The Crystal Structure of a Versatile Organic Clathrate. 4-*p*-Hydroxyphenyl-2,2,4-trimethylchroman (Dianin's Compound)

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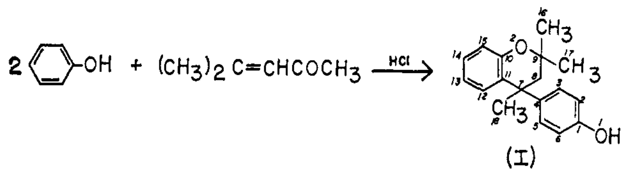
Abstract: Dianin's compound, $C_{18}H_{20}O_2$, forms crystalline inclusion compounds with a great variety of substances. The crystal structures of two adducts, one containing ethanol and the other chloroform, have been analyzed by X-ray diffraction and the size and shape of the cage have been established. Six host molecules form an hourglass-shaped cage. The guest molecules are disordered and show occupancy defects. The trigonal space group is $R\bar{3}$ with a = 26.969 and 27.116 Å, and c = 10.990 and 11.023 Å, respectively, for the ethanol and chloroform adducts. The structure of Dianin's compound was solved by means of the symbolic addition procedure. The included molecules were located in difference maps.

Inclusion compounds are defined as molecular combinations in which one component, the "guest," fits into a cavity in the other, the "host." There are six basic types of inclusion compounds characterized by the shape of the cavity found in the host. When the cavity is a three-dimensional enclosure which traps the guest molecule from all sides, the host is referred to as a clathrate or cage structure.[1]

Water clathrates, often called gas hydrates, are perhaps the best known inclusion compounds of this type and have been the subject of extensive chemical and X-ray investigations.[2] However, until this time, very little work beyond the determination of the space group and cell dimensions has been attempted on large organic inclusion compounds such as the cyclodextrins and Dianin's compound.

The cyclodextrins (inclusion compounds formed by cyclic oligosaccharides) differ from Dianin's compound in that different organic guests cause changes in the space groups of the complexes.[3] The crystal structure of one cyclohexaamylose has been solved.[4]

Dianin[5] observed that the product (I) prepared by the condensation shown below formed crystalline adducts with several common solvents. The formula of I was established by Baker and McOmie,[6] who made more than 40 different adducts and stated that Dianin's compound forms crystalline inclusion compounds with a greater variety of substances than any known organic compound. Preliminary X-ray analyses[7] established that the various crystalline inclusion compounds belong to the trigonal space group $R\bar{3}$ with cell dimensions a ~27.0 Å and c ~11.1 Å and suggested that closed cavities were formed by six host molecules.



(I)

The present investigation establishes the detailed crystal structure of the host molecule, the size and shape of the cavity, and some gross features of the included molecules such as disorder and unexpected configurations. Dianin's compound was supplied to us by Professor Mansel Davies, University College of Wales at Aberystwyth, who suggested that we undertake this investigation.

Experimental Section

The crystals used in the X-ray analyses were grown by evaporation from the solvent to be included within the cavity. Intensity data for both crystals were collected on a four-circle automatic diffractometer using the θ–2θ technique with a $2.0° + 2\theta(\alpha 2) - 2\theta(\alpha_1)$ scan over 2θ. Pertinent physical quantities are listed in Table I. The intensity data were corrected for Lorentz and polarization factors and placed on an absolute scale by means of a K curve,[8] and normalized structure factor magnitudes $|E|$ as well as structure factor magnitudes $|F|$ were derived.

Structure Determination

The structure of Dianin's compound was solved, using the ethanol adduct, with the symbolic addition procedure[9] for obtaining phases directly from the structure factor magnitudes. In space group $R\bar{3}$ only one phase is needed to specify the origin. For hexagonal indexing, the origin determining reflection must have l odd.[10] It is most convenient, although not necessary, to choose a reflection having a large $|E_{\bar{h}}|$ value for which $l = \pm 1$. The reflection used to specify the origin and three additional reflections which were assigned symbols to represent their signs in order to implement the Σ_2 formula[9,10] are listed in Table II. Since, in this space group, $F_{hkl} = F_{ihl} = F_{kil} = F_{\bar{h}\bar{k}\bar{l}}$ (where $i = -(h + k)$), the set actually consisted of 24 reflections whose signs were specified and signs for 158 additional independent reflections having $|E_{\bar{h}}| \geq 1.70$ were readily derived from them. During the phase determining process several indications arose relating the signs of the symbols. An

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(1) J. F. Brown, Jr., *Sci. Amer.*, **207**, 82 (July 1962).

(2) G. A. Jeffrey and R. K. McMullan, *Progr. Inorg. Chem.*, **8**, 43 (1967).

(3) J. A. Hamilton, L. K. Steinrauf, and R. L. Van Etten, *Acta Cryst.*, **B24**, 1560 (1968).

(4) A. Hybl, R. E. Rundle, and D. E. Williams, *J. Amer. Chem. Soc.*, **87**, 2779 (1965).

(5) A. P. Dianin, *J. Soc. Phys. Chim. Russe*, **46**, 1310 (1914).

