

Synthesis and Structure of 1,4-Bis(α,α' -dipyrromethyl)cyclohexane

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Meso-functionalized dipyrromethanes are widely used as building blocks for the synthesis of porphyrins, corroles and reduced porphyrins.¹⁻³ The importance of the porphyrin analogues in the fields of medicinal, material and biological chemistry has been well documented.¹ The synthetic methods of *meso*-substituted dipyrromethanes also have been continuously modified and optimized due to their importance in the synthesis of asymmetrically substituted porphyrins.⁴⁻⁵ Since a monumental procedure of one-pot synthesis of dipyrromethanes was developed,⁶ several macrocyclic model systems have been successfully synthesized by utilizing those dipyrromethanes.⁷ In continuation of our efforts to develop newer methods for the synthesis of simple building blocks for porphyrins, we were able to synthesize *meso*-functionalized oligopyrromethanes.⁸ These have enabled us to synthesize porphyrins as well as corroles bearing functional groups at designated positions. With these regards, we herein report the synthesis and the solid state structure of a unique dipyrromethane derivative obtained from the reaction of pyrrole and diketone.

Experimental Section

The title compound was synthesized as follows: A solution of pyrrole (6 mL, 40 mmole), 1,4-cyclohexandione (0.44 g, 4 mmol) was treated with BF₃·OEt₂ (4.8 μ L, 0.4 mmol) at 30 °C for 30 minutes. The resulting precipitated solid was collected by filtration and washed with water. The white solid was pure enough for further characterization. Yield 0.73 g (53 %). Single crystals were obtained by slow evaporation of dichloromethane. ¹H NMR (CD₂Cl₂/DMSO-d₆) δ 2.21 (bs, 8H, cyclohexane-methylene), 5.87 (s, 4H, pyrrole-H), 5.94 (s, 4H, pyrrole-H), 6.54 (s, 4H, pyrrole-H), 9.57 (bs, 4H, NH); ¹³C NMR (CD₂Cl₂/DMSO-d₆) δ 32.31, 38.92, 116.48, 116.41, 107.29, 107.16; FAB MS Calcd for C₂₂H₂₄N₄ 344.20, Found 344.13 (M⁺, 17%), 278.17, (M⁺-pyrrole, 9 %).

Crystal structure determination. Good quality of single crystal was obtained by slow evaporation of the solvent. X-Ray data of a crystal having dimensions 0.3 \times 0.3 \times 0.4 mm were collected on a Nonius CAD4-Express diffractometer equipped with graphite-monochromated MoK α radiation (λ = 0.71073 Å) at room temperature. Unit cell parameters were determined from automatic centering of 25 reflections. The data were collected using the ω -2 θ scan technique in the range 2.89 \leq θ \leq 26.27°. No absorption corrections were applied. The structure was solved by direct method and

Table 1. Crystal data and structural refinement of compound 2

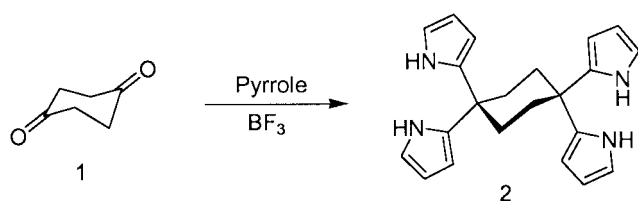
Formula	C ₂₂ H ₂₄ N ₄
Formula weight	344.45
Temperature	293(2)K
Wavelength	0.71069 Å
Space group	P21/n (No. 14)
a	7.818(1) Å
b	8.053(1) Å
c	14.137(2) Å
β	93.04(1)°
volume	888.8(2) Å ³
Z, Calculated density	2, 1.287 g/cm ³
F(000)	368
θ range of data collection	2.89 to 26.27°
Index ranges	-9 \leq h \leq 9, -10 \leq k \leq 0, -17 \leq l \leq 6
Reflection collected / unique	1893 / 1785 [R _{int} = 0.0225]
Refinement method	Full matrix least-squares on F ²
Data/restraints/parameters	1785 / 0 / 118
Goodness-of-fit on F ²	0.968
Final R indices [I > 2 σ (I)]	R ₁ ^a = 0.0873, wR ₂ ^b = 0.2087
R indices (all data)	R ₁ ^a = 0.1950, wR ₂ ^b = 0.2348
Largest diff. peak	0.284

^aR₁ = $\sum ||F_o| - |F_c|| / \sum |F_o|$. ^bwR₂ = $\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]^{1/2}$. w = 1 / [$\sigma^2(F_o)^2 + (0.1241P)^2 + 0.000P$] where P = (F_o² + 2F_c²) / 3

refined by full-matrix least-squares calculation with SHELXL-97. Anisotropic thermal parameters were used for all atoms except hydrogen. All the remaining hydrogen-atom positions were computed and refined with an overall isotropic factor in a riding model. Details on crystal and intensity data are given in Table 1 and some selected bond distances and angles are shown in Table 2.

