A New Hydrogen-Bonding Motif with Constituents Bearing Donor and Acceptor Sites 7 Å Apart

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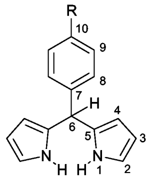
Aryl substituted dipyrromethanes [di(pyrrol-2-yl)-phenyl-methanes] with hydrogen acceptor substituents R in *para* position of the aryl ring [R = CO_2Me, CO_2H, CONH(*i*Pr) and NH_2] located 7 Å apart from the hydrogen donor pyrrole nitrogen atom are shown to self-assemble in the solid state *via* hydrogen bonds to form rings or chains.

Key words: Dipyrromethanes, Self-Assembly, Hydrogen Bonds, Bidentate Ligands, DFT



1: R = CO_2Me

2: R = CO_2H

3: R = CON(H)(*i*Pr)

4: R = NH_2

Scheme 1.

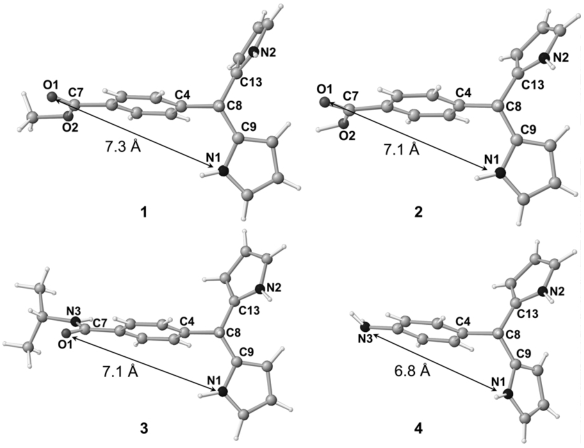


Fig. 1. View of the molecular structures of **1** – **4** along the aliphatic C8-H bond as found in the crystal lattice, numbering of relevant atoms and intramolecular distances of the hydrogen donor and acceptor atoms.

Introduction

Dipyrromethane derivatives are useful starting materials for the preparation of porphyrines [1] and coordination compounds [2, 3]. However, the use of (substituted phenyl)dipyrromethanes (Scheme 1) as building blocks (synthons [4]) in supramolecular chemistry and crystal engineering has not yet been explored. Indeed there have been only few structural reports on (substituted phenyl)dipyrromethanes: the parent compound with R = H [5], mesityl dipyrromethane [5], a bis(dipyrromethane) [6] and (nitrophenyl)dipyrromethane (R = NO_2) [7]. Only in the latter case the substitutent R is involved in hydrogen bonding to one of the acidic pyrrole hydrogen atoms while in some other cases weak N-H$\cdots\pi$(pyrrole) interactions have been found in the solid state [6, 8].

We report herein the crystal structures of four (substituted phenyl)dipyrromethanes with potential hydrogen acceptor groups R = CO_2Me (**1**), CO_2H (**2**), CONH(*i*Pr) (**3**), NH_2 (**4**) in *para* position of the phenyl ring (Scheme 1).

Results and Discussion

Dipyrromethanes **1**, **2** and **4** were prepared from the corresponding aromatic aldehyde and pyrrole in the presence of trifluoroacetic acid according to literature procedures [5], the amide **3** was formed by reaction of the acid **2** with *i*$PrNH_2$.

In the crystal structures of **1** – **4** (Fig. 1) the pyrrole hydrogen atom at N1 is identified to be involved in hydrogen bonds to the *para* substituent of a neighbouring molecule to form dimers (**1** – **3**) or helical chains (**4**) (Table 1, Fig. 2) [9]. The number of atoms separating the hydrogen donor and acceptor sites is seven atoms for **1**–**3** and six atoms for **4** (Fig. 1 and 2). The intramolecular distance of the hydrogen atom donor and

Table 1. Selected bond lengths (Å) and angles (°) of **1**, **2**, **3**, **4** and the DFT optimised structure of di(pyrrol-2-yl)-phenylmethane.

