(a) ***Cover Page***

Order and Disorder in the Structures of Two Crystal Polymorphs of the Adduct Bis(quinolinium-2-carboxylate) DL-Malic Acid

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(b) Index Abstract

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by *Graham Smith and Urs D. Wermuth*

The structure determinations of two crystal polymorphs of the 2:1 adduct of quinolinium-2-carboxylate with DL-malic acid has shown one to be triclinic and ordered while in the second monoclinic form the carboxylic acid groups of the malic acid moiety are disordered.

Figure for insertion in Index Abstract: (QAMALAB.TIF)

(c,d). Title: Authors and Affiliations

Title

Order and Disorder in the Structures of Two Crystal Polymorphs of the Adduct Bis(quinolinium-2-carboxylate) DL-Malic Acid

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(e) Abstract and Key Words

The structures of two polymorphs of the anhydrous cocrystal adduct of bis(quinolinium-2-carboxylate) DL-malic acid, one triclinic the other monoclinic and disordered, have been determined at 200 K. Crystals of the triclinic polymorph **1** have space group *P*-1, with $Z = 1$ in a cell with dimensions $a = 4.4854(4)$, $b = 9.8914(7)$, $c = 12.4670(8)$ Å, $\alpha = 79.671(5)$, $\beta = 83.094(6)$, $\gamma = 88.745(6)^{o}$. Crystals of the monoclinic polymorph **2** have space group $P2_1/c$, with $Z = 2$ in a cell with dimensions $a = 13.3640(4)$, $b = 4.4237(12)$, $c = 18.4182(5)$ Å, $\beta = 100.782(3)^{o}$.

Both structures comprise centrosymmetric cyclic hydrogen-bonded quinolinic acid zwitterion dimers [graph set $R^2_2(10)$] and 50% disordered malic acid molecules which lie across crystallographic inversion centres. However, the oxygen atoms of the malic acid carboxylic groups in **2** are 50% rotationally disordered whereas in **1** these are ordered. There are similar primary malic acid carboxyl O-H…$O_{quinaldic\ acid}$ hydrogen-bonding chain interactions in each polymorph, extended into two-dimensional structures but in **l** this involves centrosymmetric cyclic head-to-head malic acid hydroxyl-carboxyl O-H…O

interactions [graph set $R^2_2(10)$] whereas in **2** the links are through single hydroxy-carboxyl hydrogen bonds.

Key Words: Quinaldic acid; DL-malic acid adducts; polymorphism; disorder; hydrogen bonding.

Running Title:

Two polymorphs of the bis(quinoline-2-carboxylate) DL-malic acid adduct

Order and Disorder in the Structures of Two Crystal Polymorphs of the Adduct Bis(quinolinium-2-carboxylate) DL-Malic Acid

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Graham Smith and Urs D. Wermuth*

(f) Introduction

Quinoline-2-carboxylic acid (quinaldic acid, QA) [1] exists in the solid state as an aminium-carboxylate zwitterion [2]. In this structure is found a very stable N^+--H...$O_{carboxyl}$ hydrogen-bonded cyclic dimer [graph set $R^2_2(10)$ [3], which is also found in the 2:1 adduct of quinaldic acid with L-tartaric acid [4]. With the majority of the stronger organic acids e.g. 5-sulfosalicylic acid [5], picrylsulfonic acid [6] and 4,5-dichlorophthalic acid (a monohydrate) [7], protonation of the quinaldic acid occurs but a cyclic hydrogen-bonded $(QAH^+\text{-}QA)_2$ pseudo-dimeric cation is still formed. This is not the case in the 1:1 compound with 3,5-dinitrosalicylic acid (DNSA) where individual QAH^+ cations and $DNSA^-$ anions are found [8]. This is also found in the structure of the hydrochloride QAH^+ Cl^- (a monohydrate) [9]. The structure of a 1:1 DL-malic acid adduct with 4,4'-bipyridine and *trans*-1,2-bis(4-pyridyl)ethene are also known [10]. Our 1:1 stoichiometric interaction of quinaldic acid with DL-malic acid in 2-propanol was found to result in no proton transfer, instead giving the adduct bis(quinolinium-2-carboxylate) DL-malic acid which formed the major prismatic crystalline product, the disordered polymorph **2** together with minor morphologically different plates of the ordered triclinic polymorph **1**.

