ARTICLE IN PRESS

Journal of Molecular Structure xxx (2013) xxx-xxx



Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstruc



Polymorphs and salts of 4-nitro-N-(quinolin-8-yl)benzamide

Prithiviraj Khakhlary, Jubaraj B. Baruah*

Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati 781 039, Assam, India

HIGHLIGHTS

• Three polymorphs of 4-nitro-N-(quinolin-8-yl)benzamide (L) are reported.

• Head to head and head to tail arrangements in packing pattern of polymorphs are observed.

• The influence of anions on the torsion angles of amide is shown.

• Porous structure of an isomorphic desolvate is described.

ARTICLE INFO

Article history: Available online xxxx

Keywords: Amide Quinoline Polymorphs Salts Weak-interactions Torsion angle

ABSTRACT

Three polymorphs (**I–III**) of 4-nitro-N-(quinolin-8-yl)benzamide (**L**) arising from differences in their packing patterns are characterized. Out of the three polymorphs, two polymorphs (**I** and **II**) have extended chain of $R_2^2(10)$ type of hydrogen bonds involving oxygen atom of carbonyl and nitro group through C–H···O interactions. These two polymorphs have head to head arrangements of molecules in their respective crystal lattice. One polymorph has two layers of molecules which are held by $\pi \cdots \pi$ interactions; whereas another polymorph is devoid of π -interactions. The third polymorph (**III**) has head to tail arrangement of molecules and have C–H···O interactions involving carbonyl groups of amides. The polymorph **I** shows two melting points resembling liquid crystalline property. The powder X-ray diffraction studies performed on the crystals obtained from solutions of different mixed solvents showed the independent role of each solvent to guide crystallization of mixture of polymorphs. The structure of the salts of **L** having ethylsulphate (**IV**), bromide (**V**) and nitrate (**VI**) anions were determined and conformational differences are established. The nitrate salt is an isomorphic desolvate, which has a porous structure, with voids of dimension 114.8 Å³ (13.5%) per unit cell having volume of 853.4 Å³. It is found that the projection of carbonyl group with respect to the nitrogen atom of the quinoline in **LH**⁺ part in the structure of ethylsulphate salt (**IV**) with respect to bromide salt (**V**) is opposite.

© 2013 Elsevier B.V. All rights reserved.

1. Introduction

The quinoline amides find use as probes in multidrug resistance proteins [1]. Some salts of quinoline amides are known to form gels [2]. Quinoline amides generally adopt concave or S-type geometry. On the other hand, molecules of unsymmetrical quinoline amides can be arranged as head to head or head to tail type arrangements in their crystal lattices [2,3]. The 4-nitro-N-(quinolin-8-yl)benzamide is a biologically active quinoline amide [4,5]. It has several interesting structural features. First of all the molecule has two distinguishable ends for supramolecular interactions and secondly it has a partially rotatable amide bond as illustrated in Fig. 1a. Thus, it is anticipated to form polymorphs by adopting different packing patterns to form different arrangement in lattice through weak interactions. Depending on the differences in lateral or longitudinal

* Corresponding author. Tel.: +91 98640 64746. *E-mail address: juba@iitg.ernet.in* (J.B. Baruah).

0022-2860/\$ - see front matter @ 2013 Elsevier B.V. All rights reserved. http://dx.doi.org/10.1016/j.molstruc.2013.11.052 positioning of the molecules in lattice different polymorphs should be possible. Moreover, the nitrogen atom on the quinoline ring can be easily protonated to form salt by an acid, in such case the anion should play an important role to guide the torsion angles between the planes (Fig. 1b). We present here structural study of three polymorphs of **L** and show the effect of anions on geometry of the cationic part (**LH**⁺) in various salts.

2. Experimental

All reagents were purchased from Sigma Aldrich (USA) and used as received. The IR spectra were recorded using a Perkin–Elmer Spectrum One FT-IR spectrometer with KBr pellets in the range 4000–400 cm⁻¹. Powder X-ray diffraction (XRD) patterns were recorded on a Bruker D8 Advance (Germany) diffractometer with Cu K α (1.542 Å) radiation operating at 40 kV and 40 mA on glass surface of air-dried samples. The images of crystal morphologies with 10× magnifications were taken by BX-51, Olympus, Japan

P. Khakhlary, J.B. Baruah/Journal of Molecular Structure xxx (2013) xxx-xxx



Fig. 1. (a) The two aromatic planes in N-(quinolin-8-yl) 4-nitrobenzamide (L); (b) salt of L, showing that the position of an anion can influence the torsion angle of LH⁺.

optical microscope equipped with a CCD camera XC10. The differential scanning calorimetry (DSC) plots of the polymorphs were recorded by using a TA Instrument Q20 differential scanning calorimeter and SDT Q600 analyzer under nitrogen atmosphere. Calibration of the instrument was performed using indium standard with cell constant of 1.0609 and the experimental accuracy on temperature was ± 0.1 °C (calibration graph is available as

supporting figure). DSC measurements of the three polymorphs were carried out independently in three cycles: (1) heating from 35 °C to 200 °C; (2) cooling from 200 °C to 60 °C; and (3) reheating from 60 °C to 200 °C with heating and cooling rates of 3 °C/min. The high temperature images of polymorph **I** were recorded by a Carl Zeiss microscope, Axoitech 100HD-3D451007-9901 Model -TS1500.

