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Key indicators

Powder X-ray study
 $T = 298\text{ K}$
Mean $\sigma(\text{C}-\text{C}) = 0.005\text{ \AA}$
 R factor = 0.030
 wR factor = 0.039
Data-to-parameter ratio = 3.69

For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.

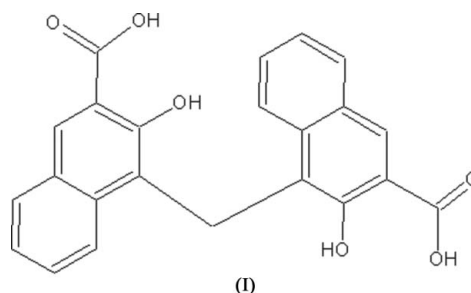
Pamoic acid determined from powder diffraction data

The title compound [systematic name: 4,4'-methylenebis(3-hydroxy-2-naphthoic acid)], $\text{C}_{23}\text{H}_{16}\text{O}_6$, has one half-molecule in the asymmetric unit. The molecular twofold rotational axis about the central C atom is preserved on crystallization. A chain formed by $R_2^2(8)$ hydrogen bonds runs along the c axis and an intramolecular $\text{O}-\text{H}\cdots\text{O}=\text{C}-\text{OH}$ hydrogen bond is also formed. The crystal structure was solved by simulated annealing from laboratory X-ray powder diffraction data, with data collected at room temperature. Rietveld refinement of this model led to a final R_{wp} value of 0.0391 at 1.39 Å resolution.

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Comment

The title compound, (I), is used in the pharmaceutical industry as a counter-ion to obtain long-acting formulations of certain basic drugs (Jorgensen, 1998), and is also of fundamental interest because of the possibility of extensive hydrogen bonding in the solid state. Attempts have been made to grow single crystals of pamoic acid for structure determination (Blackburn *et al.*, 1996, Haynes *et al.*, 2005) but these have proved unsuccessful; thus we have employed X-ray powder diffraction to solve and refine the crystal structure, which is reported here for the first time.



The compound crystallizes in the space group $C2/c$ with one half-molecule of pamoic acid in the asymmetric unit (Fig. 1). A twofold rotation axis passes through C1. The $-\text{OH}$ and $-\text{CO}_2\text{H}$ groups lie in the plane of the attached ring.

A corrugated chain of molecules running along the c axis is formed by intermolecular $R_2^2(8)$ hydrogen bonds (Fig. 2a). The hydrogen bonds themselves are oriented at approximately 45° to the chain propagation vector (Fig. 2b). Other than hydrogen bonding, the only short intermolecular contact (less than the sum of the van der Waals radii) is an aromatic $\text{C}-\text{H}\cdots\pi$ interaction (symmetry code: $\frac{1}{2} - x, \frac{1}{2} + y, \frac{3}{2} - z$) between H10 and C10 of 2.684 (8) Å, which can be compared with the van der Waals distance of 2.9 Å. Of 48362 short aromatic-aromatic $\text{C}-\text{H}\cdots\pi$ contacts in the Cambridge Structural

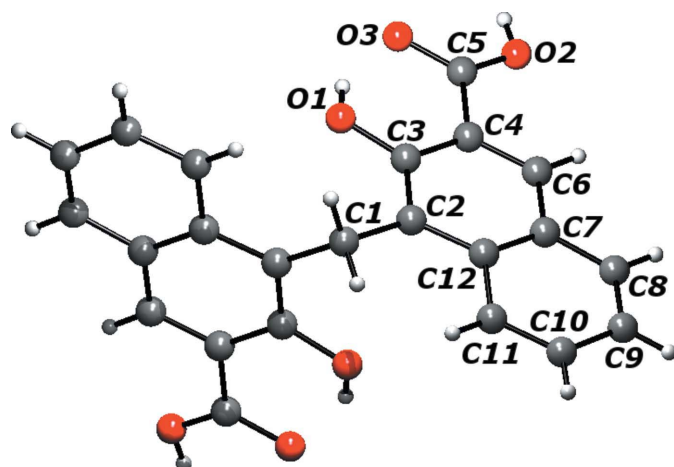


Figure 1
View of (I), with the atom-numbering scheme. The unlabelled atoms are related to the labelled ones by the symmetry operation $(1 - x, y, \frac{3}{2} - z)$.

