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ORIGINAL PAPER

Supramolecular Architecture of Two Modifications of Flavone-6,2′-dicarboxylic acid

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Abstract Two crystalline forms of flavone-6,2′-dicarboxylic acid (fla): one *N*,*N*-dimethylformamide (DMF) solvate (modification **1**) and one without any solvate molecules (modification **2**), have been obtained and their structures were determined by X-ray diffraction technique. Modification **1** crystallized in the orthorhombic space group Pbca; and modification **2** crystallized in the monoclinic space group P2(1)/c. In **1** and **2** fla molecules are both joined to helix chain structures via O–H···O hydrogen-bonds between carboxylic group of B ring and carbonyl oxygen atom of C ring, however, in **1** helix chains are further joined by DMF molecules; and in **2** helix chains are further linked via rich hydrogen-bonds between fla molecules, which result in different packing of modifications **1** and **2**.

Keywords Flavone-6,2′-dicarboxylic acid · Modification · Hydrogen-bonding · Helix chain

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Comment

Recent years, great interests have concentrated on the syntheses and characterization of the flavonoids [1–4] because flavone derivatives own potential biological activity, such as antihypertensive, antimicrobial [5], antiviral [6, 7], anti-hiv [8–10], anticancer [11, 12] properties. Flavone carboxylic acids with medicinal value [13] have also been reported, e.g., 6-carboxyl flavonoids has inhibitory effect on gastric acid secretion and have anti-anaphylaxis function [14, 15], 3-carboxyl flavonoids can be applied to antiphlogistic [16], 7-carboxyl flavonoids can be used in the treatment of rheumatisants [17] and so on. Since the varieties of biological activity, the study of structure–activity relationship on flavonoids carboxylic acids has been the hot spot all along, and our group have been working on it [18]. In this article, we report the syntheses and the supramolecular structures of two modifications of flavone-6,2′-dicarboxylic acid, a new flavonoid carboxylic acid with potential medicinal value.

Experimental

The title compound was synthesized by two steps. The first step is the synthesis of 2′-hydroxy-2,5′-dicarboxychalcone; the next step is the synthesis of flavone-6,2′-dicarboxylic acid, the synthesis route of flavone-6,2′-dicarboxylic acid is shown in Scheme 1.

The synthesis of 2′-hydroxy-2,5′-dicarboxychalcone

To an ice-cooled solution of 3-acetyl-4-hydroxybenzoic acid (5.66 g, 0.031 mol) and 2-carboxybenzaldehyde

(4.71 g, 0.031 mol) in ethanol (50 mL), 40% KOH (25 mL) and appropriate benzyl triethyl ammonium chloride were added. The resulting dark red mixture was stirred at ambient temperature for 12 h. Thereafter, the reaction mixture was slowly poured into excess 2 N HCl, and the resulting yellow precipitate was filtered off, washed with H_2O, and dried. Yield 64.1%.

The synthesis of flavone-6,2′-dicarboxylic acid

A mixture of 2′-hydroxy-2,5′-dicarboxychalcone (2.17 g, 0.007 mol), 25 mL DMSO and catalytic amount of iodine in a three necked bottle was stirred and refluxed for 2 h. After cooling, the mixture was poured into 100 g of ice, a white solid was obtained. The crude product was filtered off, washed with water, and dried, recrystallized with *N*,*N*-dimethylformamide. Yield 88.0%. Spectrosopic analysis: ^{1}H-NMR (DMSO-d_6, 400 Hz, δ, p.p.m): δ_H 6.69 (s, 1H, H3), δ_H 7.68–7.81(m, 4H, H8, H3′, H4′, H5′), δ_H 7.94 (m, 1H, H6′), δ_H 8.32 (m, 1H, H7), δ_H 8.63 (d, 1H, H5), δ_H13.39 (s, 2H, –COOH).

