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3D/2D Hydrogen-Bond Network Preferences for Five New Ryanoid Derivatives

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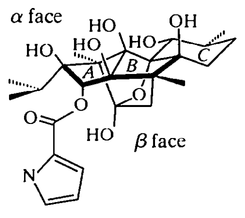
Abstract

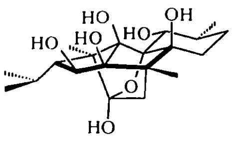
Ryanoids are a family of natural compounds that are well known for their biological activity in plants as pesticides, and in mammalian muscle tissue as calcium permeability modulators. As part of an investigation of the structure–activity relationship of ryanoids, the crystal structures of five new compounds were elucidated: 2-deoxy-3-epiryanodol ($C_{20}H_{32}O_7$), 3-deoxyryanodol hydrate (cinnzeylanol; $2C_{20}H_{32}O_7.5.15H_2O$), 2-deoxyryanodol hydrate ($2C_{20}H_{32}O_7.2.5H_2O$), 2,3-dideoxyryanodol hydrate ($C_{20}H_{32}O_6.1.5H_2O$) and 3a,4a,8,8b-tetrahydroxy-2-isopropyl-4,7-dimethyl-1-methylene-1,3a,4,4a,5,6,7,8,8a,8b-decahydro-8a,4-(epoxyethano)benzo[*a*]pentalen-10-one ($C_{20}H_{28}O_6$). The numerous hydroxyl groups on the molecules modulate the crystal packing. Successive modifications on ring *A* induce major changes in the hydrogen-bond scheme, from a three-dimensional (3D) to a two-dimensional (2D) network.

Comment

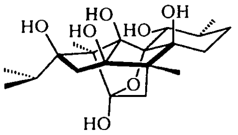
Originally extracted from the *Ryania speciosa* Vahl plant, toxic ryanodine and its congener ryanoids show interesting properties other than their primary utility in plants as botanical pesticides (Jenden & Fairhurst, 1969; Jefferies & Casida, 1994) by modulating the calcium permeability of sarcoplasmic reticulum terminal cisternal membranes (Fairhurst & Hasselbach, 1970; Meissner, 1986; Lattanzio *et al.*, 1986). The binding of ryanodine to its corresponding receptor is complex and displays multiple affinities and cooperative binding (Lai *et al.*, 1989; Chu *et al.*, 1990; Carroll *et al.*, 1991; Pessah & Zimanyi, 1991). QSAR (quantitative structure/activity analysis) and CoMFA (comparative molecular field analysis) suggest that the binding of ryanodine to its receptor involves mainly the pyrrole and isopropyl groups buried deep inside the protein cleft (Welch *et al.*, 1994). These results are based on the study of 19 natural or synthetic ryanoids. In order to identify the structural features that are necessary to enhance biological activity and selectivity, several polyhydroxylated diterpenes were isolated from the usual source or synthesized to test their biological activity (Sutko *et al.*, 1997). The crystal structures were elucidated in order to establish their stereochemistry and conformation for further QSAR and CoMFA studies.



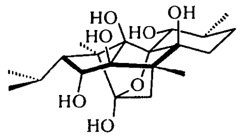
Ryanodine



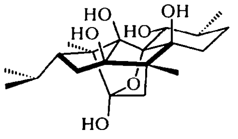
(1)



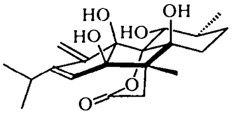
(2)



(3)



(4)



(5)

A general feature of the ryanoids is a highly polar α face opposite to a much less polar β face. The molecules tend to crystallize in the form of an optimized hydro-

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gen-bond network, in which all donors have an acceptor. This manuscript describes five new ryanoid derivatives and highlights their hydrogen-bonding capabilities. All the compounds were synthesized starting from anhydroryanodol or anhydroryanodine (Ruest & Dodier, 1996).

In a previous paper, we reported the crystal structure of 3-epiryanodol (Michel & Drouin, 1993). Its molecular packing is optimized to adopt a minimum energy as all hydroxyl donor groups have acceptors for intra- or intermolecular hydrogen bonds. The first modification to ring *A* is to remove the hydroxyl at position C2, thus giving 2-deoxy-3-epiryanodol [compound (1); Fig. 1]. All H atoms were located in a ΔF map. This compound has similar cell parameters to those of its homolog 3-epiryanodol. Therefore, the crystal packing is very similar (Fig. 2). Indeed, the intermolecular hydrogen-bond network of compound (1) is identical to that of 3-epiryanodol. Atom O23 acts as a donor to O24, and atom O26 is a donor to O27 (Table 1). The β face is linked to the α face by O28, which is a donor to O26. The intramolecular hydrogen bonds are also very similar to those of 3-epiryanodol. Atom O24 is a donor to O25, which is a donor to O23, and atom O27 is a donor to O26. This hydrogen-bond system results in an infinite 3D network.

