

Dipyrrolylpyrazoles: anion receptors in protonated form and efficient building blocks for organized structures†

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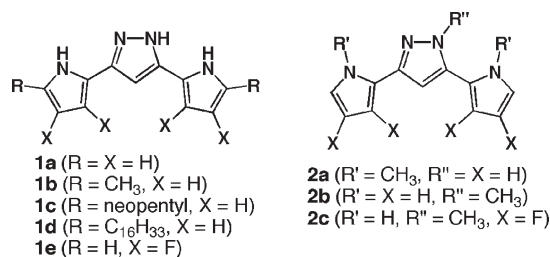
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Synthesis of dipyrrolyl-substituted pyrazoles (dpp) and anion binding studies in protonated form are reported. Dpp show [2 + 2] binding of trifluoroacetate in the solid state to afford nanometer- and micrometer-scale architectures.

Artificial discrete supramolecular structures have been prepared previously by, for example, the association of two complementary subunits,¹ such as that seen in the cooperative cation binding using pyridyl moieties.² However, of the anion binding complexes,^{3,4} only a few examples of discrete aggregates consisting of *multiple* host and guest species have been reported.^{5,6} When compared with the [1 + 1] and [1 + 2] (host + guest) binding modes, the [2 + 2] mode requires assembly of two host and guest units to form new supramolecular structures. Of the known anion receptors, oligopyrrolyl compounds are versatile complexing agents by interactions through their NH moieties.^{3,4} On the other hand, pyrazole can interact electrostatically or through hydrogen bonds with anionic or polar substrates in partly or fully protonated forms.⁷ Therefore, combination of pyrrole and pyrazole groups within one molecule could realize functionality for binding various guest species. The first example of dipyrrolylpyrazole, prepared as an *N*-substituted derivative from 1,3-dipyrrol-2'-yl-1,3-propanedione,^{8,9} was reported by Oddo and Dainotti in 1912.⁸ Recently, we have synthesized a series of dipyrrolyldiketones, which also act as precursors for efficient anion receptors.¹⁰ In this communication, [2 + 2] anion binding complexes of protonated dipyrrolyl-substituted pyrazoles (dpp, **1a–e**) are reported together with nano- and micrometer-scale architectures¹¹ based on the [2 + 2] complexes.

Dipyrrolylpyrazoles (dpp, **1a–e**) were synthesized by condensation of excess hydrazine monohydrate with the corresponding dipyrrolyldiketones^{8–10} in refluxing AcOH for 3–4 days in 63, 25, 81, 29, and 54% yields, respectively. Chemical identities of dpp **1a–e** were confirmed by ¹H NMR and FAB-MS. Proton resonances for rather soluble **1d** appear at 9.42 ppm for its



pyrrolyl NH and 6.50–5.96 ppm for its heterocyclic CH in CDCl₃, but that of the pyrazole NH could not be observed at room temperature or at 0 °C, possibly due to fast proton exchange. In contrast, in DMSO-*d*₆, the signals of each pyrrole in **1a–e** are observed independently and the pyrazole NH appear in the range of 12.40–12.93 ppm. The electronic absorption of π -conjugated dpp in CH₂Cl₂ reaches only to *ca.* 265–280 nm.

The derivative with methyl groups at pyrrole nitrogens, **2a**, was obtained in 6% yield by a similar procedure to that for **1a–e**. On the other hand, pyrazole-N-'blocked' dpp (**2b,c**) were synthesized in 93 and 28% yields, respectively, by methylation of **1a** and **1e**. Like BF₂ complexes of dipyrrolyldiketones as efficient acyclic anion receptors,¹⁰ the 1 : 1 anion binding of **2b,c** was observed through their UV/vis and ¹H NMR spectral changes. From electronic spectral changes in CH₂Cl₂, binding constants for CH₃CO₂[−] were 1600 and 28 000 mol^{−1} dm³ for **2b** and **2c**, respectively. ¹H NMR shifts of **2b** caused by the presence of CH₃CO₂[−] further confirmed the interactions of the bridging pyrazole CH (shift from 6.39 to 7.65 ppm at rt in CDCl₃) and pyrrole NH (shifts from 8.34 and 8.92 to 12.20 and 11.63 ppm, respectively). In sharp contrast to BF₂ complexes, resonances ascribable to the anion-free and binding species of **2b,c** are coalesced to a single pair of signals, implying the fast exchanges between them, possibly due to the 'hemi'-preorganized conformation and low barrier to rotation of the pyrrole rings. On the other hand, in N-free dpp like **1d**, complicated anion binding behaviors were observed in UV/vis absorption and ¹H NMR spectral changes.

