Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

(*S*,*S*)-4″-Cyano-7,7″-dimethoxy-3′,6′-dioxodispiro[indane-2,2′-piperazine-5′,2″-indane]-4-carboxamide methanol solvate: interrupting the amide-to-amide hydrogen-bonded tape

Bhumasamudram Jagadish, Michael D. Carducci, Alice Dawson, Gary S. Nichol* and Eugene A. Mash

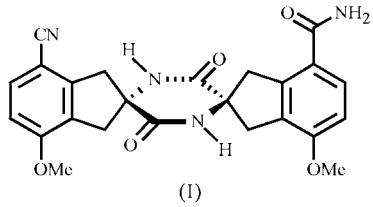
Department of Chemistry, The University of Arizona, 1306 East University Boulevard, Tucson, AZ 85721, USA
Correspondence e-mail: gsnichol@email.arizona.edu

Received 24 June 2008
Accepted 3 July 2008
Online 12 July 2008

The title methanol solvate, $C_{24}H_{22}N_4O_5\cdot CH_3OH$, forms an extended three-dimensional hydrogen-bonded structure, assisted by the presence of several good donor and acceptor sites. It shows none of the crystal packing features typically expected of piperazinediones, such as amide-to-amide $R_2^2(8)$ hydrogen bonding. In this structure the methanol solvent appears to play only a space-filling role; it is not involved in any hydrogen bonding and instead is disordered over several sites. This study reports, to the best of our knowledge, the first crystal structure of an indane-containing piperazinedione compound which exhibits a three-dimensional hydrogen-bonded structure formed by classical (N—H···O and N—H···N) hydrogen-bonding interactions.

Comment

We are pursuing a program of organic crystal engineering using a piperazinedione-based molecular scaffold to explore the effects of substituents on the crystal packing and bulk properties of such molecules (Ntirampebura *et al.*, 2008; Weatherhead-Kloster *et al.*, 2005; Kloster *et al.*, 2003; Jagadish *et al.*, 2003; Williams, Jagadish, Lansdown *et al.*, 1999; Williams, Jagadish, Lyon *et al.*, 1999). We consider the pentacyclic molecular framework depicted in Fig. 1 suitable for use in the exploration of structural effects on weak intermolecular associative forces and an appropriate scaffold for the design of compounds that could possess useful bulk properties. The conformational freedom of such molecules is restricted, limiting the number of possible packing options. At the same time, the attachment of groups to the scaffold can provide structural and functional variability. For example, incorporation of electron donor (*D*) and acceptor (*A*) groups, as shown in Fig. 1, renders the molecule chiral and dipolar. The central 1,4-piperazine-2,5-dione ring is known to favour the formation of supramolecular 'one-dimensional' tapes through reciprocal amide-to-amide $R_2^2(8)$ hydrogen bonding (Bernstein *et al.*, 1995) and in observance of the hydrogen-bonding priority rules as determined by Etter (1990). The control of order in the second and third dimensions (Fig. 1, *x* and *y* axes) depends on harnessing van der Waals interactions, arene interactions, Coulombic interactions and/or additional hydrogen-bonding interactions, all of which are affected by variation of ring substituents.



(I)

While the majority of piperazinedione-containing compounds do reliably form extended $R_2^2(8)$ hydrogen-bonded tapes, our studies and those of others (Howes *et al.*, 1983; Caira *et al.*, 2002) have shown that the crystal structure can be solvent-dependant and that not all compounds follow the $R_2^2(8)$ hydrogen-bonding pattern. We report here the methanol solvate, (I), of (*S*,*S*)-4″-cyano-7,7″-dimethoxy-3′,6′-dioxodispiro[indane-2,2′-piperazine-5′,2″-indane]-4-carboxamide, which is an example of a piperazinedione-containing compound that does not follow the general trend.

The structure of (I) is shown in the scheme and the conformer present in the crystal is shown in Fig. 2. The compound crystallizes in the space group $P2_12_12_1$, consistent with its chiral nature. The molecular dimensions are unexceptional. The indane rings, which are perpendicular to the piperazinedione ring, exhibit minimal flexibility, with the cyclopentene rings both adopting envelope conformations. A mean plane fitted through atoms C2/C5–C12 has an r.m.s. deviation of 0.1172 Å, while a mean plane fitted through atoms C4/C15–C22 has an r.m.s. deviation of 0.1084 Å. The methoxy groups are essentially coplanar with the arene unit of the indane group, while the benzamide group is not; the angle