INSERT 1 Schematic of compound 1 is given here (QAMAL.eps)

(f) Experimental Section

Preparation. The title adduct was prepared by heating together under reflux for 10 min., 1 mmol quantities of quinoline-2-carboxylic acid (quinaldic acid) and racemic malic acid in 50 mL of 50% 2-propanol. After concentration to *ca*. 30 mL, complete room temperature evaporation of the hot-filtered solution gave predominantly colourless crystal prisms of monoclinic polymorph **2**, together with minor clusters of small plates of triclinic polymorph **1**, m.p. 166 ^{o}C.

Crystallography.

X-ray diffraction data for both **1** and **2** were acquired at 200(2) K on an Oxford Diffraction Gemini-S Ultra CCD-detector diffractometer employing graphite crystal monochromatized Mo *K*α radiation (λ = 0.71073 Å). Data collection and reduction was completed using CrysAlisPro [11] with data corrected for absorption (SADABS [12]). Structures were solved by direct methods (SHELXS97 [13]) and refined (SHELXL97 [13]) (both operating within WinGX [14]), with anisotropic thermal parameters for all non-hydrogen atoms. Hydrogen atoms potentially involved in hydrogen-bonding interactions were located by difference methods and their positional and isotropic thermal displacement parameters were refined. Others were included in the respective refinements at calculated positions and treated as riding models. Refined site occupancy factors for the carboxylic acid O atoms of the rotationally disordered malic acid in **2** (O11A, O12A and O11B, O12B) were all 0.50(1) and these atoms were refined anisotropically. General crystallographic details are given in Table 1. The atom numbering scheme employed for the quinaldic acid and DL-malic acid species in **1** and **2** are shown in Figs. 1 and 2.

(g) Results and Discussion

The structures of both **1** and **2** show the presence of the common cyclic hydrogen-bonded quinolinic acid zwitterion dimer [graph set $R^2_2(10)$] which incorporates intramolecular N^+-H…$O_{carboxyl}$ interactions (Table 2). These bis(QA^{+-}) dimers are centrosymmetric, unlike those in the analogous bis(QA+-) adduct with L-tartaric acid [4]. The asymmetric units in both **1** and **2** are similar (Figs. 1, 2), each comprising a quinoline-2-carboxylate zwitterion and a 50% disordered malic acid (A) molecule which lies across a crystallographic inversion centre [symmetry code: for **1**: (v) = -*x* - 1, -*y* + 1, -*z* + 2); for **2**: (iii) -*x* + 2, -*y* + 1, -*z*]. This condition necessitates that in each structure the hydroxy group at C2A is 50% disordered across the respective inversion centres. In addition, the oxygen atoms of the malic acid carboxylic groups in **2** are 50% rotationally disordered whereas in **1**, no such disorder is present.

INSERTS 2, 3 : Figures 1 and 2 [Atom numbering scheme for the adduct species in the asymmetric units of 1 (QAMAL1.TIF) and 2 (QAMAL2.TIF)]

Strong malic acid carboxyl O--H....$O_{carboxyl}$ hydrogen bonds [2.5608(15) Å in **1** and 2.578(4) Å in **2**] link the quinaldic acid dimer units into one-dimensional chains which extend along the *c* axial direction in the unit cell in **1** (Figs. 3 and 4) and along the *a* cell direction in **2** (Fig. 5 and 6). Two-dimensional sheet structures are generated through malic acid hydroxy O--H...$O_{carboxyl}$ associations which in **1** differ significantly from those in **2**. In **1**, the extension involves centrosymmetric cyclic head-to-head malic acid interactions [graph set $R^2_2(10)$] [O21A-H...$O12A^{ii}$, 2.781(3) Å: symmetry code (ii), -*x*, -*y* + 1, -*z* + 2] while in **2**, the extension down the *b* axis of the unit cell is through single

hydrogen bonds [O21A-H...O12A, 2.712(5) Å: symmetry code (ii), x, $y + 1$, z]. In both structures, there are a number of weak aromatic C-H…O associations both within the chains and in the case of **1** between the chains, as shown in Figs. 5 and 6. The crystal packing differences between **1** and **2** are considered to be the result of conformational differences between both the malic acid and quinaldic acid species. With malic acid the defining torsion angle O11A-C1A-C2A-O21A is –95.69(18)^{o} in **1** *cf.* 132.3(2)^{o} in **2** while with the quinaldic acid species the defining torsion angle N1-C2-C21-O22 in **1** is -164.87(12)^{o} *cf*. -174.00(12)^{o} in **2**.

