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Oxidative Ring Closure and Metal Triggered Ring Opening: Syntheses of Macrocyclic and Linear Hexapyrroles

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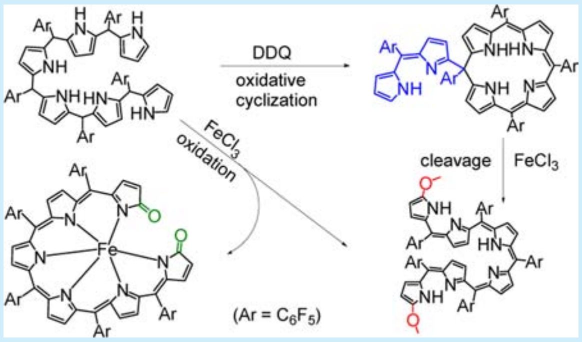
Supporting Information

ABSTRACT: A C_6F_5-substituted hexapyrrane (**1**) was synthesized in one step. Oxidative cyclization of **1** with DDQ afforded a phlorin–dipyrrin conjugate (**2**), and subsequent $FeCl_3$-assisted oxidative cleavage of **2** afforded a terminally di-α-methoxy substituted hexapyrrin (**3**). On the other hand, oxidation of **1** with $FeCl_3$ afforded **3**, a hexapyrrinone Fe^{3+} complex (**4**), and a hexaphyrin (1,1,1,1,1,0) (**5**). These results indicate that the oxidation of hexapyrranes may be developed as an effective approach for the syntheses of novel linear and macrocyclic hexapyrroles.



Pyrrole and linear oligopyrranes have been extensively used in the syntheses of porphyrins and their analogues to achieve rich optoelectronic properties.[1] Oxidation of dipyrromethanes and tripyrranes usually afford linear conjugated di- and tripyrrins, which can be used as fluorescent or colorimetric ion probes.[2] On the other hand, oxidative ring closure of relatively longer linear oligopyrranes has been developed as an effective approach for the syntheses of porphyrin analogues, such as corrole.[3] In this respect, isoamethyrin (1.0.1.0.0.0) was prepared from a hexapyrrane precursor and was developed as a colorimetric sensor for the uranyl cation.[4] Recently, we also reported the oxidation of polypyrranes with two terminal N-confused pyrroles for synthesizing unique porphyrinoids.[5] Despite these successful examples, the syntheses of linear oligopyrranes containing more than five pyrrole units are still rare.

Based on the aforementioned background, we are interested in investigating the syntheses of relatively long chain polypyrranes and their oxidation for the syntheses of novel porphyrinoids as well as linear polypyrrins. In this work, we successfully synthesized a linear hexapyrrane (**1**) from a one-step reaction. Subsequent oxidation with DDQ afforded a phlorin derivative with an appended dipyrrin (**2**). In contrast, oxidation of **1** with $FeCl_3$ afforded hexapyrrins with two terminal methoxy (**3**) or C═O (**4**) moieties as well as the hexaphyrin (1.1.1.1.1.0) (**5**).[6] Interestingly, upon treatment with $FeCl_3$, **2** also can be converted to **3** in a high yield of 88%.

Theoretically, hexapyrrane **1** can be synthesized from the corresponding bilane through successive acylation, reduction, and condensation with pyrrole. But the multistep route will be extremely tedious, and the yield will be relatively low.[7,3b] Therefore, we resorted to the one-step TFA catalyzed condensation between pyrrole and C_6F_5CHO.[8] This reaction usually yields a complicated mixture of linear oligopyrranes, and the product ratios are highly dependent on the molar ratio between pyrrole and C_6F_5CHO.[9] After repeated trials, we finally fixed the ratio at 3:1, and the crude product was separated on a silica gel column by carefully eluting with a mixture of CH_2Cl_2 and petroleum ether (1:3−1:1 v/v). Fortunately, **1** was successfully obtained in an acceptable yield of 13% from the one-step condensation reaction, and it can be synthesized at a gram scale. Thus, this reaction provides a convenient synthesis approach for **1**, which enables further research on its reactivities. Then we continued to check its oxidation reactions. Initially, it was oxidized with 5.5 equiv of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in CH_2Cl_2, which afforded a green solid of **2** in a 22% yield (Scheme 1). HRMS of **2** shows a molecular peak at 1285.1190,

