



# Synthesis and self-assembly of a novel tetrapyrrole containing dipyrin units linked at the 3,3'-positions

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## Abstract

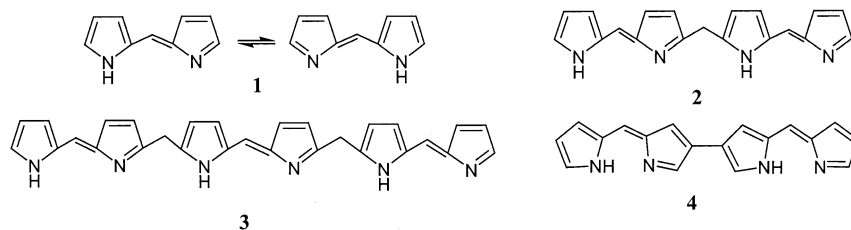
A novel ligand comprising two dipyrin units linked by a CH<sub>2</sub> spacer at the 3-position has been synthesized and used to prepare a double-stranded helical assembly. Its structure was confirmed by X-ray analysis. A new approach to 3,3'-linked dipyrromethanes with CH<sub>2</sub> as the spacer is also reported. © 2000 Elsevier Science Ltd. All rights reserved.

*Keywords:* tetrapyrrole; self-assembly; dipyrin; 3,3'-dipyrromethane; ligand.

The use of metal ions and ligands in supramolecular assemblies has been extensively studied in recent years. Among many ligands designed by chemists, the polybipyridine ligands developed by Lehn and his colleagues are particularly interesting with respect to their ability to generate helicates,<sup>1</sup> grids,<sup>2</sup> cages,<sup>3</sup> ladders,<sup>4</sup> and rings.<sup>5</sup> In contrast to bipyridine, dipyrins **1** were recently found to be ideal building blocks for supramolecular assemblies.<sup>6,7</sup> Dipyrins **1**, formerly called dipyrromethenes are important building blocks for porphyrins, bile pigments and linear polypyrroles.<sup>8,9</sup> In dipyrin **1**, the hydrogen at the N–H group can be removed and the resulting mono-anionic species is a resonance stabilized ligand. The complexes generated by dipyrins **1** and metal ions are neutral species, therefore, counterions are not needed. Consequently, it is particularly convenient to purify the complexes by column chromatography since they are not charged and are generally the least polar component in the reaction mixtures<sup>6,7</sup> (Scheme 1).

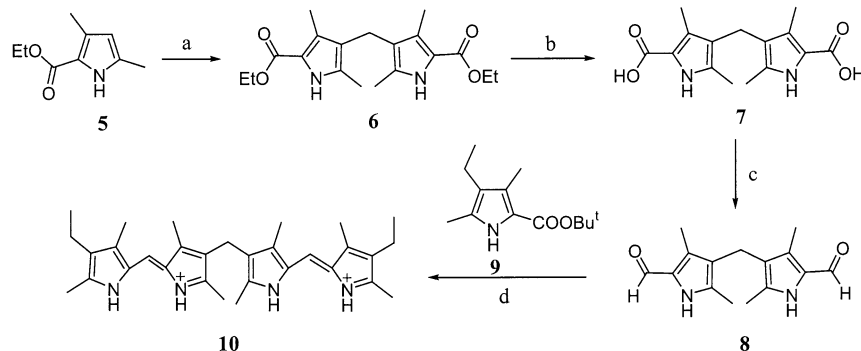
Self-assemblies of polydipyrins such as biladiene-ac **2**,<sup>6</sup> hexapyrins **3**<sup>6</sup> and 3,3'-bidipyrins **4**<sup>7</sup> have been reported. However, the self assembly of compound **10**, in which two dipyrin units are separated by a –CH<sub>2</sub>– bridge at the 3,3'-positions and rotation and twisting around the –CH<sub>2</sub>– bridge are permitted, is still unknown. Herein, we wish to report a new approach to 3,3'-linked dipyrins spaced by a methylene group and the synthesis and self-assembly of compound **10**.

