CrystEngComm

Cite this: CrystEngComm, 2011, 13, 763

www.rsc.org/crystengcomm

COMMUNICATION

Polymorphs of aromatic thiolato 1, 2 or 1,4-naphthoquinones†

Bigyan R. Jali, Marjit W. Singh and J. B. Baruah*

Received 31st August 2010, Accepted 25th November 2010 DOI: 10.1039/c0ce00591f

Two polymorphs of 4-(phenylthio)naphthalene-1,2-dione have been shown to possess distinguishable C–H···O hydrogen bond interactions; on the other hand two polymorphs of 2,3-(*bis*-4-methylphenylsulfanyl)naphthalene-1,4-dione have different orientations of methylphenylsulfenyl groups.

Weak interactions play an important role in specific drug action¹⁻³ and polymorphism.48 Weak interactions in sulfa drugs are useful in making novel cocrystals for active pharmaceutical ingredients.9 These weak interactions also provide elegant means to build assemblies of molecules in biology.¹⁰⁻¹⁵ The role of weak interactions such as C-H···O interactions in different structural studies are becoming a very prominent factor in recent days.¹⁶⁻²⁰ Quinone compounds are very attractive for polymorphism.^{17,21-23} 1,4-Quinone compounds having thiolato groups as substituents show conformational polymorphism.²⁴ However, there is ample scope to understand polymorphism in quinone derivatives due to their biological implications.^{25,26} We have chosen 4-(phenylthio)naphthalene-1,2dione, a derivative of 1,2-naphthoquinone in which the 4-position of the ring has a phenylthiolato group in anticipation of having three obvious cyclic hydrogen bonded structures as illustrated in Fig. 1. The phenyl thiolato group is chosen as a substituent as the phenyl group attached to the sulfur atom may also have some orientation effect in stabilizing such assemblies.

We have observed two such hydrogen bonded structures in 4-(phenylthio)naphthalene-1,2-dione, generated by varying the crystallization conditions. The compound 4-(phenylthio)naphthalene-1,2-dione, on crystallization from methanol, gives crystals in the *P*-1 space group (polymorph 1). It has repeated dimeric assemblies in its crystal lattice as illustrated in Fig. 2a. The compound on crystallization from ethanol led to crystals in the *P*21/*c* space group (polymorph 2). This form has repeated dimeric assemblies in the crystal lattice as shown in Fig. 2b. The important hydrogen bonds involved in self-assembly formation in these two polymorphs are listed in Table 1. The polymorph 1 (Fig. 2a) is easily transformed to

polymorph 2 (Fig. 2b) upon dissolution in ethanol. However, the reverse transformation is not observed.

The polymorph 1 melts at 178 °C whereas the polymorph 2 melts at 184 °C (please refer to supplementary DSC[†]). The powder X-ray diffraction pattern of each sample has characteristic peaks, these peaks are similar to the peaks that are obtained in the theoretically simulated powder X-ray diffraction pattern. The experimentally determined PXRD of the sample of polymorph 1 shows small amount about ($\sim 18\%$) of polymorph 2. This could be due to the higher stability of polymorph 2 (refer to supplementary figure[†]). The dimeric structures found in the polymorph 1 have the thiophenolato groups projecting cis-to each other while the polymorph 2 has the two such thiophenolato groups trans to each other. Thus, the transformation of polymorph 2 from polymorph 1 by recrystallization process can be imagined to be a reorganization of the weak interactions by a rotation cum translation of the molecules participating in self-assembly formation by rotation and translation. The methanol or ethanol on addition to amino acids leads to a particular polymorph²⁵ and the crystal habit in solvent has recently been addressed.²⁷ Further we have calculated the energy difference between the discrete molecule of 4-(phenylthio)naphthalene-1,2-dione and its dimeric pair A (as shown in Fig. 1) by using DFT and found the energy difference between these two to be insignificant. Thus, it may be mentioned that, such interactions are feeble, yet their presence causes distinguishable packing patterns.

