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Synthesis, Solid State Structures, and Properties of Linear and Tripodal Flexible Molecules with Pyrazinopyrazine Moieties

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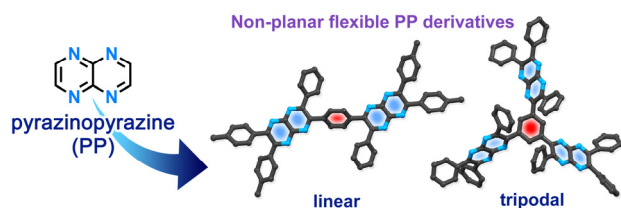
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Abstract

Pyrazino[2,3-*b*]pyrazine (PP), which is a naphthalene analogue with iminium nitrogen atoms at 1,4,5,8-positions instead of sp^2 -carbon atoms, is attractive as a building block for nitrogen-highly-contained π -conjugated systems. In this study, we synthesized PP-based linear and tripodal molecules, in which PP moieties are bonded with the central benzene ring at 1,4-positions and 1,3,5-positions, respectively, giving conformationally flexible and moderately π -conjugated molecules. It is noteworthy that the tripodal one forms unique interdigitated dimer with a small cavity in a crystalline state because of flexible tripodal molecular shape.

Keywords: pyrazinopyrazine, heterocyclic compound, flexibility, crystal engineering

Graphical abstract



Linear and tripodal flexible π -conjugated molecules possessing two and three pyrazino[2,3-*b*]pyrazine units were synthesized. Their photophysical properties in solutions, crystal structures, and acid responsiveness are presented.

1 Nitrogen-containing polycyclic aromatic hydrocarbons
 2 (N-PAHs) such as pyrazinacenes have been actively
 3 investigated because of their characteristic properties
 4 including electron accepting capacity, photo-luminescence,
 5 and responsiveness against cationic species.¹ Particularly,
 6 pyrazino[2,3-*b*]pyrazine (PP) (**1**), which is a naphthalene
 7 analogue with iminium nitrogen atoms at 1,4,5,8-positions
 8 instead of sp^2 -carbon atoms, is one of the simplest N-PAHs,
 9 and therefore, is attractive as a building block of nitrogen-
 10 highly-contained π -conjugated systems.² Tadokoro and co-
 11 workers synthesized tetraazatetracene and tetraazapentacene
 12 and showed that they can be electron acceptors that act as *n*-
 13 type semiconductors.³ Richards and co-workers reported
 14 that protonation and deprotonation significantly changed the
 15 absorption spectrum of tetradecaazadihydroheptacene.⁴
 16 Bonifazi and co-workers prepared polymeric
 17 supramolecular architectures using tetraazananthracene and
 18 boronic acids.⁵ PP-based liquid crystalline materials⁶ and
 19 hydrogen-bonded organic frameworks⁷ were also reported.
 20 In many systems, a PP moiety was annulated to other
 21 aromatic rings to achieve shape persistent rigid molecules
 22 with highly extended π -conjugation.

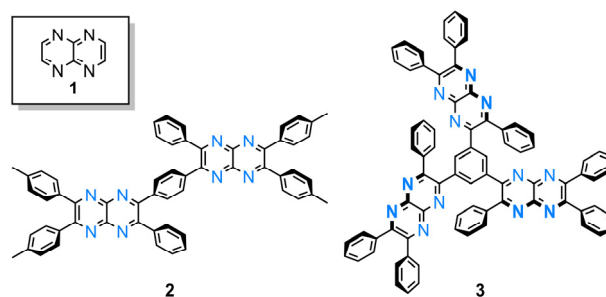
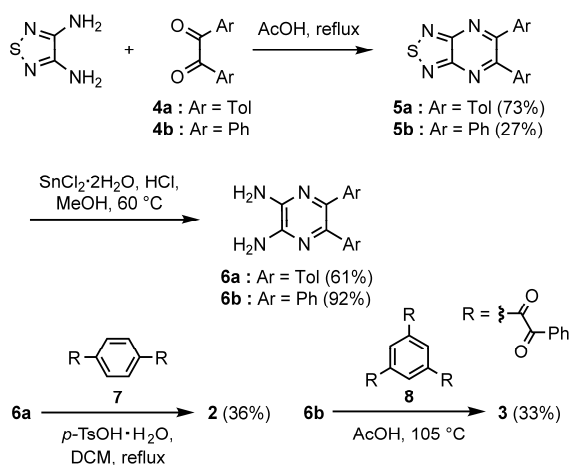


Fig. 1 Pirazinopyrazine **1** and its accumulated derivatives **2** and **3**.