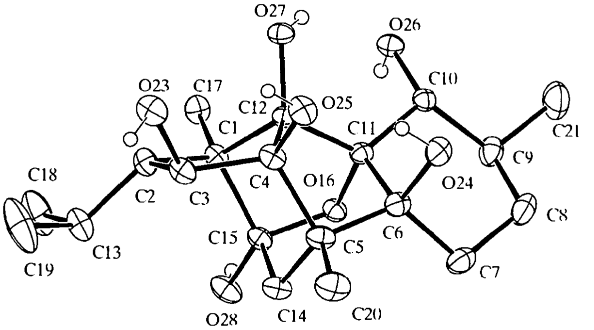

Fig. 1. Perspective view showing the labeling of the non-H atoms for compound (1). Displacement ellipsoids are shown at the 30% probability level; H atoms are drawn as small circles of arbitrary radii.

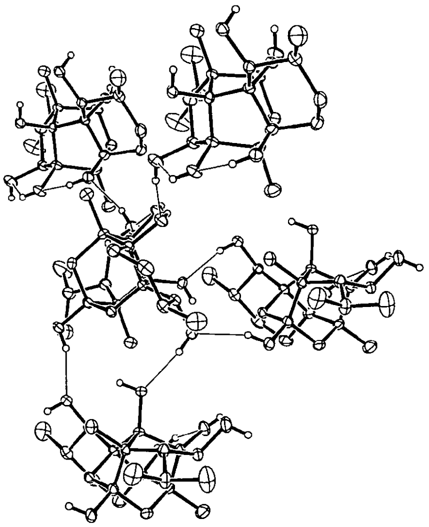

Fig. 2. Molecular packing of compound (1), showing the hydrogen-bonding interactions.

Compound (2), known as cinnzeylanol (3-deoxyryanodol; Fig. 3), crystallizes with two molecules per asymmetric unit, in which there are also 12 partially-occupied water molecule sites. The crystals are difficult to grow and were obtained by the slow vapor diffusion of water from atmospheric moisture into a methanol solution. The crystals are efflorescent. The data were collected at 173 K to avoid loss of water and crystal damage. The molecular packing is such that water molecules are disordered inside a water channel along the *a* axis (Fig. 4). The H atoms are very labile and difficult to locate. No H atoms were located for any of the water molecules. None of them is in a fully occupied position; occupancies range from 0.725 (11) to 0.253 (14). Many of the hydroxyls (O22, O22′, O24′, O25 and O27′) are donors to water molecules (Table 2). The intramolecular hydrogen bonds involve atom O24 as a donor to O25, O25 as a donor to O27, O25′ as a donor to O24′, and O27 as a donor to O22′. Atom O26 is an intermolecular donor to O26′, and atom O26′ is a donor to O16. Atom O28 is a donor to O28′, and atom O28′ is a donor to O26, which links the β face to the α face. These intermolecular hydrogen bonds form the links between the water channels.

In compound (3), 2-deoxyryanodol (Fig. 5), the polarity of the α face is reduced. The O22 atom is absent and O23 is in a pseudo-equatorial position, as found in natural ryanodol. There are two molecules of (3) in the asymmetric unit along with 2.5 water molecules. All the hydroxylic protons were located in a ΔF map. The O25 atom is now a donor to O24 for intramolecular hydrogen bonding (Table 3 and Fig. 6). Atom O23 is a donor to

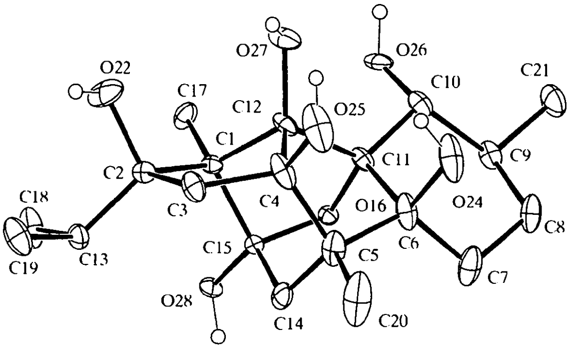

Fig. 3. Perspective view showing the labeling of the non-H atoms for compound (2). Displacement ellipsoids are shown at the 30% probability level; H atoms are drawn as small circles of arbitrary radii.

