Thiaporphyrins with One, Two and Four Unsubstituted *meso*-Carbons: Synthesis and Functionalization

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Thiaporphyrins with one, two and four unsubstituted *meso* carbons were synthesized from easily available thiophene diols. The reactivity at these carbons was demonstrated by carrying out series of reactions and some very useful functional groups were introduced.

Porphyrins have two reactive positions — the β- and *meso*-positions — at which suitable substituent(s) can be introduced to tune the electronic properties of the porphyrin for specific applications. Most of the porphyrins reported so far have aryl groups at the *meso* positions since they can be synthesized easily and are very stable to handle for applications. Reports on β-unsubstituted *meso*-unsubstituted porphyrins are scarce[1] because these porphyrins are not very stable and are difficult to synthesize. However, the *meso* carbon is highly reactive towards electrophilic and nucleophilic substitutions and very useful functional groups such as bromo, iodo, formyl, ethyne etc. can be introduced at the *meso* positions, giving access to synthetically useful precursors for the synthesis of more complicated porphyrin systems with special physical and chemical properties. Recently, the *meso*-unsubstituted porphyrins have been exploited to synthesize[2] *meso-meso* linked dimeric, trimeric and oligomeric arrays which exhibited useful electronic properties resulting from strong π-conjugation. Senge et al. have developed an efficient synthetic route to selectively introduce various substituents at the *meso* positions by treating *meso*-unsubstituted porphyrins with different organolithium reagents.[3] Shi and Wheelhouse[4] have synthesized different aryl-substituted porphyrins with very high yields by reacting the *meso*-halo porphyrins with various aryl boronic acids under Suzuki coupling conditions. Thus *meso*-unsubstituted porphyrins are highly desirable synthetic precursors for the construction of complex porphyrin-based systems. Interestingly, the few reports available on *meso*-unsubstituted porphyrins are limited to regular porphyrins (N_4 core), and reports on thia- and oxaporphyrins with N_2S_2, N_3S and N_3O porphyrin cores are very few.[5] Broadhurst and Grigg[5a] have synthesized N_3S and N_3O porphyrins with four *meso*-unsubstituted carbons by [3+1] condensation of β-substituted tripyrrane and 2,5-diformyl furan or thiophene. However, the precursors were not easy to synthesize. To be able to carry out further chemistry with *meso*-unsubstituted thiaporphyrins, one should have an easy access to these porphyrins in large quantities. Recently we reported the synthesis of thiaporphyrins having various functional groups such as pyridyl, iodo, ethyne, aldehyde etc. and showed their application in the synthesis of donor-appended thiaporphyrins and unsymmetrical covalent and non-covalent porphyrin arrays.[6] The chemistry of comparatively less known 21-thiaporphyrin could be explored in detail if *meso*-unsubstituted 21-thiaporphyrins were available easily, because the *meso*-unsubstituted porphyrins are synthetic precursors for several unique 21-thiaporphyrin-based systems. In this communication, we wish to report the synthesis of *meso*-unsubstituted thiaporphyrins with four, two and one *meso*-unsubstituted carbons **2**−**5**, respectively, using simple thiophene diols by following a well-established synthetic strategy for 21-thiaporphyrins[7] and show their importance in the synthesis of some functional thiaporphyrins. The thiaporphyrins with the desired number

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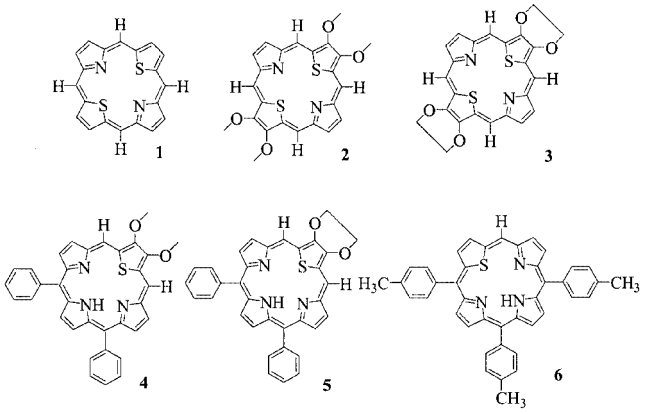
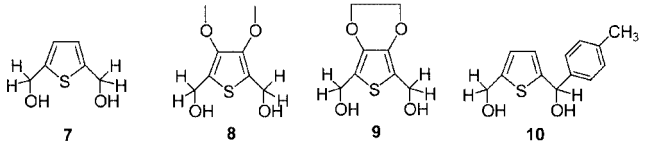
of functional groups will be key building blocks to construct novel thiaporphyrin-based systems.

