Journal of Inclusion Phenomena **1**, 169–174. 0167–7861/83/0012–0169$00.90

Crystal Structure Analysis of the Inclusion Compound of 2′-Hydroxy-2,4,4,7,4′-pentamethylflavan with 1,4-Dioxan and Water

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(Received: 18 April 1983; revised: 5 July 1983)

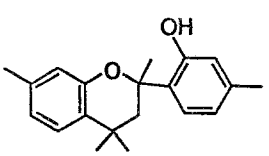
Abstract. The 2 : 1 : 2 complex of 2′-hydroxy-2,4,4,7,4′-pentamethylflavan (**1**) with 1,4-dioxan and water is triclinic, space group $P\bar{1}$, with $a = 8.164\,(1)$, $b = 8.960\,(1)$, $c = 14.644\,(1)$ Å, $\alpha = 91.56\,(1)$, $\beta = 97.19\,(1)$, $\gamma = 103.37\,(1)°$; there are two flavan host, two water molecules and a single 1,4-dioxan guest molecule in the unit cell. The dioxan molecule is linked, *via* a hydrogen-bonded water molecule, to the phenolic OH group. The second hydrogen of this water molecule is also involved in hydrogen bonding, in this case to the ring oxygen of a second host molecule. Thus a hydrogen-bonded hexameric unit, a common feature of many clathrates of phenolic hosts, is not found in the present structure.

Key words: Inclusion compound; X-ray crystal structure analysis; 2′-hydroxy-2,4,4,7,4′-pentamethylflavan; guest component 1,4-dioxan and water.

Supplementary Data relevant to this article have been deposited with the British Library Lending Division, and copies may be ordered from there, quoting Sup. 90077.

1. Introduction

In marked contrast to the wealth of structural information now available for Dianin's compound, 4-*p*-hydroxyphenyl-2,2,4-trimethylchroman [1], and related systems [2], to date no detailed structural information has appeared for 2′-hydroxy-2,4,4,7,4′-pentamethylflavan (**1**), a molecule long known to be capable of forming crystalline complexes [3].



(**1**)

Moreover, many other 2′-hydroxyflavan hosts related to (**1**) have also been discovered [4], but in no case has a full crystal structure analysis been reported. A recent detailed ESR study of the nitroxide spin label 2,2,6,6-tetramethyl-4-piperidinol-1-oxyl (tanol) as guest in (**1**) has been described [5], and the free radical guest species has been found to be well oriented at room temperature in the host lattice. We now report an investigation of an inclusion compound of (**1**), undertaken to elucidate the host conformation, the nature of host-guest interactions, and particularly the role of hydrogen-bonding in complexes of this type. The

Table I. Fractional atomic co-ordinates, and isotropic temperature factors ($Å^2$) for the hydrogen atoms, with standard deviations in the least significant digits in parentheses. Hydrogen atoms have the numbers of the carbon atoms to which they are attached