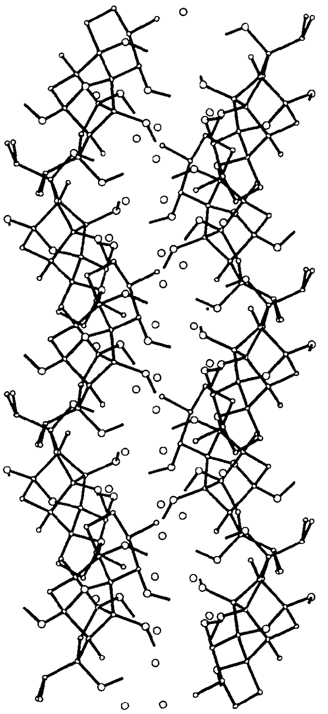

Fig. 4. Molecular packing of compound (2), showing the hydrogen-bonding interactions.

O23′, which is a donor to O41. The hydroxyl O23′ atom cannot complete the network without the help of a water molecule (O41). The hydroxyl O25 atom is a donor to O24, which is a donor to O24′. The H24′ proton does not form a hydrogen bond. Atom O25′ forms a bridge to the second water molecule (O40); atom O40 is a donor to O23 and O28′, atom O26′ is a donor to O27, atom O27 is a donor to O26, and, finally, atom O28 is a donor to O26′ and atom O28′ a donor to O26, which complete the 3D hydrogen-bond network. The β and α faces are linked by the O26 and O28 hydroxyl groups.

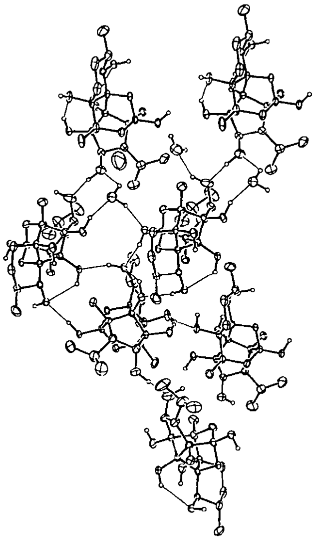

Fig. 6. Molecular packing of compound (3), showing the hydrogen-bonding interactions.

Further modifications to ring *A* produce compound (4) (2,3-dideoxyryanodol; Fig. 7). This compound also crystallizes with two molecules in the asymmetric unit, in which 1.5 water molecules are also found. The water molecules O40 and O40*a* are disordered. The water molecule O40 is located in the special position 222, whereas O40*a* lies on a twofold axis near O40. All the hydroxylic protons were located in a ΔF map. Atom O24 makes an intermolecular hydrogen bond to a symmetry-related O24 (Table 4 and Fig. 8). The hydroxyl O25 shares its H atom between O24 and O41 to form intra- and intermolecular hydrogen bonds, respectively. The positions for H25 and H25′ were located in a ΔF map and had very similar densities. Their occupancies were set to 50% and not refined. Atom O27 is an intramolecular donor to O26, atom O26 is a donor to O27, and atom O28 is a donor to

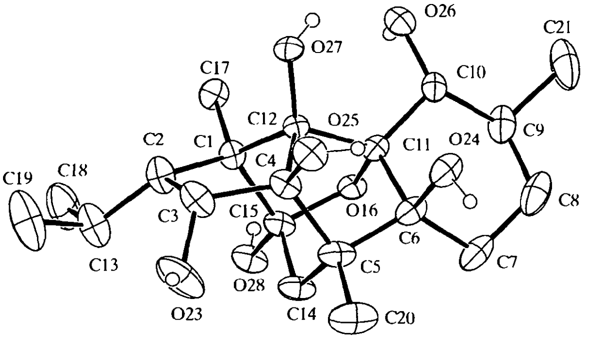

Fig. 5. Perspective view showing the labeling of the non-H atoms for compound (3). Displacement ellipsoids are shown at the 30% probability level; H atoms are drawn as small circles of arbitrary radii.

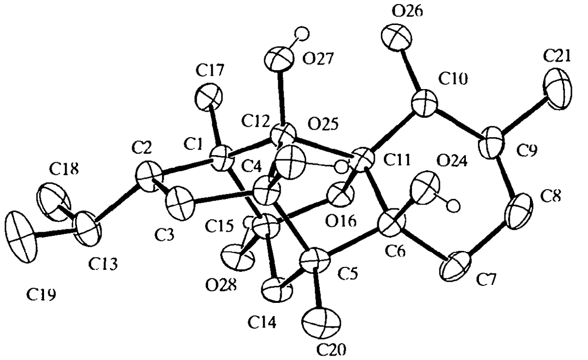

Fig. 7. Perspective view showing the labeling of the non-H atoms for compound (4). Displacement ellipsoids are shown at the 30% probability level; H atoms are drawn as small circles of arbitrary radii.

