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Synthesis and Self-Assemblies of Bithiophene Functionalized 1*H*-Pyrazole Derivatives

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Over the last decades, a great deal of attention has been devoted to synthesis, analysis, and applications of functional and high-dimensional supramolecular systems.[1-4] In general, these suprastructural entities are built from small molecular building blocks, connected *via* various secondary intermolecular forces. These include, without limitations, hydrogen bonding, electrostatic, hydrophobic, electron donor-acceptor, π–π, CH–π, and Van der Waals interactions. It is thus well recognized nowadays that the strength, directionality, and reversibility offered by these secondary interactions between discrete molecular building blocks are responsible for controlling molecular self-assemblies as well as their functionalities. Among various types of non-covalent intermolecular interactions, the hydrogen bond is one of the most important and pervasive intermolecular forces playing a key role in determining and controlling the assembly of many biological and artificial functional materials.[5-7]

Among a variety of hydrogen-bonding functional groups, 1*H*-pyrazole derivatives are a class of five-membered nitrogen heterocyclic ring compounds, containing a hydrogen-bond donor (N-H) and acceptor (N) in adjacent positions. In recent years, growing interest has been paid to studies on self-assemblies of a variety of pyrazole derivatives involving directional inter- and intra-molecular hydrogen bonding interactions.[8-11] One of the main reasons for these studies is to understand the factors that appear to govern the formation of hydrogen bond patterns in pyrazole derivatives since the core moiety in these derivatives is able to self-assemble and form a wide variety of superstructures. In fact, as shown in Figure 1, it has been observed from X-ray crystallographic analyses of pyrazole derivatives that various types of hydrogen bonding networks were formed, including dimers, trimers, tetramers, hexamers, and infinite chains (known as catemers) as a consequence of the intermolecular N–H···N hydrogen bonding interactions.[12-15] Recently, it has been also suggested that the nature of the substituents at C3 and C5 positions in terms of steric and polarizability effects appears to control hydrogen bonding motifs and secondary structures while those at C4 position appear to affect mainly the tertiary and quaternary structures.[12,16]

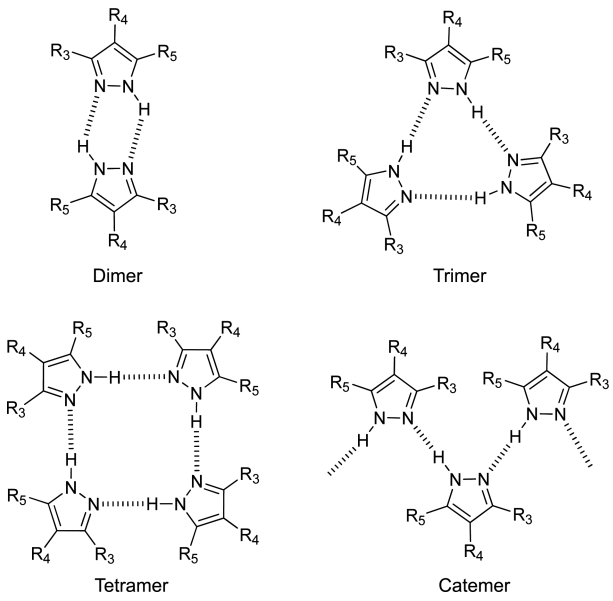
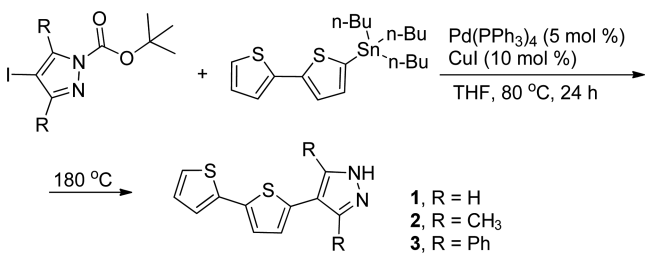


Figure 1. Various hydrogen bonding patterns found in 1*H*-pyrazole derivatives.