(6) W. Baker and J. F. W. McOmie, *Chem. Ind.* (London), 256 (1955).

(7) H. M. Powell and B. D. P. Wetters, *ibid.*, 256 (1955).

(8) J. Karle and H. Hauptman, *Acta Cryst.*, **6**, 473 (1953).

(9) J. Karle and I. L. Karle, *ibid.*, **21**, 849 (1966).

(10) H. Hauptman and J. Karle, A. C. A. Monograph, No. 3, Polycrystal Book Service, Pittsburgh, Pa., 1953.

Table I. Physical Data for Ethanol and Chloroform Adducts of Dianin's Compound[a]

	Ethanol adduct	Chloroform adduct
Habit	Colorless hexagonal prisms	Colorless hexagonal prisms
Crystal size	0.7 mm (mounting axis *c*) × 0.3 mm (maximum cross section in *ab* plane)	0.8 mm (mounting axis *c*) × 0.45 mm (maximum cross section in *ab* plane)
Space group	$R\bar{3}$	$R\bar{3}$
a	26.969 ± 0.003 Å	27.116 ± 0.003 Å
c	10.990 ± 0.002 Å	11.023 ± 0.002 Å
γ	120°	120°
V	6921.3 Å^3	7019.2 Å^3
z (Dianin's)	18	18
Molecules in asymmetric unit (Dianin's)	1	1
δ_{calcd}	1.18 g/cm^3	1.23 g/cm^3
Radiation	Cu Kα	Cu Kα
Number of independent reflections	2694	2570
Percentage of reflections significantly above background ($|F_0| > 5.0$)	89.8%	82.3%
Maximum sin θ/λ	0.5937	0.5937

[a] Molecular formula, $C_{18}H_{20}O_2$; molecular weight, 268.36.

Table II. Set of Reflections Used to Implement the Σ_2 Relation

h	*k*	*l*	Sign	E_h
6	15	$\bar{3}$	+ (origin specification)	3.73
10	8	$\bar{4}$	*a*	3.41
10	16	6	*b*	3.26
11	7	$\bar{5}$	*c*	3.22

E map computed with ~550 phases having $|E_{\vec{h}}| \geq 1.0$ contained 20 peaks of approximately equal weight corresponding to the 20 nonhydrogen atoms in the host molecule, and there were no spurious indications. The sign of the origin reflection was subsequently changed from + to − for the convenience of having one cage extend from 0 to 1 along the *c* axis. After least-squares refinement on the coordinates and thermal factors of the host molecule the hydrogen atoms and ethanol molecules were located in difference maps.

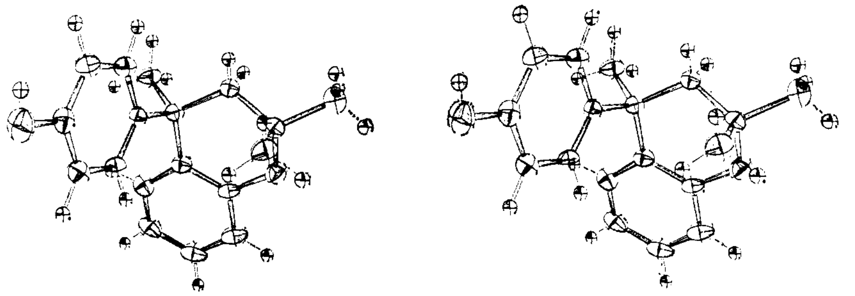

Figure 1. A stereodrawing of a single molecule of 4-*p*-hydroxyphenyl-2,2,4-trimethylchroman.

The coordinates of the carbon and oxygen atoms of Dianin's compound, as derived from the ethanol adduct data, were used as a starting point for refinement of the data from the chloroform adduct. The hydrogen atoms and chloroform molecules were then located in difference maps.

Final coordinates for the cage atoms in both adducts are listed in Table III. Approximate coordinates for hydrogen atoms are listed in Table IV.

Cage Formation and Packing

A stereodrawing of a single molecule of Dianin's compound is shown in Figure 1. Six molecules are linked together by hydrogen bonding between their OH groups, OH···O = 2.85 Å, as shown in Figure 2, to form a large complex in which alternate molecules point up or down. These complexes are stacked directly above each other, with their symmetry axes parallel to the *c* axis, to form long chains. A cage is formed when two of these complexes stack together (see Figure 3), with one hexagon of hydrogen bonded oxygens forming the floor of the cage and the next hexagon of hydrogen bonded oxygens, one unit cell away in *c*, forming the ceiling of the cage. A waist is formed in the cage by methyl groups protruding into it at $z \cong 0.5$. The nearest approaches between atoms in the upper part and the lower part of the cage are O(2)···C(3)′ at 3.65 Å and C(16)···C(17)′ at 3.70 Å. All other intermolecular, intracage approaches are considerably larger. This type of arrangement apparently persists regardless of the type of molecule trapped within the cage. However, it does seem that the cage can expand slightly to accommodate larger molecules as evidenced by the slightly larger cell dimensions for the chloroform crystal.

