 26 | H(C3) | 58 | 522 | 272 | 26 |
| H(C5) | 551 | 475 | 392 | 30 | H(C6) | 617 | 631 | 402 | 28 |
| H(C7) | 126 | 376 | 278 | 25 | H(C8) | −124 | 405 | 384 | 23 |
| H(C91) | 71 | 236 | 411 | 27 | H(C92) | −110 | 255 | 341 | 27 |
| H(C11) | 87 | 545 | 600 | 35 | H(C121) | −9 | 789 | 441 | 38 |
| H(C122)* | 226 | 783 | 481 | 38 | H(C123) | 177 | 854 | 379 | 38 |
| H(O3)* | 481 | 343 | 306 | 32 | H(O4)* | −341 | 275 | 437 | 38 |
| H(N) | 207 | 355 | 498 | 22 | | | | | |

[a] Positional parameters $\times 10^4$; thermal parameters $\times 10^3$; the expression used for the anisotropic temperature factor is $\exp(-\{2\pi^2(h^2a^{*2}U11+\cdots 2hka^*b^*U12)\})$. Estimated standard deviation in parentheses is for least significant figure. [b] All parameters $\times 10^3$; the expression used for the isotropic temperature factor is $\exp(-((8\pi^2U)\sin^2\theta/\lambda^2))$.

*Coordinates from a difference Fourier map.

in CPL[9,10] and chloramphenicol $\beta$-palmitate($C_\beta$P),[17] The only exception is the C(11)-Cl(1) distance which is longer by $4\sigma$ than the average value of 1.77 Å found in CPL and $C_\beta$P.

The least-squares planes through the atoms of the benzene ring and through the amide group and the deviations of the individual atoms from these planes are given in Table 3. The benzene ring shows a good planarity. Five atoms, C(8), N, C (10), O(5) and C(11), inclusive of the amide group, essentially from a plane. The dihedral angle between the two planes is 44.1° and the overall shape of the molecule can be depicted as a two-sided, V-shape. The stereoview of the molecule is shown in Figure 2.

A projection of the crystal structure of TPL along the $a$-axis is presented in Figure 3. There are three unique hydrogen bonds in this structure which are tabulated in Table 4. The molecules, which are related by the 2-fold screw axis parallel to $a$ at $y=1/4$ and $z=1/2$ and by one unit translation along the $a$ axis, form an infinite spiral molecular column through the hydrogen bonds (types B and C in Table 4). All of the columns generated by the symmetry operations perpendicular to the $a$ axis are interconnected by the hydrogen bonds (type A) to form a three-dimensional hydrogen-bonding network. The potential hydrogen bond donor atoms are fully utilized in the network, although the potential acceptors such as O(1) and O(5) are not used. In the crystal packing no other contacts shorter than the sum of van der Waals radii are found. Cl(2) is in close contact with N in the same molecule (Cl(2)···H(N); 2.65Å, Cl(2)···N;3.04Å, ∠Cl(2)···H(N)–N;103°) which may be regarded as an intramolecular hydrogen bond. Since Cl(1)···H(N) distance is 3.16Å, difference in the close contact distances with H(N) atom might result in the greater thermal motion of Cl(1) than Cl(2) atom.

A comparison of the crystal structures of CPL and TPL is presented in Figure 4.[19] The overall conformations of the two molecules are very similar except in the terminal groups such as the dichloroacetamide and the O(4) hydroxyl groups. Particularly the five atoms, C(4), C(7), C(8), C(9) and N,

**TABLE 3:** Least-Squares Planes for Thiamphenicol

A. Phenyl ring

2.9013x−0.3425y−14.976bz=−4.4388

Displacement (Å) of the atoms from the plane:

| | | | | | |
|---|---|---|---|---|---|
| C(1)* : | 0.001 | C(2)* : | −0.007 | C(3)* : | 0.005 |
| C(4)* : | −0.004 | C(5)* : | 0.0 | C(6)* : | −0.003 |
| S : | −0.075 | C(7) : | −0.101 | O(1) : | 0.162 |
| O(2) : | 0.791 | O(3) : | 0.293 | C(12) : | −1.758 |
| C(8) : | −1.588 | | | | |

B. Amide group

4.4660x+7.5955y−6.8439z=0.1803

Displacement (Å) of the atoms from the plane:

| | | | | | |
|---|---|---|---|---|---|
| C(10)* : | 0.0 | N* : | 0.0 | O(5)* : | 0.0 |
| C(11) : | −0.029 | C(8) : | −0.050 | | |

*atoms which are used to define the planes.

