Novel and Rapid Synthetic Routes to A_3B- and AB_3-Type 21-Thiaporphyrins and Their Use in the Construction of Unsymmetrical Covalent and Non-Covalent Porphyrin Arrays

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Novel and very simple methods were developed for the synthesis of 21-thiaporphyrins having both one functional group (A_3B) and three functional groups (AB_3). These A_3B- and AB_3-type 21-thiaporphyrin building blocks were used to synthesize both covalently and non-covalently linked unsymmetrical porphyrin arrays containing N_3S and N_4 porphyrin cores.

Introduction

21-Thiaporphyrins (with an N_3S core) resulting from the replacement of one of the pyrrole nitrogen atoms of regular porphyrins (with an N_4 core) exhibit unique properties both in terms of aromatic character and their ability to stabilize metals in unusual oxidation states.[1] These porphyrins can be synthesized by following a well-established synthetic strategy (shown in Scheme 1), in which 2,5-bis(α-aryl-α-hydroxymethyl)thiophene, a symmetrical thiophene diol, is the key precursor. According to this method, the condensation of one equivalent of thiophene diol with two equivalents of aldehyde and three equivalents of pyrrole under mild acid conditions followed by oxidation with DDQ resulted in the formation of an N_3S porphyrin. However, only the *cis*-A_2B_2 and A_4 types of N_3S porphyrins can be synthesized by this method.[1,2]

The chemistry of N_3S porphyrins is currently in its infancy, due to the lack of availability of suitable 21-thiaporphyrin building blocks. Porphyrins with one functional group are potential building blocks for the development of novel porphyrin systems.[3] However, synthesizing porphyrins with one functional group involves multi-step synthesis and tedious purification procedures.[4] To the best of our knowledge, there is no one-step method available for the synthesis of A_3B and AB_3 type 21-thiaporphyrins. In this communication, we report for the first time the synthesis of A_3B- and AB_3-type 21-thiaporphyrins **1−9** by using 2-(α-aryl-α-hydroxymethyl)thiophene(thiophene mono-ol) in place of a symmetrical thiophene diol. This method is simple; furthermore, there have been no reports so far that have shown that a thiophene mono-ol can be used as a precursor for the synthesis of N_3S porphyrins. Using this method, any desired 21-thiaporphyrin can be synthesized in reasonable quantity in one step. It is applicable to the synthesis of 21-thiaporphyrins having various functional groups, which can be used further to synthesize complex 21-thiaporphyrin-based systems. We have also developed an alternative high-yielding method, using the previously unreported unsymmetrical thiophene diols **10−17** for the synthesis of the A_3B-type 21-thiaporphyrins **18−25**. We also report the use of A_3B- and AB_3-type 21-thiaporphyrin building blocks in the synthesis of covalent and non-covalent unsymmetrical porphyrin arrays containing two different porphyrin cores.

Results and Discussion

The desired thiophene mono-ols were prepared by treating thiophene with 1.2 equivalents of *n*BuLi, followed by 1.2 equivalents of the appropriate aldehyde in THF at 0 °C. TLC analysis of the reaction mixture showed the formation of the mono-ol along with small amounts of unchanged aldehyde and thiophene. The crude mixture was subjected to silica gel column chromatography, to give the pure thiophene mono-ols as brownish-white solids in 65−70% yield.

The A_3B- and AB_3-type N_3S porphyrins **1−9** were synthesized by condensing two equivalents of the appropriate thiophene mono-ol with two equivalents of aldehyde and three equivalents of pyrrole in propionic acid (Scheme 2). We anticipated the formation of 21-thiacorrole in this reaction, but none was observed.[5] We also varied the number of equivalents of thiophene mono-ol, keeping the amounts of aldehyde and pyrrole constant. When only one equivalent (rather than two equivalents) of thiophene mono-ol was used, we observed the formation of only the N_4 porphyrin. No corrole was formed even when more than two

