

Neutral and Ionic Supramolecular Complexes of Phenanthridine and Some Common Dicarboxylic Acids: Hydrogen Bond and Melting Point Considerations

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Supporting Information

ABSTRACT: Supramolecular complexes of phenanthridine have been prepared with various dicarboxylic acids. Cocrystallization of phenanthridine with fumaric acid, succinic acid, and isophthalic acid produced neutral cocrystals. Proton transfer from maleic acid and oxalic acid to the phenanthridine moiety results in salts of these two acids. It was found that neutral cocrystals are formed when the ΔpK_a value of the complex is smaller than 2.56, whereas salts are formed when ΔpK_a is greater than 3.66. The crystal structures of supramolecular complexes have been determined. The structure of each compound depends on acid geometry, and the compounds may be described as dimers, trimers, or chains. A comparison of the melting points, hydrogen bonds, and densities of each molecular complex and



the corresponding dicarboxylic acid is presented. Utilizing the approximate relative bond strengths of hydrogen bonds, a comparison of the number of hydrogen bonds in the acid and the cocrystal is possible.

■ INTRODUCTION

The understanding of intermolecular interactions and the application of these interactions in the design of new solid-state assemblies is perhaps the main goal of supramolecular chemistry and crystal engineering.^{1,2} In recent years, advances in crystal engineering have enabled the design and the synthesis of pharmaceutical cocrystals as well as salts exhibiting improved physicochemical properties.^{3–5}

The utility of N-heterocyclic bases to obtain molecular complexes with dicarboxylic acids is well documented.⁶⁻¹² Depending on the solid state interaction between the N-heterocyclic base and a dicarboxylic acid, a neutral synthon I and II or an ionic synthon III and IV may be observed (Figure 1).

A feature of synthons I and III is that both strong O–H···N/ N⁺–H···O⁻ hydrogen bonds and weak C–H···O interactions are formed. The relatively weak C–H···O interactions can play a significant role in the stabilization of these synthons.^{10,13} The occurrence of the O–H···N/N⁺–H···O⁻ hydrogen bonds depends on the difference in pK_a values between the base and the acid. According to Johnson and Rumon,¹⁴ a pyridine– carboxylic acid system salt would be expected for $\Delta pK_a > 3.75$. Bhogala et al.¹⁵ propose that for carboxylic acid–pyridine base supramolecular systems when $\Delta pK_a < 0$ a neutral O–H···N hydrogen bond results, when $0 < \Delta pK_a < 3.75$ the synthons have an intermediate O–H···N/N⁺–H···O⁻ hydrogen bond, and when $\Delta pK_a > 3.75$ an ionic N⁺–H···O⁻ hydrogen bond forms. Although ΔpK_a values are widely used to predict proton transfer from one component to another they cannot be considered alone. Other factors such as the crystalline environment and reaction conditions (solvent, temperature, etc.) may also affect the ionization state of a compound.¹⁶

Structural studies of supramolecular complexes of N-heterocyclic bases and dicarboxylic acids show differences depending on the number of proton acceptors (nitrogen atoms) in the base molecule. The alternating chains of base and acid units are dominant in the crystal structures of the adducts containing a N-heterocyclic base with two proton acceptors and dicarboxylic acid.^{9,10,17–19} N-heterocyclic bases with one proton acceptor often form supramolecular trimers with dicarboxylic acid.^{7,11,20}

Phenanthridine is chosen as a molecular complex former because it can participate in hydrogen bonding with donor molecules such as carboxylic acids. Koshima and co-workers have reported the cocrystallization of phenanthridine with several monocarboxylic acids: diphenylacetic acid,²¹ 3-indolepropionic acid,²² 9-fluorenecarboxylic acid,²³ 3-indoleacetic acid,²⁴ and bis(thien-2-yl)acetic acid.²⁵

In order to investigate further the relation between the $\Delta p K_a$ value and the synthon species formed as a result of the interactions of a one proton acceptor N-heterocyclic base with dicarboxylic acids and determine the melting point temperatures and

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Figure 1. Supramolecular synthons I, II, III, and IV discussed in this paper. I and III represent neutral and ionic $R_2^2(7)$ synthon. II represents noncyclic dimer D. IV represents $R_2^2(5)$ synthon.

densities of the obtained cocrystals, we have prepared and determined the structures of neutral and ionic complexes of phenanthridine with the dicarboxylic acids: fumaric acid, maleic acid, isophthalic acid, succinic acid, and oxalic acid (Scheme 1).