Crystals of **1** were obtained by heating the mixture of flavone-6,2′-dicarboxylic acid (0.1 g, 0.32 mmol) and *N*,*N*-dimethylformamide (16 mL) to 363 K in water-bath until dissolving completely. Then the solution was cooled to room-temperature and single crystals of **1** suitable for X-ray diffraction analysis formed after 3 days. Elemental analysis: calculated for $C_{17}H_{10}O_6{\cdot}C_3H_7ON$: C 62.66, H 4.47, N 3.65; found: C 62.39, H 4.13, N 3.36%.

Crystals of **2** were obtained by heating the mixture of flavone-6,2′-dicarboxylic acid (0.01 g, 0.03 mmol) and *n*-propanol (10 mL) in oil-bath until dissolving completely. Then the solution was cooled to room-temperature, and single crystals of **2** suitable for X-ray diffraction analysis formed after 15 days. Elemental analysis: calculated for $C_{17}H_{10}O_6$: C 38.71, H 3.25; found: C 38.43, H 3.13%.

X-Ray Crystallography

Two different crystalline forms of flavone-6,2′-dicarboxylic acid suitable for X-ray diffraction analysis were recrystallized from *N*,*N*-dimethylformamide **1** and *n*-propanol **2**, respectively. Semi-empirical absorption corrections were applied using the SADABS program [19]. The structure was solved by direct methods and refined by full-matrix least square on F^2 using the SHELXTL-97 program [20, 21]. All non-hydrogen atoms were refined with anisotropic displacement parameters. The hydrogen atoms were generated geometrically and treated by constrained refinement.

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

Compound	**1**	**2**
Empirical formula	$C_{17}H_{10}O_6{\cdot}C_3H_7ON$	$C_{17}H_{10}O_6$
Formula weight	383.35	310.25
T (K)	291(2)	293(2)
Crystal system	Orthorhombic	Monoclinic
Space group	Pbca	P2(1)/c
a (Å)	8.449(10)	10.523(14)
b (Å)	16.976(2)	8.651(12)
C (Å)	25.793(3)	15.990(2)
β (°)	90	108.7(2)
V (Å^3)	3699.7(8)	1378.7(3)
Z	8	4
θ range (°)	2.40–25.49	2.69–25.50
μ (mm^{-1})	0.105	0.115
F(000)	1,600	640
D_c (mg m^{-3})	1.376	1.495
Goodness-of-fit on F^2(e Å^{-3})	1.022	1.038
No. data collected	25,769	10,188
No. unique data	3,440	2,564
Rint	0.0597	0.0270
$R1$, w$R2$ [I > 2σ(I)]	0.0487, 0.1183	0.0384, 0.0896
$R1$, w$R2$ (all data)	0.0838, 0.1395	0.0561, 0.1012
Largest diff. peak and hole (e Å^{-3})	0.201, −0.191	0.172, −0.204

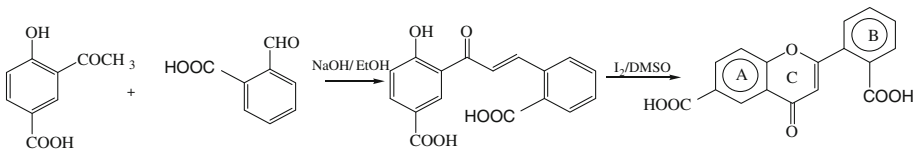
Results and Discussion

Experimental details for X-ray data collection of **1** and **2** are presented in Table 1, and the molecular structure and the atomic numbering scheme of **1** and **2** are shown in Fig. 1a and b, respectively. In the asymmetric unit of **1** DMF molecule is linked to flavone-6,2′-dicarboxylic acid via C(18)–H(18)···O(2) hydrogen-bond with C···O distance of 3.16(3) Å.

In **1** and **2**, atoms in ring A and ring C are coplanar, and atoms in ring B are quite planar too. All the bond lengths of modification **1** are very close to those of **2** except that there is little difference in C(17)–O(5) bond length of compounds **1** (1.324 Å) and **2** (1.308 Å). The atoms of the 6-carboxylic group are coplanar with ring A in **1** and **2**; however, the atoms of the 2′-carboxylic group on ring B are not coplanar with ring B, with the largest deviation of 0.5514 Å (O5) in **1** and 0.7035 Å (O2) in **2**, respectively. The dihedral angle between ring C and ring B in **1** is 45.4 (66) °, and it in **2** is 40.8 (46) °, both much larger than that in flavone-3′-sulfonamide with the dihedral of 8.3(3) ° [3].

