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# An X-Ray Crystallographic Study of the Inclusion Properties of Additionally Dimethylated Members of the 2′-Hydroxy-2,2,4-trimethylflavan Host Series

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**Abstract.** Consideration of the shape and hydrogen bonding pattern of an *entire guest unit*, in the known 2 : 1 : 2 complex of 2′-hydroxy-2,4,4,7,4′-pentamethylflavan (**1**) with 1,4-dioxan and water, has indicated a structurally compatible guest, *trans*-1,4-bis(hydroxymethyl)cyclohexane (**3b**) which is selectively clathrated from a mixture with its *cis* isomer (**3a**). The new complex is triclinic, space group $P\bar{1}$, with $a$ = 8.137(1), $b$ = 9.106(1), $c$ = 14.552(2) Å, $\alpha$ = 93.56(1), $\beta$ = 94.08(1), $\gamma$ = 98.62(1)°, and two host and one guest molecule in the unit cell. A novel hydrogen bonded host–guest arrangement has also been found for host (**1**), involving ethanol and piperazine [triclinic, space group $P\bar{1}$, with $a$ = 8.438(1), $b$ = 10.252(1), $c$ = 14.052(1) Å, $\alpha$ = 71.28(1), $\beta$ = 89.72(1), $\gamma$ = 83.88(1)°]; while for the 1 : 1 ether adduct of (**1**) the triclinic unit cell, space group $P\bar{1}$, is approximately doubled in volume [$a$ = 8.309(2), $b$ = 10.546(3), $c$ = 26.664(6) Å, $\alpha$ = 102.10(2), $\beta$ = 100.48(2), $\gamma$ = 81.04(2)°], there now being two crystallographically independent host–guest units involving $\phi$OH···OEt$_2$ hydrogen bonds of length 2.71(1) Å and 2.77(1) Å. In the 2 : 1 complex of the isomeric host 2′-hydroxy-2,4,4,6,5′-pentamethylflavan (**2**) with *N*,*N*′-dimethylpiperazine (**5**) [triclinic space group $P\bar{1}$, with $a$ = 7.411(1), $b$ = 10.143(3), $c$ = 15.109(3) Å, $\alpha$ = 98.73(2), $\beta$ = 88.30(1), $\gamma$ = 109.72(2)°] the centrosymmetric chair-shaped guest molecule is clamped by two axially oriented $\phi$OH···N hydrogen bonds of length 2.759(3) Å.

**Key words:** Inclusion compounds, X-ray crystal structure analysis, 2′-hydroxy-2,4,4,7,4′-pentamethylflavan; selective clathration; *trans*-1,4-bis(hydroxymethyl)cyclohexane guest; 2′-hydroxy-2,4,4,6,5′-pentamethylflavan host; *N*,*N*′-dimethylpiperazine guest.

**Supplementary Data** relating to this article are deposited with the British Library as Supplementary Publication SUP 82026 (138 pages).

## 1. Introduction

Although the structure [1] and wide-ranging inclusion ability [2] of 2′-hydroxy-2,4,4,7,4′-pentamethylflavan (**1**), the dimeride of 5-methyl-2-*iso*propenylphenol, were firmly established by Baker and coworkers more than thirty years ago, only recently has the crystal structure of an inclusion compound of host **1** been determined [3]. In the present work, it is demonstrated that, with due consideration of the structure and hydrogen bonding pattern of an entire guest unit found [3] earlier in **1**, it is possible to bring about, or 'engineer', the specific inclusion of an appropriately chosen isomer, *trans*-1,4-bis(hydroxymethyl)cyclohexane (**3b**), from a diastereoisomeric mixture. Here the high guest selectivity reflects efficient host–guest interactions in terms of steric compatibility and hydrogen bonding. To probe further the role of hydrogen bonding in complexes of **1** we have also determined the crystal structures of its

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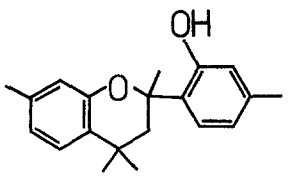
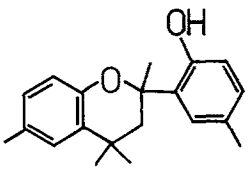
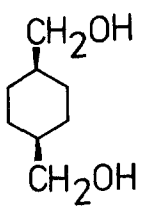
previously mentioned [3] piperazine-containing adduct as well as the 1 : 1 ether inclusion compound which was described [4] by Fries and Fickewirth as early as 1908. In addition, we have studied the guest conformation and the nature of host–guest interactions in the *N,N'*-dimethylpiperazine (**5**) complex of 2'-hydroxy-2,4,4,6,5'-pentamethylflavan (**2**), a known host [5] which is isomeric with **1**.



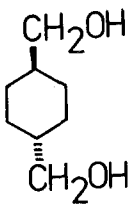
(**1**)



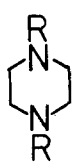
(**2**)



(**3a**)



(**3b**)



(**4**) R = H
(**5**) R = Me

## 2. Experimental

Hosts 2'-hydroxy-2,4,4,7,4'-pentamethylflavan (**1**) and 2'-hydroxy-2,4,4,6,5'-pentamethylflavan (**2**) were prepared by literature methods [1,5].

### 2.1. PREPARATION OF ADDUCTS OF (1) AND (2)

The 1,4-bis(hydroxymethyl)cyclohexane adduct of **1** was prepared by adding to 2 g of redistilled **1** dissolved in 20 ml of light petroleum, a solution of 1 g of a commercial mixture

[Aldrich] of **3a** and **3b** (molar ratio *ca.* 30 : 70, determined by 200 MHz $^1$H NMR) dissolved in 5 ml ethanol. On standing, the homogeneous solution deposited the adduct of **1** with **3b** as colourless prisms, which were collected on a sinter, washed with cold ethanol, then cold ether, and air dried. $^1$H NMR analysis gave a host–guest ratio of 2 : 1 and indicated almost exclusive incorporation of the *trans* isomer **3b** ($\geqslant$*ca.* 97%). The piperazine adduct of **1** (see text) was prepared by a method analogous to that employed previously by Baker and coworkers [2] for the dioxan water complex of **1**: thus (under nitrogen), 2 g of **1**, 1 g of piperazine, and 0.5 ml of water were brought into homogeneous solution in 20 ml of light petroleum containing 5 ml of ethanol. The precipitated adduct was collected, washed, and air dried as before.

The 1 : 1 ether adduct of **1** was crystallised from a mixture of light petroleum and ether.

The *N,N'*-dimethylpiperazine (**5**) adduct of **2** was prepared, under $N_2$, by recrystallisation of distilled **2** (2 g) from a solution of 1 g of **5** in 20 ml of light petroleum.