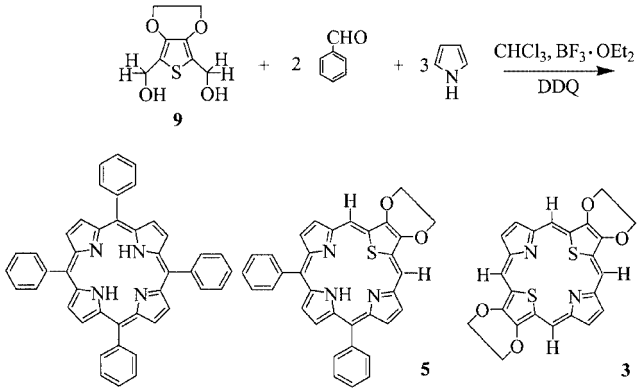


To synthesize *meso*-free thiaporphyrins, the thiophene diols **7**−**10** shown below were needed.



We first attempted to synthesize completely β- and *meso*-unsubstituted 21,23-dithiaporphyrin **1** by condensing one equivalent of diol **7** with one equivalent of pyrrole in $CHCl_3$ in the presence of a catalytic amount of $BF_3{\cdot}OEt_2$ followed by oxidation with DDQ. The absorption spectrum of the reaction mixture indicated the formation of **1**. However, we couldn't isolate **1** as it is very unstable and decomposed on the column. Thus, we used β-thiophene-substituted diols **8** and **9** to synthesize N_2S_2 porphyrins **2** and **3**, respectively, with four *meso*-unsubstituted carbons. The diols **8** and **9** were synthesized by $LiAlH_4$ reduction of the 2,5-dimethyl ester of the corresponding 3,4-disubstituted thiophene (methoxy or ethylene dioxy). The 2,5-dimethyl esters of 3,4-disubstituted thiophenes were synthesized over a sequence of steps by following a literature procedure.[8] The diols **8** and **9** were condensed with pyrrole under mild acidic conditions and the crude porphyrins were purified by silica gel column chromatography to afford crystalline purple solids **2** in 8% and **3** in 9% yields respectively. Porphyrins **2** and **3** were characterized by NMR, absorption and fluorescence spectroscopy, mass spectrometry and elemental analysis (see Supporting Information). The appearance of *meso*-H at about δ = 10.5 ppm in the ^1H NMR spectra and a corresponding *m*/*z* peak in the mass spectra confirm the formation of porphyrins **2** and **3**. The pyrrole protons of **2** and **3** are shifted downfield with respect to 5,10,15,20-*meso*-tetraphenyl-21,23-dithiaporphyrin (S_2TPP)[7] indicating the absence of electron-withdrawing phenyl groups at the *meso* positions. The absorption and fluorescence bands are blue shifted compared to S_2TPP.