EXPERIMENTAL SECTION

All chemicals were supplied by Sigma-Aldrich or by other commercial suppliers.

Synthesis of Supramolecular Complexes. *Phenanthridine– Fumaric Acid (2:1) Cocrystal,* **1**. Cocrystal formed when phenanthridine and fumaric acid in a 1:1 molar ratio (0.060 g, 0.33 mmol, and 0.039 g, 0.33 mmol, respectively) were dissolved in 5 mL of hot ethanol and allowed to crystallize.

Phenanthridine–Fumaric Acid (4:1.5) Cocrystal, **2**. Cocrystal formed when phenanthridine and fumaric acid in a 2:1 molar ratio (0.090 g, 0.50 mmol, and 0.029 g, 0.25 mmol, respectively) were dissolved in 5 mL of hot ethanol and allowed to crystallize.

Phenanthridine–Succinic Acid (2:1) Cocrystal, **3**. The cocrystals were obtained upon cocrystallization of phenanthridine (0.090 g, 0.50 mmol) and succinic acid (0.030 g, 0.25 mmol) from hot ethanol (5 mL).

Phenanthridine—Isophthalic Acid (1:1) Cocrystal, **4**. Phenanthridine (0.045 g, 0.25 mmol) and isophthalic acid (0.042 g, 0.25 mmol) were dissolved in 5 mL of hot ethanol. Slow evaporation of the solvent gave colorless crystals.

Phenanthridinium Maleate, **5**. Phenanthridine (0.090 g, 0.50 mmol) and maleic acid (0.058 g, 0.50 mmol) were dissolved in 5 mL of hot ethanol. Slow evaporation of the solvent produced colorless crystals.

Phenanthridinium Oxalate, **6**. Crystallization of phenanthridine and oxalic acid in a 2:1 molar ratio resulted in a phenanthridine oxalate with 1:1 stoichiometry. The salt was obtained by dissolving phenanthridine (0.090 g, 0.50 mmol) and 0.023g (0.25 mmol) oxalic acid in 5 mL of hot ethanol followed by slow evaporation.

Phenanthridinium Oxalate Monohydrate, **7**. Phenanthridine (0.060 g, 0.33 mmol) and oxalic acid dihydrate (0.042 g, 0.33 mmol), molar ratio 1:1, were dissolved in 5 mL of hot ethanol. Colorless crystals were formed upon evaporation of the solvent.

Single Crystal X-ray Diffraction. X-ray diffraction data were measured using a Nonius Kappa CCD diffractometer (Bruker AXS GmbH, Germany) with Mo–K $_{\alpha}$ radiation (0.71073 Å). Data were collected at 173 K. Data reduction was performed with the COLLECT/EVAL²⁶ program. All structures were solved by direct methods using SIR92²⁷ and SHELXS-86²⁸ as implemented in the program package WinGX.²⁹ Refinement was carried out by full-matrix least-squares method with the CRYSTALS³⁰ program. All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were located by the difference Fourier method. During refinement, hydrogen atoms were refined in the riding mode. The number of hydrogen bonds was determined by PLATON³¹ using the experimental results reported here and the CIF files for the dicarbocxylic acids available from the CSD.³²





X-ray Powder Diffraction (XRPD). X-ray powder diffraction analysis was performed using a Bruker AXS D8 Advance powder diffractometer (Bruker AXS GmbH, Germany) with Cu K α radiation ($\lambda = 1.5418$ Å), 40 kV, 40 mA. Data were collected at room temperature with a 0.02° step and a scan speed of 1°/min.

Thermal Analysis. Differential thermal analysis and thermogravimetric analysis (DTA/TGA) were performed using Seiko Exstar6000 TG/DTA6300 (Seiko Instruments Inc., Japan) equipment. The samples (4-7 mg) were heated in open aluminum pans at a rate of 10 °C/min in air.

RESULTS AND DISCUSSION

Crystallizing phenanthridine with several dicarboxylic acids neutral and ionic supramolecular complexes have been obtained. Regardless of an equal number of hydrogen bonding groups in each component, the observed stoichiometries of the isolated molecular complexes are different. Compounds 1 and 3 crystallized with a 2:1 ratio of base to acid stoichiometry, while 4–7 had 1:1 stoichiometry. Cocrystallizing phenanthridine with fumaric acid, the 2:1 complex (1) as well as the 4:1.5 complex (2) was also obtained. Dissolving starting components in a 1:1 molar ratio led to the generation of 1, whereas a 2:1 ratio yielded 2. This cocrystallization experiment was repeated and gave identical results. The formation of molecular complexes with different base/acid ratios has been explained by component concentration changes during solvent evaporation.³³

The solid phase of each complex was characterized by XRPD and DTA/TGA. The XRPD patterns of 1-7 are shown in Figure 2, but the respective DTA/TGA thermograms are included in the Supporting Information.