O26 and an acceptor from O41. The water molecule O41 donates only one of its two H atoms. It is placed in the unit cell such that it could be an acceptor with respect to one O40*a* disordered water molecule, but the H atoms of O40*a* were not located. The water molecule O40*a* is potentially a donor to a symmetry-related O40*a* and to O41. Again, atoms O28 and O26 form the link between the β and α faces. The system still displays a 3D hydrogen-bond network.

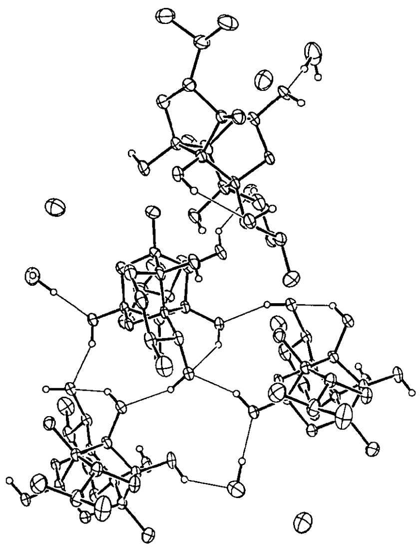

Fig. 8. Molecular packing of compound (4), showing the hydrogen-bonding interactions.

Compound (5) (Fig. 9) is produced when (4) is oxidized into a lactone (Dodier, 1996). It crystallizes with two molecules per asymmetric unit. There is only one intramolecular hydrogen bond per molecule: between O24 and O25, and O24′ and O25′ (Table 5 and Fig. 10). Atom O25 is a donor to O26, atom O25′ is a donor to O26′, atom O27 is a donor to O25, and atom O27′ is a donor to O25′. Finally, the O26 hydroxyl group is now a donor to the O28 ketone (O26′ is also a donor to O28′), providing the link between the α and β faces.

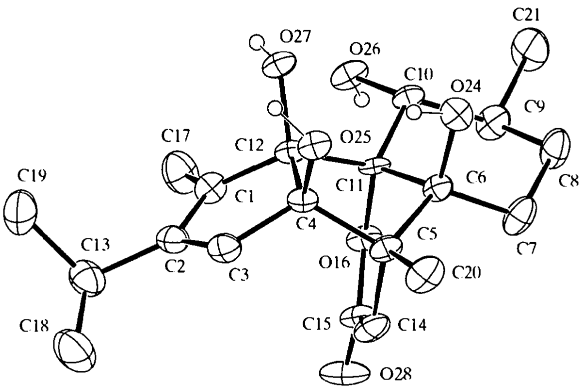

Fig. 9. Perspective view showing the labeling of the non-H atoms for compound (5). Displacement ellipsoids are shown at the 30% probability level; H atoms are drawn as small circles of arbitrary radii.

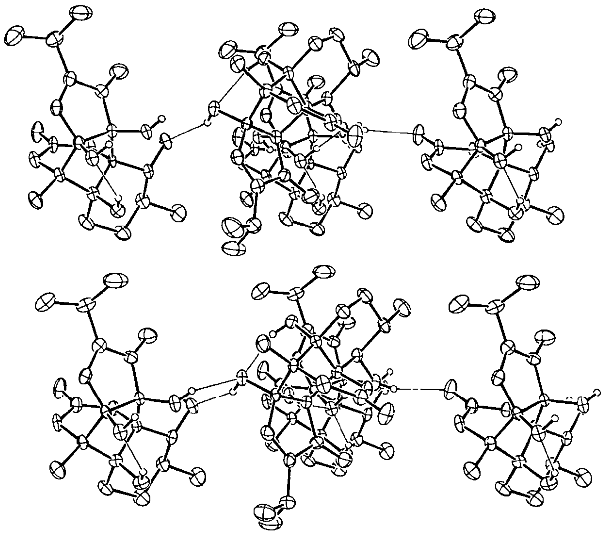

Fig. 10. Molecular packing of compound (5), showing the hydrogen-bonding interactions.