Table 1

Crystallographic parameters of I-VI.

Compound no.	Polymorph I	Polymorph II	Polymorph III	IV	V	VI
Formulae	C ₁₆ H ₁₁ N ₃ O ₃	$C_{16}H_{11}N_3O_3$	$C_{16}H_{11}N_3O_3$	C ₁₈ H ₁₇ N ₃ O ₇ S	C ₁₆ H ₁₂ N ₃ O ₃ Br	C ₁₆ H ₁₂ N ₄ O ₆
Mol. wt.	293.28	293.28	293.28	419.41	374.20	356.30
Crystal system	Monoclinic	Monoclinic	Monoclinic	Triclinic	Triclinic	Triclinic
Space group	P21/c	P21/c	Cc	P-1	P-1	P-1
Temperature (K)	296 (2)	296 (2)	296 (2)	296 (2)	296 (2)	296 (2)
a (Å)	7.5561 (8)	10.2024 (10)	3.8313 (3)	7.550 (3)	4.0181 (6)	3.7660 (3)
b (Å)	25.171 (3)	13.3545 (12)	14.6334 (7)	10.677 (3)	13.900 (2)	14.0013 (13)
<i>c</i> (Å)	7.1509 (8)	12.6962 (13)	23.5223 (13)	12.235 (5)	15.185 (2)	16.2728 (15)
α (°)	90.00	90.00	90.00	107.628 (16)	93.052 (8)	94.951 (7)
β (°)	99.671 (7)	128.364 (6)	90.851 (6)	95.921 (19)	90.676 (8)	92.379 (7)
γ (°)	90.00	90.00	90.00	94.540 (11)	93.453 (8)	92.182 (7)
$V(Å^3)$	1340.7 (2)	1356.3 (2)	1318.63 (14)	928.6 (6)	845.3 (2)	853.37 (13)
Ζ	4	4	4	2	2	2
Density g/cm ³	1.453	1.436	1.477	1.500	1.470	1.387
Abs. coeff./mm ⁻¹	0.104	0.102	0.105	0.223	2.448	0.109
Abs. correction	None	None	None	None	Multi-scan	None
F (000)	608	608	608	436	376	368
Total no. of reflections	2304	2342	1615	3289	2985	3014
Reflections, $I > 2\sigma(I)$	1128	1209	1457	2433	1438	1799
Max. 2θ (°)	50.00	50.00	50.00	50.48	50.48	50.00
Ranges (h, k, l)	$-8\leqslant h\leqslant 8$	$-12\leqslant h\leqslant 11$	$-4\leqslant h\leqslant 4$	$-8\leqslant h\leqslant 9$	$-4\leqslant h\leqslant 4$	$-4\leqslant h\leqslant 4$
	$-29\leqslant k\leqslant 27$	$-15\leqslant k\leqslant 15$	$-15\leqslant k\leqslant 16$	$-12\leqslant k\leqslant 12$	$-15\leqslant k\leqslant 13$	$-16\leqslant k\leqslant 16$
	$-8\leqslant l\leqslant 8$	$-23\leqslant l\leqslant 24$	$-27 \leqslant l \leqslant 25$	$-9\leqslant l\leqslant 14$	$-16 \leqslant l \leqslant 16$	$-19\leqslant l\leqslant 19$
Completeness to 2θ (%)	0.975	0.988	0.998	0.983	0.975	0.998
Data/Restraint/Parameters	2304/0/199	2342/0/199	1615/2/199	3289/0/263	2985/0/208	3014/0/243
GOF	1.027	1.024	1.029	1.100	1.102	1.073
R indices $[I > 2\sigma(I)]$	0.0542	0.0461	0.0427	0.0452	0.0741	0.0753
R indices (all data)	0.1247	0.1148	0.0474	0.0553	0.1428	0.1202



Fig. 2. Optical micrograph (10× magnification) of three polymorphs obtained from (a) methanol (b) dimethylformamide, (c) dichloromethane, and (d) mixture of polymorphs obtained from solution of **L** in mixed solvent comprising of *tert*-butanol and dimethylformamide.

