

2-(3-Hydroxypropyl)isoindoline-1,3-dione: competition among hydrogen-bond acceptors

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The title compound, $C_{11}H_{11}NO_3$, has two molecules in the asymmetric unit, which differ in the orientation of their side-chain OH groups, allowing them to form intermolecular O—H...O hydrogen bonds to different acceptors. In one case, the acceptor is the OH group of the other molecule, and in the other case it is an imide O=C group. This is the first example in the *N*-substituted phthalimide series in which independent molecules have different types of acceptor. Molecular-orbital calculations place the greatest negative charge on the OH group.

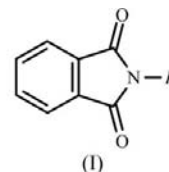
Comment

N-Substituted phthalimides, (I), are of interest for their biological activity in their own right (Lima *et al.*, 2002) and as precursors for synthesis (Couture *et al.*, 1998). Crystallographic studies have appeared recently in which the imide N atom bears a nonpolar substituent, such as ethyl, (Ia) (Liang & Li, 2006c), or allyl, (Ib) (Warzecha *et al.*, 2006). Other studies have investigated the situation when an *N*-alkyl substituent terminates with a hydrogen-bond donor, including hydroxymethyl, (Ic) (Liang & Li, 2006a), hydroxyethyl, (Id) (Liang & Li, 2006b), and a series of alkanolic acids, (Ie)–(Ii) (Feeder & Jones, 1996). The title compound, (Ij), corresponds to (If) with its carboxyl C=O group replaced by CH₂.

The two independent molecules of (Ij) are illustrated in Fig. 1. Their isoindoline ring systems are planar, with r.m.s. deviations of 0.01 Å, and the angle between these ring planes is only 1.65 (8)°. The bond distances and angles have values similar to those in related compounds. While the short-chain members of the series, (Ia)–(If), have $Z' = 1$, two of the longer-chain compounds, (Ig) and (Ii), have $Z' = 2$, the independent molecules differing in their conformation. As in (Ib) and (If)–(Ii), the alkyl chains of (Ij) lie out of the ring planes.

In the series of molecules (Ic)–(Ij), there is a single strong hydrogen-bond donor, *viz.* the OH group of the hydroxy or carboxyl group. A variety of O atoms compete to accept the

hydrogen bond, namely the OH group itself, the carboxyl O=C group if present and the two imide O atoms, which are aided by electron donation from the imide N atom. In both (Ic) and (Id), one of the imide O atoms is the acceptor. Such an O atom is even able to capture a hydrogen bond from the carboxyl group in (Ie) and (If), although the other members of this series, (Ig)–(Ii), form the familiar carboxyl dimers (Feeder & Jones, 1996).



(Ia) $R = CH_2CH_3$	(If) $R = (CH_2)_2COOH$
(Ib) $R = CH_2CH=CH_2$	(Ig) $R = (CH_2)_3COOH$
(Ic) $R = CH_2OH$	(Ih) $R = (CH_2)_4COOH$
(Id) $R = (CH_2)_2OH$	(Ii) $R = (CH_2)_5COOH$
(Ie) $R = CH_2COOH$	(Ij) $R = (CH_2)_3OH$

In (Ij), the hydrogen bonding is more complex. Torsion angles along the independent hydroxyalkyl chains of (Ij) (Table 1) start with fairly typical values, but a drastic change at the end affects the orientation of the terminal OH groups. Fig. 2 shows a superposition made with *Mercury* (Macrae *et al.*, 2006) of atoms C1 and C21, N2 and N22, and C3 and C23, which gives an r.m.s. deviation of 0.007 Å. This superposition leaves a distance of 0.680 Å between atoms O11 and O31, 1.017 Å between H11 and H31, and only 0.210 Å between H31 and O11. Alternative locations for atoms H11 and H31 can be discounted in view of their successful rotating-group refinement and the small size of the maximum difference electron density, just 0.148 e Å⁻³. Both OH groups donate hydrogen bonds (Fig. 3 and Table 2), but for O11–H11 the acceptor is imide atom O32, while for O31–H31 it is the hydroxyl atom O11 of the other independent molecule. C(10) chains (Bernstein *et al.*, 1995) (highlighted in Fig. 3) are thereby created. Both hydrogen bonds show excellent linearity (O–H...O > 170°) and nearly identical distances. Unable to accept an O–H...O hydrogen bond, atom O31 accepts a reasonably strong C–H...O hydrogen bond. Other weak C–H...O interactions with H...O greater than 2.50 Å, involving H25, H26 and H27, are not shown but may make a small contribution to the stability of the crystal structure.