The anion binding ability of the pyrrole NH sites drove us to investigate further the details of dpp as a new class of π -conjugated system. In sharp contrast to N-protected dpp, cooperative [2 + 2] binding of N-free dpp with TFA was elucidated by the X-ray analyses of **1a**·TFA, **1b**·TFA, and **1e**·TFA complexes [Fig. 1(a)–(c)].[‡] In the solid state, protonated dpp units (**1a,b,e**·H⁺) form flat structures, illustrating the association with anions by multiple units, where two TFA[−] as counter-anions use *eight* interactions in total to form a [2 + 2] assembly. The distances between N(H)···O of **1a**·TFA, **1b**·TFA, and **1e**·TFA are

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† Electronic supplementary information (ESI) available: Synthetic procedures for **1a–e**, **2a,b**, UV absorption spectral changes by anion binding, optimized structures of **1a** and **1a**·H⁺, and CIF files for the X-ray structural analyses of **1a**₂·(TFA)₂, **1b**₂·(TFA)₂, **1e**₂·(TFA)₂ and **2a**. See DOI: 10.1039/b615787d

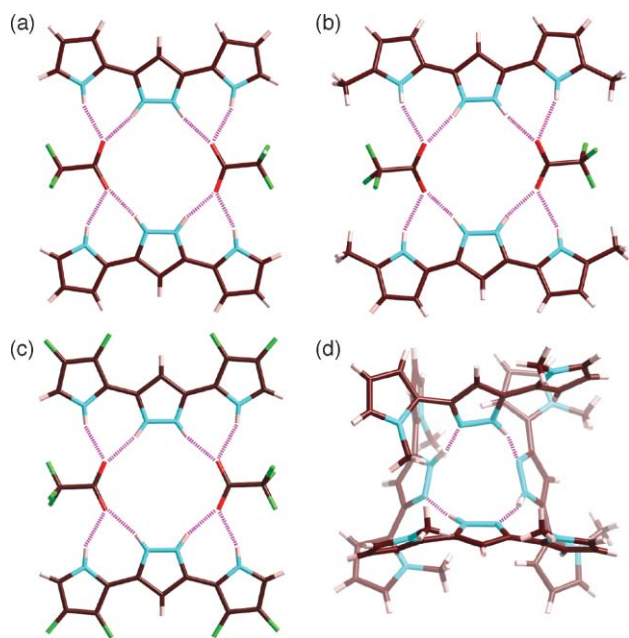


Fig. 1 Complex structures of [2 + 2] assemblies: (a) **1a**₂·(TFA)₂, (b) **1b**₂·(TFA)₂, and (c) **1e**₂·(TFA)₂, and (d) tetrameric assembly of **2a** in the solid state. Atom color code: brown = carbon, pink = hydrogen, blue = nitrogen, red = oxygen and green = fluorine.

2.681(1)–2.848(1), 2.708(3)–2.944(3), and 2.667(3)–2.803(3) Å, respectively, which are within the range of hydrogen bonding interactions,¹² and the distances between the two carboxylate carbons are 6.090, 6.101, and 6.251 Å. The dpp complexes (**1a,b,e**·TFA) exist in almost coplanar conformation, which are implied by the mean plane deviations of 0.082, 0.185, and 0.057 Å, consisting of 36 heavy atoms of six heterocycles and two carboxylates. The deviations of each dpp plane are 0.037 (**1a**·H⁺), 0.054 (**1b**·H⁺), and 0.026 (**1e**·H⁺) Å, respectively. Side alkyl groups seen in **1b** are slightly distorted from planarity. Although helical anion binding assemblies have been reported,^{3,4} the dpp TFA complexes are the first examples of planar geometries bridged by anions. Further, ‘anion’ exchanges of **1a**·TFA by AcO[−] cannot be observed even in the presence of excess AcOH, possibly because of the difference in p*K*_a of the acids (TFA: 0.2; pyrazole·H⁺: 2.5; AcOH: 4.8). On the other hand, the mean plane deviations of anion-free dpp **2a**, distorted by tetrameric self-assembly and N-substituents, were estimated to be 0.31–0.51 Å [Fig. 1(d)].§

DFT calculations of neutral and protonated dpp (**1a,e** and **1a,e**·H⁺) at the B3LYP/6-31G(d,p) level¹³ suggest distorted or flat geometries for each of the optimized structures. In the case of the unsubstituted derivative, one pyrrole ring in **1a** (i) and both in **1a**·H⁺ (ii) are inverted to the side opposing the pyrazole nitrogens in the stable conformation possibly due to the repulsion between NH groups [Fig. 2(a)]. In contrast, the ‘preorganized’ structure (iii), which is suitable for [2 + 2] assembly with two pyrrole NH groups at the same side of pyrazole NH, is 1.42 kcal mol^{−1} less stable than **1a**·H⁺ (ii). Mean plane deviations of (i)–(iii), consisting of 15 atoms, are 0.18, 0.20, and 0.23 Å, respectively, much larger than the TFA complex in the solid state. On the other hand, in the case of fluorinated **1e**, the deviations of (i)–(iii) are 0.00, 0.04, and 0.19 Å, respectively [Fig. 2(b)]. Completely planar **1e** (i),