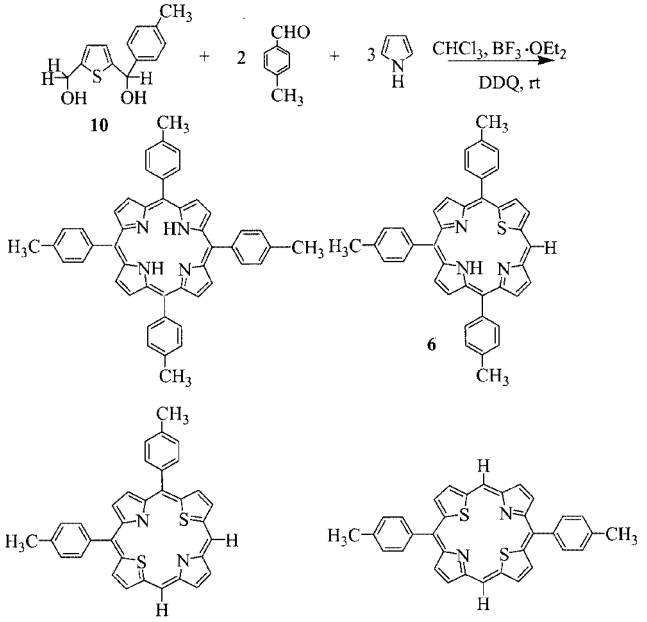
The N_3S porphyrins **4** and **5**, with two *meso*-unsubstituted carbons, were synthesized by condensing one equivalent of diol **8** or **9**, respectively, with two equivalents of benzaldehyde and three equivalents of pyrrole in $CHCl_3$ in the presence of $BF_3{\cdot}OEt_2$ followed by oxidation with DDQ (Scheme 1). The condensation resulted in the formation of a mixture of three porphyrins with three different porphyrin cores[6e,6f] and the desired N_3S porphyrins **4** and **5** were separated from this mixture by silica gel column chromatography. The porphyrins **4** and **5** were obtained in 5.5% and 8% yields, respectively, and characterized by different spectroscopic techniques. Downfield shifts in the NMR spectra and blue shifts of the absorption and fluorescence bands compared to 5,10-diphenyl-10,20-ditolyl-21-monothiaporphyrin (STPPH)[7] were again observed.



Scheme 1. Synthetic scheme for N_3S porphyrin **5**

The N_3S porphyrin with one *meso*-unsubstituted carbon **6** was synthesized from the unsymmetric thiophene diol **10**. To the best of our knowledge, there is no report on the N_3S porphyrin with one *meso*-unsubstituted carbon which is highly desirable in constructing novel 21-thiaporphyrin systems. The condensation of one equivalent of diol **10** with two equivalents of benzaldehyde and three equivalents of pyrrole under standard porphyrin-forming conditions resulted in a mixture of four porphyrins (Scheme 2): a desired N_3S porphyrin **6**, a mixture of two isomers (*cis* and *trans*) of N_2S_2 porphyrins and one N_4 porphyrin (H_2TTP). The porphyrin mixture was subjected to silica gel column chromatography to afford N_3S porphyrin **6** in 5.6% yield; its structure was confirmed by standard spectroscopic techniques.

To understand the kind of structure the *meso*-unsubstituted thiaporphyrins would adopt, we attempted to solve the crystal structure of one of the porphyrin. We successfully obtained a single crystal of **5** and its structure was solved by single-crystal X-ray diffraction analysis (CCDC-199597). In this structure one of the phenyl rings is slightly disordered. A comparison of porphyrin structure **5** with that of the reported saddle-shaped structure of 5,20-diphenyl-10,15-bis(*p*-nitrophenyl)-21-thiaporphyrin[7] indicates that the deviation of the thiophene ring with respect



Scheme 2. Synthetic scheme for the N_3S porphyrin with one *meso*-unsubstituted carbon **6**

to the mean plane of the four meso carbons in **5** is decreased and the porphyrin **5** is more planar (see supporting information for both side and top views). The novel feature observed in this structure is the presence of both intra- and intermolecular hydrogen bonding. The intramolecular hydrogen bonding interactions present in the cavity are between N−H···N [2.50(3) Å, 115(2)°] and N−H···S [2.68(2) Å, 173(2)°] which are not very common with all N_3S porphyrin systems reported so far.

In addition, the most novel feature of **5** is observed in the packing diagram (Figure 1) which reveals that there are two intermolecular C−H···O and C−H···N hydrogen bonding interactions leading to the formation of the supramolecular assembly.[9] The C-H of the *meso* phenyl of one porphyrin unit is hydrogen bonded to the O-atom of an ethylene dioxy substituent present on the thiophene ring of another porphyrin unit to form a dimeric unit [C28−H28···O1 2.47 (9) Å, 157° (7)]. This dimeric unit is further extended to form a supramolecular assembly via the formation of a hydrogen bond between the C-H of the ethylene dioxy substituent present on the thiophene ring of one of the porphyrin units of the dimer with an inner nitrogen atom of a porphyrin of another dimeric unit [C33−H33···N1 H33···N1 2.44 (3) Å, 160° (4)].[9]