### 2.2. CRYSTAL DATA

$2[C_{20}H_{24}O_2(\mathbf{1})] \cdot C_8H_{16}O_2(\mathbf{3b})$ (adduct I). Formula weight = 737.04, triclinic, $a$ = 8.137(1), $b$ = 9.106(1), $c$ = 14.552(2) Å, $\alpha$ = 93.56(1), $\beta$ = 94.08(1), $\gamma$ = 98.62(1)°, $U$ = 1060.4 Å$^3$, $Z$ = 1, $D_c$ = 1.15 g cm$^{-3}$. Space group $P\bar{1}$ (No. 2), $\mu$ = 0.69 cm$^{-1}$ for Mo$K_\alpha$ radiation, $\lambda$ = 0.71069 Å (1 Å = 10$^{-10}$ m). Prismatic, colourless crystals. Single crystal dimensions: 0.5 × 0.3 × 0.3 mm, mounted on fibre. Number of independent intensities: 4624 (all possible reflections with $\sin\theta/\lambda < 0.64$ Å$^{-1}$), of which 2630 were considered observed. Formula corresponds to two asymmetric units, hence the molecule of **3b** is crystallographically centrosymmetric. Final $R$ for observed reflections: 0.052, $R'$ 0.065. Greatest magnitude of peaks and holes in final difference map: 0.5 eÅ$^{-3}$.

$2[C_{20}H_{24}O_2(\mathbf{1})] \cdot C_4H_{10}N_2(\mathbf{4}) \cdot 2C_2H_6O$(ethanol) (adduct II). Formula weight = 771.1, triclinic, $a$ = 8.438(1), $b$ = 10.252(1), $c$ = 14.052(1) Å, $\alpha$ = 71.28(1), $\beta$ = 89.72(1), $\gamma$ = 83.88(1)°, $U$ = 1144.2 Å$^3$, $Z$ = 1, $D_c$ = 1.12g cm$^{-3}$. Space group $P\bar{1}$ (No. 2). $\mu$ = 5.40 cm$^{-1}$ for Cu$K_\alpha$ radiation, $\lambda$ = 1.5418 Å. Colourless, thin plates. Single crystal dimensions: 0.5 × 0.2 × 0.1 mm, mounted on fibre. Number of independent intensities: 4329 (all possible reflections with $\sin\theta/\lambda < 0.61$, of which 2749 were considered observed. Formula corresponds to two asymmetric units, hence the molecule of **4** is crystallographically centrosymmetric. Final $R$ for observed reflections: 0.063, $R'$ 0.088. Greatest magnitude of peaks and holes in final difference map: 0.4 eÅ$^{-3}$.

$C_{20}H_{24}O_2(\mathbf{1}) \cdot C_4H_{10}O$(diethyl ether) (adduct III). Formula weight = 370.53, triclinic, $a$ = 8.309(2), $b$ = 10.546(3), $c$ = 26.664(6) Å, $\alpha$ = 102.10(2), $\beta$ = 100.48(2), $\gamma$ = 81.04(2)°, $U$ = 2229.4 Å$^3$, $Z$ = 4, $D_c$ = 1.10 g cm$^{-3}$. Space group $P\bar{1}$ (No. 2), $\mu$ = 0.66 cm$^{-1}$ for Mo$K_\alpha$ radiation, $\lambda$ = 0.71069 Å. Platy, colourless crystals. Single crystal dimensions: 0.2 × 0.2 × 0.05 mm, mounted on fibre. Number of independent intensities: 7828 (all possible reflections with $\sin\theta/\lambda < 0.594$), of which 1815 were considered observed.

Formula corresponds to half the asymmetric unit, hence there are two symmetry-independent molecules of **1** and two independent ether molecules. Final $R$ for observed reflections: 0.078, $R'$ 0.089. Greatest magnitude of peaks and holes in final difference map: 0.8 eÅ$^{-3}$.

$2[C_{20}H_{24}O_2(\mathbf{2})] \cdot C_6H_{14}N_2(\mathbf{5})$ (adduct IV). Formula weight = 707.01, triclinic, $a$ = 7.411(1), $b$ = 10.143(3), $c$ = 15.109(3) Å, $\alpha$ = 98.73(2), $\beta$ = 88.30(1), $\gamma$ = 109.72(2)°, $U$ = 1056.4 Å$^3$, $Z$ = 1, $D_c$ = 1.11 g cm$^{-3}$. Space group $P\bar{1}$ (No. 2), $\mu$ = 0.65 cm$^{-1}$ for Mo$K_\alpha$ radiation, $\lambda$ = 0.71069 Å, Colourless, platy crystals. Single crystal dimensions:

0.5 x 0.3 x 0.1 mm, mounted in capillary. Number of independent intensities: 4582 (all possible reflections with $\sin\theta/\lambda < 0.64$), of which 1823 were considered observed. Formula corresponds to two asymmetric units, hence the molecule of **5** is crystallographically centrosymmetric. Final $R$ for observed reflections: 0.041, $R'$ 0.043. Greatest magnitude of peaks and holes in final difference map: 0.4 eÅ$^{-3}$.

X-ray intensity measurements for all four structures were made at room temperature (20°) by $\theta$–$\omega$ scan on a Nonius CAD4 diffractometer, by use of graphite-monochromated Mo$K_\alpha$ or Cu$K_\alpha$ radiation. Reflections having $F^2 > 2\sigma(F^2)$ were considered observed, where $\sigma(F^2) = [C + 4(B_1 + B_2) + 0.0009I^2]^{1/2}/t_c Lp$, $C$ is the total integrated count in time $t_c$, $B_1$ 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, except in the case of adduct II, for which correction was made by an empirical method [6]. 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 S.E.L. 32/27 computer in the laboratory (the principal computer programs used are listed in reference [6]) and the atomic scattering factors were taken from reference [7].

