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Self-assembly of pyrrole-2-carboxylates: Substituent effect on the synthon conversion

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1. Introduction

The study of synthetic assemblies linked by intermolecular noncovalent interaction such as hydrogen bonding could lead both to the creation of new structures with well-defined geometries and providing insights into biological processes [1]. Varying the overall macroscopic functional properties of a particular system by small alterations in molecular structure is of particular appeal in this field [2]. Pyrrole-based compounds are frequently observed as hosts for neutral molecules [3] and anionic species [4]. Meantime, the use of α -carbonyl-functionalized pyrrole moieties as building blocks to create hydrogen bonded self-assembled aggregates has received some attention recently [5]. For example, Sessler and coworkers [6] have reported that some ferrocene-based pyrrole-2-carboxylates can self-assemble into one-dimensional chain via pair of N-H···O hydrogen bonds. Maeda and coworkers [7] have fabricated micro- and nanometer-scale porous, fibrous, and sheet architectures from supramolecular assemblies of dipyrrolyl diketones through hydrogen bonds. In previous work [8], we have studied the robust synthon between two pyrrole-2-carboxylate moieties in the crystal structure of compound 1 (Scheme 1). Herein, we reported the solid state self-assemblies of another three pyrrole-2-carboxylate compounds, 2-4. In solid state, all the three compounds self-assembled through hydrogen bonds and the pyrrole-2-carboxylate moieties in 2-4 involved into two kinds of synthons. A phenomenon of synthon conversion of pyrrole-2-

ABSTRACT

The substituent effect on the solid state self-assemblies of three pyrrole-2-carboxylate compounds, **2–4**, with N–H…O hydrogen bonds have been studied by X-ray crystallography. Although just one group different in structure, the self-assemblies of **2–4** varied greatly. The phenyl substituted compound **2** assembled into corrugated tape structure through a $R_2^2(10)$ type dimer synthon and the benzyl substituted compound **3** assembled into 2-D layer structure through a C(5) type catemer synthon, whereas the butyl substituted compound **4** assembled into 2-D layer through both type synthons.

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carboxylate, from dimer to catemer, was found with the steric hindrance increasing.

2. Experimental

2.1. General

¹H NMR spectra were recorded in DMSO-*d*₆, with TMS as internal standard, on a BRUKER AV-400 MHz spectrometer. Mass spectra were recorded on an AEIMS-50/PS 30 mass spectrometer. Analyses of C, H and N were determined on a Perkin–Elmer 240 elemental analyzer. Melting points (mp) were recorded on an electro-thermal digital melting point apparatus and uncorrected. 2-Trichloroacetylpyrrole was prepared according to literature procedures [9]. *N*-phenyldiethanolamine, *N*-benzyldiethanolamine and *N*-*n*-butyldiethanolamine were commercial available and used without further purification.

2.2. Preparation of compounds 2-4

Diethanolamine (1 mmol), 2-trichloroacetylpyrrole (3 mmol) and triethylamine (0.5 mL) were added to acetonitrile (20 mL), and then the mixture was refluxed for 16 h. The solution was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel with ethyl acetate/petroleum ether (v:v = 1:2), affording the compounds.

Compound **2**, white powder, 67%, m.p. = $135 \,^{\circ}$ C. ¹H NMR (400 MHz, DMSO-*d*₆): δ 3.67 (t, 4H, *J* = 5.6 Hz, -CH₂-), 4.26 (t, 4H, *J* = 5.6 Hz, -CH₂-), 6.09 (s, 2H, PyCH), 6.56 (t, 1H, *J* = 7.2 Hz, PhCH),



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6.71 (s, 2H, PyCH), 6.80 (d, 1H, *J* = 8.4 Hz, PhCH), 6.96 (s, 2H, PyCH), 7.10 (t, 2H, *J* = 7.2 Hz, PhCH), 11.85 (s, 2H, PyNH); ¹³C NMR (100 MHz, DMSO-*d*₆): δ 49.1, 60.9, 109.6, 111.7, 115.2, 116.0, 121.6, 124.3, 129.2, 147.1, 160.4; ESI-MS: 368(M+1⁺). Elemental analysis: $C_{20}H_{21}N_{3}O_{4}$: Calcd: C, 65.38; H, 5.76; N, 11.44. Found: C, 65.11; H, 6.01; N, 11.59.