There are 18 molecules of Dianin's compound per unit cell which are associated into three six-molecule complexes each of which is situated on a threefold

Table III. Fractional Coordinates for Dianin's Compound[a,b]

Atom	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
O(1)	0.0644	0.1202	0.9817	4.36	3.49	3.19	1.96	0.62	1.23
	0.0653	0.1211	0.9810	6.62	6.40	5.40	3.31	0.72	1.66
O(2)	0.0869	0.2611	0.3746	3.49	3.27	3.14	2.18	−1.03	−0.62
	0.0874	0.2623	0.3750	5.52	5.30	4.76	3.09	−1.14	−0.72
C(1)	0.0883	0.1614	0.8912	3.27	2.62	2.22	1.53	0.10	0.10
	0.0892	0.1627	0.8909	4.85	4.85	3.89	2.43	0.00	0.21
C(2)	0.1407	0.1753	0.8375	3.27	3.27	2.95	2.18	−0.10	0.10
	0.1404	0.1762	0.8365	5.30	5.30	4.76	3.31	−0.41	0.21
C(3)	0.1621	0.2157	0.7444	2.62	3.05	2.80	1.74	0.00	0.00
	0.1613	0.2163	0.7437	3.97	5.07	4.47	2.65	0.00	0.00
C(4)	0.1328	0.2436	0.7040	2.18	2.18	1.93	1.31	−0.10	−0.20
	0.1327	0.2442	0.7034	3.75	3.97	3.89	2.21	−0.41	−0.52
C(5)	0.0819	0.2296	0.7617	2.40	3.05	2.56	1.74	−0.10	0.00
	0.0821	0.2296	0.7627	4.41	4.41	4.23	2.65	0.00	0.00
C(6)	0.0595	0.1887	0.8547	2.40	3.27	2.56	1.74	0.10	0.00
	0.0604	0.1898	0.8550	4.41	5.07	4.42	2.65	0.41	0.31
C(7)	0.1577	0.2868	0.5991	1.96	2.18	2.46	1.09	−0.20	−0.10
	0.1574	0.2875	0.5988	3.53	4.19	4.28	1.99	0.00	−0.10
C(8)	0.1647	0.2593	0.4814	1.96	3.05	2.37	1.31	0.20	−0.10
	0.1645	0.2609	0.4817	3.53	4.63	4.28	1.99	0.41	0.31
C(9)	0.1104	0.2239	0.4080	2.40	2.62	2.71	1.31	0.00	−0.20
	0.1109	0.2263	0.4072	3.97	4.41	4.37	2.21	−0.10	−0.21
C(10)	0.0874	0.2982	0.4620	2.18	2.18	3.09	0.87	0.10	0.20
	0.0872	0.2984	0.4625	3.75	3.97	4.52	1.99	0.21	0.41
C(11)	0.1197	0.3124	0.5682	2.18	2.18	2.37	1.09	0.20	0.20
	0.1197	0.3130	0.5687	3.53	3.75	4.28	1.76	0.52	0.62
C(12)	0.1178	0.3530	0.6441	3.71	2.84	2.80	1.96	0.51	0.31
	0.1175	0.3527	0.6452	4.85	4.19	4.62	2.43	0.52	0.31
C(13)	0.0845	0.3768	0.6177	3.71	3.27	3.96	2.40	0.72	0.41
	0.0844	0.3768	0.6190	5.52	4.85	5.74	3.31	1.24	0.72
C(14)	0.0522	0.3613	0.5110	3.05	3.05	4.83	1.96	0.72	1.03
	0.0521	0.3612	0.5134	4.41	4.63	6.42	2.87	0.72	1.14
C(15)	0.0537	0.3221	0.4329	2.62	2.84	3.72	1.53	0.00	0.72
	0.0545	0.3228	0.4355	3.97	5.29	5.39	2.43	0.00	0.93
C(16)	0.0643	0.1717	0.4718	2.62	2.84	3.86	0.87	−0.10	0.00
	0.0648	0.1740	0.4702	4.12	4.63	5.54	1.54	0.00	−0.21
C(17)	0.1260	0.2085	0.2849	4.14	4.14	3.00	2.18	−0.20	−1.23
	0.1261	0.2107	0.2862	5.74	5.96	4.57	2.87	0.21	−0.83
C(18)	0.2183	0.3355	0.6350	2.18	2.84	3.82	0.65	−0.51	−0.41
	0.2173	0.3356	0.6357	3.97	4.63	6.12	1.76	−0.83	−0.41
Standard deviations									
O	0.0002	0.0002	0.0004	0.22	0.22	0.19	0.22	0.20	0.20
	0.0001	0.0001	0.0004	0.22	0.22	0.14	0.22	0.10	0.10
C	0.0003	0.0003	0.0006	0.22	0.22	0.29	0.22	0.20	0.20
	0.0002	0.0002	0.0004	0.22	0.22	0.19	0.22	0.10	0.10

[a] The thermal parameters are of the form $T = \exp[-{}^1/_4(B_{11}h^2a^{*2} + B_{22}k^2b^{*2} + B_{33}l^2c^{*2} + 2B_{12}hka^*b^* + 2B_{13}hla^*c^* + 2B_{23}klb^*c^*)]$. The B_{ij}'s are in Å^2. [b] Coordinates for the chloroform adduct are listed below the coordinates for the ethanol adduct.