### 2.2.1. *Structure Determination*

All the structures were solved by direct methods using the MITHRIL program [6], hydrogen atoms being located in difference-Fourier maps calculated during the anisotropic least-squares refinement. Isotropic hydrogen parameters were subsequently included in the refinement. In the case of adduct III, however, the number of observed reflections was depressed by the small size of the crystal, and the precision of this analysis is therefore relatively low. For this reason

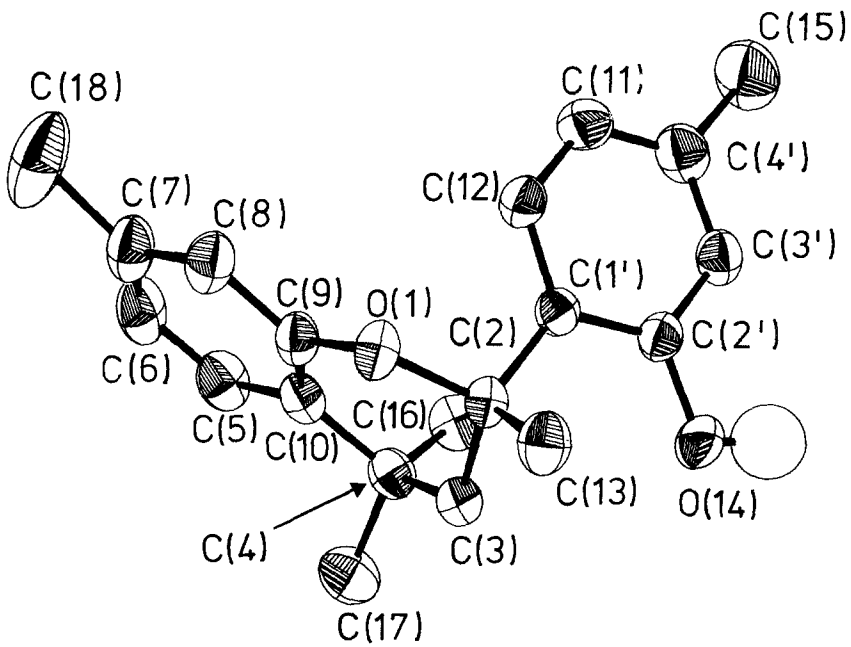



Fig. 1. A general view illustrating the conformation of the 2′-hydroxy-2,4,4,7,4′-pentamethylflavan (**1**) host molecule in its 1,4-bis(hydroxymethyl)cyclohexane (**3b**) adduct. All hydrogens have been omitted apart from the hydroxyl hydrogen. The ellipsoids represent thermal vibration envelopes of 50% probability.

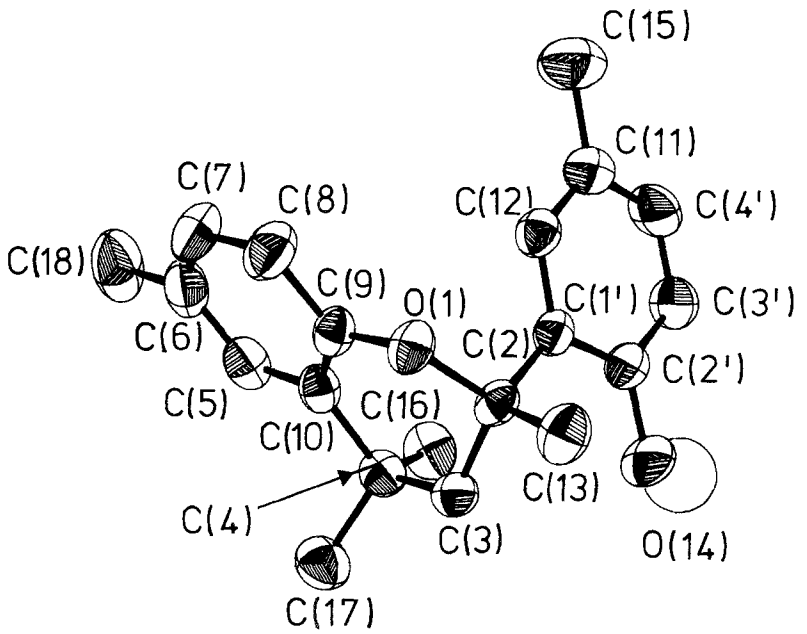



Fig. 2. A general view illustrating the host conformation of 2′-hydroxy-2,4,4,6,5′-pentamethylflavan (**2**) in its *N*,*N*′-dimethylpiperazine (**5**) complex. All hydrogen atoms have been omitted apart from the hydroxyl hydrogen. The ellipsoids represent thermal vibration envelopes of 50% probability.

all the hydrogen atoms were placed in theoretical positions with C—H bond lengths 1.084 Å for the aromatic and 1.073 Å for the alkyl-group hydrogens, and allowed to ride on their attached carbon atoms with fixed isotropic temperature factors. The same treatment was applied also to some of the hydrogen atoms on ethanol and piperazine in adduct II. The function minimised was $\Sigma w\Delta^2$, where $w = 1/\sigma^2(F_o)$, $\Delta = (|F_o| - |F_c|)$. The weighted $R$ factor $R'$ is $(\Sigma w\Delta^2/\Sigma w|F_o|^2)^{1/2}$. Difference-Fourier maps were computed from the final structure factors for all (observed and unobserved) reflections.

During the refinement of adduct II, minor a peak on difference maps indicated the presence of a low-occupancy guest partially replacing the piperazine molecule. The peak was ascribed to two centrosymmetrically or statistically-related water molecules of which the hydrogen atoms could not be located. The oxygen atom was included in the refinement with the isotropic temperature factor and occupancy both being allowed to vary, and the occupancy was constrained to 1.0 minus the occupancy of the piperazine molecule. The final value of the water occupancy was 0.151(4). The O···O distance 2.77(2) Å does not preclude the possibility of OH···O hydrogen bonding between water molecules in a particular unit cell.

Atomic coordinates are given in Table I, and selected torsion angles in Table II. The labelling of the atoms in hosts **1** and **2** is shown in Figures 1 and 2. Thermal parameters, selected bond lengths and valency angles and observed and calculated structure factors are deposited as Supplementary Publication 82026 (British Library).

Table I. Fractional atomic coordinates with standard deviations in the least significant digits in parentheses. Hydrogen atoms have the numbers of the carbon or oxygen atoms to which they are attached.

(a) Adduct I: host **1** with **3b**. Atoms of the guest are C(23–25) (ring), C(26), O(27).