Scheme 1. Multistep Oxidation of 1 (Ar = C_6F_5)

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corresponding to the phlorin framework with an appended dipyrrin, which is consistent with the crystal structure (*vide infra*). Its ^{1}H NMR spectrum in $CDCl_3$ is typical of a nonaromatic structure with pyrrolic β-H signals lying in the range 6.3−7.2 ppm. And broad signals for four NH are observed at 3.6 and 11.7 ppm.[10a] X-ray analyses[11] revealed that **2** contains a four-pyrrolic phlorin[10b] framework (Figure 1a, c) with a dipyrrin appended at the sp^3 *meso*-carbon atom C20, which interrupts the ring conjugation and affords a highly distorted macrocycle. The respective C19−C20, C20−C21, and C20−C1 bond lengths of 1.502(6), 1.525(5), and 1.521(6) Å are typical for C−C single bonds. Among the pyrrole rings, B and C are nearly coplanar, and the A and D rings are tilted from this plane with dihedral angles of 15.7(1)° and 46.9(1)°, respectively. Associated with the sp^3 carbon C20, the interplanar A/D, A/E, and D/E angles are found to be 62.4(1)°, 63.9(1)°, and 59.8(1)°, respectively. Interestingly, a clearly resolved tautomer of **2** is observed in the crystal structure, and the positions of the imino and amino N atoms can be unambiguously assigned based on the bond lengths and angles. For example, the pyrrolic C6−N2−C9 angle exhibits a small value of 104.8(4)°, and thus N2 can be assigned as an imino nitrogen. The corresponding C−N−C angles are 109.3(3)°, 111.1(4)°, and 110.3(3)° for N1, N3, and N4, respectively. And these N atoms can be assigned as the amino nitrogens.[5]

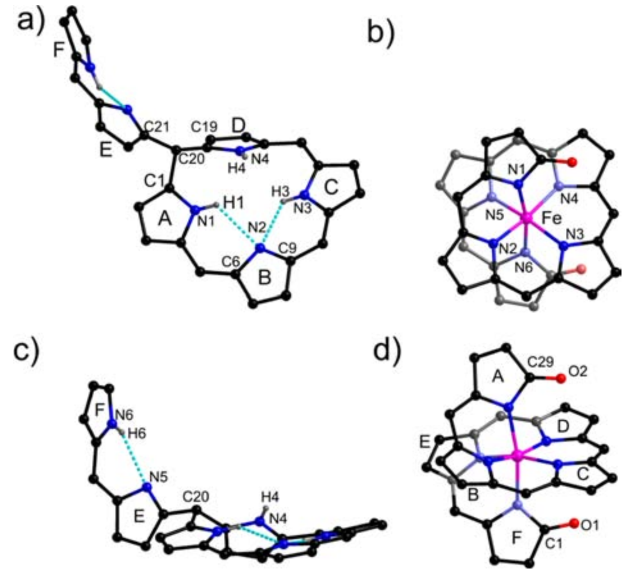


Figure 1. Crystal structures of compounds **2** (a, c) and **4** (b, d). C_6F_5 groups and the hydrogens attached to carbons are omitted for clarity.

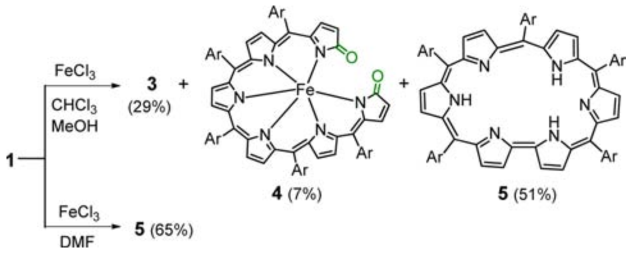
Within the macrocycle, N2 is hydrogen bonded to H1 and H3 with N2···N1 and N2···N3 distances of 2.967(5) and 2.867(5) Å, respectively. In addition, N6 in the appended dipyrrin moiety is hydrogen bonded to H5, with the N5···N6 distance at 2.764(5) Å.