23 In this study, on the other hand, we were interested in
 24 PP-accumulated molecules possessing flexible molecular
 25 conformation and moderate π -conjugation. Herein, we
 26 report synthesis, solution properties, crystal structures, and
 27 responses to HCl of flexible PP-accumulated π -conjugated
 28 molecules **2** and **3** (Fig. 1), in which multiple PP moieties
 29 are singly bonded to the central benzene ring. It is revealed
 30 that non-planar tripodal **3** shows blue-shifted absorption and
 31 red-shifted emission spectra compared to linear **2** that has a
 32 co-planar arrangement of two PP moieties. Moreover, **3**

1 forms interlocked dimers in a crystalline state. These
2 behaviors are characteristic for flexible PP derivatives,
3 particularly for **3**, suggesting the possibility of a new family
4 of N-PAH compounds.

5 Synthesis of **2** and **3** is shown in Scheme 1. 2,3-
6 Diamino-5,6-tolyl-pyrazinopyrazine (**6a**) was prepared by
7 reduction of **5a**, which was synthesized by condensation of
8 1,2,5-thiadiazole-3,4-diamine and benzyl derivative **4a**.
9 Similarly, **6b** was obtained according to the procedure
10 reported in literature.⁸ Diaminopyrazinopyrazine derivative
11 **6a** was reacted with 2,2'-(1,4-phenylene)bis(1-
12 phenylethane-1,2-dione) (**7**)⁹ to give linear PP-accumulated
13 molecule **2**. Diaminopyrazinopyrazine derivative **6b** was
14 reacted with 2,2',2''-(benzene-1,3,5-triyl)tris(1-
15 phenylethane-1,2-dione) (**8**)¹⁰ to give tripodal PP-
16 accumulated molecule **3**.



Scheme 1. Synthesis of **2** and **3**

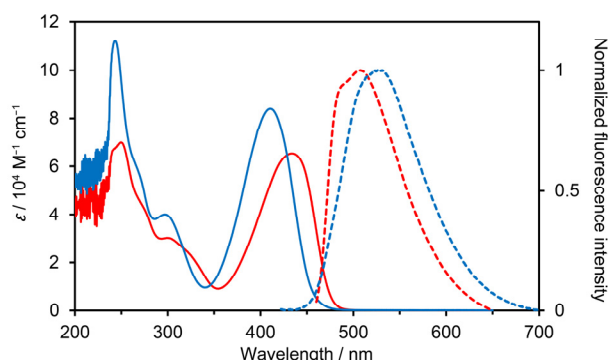


Fig. 2 Absorption (solid line) and fluorescence (dash line) spectra of linear **2** (red) and tripodal **3** (blue) in chloroform. λ_{ex} = 453 nm for **2** and 405 nm for **3**.

17 Fig. 2 shows UV-vis absorption and fluorescence
18 spectra of **2** and **3** in chloroform. Linear **2** has an absorption
19 band at 434 nm, while tripodal **3** has a band at 410 nm,
20 which is blue-shifted by 24 nm compared to that of **2**. This
21 difference causes from a meta-substituted skeleton and non-
22 planar conformation of **3**, both of which prevent effective π -
23 conjugation. Linear **2** shows a weak structureless
24 fluorescence band at 508 nm, while **3** shows the band at 526

25 nm red-shifted by 18 nm compared to that of **2**. This trend
26 of the fluorescence spectra is opposite to that of the
27 absorption spectra. These results indicate that **3** has a more
28 flexible molecular skeleton than **2** and is allowed to undergo
29 conformational relaxation at the excited state. Both of **2** and
30 **3** show very low fluorescence quantum yields ($\phi_{\text{em}} < 1\%$).

31 The redox properties of **2** and **3** were evaluated by cyclic
32 voltammetry (CV) and differential pulse voltammetry
33 (DPV) in THF solutions of 0.1 M *n*-Bu₄NBF₄ (Figs. S1 and
34 S2). The CV of **2** showed two reversible overlapped
35 reduction waves, followed by one irreversible wave. The
36 DPV results of **2** clarified that the observed first two redox
37 processes consisted of two successive steps ($E_1 = -1.51$ and
38 $E_2 = -1.57$ V vs Fc/Fc⁺) with a very small potential splitting
39 ($\Delta E = 0.06$ V), indicating a weak electronic communication
40 between the two PP moieties. Similarly, the CV of **3** showed
41 reversible overlapped reduction waves, as well as one
42 irreversible wave. The DPV revealed that two PP and the
43 other PP moieties experienced one electron reduction at
44 -1.46 and -1.61 V vs Fc/Fc⁺, respectively, also indicating
45 weak interactions among the three PP moieties in **3**.