| | X/A | Y/B | Z/C |
|---|---|---|---|
| C(1') | .4674(3) | .4614(2) | .2462(2) |
| C(2') | .4378(3) | .6083(3) | .2597(2) |
| C(2) | .5417(3) | .3816(2) | .3246(2) |
| C(3) | .7135(3) | .4550(3) | .3670(2) |
| C(3') | .3631(3) | .6766(3) | .1890(2) |
| C(4') | .3178(4) | .6035(3) | .1024(2) |
| C(4) | .8563(3) | .4580(3) | .3029(2) |
| C(5) | .9647(3) | .2657(3) | .1982(2) |
| C(6) | .9459(4) | .1301(4) | .1470(2) |
| C(7) | .8001(4) | .0319(3) | .1427(2) |
| C(8) | .6727(4) | .0716(3) | .1915(2) |
| C(9) | .6896(3) | .2063(3) | .2430(2) |
| C(10) | .8363(3) | .3078(3) | .2478(2) |
| C(11) | .3461(4) | .4586(3) | .0884(2) |
| C(12) | .4193(3) | .3903(3) | .1592(2) |
| C(13) | .4199(3) | .3591(3) | .3986(2) |
| C(15) | .2370(5) | .6820(4) | .0270(2) |
| C(16) | .8556(3) | .5815(3) | .2353(2) |
| C(17) | 1.0198(3) | .4876(3) | .3634(2) |
| C(18) | .7743(5) | -.1133(4) | .0828(2) |
| C(23) | .8431(4) | .0575(4) | .4833(2) |
| C(24) | .8819(4) | -.0067(3) | .5716(2) |
| C(25) | 1.0714(4) | .0098(4) | .5929(2) |
| C(26) | .8007(4) | .0522(4) | .6538(2) |
| O(1) | .5539(2) | .2296(2) | .2909(1) |
| O(14) | .4811(2) | .6822(2) | .3446(1) |
| O(27) | .6233(2) | .0446(2) | .6390(1) |
| H(3A) | .743(3) | .394(2) | .422(1) |
| H(3B) | .714(3) | .562(2) | .388(1) |
| H(3') | .345(3) | .782(3) | .201(2) |
| H(5) | 1.073(3) | .337(3) | .199(2) |
| H(6) | 1.030(3) | .099(3) | .112(2) |
| H(8) | .566(3) | .009(3) | .190(2) |
| H(11) | .310(3) | .404(3) | .028(2) |
| H(12) | .428(3) | .287(2) | .148(2) |
| H(13A) | .393(3) | .452(3) | .423(2) |
| H(13B) | .317(3) | .306(2) | .374(1) |
| H(13C) | .468(3) | .302(3) | .450(2) |
| H(14) | .442(4) | .769(3) | .345(2) |
| H(15A) | .281(5) | .662(4) | -.029(3) |
| H(15B) | .147(7) | .632(6) | .008(3) |
| H(15C) | .176(5) | .767(5) | .040(3) |
| H(16A) | .953(3) | .590(3) | .201(2) |
| H(16B) | .859(3) | .679(3) | .268(2) |
| H(16C) | .756(4) | .561(3) | .190(2) |
| H(17A) | 1.024(4) | .405(3) | .401(2) |
| H(17B) | 1.027(3) | .578(3) | .406(2) |
| H(17C) | 1.110(4) | .494(3) | .325(2) |
| H(18A) | .899(5) | -.133(4) | .081(3) |
| H(18B) | .708(5) | -.185(4) | .102(3) |
| H(18C) | .755(6) | -.104(5) | .015(3) |
| H(23A) | .313(6) | .964(5) | .511(3) |
| H(23B) | .091(5) | .818(5) | .490(3) |
| H(24) | .161(4) | 1.123(3) | .439(2) |
| H(25A) | -.118(5) | .906(4) | .384(3) |
| H(25B) | -.088(5) | 1.041(4) | .348(2) |
| H(26A) | .159(4) | .833(4) | .341(2) |
| H(26B) | .171(4) | 1.009(4) | .281(2) |
| H(27) | .421(3) | 1.045(3) | .345(2) |

Table I(b). Adduct II: host **1** with piperazine (**4**) and ethanol. Atoms of the guest are C(21–22), N; of the solvent C(23–24), O(3); of (low occupancy) water O(4).

| | X/A | Y/B | Z/C |
|---|---|---|---|
| C(1') | -.4529(3) | .3304(3) | .2704(2) |
| C(2') | -.5411(4) | .4579(3) | .2575(2) |
| C(2) | -.3624(3) | .3001(3) | .1835(2) |
| C(3) | -.2375(4) | .3980(3) | .1376(2) |
| C(3') | -.6260(4) | .4830(3) | .3360(2) |
| C(4) | -.0929(3) | .3891(3) | .2068(2) |
| C(4') | -.6245(4) | .3832(3) | .4296(2) |
| C(5) | .1020(4) | .1944(3) | .3199(2) |
| C(6) | .1477(4) | .0595(4) | .3734(2) |
| C(7) | .0524(4) | -.0437(3) | .3753(2) |
| C(8) | -.0920(4) | -.0029(3) | .3228(2) |
| C(9) | -.1390(3) | .1356(3) | .2691(2) |
| C(10) | -.0432(3) | .2382(3) | .2659(2) |
| C(11) | -.5394(4) | .2566(3) | .4427(2) |
| C(12) | -.4553(3) | .2298(3) | .3644(2) |
| C(13) | -.4825(4) | .2984(3) | .1028(2) |
| C(15) | -.7167(5) | .4150(4) | .5135(2) |
| C(16) | -.1296(4) | .4725(3) | .2792(2) |
| C(17) | -.9580(4) | .4521(3) | .1406(2) |
| C(18) | -.1014(5) | .1935(4) | .5653(3) |
| C(21) | .8987(6) | -1.0924(5) | 1.0583(4) |
| C(22) | 1.0227(8) | -.8823(4) | 1.0264(4) |
| C(23) | .5959(10) | -.9081(7) | .8365(6) |
| C(24) | .5000(10) | -.8628(7) | .7539(6) |
| O(1) | -.2839(2) | .1601(2) | .2177(1) |
| O(3) | .6869(4) | -.8090(3) | .8529(2) |
| O(4) | 1.0396(15) | -1.0140(12) | 1.0987(8) |
| O(14) | -.4558(3) | .4425(2) | .8349(1) |
| N | .8600(7) | -.9466(5) | 1.0359(3) |
| H(3A) | .191(4) | -.371(3) | .925(2) |
| H(3B) | .289(3) | -.494(3) | .890(2) |
| H(3') | .688(4) | -.581(3) | .678(2) |
| H(5) | -.163(4) | -.271(3) | .681(2) |
| H(6) | -.240(4) | -.034(3) | .592(2) |
| H(8) | .158(3) | .078(3) | .674(2) |
| H(11) | .543(3) | -.184(3) | .496(2) |
| H(12) | .395(4) | -.133(3) | .624(2) |
| H(13A) | .424(4) | -.272(3) | .953(2) |
| H(13B) | .569(4) | -.230(3) | .875(2) |
| H(13C) | .541(4) | -.393(3) | .922(2) |
| H(15A) | .713(5) | -.336(4) | .428(3) |
| H(15B) | .841(7) | -.412(5) | .494(4) |
| H(15C) | .720(7) | -.487(6) | .476(4) |
| H(16A) | .169(3) | -.571(3) | .765(2) |
| H(16B) | .215(4) | -.446(3) | .677(2) |
| H(16C) | .026(4) | -.454(3) | .677(2) |
| H(17A) | -.015(4) | -.531(3) | .897(2) |
| H(17B) | -.072(4) | -.405(3) | .908(2) |
| H(17C) | -.128(4) | -.455(3) | .821(2) |
| H(18A) | -.044(13) | .306(9) | .598(7) |
| H(18B) | -.179(8) | .216(6) | .580(4) |
| H(18C) | -.058(10) | .236(6) | .512(5) |
| H(O14) | .614(4) | -.654(3) | .840(2) |

