Supramolecular Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713649759

Supramolecular Interaction of Keto-substituted Pyrroles

Tatsuki Morimoto[a]; Hiroyuki Furuta[a]
[a] Department of Chemistry and Biochemistry, Graduate School of Engineering, Kyushu University, Fukuoka, Japan

First published on: 13 April 2007

To cite this Article Morimoto, Tatsuki and Furuta, Hiroyuki(2007) 'Supramolecular Interaction of Keto-substituted Pyrroles', Supramolecular Chemistry, 19: 7, 493 — 500, First published on: 13 April 2007 (iFirst)
To link to this Article: DOI: 10.1080/10610270601132129
URL: http://dx.doi.org/10.1080/10610270601132129

Supramolecular Chemistry, October–November 2007 Vol. 19(7), pp. 493–500

Supramolecular Interaction of Keto-substituted Pyrroles

TATSUKI MORIMOTO[a] and HIROYUKI FURUTA[a,b,*]

[a]*Department of Chemistry and Biochemistry, Graduate School of Engineering, Kyushu University, Fukuoka 819-0395, Japan;* [b]*PRESTO, Japan Science and Technology Agency (JST), Kawaguchi, Saitama 332-0012, Japan*

(Received 27 October 2006; Accepted 21 November 2006)

Several types of pyrrole derivatives bearing carbonyl groups were synthesized and their structures in the solid states were elucidated by single crystal X-ray analysis. In the case of α-ketopyrroles, the molecules exist as hydrogen bonding dimers between the pyrrole NH and carbonyl groups, while in the case of β-ketopyrrole derivatives, hydrogen bonding networks are formed. Both the α,β′-diketo-substituted pyrroles and their derivatives are suggested to be suitable for the construction of 1-D chain networks. Overall, the effects of substituents on the supramolecular interactions are discussed in detail.

Keywords: Ketopyrrole; Hydrogen bonding; 1-D chain; Crystal structure

INTRODUCTION

Hydrogen bonding (HB) is one of the most important and ubiquitous noncovalent interactions seen in nature and owing to its strong and directional force, it is frequently used in the artificial supramolecular systems [1]. Among a variety of HB species known, pyrrole and its derivatives have attracted considerable attention in recent years due to the medical applications [2]. The hydrogen donor property of pyrrolic NH groups [3] is known to be applicable in the anion recognition [4–7], and the oligopyrrolic amides that contain HB donor groups at α- (or β′-) positions of pyrrole rings are used for the selective DNA-binding [8].

The pyrrole derivatives bearing keto-groups at α,β′-positions are important precursors in the synthesis of *confused* oligopyrroles and N-confused porphyrins [9–16]. Previously the authors have shown the formation of hydrogen bonding 1-D networks by the doubly N-confused porphyrins (N_2CP) that possess the outward-pointing *confused* pyrrole rings in the core [17]. Depending on the relative orientation of the *confused* pyrrole rings, zigzag and rod-like types of HB networks are formed by *cis*- and *trans*-N_2CP, respectively. Here the authors are interested in the supramolecular networks of the simple pyrrole derivatives bearing both the HB donor and acceptor groups in the molecules.

In this paper the solid state structures of three classes of pyrrole derivatives are examined: (A) *with* HB acceptor, (B) *without* HB donor (N-protected pyrrole), and (C) *with* HB donor and acceptor at α,β′-positions (Fig. 1). As the representatives in class A, pyrrole and dipyrromethane bearing keto-groups at α- and β′-positions were selected. For the compounds in class B, several N-protected 2,4-pyrroledicarbaldehyde were chosen, so as to examine the HB modes around the pyrrole NH. Additionally, to explore the HB networks without pyrrole NH moiety, N-protected 2,4-bis(hydroxymethyl)pyrrole in class C was picked up (Fig. 2).

RESULTS AND DISCUSSION

Pyrrole Derivatives *with* Pyrrole NH (Class-A)

There are many reports about the formation of HB dimer with α-ketopyrroles in the solid state [18–22]. It was also shown the formation of HB dimer with 2-picolinoylpyrrole [23]. To further confirm the generality of such HB dimers formation by 2-aroylpyrroles, the structure of 2-pentafluorobenzoylpyrrole (**1**) was newly determined by X-ray single crystal analysis (Fig. 3). As expected, two HB interactions between pyrrole NH and carbonyl O atoms were observed. The atomic distance between

*Corresponding author. Tel: +81-92-802-2865. Fax: +81-92-802-2865. E-mail: hfuruta@cstf.kyushu-u.ac.jp

ISSN 1061-0278 print/ISSN 1029-0478 online © 2007 Taylor & Francis
DOI: 10.1080/10610270601132129

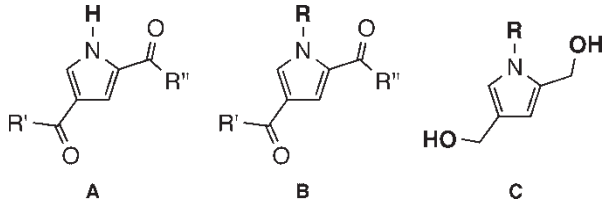

FIGURE 1 Pyrrole derivatives (A) *with* HB acceptor, (B) *without* HB donor (N-protected pyrrole), and (C) *with* HB donor and acceptor at α,β'-positions.

pyrrole N and carbonyl O is 2.843(2)Å and the angle of ∠CON is 156.6(2)°, which are comparable to those of reported dimeric structures (Fig. 3b), such as ethyl 3,5-dimethyl-4-phenylpyrrole-2-carboxylate (N–O = 2.875(2)Å, ∠CON = 158.7(2)°) [19] and ethyl 4-dodecyl-3,5-dimethylpyrrole-2-carboxylate (N–O = 2.850(2)Å, ∠CON = 160.2(2)°) [20]. Interestingly, in addition to the HB interactions, sandwich-type π-π interactions among pyrrole rings and a pentafluorophenyl ring were observed. That is, one pyrrole ring is interacting with a C_6F_5 ring on one side and with another pyrrole ring on the other side with the distances of r^1, r^2 ~ ca. 3.4 Å (Fig. 3c). Such kind of packing is not seen in the crystal of picolinoylpyrrole, where the pyrrole and pyridine rings are stacked in a staircase pattern [23].