	x/a	*y/b*	*z/c*	*U*
C(1′)	0.4797(3)	0.4515(2)	0.7447(1)	
C(2)	0.5583(3)	0.3727(2)	0.8247(1)	
C(2′)	0.4477(3)	0.5966(3)	0.7577(2)	
C(3)	0.7329(3)	0.4602(3)	0.8699(2)	
C(3′)	0.3698(3)	0.6643(3)	0.6857(2)	
C(4)	0.8769(3)	0.4799(3)	0.8096(2)	
C(4′)	0.3236(3)	0.5911(3)	0.5979(2)	
C(5)	0.9885(3)	0.2998(3)	0.7084(2)	
C(6)	0.9719(4)	0.1661(3)	0.6569(2)	
C(7)	0.8222(4)	0.0518(3)	0.6473(2)	
C(8)	0.6928(4)	0.0782(3)	0.6945(2)	
C(9)	0.7108(3)	0.2133(3)	0.7464(1)	
C(10)	0.8586(3)	0.3284(3)	0.7548(1)	
C(11)	0.3554(3)	0.4484(3)	0.5853(2)	
C(12)	0.4298(3)	0.3804(3)	0.6563(2)	
C(13)	0.4351(3)	0.3348(3)	0.8947(2)	
C(15)	0.2376(7)	0.6662(6)	0.5213(3)	
C(16)	0.8740(4)	0.6082(3)	0.7429(2)	
C(17)	1.0462(4)	0.5248(4)	0.8740(2)	
C(18)	0.7979(6)	−0.0910(4)	0.5867(3)	
C(19)	1.1573(6)	−0.0035(9)	0.0432(3)	
C(20)	1.0095(6)	−0.0351(7)	0.0910(3)	
O(D)	0.8806(3)	0.0325(2)	0.0526(1)	
O(W)	0.6106(4)	0.0658(3)	0.1456(2)	
O(1)	0.5724(2)	0.2222(2)	0.7906(1)	
O(14)	0.4939(2)	0.6715(2)	0.8432(1)	
H(WA)	0.433(5)	1.022(5)	0.831(2)	0.10(1)
H(WB)	0.290(6)	0.930(5)	0.872(3)	0.13(2)
H(3′)	0.345(3)	0.765(3)	0.698(1)	0.033(5)
H(3A)	0.762(3)	0.398(3)	0.926(2)	0.049(7)
H(3B)	0.727(3)	0.569(3)	0.898(2)	0.059(7)
H(5)	1.087(4)	0.376(3)	0.705(2)	0.057(8)
H(6)	1.065(4)	0.150(3)	0.624(2)	0.074(9)
H(8)	0.589(4)	0.002(3)	0.687(2)	0.059(8)
H(11)	0.325(4)	0.396(3)	0.524(2)	0.066(8)
H(12)	0.452(3)	0.293(3)	0.648(1)	0.031(6)
H(13A)	0.482(3)	0.271(2)	0.939(1)	0.065(7)
H(13B)	0.418(4)	0.429(3)	0.920(2)	0.086(8)
H(13C)	0.328(2)	0.272(2)	0.869(1)	0.045(5)
H(14)	0.466(5)	0.771(4)	0.853(2)	0.10(1)
H(15A)	0.311(6)	0.763(5)	0.511(3)	0.12(2)
H(15B)	0.237(10)	0.629(8)	0.478(5)	0.22(4)
H(15C)	0.145(6)	0.695(5)	0.536(3)	0.13(2)
H(16A)	0.976(4)	0.629(3)	0.712(2)	0.067(8)
H(16B)	0.778(4)	0.596(3)	0.705(2)	0.047(8)
H(16C)	0.878(4)	0.693(4)	0.772(2)	0.07(1)
H(17A)	1.140(4)	0.543(3)	0.836(2)	0.070(9)
H(17B)	1.057(4)	0.628(3)	0.921(2)	0.065(8)
H(17C)	1.054(4)	0.443(3)	0.914(2)	0.072(9)
H(18A)	0.717(6)	−0.166(5)	0.610(3)	0.14(2)

Table I. (*continued*)

	x/a	*y/b*	*z/c*	*U*
H(18B)	0.763(6)	−0.087(5)	0.520(3)	0.15(2)
H(18C)	0.903(7)	−0.134(5)	0.613(3)	0.16(2)
H(19A)	0.769(6)	0.092(5)	−0.054(3)	0.12(1)
H(19B)	0.878(6)	−0.051(5)	−0.074(3)	0.09(1)
H(20A)	−1.042(5)	−0.006(4)	0.172(3)	0.12(1)
H(20B)	0.990(5)	−0.160(5)	0.056(3)	0.12(1)

stoichiometry [3] of the complex selected for initial study was 2 : 1 : 2 for host (**1**), 1,4-dioxan, and water species, respectively.

2. Crystal Data

$2[C_{20}H_{24}O_2] \cdot C_4H_8O_2 \cdot 2H_2O$, Formula weight = 716.96. Triclinic, $a = 8.164\,(1)$, $b = 8.960\,(1)$, $c = 14.644\,(1)$, $\alpha = 91.56\,(1)$, $\beta = 97.19\,(1)$, $\gamma = 103.37\,(1)°$, $U = 1032.1$ Å^3, $Z = 1$, $D_c = 1.15$ g cm^{-3}. Space group $P\bar{1}$ (No. 2).

3. Structure Determination

A single, colourless crystal, obtained by crystallisation of (**1**) according to the conditions described in [3], was mounted in a capillary, and used for the measurement at ambient temperature (20°) of 3629 independent X-ray intensities by a θ–ω scan on a Nonius CAD4 diffractometer, using graphite-monochromated MoK_α radiation. These comprised all possible reflections with $\sin\theta/\lambda < 0.59$. 2213 reflections having $F^2 > 2\sigma(F^2)$ were considered observed, where $\sigma(F^2) = [C + 4(B_1 + B_2) + 0.0009\,I^2]^{1/2}/(t_c Lp)$, C is the total integrated count in time