Table IV. Approximate Coordinates for Hydrogen Atoms Located in Difference Maps

Atom	Bonded to	Ethanol adduct			Chloroform adduct		
		x	y	z	x	y	z
H(O1)	O(1)	0.082	0.103	0.983	0.095	0.120	0.983
H(2)	C(2)	0.162	0.154	0.867	0.167	0.125	0.858
H(3)	C(3)	0.205	0.230	0.708	0.198	0.225	0.708
H(5)	C(5)	0.060	0.248	0.733	0.065	0.250	0.733
H(6)	C(6)	0.021	0.179	0.892	−0.023	0.160	0.952
H(8a)	C(8)	0.179	0.237	0.500	0.180	0.241	0.500
H(8b)	C(8)	0.195	0.288	0.430	0.191	0.288	0.433
H(12)	C(12)	0.137	0.363	0.725	0.145	0.367	0.709
H(13)	C(13)	0.079	0.405	0.675	0.077	0.401	0.675
H(14)	C(14)	0.025	0.379	0.492	0.031	0.381	0.492
H(15)	C(15)	0.030	0.312	0.358	0.029	0.312	0.358
H(16a)	C(16)	0.051	0.180	0.542	0.052	0.187	0.542
H(16b)	C(16)	0.031	0.148	0.414	0.029	0.152	0.417
H(16c)	C(16)	0.076	0.146	0.492	0.075	0.150	0.487
H(17a)	C(17)	0.092	0.188	0.242	0.096	0.192	0.233
H(17b)	C(17)	0.138	0.188	0.303	0.142	0.188	0.293
H(17c)	C(17)	0.154	0.246	0.242	0.150	0.238	0.242
H(18a)	C(18)	0.246	0.321	0.633	0.240	0.318	0.637
H(18b)	C(18)	0.233	0.367	0.575	0.231	0.369	0.574
H(18c)	C(18)	0.218	0.352	0.717	0.216	0.350	0.725

inversion center. The packing of adjacent chains of complexes is illustrated in Figure 4 and the contents of one unit cell are shown in Figure 5. Figures 1-5 were drawn by a computer driven Calcomp plotter using the ORTEP program.[11]

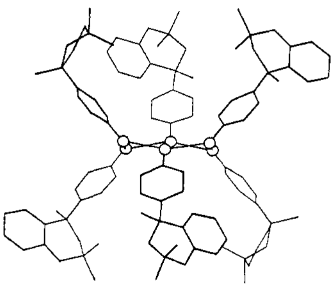

Figure 2. A complex of six molecules of Dianin's compound linked by the hydrogen bonding of the six hydroxyl groups.

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(11) C. K. Johnson, "ORTEP, A Fortran Thermal-Ellipsoid Plot

Figure 3. The stacking of two complexes along the *c* axis to form the closed cavities in the crystal. The cavity is bounded at top and bottom by the rings of six hydrogen-bonded hydroxyl groups.

There is no hydrogen bonding other than that between the OH groups, and while there are no C···C approaches closer than 3.75 Å between neighboring complexes, the only spaces in the unit cell large enough to accommodate the guest molecules are found within the cagelike areas. Bond distances and angles for Dianin's compound are illustrated in Figures 6 and 7 and are listed in Table V. Standard deviations based only on the least-squares agreement are ~0.012 Å for the bond lengths and ~0.8° for the angles.

The Cavity. Dianin's compound forms inclusion compounds of the clathrate type in a manner similar to quinol in that six molecules of the host are linked by hydrogen bonding of the OH groups to become the cage forming entity. The molecules of both substances extend alternately up and down from the hexagons of hydrogen bonded OH groups. In quinol, however, the

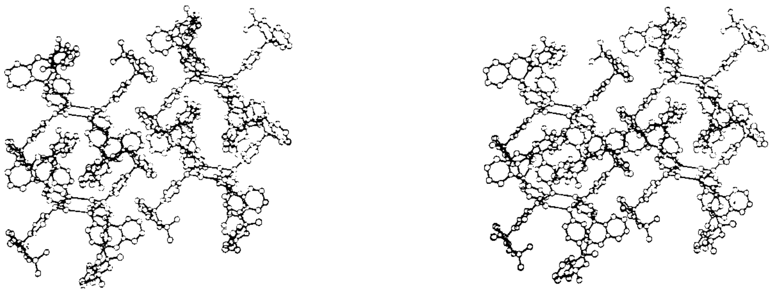

Figure 4. A stereodiagram showing the lateral packing between the chains of molecules containing the cages. The *c* axis is vertical.