Please cite this article in press as: P. Khakhlary, J.B. Baruah, J. Mol. Struct. (2013), http://dx.doi.org/10.1016/j.molstruc.2013.11.052

Synthesis of 4-nitro-N-(quinolin-8-yl)benzamide (L): to a solution of 8-aminoquinoline (0.29 g, 2 mmol) in dry THF (20 ml) triethylamine (0.28 ml, 2 mmol) was added and stirred for 15 mins. To this reaction mixture a solution of 4-nitrobenzoylchlo-ride (0.37 g, 2 mmol) solution in dry THF (20 ml) was added. The resulting mixture was stirred for 5 h at room temperature. On cooling yellow crystals separated out yield >90%. The ¹H NMR, IR

of the product was compared with authentic sample [6]. The crystals of polymorphs were prepared by allowing slow evaporation at ambient condition of saturated solutions (10 mL) independently in (a) methanol, (b) dimethylformamide and (c) dichloromethane to crystallise polymorphs **I–III** respectively.

The ethylsuphate salt of 4-nitro-N-(quinolin-8-yl)benzamide (**IV**) was prepared by reacting 4-nitro-N-(quinolin-8-yl)benzamide



Fig. 3. Weak interactions among the molecules in crystal lattices of polymorph (a) I, (b) II and (c) III (ORTEPs are drawn with 30% thermal ellipsoids).

(0.29 g, 1 mmol) in ethanol (15 ml) with few drops of conc. H_2SO_4 . White crystals of ethylsulphate salt crystallized on standing. Yield ~70%. IR (KBr, cm⁻¹): 3433 (s), 3097 (w), 1674 (s), 1634 (m), 1594 (m), 1556 (m), 1518 (s), 1483 (m), 1416 (w), 1377 (w), 1345 (m), 1259 (s), 1218 (s), 1064 (w), 1011 (m), 923 (m), 825 (w), 766 (w), 570 (w).

The bromide salt of 4-nitro-N-(quinolin-8-yl)benzamide (**V**) was prepared by reacting 4-nitro-N-(quinolin-8-yl)benzamide (0.29 g, 1 mmol) dissolved in a mixed solvent of methanol and DMF (9:1, 10 ml) with HBr (0.2 ml). On standing the bromide salt crystallized. Yield ~90%. IR (KBr, cm⁻¹): 3451 (s), 2925 (w), 2851 (w), 1681 (m), 1630 (m), 1556 (m), 1602 (m), 1520 (m), 1484 (w), 1374 (w), 1344 (w), 1259 (w), 1218 (w), 1051 (w), 850 (w), 823 (w), 760 (w), 711 (w), 600 (w).

The nitrate salt of 4-nitro-N-(quinolin-8-yl)benzamide (**VI**) was prepared by reacting 4-nitro-N-(quinolin-8-yl)benzamide (0.29 g, 1 mmol) dissolved in a mixed solvent of methanol and DMF (9:1, 10 ml) with 1 ml of concentrated nitric acid. On standing the nitrate salt crystallized. Yield ~90%. IR (KBr, cm⁻¹): 3427 (s), 2919 (w), 2849 (w), 1682 (m), 1631 (m), 1599 (m), 1535 (m), 1519 (m), 1384 (s), 1345 (m), 1310 (m), 1278 (w), 1258 (w), 1218 (w), 1102 (w), 1021 (w), 833 (w), 824 (w), 710 (w), 597 (w).

2.1. X-ray crystallography

The X-ray single crystal diffraction data for all the compounds other than polymorph III were collected with Mo $K\alpha$ radiation ($\lambda = 0.71073$ Å) using a Bruker Nonius SMART CCD diffractometer equipped with a graphite monochromator, whereas for polymorph III the data were collected on a Oxford SuperNova diffractometer. 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. For the data collected on SuperNova diffractometer data refinement and cell reductions were carried out by CrysAlisPro [7]. The structures were solved by direct methods and refined by full-matrix leastsquares calculations using SHELXTL software [8]. All the non-H atoms were refined in the anisotropic approximation against F^2 of all reflections. The crystal parameters of all the crystals are shown in Table 1.