In all compounds, several intermolecular and intramolecular hydrogen bonds occur. It is well known that the stabilization energy of a hydrogen bond is much greater than that of typical van der Waals interactions (Brock & Dunitz, 1994). Thus, intermolecular hydrogen bonds are favored during the process of crystallization. Compound (1) crystallizes in an identical fashion to its homolog 3-epiryanodol. Removing the O22 hydroxyl does not affect the crystal packing since O22 is not involved in any intermolecular hydrogen bond. In this particular crystal system, the O23 and O26 atoms are anchors on the β face. Atom O23 remains an important factor for crystal packing because it acts as a donor and an acceptor for two intermolecular hydrogen bonds. The β and α faces are linked by atom O28 as a donor to O26. In contrast, removing atom O23 changes drastically the capability for hydrogen bonding since one of the two molecular anchors disappears. The modifications in the hydroxyl groups on ring *A* result in a molecular packing in which water molecules are essential to complete the 3D network [compounds (2), (3) and (4)]. In (2), many water molecules are needed in order to complete a suitable crystal arrangement. The molecular packing is such that all hydroxyls on the α face are oriented toward the water channel. The link between the α and β faces is conserved. In (3), the orientation of O23 causes the compound to pack differently than its homolog (1). Again, it crystallizes with water molecules trapped inside the lattice. With the help of water molecules in two fully occupied sites, the crystal packing is almost completely optimized; all hydroxyls are involved in hydrogen bonding. The intermolecular hydrogen-bond network is still 3D. Again, the β face is linked to the α face by an O28-to-O26 hydrogen bond. Further reducing the hydrophilic character of the α face makes the isopropyl groups regroup, favoring van der Waals interactions, as in compounds (4) and (5). The absence of hydroxyl groups at C2 and C3 makes ring *A* more hydrophobic. Compound (4) crystallizes so as to place the isopropyl moieties face to face. One water molecule is trapped inside this hydrophilic cavity, where it cannot interact with any hydroxyl groups for hydrogen bonding. Finally, the capacity of O28 for hydrogen-bond donation is removed when oxidizing (4) is oxidized to form the lactone (5). Since atom O28 can no longer be a donor to O26, the roles are reversed: O28 is now an acceptor from O26, thus linking the α face to the β face. The 3D nature of the hydrogen-bond network is reduced to two dimensions. The resulting crystal packing is characterized by an infinite 2D hydrogen-bonded network forming a layer system. Van der Waals forces stabilize the crystal by linking the 2D layers *via* the isopropyl groups.

Experimental

The compounds were prepared as indicated in the *Comment* (Ruest & Dodier, 1996).

Compound (1)

Crystal data

$C_{20}H_{32}O_7$
$M_r = 384.46$
Orthorhombic
$P2_12_12_1$
$a = 8.9913\ (5)$ Å
$b = 13.1001\ (10)$ Å
$c = 16.6041\ (10)$ Å
$V = 1955.7\ (2)$ Å^3
$Z = 4$
$D_x = 1.306$ Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
$\lambda = 1.54184$ Å
Cell parameters from 24 reflections
$\theta = 30\text{–}40°$
$\mu = 0.807$ mm^{-1}
$T = 293\ (1)$ K
Prism
$0.30 \times 0.30 \times 0.20$ mm
Colorless

Data collection

Nonius CAD-4 diffractometer
$\theta/2\theta$ scan
Absorption correction: none
2203 measured reflections
2203 independent reflections
2134 reflections with $I > 2\sigma(I)$

$\theta_{\max} = 71.96°$
$h = 0 \rightarrow 11$
$k = 0 \rightarrow 16$
$l = 0 \rightarrow 20$
3 standard reflections
frequency: 60 min
intensity decay: <1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.030$
$wR(F^2) = 0.084$
$S = 1.052$
2203 reflections
274 parameters
H atoms constrained
$w = 1/[\sigma^2(F_o^2) + (0.0503P)^2 + 0.4105P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} = -0.001$

$\Delta\rho_{\max} = 0.210$ e Å^{-3}
$\Delta\rho_{\min} = -0.142$ e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.0032 (3)
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 1. *Hydrogen-bonding geometry (Å, °) for (1)*

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
O23—H23$\cdots$O24$^{\text{i}}$	0.84 (3)	1.94 (3)	2.779 (2)	178 (3)
O24—H24$\cdots$O25	0.86 (3)	1.78 (3)	2.585 (2)	154 (3)
O25—H25$\cdots$O23	0.78 (4)	2.03 (3)	2.547 (2)	124 (3)
O26—H26$\cdots$O27$^{\text{ii}}$	0.86 (3)	1.95 (3)	2.808 (2)	170 (3)
O27—H27$\cdots$O26	0.86 (3)	2.17 (3)	2.911 (2)	145 (3)
O28—H28$\cdots$O26$^{\text{ii}}$	0.85 (3)	1.96 (3)	2.772 (2)	161 (3)

Symmetry codes: (i) $2 - x, \frac{1}{2} + y, \frac{1}{2} - z$; (ii) $x - \frac{1}{2}, \frac{1}{2} - y, -z$.