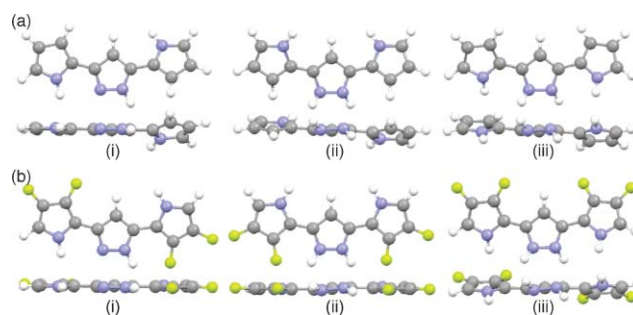


Fig. 2 Optimized structures (top and side view) of (i) neutral, (ii) protonated, and (iii) ‘preorganized’ rather unstable conformations of dpp (a) **1a** and (b) **1e**.

presumably derived from the intramolecular N–H···N and N–H···F interactions, is *ca.* 3.6–7.9 kcal mol^{−1} more stable than the other conformations. Further, the almost flat **1e**·H⁺ (ii) is more stable by 4.38 kcal mol^{−1} than the distorted (iii). From the theoretical studies as shown above, TFA anions bridged by dpp are essential to maintain the orientation of the four nitrogens and planarity.

Association of dpp (**1d** and **1e**) with TFA has been detected by UV/vis absorption spectral changes in CH₂Cl₂, for example, from 283 to 338 nm for **1d** and from 267 to 468 nm for **1e**, respectively, as rather soluble derivatives. Further, a similar trend was observed in fluorescent emission studies of **1d** and **1e** in CH₂Cl₂. The emission of **1d** at 421 nm was enhanced and shifted to 439 nm upon addition of TFA, while, in **1e**, emission at 350 nm was shifted to 398 nm. However, the behaviors in solution, containing protonated dpp as well as possibly [1 + 1] and [1 + 2] assemblies, *etc.*, were too complicated to be analyzed further.

By casting TFA complexes of dpp in CH₂Cl₂, organized structures could be observed by scanning electron microscopy (SEM) analysis. TFA complexes of unsubstituted and α -methyl-substituted dpp **1a,b** give crystalline objects. In sharp contrast, **1c** and **1d** with neopentyl and C₁₆H₃₃ chains provide petal-like objects with *ca.* 500 nm width and assembled sheet structures with <100 nm thickness, respectively [Fig. 3(a),(b)]. IR spectroscopy of **1d**·TFA (KBr pellet) displays CH₂ stretching vibrations at 2850 (*v*_{sym}) and 2919 (*v*_{asym}) cm^{−1}, which suggest the *trans*-rich geometry of C₁₆H₃₃ units. Further, β -fluorinated **1e**·TFA shows rod-like morphologies with a width of *ca.* 100–200 nm [Fig. 3(c)] as well as small amounts of microcrystals. On the other hand, TFA complexes of N-blocked **2a,b** as well as ‘anion-free’ **1b–d** show only random and amorphous structures, which imply the association with TFA as the bridging moieties between dpp planes makes possible the formation of nanometer- and micrometer-scale objects. Complexation with acid would give the planar geometry of dpp for the formation of nanometer- and micrometer-scale morphologies using intermolecular interactions such as π – π stacking, observed in the X-ray structures of **1a,b,e**·TFA. Interestingly, acid-free **1e** constructs the fibrous networks [Fig. 3(d)] possibly because of its planarity as estimated by theoretical study.

If TFA is replaced by the less acidic AcOH, sheet-like architectures form from CH₂Cl₂ solution of C₁₆-substituted **1d** [Fig. 3(e)]. In contrast, α -methyl **1b** and α -neopentyl **1c** do not show any ordered structures. On the other hand, **1e** shows the