	1 **A = O1**	**2**($\times$**H$_2$O**) **A = O1**	**3** **A = O1**	**4** **A = N3**	**DFT**
N1···A'	2.917	2.970	2.832	2.989	–
N1-H9···A'	169.2	170.9	171.8	160.2	–
N1···A	7.3	7.1	7.1	6.8	–
C4-C8-C9-N1	−35.7	−41.7	−40.5	−70.6	88.5
C4-C8-C13-N2	125.1	146.3	152.4	155.5	164.4

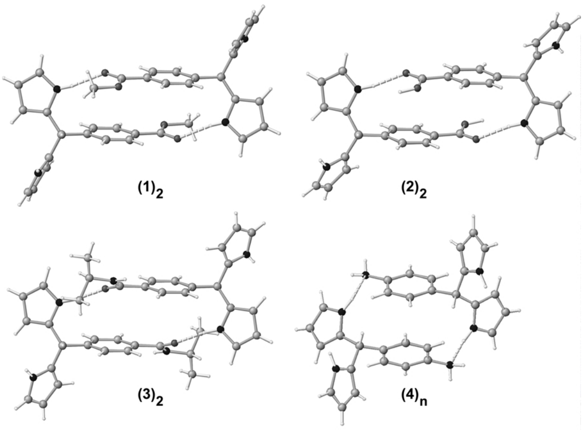
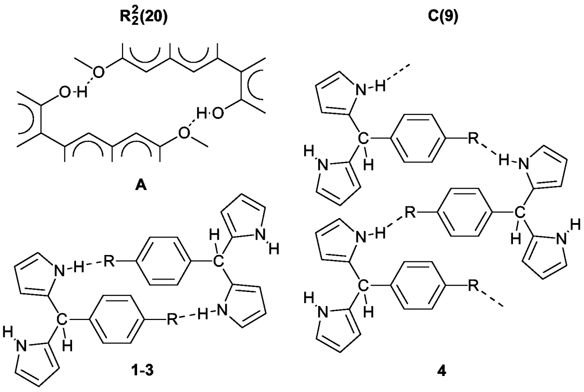


Fig. 2. View of the ring and chain motifs found in the crystal structures of **1** – **4**.

acceptor atoms amounts to 7 Å which is among the largest found in supramolecular synthons for hydrogen bonding motifs [10, 11] (*cf.* the donor acceptor distance in the common carboxylic acids or amides amounts to only 2.2 – 2.3 Å). The large intramolecular distances between donor and acceptor sites and the angles N1-C8-A of 92 – 102° (A = O1, N3) allow for the formation of small ellipsoid channels of approximately 8 – 10 Å×3.7 Å (atom-to-atom distance) running through the crystals along the short *a*-axis (**1**: 5.65; **2**: 5.87; **3**: 5.66; **4**: 6.18 Å).

Scheme 2 schematically depicts the hydrogen bonding motifs observed for **1** – **4** in the crystal lattice: dimeric ring motifs with graph set $R^2_2(20)$ [12] for **1** – **3** and a catena motif of graph set C(9) [12] for **4** [*meso*-(4-nitrophenyl)dipyrromethane [7] forms a chain of graph set C(10)]. The largest ring motif **A** [$R^2_2(20)$] with a very high probability of formation according to a statistical analysis [11] is also shown for comparison.

The probability of ring or catena formation of acceptor substituted dipyrromethanes is at present difficult to estimate due to the lack of sufficient crystal data. However, from the available data it appears that the motifs formed by **1** – **4** can successfully compete with carboxylic acid dimer formation and amide dimerisation. Even the water molecule present in the crystal lattice of **2** does not disturb the dimer formation but instead links the dimers by OH···OH$_2$···O hydrogen bonds to form a double strand [9].



Scheme 2.