Next, 4-benzoyl-2-pyrrolcarbaldehyde (**2**) [24] was investigated as an example of α,β'-diketopyrrole. Since there are two HB acceptor sites in the pyrrole ring, molecular interactions different from the self-assembled dimer are anticipated. As shown in Fig. 4, the NH hydrogen atom of **2** is pointing to the O atom of 4-benzoyl group in the neighboring molecule (N—O: 2.859(2)Å, ∠CON: 114.8(2)°), affording a HB 1-D zigzag alignment in the crystal (Fig. 4b). On the other hand, the formyl group at α-position does not interact with any other sites. This result suggests that the pyrrole NH favors the interaction with carbonyl group at β'-position rather than α-position. In fact,

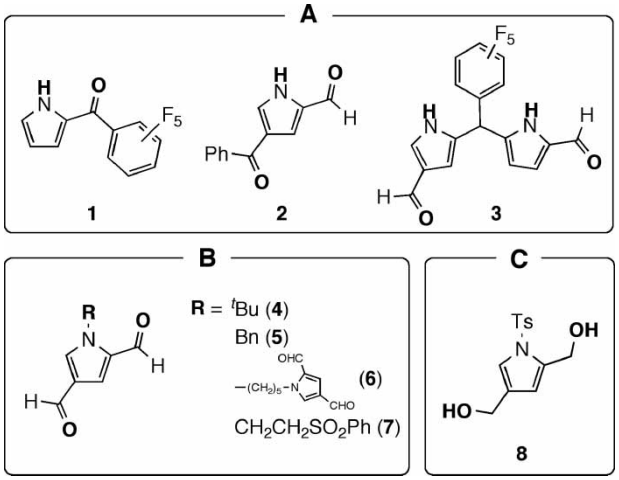

FIGURE 2 Pyrrole derivatives **1**–**8** used in this study.

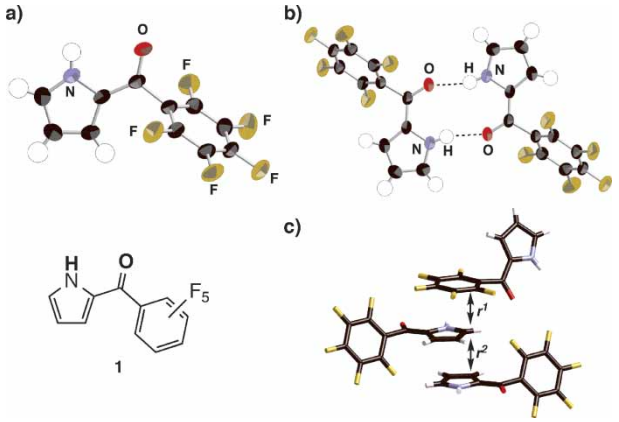

FIGURE 3 Crystal structures of **1**, a) ORTEP drawing of **1** (50% probability level), b) hydrogen bonding dimer of **1**, and c) packing diagram of three molecules (r^1, r^2 ~ 3.4 Å).

a similar 1-D structure was reported with benzyl 4-acetyl-3,5-dimethylpyrrole-2-carboxylate, previously [18].

The two X-ray crystal structures as shown above clearly indicate that N—H···O=C HB interaction is sensitive to the position of the acceptor groups on a pyrrole ring. When the two pyrrole rings having a hydrogen acceptor group at each end are connected, then, more complicated molecular interactions could occur. To confirm this, diformyl-N-confused dipyrromethane (**3**) was studied (Fig. 5). Compound **3** consists of two different pyrrole rings (*normal* and *confused*); both the pyrroles bear a formyl group at the α-positions, while the *normal* pyrrole α'-position and *confused* pyrrole β'-position are connected to *meso* carbon.

The crystal structure of **3** was shown in Fig. 5. The unsymmetrical multiple HB sites of **3** exhibits the characteristic packing structure. The two molecules are paired by the mutual HB. The *confused* pyrrole N—H interacts with the adjacent *normal* pyrrole

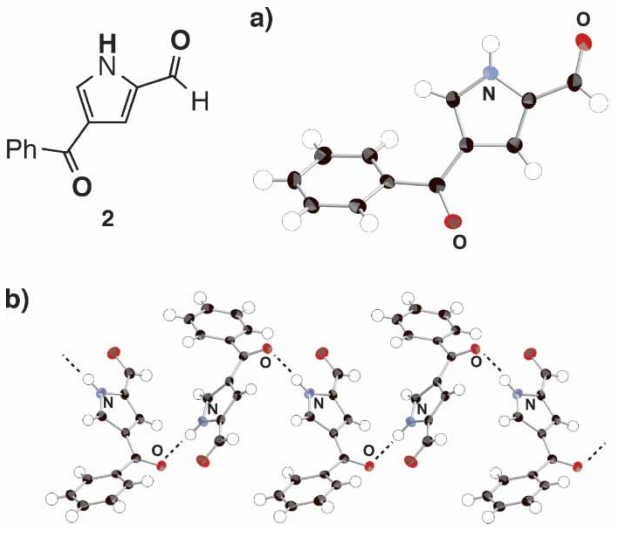

FIGURE 4 Crystal structures of **2**, a) ORTEP drawing of **2** (50% probability level) and b) Hydrogen bonding 1-D infinite chain of **2**.