The synthesis of **2** through the oxidative cyclization of **1** is similar to the oxidation of the corresponding pentapyrrane to afford a phlorin derivative.[12] These observations indicate that the formation of a tetrapyrrolic macrocycle is preferred even if a longer oligopyrrole is employed.

The *meso*-C_6F_5 moieties in **2** are favorable for improving the stability of the phlorin framework.[10] However, it is anticipated that **2** may be susceptible to ring opening or skeletal transformation reactions due to the presence of the sp^3 *meso*-carbon atom.[5a,13,14] Consistent with this expectation, when **2** was treated with anhydrous $FeCl_3$ in MeOH, it underwent an oxidative ring opening reaction to afford a high yield (ca. 88%) of a linear hexapyrrin **3**, which bears two methoxy substituents at both terminal pyrroles (Scheme 1). The reaction solvent is vital for this transformation. No target product could be obtained in CH_2Cl_2, and the reaction proceeded smoothly when a few drops of MeOH were added, implying that both terminal methoxy moieties are originated from the methanol solvent. Consistent with this structure, HRMS of **3** shows a molecular peak at 1345.1406, and the ^{1}H NMR of **3** in $CDCl_3$ displays a singlet at 3.88 ppm, which may be assigned to the methoxy hydrogens. Two NH singlets are observed at 13.65 and 12.36 ppm, respectively. And 12 pyrrolic β-hydrogens appear in the range 5.6−6.6 ppm. In addition, the di-α-methoxy substituted hexapyrrin structure of **3** could be further evidenced by the rough crystal structure of its copper complex, **3-Cu**[11] (Figure S18).

We continued to oxidize **1** with different oxidants to check the possibility of synthesizing different linear and/or macrocyclic products.[15] Compound **1** was found to be inert toward oxidants including *p*-chloranil and MnO_2. Interestingly, the oxidation reaction proceeded smoothly when it was treated with $FeCl_3$ (Scheme 2). When 100 equiv of $FeCl_3$ was heated at reflux with **1** in a mixture of $CHCl_3$/MeOH (1:1 v/v) for 4 h, three products (**3**−**5**) were isolated in yields of 29%, 7%, and 51%, respectively. And the yields are highly dependent on the reaction solvents. When DMF or $CHCl_3$ was used, **3** and **4** were not observed and the yield of **5** was increased to 65% (Scheme 2). When ethanol was used instead of methanol with the intention to obtain the ethyoxy substituted analogue of **3**, no desired compound could be obtained. Compared with the two-step synthesis of **3** (Scheme 1) through successive DDQ and $FeCl_3$ oxidation of **1** (a total yield of 19%), this direct oxidation of **1** with $FeCl_3$ provides a more convenient and efficient synthetic approach for **3**. It is also noteworthy that the hexaphyrin **5** could be obtained in a high yield of 65%, which provides an efficient new synthetic method for this compound.

Scheme 2. Oxidation of 1 with $FeCl_3$ in Different Solvents ($Ar = C_6F_5$)



HRMS of compound **4** shows a molecular peak at 1367.9999, which is in agreement with the complex structure with a Fe(III) coordinated to a hexapyrrinone. Coordination of the paramagnetic Fe(III) cation affords weak and unresolved signals in the ^{1}H NMR spectrum of **4**. More solid structural evidence for **4** comes from the single crystal X-ray diffraction analyses,[11] which reveal that the Fe(III) center adopts an octahedral coordination geometry provided by six N atoms from the trianionic hexapyrrinone ligand (Figure 1 b and 1d). Interestingly, the hexapyrrinone adopts a helical conformation. Within the ligand, the O1−C1 and O2−C29 bond lengths are found to be 1.192 and 1.203 Å, respectively. These values are typical for C═O double bonds. The Fe−N bond lengths lie in the range 1.886−1.952 Å, typical for Fe(III)−N bonds.[16] Compared to the preparation of similar tetrapyrrolic bilindiones through ring cleavage reactions of Fe(III) porphyrins,[17] the direct $FeCl_3$ oxidation of the linear hexapyrrane to complex **4** provides a new approach for the syntheses of longer conjugated oligopyrrinones.