Results and Discussions

Condensation of pyrrole with an aldehyde or a ketone usually results in the formation of dipyrromethane, which on subsequent reaction leads either to the higher oligopyrromethanes or the porphyrins depending on the reaction conditions. Ketones such as acetone and cyclohexanone condense with pyrrole to afford calix[4]pyrroles. The condensation usually resulted in the formation of different products depending on the reaction conditions. When 1,4-cyclohexandione (**1**) was condensed with pyrrole, bis-dipyrromethane (**2**) was isolated as the only product. To the best of our knowledge, there are no reports of X-ray structure available



for this class of compound. Bisdipyrromethane (**2**) formed is a versatile building block. Further condensation with either an aldehyde or a ketone would result in the formation of macrocycles such as phlorins or porphodimethenes. These partially reduced porphyrins have been demonstrated as models for molecular switch and anion binding agents.⁹ The proton NMR spectrum of the compound showed three pyrrolic signals and rather broad singlet for the cyclohexane ring protons. The mass spectral data showed the molecular ion peak and successive loss of pyrrole fragments thereof. The title compound differs from the simple dipyrromethanes in possessing a bridging cyclohexane ring between the two dipyrromethane units. Since the configuration of the pyrrole rings in the dipyrromethane units will ultimately decide its reactivity toward the carbonyl compounds, it is interesting to analyze the geometric relationship of each pyrrolic moiety in the compound. The single crystals of the title compound grown from a solution in dichloromethane possess a centrosymmetric structure with the pyrrolic N-Hs possessing alternating conformation while the cyclohexane moiety adopts somewhat flattened conformation.

As demonstrated recently in the synthesis of calix[n]-pyrroles,¹⁰ the title compound is expected to show a similar type of condensation behavior and can eventually afford larger oligomeric calix[n]pyrroles. The favorable conformation of pyrrolic moiety for the intermolecular cyclization to afford the macrocyclic oligopyrroles will be planar to each other (or driven closer each other). The crystal packing structure observed in the title compound shows that the monomeric units are arranged one above the other. The data shows that there is no H-bonding interaction present in the solidstate structure of the title compound. The cyclohexane ring is adopting a chair conformation while the two pyrrole units attached at 1 and 4 positions are almost perpendicular to each other (dihedral angle $N^1C^4C^1C^8 = 84.47^\circ$). However the solution phase NMR spectrum of the compound showed time averaged signals for the pyrrolic protons suggesting a faster equilibrium among the various conformers. One of the pyrrole rings on the same carbon is also perpendicular to the mean plane of cyclohexane. The cyclohexane ring becomes more planar than normal and the molecule as a whole possesses a center of symmetry (Figure 1). Crystal packing structure shows linear stacking of pyrrole units (Figure 2).

In conclusion, the versatile building block for the synthesis of the reduced porphyrins and calixpyrroles has been synthesized and characterized. Highly ordered oligomeric calixpyrrole could be built using this building block. The synthesis of reduced porphyrins such as phlorins, porpho-

Table 2. Selected bond distances [Å] and angles [°] for compound **2**

C2-C3	1.522(5)	C3-C2-C1	113.0(3)
C2-C1	1.550(5)	C11-N2-C8	110.2(4)
N2-C11	1.363(6)	C8-C9-C10	108.3(4)
N2-C8	1.364(5)	N1-C4-C5	105.7(4)
C9-C8	1.374(6)	N1-C4-C1	122.9(4)
C9-C10	1.410(6)	C5-C4-C1	130.8(4)
C4-N1	1.360(5)	C4-C1-C8	107.5(3)
C4-C5	1.361(6)	C4-C1-C2	122.2(3)
C4-C1	1.511(6)	C8-C1-C2	110.4(3)
C1-C8	1.513(5)	C7-N1-C4	110.3(4)
N1-C7	1.343(5)	N2-C8-C9	106.0(4)
C10-C11	1.341(6)	N2-C8-C1	123.6(4)
C5-C6	1.417(6)	C10-C11-N2	108.3(4)
C7-C6	1.320(7)	C6-C7-N1	109.2(4)

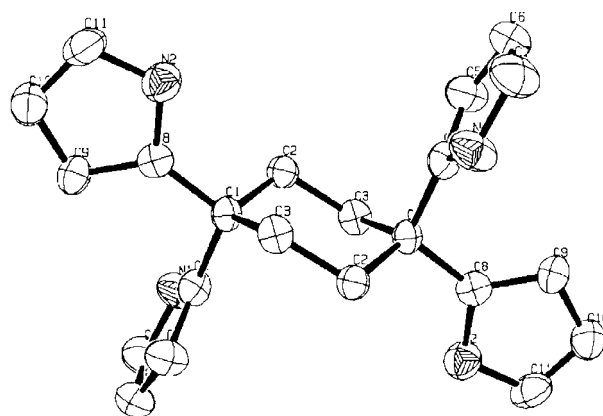


Figure 1. An ORTEP drawing of compound **2** with atomic numbering scheme.

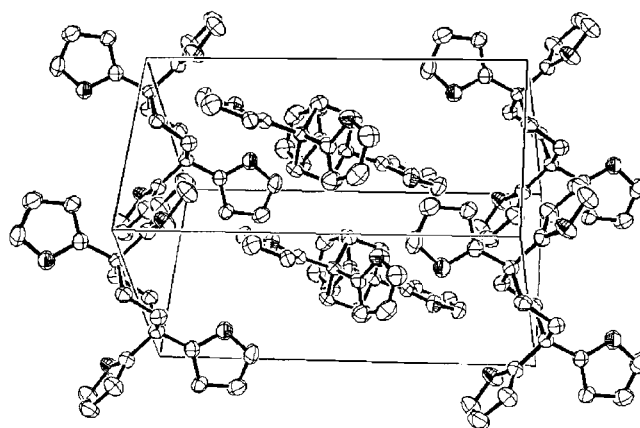


Figure 2. Crystal packing of compound **2**. The hydrogen atoms are omitted for clarity. The c-axis is vertical and b-axis is horizontal.

dimethenes by various combination of dipyrromethanes also will be possible. Works are in progress for further refinement of the synthesis and investigation for the condensation chemistry of the title compounds.

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