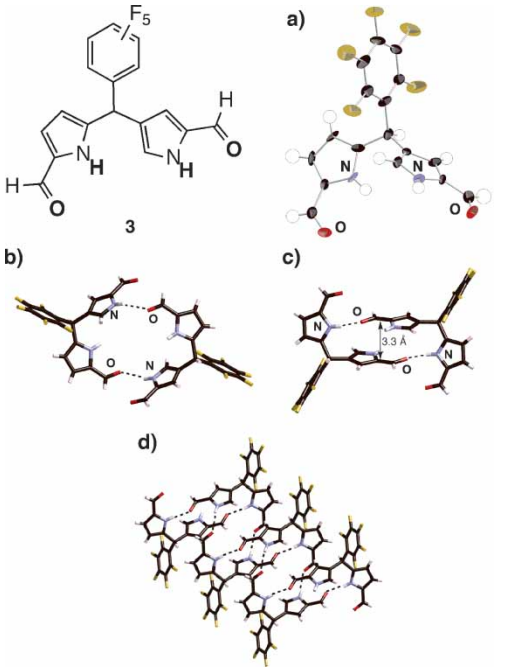

FIGURE 5 Crystal structures of **3**, a) ORTEP drawing of **3** (50% probability level), b) one type of hydrogen bonding mode (type-A), c) the other type of hydrogen bonding mode (type-B), and d) hydrogen bonding 1-D infinite alignment of **3**.

C═O group of another molecule (type-A, Fig. 5b). Similarly, the *normal* pyrrole NH interacts with the neighboring *confused* pyrrole C═O moiety of another unit (type-B, Fig. 5c). The two *confused* pyrrole rings are almost parallel and the distance is ca. 3.3 Å, which is within the distance of π-π interaction, and their formyl groups are located above the pyrrole rings of the paired molecule, respectively. Owing to these two different HB modes, the N-confused dipyrromethane **3** afforded an infinite zigzag alignment in the crystals (Fig. 5d).

Pyrrole Derivatives *Without* Pyrrole NH (Class-B)

As shown above, the pyrrole NH group is essential to construct HB assisted supramolecules. When the pyrrolic nitrogens are protected, then different kinds of interactions could be expected. To examine other potential factors for the supramolecular structures, N-protected pyrrole derivatives bearing carbonyl groups were studied.

Firstly, N-*tert*-butyl-2,4-pyrroledicarbaldehyde (**4**) was subjected to the X-ray diffraction analysis (Fig. 6). In the crystal, the pyrrole rings are placed on the same planes and interacts with each other via HB between the nearby formyl groups, affording a 1-D chain along the *a*-axis. Parallel to this, the next layer's chain is running along the *c*-axis with the distance of ca. 3.4 Å. The two pyrrole rings are partially overlapped and the formyl groups are located above or below the pyrrole ring of the adjacent molecules (Fig. 6b).

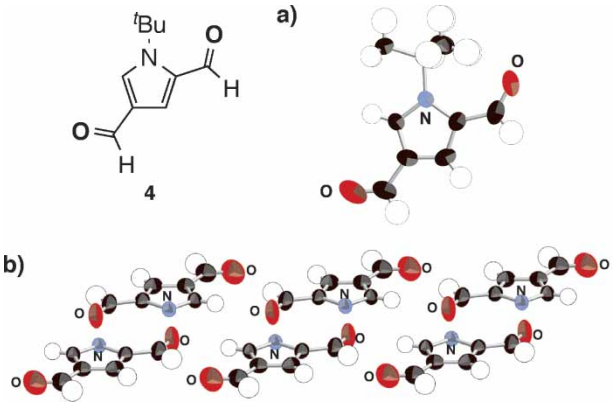

FIGURE 6 Crystal structures of **4**, a) ORTEP drawing of **4** (50% probability level) and b) packing diagram of **4**. *N-tert*-butyl groups are omitted for clarity in (b).

Secondly, the structure of 1,5-bis(2,4-diformylpyrrol-1-yl)pentane (**5**), consisting of two pyrroledicarbaldehyde moieties and an alkyl linker, was studied as another type of N-protected pyrrole derivative (Fig. 7). In the crystal, the N-alkyl chain of **5** is aligned along the *c*-axis with *anti* conformation. The pyrrole rings at both ends are stacked each other with a distance of ca. 3.5 Å. Like the case of **4**, the formyl groups are located above the pyrrole ring of the neighboring molecule.