INSERTS 4, 5 and 6: Figures 3, 4, 5 and 6 (packing of 1 and 2 in the unit cell) (QAMAL3.TIF, QAMAL4.TIF, QAMAL5.TIF and QAMAL6.TIF)

Conclusion

The structures of the two polymorphs of bis(quinoline-2-carboxylate) DL-malic acid described here provide an illustration of cocrystallization in which equilibrium conditions during the crystal growth stage resulted in later formation of the ordered triclinic form **1** (the minor component) from the disordered monoclinic form **2** (the major component). The differences are accommodated in conformational variations in both the malic acid molecules and to a lesser extent the quinaldic acid molecules as well as in the associative hydrogen-bonding between these.

Supplementary material

CCDC 773142 and 773143 contain the supplementary crystallographic data for polymorphs **1** and **2** from this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data request/cif by e-mailing data_request@ccdc.cam.ac.uk, or contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.

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(h) References

1. O'Neil MJ (ed) (2001) The Merck Index, 13th edn. Merck & Co. Inc, Whitehouse Station, NJ, USA, p1440
2. Dobrzyńska D, Jerzykiewicz LB (2004) J Chem Crystallogr 34:51
3. Etter MC, MacDonald JC, Bernstein J (1990) Acta Crystallogr B46:256
4. Smith G, Wermuth UD, White JM (2006). Acta Crystallogr C62:o694
5. Smith G, Wermuth UD, White JM (2004) Acta Crystallogr C60:o575
6. Smith G, Wermuth UD, White JM (2008) Acta Crystallogr E64:o132
7. Smith, G, Wermuth UD, White JM (2008) Acta Crystallogr C64:o180
8. Smith G, Wermuth UD, White JM (2007) Aust J Chem 60:264
9. Raisanen MT, Klinga M, Leskela M, Repo T (2007) Acta Crystallogr E63:o1926
10. Farrell DMM, Ferguson G, Lough A J, Glidewell C (2002) Acta Crystallogr B58:530
11. CrysAlisPro (2010) (version 1.171.33.55). Oxford Diffraction Ltd., Yarnton, England
12. SADABS: Absorption correction program for area detectors. Sheldrick GM (1996). University of Göttingen, Germany
13. SHELXS97 and SHELXL97: Programs for single crystal structure solution and refinement. Sheldrick GM (2008) Acta Crystallogr A64:112
14. WinGX, A suite for small-molecule single-crystal crystallography. Farrugia LJ (1999) J Appl Crystallogr 32:837
15. PLATON: A multipurpose crystallographic tool. Spek AL (2009) Acta Crystallogr D65:48

(i) Tables

Table 1. Crystal data for polymorphs **1** and **2**

Compound	**1**	**2**
CCDC reference	773142	773143
Melting point (^{o}C)	166	166
Molecular formula	$C_{24}H_{20}N_2O_9$	$C_{24}H_{20}N_2O_9$
M_r	339.32	339.32
Temperature (K)	200(2)	200(2)
Wavelength (Å)	0.71073	0.71073
Crystal system	triclinic	monoclinic
Space group	*P*-1	$P2_1/c$
a (Å)	4.4854(4)	13.3640(4)
b (Å)	9.8914(7)	4.4237(12)
c (Å)	12.4670(8)	18.4182(5)
α (^{o})	79.671(5)	90
β (^{o})	83.094(6)	100.782(3)
γ (^{o})	88.745(6)	90
V (Å^3)	540.21(7)	1069.57(10)
Z	1	2
D_c (g cm^{-3})	1.477	1.476
μ (mm^{-1})	0.115	0.115
F(000)	250	500
Instrument	Oxford Diffraction CCD	Oxford Diffraction CCD
Reflections total, θ_{max} (^{o})	5913, 25.0	6558, 26.0
Crystal size (mm)	0.30 x 0.25 x 0.15	0.40 x 0.20 x 0.20
Collection range: *h* *k* *l*	 -5 to 5 -11 to 11 -14 to 14	 -16 to 16 -5 to 5 -22 to 22
Reflections (independent)	1903	2116
Reflections [$F^2>2\sigma(F^2)$]	1496	1546
R_{int}	0.0203	0.0214
$R1$ [a] [$F^2>2\sigma(F^2)$]	0.0337	0.0352
$wR2$ [a] (all data)	0.0961	0.0922
S [a]	1.02	1.00
n_p	175	194
Transmission factors (max/min)	0.942/0.982	0.934/0.980
Residuals:	0.130/-0.197	0.155/-0.159