The *meso*-unsubstituted porphyrins are highly reactive and rapidly undergo electrophilic and nucleophilic substitution reactions. We carried out some recently reported reactions with *meso*-unsubstituted thiaporphyrins to introduce suitable functional groups at the *meso* carbons which can be used to further synthesize novel photosynthetic model compounds. Porphyrin **5** was treated with two equivalents of *N*-bromosuccinimide[10] at room temperature for 10 min followed by silica gel column chromatography with

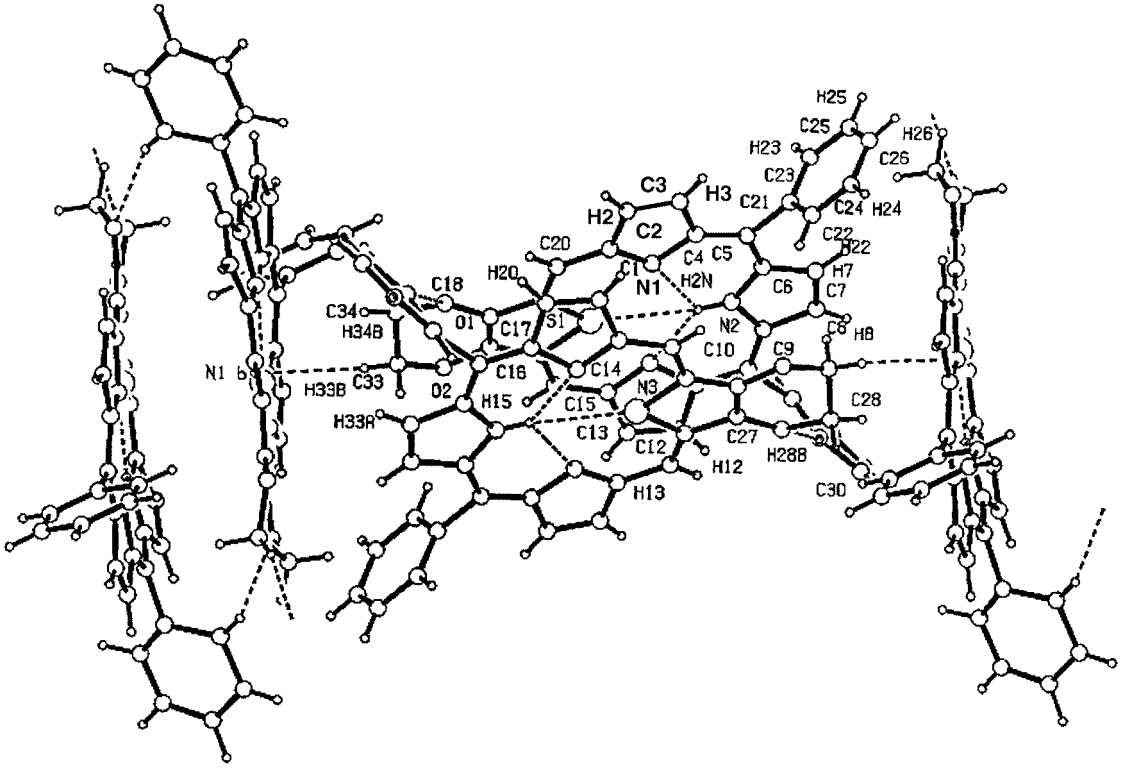
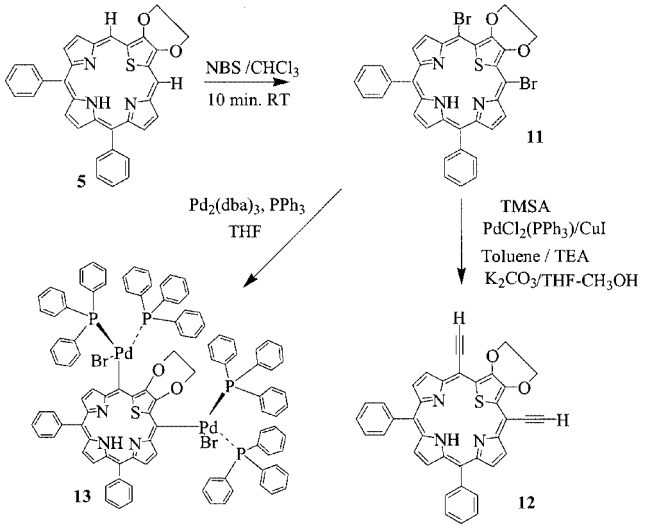


Figure 1. Hydrogen bond-assisted supramolecular assembly of **5** (dotted line showing the hydrogen bonds)



Scheme 3. Synthetic scheme for **11**, **12** and **13**

CH_2Cl_2 as eluent to give dibromo derivative **11** in 55% yield (Scheme 3).