The crystal and molecular structures of all seven compounds have been determined by single crystal X-ray diffraction. Crystallographic data are summarized in Table 1. Hydrogen bond parameters are listed in Table 2.

Phenanthridine—Fumaric Acid (2:1) Cocrystal, 1. The cocrystal crystallizes in the monoclinic space group $P2_1/n$. The fumaric acid molecule is located on an inversion center and links two phenanthridine molecules through O—H····N hydrogen bonds, forming centrosymmetric trimers. The angle between the plane of the carboxylic acid group and the pyridyl ring plane is 13.6°. The fumaric acid molecule in the compound has *S*-*trans*/*S*-*trans* conformation. The crystal structure along the *a* axis shows phenanthridine—fumaric acid—phenanthridine trimer arrangement in which the trimer units pack alongside one another (Figure 3).

The packing motif of this cocrystal along the *a* axis is similar to that of acridine – fumaric acid complex.¹¹ However, in **1** the angle

between planes of the carboxylic acid and the acridine molecule is significantly larger: 60.26°.

Phenanthridine–Fumaric Acid (4:1.5) Cocrystal, 2. The compound crystallizes in the triclinic $P\overline{1}$ space group. The asymmetric unit contains four symmetry independent phenanthridine molecules (**a**, **b**, **c**, **d**) and one and one-half symmetry independent fumaric acid molecules (**e**, **f**).

The fumaric molecule f lies on an inversion center. Three (a, b, c) phenanthridine molecules are oriented perpendicular to the fourth (d) phenanthridine molecule. The two acid molecules are parallel to each other. The angles between the carboxylic acid group plane O11, C10, O12 (fumaric acid e molecule) and the pyridyl ring plane N60, C59, C68, C67, C62, C61 and between the carboxylic acid group plane O5, C7, O6 (fumaric acid e molecule) and the pyridyl ring plane N32, C33, C34, C39, C40, C31 are 20.3° and 38.1° , respectively. In the case of the fumaric acid f molecule, which is located on an



Figure 2. XRPD patterns for complexes of phenanthridine with dicarboxylic acids.

inversion center, the angle between the plane of the carboxylic acid group and pyridyl ring plane is 22.4°. The fumaric acid molecules have *S*-*trans/S*-*trans* conformation. In the solid state, phenanthridine and fumaric acid molecules form a two-layered structure (Figure 4a).

The first layer consists only of phenanthridine **a**, **b**, **c** molecules with an $-[\mathbf{a}-\mathbf{b}-\mathbf{a}-\mathbf{c}-\mathbf{c}]_{n}$ - arrangement. In a row of phenanthridine molecules, three (**a**, **b**, **c**) molecules are oriented in one direction, but the next three are oriented in the opposite direction as determined by the packing of these molecules and shown in Figure 4b. The distance between phenanthridine molecule planes is 3.46 Å. Alternating fumaric acid **e** and **f** molecules and phenanthridine **d** molecules form the second layer of the crystal structure. Both layers are connected through $O-H \cdot \cdot \cdot N$ hydrogen bonds that involve two fumaric acids and one phenanthridine molecule. Additional $C-H \cdot \cdot \cdot O$ hydrogen bonds between oxygen and the hydrogen atoms of the carboxyl group and phenanthridine **d** molecule are also formed.

Phenanthridine–**Succinic Acid (2:1) Cocrystal, 3.** The cocrystals crystallize in the monoclinic $P2_1/n$ space group. The succinic acid molecule is located on an inversion center. The angle between the plane of the carboxylic acid group and pyridyl ring plane is 21.5° . In the solid state, the cocrystal structure is a centrosymmetric trimer: two molecules of phenanthridine are linked by one molecule of succinic acid through $O-H \cdots N$ hydrogen bonds. Unlike cocrystal **1**, the trimers are placed in a herringbone arrangement when viewed along the *a* axis (Figure 5).

Weak $C-H\cdots O$ hydrogen bonds between trimers are observed and result in planar supramolecular sheets.