However, there are significant differences in the connections of the two modifications which bring out different packing motifs of them.

Scheme 1 Synthesis route of flavone-6,2′-dicarboxylic acid



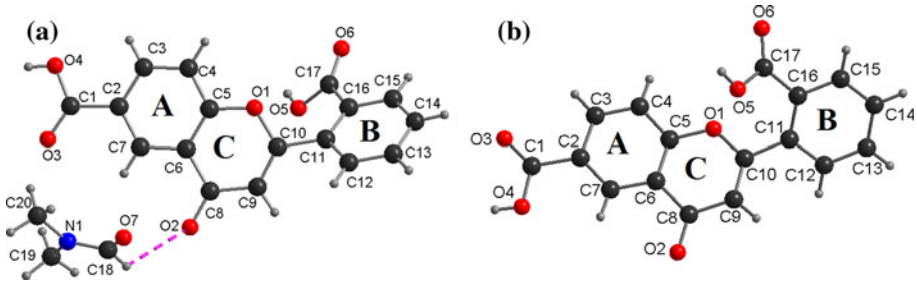


Fig. 1 The molecular configuration and atom-numbering scheme for **1** (**a**), **2** (**b**), atoms are shown as 30% probability ellipsoids

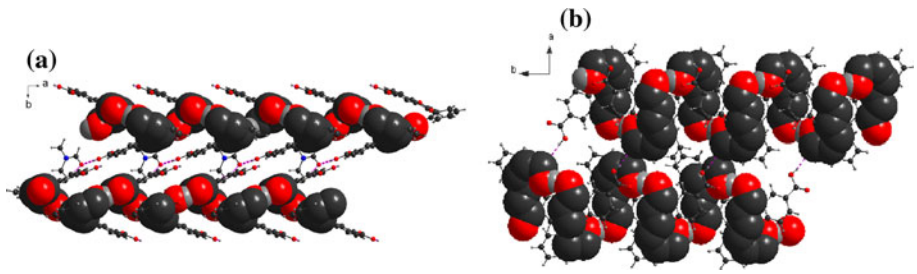


Fig. 2 View of 2-D supramolecular structure composed of hydrogen-bonding helix chains (shown as *spacing filling models*) along the *c*-axis for **1** (**a**), **2** (**b**)

Table 2 Hydrogen-bonding geometry (Å and °) for **1** and **2**

D–H	d(D–H)	d(H···A)	<DHA	d(D···A)	A
1					
O(4)–H(4)	0.82	1.77	165.4	2.57(2)	O(7) [x − 1, y, z]
O(5)–H(5)	0.82	1.80	169.1	2.61(3)	O(2) [x − 1/2, −y + 1/2, −z + 1]
C(4)–H(4A)	0.93	2.49	166.6	3.40(3)	O(7) [−x + 1, −y, −z + 1]
C(18)–H(18)	0.93	2.59	119.7	3.16(3)	O(2)
C(14)–H(14)	0.93	2.59	142.0	3.37(3)	O(6) [x + 1/2, y, −z + 3/2]
C(19)–H(19C)	0.93	2.58	153.0	3.46(4)	O(3) [x + 1/2, y, −z + 1/2]
2					
O(5)–H(5)	0.82	1.78	166.9	2.58(17)	O(2) [−x + 1, y + 1/2, −z + 1/2]
O(4)–H(4)	0.82	1.83	168.4	2.64(19)	O(6) [x − 1, −y + 3/2, z − 1/2]
C(3)–H(3)	0.93	2.34	149.4	3.17(5)	O(3) [−x + 1, −y + 2, −z]