Compound (2)

Crystal data

$2C_{20}H_{32}O_7.5.15H_2O$
$M_r = 861.50$
Orthorhombic
$P2_12_12_1$
$a = 10.321\ (3)$ Å
$b = 13.917\ (5)$ Å
$c = 29.196\ (4)$ Å
$V = 4194\ (2)$ Å^3
$Z = 4$
$D_x = 1.364$ Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 24 reflections
$\theta = 15\text{–}20°$
$\mu = 0.10$ mm^{-1}
$T = 293$ K
Block
$0.30 \times 0.30 \times 0.30$ mm
Colorless

Data collection

Nonius CAD-4 diffractometer
$\theta/2\theta$ scan
Absorption correction: none
6905 measured reflections
6176 independent reflections
4475 reflections with $I_{\text{net}} > 2\sigma(I_{\text{net}})$

$R_{\text{int}} = 0.012$
$\theta_{\max} = 24.89°$
$h = 0 \rightarrow 11$
$k = 0 \rightarrow 16$
$l = 0 \rightarrow 34$
2 standard reflections
frequency: 60 min
intensity decay: <1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.062$
$wR(F^2) = 0.152$
$S = 1.038$
6176 reflections
560 parameters
H atoms constrained
$w = 1/[\sigma^2(F_o^2) + (0.0796P)^2 + 1.0322P]$
where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} = 0.021$
$\Delta\rho_{\max} = 0.374$ e Å^{-3}
$\Delta\rho_{\min} = -0.297$ e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)

Table 2. *Hydrogen-bonding geometry (Å, °) for (2)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O22—H22···O41	0.82	2.155 (15)	2.848 (6)	142 (2)
O22—H22···O46^{i}	0.82	2.15 (4)	2.802 (10)	139 (5)
O22′—H22′···O43^{ii}	0.82	2.07 (1)	2.680 (9)	130.7 (8)
O22′—H22′···O48^{ii}	0.82	2.14 (3)	2.758 (13)	132 (4)
O24—H24···O25	0.82	2.01 (5)	2.611 (6)	129 (5)
O24′—H24′···O40	0.82	2.102 (16)	2.917 (16)	172 (2)
O24′—H24′···O50	0.82	1.966 (13)	2.665 (12)	142.7 (9)
O24′—H24′···O51	0.82	2.042 (15)	2.847 (10)	167 (4)
O25—H25···O27	0.82	2.390 (17)	2.846 (6)	116 (1)
O25—H25···O44	0.82	2.37 (6)	2.925 (10)	125 (7)
O25′—H25′···O24′	0.82	1.923 (9)	2.592 (5)	138 (1)
O26—H26···O26′	0.82	1.920 (4)	2.700 (4)	159 (2)
O26′—H26′···O16^{iii}	0.82	2.46 (1)	3.229 (4)	156 (2)
O27′—H27′···O22′	0.82	2.53 (3)	3.053 (5)	122 (3)
O27′—H27′···O43^{ii}	0.82	2.49 (2)	3.206 (10)	146 (3)
O27′—H27′···O48^{ii}	0.82	2.378 (14)	3.173 (14)	164 (3)
O28—H28···O28′^{iv}	0.82	2.086 (5)	2.897 (4)	170 (2)
O28′—H28′···O26^{iii}	0.82	1.903 (6)	2.683 (4)	159 (1)

Symmetry codes: (i) $x, y, z-1$; (ii) $\frac{1}{2}+x, \frac{3}{2}-y, 1-z$; (iii) $2-x, y-\frac{1}{2}, \frac{1}{2}-z$; (iv) $x, 1+y, z$.

Compound (3)

Crystal data

$2C_{20}H_{32}O_7.2.5H_2O$
$M_r = 813.98$
Orthorhombic
$P22_12_1$
$a = 9.0121$ (10) Å
$b = 18.080$ (4) Å
$c = 25.476$ (3) Å
$V = 4150.9$ (11) Å^3
$Z = 4$
$D_x = 1.302$ Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
$\lambda = 1.54184$ Å
Cell parameters from 24 reflections
$\theta = 30$–$40°$
$\mu = 0.83$ mm^{-1}
$T = 293$ K
Prism
$0.20 \times 0.20 \times 0.20$ mm
Colorless

Data collection

Nonius CAD-4 diffractometer
$\theta/2\theta$ scan
Absorption correction: none
4670 measured reflections
4541 independent reflections
3995 reflections with $I > 2\sigma(I)$