Since π -stacking interactions are also important in supramolecular chemistry²⁸ and guide many structural factors we examined the orientations of 1,2-naphthoquinone rings in the respective crystal lattice. In both polymorphs 1 and 2 the 1,2-naphthoquinone rings are parallel when viewed along a definite crystallographic axis. In the polymorph 1, the naphthoquinone rings are positioned in the opposite face with carbonyl groups projected away from each other. This is to compensate the intrinsic polarity (dipole) within the rings, so that oppositely charged sides are close to each other. The distance of separation between C1-C8 is 3.39 Å (Fig. 3a). Although the rings look to be on top of each other; the effective overlaps are only through C1-C8 as these portions of the rings are geometrically suitable to overlap. In the polymorph 2 the naphthoquinone rings of two molecules are stacked parallel; they are eclipsed when viewed along the crystallographic a-axis; each ring is positioned so that the atom C5 of one ring is on top of the atom C8 of another ring with a separation distance of 3.40 A (Fig. 3b). Although the rings are eclipsed, the contributions from interactions between these rings have to be compensated by the repulsion between the rings arising from

Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati, 781 039, Assam, India. E-mail: juba@iitg.ernet.in

[†] Electronic supplementary information (ESI) available: DSC of polymorph **1** and **2** and powder XRD of all the polymorphs. CCDC reference numbers 662871,³⁴ 699026, 789552, 789553. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0ce00591f



Fig. 1 Three possible types of cyclic hydrogen bond structure through C-H…O interactions in 4-(alkyl/aryl) naphthalene-1,2-dione.



Fig. 2 Repeated dimeric assemblies in the two polymorphs of 4-(phenylthio)naphthalene-1,2-dione.

Table 1 Hydrogen bond parameters for polymorphs 1 and 2

D–H···A	$d_{\rm D-H}/{ m \AA}$	$d_{\mathrm{H}\cdots\mathrm{A}}/\mathrm{\AA}$	$d_{\mathbf{D}\cdots\mathbf{A}}/\mathbf{\mathring{A}}$	<d–h···a th="" °<=""></d–h···a>
For polymorph 1				
$C(3) - H(3) \cdots O(1) [x, 1 + y, z]$	0.93	2.55	3.395(2)	152
$C(4)-H(4)\cdots O(2)[x, 1+y, z]$	0.93	2.55	3.392(2)	151
For polymorph 2				
$C(7) - H(7) \cdots O(1) [-1 + x, 1/2 - v, 1/2 + z]$	0.93	2.50	3.370(2)	155
$C(8)-H(8)\cdots O(2)[-1 + x, 1/2 - y, 1/2 + z]$	0.93	2.57	3.366(18)	143



Fig. 3 Stacking interactions in the crystal lattices of polymorphs of 4-(phenylthio)naphthalene-1,2-dione (a) 1 and (b) 2.

stacking of similar dipoles on top of each other. Thus, stacking interactions become less significant in this pair of polymorphs. But the dipolar interactions (repulsive as well as attractive) between such stacks can not be ignored; such interactions can contribute to the crystal energy barrier to transform one polymorphic form to another.²⁹ The C–H frequency in IR has been a useful tool to depict C–H···O interactions.¹⁸ Based on this report, we have examined the solid state IR spectra of the two polymorphs in the region of



Fig. 4 FT-IR of polymorphs in KBr and CCl₄ (a) 1 and (b) 2 in the region of 3000-2500 cm⁻¹.

 $3000-2000 \text{ cm}^{-1}$ and found that the two polymorphs have different C-H absorption frequencies (Fig. 4). This clearly supports participation of the C-H in weak interactions and these interactions are distinguishable in the polymorphic forms 1 and 2.

We have also observed two conformation polymorphs of 2,3-(*bis*-4-methylphenylsulfanyl) naphthalene-1,4-dione; their structures are shown in Fig. 5. These polymorphs are also obtained by changing the crystallization conditions. The structures of conformational polymorphs are generally guided by weak interactions.^{17,30-33} In the present case we have not obtained solvated species to make deeper comment on the intermediate species responsible for making different conformers. However, in one case we have used copper(II) ions as catalyst for the oxidation process, thus the process of formation of polymorph **3** may be guided by coordination effects.