Table I(c). Adduct III: host 1 with diethyl ether. Atoms of the guest are C(23,24,26,27), O(25). Suffixes A and B denote the crystallographically independent molecules.

| | X/A | Y/B | Z/C |
|---|---|---|---|
| C(1'A) | .5879(14) | .2769(12) | .1147(5) |
| C(2'A) | .5042(15) | .4054(13) | .1215(6) |
| C(2A) | .7008(15) | .2236(11) | .1588(5) |
| C(3A) | .8400(16) | .3025(11) | .1862(4) |
| C(3'A) | .4036(15) | .4461(11) | .0808(6) |
| C(4'A) | .3788(15) | .3723(14) | .0326(7) |
| C(4A) | .9728(15) | .3083(12) | .1550(5) |
| C(5A) | 1.1473(14) | .1432(12) | .0953(5) |
| C(6A) | 1.1812(15) | .0208(15) | .0655(5) |
| C(7A) | 1.0830(17) | -.0762(12) | .0605(5) |
| C(8A) | .9460(14) | -.0442(11) | .0862(5) |
| C(9A) | .9111(15) | .0772(12) | .1156(4) |
| C(10A) | 1.0113(15) | .1765(12) | .1222(5) |
| C(11A) | .4594(15) | .2447(12) | .0241(5) |
| C(12A) | .5602(14) | .2026(11) | .0658(6) |
| C(13A) | .5946(14) | .2051(11) | .1966(5) |
| C(15A) | .2688(17) | .4204(12) | -.0124(5) |
| C(16A) | .9206(14) | .4109(10) | .1200(5) |
| C(17A) | 1.1269(16) | .3457(11) | .1924(5) |
| C(18A) | 1.1217(17) | -.2054(12) | .0279(5) |
| C(23A) | 1.627(4) | -.210(2) | .158(1) |
| C(24A) | .505(3) | .833(2) | .173(1) |
| C(26A) | .745(2) | .190(2) | .805(1) |
| C(27A) | .868(2) | .279(2) | .814(1) |
| C(1'B) | .4701(13) | .6643(11) | .3881(5) |
| C(2'B) | .3798(14) | .7875(11) | .3799(6) |
| C(2B) | .5319(15) | .5674(11) | .3433(5) |
| C(3B) | .6395(15) | .6188(10) | .3132(4) |
| C(3'B) | .3180(14) | .8706(10) | .4235(6) |
| C(4'B) | .3463(15) | .8410(12) | .4723(6) |
| C(4B) | .8095(15) | .6549(11) | .3435(5) |
| C(5B) | 1.0473(17) | .5499(11) | .4034(5) |
| C(6B) | 1.1123(15) | .4585(15) | .4328(5) |
| C(7B) | 1.0172(18) | .3667(11) | .4402(5) |
| C(8B) | .8544(16) | .3713(11) | .4150(5) |
| C(9B) | .7905(15) | .4632(12) | .3857(5) |
| C(10B) | .8834(16) | .5562(12) | .3767(5) |
| C(11B) | .4328(14) | .7216(12) | .4794(4) |
| C(12B) | .4908(13) | .6357(10) | .4374(5) |
| C(13B) | .3905(14) | .5122(10) | .3064(4) |
| C(15B) | .2845(15) | .9352(12) | .5170(5) |
| C(16B) | .9215(15) | .6564(11) | .3043(5) |
| C(17B) | .7940(13) | .7925(10) | .3767(4) |
| C(18B) | 1.0895(17) | .2675(13) | .4726(6) |
| C(23B) | -.051(3) | .030(2) | .309(1) |
| C(24B) | .056(3) | .114(2) | .309(1) |
| C(26B) | .326(4) | .166(3) | .335(1) |
| C(27B) | 1.470(3) | .136(2) | .336(1) |
| O(1A) | .7737(9) | .0911(7) | .1403(3) |
| O(14A) | .5240(9) | .4833(7) | .1694(3) |
| O(25A) | .6104(12) | .2589(9) | .8301(3) |
| O(1B) | .6278(9) | .4539(6) | .3616(3) |
| O(14B) | .3487(10) | .8223(7) | .3328(3) |
| O(25B) | .2171(14) | .0728(10) | .3290(4) |

Table I(d). Adduct IV: host **2** with *N,N'*-dimethylpiperazine (**5**). Atoms of the guest are C(23,25,26), N.

| | X/A | Y/B | Z/C |
|---|---|---|---|
| C(1') | .0992(4) | -.2014(3) | .2869(2) |
| C(2) | .1622(3) | -.0523(3) | .3407(2) |
| C(2') | -.0487(4) | -.3143(3) | .3153(2) |
| C(3) | .0063(4) | .0115(3) | .3648(2) |
| C(3') | -.0925(5) | -.4489(3) | .2673(2) |
| C(4) | -.0957(4) | .0398(3) | .2871(2) |
| C(4') | .0084(5) | -.4746(3) | .1933(2) |
| C(5) | -.0016(5) | .1315(3) | .1391(2) |
| C(6) | .1223(6) | .1764(3) | .0713(2) |
| C(7) | .3061(6) | .1777(4) | .0813(2) |
| C(8) | .3639(5) | .1334(3) | .1543(2) |
| C(9) | .2332(4) | .0866(3) | .2200(2) |
| C(10) | .0486(4) | .0870(3) | .2140(2) |
| C(11) | .1591(4) | -.3685(3) | .1648(2) |
| C(12) | .1990(4) | -.2339(3) | .2125(2) |
| C(13) | .2743(5) | -.0514(4) | .4234(2) |
| C(15) | .2802(9) | -.3970(6) | .0875(3) |
| C(16) | -.2620(5) | -.0924(4) | .2479(3) |
| C(17) | -.1768(6) | .1580(4) | .3230(3) |
| C(18) | .0552(12) | .2167(6) | -.0105(3) |
| C(23) | -.5278(5) | -.6166(3) | .4325(3) |
| C(25) | -.5761(5) | -.3979(4) | .4825(3) |
| C(26) | -.6097(8) | -.4945(6) | .3239(3) |
| O(1) | .3038(2) | .0437(2) | .2898(1) |
| O(14) | -.1430(3) | -.2884(2) | .3915(1) |
| N | -.5056(3) | -.4779(2) | .4089(2) |
| H(3A) | .059(3) | .098(3) | .404(1) |
| H(3B) | -.089(4) | -.048(2) | .403(1) |
| H(3') | -.197(5) | -.527(3) | .290(2) |
| H(4') | -.018(4) | -.567(3) | .165(2) |
| H(5) | -.130(4) | .131(3) | .133(2) |
| H(7) | .395(5) | .201(3) | .037(2) |
| H(8) | .489(4) | .128(3) | .162(2) |
| H(12) | .303(3) | -.156(2) | .194(1) |
| H(13A) | .196(4) | -.118(3) | .461(2) |
| H(13B) | .314(3) | .040(3) | .458(1) |
| H(13C) | .396(4) | -.082(3) | .404(2) |
| H(14) | -.250(6) | -.356(4) | .397(2) |
| H(15A) | .364(9) | -.319(6) | .072(4) |
| H(15B) | .336(8) | -.457(6) | .096(3) |
| H(15C) | .203(7) | -.423(5) | .031(4) |
| H(16A) | -.351(5) | -.128(4) | .293(2) |
| H(16B) | -.331(5) | -.075(3) | .197(2) |
| H(16C) | -.217(4) | -.176(3) | .219(2) |
| H(17A) | -.248(5) | .177(3) | .274(2) |
| H(17B) | -.267(4) | .132(3) | .373(2) |
| H(17C) | -.073(5) | .244(4) | .347(2) |
| H(18A) | -.002(7) | .144(5) | -.057(3) |
| H(18B) | .139(8) | .273(6) | -.029(3) |
| H(18C) | -.022(8) | .283(6) | .005(3) |
| H(23A) | -.666(5) | -.666(3) | .440(2) |
| H(23B) | -.476(4) | -.665(3) | .385(2) |
| H(25A) | -.721(5) | -.455(3) | .484(2) |
| H(25B) | -.559(4) | -.301(3) | .466(2) |
| H(26A) | -.556(7) | -.554(5) | .267(3) |
| H(26B) | -.748(7) | -.533(5) | .334(3) |
| H(26C) | -.594(7) | -.400(5) | .312(3) |