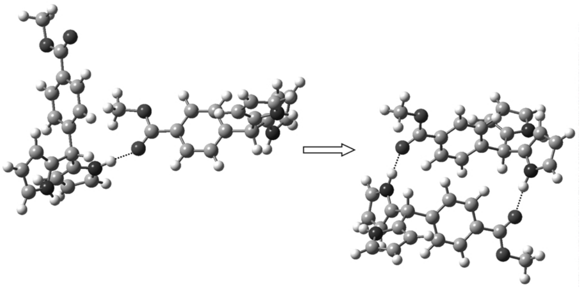


Fig. 3. DFT optimised geometries of (**1**)$_2$ in single-bonded and double-bonded arrangements.

In contrast to typical synthons (*e.g.* **A** or carboxylic acids) the dipyrromethanes **1** – **4** are flexible and thus non-preorganised for self-assembly. In order to gain some insight into the flexibility of dipyrromethanes the gas phase minimum geometry of the parent unsubstituted dipyrromethane was determined by means of DFT calculations (B3LYP, 6-31G+(d,p) basis set). The largest conformational difference between the calculated gas phase geometry and the solid state structures involves the hydrogen bonded pyrrole ring. The torsional angle C4-C8-C9-N1 differs by 124 – 159 ° while the orientation of the second pyrrole ring (C4-C8-C13-N2) differs by only 9 – 39° (Table 1, Fig. 2). Thus the rather flexible orientation of the pyrrole rings has to be adjusted for self-assembly. However, the energy required for ring rotation is small and can easily be compensated for by the formation of hydrogen bonds. One hydrogen bond suffices to force two dipyrromethanes

Table 2. X-ray crystallographic data for **1**, **2**, **3** and **4**.

	1	**2•H_2O**	**3**	**4**
Formula	$C_{17}H_{16}N_2O_2$	$C_{16}H_{16}N_2O_3$	$C_{19}H_{21}N_3O$	$C_{15}H_{15}N_3$
Molecular mass	280.32	284.31	307.39	237.30
Crystal dimension / mm	$0.20 \times 0.10 \times 0.03$	$0.10 \times 0.10 \times 0.01$	$0.40 \times 0.30 \times 0.10$	$0.05 \times 0.04 \times 0.02$
Crystal system	triclinic	triclinic	triclinic	orthorhombic
Space group (no.)	$P\bar{1}$ (2)	$P\bar{1}$ (2)	$P\bar{1}$ (2)	$P2_12_12_1$ (19)
a [Å]	5.648(1)	5.869(1)	5.655(2)	6.177(1)
b [Å]	7.623(2)	7.527(2)	10.990(2)	7.737(2)
c [Å]	16.337(3)	16.204(3)	13.243(3)	26.002(5)
α [°]	96.56(3)	79.40(3)	85.67(3)	90.0(0)
β [°]	95.27(3)	86.32(3)	80.36(3)	90.0(0)
γ [°]	95.58(3)	81.73(3)	87.49(3)	90.0(0)
Cell volume [Å^3]	691.7(2)	695.8(2)	808.7(3)	1242.7(4)
Molecular units per cell	2	2	2	4
μ [mm^{-1}]	0.090	0.095	0.080	0.077
Density (calcd) [g cm^{-3}]	1.346	1.357	1.262	1.268
T [K]	200	200	200	200
Scan range (2Θ)	2.5 – 55.1	5.1 – 54.8	3.7 – 59.9	3.1 – 55.0
Scan speed / sec frame^{-1}	16	50	6	60
Measured reflections	4313	4636	6364	2856
Unique reflections	2934	3104	4529	2831
Obs. reflections $(I \geq 2\sigma)$	2215	1479	2906	2359
Parameters refined	196	210	292	224
Max. of residual electron density [e Å^{-3}]	$0.37/-0.36$	$0.42/-0.27$	$0.35/-0.33$	$0.18/-0.21$
Agreement factors^{a,b} (F^2 refinement)	$R_1 = 8.2\%$ $R_w = 27.4\%$	$R_1 = 8.2\%$ $R_w = 21.3\%$	$R_1 = 8.1\%$ $R_w = 24.4\%$	$R_1 = 5.2\%$ $R_w = 13.7\%$