Phenanthridine–Isophthalic Acid (1:1) Cocrystal, 4. The compound crystallizes in the monoclinic space group Pc. The angle between the plane of the carboxylic acid group and the pyridyl ring plane is 42.9°. Isophthalic acid molecules are

Table 1. Crystallographic Data and Structure Refinement Parameters for Supramolecular Complexes 1-7

supramolecular complex	1	2	3	4	5	6	7
chemical formula	$C_{13}H_9N \cdot (C_4H_4O_4)_{0.5}$	$(C_{13}H_9N)_4 \cdot (C_4H_4O_4)_{1.5}$	$C_{13}H_9N \cdot (C_4H_6O_4)_{0.5}$	C ₁₃ H ₉ N∙ C ₈ H ₆ O ₄	$C_{13}H_{10}N^{+}$. $C_{4}H_{3}O_{4}^{-}$	$C_{13}H_{10}N^{+} \cdot C_{2}HO_{4}^{-}$	$\begin{array}{c} C_{13}H_{10}N^{+} \cdot\\ C_{2}HO_{4}^{-} \cdot H_{2}O\end{array}$
formula weight	237.26	890.99	238.27	345.35	295.29	269.26	287.27
crystal system	monoclinic	triclinic	monoclinic	monoclinic	monoclinic	triclinic	monoclinic
space group	$P2_1/c$	$P\overline{1}$	$P2_1/n$	Pc	$P2_1$	$P\overline{1}$	$P2_1/c$
a (Å)	3.900(1)	11.299(2)	4.901(1)	11.915(2)	5.712(1)	5.584(1)	7.557(2)
b (Å)	20.070(4)	13.591(3)	17.210(3)	3.8719(8)	8.131(2)	10.230(2)	9.469(2)
c (Å)	14.489(3)	15.293(3)	13.989(3)	17.285(4)	14.943(3)	10.962(2)	18.562(4)
α (°)	90	78.55(3)	90	90	90	75.17(3)	90
β (°)	97.58(3)	75.83(3)	90.90(3)	91.79(3)	93.42(3)	84.53(3)	95.51(3)
γ (°)	90	75.89(3)	90	90	90	86.35(3)	90
$V(Å^3)$	1124.2(4)	2184.1(9)	1179.8(3)	797.1(3)	692.8(2)	602.1(2)	1322.1(5)
Ζ	4	2	4	2	2	2	4
$T(\mathbf{K})$	173	173	173	173	173	173	173
reflections collected	13715	39870	15813	11136	12841	9799	23655
independent reflection	2534	9991	2676	1823	1704	2743	3038
observed reflection	1339	5390	1455	1733	1369	1636	1857
threshold expression	$>2\sigma(I)$	$>1.5\sigma(I)$	$>3\sigma(I)$	$>0\sigma(I)$	$>3\sigma(I)$	>3 <i>\sigma(I)</i>	>2 <i>\sigma(I)</i>
R_1	0.0462	0.0656	0.0350	0.0582	0.0320	0.0402	0.0384
wR ₂	0.1088	0.1536	0.0962	0.1120	0.0829	0.1011	0.0772
GOF	0.9876	1.0412	1.0653	1.0000	1.0103	1.0248	1.0274