3. Results and discussion

We obtained three polymorphs of 4-nitro-N-(quinolin-8-yl)benzamide, each of which has different crystal morphologies as illustrated in Fig. 2. For easy description we refer these three polymorphs as polymorph I, polymorph II and polymorph III which were obtained from the solution of L in methanol or dimethylform-amide (DMF) or dichloromethane (DCM) respectively by crystallization at ambient conditions. From the literature we find that the crystal structure of the 4-nitro-N-(quinolin-8-yl)benzamide (L) at low temperature was determined earlier [6]. For an adequate

Table 2	
Hydrogen bond parameters of polymorphs I, II, an	nd II



Fig. 4. The experimental powder X-ray diffraction of the polymorph (a) I, (b) II and (c) III.

comparison we have also re-determined the structure of L at room temperature; this structure is designated as polymorph I. The crystals of this polymorph belong to monoclinic space group $P2_1/c$. It has a chain like structure with cyclic $R_2^2(10)$ type [9] hydrogen bond motifs (Fig. 3a). These $R_2^2(10)$ type hydrogen bond motifs are formed with the aid of the C15-H15...O1 and C12-H12...O3 interactions (Table 1). In the crystal lattice, the neighboring molecules interact through hydrogen bonds leading to chain like structures. The hydrogen bonded chains are arranged in two layers by $\pi \cdots \pi$ interactions [10] between the phenyl rings ($d_{\pi \dots \pi}$, 3.351 Å). Overall there are two parallel chains, these chains are repeated as units, in the lattice these molecules are arranged slightly offset to each other. The molecules in one of the chain are linked by C-H--O bonds [11] along the *a*-axis. The molecules present on the other chain are related to the molecules of this chain by 2_1 screw-axis. These adjacent double chains are related to each other by inversion symmetry. When viewed along a pair of the interacting chains, the parent molecules appear to be organized in head to head arrangements. However, when the two molecules across the two layers of non-interacting chains are compared, they appear to be organized in head to tail arrangements across the two layers.

The crystals of the polymorph **II** belong to monoclinic space group $P2_1/c$. This polymorph in its lattice has molecules that form chain like structures with head to tail arrangements. One of the oxygen atoms of the nitro group is involved in C3–H3···O2 ($d_{D...A}$, 2.50 Å) interactions; such interactions result in the formation of chain like structure (Fig. 3b). The carbonyl oxygen atom of amide group is engaged in C15–H15···O1 interactions with neighboring molecules (Table 2). The phenyl and quinoline rings are nearly parallel to each other and have favorable geometry to have $\pi \cdots \pi$ interactions ($d_{\pi \cdots \pi}$ 3.36 Å) as they and are also in favorable proximity to have such interactions.

The crystals of polymorph **III** belong to monoclinic *Cc* space group. The packing patterns of **I** and **III** are almost identical, both have chain type of arrangements of molecules in respective lattice.

D−H···A	<i>d</i> _{D-Н} (Å)	$d_{H\cdotsA}$ (Å)	$d_{D\cdotsA}$ (Å)	∠D–H···A (°)
Polymorph I				
$C12-H12\cdots O3 [1+x, y, z]$	0.93	2.45	3.35	164
$C15-H15\cdots O1 [-1+x, y, z]$	0.93	2.41	3.29	160
Polymorph II				
$C3-H3\cdots O2 [-1+x, 1/2-y, 1/2+z]$	0.93	2.50	3.42 (6)	171
C15-H15O1 [2-x, -1/2+y, 1/2-z]	0.93	2.40	3.27 (3)	158
Polymorph III				
C12–H12···O3 [–1/2+x, 1/2+y, z]	0.93	2.53	3.42 (5)	160
C15-H15···O1 [1/2+x, -1/2+y, z]	0.93	2.42	3.29 (5)	156

Please cite this article in press as: P. Khakhlary, J.B. Baruah, J. Mol. Struct. (2013), http://dx.doi.org/10.1016/j.molstruc.2013.11.052

The polymorph III has also chain-like structure that can be distinguished from the chains in polymorph I or II. The chains in III are arranged in such a way that the molecules in the first chain are related by a diagonal translation (related as C-centering) and the molecules in the second chain are related to the first by a glide-plane. These double chain-like structures are repeated as pairs and the pairs of chain next to each other are related by C-centering. Both the polymorphs I and III have C12–H12···O3 and C15–H15···O1 interactions. These interactions present in the lattice of III result in the formation of $R_2^2(10)$ motifs. All the aromatic rings positioned on one side of the chain have similar orientation. Thus, an one dimensional chain-like structure extended through $R_2^2(10)$ hydrogen bond motifs (Fig. 3c) are observed.