Both **4** and **5** exhibit the preference of π-π interactions between the pyrrole-carbonyl planes in the crystals. When the *N*-protecting alkyl groups are substituted by the aromatic ones, further interactions could be anticipated. For such an example, the benzyl protected 2,4-diformylpyrrole (**6**) was studied. In the crystal, the molecule **6** exists in a dimer form, but the structure is entirely different from those of **4** and **5** (Fig. 8). Apart from the π-π interactions between the pyrrole rings, the additional different type of π-π interaction was observed between the pyrrole and the phenyl ring of benzyl group in the dimeric structures (Fig. 8b). Namely, similar to the case of **4** and **5**, the two pyrrole rings are partially overlapped and the pyrrole β-CH group is pointing toward the phenyl ring of the countered molecule with a dihedral angle of 73.9(1)°, just like a T-shaped edge-to-face interaction [25]. The distance between the pyrrole β-C atom and the phenyl ring is 3.500(2)Å, which is less than the

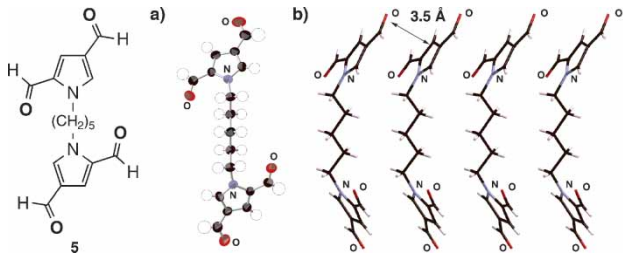

FIGURE 7 Crystal structures of **5**, a) ORTEP drawing of **5** (50% possibility level), and b) packing of **5**.

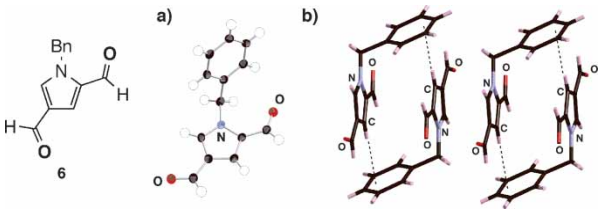

FIGURE 8 Crystal structures of **6**, a) ORTEP drawing of **6** (50% probability level) and b) packing diagram of **6.**

sum of van der Waals radii of carbon and hydrogen atoms [26]. Moreover, the pyrrole rings in the dimer are further stacked with pyrrole rings of the adjacent molecules, resulting in the formation of infinite layers of pyrrole rings along the *a*-axis.

On the other hand, the *N*-protected pyrrole derivative with a phenyl group apart from the pyrrole ring moiety, adopts another type of structures in the crystals. For example, *N*-benzensulfonylethyl-2,4-pyrroledicarbaldehyde (**7**) does not form a stacked structure between the pyrrole moieties, but it shows an intramolecular π-π interaction between the pyrrole and phenyl rings (Fig. 9a). The bridging ethyl group adopts *gauche* conformation, which enables the two aromatic planes to face in a short distance (Fig. 9a,b). In the molecule, the dihedral angle of the planes is 20.6(2)°, and the closest *ortho*-cabon atom of the phenyl group is separated by 3.313(3)Å from the pyrrole ring. The molecules are arranged along the *c*-axis with facing the each π-ring (Fig. 9b).

As shown above, the structures of **4**–**7** indicate that the face-to-face π-π interactions are preferable when the HB donor NH groups are missing, and additionally, the N-protected pyrrole rings can also interact with π-face in the edge-to-face fashion in the crystals.

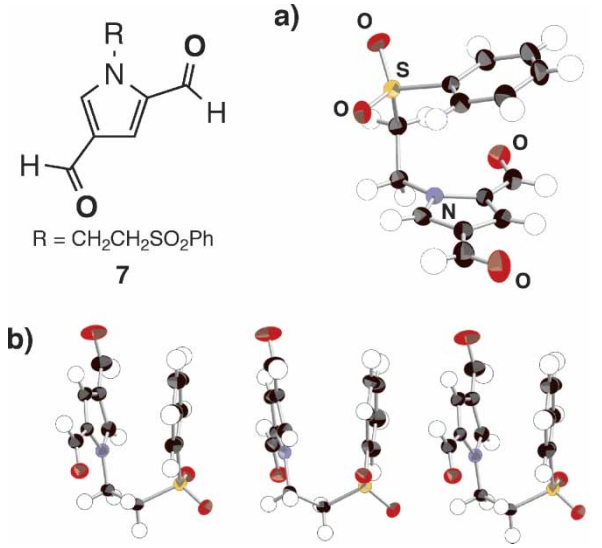

FIGURE 9 Crystal structures of **7**, a) ORTEP drawing of **7** (50% probability level) and b) packing diagram of **7**.

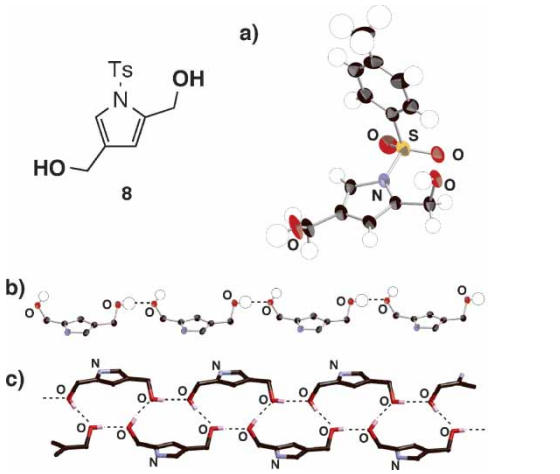

FIGURE 10 Crystal structures of **8**, a) ORTEP drawing of **8** (50% probability level), b) infinite 1-D chain along the *b*-axis, and c) complementary hydrogen bonding network by the infinite OH···O interactions.