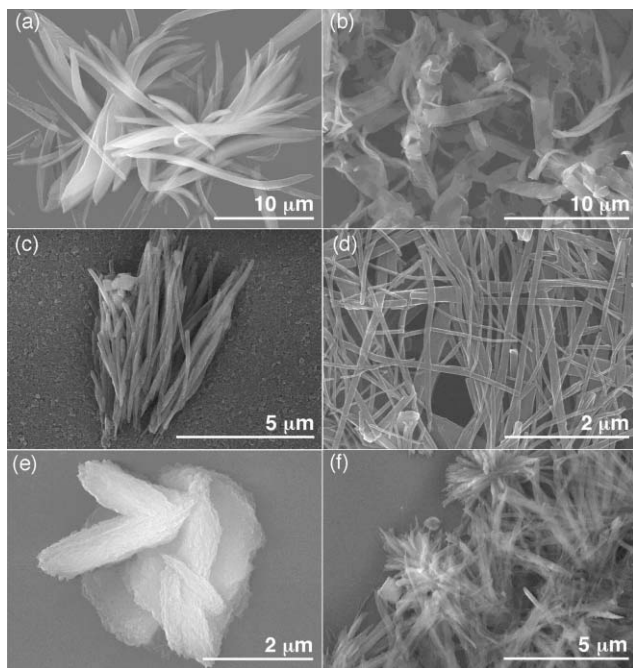


Fig. 3 Scanning electron micrographs (SEM) of (a) **1c**·TFA, (b) **1d**·TFA, (c) **1e**·TFA, (d) acid-free **1e**, (e) **1d**·AcOH, and (f) **1e**·AcOH from CH₂Cl₂.

similar rods or fibers [Fig. 3(f)] as seen in its TFA complex [Fig. 3(c)]. While the interactions of TFA and AcOH complexes may be different, *i.e.* charged hydrogen bonding between cation (host) and anion (guest) and neutral ones between base (host) and acid (guest), supramolecular assemblies could be obtained, possibly assisted by other intermolecular interactions.

In summary, the planar cooperative anion binding self-assemblies of protonated dipyrrolylpyrazoles (dpp) and carboxylates have been elucidated by SEM analysis (nanometer- and micrometer-scale) as well as by X-ray crystallography (molecular level). Dpp are potential functional subunits for π -conjugated polymers and larger macrocyclic systems. Efforts to generate such systems are in progress.

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Notes and references

‡ *Crystal data for 1a*·TFA (from CH₂Cl₂/hexane): C₁₁H₁₁N₄·C₂O₂F₃, $M_w = 312.26$, $P2_1/c$ (no. 14), $a = 14.3569(10)$, $b = 15.2520(11)$, $c = 6.0571(4)$ Å, $\beta = 91.1800(10)^\circ$, $V = 1326.05(16)$ Å³, $Z = 4$, $D_c = 1.564$ g cm⁻³, $\mu(\text{MoK}\alpha) = 0.137$ mm⁻¹, reflections collected = 8027, independent reflections = 3018 ($R_{\text{int}} = 0.0175$), $R_1 = 0.0411$, $wR_2 = 0.1095$, GOF = 1.133 [$I > 2\sigma(I)$]. CCDC 625142. *Crystal data for 1b*·TFA (from

CH₂Cl₂/hexane): C₁₃H₁₅N₄·C₂O₂F₃, $M_w = 384.23$, $P\bar{1}$ (no. 2), $a = 8.307(5)$, $b = 9.278(6)$, $c = 10.960(8)$ Å, $\alpha = 85.90(3)$, $\beta = 87.73(3)$, $\gamma = 65.63(2)^\circ$, $V = 767.5(9)$ Å³, $Z = 2$, $D_c = 1.472$ g cm⁻³, $\mu(\text{MoK}\alpha) = 0.125$ mm⁻¹, reflections collected = 7620, independent reflections = 3484 ($R_{\text{int}} = 0.0264$), $R_1 = 0.0624$, $wR_2 = 0.1748$, GOF = 1.089 [$I > 2\sigma(I)$]. CCDC 625143. *Crystal data for 1e*·TFA (from CH₂Cl₂/hexane): C₁₁H₇N₄F₄·C₂O₂F₃, $M_w = 384.21$, $P2_1/c$ (no. 14), $a = 7.200(4)$, $b = 24.567(1)$, $c = 8.844(3)$ Å, $\beta = 111.44(2)^\circ$, $V = 1456(1)$ Å³, $Z = 4$, $D_c = 1.752$ g cm⁻³, $\mu(\text{MoK}\alpha) = 0.181$ mm⁻¹, reflections collected = 12 803, independent reflections = 3170 ($R_{\text{int}} = 0.0403$), $R_1 = 0.0663$, $wR_2 = 0.1768$, GOF = 1.085 [$I > 2\sigma(I)$]. CCDC 625144. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b615787d.

§ *Crystal data for 2a* (from CH₂Cl₂/hexane): C₁₃H₁₄N₄, $M_w = 226.28$, $C2/c$ (no. 15), $a = 16.129(5)$, $b = 16.450(4)$, $c = 36.383(9)$ Å, $\beta = 90.02(1)^\circ$, $V = 9653(4)$ Å³, $Z = 32$, $D_c = 1.245$ g cm⁻³, $\mu(\text{MoK}\alpha) = 0.078$ mm⁻¹, reflections collected = 45 036, independent reflections = 10 976 ($R_{\text{int}} = 0.1009$), $R_1 = 0.0870$, $wR_2 = 0.2030$, GOF = 1.022 [$I > 2\sigma(I)$]. CCDC 625145. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b615787d.

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