Table 2. Selected Hydrogen Bond Parameters for Supramolecular Complexes 1-7

supramolecular					
complex	$d_{\mathrm{D-H}}$ (Å)	$d_{\mathrm{H}\cdots\mathrm{A}}$ (Å)	$d_{\mathrm{D} \dots \mathrm{A}} (\mathrm{\AA})$	$\angle D-H\cdots A(^{\circ})$	symmetry code
01 1111 115	0.05	1.50	1	17/	
OI-HII···NS	0.85	1.78	2.627(4)	1/6	
			2		
O1-H11N46	0.84	1.78	2.614(6)	174	
O5-H51N32	0.83	1.80	2.621(6)	170	
O11-H111N60	0.84	1.78	2.617(6)	173	3 - x, -y, 1 - z
C24-H241···O2	0.93	2.45	3.368(6)	170	-1 + x, y, z
C23-H231O6	0.94	2.42	3.362(6)	179	-1 + x, y, z
			3		
O3-H31N6	0.86	1.80	2.652(3)	175	-1 + x, y, z
C15-H151O1	0.94	2.53	3.359(3)	147	1/2 - x, $1/2 + y$, $3/2 - z$
C17-H171O3	0.95	2.57	3.461(3)	158	-1/2 + x, $3/2 - y$, $1/2 + z$
			4		
Q12 H121 N10	1.01	1.59	T 2.570(5)	172	1
012-H121···N19	1.01	1.30	2.379(3)	1/3	-1 + x, y, z
C_{14} H_{141} C_{23}	0.80	1.85	2.078(3)	124	x, 1 - y, 1/2 + z
$C_{14} = 11141 \cdots O_{3}$	0.83	2.50	3.207(3)	134	x, 1 - y, -1/2 + z
$C_{20} = H_{20} + H$	0.92	2.54	3.294(3)	140	1 + x, -1 + y, z
025-11251012	0.94	2.39	5.511(5)	107	1 + x, -y, -1/2 + z
			5		
N9-H9101	0.87	1.77	2.636(3)	173	1 + x, y, z
C14-H141O3	0.93	2.51	3.180(3)	129	1 + x, y, z
C18-H181O8	0.94	2.36	3.292(3)	175	-1 + x, -1 + y, z
C20-H201O1	0.94	2.56	3.319(3)	138	-x, $-1/2 + y$, $1 - z$
C22-H221O8	0.93	2.46	3.386(3)	176	-1 + x, -1 + y, z
07–H71…O3 (intra)	0.85	1.61	2.453(3)	168	
			6		
N7-H71O6	0.89	1.93	2.800(3)	166	
N7-H7101	0.89	2.39	2.907(3)	117	
01-H1105	0.87	1.61	2.474(3)	171	-1 + x, y, z
C12-H121O5	0.93	2.34	3.252(3)	164	1 - x, 2 - y, 2 - z
С13-Н131О3	0.95	2.51	3.319(3)	144	-x, 2 - y, 2 - z
01-H11C4	0.87	2.50	3.258(3)	146	-1 + x, y, z
			7		
N8-H8101	0.92	1.79	2.701(3)	168	$x_{1} \frac{3}{2} - v_{2} - \frac{1}{2} + z_{1}$
N8-H8105	0.92	2.51	3.055(2)	118	$x_{1} \frac{3}{2} - y_{1} - \frac{1}{2} + z$
07-H7103	0.82	1.94	2.723(3)	159	, 0, = ,, 1, 2, 2, 2
07-H7106	0.82	2.49	3.029(3)	124	
07-H72···01	0.82	1.90	2.699(3)	166	$1 - x_1 - \frac{1}{2} + v_1 \frac{3}{2} - \tau$
05-H5107	0.84	1.68	2.522(3)	175	$2 - x_1 \frac{1}{2} + y_1 \frac{3}{2} - z$
C9-H9106	0.94	2.52	3.193(3)	129	2 - x, 1 - v, 1 - z
C15-H15101	0.94	2.56	3.458(3)	161	1 - x, 1/2 + v, 3/2 - z
	0.71	2.50	0.100(0)	101	

held in infinite linear chains by $O-H\cdots O$ hydrogen bonds. Furthermore, each acid molecule interacts with phenanthridine via an $O-H\cdots N$ hydrogen bond (Figure 6). of isophthalic acid—pyridine solvate,¹² chains are formed by the molecules, with two pyridine moieties hydrogen bonded to each acid moiety.

Adjacent chains are linked through weak C–H···O interactions between base and acid molecules. The crystal structure is stabilized by $\pi - \pi$ interactions of phenanthridine as well as of isophthalic acids moieties in neighboring chains. The distance between the phenanthridine rings is 3.42 Å, but the distance between acid rings is 3.34 Å. In the crystal structure **Phenanthridinium Maleate (2:1), 5.** The salt crystallizes in the monoclinic $P2_1$ space group. The angle between the plane of the carboxylate group and the pyridinium ring plane is 6.7°. One phenanthridine moiety interacts with one maleate moiety via $N^+-H\cdots O^-$ and $C-H\cdots O$ hydrogen bonds to form dimers (Figure 7).



Figure 3. Packing motif of 1 along the *a* axis.



Figure 4. (a) Layered structure of 2 (colored according to symmetry equivalence) viewed along the *b* axis. (b) The π -stacking of phenan-thridine molecules.

These dimers are further extended through weak $C-H\cdots O$ hydrogen bonds to produce infinite chains (Figure 8).

These chains are cross-linked via $C-H\cdots O$ bonds. Baseacid dimer formation is observed in the crystal structure of acridinium hydrogen maleate¹¹ in which, unlike **5**, synthon II is distorted due to molecular geometry of the acridine molecule. In the maleate anion of **5**, an intramolecular $O-H\cdots O^-$ hydrogen bond is also observed as a result of the short distance between the carboxyl group and carboxylate anion.