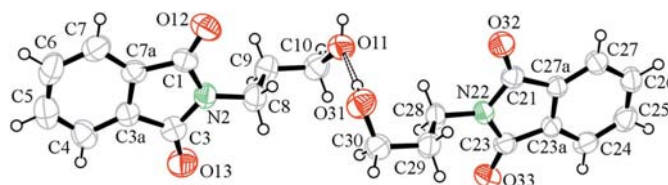


Figure 1
The molecular structure and the atom-numbering scheme for (Ij). Displacement ellipsoids are drawn at the 50% probability level.

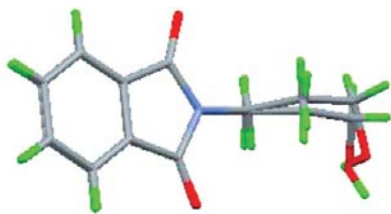


Figure 2
Superposition with *Mercury* (Macrae *et al.*, 2006) of the phthalimide N atoms and the carbonyl C atoms in the two independent molecules of (Ij).

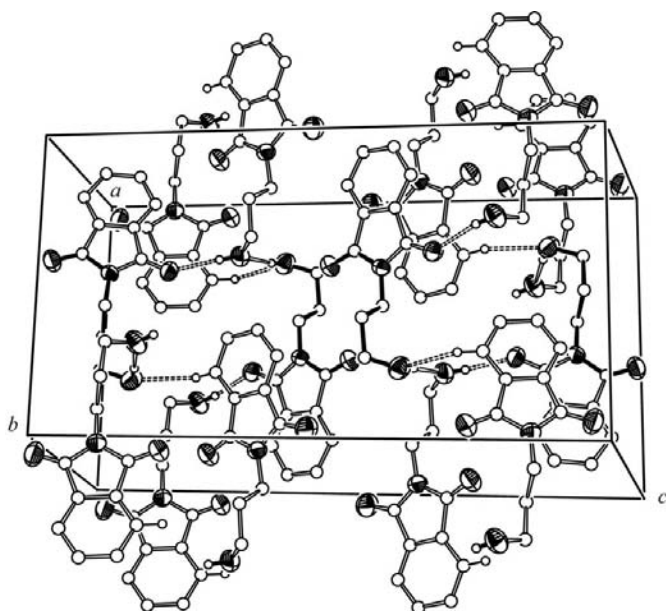


Figure 3
The unit-cell contents of (Ij). Heteroatoms are shown as ellipsoids and C atoms as spheres; H atoms have been omitted except for those involved in hydrogen bonds, which are shown as dashed lines. The C(10) motif is traced in solid lines. Other covalent bonds are shown as open bonds.

A derivative of (Ij) with complete 4,5,7-trichloro-6-(2,4-dimethylthiazol-5-yl) substitution on the benzene ring (Fun *et al.*, 2007) has successive torsion angles along the alkyl chain that are similar in magnitude within 18° to those for the C8–C10/O11 unit of (Ij), but the C8–C9–C10–O11 angle is opposite in sign. The hydrogen bonding is entirely different, with a thiazole N atom acting as acceptor for the OH group. The similar structure (If) is constructed from just one type of independent molecule and has a stronger intermolecular O–H \cdots O hydrogen bond to an imide O atom, forming chains; the H \cdots O and O \cdots O distances are 1.82 and 2.689 Å (Feeder & Jones, 1996). The carboxyl O(=C) atom only accepts C–H \cdots O hydrogen bonds, and C–H \cdots O hydrogen bonds link the chains into sheets.