46 To explore their solid-state structures, each of **2** and **3**
47 was recrystallized by slow evaporation of
48 chloroform/acetone mixed solutions, yielding platelet small
49 crystals of **2** and block crystals of **3** (Fig. S3) suitable for
50 single crystalline X-ray diffraction analysis (Table S1).
51 Linear **2** was crystallized in the space group *P*-1 (Fig. 3). A
52 half of the molecule is crystallographically independent, and

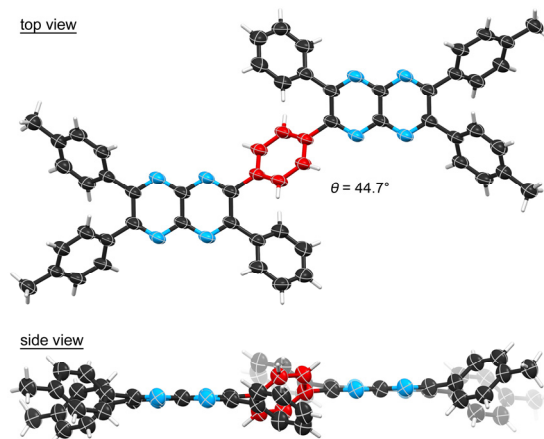


Fig. 3 Crystal structure of **2** drawn by isotropic displacement ellipsoids with 50% probability. The central benzene ring is colored by red.

Table 1. Structural parameters for flexibility.

	2 _{obs} ^a	2 _{calc} ^b	3 _{obs} ^c	3 _{calc} ^b
$\theta^d / ^\circ$	44.1	37.4–42.2	42.5–54.3	38.9–43.4
$\omega_{\text{in}}^e / ^\circ$	35.7	37.7–42.4	40.8–76.0	39.7–44.6
$\omega_{\text{out}}^f / ^\circ$	17.8–48.6	37.1–41.5	24.2–85.6	37.8–42.4

[a] Molecular conformation in crystal of **2**. [b] Geometrically optimized structure calculated at CAM-B3LYP/6-311G** level of theory. [c] Molecular conformation in crystal **3**-(acetone-CHCl₃). [d] Dihedral angle between planes of the central benzene ring and PP moiety. [e] Dihedral angle between planes of the PP moiety and inner phenyl groups. [f] Dihedral angle between planes of the PP moiety and outer tolyl groups.

1 therefore, the molecule has an inversion center at the central
 2 benzene ring. Two PP groups of **2** have a nearly co-planar
 3 arrangement. The central benzene ring is twisted by 44.1°
 4 against the PP planes. The outer four tolyl groups of **2**
 5 twisted from the PP groups by 47.8° – 48.6° , while the inner
 6 phenyl groups did by 35.7° . These conformational
 7 parameters are similar to these of theoretical structure
 8 optimized in vacuum (Tables 1 and S2). Because of the
 9 twisted aryl groups, π/π stacking between the PP moieties is
 10 limited, on the other hand, the PP moiety has edge-to-face
 11 contacts with the peripheral aryl groups and the central
 12 benzene ring (Fig. S4). Namely, the nitrogen atoms in the
 13 PP parts participate in formation of CH/N interactions with
 14 the phenylene group with a H \cdots N distance of 2.58 Å and a
 15 C–H–N angle of 165.7° and CH/N interactions with the
 16 methyl groups in the peripheral tolyl groups with a N \cdots H
 17 distance of 2.49 Å and a C–H–N angle of 156.1° . Interlayer
 18 distances of the neighboring molecules are 3.52 Å and 3.74
 19 Å, which are longer than that of a typical π/π stacked
 20 structure (Fig. S5). The crystal structure of **2** has small,
 21 discrete voids located near by the peripheral phenyl groups
 22 and N atoms of the PP moieties (Fig. S6).