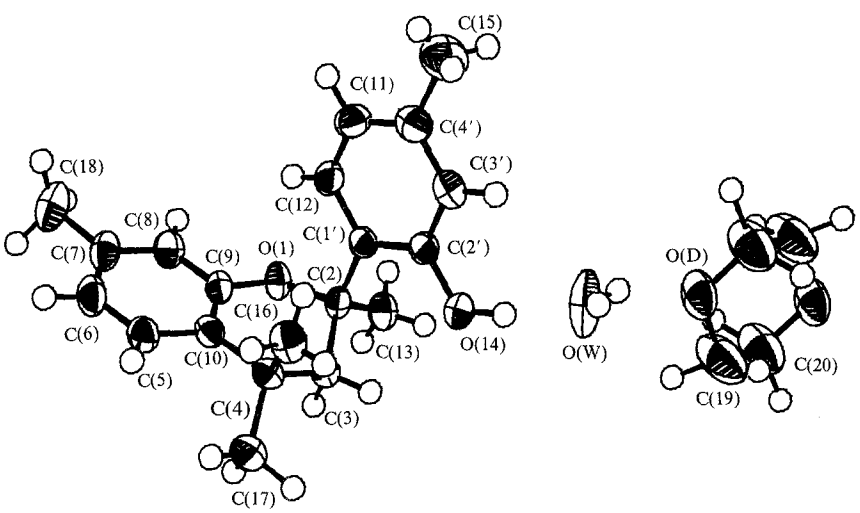


Fig. 1. A general view showing the host and guest molecules in the inclusion compound of 2′-hydroxy-2,4,4,7,4′-pentamethylflavan (**1**) with 1,4-dioxan and water as guests. Hydrogen atoms have the same numbers as the atoms to which they are attached.

t_c, B_1 and B_2 are background counts, $I = C-2(B_1 + B_2)$, Lp is the correction factor for Lorentz and polarisation effects, and $F^2 = I/(t_c Lp)$. Intensities were not corrected for absorption. Counting-coincidence errors were avoided by use of an attenuator on high intensities. Unit cell parameters were determined by least-squares refinement of diffractometer setting angles for 25 reflections. Computations were carried out on a Gould-SEL 32/27 computer in the laboratory; the principal computer programs used are listed in reference [6]. Atomic scattering factors were taken from reference [7].

The formula corresponds to two asymmetric units, so that the unit cell contains two host molecules, two water molecules, and one crystallographically centrosymmetric dioxan guest molecule. The structure was solved by the MITHRIL program [6], all hydrogen atoms being located in difference-Fourier maps calculated during the anisotropic least-squares refinement. The isotropic hydrogen parameters were included in the refinement, which gave a final R factor of 0.043 for 2213 reflections.

Table 2. Selected bond lengths (Å) and valency angles (°), with standard deviations in parentheses.

C(1′)–C(2)	1.534(3)	C(1′)–C(2′)	1.396(4)
C(1′)–C(12)	1.396(4)	C(2)–C(3)	1.517(4)
C(2)–C(13)	1.515(4)	C(2)–O(1)	1.460(3)
C(2′)–C(3′)	1.389(4)	C(2′)–O(14)	1.371(3)
C(3)–C(4)	1.538(4)	C(3′)–C(4′)	1.395(4)
C(4)–C(10)	1.525(4)	C(4)–C(16)	1.532(4)
C(4)–C(17)	1.535(4)	C(4′)–C(11)	1.374(4)
C(4′)–C(15)	1.506(6)	C(5)–C(6)	1.368(4)
C(5)–C(10)	1.397(4)	C(6)–C(7)	1.390(4)
C(7)–C(8)	1.392(4)	C(7)–C(18)	1.497(5)
C(8)–C(9)	1.379(4)	C(9)–C(10)	1.384(4)
C(9)–O(1)	1.387(3)	C(11)–C(12)	1.367(4)
C(19)–C(20)	1.445(7)	C(19)–O(D)	1.402(6)
C(20)–O(D)	1.399(6)	O(W)–H(WA)	0.89(4)
O(W)–H(WB)	0.88(5)	O(14)–H(14)	0.98(4)
C(2)–C(1′)–C(2′)	121.3(2)	C(2)–C(1′)–C(12)	122.2(2)
C(2′)–C(1′)–C(12)	116.4(3)	C(1′)–C(2)–C(3)	114.9(2)
C(1′)–C(2)–C(13)	109.5(2)	C(1′)–C(2)–O(1)	108.7(2)
C(3)–C(2)–C(13)	111.5(2)	C(3)–C(2)–O(1)	108.0(2)
C(13)–C(2)–O(1)	103.6(2)	C(1′)–C(2′)–C(3′)	120.9(3)
C(1′)–C(2′)–O(14)	118.8(2)	C(3′)–C(2′)–O(14)	120.2(3)
C(2)–C(3)–C(4)	116.3(2)	C(2′)–C(3′)–C(4′)	121.2(3)
C(3)–C(4)–C(10)	108.4(2)	C(3)–C(4)–C(16)	112.5(3)
C(3)–C(4)–C(17)	107.7(2)	C(10)–C(4)–C(16)	109.3(2)
C(10)–C(4)–C(17)	111.6(3)	C(16)–C(4)–C(17)	107.4(3)
C(3′)–C(4′)–C(11)	117.7(3)	C(3′)–C(4′)–C(15)	120.2(3)
C(11)–C(4′)–C(15)	122.1(3)	C(6)–C(5)–C(10)	122.3(3)
C(5)–C(6)–C(7)	121.2(3)	C(6)–C(7)–C(8)	116.9(3)
C(6)–C(7)–C(18)	121.9(3)	C(8)–C(7)–C(18)	121.2(3)
C(7)–C(8)–C(9)	121.5(3)	C(8)–C(9)–C(10)	121.7(3)
C(8)–C(9)–O(1)	115.0(3)	C(10)–C(9)–O(1)	123.3(2)
C(4)–C(10)–C(5)	121.8(3)	C(4)–C(10)–C(9)	121.9(2)
C(5)–C(10)–C(9)	116.3(3)	C(4′)–C(11)–C(12)	121.3(3)
C(1′)–C(12)–C(11)	122.5(3)	C(20)–C(19)–O(D)	113.9(4)
C(19)–C(20)–O(D)	113.2(5)	C(19)–O(D)–C(20)	112.4(4)
H(WA)–O(W)–H(WB)	113.6(38)	C(2)–O(1)–C(9)	118.6(2)
C(2′)–O(14)–H(14)	118.9(20)		