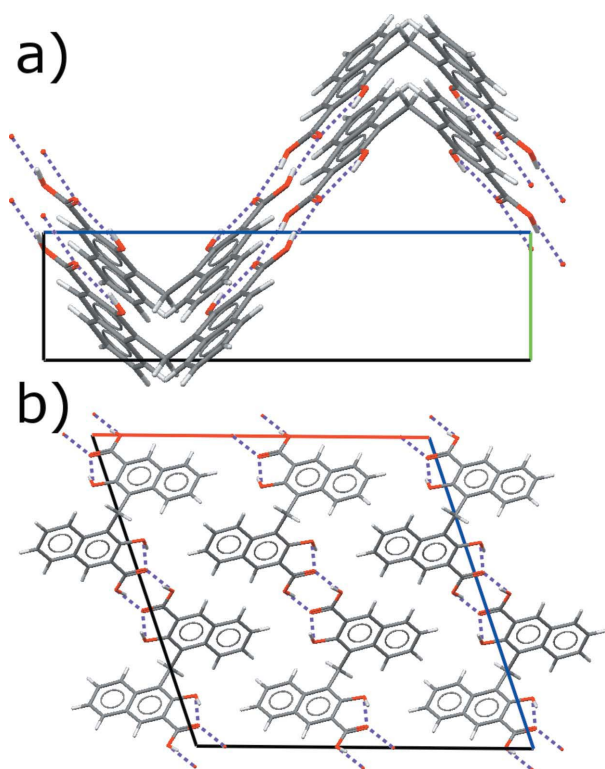


Figure 2
The crystal packing viewed (a) along the a axis and (b) along the b axis. The O—H...O hydrogen bonds are indicated by dashed lines.

Database (CSD; Version 5.26 of November 2005; Allen, 2002), only 624 (1.3%) are as short or shorter; the median is 2.837 Å. The bis-pyridinium salt of pamoic acid (CSD refcode TABMAK; Blackburn *et al.*, 1996) exhibits a similar C—H... π distance of 2.646 Å, although between a different pair of atoms. This type of contact may therefore play a role in stabilizing the observed crystal structures in pamoic acid

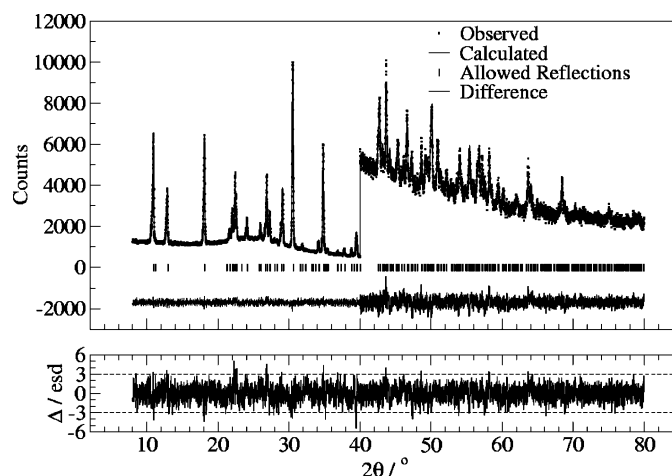


Figure 3
Final observed (points), calculated (line), difference $[(y_{\text{obs}} - y_{\text{calc}})]$ and weighted difference $[(y_{\text{obs}} - y_{\text{calc}})/\sigma]$ profiles for the Rietveld refinement of the title compound. Change of scale at 40° is a factor of 10 and the increment in 2θ is 0.01° .

derivatives; however, further work will be necessary to confirm this.