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Scheme 1.

The novel tetrapyrrole ligand **10** was synthesized in four steps with an overall yield of 39% starting from the 3-unsubstituted pyrrole **5**, as shown in Scheme 2. Obviously the 3,3'-dipyrromethane **6** was a crucial intermediate. Although its analogs, 2,2'-dipyrromethanes, have been known for a long time,<sup>8,9</sup> 3,3'-dipyrromethanes have been less explored. To the best of our knowledge, there are only a few examples reported in the literature.<sup>10,11</sup> Unfortunately, these do not include detailed synthetic procedures or proper characterization. We tried to couple a 4-unsubstituted pyrrole with paraformaldehyde under acidic conditions in different solvent systems. It was found that the best yield of the key intermediate 3,3'-dipyrromethane **6**<sup>12</sup> was obtained by coupling 2-ethoxycarbonyl-3,5-dimethylpyrrole **5**<sup>13</sup> with paraformaldehyde in hydrogen chloride–glacial acetic acid at room temperature. It is worth noting that if the same reaction was run at low temperature (below 0°C), the unsubstituted position of pyrrole **5** was chloromethylated to yield 2-ethoxycarbonyl-4-chloromethyl-3,5-dimethylpyrrole.<sup>14</sup> The purification of compound **6** was particularly convenient since it precipitated out during the reaction and could be isolated simply by suction filtration.



Scheme 2. Reagents and conditions: (a) paraformaldehyde and HCl in HOAc at rt (83%); (b) 4.0 equiv. NaOH reflux in 95% ethanol for 4 h, then in 1 M H<sub>2</sub>SO<sub>4</sub> (84%); (c) reflux in DMF for 30 min, benzoyl chloride at 0° for 15 min, then aqueous sodium carbonate (77%); (d) **9** was dissolved in CF<sub>3</sub>COOH for 5 min, then **8** and HBr–HOAc were added (73%)

Unlike 2,2'-dipyrromethane analogs,<sup>15</sup> saponification of **6** using a large excess of sodium hydroxide (4 mole equiv.) in aqueous ethanol under reflux for 5 h afforded the diacid product **7**<sup>12</sup> in quantitative yield. The diacid **7** was converted to the corresponding diformyl intermediate **8**<sup>12</sup> according to the standard *Vilsmeier* formylation procedure.<sup>16</sup> Condensation of **8** with 3,5-dimethyl-4-ethyl-2-carboxypyrrole, generated in situ by treating the corresponding *tert*-butyl ester **9**<sup>17</sup> with trifluoroacetic acid, gave the expected tetrapyrrole **10**<sup>12</sup> in high yield. Following the same procedures we also synthesized bis(2,4,7,9-tetramethyl-8-methoxy-carbonyl)ethyldipyrroin-3-

yl)methane and bis(2,4,9-trimethyl-7,8-diethyldipyrrin-3-yl)methane.<sup>18</sup> When a solution of  $\text{Zn}(\text{OAc})_2$  and MeOH was added to a solution of **10** in  $\text{CHCl}_3$  a single complex **11**<sup>12</sup> was formed in 92% yield, and had a molecular weight of 1060.5 as confirmed by MALDI-TOF mass spectroscopy. It was a dimeric complex with a ligand:metal ratio of 2:2. The X-ray structure<sup>12</sup> of this zinc complex (Fig. 1) of **10** shows that it has double stranded helical geometry, resulting from a twist around the  $-\text{CH}_2-$  bridge in **10**. The distance between the two metal centers along the axis of the helix is 7.7632 Å.