Atomic coordinates are given in Table I, bond lengths and angles in Table II, and thermal ellipsoids and atom labelling are shown in Figure 1. Thermal parameters and observed and calculated structure factors are in Supplementary Publication 90077.

4. Discussion of the Structure

Figure 1 gives an illustration of the host and guest molecules. The most salient features of the host are the half-chair conformation of the heterocyclic ring and the outward-facing disposition of the phenolic hydroxyl group, which is not involved in intra-molecular hydrogen bonding. The half-chair conformation of the oxygen-containing ring is characterised by displacements of 0.34 and 0.29 Å above and below the mean plane of the fused benzene ring. A distorted half-chair conformation has also been found for the six-membered oxygen-containing ring in Dianin's compound [8]. The rotational orientation around the bond C(2)–C(1′) is shown by the torsion angles C(12)–C(1′)–C(2)–O(1) $-1.4(2)°$ and C(2′)–C(1′)–C(2)–C(3) $+60.2(3)°$.

The 1,4-dioxan guest molecule, located at a centre of inversion, has a chair conformation and, as a result of the favourable orientation of the flavan's phenyl group, the phenolic hydroxyl is linked indirectly *via* a water molecule to a dioxan oxygen atom, as illustrated in the stereoview shown in Figure 2. The relevant hydrogen-bonding distances are O(14)...O(W) 2.690(3), O(W)...O(D) 2.799(4) Å. Both hydrogen atoms of the bridging water molecule are involved in hydrogen bonds, the second being associated with the ether

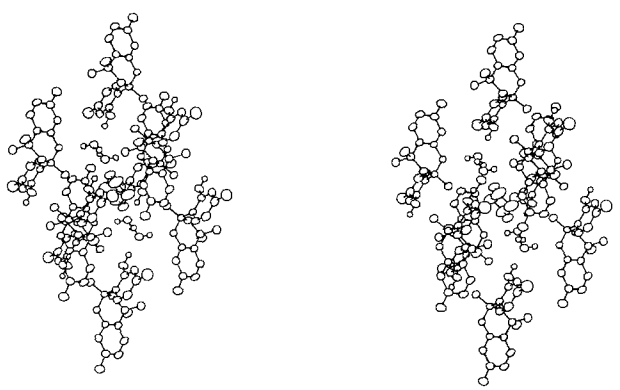


Fig. 2. A stereoview illustrating the host-guest packing in the 2 : 1 : 2 adduct of compound (**1**) with 1,4-dioxan and water. All hydrogen atoms have been omitted except those involved in hydrogen bonding.

oxygen of another host molecule of (**1**), as shown in Figure 2. This second hydrogen bond is characterised by a distance O(W)...O(1) 2.909(3) Å. Since the host molecule (**1**) occupies a general position in the unit cell, both enantiomers are present in the inclusion compound, as is the case for clathrates of Dianin's compound. However, in marked contrast to Dianin's compound, hydrogen-bonded hexamers of phenolic oxygens are not found in the structure described here. Rather, the phenolic OH group is involved in host–guest interaction.

Interestingly, the use of the isoelectronic guest piperazine does not lead to the formation of an isostructural adduct. Analogous conditions were employed, with aqueous ethanol as solvent, and the triclinic adduct (space group $P\bar{1}$) contains two molecules of ethanol per unit cell. Further work on this and other adducts of (**1**) is in progress.

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