Powder X-ray diffraction (PXRD) patterns of the three polymorphs are distinguishable; the experimental powder-XRD patterns of the polymorphs are shown in Fig. 4. The simulated powder-XRD patterns resemble the experimental ones (Supporting Fig. S1); these confirm the purity of the polymorphs. The polymorphs I, II and III have characteristic PXRD patterns, which are well distinguishable from each other, hence in a mixture of crystals of these polymorphs can be easily analyzed. Besides this, the solvent [12–14] and anion guided [15,16] crystallization or transformation of crystals is an important issue. To see the influence of different solvents in the crystallization process, the PXRD patterns of the crystalline materials obtained on crystallizations of L from different solutions prepared in mixed solvents were analyzed. We have chosen methanol, DMF, DCM, dioxane as solvents to crystallize L by making its solution in binary or ternary mixtures of the solvents at different proportions. The powder X-ray diffractions crystals obtained at ambient condition after complete evaporation of solvents after several days were analyzed (Supporting Fig. S3). We find that PXRD patterns of the crystals obtained from the crystallization of L from an equal volume mixed solvent comprising of tert-butanol and dimethylformamide show the PXRD peaks of polymorphs II as well as that of polymorph III (Supporting Fig. S2). This suggests that this simultaneous crystallization of polymorphs II and III can be done from mixed solvents. The use of 1:1 ratio of methanol and DCM led to a mixture of I and II with minor amount of **III**, whereas use of same combination of solvents in 1:4 ratio vielded I and II: it shows that the methanol has a higher tendency to control the crystallization process over the dichloromethane. The use of DMF: methanol in 1:1 mixture led to the formation of I and II as the major components and polymorph III as minor component. The trend supports the preferential crystallization of the polymorph I from methanol, polymorph II from DMF independently. In binary mixed solvent, the two solvents compete independently to guide crystallization of the selective polymorph or mixture of polymorphs. Analogously, a mixture of DMF and DCM 1:1 led to crystals of polymorph II and III predominantly with trace amount of crystals of polymorph I; however, changing the ratio of DMF:DCM to 1:4 resulted in the crystallization of polymorphs I, II and III but lesser quantity of crystals of polymorph



Fig. 5. DSC plots obtained from cyclic heating and cooling at a rate of 3 °C/min. of the polymorph (a) I; (b) II; (c) III. DSC plot from second time heating at 3 °C/min after first cycle of heating and cooling of polymorph (d) I, (e) II, (f) III.

Please cite this article in press as: P. Khakhlary, J.B. Baruah, J. Mol. Struct. (2013), http://dx.doi.org/10.1016/j.molstruc.2013.11.052



Scheme 1. Formation of salts of L with various inorganic acids.

III was obtained with respect to the other two polymorphs. Thus, to a large extent the binary mixture of solvents did not alter the signature or proportion of the crystals of the polymorphs from the ones that were independently crystallized from the constituent solvents.

The differential scanning calorimetry (DSC) has been used [17,18] to understand thermal inter-conversion between the different polymorphs. The DSC of the polymorphs in the range of 30–200 °C were recorded for two heating cycles (Fig. 5a). While heating polymorph I showed two endothermic peaks and while cooling it showed one exothermic peak. We also checked the images of the polymorph under hot stage microscope with a heating rate 3 °C/min under inert atmosphere. The images at various temperatures are shown in supporting information (Supporting Fig. S7). The endothermic peak at 157 °C with the onset temperature of 151 °C corresponds to melting of the polymorph and the second melting peak with an onset temperature of 167 °C and peak at 173 °C; this suggests the polymorph to have liquid crystal like property. In fact, if larger amount of samples were taken for recording images, above 157 °C it forms milky hazy liquid on the glass surface. While cooling, the formation of exothermic peak with onset temperature of 101 °C and peak at 99 °C is attributed to the recrystallization of the melt (Fig. 5a). Similar DSC plot was observed to that of the first heating, when the sample of polymorph I used for first cycle of heating was heated again (Fig. 5d).

Table	3
-------	---

Hydrogen bond parameters in the salts of **L** (**IV–VI**).

No changes prior or after melting of the polymorphs II and III were observed. On heating, the polymorphs II and III show one endothermic peak each, corresponding to the respective melting; subsequent cooling gave one exothermic peak for recrystallization in each case. In polymorph II endothermic peak appears with onset temperature of 184 °C and peak at 186 °C. While cooling, the exothermic peak for II occurs at 138 °C. Endothermic peak corresponding to melting appear at same temperature on second heating cycle for each polymorph I, II and III as illustrated in Fig. 5d–f. Similarly, the polymorph **III** shows an endothermic peak with onset temperature of 186 °C and peak at 187 °C. While cooling it showed an exothermic peak at 144 °C which is attributed to recrystallization (Fig. 5f). The enthalpy of melting for polymorph I, polymorph II and polymorph III are 15.50 J/g, 75.64 J/g and 65.12 J/g respectively. It is a general fact that polymorphs of amide compounds interconvert among themselves, which are reflected in their DSC curves [19]. However, in such studies by DSC, the melting temperature of individual polymorph in each mixture may slightly differ [20]. In our case, there is no conversion between the polymorphs, accordingly in the second heating of the polymorphs we obtained almost identical profiles as that of first cycles. These show that there were no noticeable changes of structures within the temperature where DSC were recorded. It could be one of the reasons that polymorph I having suitable alignments of molecules to exhibit liquid crystal like properties shows two melting points. From crystallography it is already shown that the molecules of polymorph I are arranged as chain like arrangements. The crystal densities of three polymorphs are 1.453 g/cm³, 1.436 g/cm³ and 1.477 g/cm³, which are comparable to each other. All these polymorphs show melting point on second heating at identical temperature as that is observed in the first heating, thus it may be suggested that the original packing pattern in each case is recovered when they recrystallise from their melt.