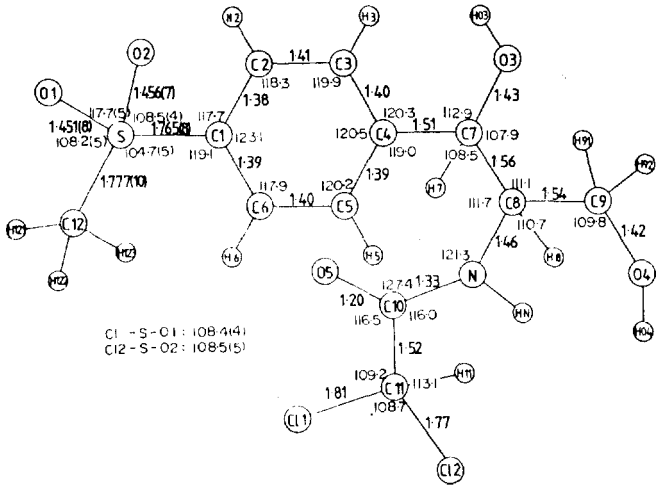



**Figure 1.** Schematic representation of the thiamphenicol molecule showing the atomic numbering scheme, the bond distances(Å) and angles(°). Estimated standard deviation in parentheses is for the least significant digit. All the standard deviations not shown in the figure are 0.01Å for the bond distances and 0.6 to 0.8° for the bond angles.

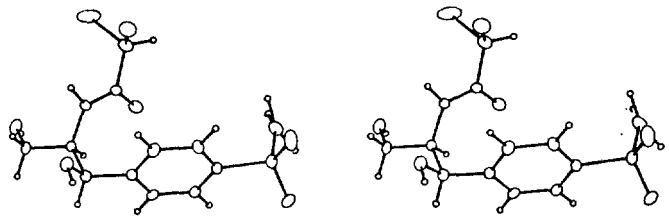


**Figure 2.** Stereoscopic ORTEP[18] drawing of the thiamphenicol molecule. The thermal ellipsoid boundaries are at the 30 % probability level except those for the hydrogen atoms which are represented by spheres of a fixed arbitrary radius.

**TABLE 4: Hydrogen Bonds in Thiamphenicol**

| Type | a | b | c | a-c(Å) | b-c(Å) | ∠abc(°) | Position of c |
|---|---|---|---|---|---|---|---|
| A | O(3)-H(O3)··· | O(2) | 2.86 | 2.02 | 164 | 1−x, $-\frac{1}{2}$+y, | $\frac{1}{2}$−z |
| B | N-H(N) ····· | O(4) | 2.88 | 2.01 | 145 | $\frac{1}{2}$+x, $\frac{1}{2}$−y, | 1−z |
| C | O(4)-H(O4)··· | O(3) | 3.00 | 2.25 | 154 | −1+x, y, | z |