The absorption spectra of **2**, **3**, and **4** in CH_2Cl_2 are shown in Figure 2. Compound **2** exhibits characteristics of a phlorin chromophore with a broad absorption band in the region 400−500 nm and near-infrared (NIR) absorption bands at 641 and 800 nm. Compared with **2**, the absorption spectrum of the linear hexapyrrole **3** was drastically changed. It displays a relatively sharp peak at 533 nm, and a low energy NIR band centered at 890 nm, which is related to its large hexapyrrolic π-conjugation structure.[18] Different from **2** and **3**, the Fe(III) complex **4** shows a strong peak at 336 nm and relatively weaker peaks at longer wavelengths.

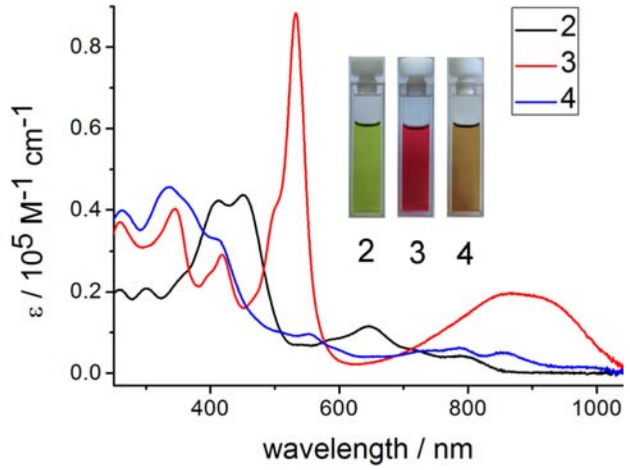
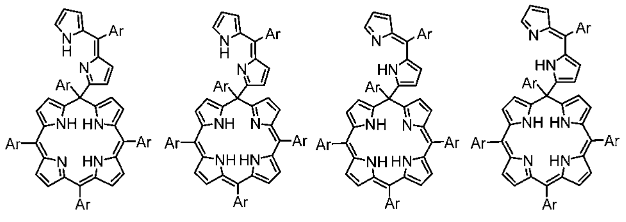


Figure 2. UV−vis spectra of **2**, **3**, and **4** in CH_2Cl_2. The inset shows the phtographs of these compounds in CH_2Cl_2.

Theoretically, **2** has three possible isomers, **2-a**−**2-c** (Figure 3). In fact, only **2** was oberved in the crystal structure (*vide supra*). Density functional theory (DFT) calculations were carried out to understand relative energies of **2** and its isomers using the Gaussian 09 program package,[19] and the results are listed in Figure 3, Figure S15, and Table S1, from which we can see that **2** is the most stable isomer, with its energy 10.7−21.0 kJ/mol lower than the potential isomers **2-a**−**2-c**. These data are consistent with the fact that **2** was the only one isomer observed in the crystal structure.



2 0.0 kJ/mol
2-a 11.8 kJ/mol
2-b 21.0 kJ/mol
2-c 10.7 kJ/mol

Figure 3. Relative free energies (kJ/mol) for **2** and its possible isomers (Ar = C_6F_5).

Compound **3** has five *Z*/*E* stereopositions. We employed a two-step computational screening procedure to elucidate the most probable isomer without looping over all the isomers (see the computation details in SI, Figures S16, S17 and Tables S2 and S3).

In conclusion, a C_6F_5-sbustituted hexapyrrane (**1**) was synthesized in one-step with a moderate yield. And oxidation of **1** with DDQ or $FeCl_3$ has been demonstrated to be effective for the syntheses of novel linear hexapyrrin derivatives as well as macrocyclic hexapyrrolic compounds.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Synthetic procedures and complete experimental details; crystallographic details (CIF) for **2**, **3-Cu**, **4**, **5**; spectroscopic and analytical data; details on DFT calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(11) CCDC 1030534 (**2**), 1034362 (**3-Cu**), and 1030535 (**4**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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(19) All the calculations were achieved with the Gaussian09 program package at the B3LYP/6-31G* level. See Supporting Information for calculation details.