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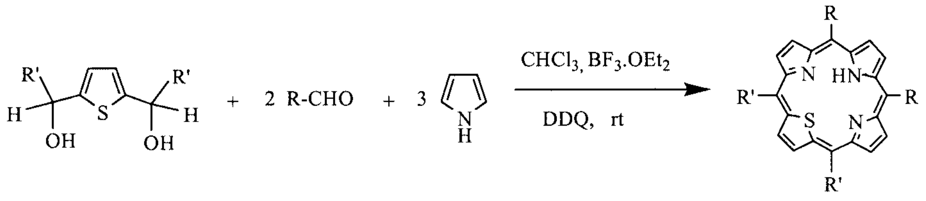
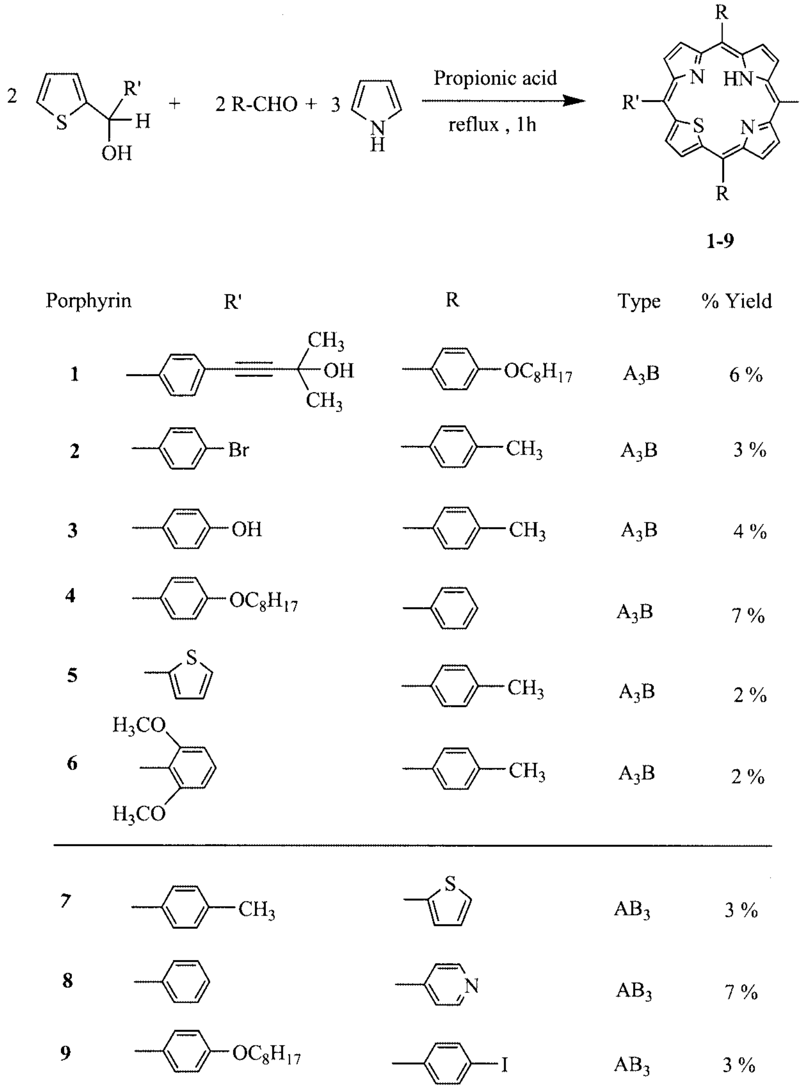


Scheme 1. A general literature procedure for the synthesis of 21-thiaporphyrins

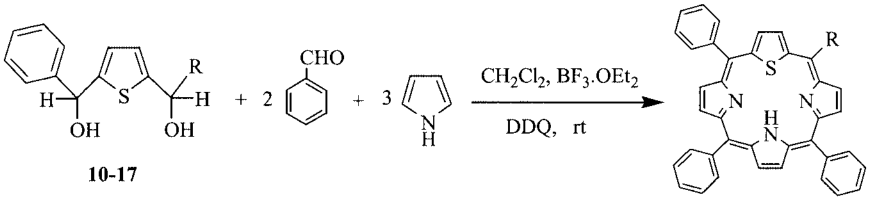
equivalents of thiophene mono-ol was used, but the yields of N_3S porphyrins were reduced drastically.

Therefore, we used two equivalents of thiophene mono-ol to prepare the A_3B- and AB_3-type N_3S porphyrins **1−9**. The crude mixtures were purified by double silica gel column chromatography, to afford the desired products in yields of 2−7%. Although the yields of porphyrin are low, this method presents the first facile preparation of mono- and tri-functionalized N_3S porphyrins from one precursor. The desired N_3S porphyrin can be prepared easily on a 100-mg scale in a one-pot reaction, since the precursor thiophene mono-ols can be synthesized in multigram quantity, and the chromatographic separation of the N_3S from the N_4 porphyrins is simple and straightforward. Characterization data (NMR, mass, UV/vis and fluorescence spectra) for the A_3B- and AB_3-type N_3S porphyrins **1−9** is given in the Supporting Information.