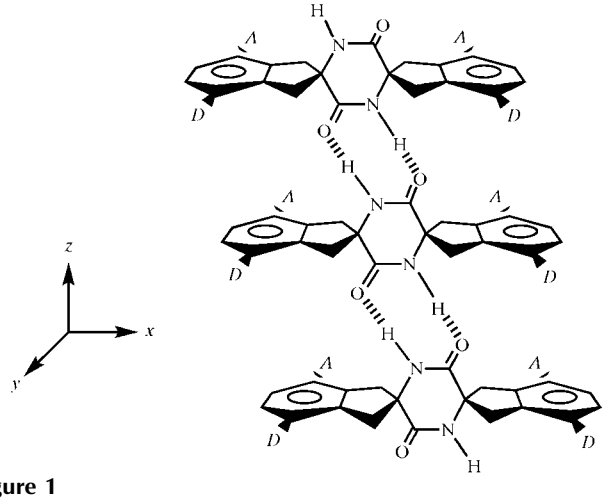


Figure 1
Intermolecular $R_2^2(8)$ hydrogen-bonding interactions (dashed lines) in piperazinediones.

 DOI: 10.1107/S010827010802057X

between the mean plane through atoms O4, N3, C14 and C10, and the plane through the six-membered ring is 41.40 (9)°.

The crystal packing of (I) is very different from most other piperazinedione compounds. The presence of benzamide and nitrile groups permits the formation of an alternative extended three-dimensional hydrogen-bonded network. The methanol solvent molecule, removed using the SQUEEZE routine of *PLATON* (Spek, 2003), has no role in the hydrogen bonding; this explains the desolvation observed when the crystals were removed from the mother liquor. Fig. 3 shows (I) in a space-filling representation, with the methanol molecule shown in one of its several orientations. It would seem that the methanol molecule occupies space between the two methoxy groups but, suprisingly, with no appreciable interactions between the dispiro molecule and solvent to anchor the methanol in one orientation. Instead, it is disordered over several positions in this 'pocket'. An *a*-axis projection (Fig. 4) shows how the $R_2^2(8)$ motif is avoided. Two motifs are found, each sharing a single N—H···O interaction between the piperazinedione rings. One motif can be described as $R_2^2(13)$, in which the acetamide group acts as a donor, and the second can be described as $R_2^2(12)$, in which the acetamide group acts as an acceptor. These two motifs allow the structure to extend in the *a* and *b* directions. The second N—H acetamide H atom forms an N—H···N interaction with an adjacent cyano group, and this interaction allows the crystal structure to propagate along the *c* axis (Fig. 5). From this analysis, it can be seen that no good hydrogen-bond donor or acceptor is left without a partner, and so the methanol solvent molecule, while perhaps playing a space-filling role for the three-dimensional structure, does not itself form part of the three-dimensional hydrogen-bonded framework. Unlike other indane-containing piperazinedione crystal structures, arene interactions are not a significant force in this crystal structure, there being essentially just one interaction (Fig. 6), which most probably results from the orientation of the molecules to maximize hydrogen bonding.

In summary, while the majority of indane-containing piperazinedione compounds produce predicatable $R_2^2(8)$ crystal packing motifs, the properties of which can be tuned by appropriate ring subsitution, there are compounds which do not follow this trend. In the case of (I), the benzamide group provides the piperazinedione ring with competition for hydrogen-bonding donor and acceptor sites, and also involves the cyano group as an acceptor. Maximization of hydrogen bonding in this compound requires that the amide-to-amide $R_2^2(8)$ motif be displaced in favour of a more complex and extensive hydrogen-bonded network.

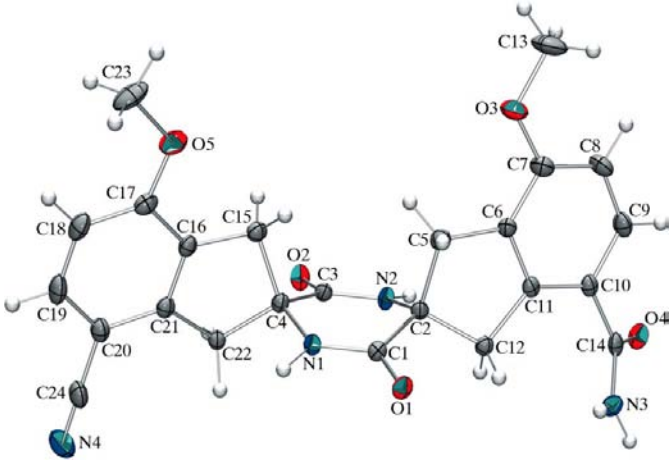


Figure 2
The molecular structure of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