We have prepared three salts namely ethylsulphate (IV), bromide (**V**) and nitrate (**VI**) of **L** as shown in Scheme 1. The structures of these salts of **L** were determined. The salt **IV** having ethylsulphate anion was generated *in-situ* from the reaction of sulphuric acid with ethanol in the presence of **L**. In the structure of this salt, there are two oxygen atoms from the anion involved in bifurcated hydrogen bonds formation in the packing. The oxygen atom, namely the atom O5 interacts with C1–H bond and C2–H bond whereas the atom O6, interacts with N2–H bond as well as with C13–H bond (Table 3). The atom O4 forms strong hydrogen bond with N1–H bond (Fig. 6a). Both the oxygen atoms O2 and O3 of the nitro group are involved in C–H···O interactions with C7–H7 and C2–H2 bonds respectively. Apart from these, phenyl ring is

, , , , , , , , , , , , , , , , , , ,				
D–H···A	d _{D-Н} (Å)	$d_{H\cdots A}$ (Å)	$d_{D\cdotsA}(\AA)$	$\angle D-H \cdot \cdot \cdot A$ (°)
Ethylsulphate salt (IV)				
N1-H04 $[-x, 1-y, 1-z]$	0.86	1.97	2.763 (3)	153
N2-H···O6 $[1-x, 1-y, 1-z]$	0.86	2.29	2.903 (3)	129
C5-H···O1 $[-x, -y, -z]$	0.93	2.59	3.413 (3)	147
C13-H···06	0.93	2.58	3.464 (4)	160
Bromide salt (V)				
N1–H···Br1 $[-1+x, y, z]$	0.86	2.43	3.213 (9)	152
N2-H···Br1	0.86	2.62	3.377 (11)	148
$C1-H\cdots Br1 [-x, 1-y, -z]$	0.93	2.87	3.620 (13)	138
C16–H···Br1	0.92	2.98	3.889	165
C5−H···O2	0.93	2.66	3.522	153
Nitrate salt (VI)				
N1-H1A $\cdot \cdot \cdot O4 [1-x, 1-y, 1-z]$	0.86	1.94	2.753 (6)	157
N2-H2A···O4 $[-x, 1-y, 1-z]$	0.83 (6)	2.09 (6)	2.840 (6)	149 (5)
$C1-H1\cdots O6 [1+x, 1+y, z]$	0.93	2.42	3.243 (7)	147
C5-H $\cdot \cdot 02 [1+x, -1+y, z]$	0.93	2.65	3.482	149

P. Khakhlary, J.B. Baruah/Journal of Molecular Structure xxx (2013) xxx-xxx



Fig. 6. Hydrogen bond interactions in (a) ethylsulphate salt (IV), (b) bromide salt, (V) and (c) nitrate salt (VI) of L.

almost perpendicular to quinoline ring in the cationic part, this occurs to accommodate the ethylsulphate anions in the lattice. In-situ generation and stabilization of ethylsulphate anions by various supramolecular assemblies [21,22] has been well studied. However, we observe formation of such species in the presence of an amide bond containing molecule, which is easy to synthesize as compared to many complex receptors reported earlier.

The bromide salt (**V**) crystallizes in triclinic P-1 space group. In comparison to the structure of **L**, the plane of the phenyl ring in the bromide salt is significantly away from the plane containing quinoline ring. The crystal lattice is stabilized by strong electrostatic N-H···Br interactions (Table 3). Each bromide ion is held by four prominent interactions, two of them are N-H···Br interactions and other interactions are C1-H1···Br and C16-H16···Br interactions (Fig. 6b). The bromide ions are generally known to form spherically symmetric coordinated geometry [23]. There are also examples of bromide ions having T-shaped environments [24] in crystal lattice. Whereas, the bromide ions in the crystal lattice of the salt **V** has distorted tetrahedron environment.