Experimental

Pamoic acid (97%+) was obtained from Sigma and used without further purification. No impurities were detected by X-ray powder diffraction. The sample was lightly ground and loaded into a 0.7 mm-diameter Lindemann glass capillary. Data were collected in Debye-Scherrer geometry employing Co $K\alpha_1$ radiation.

Crystal data

$C_{23}H_{16}O_6$
 $M_r = 388.37$
Monoclinic, $C2/c$
 $a = 19.7348$ (7) Å
 $b = 4.78768$ (12) Å
 $c = 19.2544$ (4) Å
 $\beta = 108.9622$ (17) $^\circ$
 $V = 1720.5$ (1) Å 3

$Z = 4$
 $D_x = 1.499$ Mg m $^{-3}$
Co $K\alpha_1$ radiation
 $\mu = 2.19$ mm $^{-1}$
 $T = 298$ K
Specimen shape: cylinder
12 × 0.7 × 0.7 mm
Specimen prepared at 298 K

Data collection

Stoe linear PSD diffractometer
Specimen mounting: 0.7 mm
Lindemann glass capillary
Specimen mounted in transmission mode

Scan method: step
Absorption correction: none
 $2\theta_{\text{min}} = 2.0$, $2\theta_{\text{max}} = 80.0^\circ$
Increment in $2\theta = 0.0^\circ$

Refinement

Refinement on I_{net}
 $R_p = 0.030$
 $R_{\text{wp}} = 0.039$
 $R_{\text{exp}} = 0.035$
 $S = 1.20$
Profile function: pseudo Voigt
(Thompson *et al.*, 1987) with the asymmetry correction (Finger *et al.*, 1994)

362 reflections
98 parameters
H-atom parameters constrained
Weighting scheme based on measured s.u.'s $w = 1/\sigma(Y_{\text{obs}})^2$
 $(\Delta/\sigma)_{\text{max}} = 1.61$
Preferred orientation correction: none

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

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
O2—H2A...O3 ⁱ	0.82	1.85	2.643 (4)	166
O1—H1A...O3	0.90	1.72	2.529 (4)	147

Symmetry code: (i) $-x + 1, -y - 1, -z + 1$.

As noted in *_pd_proc_ls_special_details*, the refinement was characterised by a relatively shallow minimum with respect to the lattice parameters and zero point which were refined for the final cycle to generate s.u.'s.

Two powder diffraction patterns were collected. Initially a pattern was collected using a Philips Xpert diffractometer operating in Bragg–Brentano mode with a flat-plate sample. No monochromation or collimation was employed. A full pattern was collected in under five minutes; this was used to solve the crystal structure. Subsequent attempts to use this pattern in a Rietveld analysis were not successful owing to difficulties in modelling the diffraction peak shapes from the high-intensity operation mode. Thus a second pattern was collected for approximately 24 h using a monochromatic Stoe Stadi-P instrument operating in Debye–Scherrer geometry with the sample contained in a glass capillary. The resulting pattern proved suitable for a full Rietveld analysis.