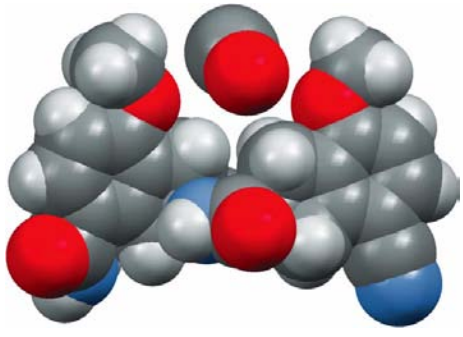


Figure 3
A space-filling representation of the asymmetric unit of (I), with the methanol solvent molecule shown in one of several orientations.

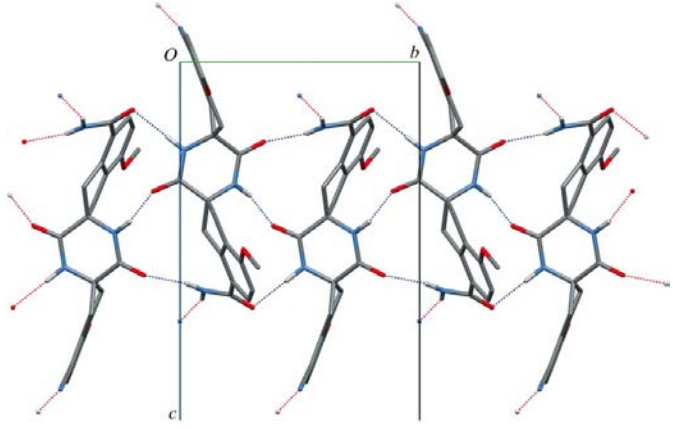


Figure 4
Hydrogen-bonding interactions parallel to the *b* axis in (I). The long *c* axis of the unit cell has been truncated for clarity.

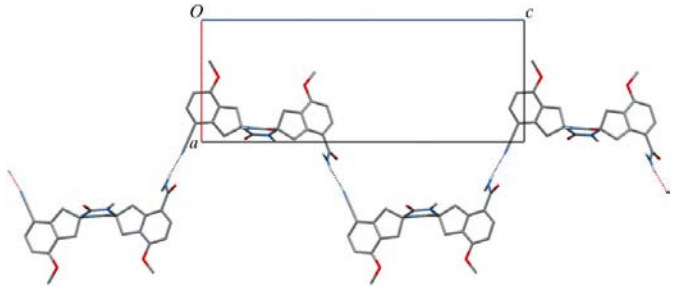


Figure 5
Illustration of how N—H···N hydrogen bonds allow the structure of (I) to propagate parallel to the *c* axis.

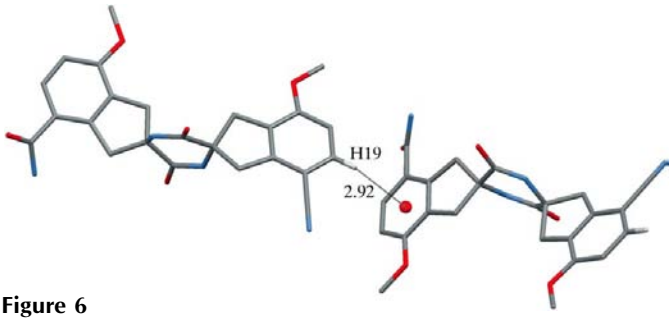


Figure 6
The only aromatic stacking interaction in (I); the distance is approximate and in Å.

Experimental

The synthesis of (I) has been described elsewhere (Jagadish *et al.*, 2003). Crystallization was effected by heating a suspension of the compound in methanol until dissolution was complete. The hot methanol solution was allowed to cool slowly in an oil bath overnight.