In the crystal lattice of nitrate salt (**VI**) (space group Triclinic P-1) two oxygen atoms involve in C-H···O interaction namely the atom O5 interacts with C16-H and O6 with C1-H (Fig. 6c). Similarly C-H···O interactions are observed with the carbonyl oxygen atom O1 with C6-H and that of the O2 with C5-H. The nitrate oxygen atom O4 is involved in strong hydrogen bond with N1-H. The nitrate salt is highly porous (Supporting Fig. S4). The analysis of the packing pattern of the salt shows void with dimension 114.8 Å³ (13.5%) per unit cell having volume 853.4 Å³. Generally porous structures are isomorphic desolvate, by definition they have three dimensional structures of their parent solvates which are formed upon loss of solvent molecules. Such desolvates were



Fig. 7. (a) Atom numbering to describe the torsion angles of **L**; (b) projections of the carbonyl group of amide with respect to the of the quinoline ring in salts **IV–VI**.

Tapic T	Tabl	e	4
---------	------	---	---

Torsion angles in the polymorphs and salts.

demonstrated by Stephenson et al. [25] in spirapril hydrochloride. In the present case the bromide and nitrate salts (**V** and **VI**) are air stable as well as not hygroscopic. However, close analysis reveals that the packing patterns of nitrate and bromide salts have similar principal weak interactions between the hosts. But differences arise in these cases in the interactions of the parent **LH**⁺ with the anions. Bromide ion has spherical structure whereas the nitrate ion has a planar structure. Size-wise nitrate is smaller than bromide, hence solvent might have been present in the nitrate salt as filler molecules to make a packed structure which is comparable to bromide salt. Such solvent molecules might have got lost of the nitrate salt during crystallization, causing formation of an isomorphic desolvate having a porous structure.

Since we have described a set of polymorphs, it is interesting to look at the torsion angles as defined in Fig. 7a, C7-C8-N2-C10, C8-N2-C10-O1. O1-C10-C11-C16 and C13-C14-N3-O2 in each case. The torsion angles from the individual crystal structures are listed in the Table 4. The differences in the torsion angle C7–C8–N2–C10 in each case, show the dissimilar projection of the carbonyl group of amide across the quinoline ring. The torsion angles of the three polymorphs differ, this attributes to the formation of different packing patterns in the three polymorphs. The origin of the differences in the geometries of the polymorphs arises from the synergic effects of partial rotation of the amide bond and resonance effect of the nitro group. In none of the case we could isolate solvate, where one could have anticipated large variation of torsion angles by strong interactions of solvent molecules with the parent molecules. Large changes in the C7-C8-N2-C10 torsion angles with respect to the parent compound (L) could be brought about in the salts of L in which L got protonated at nitrogen atom of the quinoline ring. In addition to size differences between a bromide and a nitrate anion, bromide ion has spherical charge distribution whereas the nitrate ion has charge distributed among the three oxygen atoms. On the other hand, the relatively larger ethylsulphate anion is nonplanar and has multiple sites for weak interactions. These factors affect the packing patterns in each case. Accordingly, the carbonyl group of HL⁺ of the salts differ (Fig. 7b). It is found that the projection of carbonyl group with respect to the nitrogen atom of the quinoline in **LH**⁺ part in the structure of ethylsulphate salt (**IV**) with respect to bromide salt (V) is opposite. Thus, differences in the shape, size and weak interaction of the anions cause the differences in the torsion angles of the cationic counterparts.

In conclusion, three polymorphs **I–III** of **L** were prepared in pure from by independent crystallization. Highly ordered structures are observed in each case, which led the polymorph **I** to show two melting points resembling liquid crystal. The differential scanning calorimetry analysis established that the three polymorphs **I–III** independently retain their original structure after melting. The polymorphs have characteristic dihedral angles. The dihedral angles of aromatic plane across the amide bond of protonated **L** are dependent on the size and shape of the counter anion.

Polymorph I	Torsion angle	Polymorph II	Torsion angle	Polymorph III	Torsion angle
C7-C8-N2-C10	-4.6	C7-C8-N2-C10	-6.4	C7-C8-N2-C10	-3.5
C8-N2-C10-O1	1.7	C8-N2-C10-O1	-4.4	C8-N2-C10-O1	-1.9
01-C10-C11-C16	158.4	01-C10-C11-C16	164.3	01-C10-C11-C16	175.6
C13-C14-N3-O2	-1.3	C13-C14-N3-O2	7.3	C13-C14-N3-O2	-9.3
Ethylsulphate salt	Torsion angle	Bromide salt	Torsion angle	Nitrate salt	Torsion angle
C7-C8-N2-C10	112.3	C7-C8-N2-C10	-42.8	C7-C8-N2-C10	-38.6
C8-N2-C10-O1	7.0	C8-N2-C10-O1	-0.29	C8-N2-C10-O1	-1.7
01-C10-C11-C16	148.4	01-C10-C11-C16	177.5	01-C10-C11-C16	-179.2
C13-C14-N3-O2	-15.0	C13-C14-N3-O2	-4.0	C13-C14-N3-O2	-4.0

Acknowledgements

The authors are grateful to the referees for invaluable comments and also expresses thanks to Prof. P.S. Robi of IIT Guwahati for extending help in getting the high temperature images.