Table II. Selected torsion angles for adducts I–IV specified in the headings of Table I.

| | | | |
|---|---|---|---|
| **Adduct I:** | | | |
| C(2') - C(1') - C(2) - C(3) | 59.7(3) | C(12) - C(1') - C(2) - O(1) | -1.2(2) |
| O(1) - C(2) - C(3) - C(4) | -57.0(2) | C(3) - C(2) - O(1) - C(9) | 43.9(2) |
| C(2) - C(3) - C(4) - C(10) | 41.8(3) | C(3) - C(4) - C(10) - C(9) | -14.4(3) |
| C(10) - C(9) - O(1) - C(2) | -19.3(3) | O(1) - C(9) - C(10) - C(4) | 3.3(3) |
| **Adduct II:** | | | |
| C(2') - C(1') - C(2) - C(3) | 58.9(3) | C(12) - C(1') - C(2) - O(1) | -1.7(3) |
| O(1) - C(2) - C(3) - C(4) | -56.2(3) | C(3) - C(2) - O(1) - C(9) | 43.9(3) |
| C(2) - C(3) - C(4) - C(10) | 40.2(3) | C(3) - C(4) - C(10) - C(9) | -12.5(3) |
| C(10) - C(9) - O(1) - C(2) | -18.9(3) | O(1) - C(9) - C(10) - C(4) | 1.7(3) |
| **Adduct III:** | | | |
| C(2'A)- C(1'A)- C(2A) - C(3A) | 55.7(13) | C(12A)- C(1'A)- C(2A) - O(1A) | -2.3(11) |
| O(1A) - C(2A) - C(3A) - C(4A) | -57.2(11) | C(3A) - C(2A) - O(1A) - C(9A) | 45.4(10) |
| C(2A) - C(3A) - C(4A) - C(10A) | 40.0(11) | C(3A) - C(4A) - C(10A)- C(9A) | -12.0(11) |
| C(10A)- C(9A) - O(1A) - C(2A) | -21.1(11) | O(1A) - C(9A) - C(10A)- C(4A) | 2.8(11) |
| C(2'B)- C(1'B)- C(2B) - C(3B) | 55.1(13) | C(12B)- C(1'B)- C(2B) - O(1B) | -6.6(11) |
| O(1B) - C(2B) - C(3B) - C(4B) | -57.0(10) | C(3B) - C(2B) - O(1B) - C(9B) | 47.6(10) |
| C(2B) - C(3B) - C(4B) - C(10B) | 39.8(11) | C(3B) - C(4B) - C(10B)- C(9B) | -12.2(11) |
| C(10B)- C(9B) - O(1B) - C(2B) | -23.4(11) | O(1B) - C(9B) - C(10B)- C(4B) | 3.9(11) |
| **Adduct IV:** | | | |
| C(2') - C(1') - C(2) - C(3) | 53.0(3) | C(12) - C(1') - C(2) - O(1) | -12.2(3) |
| O(1) - C(2) - C(3) - C(4) | -57.6(3) | C(3) - C(2) - O(1) - C(9) | 49.3(3) |
| C(2) - C(3) - C(4) - C(10) | 35.8(3) | C(3) - C(4) - C(10) - C(9) | -5.7(3) |
| C(10) - C(9) - O(1) - C(2) | -23.1(3) | O(1) - C(9) - C(10) - C(4) | -.7(3) |