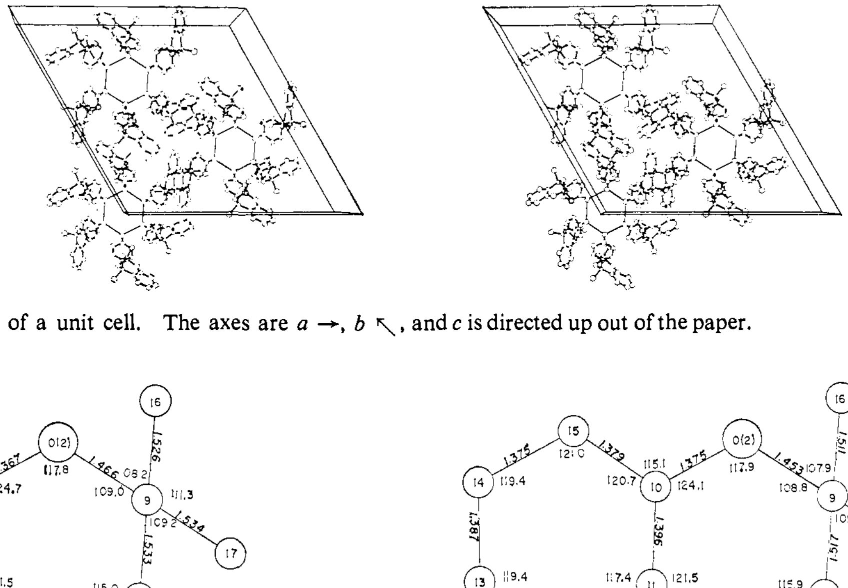

Figure 5. The contents of a unit cell. The axes are *a* →, *b* ↖, and *c* is directed up out of the paper.

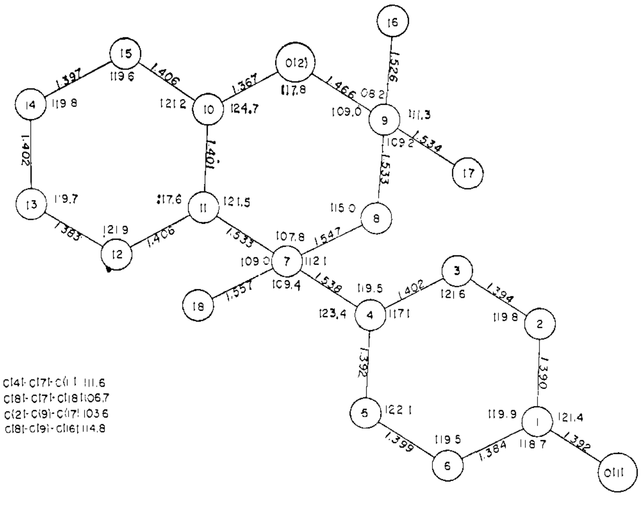

Figure 6. Bond distances and angles for the ethanol adduct.

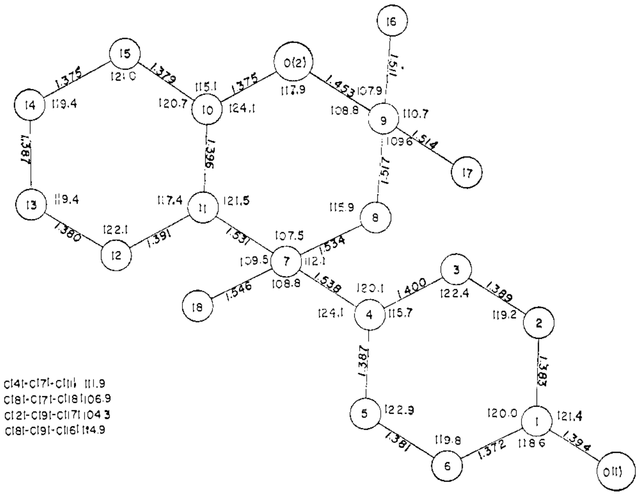

Figure 7. Bond distances and angles for the chloroform adduct.

Program for Crystal Structure Illustrations," U. S. Atomic Energy Commission Report ORNL-3794, 1965. These pictures should be seen with a three-dimensional viewer for printed stereophotographs. The viewers are commercially available from either The Taylor Merchant Corp., 25 West 45th St., New York, N. Y. 10036, or from Hubbard Scientific Co., 2855 Shermer St., Northbrook, Ill. 60062.