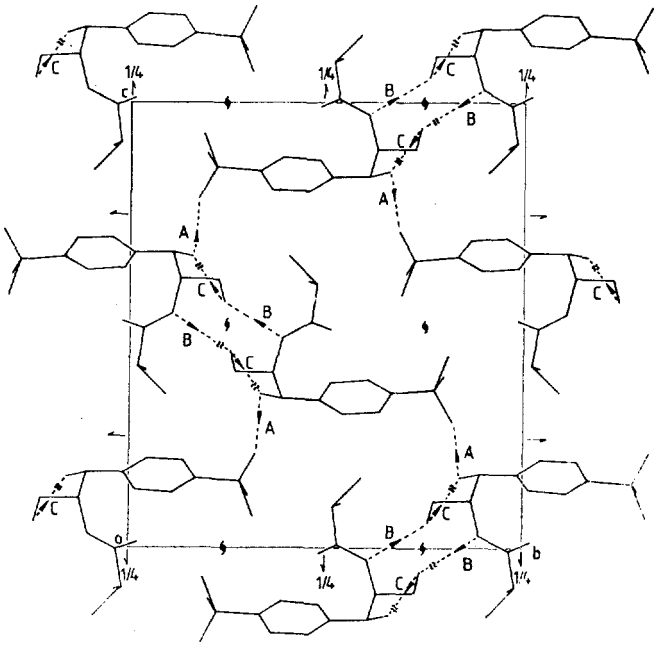


**Figure 3.** Schematic drawing of crystal packing in thiamphenicol projected along the *a* axis. Hydrogen atoms are omitted in the drawing. Dotted lines represent the hydrogen bonds, arrows the donor directions. The symbols (≈) denote the hydrogen bonds to the molecules translated by ± *a*.

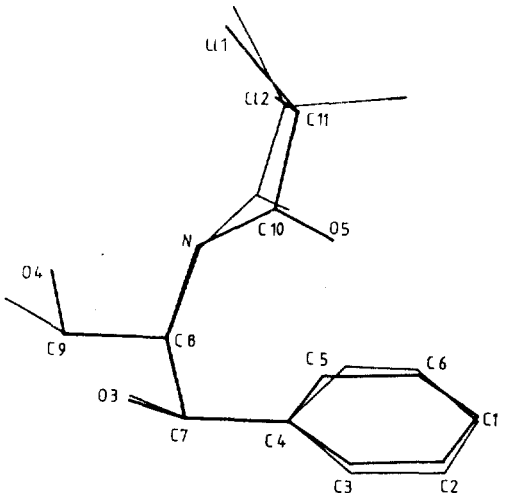


**Figure 4.** Schematic representation of the best least-squares molecular fitted TPL (heavy lines) and CPL (lighter lines) molecules.

**TABLE 5: Comparison of Torsion Angles***

| | $\tau_1$ | $\tau_2$ | $\tau_3$ | $\tau_4$ | $\tau_5$ | Ref. |
|---|---|---|---|---|---|---|
| Thiamphenicol[a] | −77.9 | −59.0 | −171.8 | 102.5 | −15.9 | this study |
| Chloramphenicol[a] | −89.4 | −54.9 | 67.0 | 124.1 | −171.3 | 10 |
| Chloramphenicol[b] | −90 | −60 | 180 | 120 | 60 | 6 |
| Chloramphenicol[c] | −90 | −65 | 180 | 95 | 0 | 8 |
| Chloramphenicol[a] β-palmitate | −76.8 | −68.7 | 69.4 | 155.1 | −49.3 | 17 |

*$\tau_1$=C(3)−C(4)−C(7)−C(8), $\tau_2$=C(4)−C(7)−C(8)−N, $\tau_3$=C(7)−C(8)−C(9)−O(4), $\tau_4$=C(7)−C(8)−N−C(10), $\tau_5$=O(5)−C(10)−C(11)−H(C11)

[a] crystal structure; [b] extended Hückel theory; [c] nonbond calculation

which constitute the base part of the V-shaped molecule, match almost perfectly. This similarity can be seen in the dihedral angles which are tabulated in Table 5. Even the crystal structure of $C_\beta$ P shows a great similarity in the overall conformation. It is very significant to find that the overall conformations of the CPL and its congeners are similar despite the different intermolecular hydrogen bonding patterns and thus the different crystal packing environments and despite the presence of the different substituents either at the para position of the phenyl ring or at the O(4) hydroxyl group. Structural models proposed from the nmr studies[7,8] and the energy calculations[6,8] (see the torsion angles in Table 5) also support the idea that CPL and its congeners are rather rigid molecules even though there are, in principle, many freely rotatable single bonds in the molecules. From the recent nmr studies of the ribosome-CPL complex[20], any conformational change in CPL upon binding to the ribosome was not observed and the binding process has been considered to be static rather than dynamic. This strongly implicates that the active conformation of the CPL molecule may be same as the intrinsically stable conformation, *i.e.*, the V-shaped conformation.