Crystal data

$C_{24}H_{22}N_4O_5\cdot CH_4O$
M_r = 478.50
Orthorhombic, $P2_12_12_1$
a = 9.6409 (7) Å
b = 10.4629 (8) Å
c = 25.5588 (19) Å
V = 2578.2 (3) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.09 mm^{-1}
T = 170 (2) K
0.44 × 0.19 × 0.10 mm

Data collection

Bruker SMART 1000 CCD diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.962, T_{max} = 0.992
20487 measured reflections
2821 independent reflections
2290 reflections with $I > 2\sigma(I)$
R_{int} = 0.053

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.029
$wR(F^2)$ = 0.068
S = 0.98
2821 reflections
317 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.12 e Å^{-3}
$\Delta\rho_{min}$ = −0.15 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N2—H2N···O1^{i}	0.93 (2)	1.98 (2)	2.889 (2)	165.7 (19)
N1—H1N···O4^{ii}	0.94 (2)	1.93 (2)	2.867 (2)	173.6 (18)
N3—H3*A*···O2^{ii}	0.91 (2)	2.05 (2)	2.944 (2)	166.3 (19)
N3—H3*B*···N4^{iii}	0.94 (2)	2.19 (2)	3.078 (3)	156 (2)

Symmetry codes: (i) $-x+2, y+\frac{1}{2}, -z+\frac{1}{2}$; (ii) $-x+2, y-\frac{1}{2}, -z+\frac{1}{2}$; (iii) $-x+\frac{5}{2}, -y, z+\frac{1}{2}$.

H atoms were initially located in a difference Fourier map. N-bound H atoms were refined freely. C-bound H atoms were refined using a riding model, with U_{iso}(H) = 1.5U_{eq}(C) for methyl H atoms and 1.2U_{eq}(C) for all others. C—H distances were constrained to 0.95 Å for aryl H atoms, 0.98 Å for methyl H atoms and 0.99 Å for methylene H atoms. The unit cell contains two solvent-accessible voids of 279 Å^3 each. A difference map revealed a series of electron-density peaks corresponding to partially desolvated methanol disordered over many positions. No multi-part disorder model could be refined satsfactorily and so the residual electron density was removed using the SQUEEZE routine of *PLATON* (Spek, 2003). Friedel pairs were merged during refinement.

Data collection: *SMART* (Bruker, 2007); cell refinement: *SAINT* (Bruker, 2007); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 2008); program(s) used to refine structure: *SHELXTL*; molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997) and *Mercury* (Version 2.0; Macrae *et al.*, 2006); software used to prepare material for publication: *SHELXTL*, *publCIF* (Westrip, 2008) and local programs.

This work was supported by the Office of Naval Research through the Center for Advanced Multifunctional Nonlinear Optical Polymers and Molecular Assemblies, by the National Science Foundation (grant No. CHE9610374), by Research Corporation, and by the University of Arizona through the Materials Characterization Program and the Office of the Vice President for Research.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK3252). Services for accessing these data are described at the back of the journal.

References

Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Bruker (2007). *SAINT* and *SMART*. Bruker AXS Inc., Madison, Wisconsin, USA.
Caira, M. R., Buyukbingol, E., Adejare, A. & Millington, W. R. (2002). *Anal. Chem.* **18**, 1175–1176.
Etter, M. C. (1990). *Acc. Chem. Res.* **23**, 120–126.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Howes, C., Alcock, N. W., Golding, B. T. & McCabe, R. W. (1983). *J. Chem. Soc. Perkin Trans. 1*, pp. 2287–2291.
Jagadish, B., Carducci, M. D., Bosshard, C., Günter, P., Margolis, J. I., Williams, L. J. & Mash, E. A. (2003). *Cryst. Growth Des.* **3**, 811–821.
Kloster, R. A., Carducci, M. D. & Mash, E. A. (2003). *Org. Lett.* **5**, 3683–3686.
Macrae, C. F., Edgington, P. R., McCabe, P., Pidcock, E., Shields, G. P., Taylor, R., Towler, M. & van de Streek, J. (2006). *J. Appl. Cryst.* **39**, 453–457.
Ntirampebura, D., Jagadish, B., Nichol, G. S., Carducci, M. D., Dawson, A., Rajapakshe, A., Oliver, A. G., Clegg, W., Harrington, R. W., Layne, L., Margolis, J. I. & Mash, E. A. (2008). *Cryst. Growth Des.* In the press.
Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
Weatherhead-Kloster, R. A., Selby, H. D., Miller, W. B. & Mash, E. A. (2005). *J. Org. Chem.* **70**, 8693–8702.
Westrip, S. P. (2008). *publCIF*. In preparation.
Williams, L. J., Jagadish, B., Lansdown, M. G., Carducci, M. D. & Mash, E. A. (1999). *Tetrahedron*, **55**, 14301–14322.
Williams, L. J., Jagadish, B., Lyon, S. R., Kloster, R. A., Carducci, M. D. & Mash, E. A. (1999). *Tetrahedron*, **55**, 14281–14300.