Table V. Bond Lengths and Angles

	Bond length, A			Bond angle, deg	
	Ethanol adduct	Chloroform adduct		Ethanol adduct	Chloroform adduct
O(1)-C(1)	1.392	1.394	O(1)-C(1)-C(2)	121.4	121.4
O(2)-C(9)	1.466	1.453	O(1)-C(1)-C(6)	118.7	118.6
O(2)-C(10)	1.367	1.375	C(2)-C(1)-C(6)	119.9	120.0
C(1)-C(2)	1.390	1.383	C(1)-C(2)-C(3)	119.8	119.2
C(1)-C(6)	1.384	1.372	C(2)-C(3)-C(4)	121.6	122.4
C(2)-C(3)	1.394	1.389	C(3)-C(4)-C(5)	117.1	115.7
C(3)-C(4)	1.402	1.400	C(3)-C(4)-C(7)	119.5	120.1
C(4)-C(5)	1.392	1.387	C(5)-C(4)-C(7)	123.4	124.1
C(4)-C(7)	1.538	1.538	C(4)-C(5)-C(6)	122.1	122.9
C(5)-C(6)	1.389	1.381	C(5)-C(6)-C(1)	119.5	119.8
C(7)-C(8)	1.547	1.534	C(4)-C(7)-C(8)	112.1	112.1
C(7)-C(11)	1.533	1.531	C(4)-C(7)-C(11)	111.6	111.9
C(7)-C(18)	1.557	1.546	C(4)-C(7)-C(18)	109.4	108.8
C(8)-C(9)	1.533	1.517	C(8)-C(7)-C(11)	107.8	107.5
C(9)-C(16)	1.526	1.511	C(8)-C(7)-C(18)	106.7	106.9
C(9)-C(17)	1.534	1.514	C(11)-C(7)-C(18)	109.0	109.5
C(10)-C(11)	1.401	1.396	C(7)-C(8)-C(9)	115.0	115.9
C(10)-C(15)	1.406	1.379	O(2)-C(9)-C(8)	109.0	108.8
C(11)-C(12)	1.406	1.391	O(2)-C(9)-C(16)	108.2	107.9
C(12)-C(13)	1.383	1.380	O(2)-C(9)-C(17)	103.6	104.3
C(13)-C(14)	1.402	1.387	C(8)-C(9)-C(16)	114.9	114.9
C(14)-C(15)	1.397	1.375	C(8)-C(9)-C(17)	109.2	109.6
			C(16)-C(9)-C(17)	111.3	110.7
			O(2)-C(10)-C(11)	124.7	124.1
			O(2)-C(10)-C(15)	114.1	115.1
			C(11)-C(10)-C(15)	121.2	120.7
			C(7)-C(11)-C(10)	121.5	121.5
			C(7)-C(11)-C(12)	120.9	121.1
			C(10)-C(11)-C(12)	117.6	117.4
			C(11)-C(12)-C(13)	121.9	122.1
			C(12)-C(13)-C(14)	119.7	119.4
			C(13)-C(14)-C(15)	119.8	119.4
			C(10)-C(15)-C(14)	119.6	121.0
			C(9)-O(2)-C(10)	117.8	117.9

second OH groups are involved in identical hydrogen bonding which gives rise to a giant molecule extending to infinity in three dimensions.[12] The cavities in quinol are roughly spherical and ~4 Å in diameter. Owing to the size of the cavity only relatively small guest molecules (such as H_2S, SO_2, CH_3OH, etc.) can be accommodated.

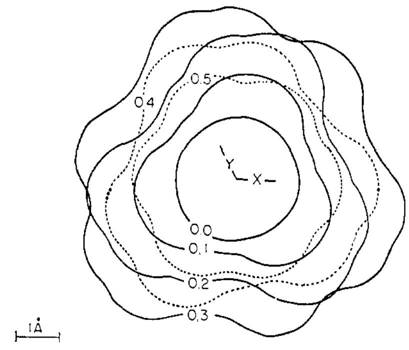

Figure 8. The space available in the cage in cross-sections at various levels along the *c* axis. The van der Waals volumes about the atoms forming the cage have been accounted for.

In contrast, in Dianin's compound there is only one OH group available for hydrogen bonding, so that, instead of an infinite network of cages, there are separate columns of independent cages as described in the previous section. The cage is twice as long (along the *c* direction) in Dianin's compound as in quinol. It is not spherical but, rather, has an hourglass shape with the indentation at the center caused by the methyl groups which protrude into the cage at $z \simeq 0.5$.

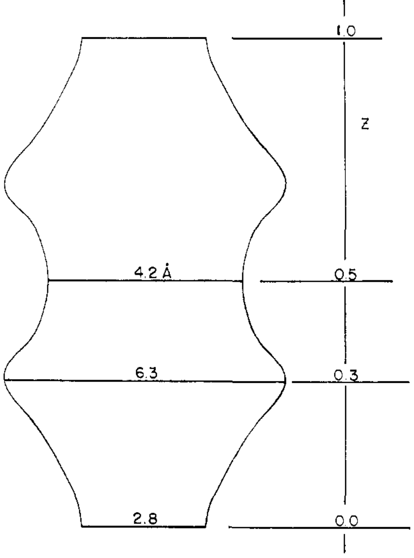

Figure 9. The shape and size of the largest figure of revolution which can fit into the cage. There is actually more space for shapes that vary from cylindrical symmetry. The height is 11.0 Å.

The cage is quite large—~11 Å long and ~ 6.2 Å wide at its point of maximum extension at $z \sim 0.3$ and ~ 0.7. Figures 8 and 9 illustrate the size and shape of

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(12) D. E. Palin and H. M. Powell, *J. Chem. Soc.*, 815 (1948).

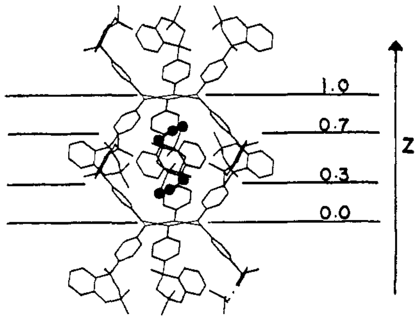

Figure 10. The orientation of the two ethanol molecules in the cage. Each ethanol molecule is triply disordered since the crystal symmetry requires a threefold rotation axis.