Here, as a part of our ongoing research on studying supramolecular, organic, and inorganic functional materials, we report synthesis of a series of new 2,2'-bithiophene functionalized N-unsubstituted pyrazole derivatives, their primary and secondary structures, and photochemical properties, UV/Vis absorption and fluorescence spectra. The bithiophene moiety was substituted at the 4-position of pyrazole ring to produce extended conjugated systems for potential optoelectronic applications as well as new building blocks for synthesis of pyrazolyl based multi-dentate ligands and the corresponding metal complexes.[17-20] Furthermore, we are particularly interested in examining the effects of such substitution on the intermolecular hydrogen bonding modes, comparing with their parent 4-unsubstituted pyrazole derivatives.

A series of the 2,2'-bithiophene conjugated pyrazole derivatives 4-(2,2'-bithiophen-5-yl)-1*H*-pyrazole **1**, 4-(2,2'-



Scheme 1. Synthetic procedure for **1-3**.

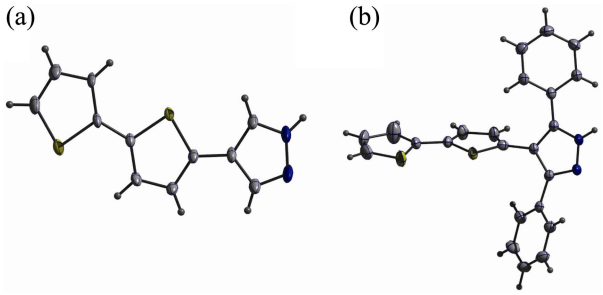


Figure 2. Molecular structures of **1** (a) and **3** (b). Displacement ellipsoids are drawn at 50% probability level.

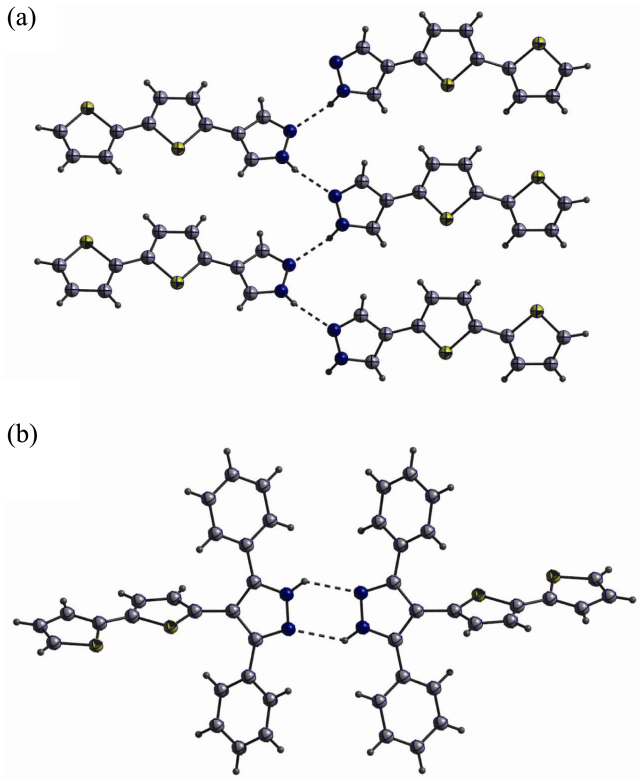


Figure 3. View of hydrogen bonding patterns of **1** (a) and **3** (b), displaying catemer (top) and dimer motifs (bottom) respectively.

bithiophen-5-yl)-3,5-dimethyl-1*H*-pyrazole **2**, and 4-(2,2'-bithiophen-5-yl)-3,5-diphenyl-1*H*-pyrazole **3** were systematically synthesized by Pd-catalysed Stille cross-coupling reactions of three 1-Boc-4-iodo pyrazole derivatives with [2,2'-bithiophen]-5-yltributylstannan, as shown in Scheme 1. The resulting cross coupling products **1-3** were thoroughly characterized by means of ^{1}H- and ^{13}C-NMRs, mass spectrometry, and single crystal X-ray crystallographic analyses. It should be noted that a catalytic amount of copper(I) iodide is necessary to obtain the cross-coupled products **1-3**, otherwise the yields of the desired products significantly reduced to less than 10%.