A_3B-type 21-thiaporphyrins were also synthesized from the unsymmetrical thiophene diols **10−17** (Scheme 3). These novel diols were prepared by treating 2-[α-hydroxy-α-phenyl]methylthiophene (**26**) with two equivalents of *n*BuLi, followed by 1.2 equivalents of the desired aromatic

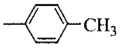
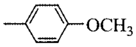
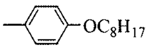
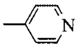
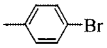
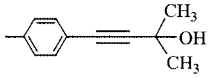
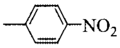
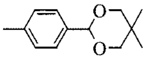


Scheme 2. Synthesis of A_3B- and AB_3-type 21-thiaporphyrins from thiophene mono-ols

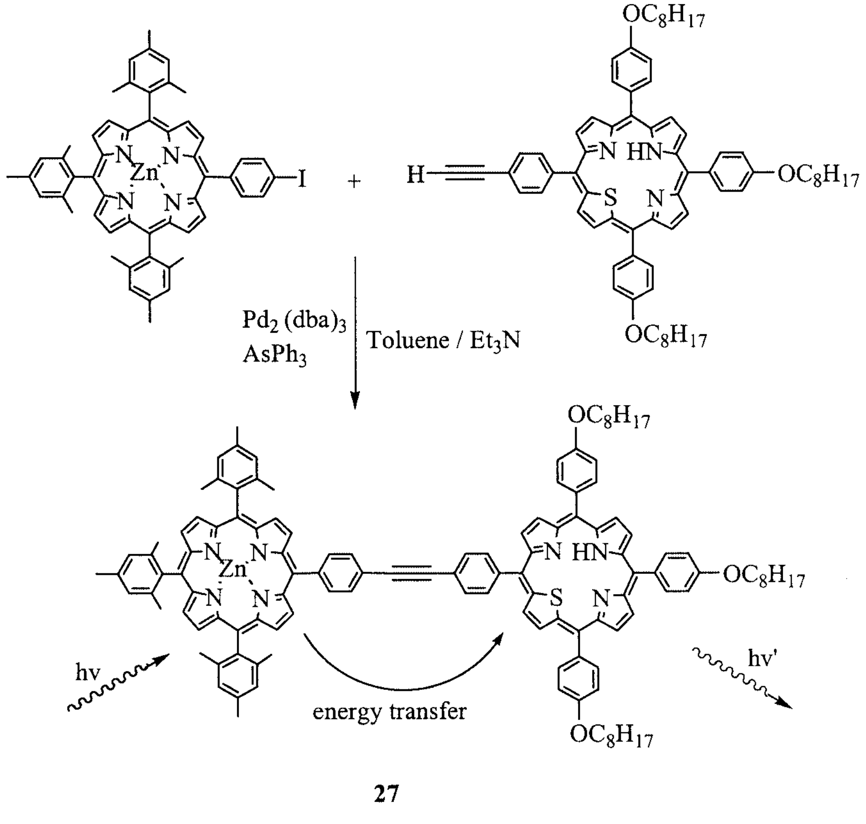


10-17

18-25

R	Thiophene diol, Yield	Porphyrin, Yield
	**10**, 35%	**18**, 10%
	**11**, 42%	**19**, 11%
	**12**, 45%	**20**, 16%
	**13**, 30%	**21**, 2%
	**14**, 40%	**22**, 10%
	**15**, 26%	**23**, 9%
	**16**, 28%	**24**, 12%
	**17**, 35%	**25**, 2%

Scheme 3. Synthesis of A$_3$B-type 21-thiaporphyrins from unsymmetric thiophene diols