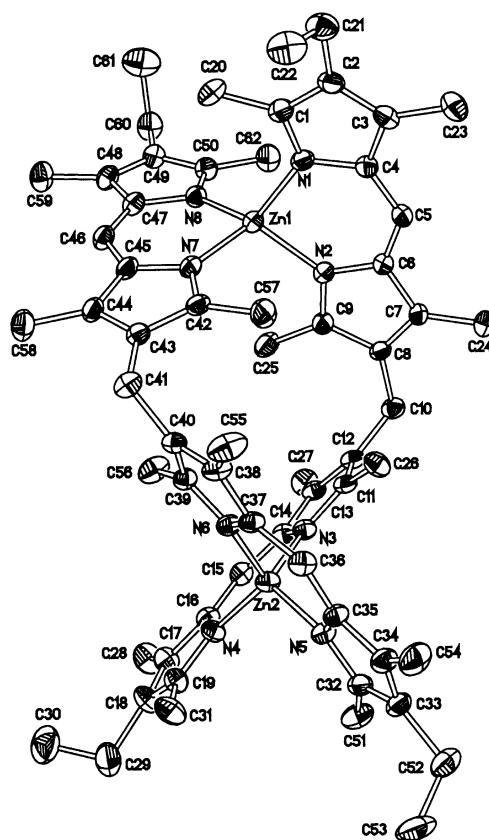


Figure 1. X-ray structure of **11** (hydrogen atoms are omitted for clarity)

In summary, our work has provided an efficient route to 3,3'-linked dipyrins, which are very useful building blocks for helical supramolecular architectures. Further work will focus on the syntheses and self-assembly of a non-twisted biladiene-ac, in which two dipyrin units are fixed in the same plane and the twist or rotation around the 3,3'- $\text{CH}_2-$  is restricted.