$\Delta_{max./min}$ (eÅ^{-3})		

[a] $R1 = (\Sigma\ |F_o| - |F_c|\ )/\ \Sigma\ |F_o|)$; $wR2 = \{\Sigma\ [w(F_o^2 - F_c^2)^2] / \Sigma\ [w(F_o^2)^2]\}^{½}$;

$S = \{\Sigma\ [w(F_o^2 - F_c^2)^2] / (n\text{-}p)\}^{½}$.

Table 2. Hydrogen-bonding interactions (Å/ °) for **1** and **2**

1

D-H…A	D-H	H…A	D…A	∠ DH..A
N1-H1…O21	0.888(16)	2.331(15)	2.6916(14)	101.3(12)
N1-H1…O21^{i}	0.888(16)	1.923(17)	2.7837(16)	162.7(14)
O11A-H11A…O22	1.00(2)	1.56(2)	2.5608(15)	179(2)
O21A-H21A…O12A^{ii}	0.90(3)	1.89(3)	2.781(3)	179(4)
C3-H3…O22^{iii}	0.93	2.54	3.3357(17)	144
C4-H4…O12A^{iv}	0.93	2.46	3.2826(19)	148
C5-H5…O12A^{iv}	0.93	2.50	3.311(2)	146
C8-H8…O11A^{i}	0.93	2.53	3.2754(19)	138
C8-H8…O12A^{i}	0.93	2.53	3.2433(17)	134

Symmetry codes: (i) $-x, -y+2, -z+1$; (ii) $-x, -y+1, -z+2$; (iii) $-x, -y+1, -z+1$; (iv) $-x+1, -y+1, -z+1$.

2

D-H…A	D-H	H…A	D…A	∠ DH..A
N1-H1…O21	0.881(18)	2.334(18)	2.6793(18)	102.1(19)
N1-H1…O21^{i}	0.881(18)	1.948(18)	2.8047(17)	163(3)
O11A-H11A…O22	1.01(3)	1.59(3)	2.556(3)	172(3)
O21A-H21A…O12A^{ii}	0.87(4)	1.88(4)	2.712(5)	158(5)
C8-H8…O11A^{i}	0.93	2.59	3.384(4)	144
C8-H8…O21^{i}	0.93	2.54	3.2519(17)	134

Symmetry codes: (i) $-x+1, -y, -z$; (ii) $x, y+1, z$.

(j) Figures

Figure 1. Molecular configuration and atom naming scheme for the zwitterionic quinaldic acid species and the malic acid molecule (A) in **1**. The pseudo-inversion related atoms of the malic acid have the symmetry code (v) (-*x* - 1, -*y* + 1, -*z* + 2), with O21A having 50% occupancy. The inter-species hydrogen bond is shown as a dashed line and displacement ellipsoids are drawn at the 40% probability level [15].

Figure 2. Molecular configuration and atom naming scheme for **2**. The pseudo-inversion related atoms of the malic acid molecule have the symmetry code (iii) (-*x* + 2, -*y* + 1, -*z*), with O21A having 50% occupancy. Oxygen atoms of the rotationally disordered carboxylic acid group are O11A, O12A and O11B, O12B and are also 50% disordered. The inter-species hydrogen bond is shown as a dashed line and displacement ellipsoids are drawn at the 40% probability level.

Figure 3. A perspective view of the unit cell of **1** showing the cyclic hydrogen-bonded quinolinium-2-carboxylate dimer and its extension *via* the cyclic hydrogen-bonded malic acid dimer. For symmetry codes, see Table 2.

Figure 4. A comparative view of the hydrogen-bonded quinolinium-2-carboxylate dimer in **2** and its hydrogen bonding extensions *via* single malic acid hydroxyl O-H...$O_{carboxyl}$ extensions.

Figure 5. Molecular packing in the unit cell of **1**, viewed down the *a* cell direction, including the O-H…O hydrogen bonds as well as the weak aromatic C-H…O hydrogen-bonding associations, shown also as dashed lines.

Figure 6. A comparative view of the view of the packing of **2** in the unit cell viewed down the *b* cell direction. The half-occupancy (B) oxygen atoms of the disordered carboxylic acid groups are omitted for clarity.