$R_{int} = 0.036$
$\theta_{max} = 71.92°$
$h = 0 \rightarrow 10$
$k = 0 \rightarrow 21$
$l = 0 \rightarrow 31$
2 standard reflections
frequency: 60 min
intensity decay: <1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.055$
$wR(F^2) = 0.159$
$S = 1.041$
4540 reflections
523 parameters
H atoms constrained
$w = 1/[\sigma^2(F_o^2) + (0.1016P)^2 + 1.0931P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.489$ e Å^{-3}
$\Delta\rho_{min} = -0.220$ e Å^{-3}

Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.00023 (8)
Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)
Absolute structure: Flack (1983)
Flack parameter = 0.3 (3)

Table 3. *Hydrogen-bonding geometry (Å, °) for (3)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O23—H23···O23^{i}	0.820	1.783 (11)	2.592 (5)	169 (5)
O23′—H23′···O41^{ii}	0.820	2.122 (9)	2.724 (6)	130.1 (8)
O24—H24···O24′^{iii}	0.820	2.027 (19)	2.793 (4)	155 (4)
O25—H25···O24	0.820	1.901 (5)	2.586 (4)	140.4 (5)
O25′—H25′···O40	0.820	1.949 (15)	2.710 (4)	154 (3)
O26—H26···O27′	0.820	2.044 (3)	2.855 (3)	169.9 (8)
O26′—H26′···O27^{iv}	0.820	2.075 (3)	2.888 (3)	171.0 (9)
O27—H27···O26	0.820	2.206 (8)	2.899 (3)	142 (1)
O27′—H27′···O26′	0.820	2.263 (15)	2.922 (3)	138 (2)
O28—H28···O26′	0.820	2.009 (4)	2.801 (3)	162.1 (9)
O28′—H28′···O26^{iv}	0.820	1.969 (4)	2.763 (3)	162.9 (7)
O40—H40*A*···O23^{v}	1.896	2.225 (4)	2.776 (5)	119.3 (2)
O40—H40*B*···O28′^{vi}	1.017	1.867 (2)	2.821 (4)	154.9 (2)

Symmetry codes: (i) $1-x, \frac{3}{2}-y, z-\frac{1}{2}$; (ii) $2-x, \frac{3}{2}-y, \frac{1}{2}+z$; (iii) $1-x, y-\frac{1}{2}, \frac{1}{2}-z$; (iv) $1+x, y, z$; (v) $1-x, \frac{3}{2}-y, \frac{1}{2}+z$; (vi) $x-1, y, z$.

Compound (4)

Crystal data

$C_{20}H_{32}O_6.1.5H_2O$
$M_r = 395.49$
Orthorhombic
$I222$
$a = 8.9140$ (5) Å
$b = 18.1678$ (13) Å
$c = 25.326$ (2) Å
$V = 4101.3$ (5) Å^3
$Z = 8$
$D_x = 1.281$ Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
$\lambda = 1.54184$ Å
Cell parameters from 24 reflections
$\theta = 30$–$40°$
$\mu = 0.80$ mm^{-1}
$T = 293$ (2) K
Thin plate
$0.40 \times 0.30 \times 0.02$ mm
Colorless

Data collection

Nonius CAD-4 diffractometer
$2\theta/\omega$ scans
Absorption correction: empirical *via* ψ scans on 9 azumital reflections (*NRCCAD*; Le Page *et al.*, 1986)
$T_{min} = 0.886$, $T_{max} = 0.999$
5597 measured reflections
4020 independent reflections

3665 reflections with $I > 2\sigma(I)$
$R_{int} = 0.020$
$\theta_{max} = 71.87°$
$h = -10 \rightarrow 10$
$k = -21 \rightarrow 21$
$l = -30 \rightarrow 31$
2 standard reflections
frequency: 60 min
intensity decay: <1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.039$
$wR(F^2) = 0.108$
$S = 1.024$
4020 reflections
289 parameters
H atoms constrained
$w = 1/[\sigma^2(F_o^2) + (0.0754P)^2 + 0.3481P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.006$

$\Delta\rho_{max} = 0.239$ e Å^{-3}
$\Delta\rho_{min} = -0.201$ e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.00025 (6)
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 4. *Hydrogen-bonding geometry (Å, °) for (4)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O24—H24···O24^{i}	0.68 (4)	2.09 (4)	2.766 (3)	171 (4)
O25—H25···O41^{ii}	0.79 (5)	2.11 (6)	2.785 (3)	144 (5)
O25—H25′···O24	0.89 (6)	1.73 (6)	2.566 (2)	153 (6)
O26—H26···O27^{iii}	0.77 (3)	2.07 (7)	2.812 (2)	160 (3)

O27—H27···O26	0.83 (2)	2.19 (2)	2.894 (2)	142 (2)
O28—H28···O26$^{\rm iii}$	0.96 (2)	1.86 (3)	2.767 (2)	158 (2)
O41—H41*B*···O28	0.86 (4)	2.02 (5)	2.848 (3)	161 (4)

Symmetry codes: (i) $-x, 1-y, z$; (ii) $x-1, y, z$; (iii) $\frac{1}{2}+x, \frac{1}{2}-y, \frac{1}{2}-z$.