Pyrrole Derivatives with Extra HB Sites (Class-C)

The formyl groups of **4**–**7** mentioned above are readily converted into the hydroxymethyl groups, which can serve as both HB donor and acceptor groups. For example, *N*-tosyl-2,4-pyrroledicarbaldehyde was reduced to the corresponding diol (**8**) quantitatively and the X-ray crystal (Fig. 10a) shows the infinite 1-D chain along the *b*-axis where the two OH groups in the molecule interact with the OH groups of adjacent molecules (Fig. 10b). Furthermore, the two 1-D chains interact mutually by the complementary infinite OH···O HB interactions (Fig. 10c). In details, the HB interactions of two OH groups of the neighboring 1-D chain are pinched by the two OH groups of another 1-D chain through four successive OH···O HB interactions. As a result, the OH groups are arranged to form the 1-D infinite OH···O HB chain (averaged O–O distance is 2.707 (3)Å) along the *b*-axis, and the O—O distance is comparable to that of 1-D OH···O network, reported previously [27–29].

This result implies that 2,4-bis(hydroxymethyl)pyrrole serves as a suitable platform for the infinite 1-D chain structure, because of the favorable distance and the regular alignment of the OH groups. By utilizing this packing pattern, it could be possible to arrange the particular functional groups on the pyrrole N atoms, along an axis.

CONCLUSION

The X-ray analyses of α,β-diketopyrrole and its derivatives revealed the versatile interaction modes in the solid states. The α-ketopyrroles form HB dimers, in contrast to β-ketopyrroles; the pyrrole NH moieties prefer to interact with the β-carbonyl group

of adjacent pyrrole molecules to form 1-D networks. In the *N*-protected pyrrole derivatives, the pyrrole rings become major interaction sites and the planes composed of pyrrole rings and the carbonyl groups interact with each other in a parallel face-to-face fashion. Pyrrole derivatives with two HB carbonyl groups at the α,β'-ends and its reduced form afford infinite 1-D chains in the solid state.

Because of the sensitivity of HB interactions between the pyrrole NH and carbonyl O atoms to the surrounding substituents, even the simple pyrrole derivatives could serve as useful building blocks for the supramolecules. By introducing further HB sites around the pyrrole rings using the accumulated methods for pyrrole modifications, the construction of more sophisticated high-ordered structures would be possible.

MATERIALS AND METHOD

Commercially available solvents and reagents were used without further purification. Dry THF was distilled from sodium chips under argon with benzophenone/ketyl as indicator. Dry CH_2Cl_2 was distilled from CaH_2. Dry DMF was distilled from alumina. Compound **2** was prepared according to the previous literature [24]. Silica gel column chromatography was performed on Wakogel C-200 and C-300. ^{1}H NMR spectra were recorded on JEOL JNM-AL270 (operating at 300 MHz). The residual ^{1}H NMR resonances of the deuterated solvents were used as the internal references. Mass spectrometry was performed on JEOL HX110 using fast atom bombardment (FAB) method in the positive ion mode with a 3-nitrobenzylalcohol matrix, and Bruker AUTOFLEX using positive-MALDI-TOF method with a dithranol matrix.

X-ray Crystallography

Data of compounds **1**–**8** were collected on a Bruker SMART APEX with graphite monochromated Mo-K_α radiation ($\lambda = 0.71073$ Å). Single crystals of **1** and **4**–**7** were obtained by vapor diffusion of hexane into the corresponding CH_2Cl_2 solutions. A single crystal of **2** was obtained by slow evaporation of a $CHCl_3$ solution. Single crystals of **3** and **8** were obtained by slow evaporation of the CH_2Cl_2 solutions. Crystal data and experimental parameters are summarized in Table I. Crystallographic data for compounds **1**–**8** have been deposited with Cambridge Crystallographic Data Center with CCDC number 620230, 620223, 620224, 620228, 620225–7, and 620229, respectively. Copies can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033. E-mail: deposit@ccdc.cam.ac.uk).

2-Pentafluorobenzoylpyrrole (1)

Compound **1** was prepared in 25% yield according to the reported method [30]. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.83 (br, 1H, N*H*), 7.25 (m, 1H, pyrrole-*H*), 6.72 (m, 1H, pyrrole-*H*), 6.37 (m, 1H, pyrrole-*H*).

N-Confused 5-Pentafluorophenyldipyrromethane-1,9-Dicarbaldehyde (3)

To a Vilsmeier reagent prepared from DMF (0.32 mL, 4.2 mmol) and $POCl_3$ (0.39 mL, 4.2 mmol) in dichloro ethane (15 mL), N-confused 5-pentafluorophenyldipyrromethane (500 mg, 1.6 mmol) [31] in dichloroethane (20 mL) was added over 20 min at 0°C. After stirring for 0.5 h at room temperature, the reaction mixture was refluxed for 2 h. Sodium acetate (1.28 g, 15.6 mmol) in water (40 mL) was added and the resulting solution was refluxed for 0.5 h. After cooling to room temperature, the organic layer was separated and the aqueous phase was extracted five times with CH_2Cl_2 (40 mL × 5). The combined organic layer was washed with water and brine, and dried over Na_2SO_4. The solvent was removed in vacuo and the residue was purified by a silica gel column (eluent: 5% MeOH/CH_2Cl_2) to afford **3** (362 mg, 0.98 mmol) in 61% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.50 (s, 1H, C*H*O), 9.47 (br, 1H, N*H*), 9.44 (s, 2H, C*H*O), 9.20 (br, 1H, N*H*), 7.03 (s, 1H, pyrrole-*H*), 6.92 (m, 1H, pyrrole-*H*), 6.89 (s, 1H, pyrrole-*H*), 6.13 (m, 1H, pyrrole-*H*), 6.13 (s, 1H, *meso*-*H*); FABMS: *m/z*: 369.0 $[M + H]^+$.