Phenanthridinium Oxalate (1:1), 6. The salt crystallizes in the triclinic $P\overline{1}$ space group. The oxalate anion has a twisted geometry; the C-C twist angle is 20.7°. The oxalate anions form linear chains via O-H···O hydrogen bonds. The anions in a chain are bound to phenanthridinium cations by asymmetric bifurcated O-H···N hydrogen bonds (Figure 9).

This mode of bonding between oxalate chains and phenanthridinium moieties is similar to previously reported phthalazinium oxalate.³⁴ In the solid state, the phenanthridinium and



Figure 5. Packing motif of 3 along the *a* axis.



Figure 6. Formation of extended chains in the crystal structure of 4.



Figure 7. Packing motif of 5 along the *a* axis.

oxalate moieties in **6** are arranged in separate layers which are connected through weak $C-H\cdots O$ interactions.

Phenanthridinium Oxalate (1:1) Monohydrate, 7. The compound crystallizes in the monoclinic space group $P2_1/c$. The asymmetric unit of 7 contains one phenanthridinium cation, one oxalate anion, and one water molecule. The oxalate anion has an almost planar conformation with the C–C twist angle of 2.2°. Analysis of the CSD³² for oxalate anion geometry in organic compounds indicates that a twisted or a planar conformation can be expected. The oxalate anion with two bifurcated hydrogen bonds is planar due to intermolecular interactions that stabilized the structure. Similar to the structure of 6, in 7 the oxalate anion interacts with phenanthridinium cation through asymmetric bifurcated O–H···N hydrogen bonds and in addition forms asymmetric bifurcated O–H···O hydrogen bonds with the water molecule (Figure 10).



Figure 8. Arrangement of molecules in the crystal structure of 5.



Figure 9. Hydrogen bond formation in 6.

The water molecule connects two anions via $O-H\cdots O_{water}$ and $O_{water}-H\cdots O$ hydrogen bonds.

Some Supramolecular Features of 1-7. Pyridine and carboxylic acid functional groups are known to form robust intermolecular interactions, and cocrystallizing an N-heterocyclic base with a carboxylic acid should form synthon I and II or III and IV depending on the acidity of acid. Molecular complexes of phenanthridine with dicarboxylic acids are based on either the neutral synthon II or ionic synthon III and IV. The $O-H \cdots N$ hydrogen bond present in synthon I and II is strong and directional, whereas weak C-H···O interaction cannot form in all cases. For ring motif $R_2^2(7)$ formation, strong geometrical complementarity between base and acid molecules is necessary. Our results show that in cocrystals 1-4 the noncyclic motif D is formed probably due to relatively large dihedral angles observed between the carboxylic acid group and pyridyl ring; these angles range from 13.6 to 42.9°. In phenanthridinium salt 5, this angle is 6.7° and an ionic ring motif $R_2^2(7)$ is observed. Other factors such as conformational flexibility of molecules may also affect synthon formation. In the compounds 6 and 7 the ionic synthon $R_2^2(7)$ is absent. The crystal structure of both salts display motif $R_1^2(5)$ between oxalate anion and phenanthridinium cation. Interestingly, $R_2^2(7)$ synthon formation takes place generally in neutral molecular complexes of oxalic acid with N-heterocyclic bases, 9,10,18,34,35 whereas in ionic complexes 36,37 the $R_1^2(5)$ synthon is present. Dale and co-workers¹² reported poor predictability of the carboxylic acid-pyridine $\hat{R}_2^2(7)$ heterosynthon



Figure 10. Hydrogen bonding in compound 7.

when simple pyridine derivatives combine with highly oxygenated carboxylic acids.

In the supramolecular complexes, the phenanthridine moiety does not change and the structures of the compounds 1-7 is based on acid geometry. Because the linear nature of the fumaric and the succinic acid molecules, in the solid state centrosymmetric base-acid-base trimers formed with phenanthridine. In the structure of 4, the carboxyl groups of isophthalic acid are located in the para position, and only one of these is bound by a hydrogen bond to a phenanthridine moiety. In this instance, minimal spatial interferences permit hydrogen bonds with other acid as well as the phenanthridine molecule, and chain formation in the crystal structure of 4 is preferred. Maleic acid geometry permits intramolecular hydrogen bonding, and only one carboxyl group is available for carboxylic acid-pyridine synthon formation resulting in phenanthridinium-maleate dimers, 5. The oxalate ion structure enhances bifurcated bond formation in 6 and 7.