Single crystals of **1** and **3** suitable for X-ray diffraction analysis were grown by slow diffusion of hexane into a solution of **1** or **3** in tetrahydrofuran. The resulting molecular structures of **1** and **3** are displayed in Figure 2. X-ray crystallographic analysis reveals that the complex **1**, having hydrogen atoms at 3- and 5-position of pyrazole ring, adopts nearly planar configuration, where the angle defined by mean planes of the pyrazole ring and neighbor thiophene rings is 2.1°. However, in the case of the complex **3**, the neighbor thiophene ring is rotated with respect to the pyrazole ring plane by 68.4°, showing evidence for largely disrupted conjugation between the pyrazole and bithiophene moieties. It is also worthy of noting that two phenyl substituents are severely deviated from the planarity by an angle of 28.4° for 3-position and 34.3° for 5-position. These structural characteristics of the compound **3** can be explained by severe steric crowding of three aryl substituents attached to three neighboring carbon atoms in the pyrazole ring.

In order to investigate effects of bithiophene attachement on intermolecular hydrogen bonding motif, the secondary structures of **1** and **3** are examined (Figure 3(a) and Figure 3(b)). The N–H of the pyrazole in both **1** and **3** is engaged in hydrogen bonding interactions with the nearest-neighbor N atom in another molecule as evidenced by short hydrogen bonding distance of 2.88 Å for **1** and 2.90 Å for **3** respectively. Through this N–H···N hydrogen bonding interaction, the complex **1** forms a polymeric chain-like structure known as a catemer similar to that found in the unsubstituted parent pyrazole ($C_3N_2H_4$).[21,22] However, it is worth noting that their tertiary structures are clearly different from each other, where the former adopts a two-fold helical arrangement while the latter displays a four-fold helical structure. Although it was unsuccessful in obtaining publication-quality X-ray data of the complex **2**, it is confirmed that the complex **2** display a catemeric hydrogen-bond motif in the solid state. This is significantly different from that of its precursor, 3,5-dimethylpyrazole showing a trimeric structure (S-Figure 1 in Supporting Information). In the case of the complex **3**, a dimeric structure was found in the solid state. This striking difference in hydrogen bonding modes between **1** and **3** can be explained by the previous experimental observations as well as theoretical calculations that pyrazole derivatives with small substituents at 3- and 5-position have a tendency to form trimers or catemers while those with small substituents give rise to produce dimers or tetramers.[12,16] However, the hydrogen bonding motif in the compound **3**, a dimeric structure is different from its parent compound (3,5-diphenylpyrazole), displaying a cyclic tetramer with tetrahedral geometry.[23] This is possibly due to the change in steric and polarizability effects caused by bulky aryl substitution at 4-position of the pyrazole ring.[12,16]

UV-Vis absorption and fluorescence emission spectra were measured to study electronic and optical properties of the compounds **1-3**. It is observed from our X-ray crystallographic studies that the degree of deviation from the planarity between pyrzole and bithiophene fragments is increased as the substituent size at 3- and 5-position of pyrazole ring is enlarged. It is thus anticipated that this would certainly lead to lesser degrees of pi-conjugation between two aromatic systems. As displayed in Figure 4, the complex **3** exhibits the shortest λ_{max} absorption wavelength (325 nm), followed

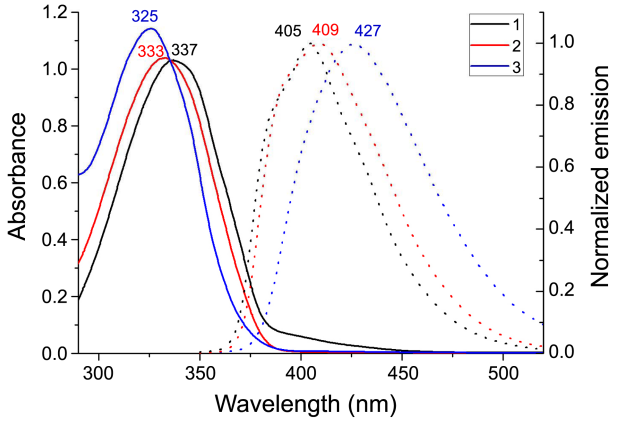


Figure 4. Absorption and emission spectra of **1-3** in dichloromethane at room temperature.