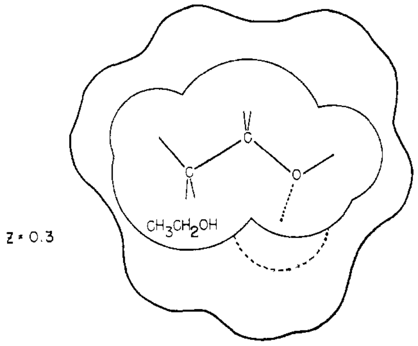

Figure 11. The size of the ethanol molecule, surrounded by van der Waals radii, as compared to the space in the cage at the level accommodating the ethanol molecule.

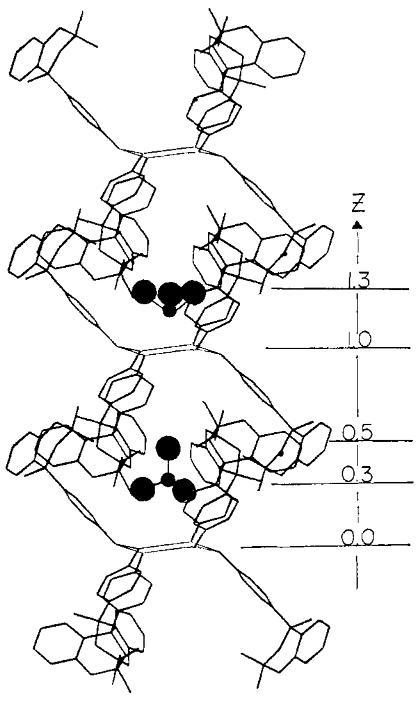

Figure 12. Chloroform molecules in their two different orientations.

the cavity. The cross-sectional contours in Figure 8, seen looking down the *c* axis, were drawn using van der Waal's radii for the cage atoms. They represent the greatest degree of freedom for a hydrogen atom at each level. Figure 8 represents only half of the cage, 0.0–0.5 in *z*. Figure 9 shows the entire cage along the *c* axis and was obtained from the diameters of the largest circles which could be inscribed in each of the sections in Figure 8. The cage is widest from $z = 0.25$ to 0.35 and one would expect to find the included molecules in this region.

The Included Molecules. The included molecules, ethanol and chloroform, were located by means of difference maps after least-squares refinement of the coordinates and thermal factors of the host atoms. The ethanol molecules make use of the largest cross-sections in the cage with the atoms having *z* coordinates between 0.25 and 0.35 and between 0.65 and 0.75, as shown in Figure 10. Space group symmetry requires a threefold rotation axis; hence the molecules are triply disordered. The ethanol molecules have more than sufficient space in the cage as illustrated in Figure 11. The large thermal parameters associated with the ethanol atoms as determined by the least-squares refinement indicate that the ethanol is not rigidly fixed in the cavity. These large values may, in part, be due to an occupancy deficiency, *i.e.*, not all cages have two ethanol molecules.

The chloroform molecule has a threefold axis and could satisfy the crystal symmetry without being disordered. As expected, a chloroform molecule was located having a carbon atom on the *c* axis with the Cl atoms (at $z \simeq 0.3$) around it in a trigonal configuration (molecule I in Table VI). However, a second orientation was found for a chloroform molecule with one Cl atom at 0, 0, $^1/_2$ and the other two Cl atoms disordered among three positions (molecule II in Table VI). The orientations in the cage of both $CHCl_3$ molecules are illustrated in Figure 12. The large thermal factor for the Cl atoms may be due, in part, to the fact that the same coordinates were used for the nonaxial Cl atoms in both molecules whereas they may be slightly displaced from one another. Refinement on the occupancies indicated that the ratio of Dianin's compound to chloroform is 6:1 or an average of only one molecule per cage. In addition, there is approximately a 1:1 ratio of molecule I to molecule II. Because of space limitations, there can be only one molecule of type II per cage but there can be two molecules of type I per cage. Hence, there is the possibility that some cages are completely empty.

Table VI. Approximate Coordinates for Chloroform Molecules

Atom	*x*	*y*	*z*	*B*
		Molecule I		
Cl	0.058	0.057	0.287	15.3
C	0.000	0.000	0.202	11.6
		Molecule II		
Cl′	0.000	0.000	0.500	9.9
Cl	0.058	0.057	0.287	15.3
C	0.000	0.000	0.337	8.9

Both adducts were refined using a full matrix three-dimensional least-squares program RFINE[13] which allows constraints to be placed upon dependent param-

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[13] W. Finger, "RFINE—A Fortran IV Computer Program for Structure Factor Calculation and Least-Squares Refinement of Crystal Structures," Geophysical Laboratory, Carnegie Institution of Washington, Washington, D. C., 1969.

eters. The final R factors for the ethanol and chloroform adducts are, respectively, 8.0 and 13.0% for all the data and 6.7 and 10.2% if the weakest reflections ($|F_o| \leq 5.0$) and those having large extinction errors are omitted.[14]

Finding a Cl atom at $z = 1/2$, the waist of the cage, suggested the possibility of including a larger molecule which could extend throughout the entire length of the cage. No such molecules were included in published studies.[6] However, an investigation on the occupancy of various isomers of heptane has been made by Goldup.[15] The cross section of the waist of the cage is large enough to accommodate CH_2 groups arranged in a zigzag chain. Crystals of an adduct with n-heptyl alcohol, which has an overall molecular length of ~10 Å, have been prepared and the structure is currently under investigation.