[a] $R_1 : I > 2\sigma(I)$; [b] R_w: all data.

into the correct conformation according to DFT calculations (B3LYP, 3-21G$*$ basis set) of $(1)_2$ in a single-bonded arrangement and $(\mathbf{1})_2$ in the experimentally determined and DFT optimised double-bonded ring structure (Fig. 3).

Thus suitably substituted (substituted phenyl)dipyrromethanes are useful synthons for the construction of hydrogen-bonded supramolecular systems – in spite of the facts that donor and acceptor sites are 7 Å apart and that their relative orientation is quite flexible.

Experimental Section

Unless noted otherwise, all manipulations were carried out under argon by means of standard Schlenk techniques. All solvents were dried by standard methods and distilled under argon prior to use. All other reagents were used as received from commercial sources.

NMR: Bruker Avance DPX 200 at 200.15 MHz (^{1}H), 50.323 MHz (^{13}C) at 303 K; chemical shifts (δ) in ppm with respect to residual solvent peaks as internal standards: $CDCl_3$ (^{1}H: $\delta = 7.24$; ^{13}C: $\delta = 77.0$); CD_2Cl_2 (^{1}H: $\delta = 5.32$; ^{13}C: $\delta = 53.5$); [D$_6$]-acetone (^{1}H: $\delta = 2.04$; ^{13}C: $\delta = 29.8$). – IR spectra were recorded on a BioRad Excalibur FTS 3000 spectrometer using CsI disks. – Mass spectra were recorded on a Finnigan MAT 8400 spectrometer. – Elemental analyses were performed by the microanalytical laboratory of the Organic Chemistry Department, University of Heidelberg.

Computational method

Density functional calculations were carried out with the Gaussian03/DFT [13] series of programs. The B3LYP formulation of density functional theory was used employing the 6-31G+(d,p) and 3-21G* basis sets, respectively [13]. Harmonic vibrational frequencies and infrared intensities were calculated by numerical second derivatives using analytically calculated first derivatives.

Crystallographic structure determinations

The measurements were carried out on an Enraf-Nonius Kappa CCD diffractometer using graphite monochromated Mo-K_α radiation. The data were processed using the standard Nonius software [14]. All calculations were performed using the SHELXT PLUS software package. Structures were solved using direct or Patterson methods with the SHELXS-97 program and refined with the SHELXL-97 program [15]. Graphical handling of the structural data during refinement was performed using XMPA [16] and WinRay [17]. Atomic coordinates and anisotropic thermal parameters of the non-hydrogen atoms were refined by full-matrix least-squares calculations.

Crystallographic data for the structures have been deposited with Cambridge Crystallographic Data Centre, CCDC-258022 – CCDC-258025. Copies of the data can be obtained free of charge on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK

Table 3. Analytical data of **1**, **2**, **3** and **4** (atom numbering according to Scheme 1).