There is a major descrepancy in the observed structures of CPL and TPL. While the crystal structure of CPL shows the existence of an intramolecular hydrogen bond between the two hydroxyl oxygen atoms, O(3) and O(4), of the propanediol moiety, the crystal structures of TPL and $C_\beta$P do not. There fore the formation of an acyclic ring from the propanediol moiety through an intramolecular hydrogen bond does not seem to be a prerequisite for the CPL congeners to assume a stable conformation.

*Acknowledgement.* This research was supported by Grant No. ED81-302 of the Ministry of Education.

## References

(1) F. E. Hahn and P. Gund, "Topics in Infectious Diseases," (J. Drews and F. E. Hahn eds.). p. 245, University Park Press, Baltimore, Md., 1975.

(2) R. Werner, A. Kollak, D. Nierhaus, G. Schreiner and K. H. Nierhaus, *ibid.*, p. 217.

(3) P. Bhuta, H. L. Chung, J-S. Hwang and J. Zemlicka, *J. Med. Chem.*, **23**, 1299 (1980).

(4) B. V. Cheney, *J. Med. Chem.*, **17**, 590 (1974).

(5) J. D. Dunitz, *J. Amer. Chem.*, **74**, 995 (1952).

(6) H-D, Höltje and L. B. Kier, *J. Med. Chem.*, Soc., **17**, 814 (1974).

(7) O. Jardetzky, *J. Biol. Chem.*, **238**, 2498 (1963).

(8) T. M. Bustard, R. S. Egan, and T. J. Perun, *Tetrahedron*, **19**, 1961 (1973).

(9) K. Ravindra Acharya, D. S. Sake Gowda and M. Post, *Acta. Cryst.*, **B35**, 1360 (1979).

(10) C. Chatterjee, J. K. Dattagupta, N. N. Saha, W. Saenger and K. Müller, *J. Cryst. Mol. Struc.*, **9**, 295 (1979).

(11) The DCLT softwares for diffractometer control, data collection, and data reduction were obtained with the AFC system from Rigaku Corp.

(12) J. P. Declercq, G. Germain, P. Main and M. M. Woolfson, *Acta Cryst.*, **A29**, 231 (1973).

(13) J. D. Dunitz, "X-ray Analysis and the Structure of Organic Molecules," p. 52, Cornell University Press, Ithaca, N.Y., 1979.

(14) G. M. Sheldrick, The SHELX Program System, University Chemical Laboratory, Cambridge, England, 1976.

(15) "International Tables for X-ray Crystallography," Vol. IV, Kynoch Press, Birmingham, England, 1974.

(16) Par D. Tranqui, J. Vicat, and H. Fillion, *Acta Cryst.*, **B32**, 1228 (1976).

(17) K. Szulzewsky, S. Kulpe, B. Schulz and D. Kunath, *Acta Cryst.*, **B37**, 1673 (1981).

(18) C. K. Johnson, ORTEP, Report ORNL-3794, Oak Ridge National Laboratory, Tennessee, 1965.

(19) S. C. Nyburg, *Acta Cryst.*, **B30**, 251 (1974). Initially all of the atoms shown in Fig. 5 except Cl (1), Cl (2) and O (4) were used in the best molecular fitting Procedure (BMFIT). Since the five atoms C (4), C (7) ,C (8), C (9) and N in both structures gave a good fit, only these atoms were fitted again and the results are shown in Fig. 4. The average distance between these five pairs of the atoms is 0.03 Å.

(20) T. R. Tritton, *Arch. Biochem. Biophys.*, **197**, 10 (1979).