1-*tert*-Butyl-2,4-Pyrroledicarbaldehyde (4)

To a stirred solution of *tert*-butylamine (24.5 mL, 233 mmol) in acetic acid (48 mL), 2,5-dimethoxytetrahydrofuran (30.2 mL, 232 mmol) was added and refluxed for 5 h. Water and saturated $NaHCO_3$ aq. were added into the reaction mixture and the resulting solution was extracted with ether. The organic phase was separated, washed with water and brine and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by bulb-to-bulb distillation to afford 1-*tert*-butylpyrrole (11.5 g, 93.5 mol) in 40% yield. To a Vilsmeier reagent preapared from oxalyl chloride (9.0 mL, 103 mmol) and DMF (10 mL, 129 mmol) in dichloroethane (65 mL), a solution of 1-*tert*-butylpyrrole (11.5 g, 93.5 mol) in dichloroethane (28 mL) was added over 15 min. The solution was allowed to stir for 12 h at room temperature, and subsequently, nitromethane (6.5 mL) was added. To the solution cooled by ice bath, dichloromethyl methyl ether (8.5 mL, 94 mmol) and aluminum chloride (27.6 g, 206 mmol) were added and the ice bath was removed after vigorous evolution of HCl gas. After stirring for 2 h at room temperature, the reaction mixture was

TABLE I Crystal data and selected details of the data collection and refinement calculations of compounds **1**–**8**

Parameter	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
empirical formula	$C_{11}H_4NOF_5$	$C_{12}H_9NO_2$	$C_{17}H_9N_2O_2F_5$	$C_{10}H_{13}N_2O_2$	$C_{17}H_{18}N_2O_4$	$C_{13}H_{11}NO_2$	$C_{14}H_{13}N_2O_4S$	$C_{13}H_{15}NO_4S$
Fw	261.15	199.2	368.26	179.21	314.33	213.23	291.31	281.32
space group (No.)	$P2_1/c$ (no. 14)	$P2_12_12_1$ (no. 19)	$P2_1/c$ (no. 14)	$P2_1/m$ (no. 14)	$Fdd2$ (no. 43)	$P2_1/c$ (no. 14)	$C2/c$ (no. 15)	$P2_1/n$ (no. 14)
cryst syst	monoclinic	orthorhombic	monoclinic	monoclinic	orthorhombic	monoclinic	monoclinic	monoclinic
a,Å	12.2725(9)	7.857(2)	17.799(4)	7.5270(7)	26.085(1)	6.9977(4)	28.796(2)	11.0823 (9)
b,Å	6.4027(5)	9.750(2)	6.677(1)	6.7578(7)	81.761(4)	15.7524(9)	7.0461(5)	8.7293(7)
c,Å	13.098(1)	12.486(3)	13.538(3)	9.5907(9)	4.4434(2)	9.6024(6)	13.855(1)	13.843(1)
α, deg	90	90	90	90	90	90	90	90
β, deg	98.351(2)	90	102.72(3)	98.046(2)	90	91.813(1)	109.849(2)	99.717(2)
γ, deg	90	90	90	90	90	90	90	90
V,Å^3	1018.3(1)	956.4(3)	1569.4(6)	483.04(8)	9476.8(8)	1058.0(1)	2644.0(3)	1320.0(2)
T, °C	−50	23	23	20	−50	23	−50	−50
Z	4	4	4	2	24	4	8	4
D_{calcd}, g cm^{-3}	1.703	1.383	1.559	1.328	1.322	1.339	1.464	1.416
Cryst size, mm	0.39 x 0.16 x 0.13	0.40 x 0.40 x 0.05	0.20 x 0.10 x 0.10	0.50 x 0.48 x 0.31	0.30 x 0.05 x 0.05	0.27 x 0.24 x 0.16	0.18 x 0.12 x 0.16	0.11 x 0.11 x 0.06
θ, deg	24.7	26.4	24.7	23.3	20.8	24.7	24.7	24.7
No. of reflectns measd	1738	1951	1632	757	2487	1804	2265	2248
No. of reflectns obsd	1502	1761	1385	702	2118	1641	1866	1560
Radiation λ, Å	0.71073 (MoK_α)	0.71073 (MoK_α)	0.71073 (MoK_α)	0.71073 (MoK_α)	0.71073 (MoK_α)	0.71073 (MoK_α)	0.71073 (MoK_α)	0.71073 (MoK_α)
μ(MoK_α), cm^{-1}	0.173	0.095	0.143	0.094	0.095	0.091	0.257	0.255
GOF ($I > 2\sigma(I)$)	1.069	1.001	1.279	1.121	1.045	1.043	1.028	1.004
R ($I > 2\sigma(I)$)	0.036	0.033	0.112	0.067	0.035	0.033	0.041	0.044
R_w	0.093	0.070	0.190	0.180	0.075	0.088	0.099	0.100

poured into ice-cold water and stirred for 1 h in ambient conditions. The product was extracted with CH_2Cl_2 and purified by a silica gel column (eluent: CH_2Cl_2) to afford **4** in 15% from 2,5-dimethoxytetrahydrofuran: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.81 (s, 1H, C*H*O), 9.56 (d, $J = 1.2$ Hz, 1H, C*H*O), 7.82 (m, 1H, pyrrole-*H*), 7.53 (m, 1H, pyrrole-*H*), 1.70 (s, 9H, C(CH_3)$_3$; MALTI-TOFMS: *m/z*: 179.8 [M] $^+$.