The polymorph **3** was obtained from oxidation of 2,3-*bis*-4methylphenylsulfanyl 1,4-naphthalenediol by copper(II) acetate catalyst; while the polymorph **4** was obtained by slow aerial oxidation of the 2,3-bis-4-methylphenylsulfanyl 1,4-naphthalenediol in ethanol. The polymorph **3** (Fig. 5a) crystallizes in centrosymmetric *Pnma*



Fig. 5 Structure of polymorphs (a) 3 and (b) 4 of 2, 3-(bis-4-methylphenylsulfanyl) naphthalene-1,4-dione.



Fig. 6 Weak interactions of polymorph 3 (ORTEP drawn with 50% thermal ellipsoid, disorder in sulfur is not shown for clarity).



Fig. 7 Weak interactions of polymorph **4** (ORTEP drawn with 50% thermal ellipsoid).

space group and it has a highly symmetric structure, having a mirror plane bisecting the molecule. The two 4-methylphenylsulfanyl groups are *syn* with respect to the naphthoquinone rings. The 4-methylphenyl groups are placed away from the naphthoquinone ring (out of plane of the naphthoquinone ring) and are almost perpendicular. The packing pattern of the molecules are decided by the C–H···O (C10–H10···O1; $d_{D...A}$, 3.39 Å, and <D–H···A 130.28° and C–H··· π (C7–

 Table 2
 Crystallographic parameters of polymorphs 1–4

 $H7\cdots\pi_{C8}$; d = 2.866 Å) interactions as shown in Fig. 6. The methyl hydrogens of the 4-methylphenyl group are involved in C–H···O interactions. These weak interactions lead to an infinitely extended 1D hydrogen bonded network. The sulfur atoms are disordered in the structure (Fig. 5a).

Polymorph **4** crystallizes in centrosymmetric space group $C222_1$. The 4-methylphenylsulfenyl groups are *anti* with respect to the naphthoquinone ring. One of the 4-methylphenyl rings is placed away from the carbonyl–C(1)==O(1) of the naphthoquinone ring (out of the plane of the naphthoquinone ring) while the other 4-methylphenyl ring is placed toward the carbonyl –C(8)==O(2) of the naphthoquinone ring.

In the crystal lattice of polymorph 4, the methyl hydrogen atoms of the 4-methylphenyl groups do not participate in weak interactions but in the case of polymorph 3, methyl groups participate in weak interactions. The crystal lattice is stabilized by the C-H···O (C16-H16...O1; $d_{D...A}$, 3.465 Å, and <D-H...A 162.64° and C23-H23... O2; $d_{D...A}$, 3.409 Å, and <D–H···A 164.25°), C7–H7··· π (C4–H4··· π_{C12} ; d = 2.835 Å and C6–H6… π_{C14} ; d = 2.803 Å) and $\pi \dots \pi$ (between two aromatic benzene ring of 1, 4-naphthoquinone) interactions as shown in Fig. 7. The experimentally determined powder X-ray diffraction patterns of these polymorphs in solid state tallies with the simulated pattern (supplementary material[†]). A density functional theory calculation by using Gaussian program at the B3LYP/6-31++G** level calculation was carried out with the two conformers and found that the energy of the two conformers differs by 0.746 Kcal mol⁻¹. This subtle difference is attributed to the difference in weak interactions that arises from the differences in the collections of weak interactions in two systems as illustrated, which are generally of the magnitude of 1–3 Kcal mol^{-1,17}