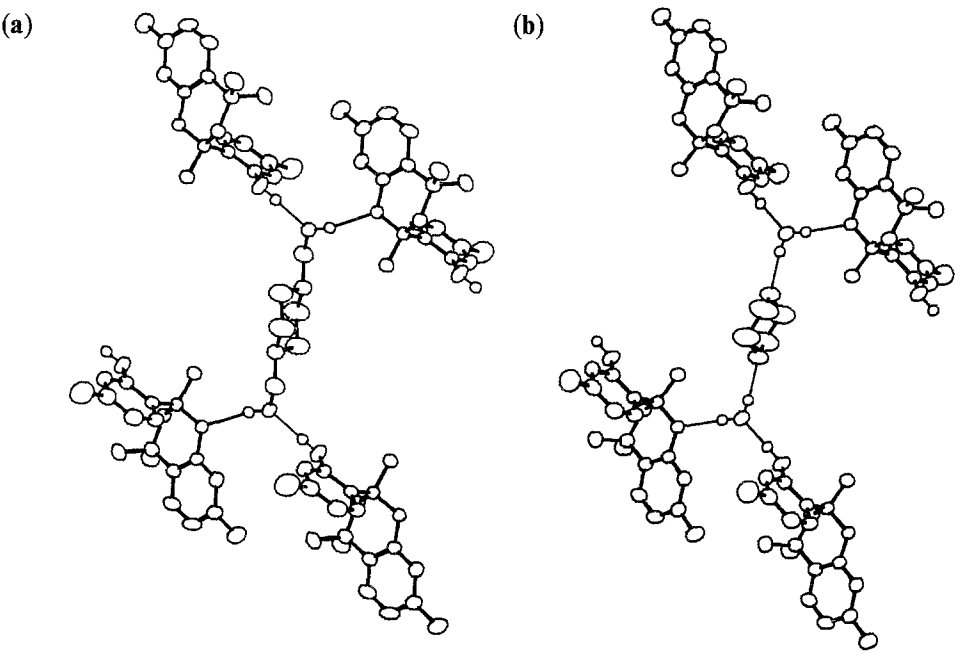



Fig. 3. A comparison of the host–guest interactions in (a) the *trans*-1,4-bis(hydroxymethyl)cyclohexane (**3b**) adduct of 2′-hydroxy-2,4,4,7,4′-pentamethylflavan (**1**) with (b) the corresponding 2 : 1 : 2 adduct of **1** with 1,4-dioxan and water. In each case only the hydrogens involved in hydrogen bonding (denoted by thin lines) are shown.

## 3. Discussion

The key hydrogen bonding scheme and the related host–guest arrangement in the 2 : 1 : 2 adduct [3] of 2′-hydroxy-2,2,4,7,4′-pentamethylflavan (**1**) with 1,4-dioxan and water are illustrated in Figure 3b. Consideration of the geometry of the host–guest interactions suggested the previously mentioned possibility that *trans*-1,4-bis(hydroxymethyl)cyclohexane (**3b**) in its di-equatorial conformation might, employing a corresponding hydrogen bonding scheme, be capable of replacing the entire dioxan-water guest unit. Significantly, the *trans*--isomer **3b** is selectively included by host **1** (see *Experimental* section), and the unit cell parameters for the new adduct are remarkably similar to those of the parent complex. As shown in Figure 3a, a closely related juxtaposition of host and guest components has indeed been produced, the di-equatorial location of the $-CH_2OH$ groups being compatible with hydrogen bonding involving *two* host molecules of **1** at each end of the centrosymmetric, chair-shaped guest. The hydrogen atom of the phenolic OH group participates in an OH···O hydrogen bond, length 2.749(2) Å, to the hydroxymethyl group's oxygen atom, while the hydrogen atom of the $CH_2OH$ group is involved in an OH···O hydrogen bond of length 2.967(2) Å to the ether oxygen of a second host molecule. Although the parallel between the two structures is close, it is interesting to note that the guest chair of **3b**, in fact, corresponds to a 'ring-inverted' form of the dioxan chair, as may be appreciated by a close inspection of Figures 3a and 3b. The host conformation of **1** in its **3b** adduct is shown in Figure 1. In the flavan's oxygen-containing ring, the displacements of C(2) and C(3) above and below the mean plane defined by the fused benzene ring, 0.33 Å and 0.32 Å, are more nearly equal than in the dioxan–water adduct where the corresponding respective values [3] are 0.34 Å and

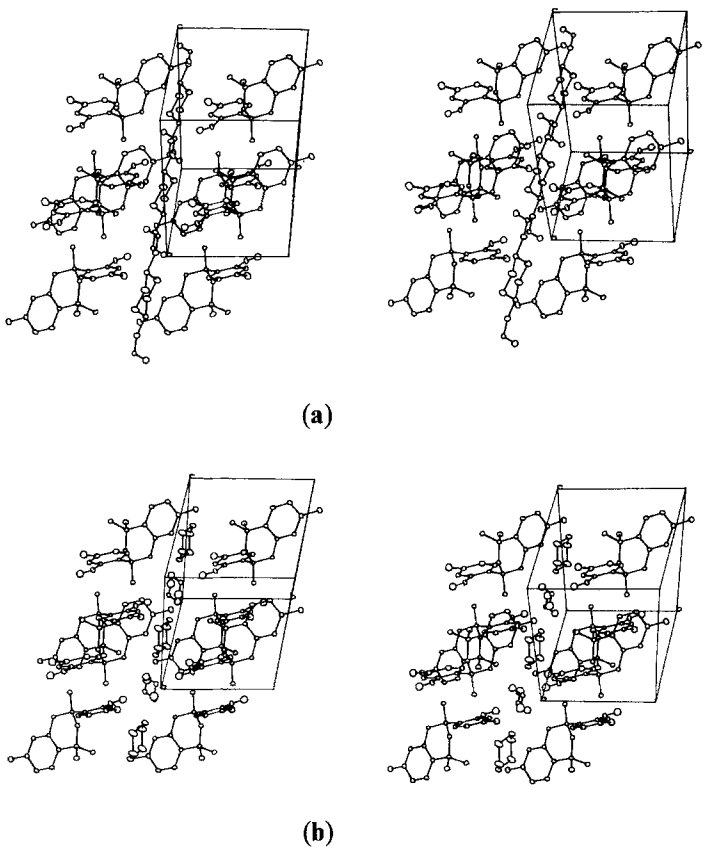



Fig. 4. Comparative stereoviews showing packing diagrams for (a) the adduct of host **1** with *trans*-1,4-bis(hydroxymethyl)cyclohexane (**3b**) and (b) the same host in its 2 : 1 : 2 adduct with 1,4-dioxan and water.

0.29 Å. The host–guest packing modes for the two analogous systems are illustrated in Figure 4. As can be seen, host molecules of **1** a *b*-translation apart are indirectly linked head-to-tail *via* an OH group belonging to a molecule of **3b** or a water molecule; this type of packing is dependent upon the common outward-facing disposition of the phenolic OH group of the host molecule.

An attempt [3] to prepare a piperazine(**4**)–water complex of **1** directly analogous to the dioxan–water adduct gave, for similar conditions with ethanol as solvent (see *Experimental*), ethanol-containing crystals ($^1$H NMR analysis) with unit cell parameters significantly different from those of the dioxan–water adduct. Crystal structure analysis of this new adduct reveals (see Figure 5) a chair-shaped piperazine guest molecule which is linked, again indirectly, to enantiomerically related host molecules; here, however, the indirect linking at each end of the centrosymmetric guest occurs *via* an ethanol molecule, rather than *via* a water molecule as in the dioxan–water complex. The X-ray results indicate an approximately axially oriented OH···N hydrogen bond of length 2.83(1) Å involving the ethanol molecule, while the (unionised) phenolic OH group is linked by a $\phi$OH···O hydrogen bond, length 2.66(1) Å, to the ethanol's oxygen atom. A nitrogen-to-ring ether oxygen contact [3.27(1) Å] may indicate a weak NH···O interaction. The observed packing mode is again characterised by the outward-facing OH location. The half-chair conformation found in this case is remarkably