Compound **3**, white powder, 60%, m.p. = 92 °C. ¹H NMR-(400 MHz, δ ppm, DMSO- d_6) : δ 2.83 (t, 4H, J = 5.2 Hz, -CH₂-), 3.73 (s, 2H, -CH₂-), 4.25 (t, 4H, J = 5.2 Hz, -CH₂-), 6.14 (s, 2H, PyCH), 6.74 (s, 2H, PyCH), 7.00 (s, 2H, PyCH), 7.19–7.30 (m, 5H, PhCH), 11.83 (s, 1H, PyNH); ¹³C NMR (100 MHz, DMSO- d_6): δ 51.9, 58.3, 64.5, 109.4, 114.9, 121.6, 123.9, 126.7, 128.0, 128.3, 139.3, 160.3; ESI-MS: 382(M+1⁺). Elemental analysis: C₂₁H₂₃N₃-O₄: Calcd: C, 66.13; H, 6.08; N, 11.02. Found: C, 66.27; H, 6.11; N, 10.78.

Compound **4**, white powder, 65%, m.p. = 60 °C. ¹H NMR-(400 MHz, δ ppm, CDCl₃) : δ 0.88 (t, 3H, *J* = 7.5 Hz, -CH₃), 1.25– 1.48 (m, 4H, -CH₂CH₂-), 2.59 (t, 2H, *J* = 7.5 Hz, -CH₂-), 2.91 (t, 4H, *J* = 6 Hz, -CH₂-), 4.35 (t, 4H, *J* = 6 Hz, -CH₂-), 6.23-6.25 (m, 2H, PyCH), 6.91–6.95 (m, 4H, PyCH), 9.62 (s, 1H, PyNH); ¹³C NMR (100 MHz, CDCl₃): δ 14.0, 20.4, 29.6, 53.1, 55.0, 62.7, 110.4, 115.6, 122.6, 123.1, 161.2; ESI-MS: 348(M+1⁺). Elemental analysis: C₁₈H₂₅N₃O₄: Calcd: C, 62.23; H, 7.25; N, 12.10. Found: C, 62.33; H, 6.99; N, 12.17.

2.3. X-ray crystallography

The single crystal of compound **2** suitable for X-ray crystallography studies was grown by slowly evaporating its MeOH solution. Crystals of compounds **3** and **4** were obtained by the diffusion of petroleum ether to the ethyl acetate solution of compounds **3** and **4**, respectively. The diffraction data were measured on a BRU-KER SMART APEX II CCD diffractometer with Mo K α radiation ($\lambda = 0.71073$ Å) by ω scan mode at 293(2) K. All data were corrected by semi-empirical method using SADABS program. The program SAINT [10] was used for integration of the diffraction profiles. The structure was solved by the direct methods using SHELXS program of the SHELXL-97 package and refined with SHELXL [11]. The final refinement was performed by full matrix least-squares methods with anisotropic thermal parameters for all non-hydrogen atoms on F^2 . Crystallographic data and refinement parameters of the three crystals were summarized in Table 1.

2.4. DFT calculation

 $R_2^{2}(10)$ hydrogen bonding motif (synthon I) linked 2.2 dimer and its two monomers units were cut out as the calculation models from the crystal of 2. All hydrogen atoms were included in the models. Single point energies of the monomers and dimer were calculated at the B3LYP/6-31G^{*} level by using the Gaussian 98 program [12]. The energies of the synthon I in crystal 2 was computed as the difference in the single point energies between the 2.2 dimer and its two monomers [13]. The energies of the catemer A and B in crystal **3** and the catemer **C** and synthon **I** in crystal **4** were also calculated using the same procedure.

2.5. Scanning electron microscopy studies

SEM images were obtained with a LX30W/TMP scanning electron microscope at acceleration voltages of 20 kV. The samples were prepared by dropping a small amount of ethyl acetate solution of **2–4** onto a silicon plate and evaporating the solvent.