Appendix A. Supplementary material

The simulated and experimental PXRD patterns of the polymorphs, packing pattern of nitrate salt, calibration plot for DSC measurements, DSC of polymorph I at different conditions, images of the crystalline samples of polymorph I heated at different temperature are available. The CIFs are deposited to Cambridge Structure Database and have the CCDC Nos. 902576, 902577, 902578, 902579, 902580 and 956990.

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.molstruc.2013.11. 052.

References

- R. Daoud, J. Desneves, L.W. Deady, L. Tilley, R.J. Scheper, P. Gros, E. Georges, Biochemistry 39 (2000) 6094–6102.
- [2] A. Karmakar, R.J. Sarma, J.B. Baruah, Cryst. Eng. Comm. 9 (2007) 378-388.
- [3] D. Kalita, J.B. Baruah, Cryst. Eng. Comm. 12 (2010) 1562-1567.
- [4] Y. Yang, L. Shi, Y. Zhou, H.-Q. Li, Z.-W. Zhu, H.-L. Zhu, Bioorg. Med. Chem. Lett. 20 (2010) 6653–6656.

- [5] M. Lanier, D. Schade, E. Willems, M. Tsuda, S. Spiering, J. Kalisiak, M. Mercola, J.R. Cashman, J. Med. Chem. 55 (2012) 697–708.
- [6] G. Lei, L.-H. Jing, L. Zhou, Acta Crystallogr. E64 (2008) o2401.
- [7] CrysAlisPro, Oxford Diffraction Ltd., version 1, 171. 33. 34d (release 27-02-2009 crysAlis 171.NET).
- [8] G.M. Sheldrick, Acta. Crystallogr. 64 (2008) 112.
- [9] M.C. Etter, Acc. Chem. Res. 23 (1990) 120–126.
- [10] C.R. Martinez, B.L. Iverson, Chem. Sci. 3 (2012) 2191–2201.
- [11] G.R. Desiraju, T. Steiner, The weak hydrogen bond in structural chemistry and biology, Oxford University Press, Oxford, 1999.
- [12] W.M. Bloch, C.J. Sumby, Chem. Commun. 48 (2012) 2534-2536.
- [13] Z. Duan, Y. Zhang, B. Zhang, D. Zhu, Cryst. Eng. Comm. 13 (2011) 680-6810.
- [14] Z.-Y. Liu, E.-C. Yang, L.-L. Li, X.-J. Zhao, Dalton Trans. 41 (2012) 6827–6832.
- [15] A. Aijaz, P. Lama, P.K. Bharadwaj, Inorg. Chem. 49 (2010) 5883-5889.
- [16] X. Cui, A.N. Khlobystov, X. Chen, D.H. Marsh, A.J. Blake, W. Lewis, N.R. Champness, C.J. Roberts, M. Schroder, Chem. Eur. J. 15 (2009) 8861–8873.
- [17] K. Kawakami, J. Pharm. Sci. 06 (2007) 982–989.
- [18] G.W.H. Hohne, W. Hemminger, H.-J. Flammersheim, Differential Scanning Calorimetry, second rev. ed., Spinger-Verlag Publisher, Berlin, Heidelberg, 2003.
- [19] A.L. Grzesiak, M. Lang, K. Kim, A.J. Matzger, J. Pharm. Sci. 92 (2003) 2260–2271.
- [20] R.J. Sarma, J.B. Baruah, Solid State Sci. 10 (2008) 580–586.
- [21] S.G. Bott, A.W. Coleman, J.L. Atwood, J. Am. Chem. Soc. 110 (1988) 610-611.
- [22] A.J. Blake, P. Hubberstey, U. Suksangpanya, C.L. Wilson, J. C. S. Dalton Trans. (2000) 3873–3880.
- [23] C.A. Ilioudis, K.S.B. Hancock, D.G. Georganopoulou, J.W. Steed, New J. Chem. 24 (2000) 787–798.
- [24] C. Tamuly, R.J. Sarma, A.S. Batsanov, A. Goeta, J.B. Baruah, Acta Crystallogr. 61C (2005) 0324-0327.
- [25] G.A. Stephenson, E.G. Groleau, R.L. Kleemann, W. Xu, D.R. Rigsbee, J. Pharm. Sci 87 (1998) 536–542.