(14) For a complete list of observed and calculated structure factors order Document NAPS-00958 from ASIS National Auxiliary Publications Service, % CCM Information Corp., 909 Third Ave., New York, N. Y. 10022, remitting $1.00 for microfiche or $3.00 for photocopies. Make checks payable to CCMIC-NAPS.

(15) A. Goldup, British Petroleum Co., Ltd., private communication.

The Conformation and Crystal Structure of the Cyclic Polypeptide ┌Gly-Gly-D-Ala-D-Ala-Gly-Gly┐ ·$3H_2O$

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Abstract: A single-crystal X-ray diffraction analysis has been made on the structure of the cyclic polypeptide ┌Gly-Gly-D-Ala-D-Ala-Gly-Gly┐·$3H_2O$. If the CH_3 groups in the alanine residues are disregarded, the molecule very nearly has a center of symmetry. All the peptide units are planar and in the *trans* conformation. In order to close the ring, the residues, from N to N, have the conformations *cis,trans,cis,cis,trans,cis*. The 18-membered ring is stabilized by two intramolecular hydrogen bonds and by hydrogen bonding to H_2O molecules. Each NH and CO moiety participates in one or more hydrogen bonds. The material crystallizes in the orthorhombic space group $P2_12_12_1$ with cell parameters $a = 12.662$, $b = 18.102$, and $c = 8.678$ Å. The X-ray intensity data were collected with an automatic diffractometer and refined to an $R = 6.5\%$. The crystal structure was solved by the symbolic addition procedure for phase determination for noncentrosymmetric crystals.

The conformation of cyclic polypeptides is of fundamental importance in understanding the relationship between the structure and function of natural products.[1] Detailed structural information obtained from single-crystal X-ray diffraction analyses has been published for the cyclic tetradepsipeptide ┌D-HyIv-L-MeIleu-D-HyIv-L-MeLeu┐,[2] for ferrichrome-A·$4H_2O$,[3] and for cyclohexaglycyl·$1/2H_2O$.[4] In the cyclic tetradepsipeptide, the two peptide units assumed the *cis* conformation, contrary to the general observation from linear polypeptides that the *trans* conformation prevails. In the crystal of the cyclic hexaglycyl, there are four distinct conformers in the same unit cell. Only one of the conformers has intramolecular hydrogen bonds. Accordingly, it seemed appropriate to investigate the crystal structure of another cyclic hexapeptide in order to compare its conformation with that of the cyclohexaglycyl. The material reported in this investigation is the cyclic polypeptide I. It was prepared by

┌Gly-Gly-D-Ala-D-Ala-Gly-Gly┐

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the method of Gerlach, Ovchinnikov, and Prelog[5] anp made available to us by Dr. Bernhard Witkop of the National Institutes of Health.

Experimental Section

The crystal was a thin plate, roughly hexagonal in shape. The b axis was perpendicular to the plate, and the crystal was mounted along the c axis. Cell constants and other physical data are listed in Table I.

Table I. Physical Data

Mol formula	$C_{14}H_{22}O_6N_6 \cdot 3H_2O$
Mol wt	424.4
Habit	Thin tabular (010)
Crystal size	0.7 × 0.08 × 0.7 mm
Space group	$P2_12_12_1$
a	12.662 ± 0.003 Å
b	18.102 ± 0.005 Å
c	8.678 ± 0.002 Å
V	1989.06 Å^3
ρ calcd	1.417 g/cm^3
Radiation	Cu Kα, 1.5418 Å
No. of independent reflections	1975
Molecules per unit cell	4

The X-ray intensity data were collected from one crystal on a four-circle automatic diffractometer using the θ,2θ (moving crystal–

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(1) See, *e.g.* M. M. Shemyakin and Yu. A. Ovchinnikov, *Recent Develop. Chem. Natur. Carbon Compounds*, **2**, 1 (1967); *Chem. Abstr.*, **68**, 87510 (1968); and Conformation of Biopolymers, International Symposium in Madras, G. N. Ramachandran, Ed., 1967.

(2) J. Konnert and I. L. Karle, *J. Amer. Chem. Soc.*, **91**, 4888 (1969).

(3) A. Zalkin, J. D. Forrester, and D. H. Templeton, *ibid.*, **88**, 1810 (1966).

(4) I. L. Karle and J. Karle, *Acta Crystallogr.*, **16**, 969 (1963).

(5) H. Gerlach, Yu. A. Ovchinnikov, and V. Prelog, *Helv. Chim. Acta*, **47**, 2294 (1964).