	1	**2**	**3**	**4**
M. p. [°C]	164	164	110	62
IR (CsI) [cm^{-1}]	3350 (NH, s), 1700 (C=O, s)	3550 (NH, OH, s), 3350 (NH, OH, s), 1680 (C=O, s)	3346 (NH, s), 3226 (NH, s), 1650 (C=O, s)	3400 – 3310 (NH, s), 3200 (NH, m), 1250 (CN, s)
^{1}H NMR	[a]	[b]	[c]	[b]
H^1	8.15 (br.s)	8.00 (br.s)	9.74 (br.s)	7.95 (br.s)
H^2	6.77 (dd, $J = 2.7$; 1.6 Hz)	6.76 (dd, $J = 2.7$; 1.4 Hz)	7.71 (dd, $J = 2.7$; 1.6 Hz)	6.68 – 6.75 (m)
H^3	6.17 (dd, $J = 2.7$; 2.7 Hz)	6.22 (dd, $J = 3.1$; 2.7 Hz)	6.02 (dd, $J = 2.7$; 2.7 Hz)	6.19 (dd, $J = 3.1$; 2.7 Hz)
H^4	5.90 – 5.95 (m)	5.90 – 6.00 (m)	5.74 – 5.82 (m)	5.90 – 6.00 (m)
H^6	5.59 (s)	5.59 (s)	5.53 (s)	5.41 (s)
H^8	7.35 (d, $J = 8.2$ Hz)	7.37 (d, $J = 8.3$ Hz)	7.28 (d, $J = 8.0$ Hz)	7.04 (d, $J = 8.3$ Hz)
H^9	8.02 (d, $J = 8.2$ Hz)	8.10 (d, $J = 8.3$ Hz)	7.80 (d, $J = 8.0$ Hz)	6.68 (d, $J = 8.3$ Hz)
other hydrogen atoms	3.94 (s, CH_3)	–	1.25 (d, $J = 6.7$ Hz, CH_3); 4.15 – 4.35 (m, CH); 7.42 (br.s., NH)	3.7 (br.s, NH_2)
^{13}C{^{1}H} NMR	[a]	[b]	[c]	[b]
C^2	117.9	118.0	117.7	115.8
C^3	108.9	109.1	107.9	108.8
C^4	107.7	108.0	107.1	107.4
C^5	148.7	148.8	147.1	133.6
C^6	44.4	44.5	44.3	43.8
C^7	131.8	131.9	134.0	132.5
C^8	128.8	128.4	128.8	129.8
C^9	130.2	131.0	127.4	120.0
C^{10}	129.0	129.0	133.2	145.0
other carbon atoms	52.4 (CH$_3$); 167.0 (CO$_2$Me)	171.7 (CO$_2$H)	22.4 (CH$_3$); 42.0 (CH); 166.1 (CON)	–
MS (EI, 70 eV): *m/z* (%)	280 (100) [M$^+$], 214 (50) [M$^+$-pyrrole], 145 (72) [M$^+$-$C_8H_7O_2$]	266 (100) [M$^+$], 200 (34) [M$^+$-pyrrole], 145 (52) [M$^+$-$C_7H_5O_2$]	307 (100) [M$^+$], 241 (46) [M$^+$-pyrrole], 145 (97) [M$^+$-$C_{11}H_{13}NO$]	237 (100) [M$^+$], 170 (35) [M$^+$-pyrrole], 145 (32) [M$^+$-C_6H_6N]
HR-MS (EI) calcd. found	280.1212 280.1194	266.1055 266.1035	307.1785 307.1662	237.1266 237.1247

[a] In CD_2Cl_2; [b] in $CDCl_3$; [c] in [D_6]-acetone.

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Synthesis of 1, 2 *and* 4

Following the general procedure of Lindsey *et al.* [5] a mixture of pyrrole, the corresponding aldehyde and trifluoroacetic acid (50:1:0.004) was stirred at room temperature for 10 min. 0.1 M NaOH and ethyl acetate were added, and the layers were separated. The aqueous layer was acidified with diluted HCl and extracted again with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated to remove the excess pyrrole. Column chromatography [silica, CH_2Cl_2/ethyl acetate (3:1)], washing with water and recrystallisation from ethanol/water (10:1) afforded the pure dipyrromethanes in 95% (**1**), 75% ($\mathbf{2 \bullet H_2O}$) and 50% (**4**) yield, respectively. The presence of one water molecule in $\mathbf{2 \bullet H_2O}$ was confirmed by elemental analysis for $C_{16}H_{16}N_2O_3$: calcd. C 67.59, H 5.67, N 9.85; found C 67.87, H 5.66, N 9.95.