3. Results and discussion

3.1. Crystal structures of 2-4

The molecular structures of **2–4** were shown in Fig. 1, respectively. In the three structures, all the pyrrole-2-carboxylate moieties adopt *syn* conformation, with the carbonyl group arranged *syn* to its adjacent pyrrole NH. In the crystal of compound **2**, each molecule **2** connected with its two neighbors through a pair of N–H···O hydrogen bonds and then formed into one-dimensional corrugated tape (Fig. 2). The parameters of the hydrogen bonds were listed in Table 2. In terms of Etter's graph-set formalism, this pair of hydrogen bonds motif can be described as an $R_2^2(10)$ system [14], which has been frequently observed in the crystal structures of pyrrole-2-carboxylate compounds [8,15]. Different from previous results, however, the $R_2^2(10)$ motif in crystal of compound **2** is unsymmetrical.

In the crystal of compound **3**, the molecules adopt a convergent conformation which may ascribe to the intramolecular $C-H\cdots O$

 Table 1

 Crystal data of compounds 2–4.

Crystals	2	3	4
CCDC No.	725706	725704	725705
Empirical formula	$C_{20}H_{21}N_3O_4$	$C_{21}H_{23}N_3O_4$	$C_{18}H_{25}N_3O_4$
Formula weight	367.40	381.42	347.41
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	P2(1)/n	P2(1)	P2(1)/n
a (Å)	13.057(4)	11.735(5)	17.060(7)
b (Å)	8.138(3)	6.212(3)	6.159(3)
c (Å)	17.660(6)	14.612(6)	18.485(8)
α(°)	90	90	90
β (°)	94.412(5)	100.797(7)	103.062(7)
γ(°)	90	90	90
V (Å ³)	1870.8(11)	1046.4(7)	1892.1(14)
Ζ	4	2	4
D _{calc} (g/cm ³)	1.304	1.211	1.220
μ (mm ⁻¹)	0.092	0.085	0.087
Total reflections	9840	5411	9196
Unique reflections	3296	3390	3347
$R_1/wR_2 [I > 2\sigma(I)]$	0.0387/0.0828	0.0337/0.0787	0.0367/0.0947
R_1/wR_2 (all data)	0.0702/0.0959	0.0409/0.0831	0.0527/0.1055
Go F on F ²	1.006	1.026	1.010



Fig. 1. ORTEP view of compound 2 (a), 3 (b) and 4 (c); showing 30% probability displacement ellipsoids with atom numbering.

hydrogen bond (C12–H12···O1, 2.57 Å, 3.43 Å, 153°). Molecules of **3** assembled into 2-D structure through two types helical catemer hydrogen bonding motifs (Fig. 3). The catemer **A** consisted of N1–

 $H1\cdots O1$ hydrogen bonds and the catemer **B** consisted of N2– $H2\cdots O3$ hydrogen bonds. The parameters of the two hydrogen bonds were also listed in Table 2.



Fig. 2. Self-assembly of compound 2 with dimeric N-H--O hydrogen bonding motif.

Table 2Hydrogen bonds parameters in crystals of 2–4.

Compounds	$D{-}H{\cdot}{\cdot}{\cdot}A$	D···A (Å)	H· · ·A (Å)	$\angle D - H \cdot \cdot \cdot A$ (deg)
2	$N2\text{-}H2{\cdots}O3^i$	3.094	2.278	158
	N3−H3···O1 ⁱⁱ	2.805	2.005	154
3	N1−H1···O1 ⁱⁱⁱ	2.919	2.118	155
	N2-H2···O3 ^{iv}	2.903	2.054	169
4	$N1-H1\cdots O2^{v}$	2.831	2.010	159
	N2-H2···O3 ^{vi}	2.921	2.125	154

Symmetry code i: x + 1/2, -y + 1/2, z - 1/2; ii: x - 1/2, -y + 1/2, z + 1/2; iii: -x, y - 1/2, -z; iv: -x, y - 1/2, -z + 1; v: -x, -y + 2, -z; vi: -x - 1/2, y + 1/2, -z + 1/2.