1,5-Bis(2,4-Diformylpyrrol-1-yl)pentane (5)

To a stirred solution of DMF (2.5 mL, 32 mmol) in dichloroethane (20 mL) under N_2 atmosphere, oxalyl chloride (2.6 mL, 30 mmol) in dichloroethane (20 mL) was added at 0 °C over a period of 10 min. After stirring the white suspension for 30 min at room temperature, a solution of 1,5-di(pyrrol-1-yl)pentane (2.71 g, 13.4 mmol) [32] in dichloroethane (15 mL) was added over 10 min. The reaction mixture was allowed to stir for 2.5 h at room temperature, and subsequently, nitromethane (3.5 mL) was added. To the solution cooled by ice bath, dichloromethyl methyl ether (2.7 mL, 30 mmol) and aluminum chloride (4.10 g, 30 mmol) was added, and the ice bath was removed after vigorous evolution of HCl gas. After stirring for 2.5 h at room temperature, the reaction mixture was poured into ice cold water and stirred for 2 h under ambient conditions. The product was extracted with CH_2Cl_2 or ethyl acetate and purified by column chromatography on silica gel (eluent: 1% MeOH/CH_2Cl_2) to afford **5** (564 mg, 1.79 mmol) in 13.4% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.81 (s, 1H, C*H*O), 9.62 (d, $J = 1.2$ Hz, 1H, C*H*O), 7.53 (s, 1H, pyrrole-*H*), 7.38 (d, $J = 1.2$ Hz, 1H, pyrrole-*H*), 4.34 (t, $J = 7.5$ Hz, 4H, N–CH_2), 1.83 (m, 4H, N–CH_2CH_2), 1.34 (m, 2H, N–CH_2CH_2CH_2); MALTI-TOFMS: *m/z*: 315.0 [M + H] $^+$.

1-Benzyl-2,4-Pyrroledicarbaldehyde (6)

Prepared in a similar procedure to that of **4**; 64% from pyrrole: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.80 (s, 1H, C*H*O), 9.65 (s, 1H, C*H*O), 7.52 (s, 1H, pyrrole-*H*), 7.36 (m, 4H, Ph-*H* and pyrrole-*H*), 7.20 (m, 2H, Ph-*H*), 5.59 (s, 2H, CH_2); MALTI-TOFMS: *m/z* (%): 213.0 [M] $^+$.

1-(2-Benzensulfonylethyl)-2,4-Pyrroledicarbaldehyde (7)

To a suspension of NaH (60% dispersion in mineral oil; 197 mg, 4.03 mmol) in DMF (2 mL), 2,4-pyrroledicarbaldehyde (496 mg, 4.03 mmol) in DMF (3 mL) was added. After 2 h, 2-benzensulfonylethyl chloride (1.66 g, 8.12 mmol) in DMF (5 mL) was added for 15 h. The reaction was quenched by H_2O (50 mL) and the products were extracted with ethyl acetate. The organic layer was washed with water, dried over Na_2SO_4, and the solvent was removed in vacuo. The residue was purified by a silica gel column, and recrystallized from CH_2Cl_2/hexane to afford **7** in 63% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.79 (s, 1H, C*H*O), 9.50 (d, 1H, C*H*O), 7.82 (m, 2H, Ph-*H*), 7.66 (m, 1H, Ph-*H*), 7.62 (s, 1H, pyrrole-*H*), 7.54 (m, 2H, Ph-*H*), 7.31 (s, 1H, pyrrole-*H*), 4.74 (d, $J = 6.0$ Hz, 2H, CH_2), 3.65 (d, $J = 6.0$ Hz, 2H, CH_2); MALTI-TOFMS: *m/z*: 291.9 [M + H] $^+$.

1-Tosyl-2,4-Bis(hydroxymethyl)pyrrole (8)

To a suspension of NaH (60% dispersion in mineral oil; 819 mg, 20.4 mmol) in THF (10 mL), 2,4-pyrroledicarbaldehyde (1.97 g, 16.0 mmol) in THF (30 mL) was added. After 3 h, tosyl chloride (3.12 g, 16.4 mmol) in THF (10 mL) was added for 5 min. The reaction was quenched by a saturated NH_4Cl aqueous solution (50 mL), and the products were extracted with ethyl acetate. The organic layer was washed with water, dried over Na_2SO_4, and the solvent was removed in vacuo. The residue was purified by a silica gel column, and recrystallized from CH_2Cl_2/hexane to afford 1-tosyl-2,4-pyrroledicarbaldehyde (3.44 g, 12.4 mmol) in 80% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.92 (s, 1H, C*H*O), 9.90 (d, 1H, C*H*O), 8.21 (d, $J = 1.8$ Hz, 1H, pyrrole-*H*), 7.89 (d, $J = 8.4$ Hz, 1H, tosyl-*H*), 7.48 (d, $J = 1.8$ Hz, 1H, pyrrole-*H*), 7.38 (d, $J = 8.4$ Hz, 1H, tosyl-*H*), 2.44 (s, 3H, CH_3). 1-Tosyl-2,4-pyrroledicarbaldehyde (500 mg, 1.80 mmol) was reduced quantitatively by $NaBH_4$ (686 mg, 18.1 mmol) in THF/MeOH (40 + 8 mL). The reaction was quenched with H_2O and the products were extracted with CH_2Cl_2. After removing of the solvents in vacuo, compound **8** was obtained in a pure form as a white crystal; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.92 (s, 1H, C*H*O), 9.90 (d, 1H, C*H*O), 8.21 (d, $J = 1.8$ Hz, 1H, pyrrole-*H*), 7.89 (d, $J = 8.4$ Hz, 1H, tosyl-*H*), 7.48 (d, $J = 1.8$ Hz, 1H, pyrrole-*H*), 7.38 (d, $J = 8.4$ Hz, 1H, tosyl-*H*), 2.44 (s, 3H, CH_3).