Melting Points and ΔpK_a of Molecular Complexes. The neutral cocrystals reported here have higher melting points than phenanthridine (107.4 °C) but lower melting points than the individual dicarboxylic acids (Table 3).

Phenanthridine and fumaric acid cocrystals with 2:1 and 4:1.5 stoichiometries have different melting points. 1 with a stoichiometric ratio 2:1 melts at higher temperature than 2 with a stoichiometric ratio of 4:1.5. This difference is probably the result of closer molecular packing in the crystal structures. Notwithstanding stabilization effects of $\pi - \pi$ interactions in 2, the calculated density of 1 is higher than 2. Comparing the melting points and densities of phenanthridine-fumaric acid cocrystal 1 and phenanthridine-succinic acid cocrystal 3, in both cases a centrosymmetric structure is observed and the cocrystal with the higher density has the higher melting point. The melting point of fumaric acid cocrystal (1) is higher than that of the succinic acid cocrystal (3). Both structures are trimers; however, the angle between the carboxylic acid plane and the pyridyl ring plane in trimer 1 is smaller than in trimer 3, and closer packing is found in 1 resulting in a higher density and higher melting point of 1. The density of the cocrystals is also either less or slightly higher that of the dibasic acids, and packing in the solid state may

		number of						number of			
	number of weak	strong	total possible		melting		number of weak	strong	total possible		melting
	$C-H\cdots O$	$O{-}H{\cdots}N$	strong	density	point	dicarboxylic	$C-H\cdots O$	$O{-}H{\cdots}N$	strong	density	point
compd	bonds	$(or \ O) \ bonds$	H-bonds	$(\mathrm{g}~\mathrm{cm}^{-3})$	$(^{\circ}C)$	acid	bonds	$(or \ O) \ bonds$	H-bonds	$(g \ cm^{-3})^{38}$	$(^{\circ}C)^{38}$
1		1	1	1.402	164	fumaric acid	3	3	4	1.635	287
2	2	3	3.66	1.355	160						
3	2	1	1.66	1.341	115	succinic acid		2	2	1.572	187.9
4	3	1	2	1.439	150	isophthalic acid	2	3	3.66	1.526	347
5	4	1	2.33	1.416	141	maleic acid	2	2	2.66	1.590	139
6	4	2	3.33	1.485	169	oxalic acid		2	2	1.900	189.5

Table 3. The Number of Hydrogen Bonds, Density, and Melting Point of each Compound 1-6 and Dicarboxylic Acid

also affect the melting point of each compound. Similar correlation between melting points of cocrystals and starting compounds is observed in cocrystals obtained from acridine and dicarboxylic acids.¹¹

Intermolecular hydrogen bonding also affects the melting point of the compound. To compare the number of hydrogen bonds in the crystal structure, it is important to take into account the fact that there are relatively weak and relatively strong interactions. It has been reported that the $C-H \cdot \cdot \cdot O$ hydrogen bond strength is approximately 25-50% of an O-H···O and an O-H...N hydrogen bond. 39,40 Assuming that three $C-H\cdots O$ bonds are energetically equivalent to one full strength hydrogen bond such as $O-H\cdots O$ (or $O-H\cdots N$), it is possible to assign strong hydrogen bonds to the cocrystals and the respective dicarboxylic acids (total possible strong H-bonds). The results are presented in Table 3. Using the assumption regarding the relative strengths of hydrogen bonds mentioned above, in the nonionic cocrystals studied the number of possible strong hydrogen bonds in the acids is equal to or larger than the number of strong hydrogen bonds in the cocrystal. This would suggest that the formation of fewer hydrogen bonds in the cocrystal results in a lower melting point of the cocrystals but a higher melting point of the dibasic acid having a larger number of possible strong hydrogen bonds. However, in cocrystals of isonicotinamide with dicarboxylic acids,40 the cocrystals have higher melting points than the corresponding individual acids. Possibly supramolecular systems with a larger number proton donor and acceptor sites for hydrogen bond formation, as opposed to packing in the unit cell, are better suited for formation of cocrystals with higher melting points than the pure dicarboxylic acids. It may be concluded that both hydrogen bond formation and packing forces influence the melting point of cocrystals. These are examples of the influence of structure on physical properties, and hydrogen bonds and crystal packing do have an impact on physical properties such as the density and melting point.