23 Tripodal **3** was crystallized in the space group $P31c$. The
 24 resultant crystal **3**·(acetone-CHCl₃) consists of two
 25 independent molecules (A and B) of **3** and at least one
 26 acetone and one chloroform molecules. Some of peripheral
 27 phenyl groups are crystallographically disordered because
 28 of high degree of conformational freedom (Fig. S7). The
 29 structure of **3**·(acetone-CHCl₃) is shown in Fig. 4. The
 30 molecules have a quasi- C_3 symmetric nonplanar
 31 conformation with *P*- or *M*-helicity. Three PP groups are
 32 twisted from the central benzene ring by 46.3° to 51.4° for
 33 molecule A (Fig. 4a) and 42.5° to 54.3° for molecule B
 34 (Table S3). Basically, molecules A and B have similar
 35 molecular conformation to each other. Dihedral angles

36 between the inner phenyl groups and the PP groups range
 37 from 40.8° to 76.0° , which are more varied than those of
 38 theoretical structure optimized in vacuum, i.e. 39.7° – 44.6° ,
 39 due to packing force. Similarly, dihedral angles between the
 40 outer phenyl groups and the PP groups have wide range of
 41 values from 30.7° to 85.6° .

42 Interestingly, tripodal molecules A and B with the same
 43 helicity form an interdigitated dimer (Fig. 4b). The
 44 staggered angle of the central benzene rings of the two
 45 molecules forming the dimer is 18.4° , although the benzene
 46 rings are not perfectly parallel. The distance between the
 47 centroids of the benzene rings is 3.94 Å. This distance is so
 48 far apart that the π - π interactions are completely negligible,
 49 while there is no enough space to encapsulate a guest
 50 molecule. This “non-utilizable” space seems to be a
 51 characteristic of the present system. The dimer structure is
 52 supported by intermolecular interactions involving the
 53 peripheral phenyl groups, such as CH/ π interactions
 54 between the peripheral phenyl groups (denoted by 1, 2, 3)
 55 and CH/N interactions between and the phenyl group and
 56 PP moiety (denoted by 4). Fig. 4c shows relative orientation
 57 of three sets stacked PP moieties observed in the dimer. In
 58 these cases, the PP moieties are stacked with a center-to-
 59 center distance ranging from 3.39 Å to 3.74 Å and a
 60 staggered angle ranging from 75° to 80° . The dimers with
 61 the same helicity are then gathered with three-fold axis to
 62 give a chiral sheet structure parallel to the *ab* plane, while a
 63 neighboring sheet has the opposite chirality, resulting
 64 entirely achiral crystal structure (Fig. S8). In the crystal
 65 structure of **3**·(acetone-CHCl₃), trefoil-shaped inclusion
 66 spaces are connected through a narrow bottleneck, forming
 67 a two-dimensional network parallel to the *ab* plane (Fig. S9).
 68 The space includes acetone and chloroform molecules with
 69 an approximate host-guest ratio of 2:3:2
 70 (**3**/acetone/chloroform), which was based on electron counts