Compound No.	Polymorph 1	Polymorph 2	Polymorph 3	Polymorph 4
Formulae	C ₁₆ H ₁₀ O ₂ S	$C_{16}H_{10}O_{2}S$	$C_{24}H_{18}O_2S_2$	$C_{24}H_{18}O_2S_2$
Mol. wt.	266.30	266.30	402.50	402.50
Crystal system	Triclinic	Monoclinic	Orthorhombic	Orthorhombic
Space group	<i>P</i> -1	P2(1)/c	Pnma	C222(1)
aĺÅ	7.7573	4.5694	16.3268	6.7587
b/Å	8.3355	23.812	22.0140	19.4871
c/Å	10.1969	11.7744	5.34810	31.0120
$\alpha /^{\circ}$	75.158	90.00	90.00	90.00
βI°	89.963	99.299	90.00	91.056
$\gamma/^{\circ}$	86.091	90.00	90.00	90.00
V/Å ³	635.76	1264.31	1922.20	4084.5
Ζ	2	4	4	8
Density/Mg m ⁻³	1.391	1.399	1.391	1.309
Abs. Coeff./mm ⁻¹	0.248	0.249	0.295	0.277
Abs. correction	None	none	None	none
F (000)	276	552	840	1680
Total no. of reflections	7501	9095	24597	20811
Reflections, $I > 2\sigma(I)$	2279	2252	2424	5044
Max. $2\theta/^{\circ}$	50.48	50.48	56.56	56.58
Ranges (h, k, l)	$-9 \le h \le 9$	$-5 \le h \le 5$	$-21 \le h \le 19$	$-6 \le h \le 8$
	$-9 \le k \le 9$	$-28 \le k \le 25$	$-29 \le k \le 26$	$-25 \le k \le 25$
	$-12 \le l \le 11$	$-13 \le l \le 14$	$-7 \le l \le 7$	$-41 \le l \le 41$
Completeness to 2θ (%)	99.0	98.3	99.4	99.7
Data/Restraints/Parameters	2279/0/172	2252/0/172	2424/7/138	5044/0/255
Goof (F2)	1.084	0.969	1.025	1.051
R indices $[I > 2\sigma(I)]$	0.0402	0.0528	0.0807	0.0553
R indices (all data)	0.0491	0.0887	0.1780	0.0942
wR indices	0.1467	0.1661	0.2911	0.1758

In conclusion, we have demonstrated two different types of polymorphs in two independent naphthoquinone derivatives; solid state closed packing of these polymorphs have differences in the C–H···O interactions or in π -stacking interactions.

Experimental

The X-ray single crystal diffraction data were collected at 296 K with $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å) using a Bruker Nonius SMART CCD diffractometer equipped with a graphite monochromator. The SMART software was used for data collection and also for indexing the reflections and determining the unit cell parameters; the collected data were integrated using SAINT software. The structures were solved by direct methods and refined by full-matrix least-squares calculations using SHELXTL software. All the non-H atoms were refined in the anisotropic approximation against F^2 of all reflections. The H-atoms were placed at their calculated positions and refined in the isotropic approximation. The crystallographic parameters of the compounds are tabulated in Table 2.

Synthesis of 4-(phenylthio)naphthalene-1,2 dione. To a solution of 1, 2-naphthoquinone (0.474 g, 3 mmol) in methanol (15 mL) thiophenol (0.306 mL, 3 mmol) was added slowly. After addition of thiophenol, the colour of the reaction mixture turns red. The reaction mixture was stirred at room temperature for 8 h. A precipitate appeared was filtered off and dried in air. Isolated yield: 58%. ¹H NMR (DMSO- d^8 , 400 MHz): 8.0 (d, J = 7.6 Hz,1H); 7.9 (d, J = 7.6 Hz, 1H); 7.8 (t, J = 7.6Hz, 1H); 7.6 (m, 6H); 5.5 (s, 1H); IR (KBr, cm⁻¹): 1692 (m), 1646 (s), 1543 (m), 1384 (w), 1322 (m), 1250 (m), 1168 (w), 932 (m). Polymorph **1** was obtained by recrystallization from methanol whereas polymorph **2** was obtained by recrystallization from ethanol.

The polymorphs **3** and **4** are prepared from oxidation³³ of 2,3-*bis*-4-methylphenylsulfanyl 1,4-naphthalenediol. Polymorph **3** was obtained from oxidation by using a catalytic amount of copper(II) acetate monohydrate in ethanol, whereas polymorph **4** was formed by ordinary aerial oxidation in ethanol.

Acknowledgements

The authors thank the Council of Scientific and Industrial Research, New-Delhi (India) for financial support.

References

- L. L. Shen, J. Baranowski and A. G. Pernet, *Biochemistry*, 1989, 28, 3879.
- 2 X. Chen and B. Ramakrishnan, J. Mol. Biol., 1997, 267, 1157.