## Acknowledgements

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## References

- Hasenknopf, B.; Lehn, J.-M.; Baum, G.; Fenske, D. *Proc. Natl. Acad. Sci. USA* **1996**, *93*, 1397–1400. Piguet, C.; Bernardinelli, G.; Hopfgartner, G. *Chem. Rev.* **1997**, *97*, 2005–2062
- Weissbuch, I.; Baxter, P. N. W.; Cohen, S.; Cohen, H.; Kjaer, K.; Howes, P. B.; Als-Nielsen, J.; Hanan, G. S.; Schubert, U. S.; Lehn, J.-M.; Leiserowitz, L.; Lahav, M. *J. Am. Chem. Soc.* **1998**, *120*, 4850–4860.
- Fujita, M.; Yu, S.-Y.; Kusakawa, T.; Funaki, H.; Ogura, K.; Yamaguchi, K. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2082–2085.
- Baxter, P. N. W.; Hanan, G. S.; Lehn, J.-M. *Chem. Commun.* **1996**, 2019–2020.
- Funeriu, D. P.; Lehn, J.-M.; Baum, G.; Fenske, D. *Chem. Eur.* **1997**, *3*, 99–104.
- Zhang, Y.; Thompson, A.; Rettig, S. J.; Dolphin, D. *J. Am. Chem. Soc.* **1998**, *120*, 13537–13538.
- Thompson, A.; Rettig, S. J.; Dolphin, D. *Chem. Commun.* **1999**, 631–632.
- Falk, H. *The Chemistry of Linear Oligopyrroles and Bile Pigments*; Springer-Verlag: Wien, 1989.
- Dolphin, D. *The porphyrins*; Academic Press: New York, 1979; Vols. I–VII.
- John, B.; Paine, I.; Dolphin, D. *Can. J. Chem.* **1978**, *56*, 1710–1712.
- Hoef, K. V. D.; Hempenius, M. A.; Koek, J. H.; Lugtenburg, J.; Fokkens, R. *Recl. Trav. Chim. Pay-Bas* **1987**, *106*, 77–84.
- Compound 2,2',4,4'-tetramethyl-5,5'-diethoxycarbonyl-3,3'-dipyrromethane **6**  
mp: 236–238°C; EI-MS: *m/e* 346; UV–Vis:  $\lambda_{\max}$  (282.50 nm,  $\text{\AA}36,100$ );  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.34 (t, 6H,  $\text{CH}_3$ ), 2.05 (s, 6H,  $\text{CH}_3$ ), 2.17 (s, 6H,  $\text{CH}_3$ ), 3.46 (s, 2H,  $\text{CH}_2$ ), 4.28 (q, 4H,  $\text{CH}_2$ ), 8.73 (s, 2H, NH);  $^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  10.60, 11.13, 19.03, 58.79, 115.73, 119.25, 126.16, 130.47, 160.95. Anal. calcd for  $\text{C}_{19}\text{H}_{26}\text{N}_2\text{O}_4$ : C, 65.87; H, 7.56; N, 8.09. Found: C, 65.88; H, 7.38; N, 7.85.  
Compound 2,2',4,4'-tetramethyl-5,5'-biscarboxy-3,3'-dipyrromethane **7**  
mp: 128–130°C;  $^1\text{H}$  NMR (200 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  1.90 (s, 6H,  $2\text{CH}_3$ ), 2.10 (s, 6H,  $2\text{CH}_3$ ), 3.20 (s, 2H,  $\text{CH}_2$ ), 10.95 (s, 4H,  $2\text{COOH}$ , 2NH);  $^{13}\text{C}$  NMR (50 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  11.20, 11.34, 19.50, 121.33, 127.67, 130.32, 136.43, 161.55.  
Compound 2,2',4,4'-tetramethyl-5,5'-diformyl-3,3'-dipyrromethane **8**  
mp: >300°C; EI-MS: *m/e* 258; UV–Vis:  $\lambda_{\max}$  ( $\text{DMSO}$ ) 314.10 nm ( $\text{\AA}29,600$ );  $^1\text{H}$  NMR (200 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  2.04 (s, 6H,  $\text{CH}_3$ ), 2.09 (s, 6H,  $\text{CH}_3$ ), 3.39 (s, 2H,  $\text{CH}_2$ ), 9.40 (s, 2H, CHO), 11.43 (s, 2H, NH).  $^{13}\text{C}$  NMR (50 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  8.91, 11.34, 18.42, 119.92, 127.54, 130.70, 135.17, 175.83. Anal. calcd for  $\text{C}_{19}\text{H}_{26}\text{N}_2\text{O}_4$ : C, 69.74; H, 7.02; N, 10.84. Found: C, 69.63; H, 7.04; N, 10.71.  
Compound bis(2,4,7,9-tetramethyl-8-ethyl-dipyrin-3-yl)methane **10**  