Compound (5)

Crystal data

$C_{20}H_{28}O_6$
$M_r = 728.85$
Monoclinic
$P2_1$
$a = 9.7509\ (5)$ Å
$b = 10.3005\ (8)$ Å
$c = 19.5609\ (13)$ Å
$\beta = 101.937\ (5)°$
$V = 1922.2\ (2)$ Å^3
$Z = 2$
$D_x = 1.259$ Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 24 reflections
$\theta = 30–40°$
$\mu = 0.092$ mm^{-1}
$T = 293\ (2)$ K
Irregular
0.20 × 0.20 × 0.20 mm
Colorless

Data collection

Nonius CAD-4 diffractometer
$\theta/2\theta$ scans
Absorption correction: none
3460 measured reflections
3321 independent reflections
2517 reflections with $I > 2\sigma(I)$

$R_{\rm int} = 0.007$
$\theta_{\rm max} = 22.42°$
$h = -10 \rightarrow 10$
$k = 0 \rightarrow 10$
$l = 0 \rightarrow 20$
2 standard reflections
frequency: 60 min
intensity decay: <1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.038$
$wR(F^2) = 0.094$
$S = 1.036$
3321 reflections
486 parameters
H atoms constrained
$w = 1/[\sigma^2(F_o^2) + (0.0406P)^2 + 0.4793P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} = -0.021$

$\Delta\rho_{\rm max} = 0.157$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.138$ e Å^{-3}
Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.0047 (5)
Scattering factors from *International Tables for Crystallography* (Vol. C)

Table 5. *Hydrogen-bonding geometry (Å, °) for (5)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O24—H24···O25	0.82 (5)	1.91 (5)	2.713 (5)	162 (6)
O24′—H24′···O25′	0.76 (4)	2.05 (4)	2.725 (5)	148 (5)
O25—H25···O26$^{\rm i}$	0.86 (7)	1.90 (7)	2.684 (5)	149 (6)
O25′—H25′···O26′$^{\rm ii}$	0.89 (10)	1.93 (10)	2.678 (5)	141 (9)
O26—H26···O28$^{\rm iii}$	0.85 (5)	2.00 (5)	2.827 (5)	162 (5)
O26′—H26′···O28′$^{\rm iv}$	0.90 (8)	2.10 (8)	2.764 (5)	130 (7)
O27—H27···O25$^{\rm v}$	0.84 (6)	2.18 (6)	2.960 (4)	154 (5)
O27′—H27′···O25′$^{\rm vi}$	0.90 (6)	1.99 (7)	2.866 (5)	164 (6)

Symmetry codes: (i) $1-x, y-\frac{1}{2}, 1-z$; (ii) $1-x, y-\frac{1}{2}, -z$; (iii) $2-x, \frac{1}{2}+y, 1-z$; (iv) $2-x, \frac{1}{2}+y, -z$; (v) $1-x, \frac{1}{2}+y, 1-z$; (vi) $1-x, \frac{1}{2}+y, -z$.

It should be noted that the two independent molecules of compound (2) are related by a non-crystallographic 2_1 screw axis parallel to the *c* axis, and that the two independent molecules of compound (3) are related by a non-crystallographic 2_1 screw axis parallel to the *a* axis.

Data collection and cell refinement were performed with *NRCCAD* (Le Page *et al.*, 1986). For (1) and (2), equivalent reflections were grouped and averaged according to Le Page & Gabe (1979). For all compounds, data reduction was performed using the *NRCVAX* package (Gabe *et al.*, 1989). *NRCVAX* was used for the solution of structures (2) and (3), while *SIR*92 (Altomare *et al.*, 1993) was used for structures (1), (4) and (5). *SHELXL*93 (Sheldrick, 1993) was used for all refinements. Molecular graphics were prepared using versions of *ORTEP*II (Johnson, 1976) in *NRCVAX* and *Xtal_GX* (Hall & du Boulay, 1995). *SHELXL*93 was used to prepare the data for publication.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BS1023). Services for accessing these data are described at the back of the journal.

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