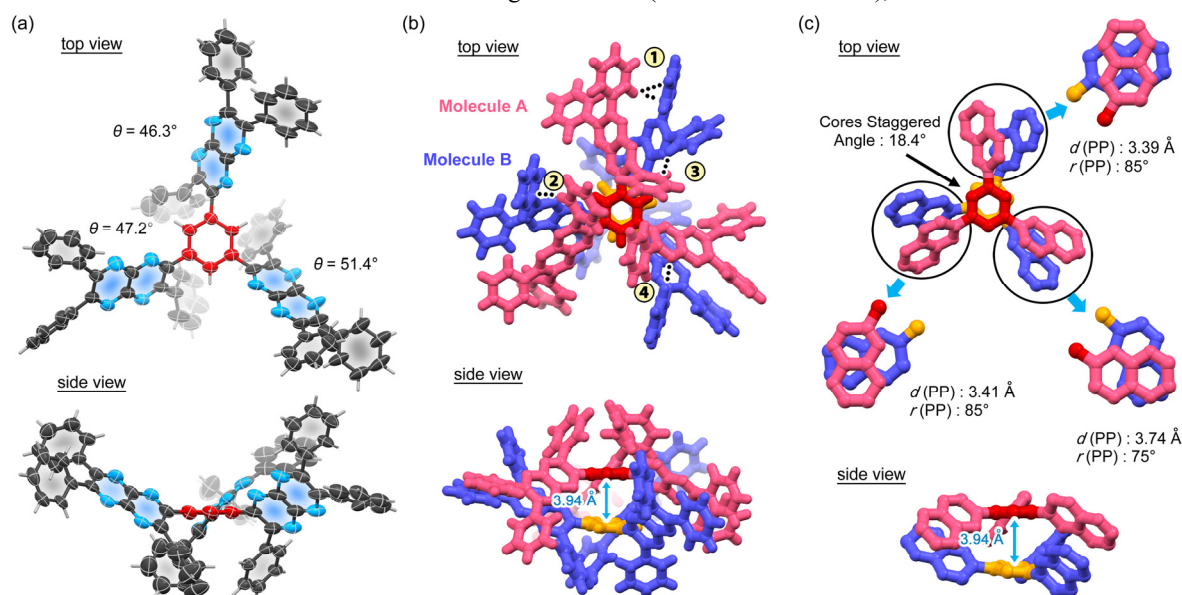


Fig. 4 Crystal structure of **3**·(acetone-CHCl₃). (a) Anisotropic displacement ellipsoids plot of molecule A with 50% probability from top and side of the central benzene ring (red color). (b) Interdigitated dimer composed of molecules A (pink) and B (purple), where the central benzene rings are colored by orange and red. Typical intermolecular interactions are noted by 1, 2, 3, and 4. (c) Relative orientations of the neighboring PP groups in the dimer, where *d*(PP) and *r*(PP) denote a distance and rotation angle between the stacked PP moieties, respectively.

1 estimated by SQUEEZE process¹² and ¹H NMR spectrum of
2 **3**·(acetone-CHCl₃) dissolved in DMSO-*d*₆ (Fig. S10).
3 Thermogravimetric analysis revealed that the crystals
4 gradually released the included solvent under ambient
5 temperature and lost all solvent up to ca. 160 °C (Fig. S11).

6 Molecules containing pyrazine moieties often show acid
7 responsiveness, as reported in several previous studies.¹¹ We
8 also investigated whether **2** and **3** show acid responsiveness.
9 Crystalline bulks of **2** and **3**·(acetone-CHCl₃) were exposed
10 to hydrochloric acid vapor, resulting gradual changes of
11 their colors from yellow to reddish yellow as a result of
12 protonation of the PP moieties (Fig. 5). Diffuse reflectance
13 spectra of as-formed crystals show closely similar profiles
14 to each other. A crystalline bulk of **2** shows a new shoulder
15 at ca. 550–610 nm in the spectrum with moderate intensity
16 after the exposure. That of **3**·(acetone-CHCl₃) also showed
17 red shifted band at ca. 500–580 nm. TDDFT calculations
18 disclose that these new bands are ascribable to electron
19 transition from neutral PP to protonated PP moieties (Figs.
20 S12–S18). When the reddish crystals were heated or left at
21 room temperature, they gradually returned to yellow.

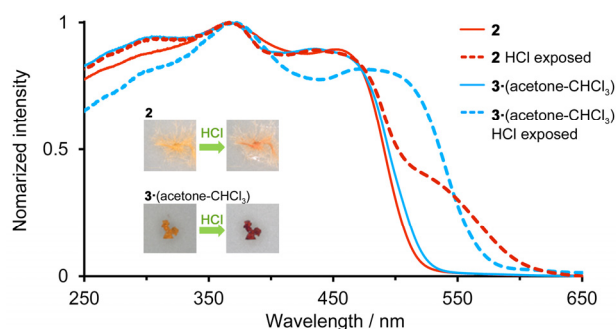


Fig. 5 Reflectance spectra of crystalline bulks of **2** and **3**·(acetone-CHCl₃) before and after exposed to hydrochloric acid. Inset: photographs of crystals.

22 In summary, we synthesized pyrazinopyrazine (PP)-
23 based linear **2** and tripodal **3**, in which PP moieties are
24 introduced at 1,4-positions and 1,3,5-positions of the central
25 benzene ring, respectively, giving conformationally flexible
26 and moderately π -conjugated molecules. Their solution
27 properties, crystal structures, and hydrochloric acid
28 responsiveness were revealed. Nonplanar **3** shows blue-
29 shifted absorption and red-shifted emission spectra
30 compared to planar **2** due to conformational flexibility of **3**.
31 Moreover, **3** forms an unique interdigitated dimer with a
32 small cavity in the crystalline state because of tripodal non-
33 planar molecular shape. These PP derivatives can open a
34 new family of N-contained π -conjugated systems.

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Supplementary data

49 Supplementary material is available at *Chemistry Letters*

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