The initial X-ray powder diffraction pattern was used for structure determination with the program *DASH* (David *et al.*, 2004). The powder pattern was truncated to $45.3^\circ 2\theta$ (Cu $K\alpha$), corresponding to a real-space resolution of 2.0 Å. The background was subtracted with a Bayesian high-pass filter (David & Sivia, 2001). Peak positions for indexing were obtained by fitting with an asymmetry-corrected Voigt function, followed by indexing with the program *DICVOL* (Boultif & Louer, 1991). Pawley refinement was used to extract integrated intensities and their correlations, from which the space group was determined using Bayesian statistical analysis (Markvardsen *et al.*, 2001). Possible space groups were *Cc* or *C2/c*, the latter implying that the molecule sits on a special position; both space groups were tried. Simulated annealing was used to solve the crystal structure from the powder pattern in direct space. The starting molecular geometry was taken from entry TABMAK (Blackburn *et al.*, 1996) from the CSD. When choosing *Cc* as the space group, the asymmetric unit consists of a full pamoic acid molecule, which then has four independent flexible torsions, one for each of the two carboxylic acid groups and two across the central C atom. All these four torsion angles were left fully flexible during the simulated annealing, which, combined with three translational and three rotational degrees of freedom, gives a total of ten degrees of freedom. When choosing *C2/c* as the space group, the pamoic acid molecule is constrained by symmetry to sit on a twofold rotation axis through the central C atom, C1. Suitable constraints for atom C1 were therefore included in the simulated annealing runs for that space group, namely fixing its *x* coordinate at 1/2, fixing its *z*

coordinate at 3/4 and setting its occupancy to 0.5 to account for site multiplicity. Imposing these constraints reduces the number of degrees of freedom from ten to five. The background subtraction, peak fitting, indexing, Pawley refinement, space-group determination and simulated annealing algorithms used are as implemented in the program *DASH*. With the default settings for the simulated annealing, ten simulated annealing runs for each of both space groups readily yielded ten identical crystal structures. The two space groups *Cc* and *C2/c* gave identical crystal structures with comparable figures of merit, indicating that the higher-symmetry space group was the correct one, and Rietveld refinement was carried out in *C2/c* only. Suitable constraints were imposed on bond lengths, angles and planar groups, including bonds to H atoms. The CH and CH₂ C—H distances were constrained to be 0.93 and 0.97 Å respectively, with C—C and C—O constraints taken from CSD entry TABMAK (Blackburn *et al.*, 1996). The refinement (Fig. 3), using the *GSAS* software suite (Larson & Von Dreele, 2000), converged readily to yield acceptable figures of merit ($\chi^2 = 1.425$, $R_p = 0.0298$ and $R_{wp} = 0.0392$) and a chemically reasonable structural model. An overall isotropic displacement parameter was employed to model the entire molecule. Standard deviations are taken from the program employed and represent statistical uncertainties rather than estimates of the absolute error, which are likely to be considerably greater.

Data collection: *WinXPow* (Stoe & Cie, 1999); cell refinement: *GSAS* (Larson & Von Dreele, 2000); program(s) used to solve structure: *DASH* (David *et al.*, 2004); program(s) used to refine structure: *GSAS*; molecular graphics: *PLATON* (Spek, 2003).

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References

- Allen, F. H. (2002). *Acta Cryst.* **B58**, 380–388.
 Blackburn, A. C., Dobson, A. J. & Gerkin, R. E. (1996). *Acta Cryst.* **C52**, 1269–1272.
 Boultif, A. & Louer, D. (1991). *J. Appl. Cryst.* **24**, 987–993.
 David, W. I. F., Shankland, K., Van de Streek, J., Pidcock, E. & Motherwell, S. (2004). *DASH*. Version 3.0. Cambridge Crystallographic Data Centre, England.
 David, W. I. F. & Sivia, D. S. (2001). *J. Appl. Cryst.* **34**, 318–324.
 Haynes, D. A., Jones, W. & Motherwell, W. D. S. (2005). *CrystEngComm*, **7**, 538–543.
 Jorgensen, M. (1998). *J. Chromatogr. B Biomed. Sci. Appl.* **716**, 315–323.
 Larson, A. C. & Von Dreele, R. B. (2000). *General Structure Analysis System (GSAS)*. (2000). Report LAUR 86-748, Los Alamos National Laboratory, New Mexico, USA.
 Markvardsen, A. J., David, W. I. F., Johnson, J. C. & Shankland, K. (2001). *Acta Cryst.* **A57**, 47–54.
 Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.
 Stoe & Cie (1999). *WinXPow*. Version 1.06. Stoe & Cie, Darmstadt, Germany.