mp: >230°C (dec.); FAB-MS: *M*+1 469; UV–Vis:  $\lambda_{\max}$  ( $\text{CH}_2\text{Cl}_2$ ) 504.4 nm ( $\text{\AA}316,900$ ); 461.2 nm ( $\text{\AA}98,400$ );  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.08 (t, 6H,  $\text{CH}_3$ ), 2.15 (s, 6H,  $\text{CH}_3$ ), 2.28 (s, 6H,  $\text{CH}_3$ ), 2.44 (q, 4H,  $\text{CH}_2$ ), 2.57 (s, 6H,  $\text{CH}_3$ ), 2.68 (s, 6H,  $\text{CH}_3$ ), 3.57 (s, 2H,  $\text{CH}_2$ ), 7.04 (s, 2H,  $-\text{CH}=\text{}$ ), 13.07 (s, 1H, NH), 13.16 (s, 1H, NH).  $^{13}\text{C}$  NMR (50 Hz,  $\text{CDCl}_3$ ):  $\delta$  9.99, 10.36, 12.90, 14.30, 17.16, 19.47, 118.82, 124.32, 125.43, 126.76, 131.34, 140.84, 142.34, 151.89, 155.97. Anal. calcd for  $\text{C}_{31}\text{H}_{42}\text{Br}_2\text{N}_4$ : C, 59.05; H, 6.71; N, 8.89. Found: C, 58.83; H, 6.68; N, 8.87.  
Zinc complex **11**  
mp: >230°C (dec.); MALDI-TOF-MS: 1060; UV–Vis:  $\lambda_{\max}$  ( $\text{CH}_2\text{Cl}_2$ ) 526.8 nm ( $\text{\AA}326,700$ ); 477.8 nm ( $\text{\AA}130,000$ );  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.01 (t, 12H,  $\text{CH}_3$ ), 1.38 (s, 12H,  $\text{CH}_3$ ), 1.99 (t, 12H,  $\text{CH}_3$ ), 2.19 (s, 12H,  $\text{CH}_3$ ), 2.20 (s, 12H,  $\text{CH}_3$ ), 2.34 (q, 8H,  $\text{CH}_2$ ), 3.40 (s, 4H,  $\text{CH}_2$ ), 5.87 (s, 4H, CH), 7.25 (s, 4H, CH).  $^{13}\text{C}$  NMR (50 MHz,  $\text{CDCl}_3$ ):  $\delta$  9.86, 14.90, 15.10, 17.97, 20.47, 120.28, 125.55, 129.19, 135.06, 135.26, 136.01, 136.31, 155.79, 157.16. Anal. calcd for  $\text{C}_{62}\text{H}_{76}\text{N}_8\text{Zn}_2\cdot\text{H}_2\text{O}$ : C, 68.82; H, 7.27; N, 10.36. Found: C, 68.86; H, 7.21; N, 10.30.  
X-ray crystal data of **11**  
 $\text{C}_{62}\text{H}_{76}\text{N}_8\text{Zn}_2\cdot 2\text{H}_2\text{O}$ : *M* = 1100.08, monoclinic, space group  $P2_1/c$  (No. 14), *a* = 11.3915(9), *b* = 2.5671(10), *c* = 42.419(3) Å,  $\beta$  = 95.698(3)°, *V* = 6042.7(8) Å<sup>3</sup>, *Z* = 4, *D*<sub>calcd</sub> = 1.209 g/cm<sup>3</sup>, *F*(000) = 2336,  $\mu$  = 0.841 mm<sup>-1</sup>, crystal size 0.24 × 0.14 × 0.07 mm NONIUS Kappa CCD diffractometer, *T* = 293(2) K, graphite-monochromated Mo *K*α radiation,  $\lambda$  = 0.71073 Å,  $\theta_{\max}$  = 25.35°, 46 819 reflections measured, 10 725 unique with *R*<sub>int</sub> = 0.122. The final unit cell parameters were obtained by least-squares using 46 819 reflections with  $2\theta$  = 3.54–50.7°. Data were corrected for *L*<sub>p</sub> factors and absorption with transmission factors of 0.888–0.954. The structure was solved by direct methods. Non-H atoms were refined anisotropically and H atoms were added by calculated positions. The refinement converged at *R*<sub>1</sub> = 0.077 for 5827 observations with  $I \geq 2\sigma(I)$ . Calculations were performed using SHELX-97 (Sheldrick, 1997).

13. Robinson, J. A.; MacDonald, E.; Battersby, A. R. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1699–1709.
14. MacDonald, S. F.; Markovac, A. *Can. J. Chem.* **1965**, *43*, 3247–3252.
15. Shrout, D. P.; Lightner, D. A. *Synthesis* **1990**, 1062–1064.
16. Chong, R.; Clezy, P. S.; Liepa, A. J.; Nichol, A. W. *Aust. J. Chem.* **1969**, *22*, 229–238.
17. Jonnson, A. W.; Kay, I. T.; Markham, E.; Price, R.; Shaw, K. B. *J. Chem. Soc.* **1959**, 3416–3424
18. Zhang, Y.; Ma, J.-S., full paper in preparation.