Acknowledgements

T. M. thanks to JSPS for a Research Fellowship for Young Scientists.

References

[1] Jeffrey, G. A.; Saenger, W. *Hydrogen Bonding in Biological Structures*; Springer: Berlin, 1991.
[2] Gottesfeld, J. M.; Neely, L.; Trauger, J. W.; Baird, E. E.; Dervan, P. B. *Nature* **1997**, *387*, 202.
[3] Sessler, J. L.; Berthon-Gelloz, G.; Gale, P. A.; Camiolo, S.; Anslyn, E. V.; Anzenbacher, Jr., P.; Furuta, H.; Kirkovits, G. J.; Lynch, V. M.; Maeda, H.; Morosini, P.; Scherer, M.; Shriver, J.; Zimmerman, R. S. *Polyhedron* **2003**, *22*, 2963.
[4] Gale, P. A.; Sessler, J. L.; Král, V. *Chem. Commun.* **1998**, 1.
[5] Beer, P. D.; Gale, P. A. *Angew. Chem. Int. Ed.* **2001**, *40*, 486.
[6] Sessler, J. L.; Davis, J. M. *Acc. Chem. Res.* **2001**, *34*, 989.

[7] Sessler, J. L.; Camiolo, S.; Gale, P. A. *Coord. Chem. Rev.* **2003**, *240*, 17.
[8] White, S.; Szewczyk, J. W.; Turner, J. M.; Baird, E. E.; Dervan, P. B. *Nature* **1998**, *391*, 468.
[9] Furuta, H.; Asano, T.; Ogawa, T. *J. Am. Chem. Soc.* **1994**, *116*, 767.
[10] Chmielewski, P. J.; Latos-Grażyński, L.; Rachlewicz, K.; Głowiak, T. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 779.
[11] Latos-Grażyński, L. In *The Porphyrin Handbook*; Kadish, K., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, 2000; vol. 2, chapter 14.
[12] Furuta, H.; Maeda, H.; Osuka, A. *Chem. Commun.* **2002**, 1795.
[13] Harvey, J. D.; Ziegler, C. J. *Coord. Chem. Rev.* **2003**, *247*, 1.
[14] Chmielewski, P. J.; Latos-Grażyński, L. *Coord. Chem. Rev.* **2005**, *249*, 2510.
[15] Srinivasan, A.; Furuta, H. *Acc. Chem. Res.* **2005**, *38*, 10.
[16] Harvey, J. D.; Ziegler, C. J. *J. Inorg. Biochem.* **2006**, *100*, 869.
[17] Maeda, H.; Osuka, A.; Furuta, H. *Supramol. Chem.* **2003**, *15*, 447.
[18] Senge, M. O.; Smith, K. M. *Acta Crystallogr. Sect. C* **2005**, *61*, o538.
[19] Paixao, J. A.; Ramos Silva, M.; Matos Beja, A.; Sobral, A. J. F. N.; Lopes, S. H.; Rocha Gonsalves, A. M. d'A. *Acta Crystallogr., Sect. C* **2002**, *58*, o721.
[20] Ramos Silva, M.; Matos Beja, A.; Paixao, J. A.; Sobral, A. J. F. N.; Lopes, S. H.; Rocha Gonsalves, A. M. d'A. *Acta Crystallogr., Sect. C* **2002**, *58*, o572.
[21] Light, M. E.; Camiolo, S.; Gale, P. A.; Hursthouse, M. B. *Acta Crystallogr., Sect. E* **2001**, *57*, o1245.
[22] Despinoy, X. L. M.; Harris, S. G.; MacNab, H.; Parsons, S.; Withell, K. *Acta Crystallogr., Sect. C* **1998**, *54*, 231.
[23] Ono, Y.; Furuta, H. *Chem. Lett.* **2006**, *35*, 750.
[24] Anderson, H. J.; Loader, C. E.; Foster, A. *Can. J. Chem.* **1980**, *58*, 2527.
[25] Carver, F. J.; Hunter, C. A.; Livingstone, D. J.; McCabe, J. F.; Seward, E. M. *Chem. Eur. J.* **2002**, *8*, 2847.
[26] Nishio, M.; Umezawa, Y.; Hirota, M.; Takeuchi, Y. *Tetrahedron* **1995**, *51*, 8665.
[27] Hong, B. H.; Lee, J. Y.; Lee, C. -W.; Kim, J. C.; Bae, S. C.; Kim, K. S. *J. Am. Chem. Soc.* **2001**, *123*, 10748.
[28] Neogi, S.; Bharadwaj, P. K. *Inorg. Chem.* **2005**, *44*, 816.
[29] Ghosh, S. K.; Bharadwaj, P. K. *Inorg. Chem.* **2005**, *44*, 5553.
[30] Cadamuro, S.; Degani, I.; Dughera, S.; Fochi, R.; Gatti, A.; Piscopo, L. *J. Chem. Soc., Perkin Trans.* **1993**, *1*, 273.
[31] Furuta, H.; Maeda, H.; Osuka, A. *J. Am. Chem. Soc.* **2000**, *122*, 803.
[32] Hlavaty, J.; Papez, V.; Kavan, L. *Synthetic Metals* **1994**, *63*, 209.