In the crystal structure of **1**, carboxylate oxygen atom O(5) in the molecule at (x, y, z) acts as a hydrogen-bond donor to carbonyl atom O(2) in the molecule at (x − 1/2, −y + 1/2, −z + 1), leading to a hydrogen-bonding helix chain structure; and carbonyl oxygen atom of DMF molecule O(7) acts as a hydrogen-bond acceptor to O(4)–H(4) group in the molecule at (x − 1, y, z) and C(4)–H(4A) group in the molecule at (−x + 1, −y, −z + 1), which joins the helix chains to a 2-D layer structure, as shown in Fig. 2a. Further C(14)–H(14)···O(6) (symmetry code: x + 1/2, y, −z + 3/2) and C(19)–H(19C)···O3 (symmetry code: x + 1/2, y, −z + 1/2) hydrogen-bonds (as shown in Table 2) join the layers to form the final supramolecular structure of **1**, as shown in Fig. 3a.

Similar to **1**, carboxylate oxygen atom O(5) in the ring B at (x, y, z) acts as a hydrogen-bond donor to carbonyl atom O(2) in the ring C at (−x + 1, y + 1/2, −z + 1/2), forming hydrogen-bonding helix chains along the b-axis in the modification **2**, as shown in Fig. 2b, which are further joined to 2-D layer structure via O(4)–H(4)···O(6) hydrogen-bonds along the *c*-axis. In addition, the planes of benzopyran ring of adjacent molecules are mutual parallel,

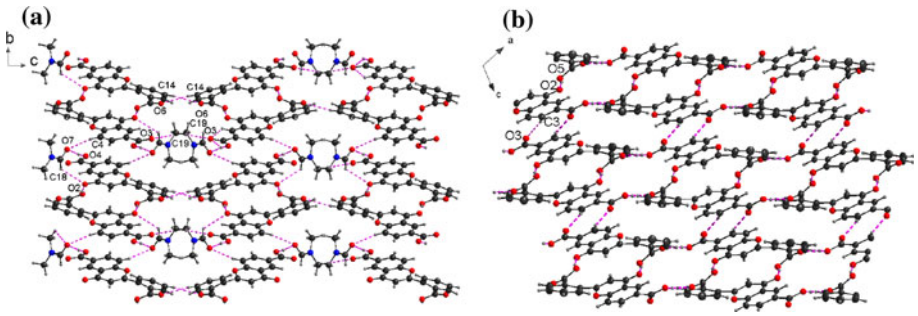


Fig. 3 **a** The packing diagram for **1** viewed along the *a*-axis; **b** The packing diagram for **2** viewed along the *b*-axis, the hydrogen-bonding interactions are represented by *dashed lines*

the average distance between the two planes is 3.46 Å, and the distance between the two ring center is 3.76 Å, showing that weak π–π aromatic interaction exit between the phenyl rings in **2**; meanwhile the carboxylate oxygen atoms of ring *A* form O(3)···H(3)–C(3) hydrogen-bonds with the C–H of ring A in the adjacent layer with C···O distance of 3.18 Å; these weak interactions result in the ultimate supramolecular structure of **2**, as shown in Fig. 3b.

In **1** and **2**, the dihedral angles between ring B and C are 45.4 (66) ° and 40.8 (46) °, respectively, showing that rings B and C are severely twisted across the C–C single bond, which provide the potentiality of the formation of a helix structure. X-ray single crystal diffraction studies show that O–H···O hydrogen-bonds exit between the carboxylate group of ring C and carbonyl oxygen atom of ring B, which help to link the fla molecules into a helix chain structure in **1** and **2**. However, in **1** helix chains are further joined by DMF molecules; and in **2** helix chains are further linked via hydrogen-bonds between fla molecules; which result in different packing of modifications **1** and **2**.

Conclusion

Flavone-6,2′-dicarboxylic acid (fla) was found to exhibit two different conformations. One crystallizes from *N*,*N*-dimethylformamide in orthorhombic group Pbca and the other crystallizes from *n*-propanol in monoclinic group P2(1)/c without any solvent molecules. Rich hydrogen-bonds and aromatic-aromatic interactions link fla molecules to two different supramolecular structures.

Supplementary Material

CCDC 793602 and 793603 contain the supplementary crystallographic data for this article. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44)1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.32.

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