The melting points of **5** and **6** are influenced by the ionic character of these compounds, and hydrogen bonding influence seems to be reduced. A comparison of melting point of these salts (Table 3) shows that **5** melts at higher temperature than phenanthridine and maleic acid, whereas **6** melts at higher temperature that phenanthridine but lower than oxalic acid. Compound 7 crystallize as hydrate and DTA/TGA thermogram indicates a loss of the weight (6.3%) that corresponds to the theoretical mass of water (6.3%) in a monohydrate. Dehydration of the compound occurs at 70 and 100 °C, followed by melting of the anhydrous form. The melting temperature of the anhydrous

Table 4. pK_a and ΔpK_a Values for Neutral and Ionic Complexes of Phenanthridine

compound	dicarboxylic acid	pK_a	$\Delta p K_a$	nature of compound
1, 2	fumaric acid	3.02	2.56	neutral
3	succinic acid	4.21	1.37	neutral
4	isophthalic acid	3.70	1.88	neutral
5	maleic acid	1.92	3.66	ionic
6	oxalic acid	1.25	4.33	ionic

form agrees with the melting temperature of **6**. XRPD of the anhydrous form also confirmed that after 2 h dehydration of the hydrate at 100 $^{\circ}$ C **6** was obtained. There appears to be no clear correlation between the melting point and the neutral or ionic nature of the compound.

Phenanthridine is a relatively basic compound $(pK_a = 5.58)$.³⁸ Depending on the acidity of the studied acid, salts or cocrystals may form. A comparison of the ΔpK_a ($\Delta pK_a = pK_a$ base $- pK_a$ acid) values of 1-6 (Table 4) shows that when the value ΔpK_a is less than 2.56 formation of the neutral hydrogen bonded synthon I takes place.

The formation of the phenanthridine salts occurred when $\Delta p K_a > 3.66$. On the basis of the considerations of Bhogala et al.,¹⁵ when $0 < \Delta p K_a < 3.75$ it is difficult to predict neutral or ionic hydrogen bond formation in the supramolecular structure. The $\Delta p K_a$ values of 1-5 are located in the interval when cocrystals and/or salts can be expected, but **6** is an ionic complex. These observations are in good agreement with Brittain's method⁴¹ for predicting salt formation in aqueous solution by calculating the percentage of salt formation as a function of $p K_a$ and $p K_b$.

CONCLUSIONS

Phenanthridine can form neutral or ionic supramolecular complexes with dicarboxylic acids depending on the acidity of the acids. The formation of $O-H\cdots N$ hydrogen bonds in supramolecular complexes of N-heterocyclic bases and dicarboxylic acids is generally predictable, but weak $C-H\cdots O$ interactions may be affected by geometrical compatibility between base and acid molecules, depending on the dihedral angle between the planes of the carboxylic group and the phenathridine moiety. As a result of distortion between the carboxylic acid group and pyridyl ring, the crystal structures of the neutral cocrystals exhibited a noncyclic dimer motif but not an $R_2^2(7)$ ring motif. An ionic $R_2^2(7)$ heterosynthon is observed in phenanthridinium maleate, whereas phenanthridine salts such as the

oxalate and its hydrate display motif $R_1^2(5)$ between the base and the acid.

The number of weak and strong hydrogen bonds in the studied neutral cocrystals is an approximate guide for predicting melting points. In the studied neutral cocrystals using the approximation that the strength of a weak $C-H \cdots O$ hydrogen bond is equal to 33% of a strong $O-H \cdots N$ (or O) hydrogen bond, it is possible to correlate the melting points of the cocrystals with the number of hydrogen bonds in the cocrystal and the respective dibasic acid. The number of hydrogen bonds in the cocrystal structures reported here is either less than or almost equal to that of the dicarboxylic acid and the melting points are below those of the dicarboxylic acids. Examining the densities of both cocrystals and the dicarboxylic acids, the cocrystals have lower densities and lower melting points. While there does not seem to be a monotonic trend, the results indicate that packing in the unit cell as well as the number and type of hydrogen bonds has an influence on the melting point of the cocrystal.

ASSOCIATED CONTENT

Supporting Information. DTA/TGA data and X-ray crystallographic information files (CIF) are available. The crystal structures in this paper have been deposited at the Cambridge Crystallographic Data Centre with deposition numbers CCDC 816162 (1), 816163 (2), 791362 (3), 816166 (4), 791363 (5), 816165 (6), and 816164 (7). This material is available free of charge via the Internet at http://pubs.acs.org.

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