The ethyne derivative **12** was prepared[11] in 58% yield by treating porphyrin **11** with trimethylsilylacetylene in the presence of a catalytic amount of $[PdCl_2(PPh_3)_2]$/CuI in THF/triethylamine followed by deprotection of the trimethylsilyl group with K_2CO_3 in THF/CH_3OH. The bromo and ethyne functional groups are very useful to synthesize multiporphyrin arrays.[12] *meso*-Bis(palladio)porphyrin **13** was prepared by following the method of Arnold et al.[13] Porphyrin **11** was treated with two equivalents of $Pd_2(dba)_3$/PPh_3 in toluene at room temperature and the crude compound was purified by column chromatography to afford the palladioporphyrin **13** in 28% yield. The introduction of substituents at the *meso* carbons resulted in large red shifts of the absorption (Figure 2) and fluorescence bands and maximum shifts were observed for porphyrins **12** and **13** indicating that the electronic properties of the *meso*-unsubstituted porphyrins are altered drastically by introducing substituents at the *meso* carbons (see Supporting Information).

We also tested the reactivity of *meso*-unsubstituted thiaporphyrins by reacting *meso*-unsubstituted porphyrins with

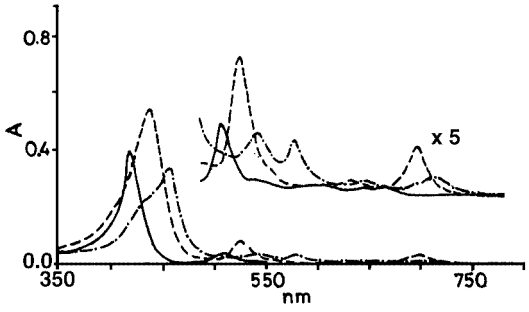
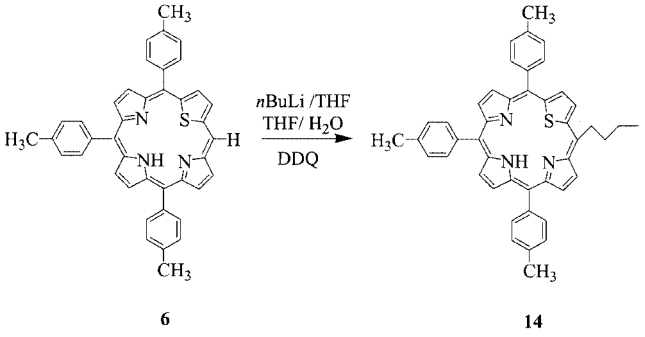


Figure 2. Absorption spectra, recorded in toluene for **5** (−), **11** (---) and **12** (-·-·-).



Scheme 4. Synthetic scheme for porphyrin **14**

organolithium reagents, as developed by Senge et al.[3] Reaction of **6** with *n*-butyllithium at 0 °C in THF followed by oxidation with DDQ at room temperature afforded the butyl derivative **14** in 65% yield (Scheme 4).

In conclusion, we have prepared *meso*-unsubstituted thiaporphyrins with one, two and four *meso*-unsubstituted carbons using simple thiophene diols. Previously no one has explored the synthesis of *meso*-unsubstituted thiaporphyrins in detail which has several applications in porphyrin synthetic chemistry. We demonstrated the reactivity of *meso*-unsubstituted thiaporphyrins by carrying out the recently reported reactions and synthesized some important functionalized *meso*-thiaporphyrins. These functionalized porphyrins can be used to construct some complicated thiaporphyrin systems with novel physical and chemical properties and such efforts are presently underway in our laboratory.

Supporting Information Available (see also footnote on the first page of this article)**:** Mass spectra, NMR spectra, X-ray crystal structures and absorption data of selected compounds and tables of crystal data.

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