by **2** (333 nm) and **1** (337 nm). This observation is consistent with the relationship between planarity and degrees of conjugation enforced by steric bulkiness of the substituents in the compounds **1-3**. The fluorescence emission spectra of the complex **1-3** upon the irradiation of their corresponding absorption λ_{max} were also measured to characterize the luminescent properties of the compounds **1-3**. The resulting emission spectra are also displayed in Figure 4. The solution phase emission spectra for **1-3** show single emission bands in the near-UV and blue regions (from 360 nm and 560 nm). Interestingly, the complex **3** display the largest red shifted emission band centered at 427 nm ($\Delta\lambda$ = 102 nm) with respect to its maximum absorption λ_{max}, followed by the complex **2** ($\Delta\lambda_{max}$ = 76 nm) and **1** ($\Delta\lambda_{max}$ = 65 nm). Accordingly, the emission λ_{max} is the reverse order of their absorption λ_{max} likely due to change in the geometry of the emitting state following excitation.[24]

In summary, three new bithiophene functionalized pyrazole derivatives were successfully prepared by Pd-catalyzed Stille cross-coupling reactions in good yields and their molecular structures were determined by X-ray single crystallographic analyses. In the solid state, these pyrazole derivatives were self-assembled by intermolecular N–H···N hydrogen bonding interactions. It is found that attachment of 2,2'-bithiophene at 4-position of pyrazole ring causes the change in hydrogen bonding patterns in either the secondary or tertiary structure from the parent pyrazole derivatives. In addition, absorption and emission characteristics of the complex **1-3** were investigated. It is found that the observed absorption λ_{max} is related to the steric factor of substituents on 3,5-postion of pyrazole ring causing distortion from planarity between two aromatic systems.

Experimental

All reactions were carried out under an inert atmosphere of argon. THF was distilled from sodium with benzophenone. Dichloromethane and DMF were distilled over CaH_2. $Pd(PPh_3)_4$ and CuI were purchased from Aldrich and used without further purification. The compounds, 2,2'-bithiophen-5-yltributylstannane, *tert*-butyl 4-iodo-1*H*-pyrazole-1-carboxylate, *tert*-butyl 4-iodo-3,5-dimethyl-1*H*-pyrazole-1-carboxylate, and *tert*-butyl 4-iodo-3,5-diphenyl-1*H*-pyrazole-1-carboxylate were synthesized according to the reported procedures.[25,26] NMR spectra were recorded on a Varian Inova 400 MHz FT-NMR spectrometer at ambient temperature.

Synthesis of 4-([2,2'-Bithiophen]-5-yl)-1*H*-pyrazole (1). A mixture of 2,2'-bithiophen-5-yltributylstannane (5.02 g, 11 mmol), *tert*-butyl 4-iodo-1*H*-pyrazole-1-carboxylate (2.94 g, 10 mmol), $Pd(PPh_3)_4$ (0.58 g, 0.5 mmol), and CuI (0.19 g, 1 mmol) in 50 mL of THF was stirred for 24 h under reflux condition and then cooled to room temperature. The solvent removed by vacuum and the residue was heated for 30 minutes under vacuum at 180 °C. After cooling at room temperature, purification of the product by flash column chromatography (SiO_2: *n*-hexanes/DCM) provided the corresponding product **1** in 65% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.09 (s, 1H), δ 7.97 (br s, 2H), δ 7.45 (dd, J = 5.1, 1.1 Hz, 1H), δ 7.24 (dd, J = 3.6, 1.1 Hz, 1H), δ 7.21 (d, J = 3.7 Hz, 1H), δ 7.16 (d, J = 3.7 Hz, 1H), δ 7.06 (dd, J = 5.1, 3.6 Hz, 1H); ^{13}C NMR (101 MHz, DMSO) δ 136.7, 134.5, 133.3, 128.3, 124.9, 124.6, 123.5, 123.2, 115.0; HRMS (ESI) *m/z* calcd. for $C_{11}H_8N_2S_2$ $[MH]^+$ 233.0207; found 233.0096.