- 3 Y. Umezawa and M. Nishio, Biopolymers, 2005, 79, 248.
- 4 G. R. Desiraju, Science, 1997, 278, 404.
- 5 D. Braga, L. Maini, C. Fagnano, P. Taddei, M. R. Chierotti and R. Gobetto, *Chem.-Eur. J.*, 2007, **13**, 1222.
- 6 I. Bernal in *Models, mysteries and magic of molecules*, ed. J. C. A. Boeyens, J. F. Ogilvie, Springer, Dordrecht, The Netherlands, 2008, pp. 137–166.
- 7 A. Nangia in *Models, mysteries and magic of molecules*, ed. J. C. A. Boeyens, J. F. Ogilvie, Springer, Dordrecht, The Netherlands, 2008, pp. 63–86.
- Braga, F. Grepioni, L. Maini and M. Polito, *Struct. Bonding*, 2009, 132, 25.
- 9 M. R. Caira, Mol. Pharmaceutics, 2007, 4, 310.
- 10 A. M. Bittner, P. Behrens and E. Baeuerlein, *Handbook of Biomineralization: Biomimetic and Bioinspired Chem.*, 2007, 335.
- E. N. Baker and R. E. Hubbard, *Prog. Biophys. Mol. Biol.*, 1984, 44, 97.
 G. A. Jeffrey, W. Saenger, *Hydrogen bonding in Biological Structures*,
- Springer-Verlag, NY, 1991.
 13 G. Desiraju, T. Steiner, *The Weak Hydrogen bond in Structural Chemistry and Biology*, Oxford University Press, Oxford, 1999.
- 14 Z. S. Derewenda, L. Lee and U. Derewenda, J. Mol. Biol., 1995, 252, 248.
- 15 M. Brandl, M. S. Weiss, A. Jabs, J. Sühnel and R. Hilgenfeld, J. Mol. Biol., 2001, 307, 357.
- 16 G. R. Desiraju, Chem. Commun., 2005, 2995.
- 17 A. Nangia, Acc. Chem. Res., 2008, 41, 595.
- 18 T. Steiner, B. Lutz, J. van der Maas, A. M. M. Schreurs, J. Kroon and M. Tamm, *Chem. Commun.*, 1998, 171.
- 19 K. Ramanathan, V. Shanthi and R. Sethumadhavan, Interdiscip. Sci.: Comput. Life Sci., 2009, 1, 263.
- 20 S. Anand, A. Anbarasu and R. Sethumadhavan, App. Biochem. Biotech, 2009, 159, 2343.
- 21 S. K. Chandran, N. K. Nath, S. Roy and A. Nangia, *Cryst. Growth Des.*, 2008, 8, 140.
- 22 T. W. Lewis, D. Y. Curtin and I. C. Paul, J. Am. Chem. Soc., 1979, 101, 5717.
- 23 W. M. Singh and J. B. Baruah, J. Mol. Struct., 2009, 931, 82.
- 24 R. P. Kashyap, D. Sun and W. H. Watson, J. Chem. Crystallogr., 1995, 25, 339.
- 25 Y. Fu, L. Buryanovskyy and Z. Zhang, J. Biol. Chem., 2008, 283, 23829.
- 26 I. Weissbuch, V. Y. Torbeev, L. Leiserowitz and M. Lahav, Angew. Chem., Int. Ed., 2005, 44, 3226.
- 27 J. Chen, J. Wang, J. Ulrich, Q. Yin and L. Xue, *Cryst. Growth Des.*, 2008, 8, 1490.
- 28 G. R. Desiraju, In Crystal Engineering: The Design of Organic Solids. Amsterdam: Elsevier, 1989.
- 29 S. L. Price, Phys. Chem. Chem. Phys., 2008, 10, 1996.
- 30 A. Kalman, L. Fabian, G. Argay, G. Bernath and Z. Gyarmati, J. Am. Chem. Soc., 2003, 125, 34.
- 31 M. Morimoto, S. Kobatake and M. Irie, Chem.-Eur. J., 2003, 9, 621.
- 32 P. Raiteri, R. Martonak and M. Parrinello, Angew. Chem., Int. Ed., 2005, 44, 3769.
- 33 P. K. Thallapally, R. K. R. Jetti, A. K. Katz, H. L. Carrell, K. Singh, K. Lahiri, S. Kotha, R. Boese and G. R. Desiraju, *Angew. Chem., Int. Ed.*, 2004, 43, 1149.
- 34 This structure was reported earlier in J. B. Baruah, W. M. Singh and A. Karmakar, *J. Mol. Struct.*, 2008, **892**, 84; the structure is determined again to resolve the disorder in sulfur atom.