To provide some insight into hydrogen-bond acceptor strength, Löwdin charges were calculated for the O atoms of (Ij) after optimization of the geometry with *GAMESS* (Schmidt *et al.*, 1993) in the 6–31G* basis set. The charge of -0.519 on the hydroxy O atom is considerably greater than those of -0.311 and -0.308 on the imide O atoms, suggesting that the former should be a more attractive hydrogen-bond acceptor. Taken together, the molecular orbital results for (Ij)

and crystallographic results for (Ic), (Id) and (Ij) suggest that once the linkage between the phthalimide ring and the hydroxy group becomes sufficiently long and flexible to position it properly, the latter group can assert its acceptor strength and receive an O–H \cdots O or a C–H \cdots O hydrogen bond.

Experimental

Crystals of (Ij) suitable for X-ray diffraction were obtained by slow evaporation of a solution in dichloromethane/hexane (8:1).

Crystal data

$C_{11}H_{11}NO_3$	$V = 1999.9 (4) \text{ \AA}^3$
$M_r = 205.21$	$Z = 8$
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation
$a = 12.2439 (17) \text{ \AA}$	$\mu = 0.10 \text{ mm}^{-1}$
$b = 7.4543 (8) \text{ \AA}$	$T = 294 (2) \text{ K}$
$c = 21.973 (2) \text{ \AA}$	$0.43 \times 0.42 \times 0.40 \text{ mm}$
$\beta = 94.282 (10)^\circ$	

Data collection

Enraf–Nonius CAD-4 diffractometer	$R_{\text{int}} = 0.052$
4424 measured reflections	3 standard reflections
3583 independent reflections	frequency: 120 min
1805 reflections with $I > 2\sigma(I)$	intensity decay: 6%

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.043$	273 parameters
$wR(F^2) = 0.124$	H-atom parameters constrained
$S = 0.97$	$\Delta\rho_{\text{max}} = 0.15 \text{ e \AA}^{-3}$
3583 reflections	$\Delta\rho_{\text{min}} = -0.17 \text{ e \AA}^{-3}$

Table 1

Selected torsion angles ($^\circ$).

C1–N2–C8–C9	$-85.0 (3)$	C21–N22–C28–C29	$-92.8 (3)$
C3–N2–C8–C9	$99.5 (3)$	C23–N22–C28–C29	$88.1 (3)$
N2–C8–C9–C10	$173.6 (2)$	N22–C28–C29–C30	$176.9 (2)$
C8–C9–C10–O11	$-59.0 (3)$	C28–C29–C30–O31	$-71.6 (3)$
C9–C10–O11–H11	-89	C29–C30–O31–H31	76

Table 2

Hydrogen-bond geometry (\AA , $^\circ$).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O31–H31 \cdots O11	0.82	2.02	2.832 (3)	173
O11–H11 \cdots O32 ⁱ	0.82	2.04	2.851 (3)	171
C7–H7 \cdots O31 ⁱⁱ	0.93	2.47	3.269 (3)	144

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

H atoms attached to C atoms were positioned geometrically at C–H distances 0.93 or 0.97 Å and refined using a riding model with $U_{\text{iso}}(\text{H})$ values of $1.2U_{\text{eq}}(\text{C})$. H atoms in the OH groups were refined as rotating groups with an O–H distance of 0.82 Å and $U_{\text{iso}}(\text{H})$ values of $1.5U_{\text{eq}}(\text{O})$.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: *CADABS* (Gould & Smith, 1986); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *SHELXL97*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: HJ3075). Services for accessing these data are described at the back of the journal.

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