Synthesis of 4-([2,2'-Bithiophen]-5-yl)-3,5-dimethyl-1*H*-pyrazole (2). The reaction procedures was similar to the preparation of compound **1** except using *tert*-butyl 4-iodo-3,5-dimethyl-1*H*-pyrazole-1-carboxylate instead of *tert*-butyl 4-iodo-1*H*-pyrazole-1-carboxylate. (Yield 59%) ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.49 (s, 1H), δ 7.46 (dd, J = 5.1, 1.0 Hz, 1H), δ 7.30-7.22 (m, 2H), δ 7.07 (dd, J = 5.1, 3.6 Hz, 1H), δ 6.94 (d, J = 3.7 Hz, 1H), δ 2.30 (s, 6H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 145.4, 136.6, 135.0, 134.01, 128.3, 124.9, 124.9, 124.3, 123.5, 110.1, 13.4, 10.5; HRMS (ESI)

Table 1. Crystallographic data for **1** and **3**

	1	**3**
Empirical formula	$C_{11}H_8N_2S_2$	$C_{23}H_{16}N_2S_2$
Formula weight	232.31	384.50
Temperature (K)	125(2)	125(2)
Wavelength (Å)	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1$	$P2_1/n$
a (Å)	9.863(2)	12.758(3)
b (Å)	5.6200(11)	9.2814(19)
c (Å)	12.301(3)	16.324(3)
β (°)	109.79(3)	106.06(3)
V (Å^3)	641.6(2)	1857.5(7)
Z	2	4
D_{cald}(Mg/m^3)	1.203	1.375
Absorption coefficient (mm^{-1})	0.385	0.297
Reflections collected/ unique	6055 / 2003	12394/3268
	R(int) = 0.0339	R(int) = 0.0480
Goodness-of-fit on F2	1.102	1.018
Final R indices [I > 2σ(I)]	R_1 = 0.0336	R_1 = 0.0434
	wR_2 = 0.0815	wR_2 = 0.1054
R indices (all data)	R_1 = 0.0378	R_1 = 0.0523
	wR_2 = 0.0845	wR_2 = 0.1109

m/z calcd. for $C_{13}H_{12}N_2S_2$ $[MH]^+$ 261.0520; found 261.0408.

Synthesis of 4-([2,2'-Bithiophen]-5-yl)-3,5-diphenyl-1*H*-pyrazole (3). The reaction procedure was similar to the preparation of compound **1** except using *tert*-butyl 4-iodo-3,5-diphenyl-1*H*-pyrazole-1-carboxylate instead of *tert*-butyl 4-iodo-1*H*-pyrazole-1-carboxylate. (Yield 49%) ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.59 (s, 1H), δ 7.52 (m, 4H), δ 7.46 (dd, J = 5.1, 0.9 Hz, 1H), δ 7.37 (m, 6H), δ 7.26 (d, J = 3.6 Hz, 1H), δ 7.24 (dd, J = 3.6, 0.9 Hz, 1H), ä 7.04 (dd, J = 5.1 , 3.6 Hz, 1H), δ 6.92 (d, J = 3.7 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 137.3, 136.4, 133.5, 129.8, 129.0-128.4 (br), 128.3, 127.4, 125.3, 125.1, 124.2, 123.9, 108.3, 99.6; HRMS (ESI) *m/z* calcd. for $C_{23}H_{16}N_2S_2$ $[MH]^+$ 385.0833; found 385.0685.

X-ray Crystallography. All X-ray crystallographic data were collected on a Nonius Kappa CCD diffractometer using a graphite monochromator with MoK_α radiation (λ = 0.71073 Å). The data were collected at 153 K using an Oxford Cryostream low temperature device. Details of crystal data, data collection and structure refinement are listed in Table 1. Data reductions were performed using DENZO-SMN.[27] The structure was solved by direct methods and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-H atoms using SHELXL-97.[28] The hydrogen atoms were calculated in ideal positions with isotropic displacement parameters set to 1.2xUeq of the attached atom (1.5 × Ueq for methyl hydrogen atoms). All the calculations were carried out with the SHELXTL program.[29]

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Supporting Information. Further details of the individual structures can be obtained from the Cambridge Crystallographic Data Centre by quoting reference numbers CCDC 969009 for **1** and CCDC 969010 for **3**.

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