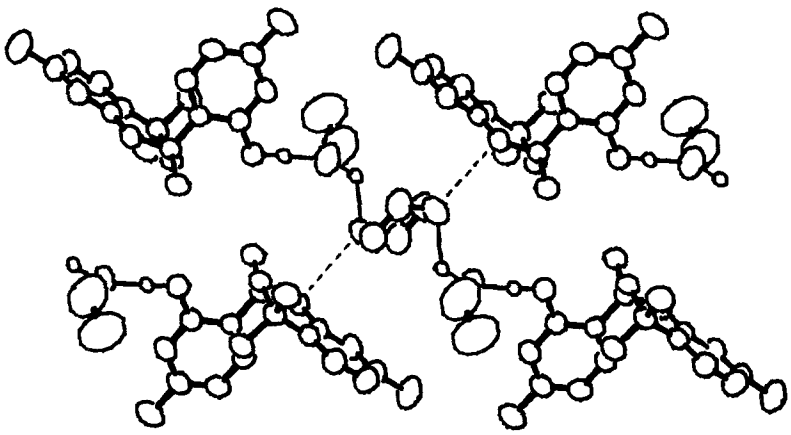


Fig. 5. A general view illustrating host–guest interactions in the inclusion compound of host **1** with piperazine (**4**) and ethanol. The only hydrogen atoms shown are hydroxyl hydrogens, and broken lines denote possible weak NH···O interactions.

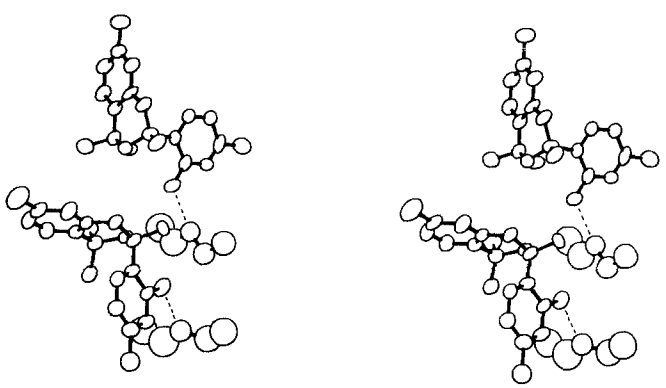


Fig. 6. A stereoview illustrating the two independent host and the two independent guest molecules in the 1 : 1 adduct of 2′-hydroxy-2,4,4,7,4′-pentamethylflavan (**1**) with diethyl ether. Broken lines denote OH···O hydrogen bonds.

similar to that in the complex of **1** with **3b**, equal displacements of ± 0.33 Å now being found for C(2) and C(3).

It should be noted, however, that while the above analysis is successful in determining the overall host–guest packing scheme in this adduct, the high thermal motion and disorder associated with the guest components makes detailed structural interpretation difficult, as may be appreciated from the large thermal parameters of the ethanol carbon atoms and the partial occupancy of the piperazine.

In the long-known ether adduct of **1** there are two crystallographically independent host molecules, and each of these is present in the triclinic unit cell along with its enantiomer. The salient host–guest interactions are $\phi OH\cdots OEt_2$ hydrogen bonds, the two independent types having lengths 2.77(1) Å and 2.71(1) Å. The independent host molecules of **1** both have distorted half-chair conformations for the heterocyclic ring; the displacements of C(2) and C(3) from the mean plane defined by the fused benzene ring are, respectively, 0.36 Å and − 0.30 Å for the first molecule and 0.39 Å and − 0.29 Å for the second. The host confor-

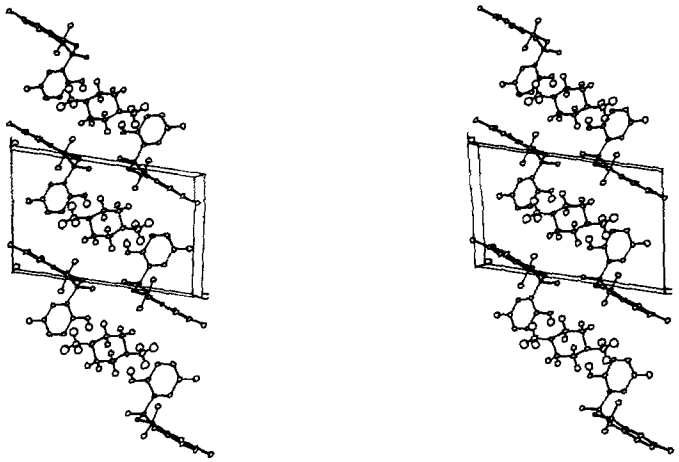


Fig. 7. A stereoview looking along the *a* axis illustrating the packing in the triclinic crystal of the *N,N'*-dimethylpiperazine (**5**) adduct with host (**2**). All hydrogen atoms have been omitted except those involved in hydrogen bonding, and those on the guest molecule.

mations and host–guest interactions are illustrated in the stereoview shown in Figure 6. The two crystallographically independent diethyl ether molecules, hydrogen bonded to the outward-projecting host OH groups, exhibit very high thermal motion and, possibly, disorder. The two guests appear to have approximately *trans,trans*-conformations [9].

In order to study the host–guest packing in a host isomeric with **1**, the *N,N'*-dimethylpiperazine (**5**) adduct of 2'-hydroxy-2,4,4,6,5'-pentamethylflavan (**2**) was investigated. The unit cell is triclinic, space group $P\bar{1}$, and contains two host molecules and a single guest molecule. The host molecule, shown in Figure 2, has a very distorted half-chair conformation for the oxygen-containing ring, the atoms C(2) and C(3) being displaced above and below the mean plane of the fused aromatic ring by 0.53 Å and 0.18 Å, respectively. The hydroxyl group of the host again points outward with the O—H bond directed away from the centre of the molecule, but the C(1')—C(12) bond does not so accurately eclipse the C(2)—O(1) bond as for host **1** (see Table II). The arrangement of the centrosymmetric *N,N'*-dimethylpiperazine (**5**) guest molecule with respect to the two (unionised) host molecules to which it is *directly* hydrogen bonded is depicted in the stereo packing diagram in Figure 7. The chair-shaped guest is clamped by two centrosymmetrically related OH···N hydrogen bonds of length 2.759(3) Å. The guest conformation, with both *N*-$CH_3$ groups equatorial, corresponds to the predominant solution conformation [8]; and the N—C—C—N ring torsion angle for the guest in adduct IV is 59.2(3)°. The methyl group is staggered with respect to the two ring N—C bonds and the lone pair involved in hydrogen bond formation to the host. The well-defined guest molecule disposition is illustrated in Figure 7. For host **2**, as well as for **1** in the adducts described, each aromatic ring is planar to within 0.02 Å.

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