In the solid state, the compound **4**, which also adopt a convergent conformation due to the intramolecular C-H···O hydrogen bond (C3-H3···O3, 2.55 Å, 3.40 Å, 152°), has the similar conformation to compound **3**. Molecules of **4** assembled into 1-D chain through a hydrogen bonding catemer **C** which consisted of N2-H2···O3 hydrogen bonds. The chains form 2-D layer structure with the contribution of a symmetrical $R_2^2(10)$ hydrogen bonding motif (Fig. 4).

3.2. Comparison of the hydrogen bond synthons in crystal structures of **2–4**

In the three crystal structures, the hydrogen bonding synthons in which pyrrole-2-carboxylate moieties involved are $R_2^2(10)$ type dimer (synthon I, Scheme 2) and C(5) type helical catemer (synthon II, Scheme 2). The two kinds of hydrogen bonding motifs are reminiscent of the hydrogen bonding dimer and catemer of carboxylic acid [16], oxime [17] and pyrazole [17-18] compounds. In the crystals of compound 2 and 3, just one kind synthon was observed, synthon I and synthon II, respectively. In the crystal of compound 4, both kinds synthon were found. Obviously, the different synthon resulted from the different substituent groups on nitrogen atom in molecules of 2-4. The change of substituent groups from phenyl in 2 to benzyl in 3 and butyl in 4 caused the sp² hybrid to sp³ hybrid of the nitrogen atom and consequent steric hindrance increasing. Similar substituent effects on the formation of dimer and catemer of carboxylic acid have been reported by Desiraju [19]. The coexistence of synthon I and II in the crystal of compound **4** should ascribed to that butyl group is smaller than



Fig. 3. Self-assembly of compound 3 with helical catemeric N-H---O hydrogen bonding motifs.



Fig. 4. Self-assembly of compound 4 with helical catemeric N-H···O hydrogen bonding motifs and dimeric hydrogen bonding motifs.



Scheme 2. Diagram of synthon I (left) and synthon II (right).

benzyl group. It should be the transition structure of steric hindrance effects on the synthon conversion.

The hydrogen bond energy of synthon **I** and synthon **II** were calculated to evaluate their strength by using DFT calculations. The calculated energy of synthon **I** is about 9.8 kcal/mol for which observed in the crystal of compound **2** and 11.9 kcal/mol for which observed in the crystal of compound **4**. The energies of catemers **A**, **B** and **C** are 6.5, 7.0 and 6.6 kcal/mol, respectively. It means that the hydrogen bonds in the catemer synthon is more stable than that in the dimer synthon. Calculations with PLATON [20] revealed that the available volume for solvent is 6.7% of per unit cell in the crystal **3** and none in the crystal **2**. It indicates that the catemer synthon is geometry disadvantaged which cause loose packing of the pyrrole-2-carboxylate compounds [21]. Self-assembled nanoscale structures of **2–4** were fabricated by the deposition of target compounds from a saturated solution onto clean substrates. Scanning electron microscopy (SEM) studies revealed that distinct morphologies were formed. As shown in Fig. 5, compounds **2** and **4** generated nanorod and block, respectively, while compound **3** formed porous structure. It is consistent with above X-ray structures and PLATON calculation results that the catemer synthon cause the loose packing of molecules.

4. Conclusions

In conclusion, three structural similar pyrrole-2-carboxylate compounds **2–4**, just different in one substituent group, were syn-



Fig. 5. SEM images of (a) 2, (b) 3 and (c) 4.

thesized and their crystal structures were characterized by X-ray crystallography. In the three crystals, the pyrrole-2-carboxylate moieties involve into two kinds of synthons, $R_2^2(10)$ type dimer and C(5) type catemer. DFT calculation rationalized that the catemer synthon is energy more stable but is geometry disadvantaged. Most importantly, a phenomenon of synthon conversion of pyrrole-2-carboxylate, from dimer to catemer, was found with the steric hindrance increasing of the substituted groups and which caused distinct assemblies of **2–4**. This observation would be helpful to obtain desired supramolecular structures by purposefully controlling the molecular structure of pyrrole-2-carboxylate has good perspective on application to crystal engineering.

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