Synthesis of 3

The acid **2** was activated with 1-hydroxybenzotriazole (1 eq) in the presence of 1,3-dicyclohexylcarbodiimide (1 eq) for 12 h and treated with 1.1 equivalents of isopropylamine in CH_2Cl_2 for 12 h at room temperature. After removal of the solvent and recrystallisation from ethanol/water (10:1) **3** was obtained in 90% yield.

Analytical data of **1** – **4** are summarised in Table 3.

Acknowledgements

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[1] P. D. Rao, S. Dhanalekshmi, B. J. Littler, J. S. Lindsey, J. Org. Chem. **65**, 7323 (2000).

[2] S. R. Halper, M. R. Malachowski, H. M. Delaney, S. M. Cohen, Inorg. Chem. **43**, 1242 (2004).

[3] S. R. Halper, S. M. Cohen, Chem. Eur. J. **9**, 4661 (2003).

[4] G. R. Desiraju, Angew. Chem. **107**, 2541 (1995); Angew. Chem. Int. Ed. Engl. **34**, 2311 (1995).

[5] B. J. Littler, M. A. Miller, C.-H. Hung, R. W. Wagner, D. F. O'Shea, P. D. Boyle, J. S. Lindsey, J. Org. Chem. **64**, 1391 (1999).

[6] V. Bennis, J. F. Gallagher, Acta Crystallogr. **C54**, 130 (1998).

[7] G. K. Patra, Y. Diskin-Posner, I. Goldberg, Acta Crystallogr. **E58**, o530 (2002).

[8] J. F. Gallagher, E. Moriarty, Acta Crystallogr. **C55**, 1079 (1999). [9]

[9] In the lattice of **2•H$_2$O** the water molecule connects the dimers along the crystallographic *a*-axis to form columns of dimers through O2-H$\cdots$O$_W$ and O$_W$-H$\cdots$O1' hydrogen bonds with O2-O$_W$ = 2.583(4) Å and O$_W$$\cdots$O1 = 2.774(5) Å.

[10] T. Steiner, Angew. Chem. **114**, 50 (2002); Angew. Chem. Int. Ed. **41**, 48 (2002).

[11] F. H. Allen, W. D. S. Motherwell, P. R. Raithby, G. P. Shieldsa, R. Taylor, New. J. Chem. 25 (1999).

[12] $R^x{}_y(n)$: The superscript x denotes the number of hydrogen acceptors, the subscript y the number of hydrogen donors and n the ring size. C(n) denotes a chain with n atoms in the repeating unit. J. Bernstein, R. E. Davis, L. Shimoni and N.-L. Chang, Angew. Chem. **107**, 1689 (1995); Angew. Chem. Int. Ed. Engl. **34**, 1555 (1995).

[13] Gaussian 03, Revision B.03, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, (Jr.), T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Pittsburgh PA (2003).

[14] R. Hooft, Collect, Data Collection Software, Nonius, The Netherlands (1998); http://www.nonius.com.

[15] G. M. Sheldrick, SHELXS-97, Program for Crystal Structure Solution, University of Göttingen, Germany (1997); http://www.shelx.uni-ac.gwdg.de/shelx/index.html; G. M. Sheldrick, SHELXL-97, Program for Crystal Structure Refinement, University of Göttingen, Germany (1997); http://www.shelx.uni-ac.gwdg.de/shelx/index.html; International Tables for X-ray Crystallography, **Vol. 4**, Kynoch Press, Birmingham (1974).

[16] L. Zsolnai and G. Huttner, XPMA, University of Heidelberg, Germany (1998); http://www.rzuser.uni-heidelberg.de/∼il1/laszlo/xpm.html.

[17] R. Soltek and G. Huttner, WinRay, University of Heidelberg, Germany (1999); http://www.uni-heidelberg.de/institute/fak12/AC/huttner/frame/frame_soft.html.