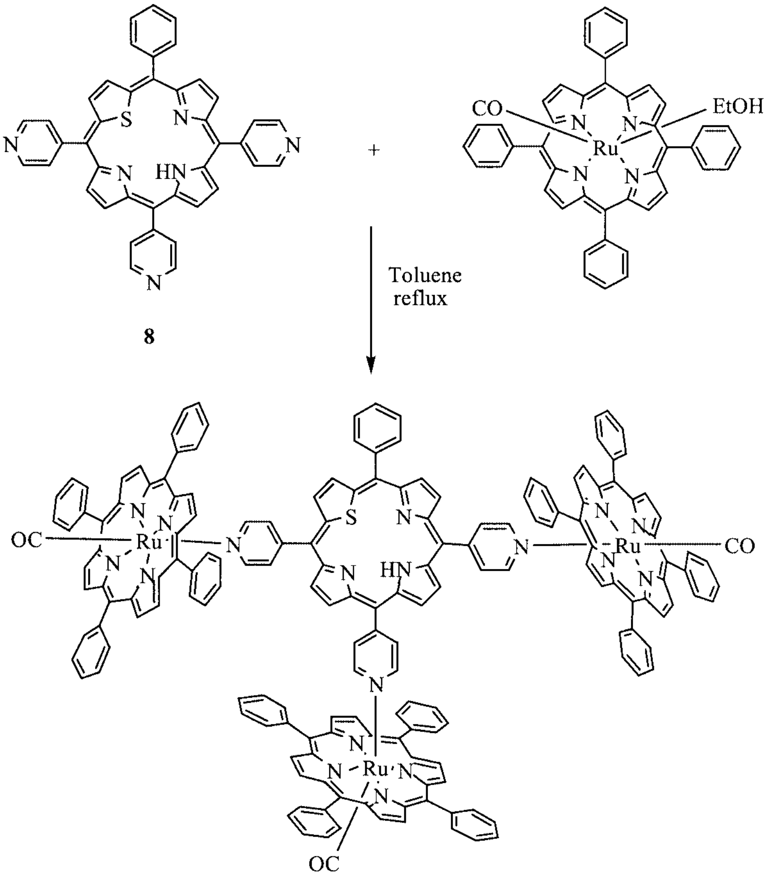
27

Scheme 4. Synthesis of the unsymmetrical covalently linked dimer **27** aldehyde in THF at 0 °C. TLC analysis of the crude reaction mixture indicated the formation of the diol, along with unchanged aldehyde and the thiophene mono-ol **26**. Purification of the crude reaction mixture by silica gel column chromatography afforded the pure unsymmetrical diols **10−17** in 26−45% yield.

To optimize the reaction conditions for the synthesis of unsymmetrical thiophene diols, we varied the number of equivalents of *n*BuLi; the best diol yields were obtained with two equivalents of *n*BuLi. Diol yields were much lower with one equivalent of *n*BuLi, and were not much improved when we used more than two equivalents of *n*BuLi. It seems likely that at least two equivalents of *n*BuLi are needed for this reaction because the hydroxyl group of thiophene mono-ol gets lithiated during the reaction. Although the yields of diols are moderate, the preparation of large quantities of unsymmetrical diols is simple by this method. Furthermore, the desired mono-functional group of N_3S porphyrins can be incorporated easily at the thiophene diol stage.

To synthesize the 21-thiaporphyrins, one equivalent of the appropriate unsymmetrical diol was condensed with two equivalents of an aromatic aldehyde and three equivalents of pyrrole under standard porphyrin-forming conditions (Scheme 3). The condensation resulted in the formation of a mixture of four porphyrins; 5,10,15,20-tetraphenylporphyrin (H_2TPP), the desired A_3B-type 21-thiaporphyrin and a mixture of *cis*- and *trans*-A_2B_2-type 21,23-dithiaporphyrins. The crude mixture was purified by silica gel column chromatography; the desired 21-thiaporphyrin always eluted as the second chromatographic band, and the 21,23-dithiaporphyrins eluted together in the last band. The 21-thiaporphyrins (with small impurities of the other porphyrins) were subjected to a second silica gel column chromatography, to afford the pure 21-thiaporphyrins **18−25** in 2−15% yield (Scheme 3). No attempts were made to separate the *cis*- and *trans*-21,23-dithiaporphyrins. The identities of the 21-thiaporphyrins **18−25** were confirmed by spectroscopy (see Supporting Information).

We sought to broaden the scope of A_3B- and AB_3-type N_3S porphyrin building blocks by constructing covalent and non-covalent unsymmetrical porphyrin arrays containing two different porphyrin cores. Such unsymmetrical porphyrin arrays are suitable models for mimicking the energy-transfer and electron-transfer processes of photosynthesis, because of the feasibility of selective excitation of one porphyrin unit and energy transfer to another porphyrin unit. Recently, several unsymmetrical porphyrin dimers (such as porphyrin−chlorin and porphyrin− corrole) have been synthesized in order to obtain long-lived charge-transfer states.[6] Interestingly, there is only one report on unsymmetrical arrays containing N_3S and N_4 porphyrin cores.[7]



Scheme 5. Synthesis of the unsymmetrical non-covalently linked tetramer **28**

Therefore, we decided to synthesize the covalently linked diarylethyne-bridged unsymmetrical porphyrin dimer **27** containing one N_3S and one N_4 porphyrin core. Coupling of the deprotected (terminal alkyne) form of **1** with the zinc(II) complex of 5,10,15-tri(mesityl)-20-(4-iodophenyl)porphyrin in toluene/triethylamine at 35 °C in the presence of $Pd_2(dba)_3$ and $AsPh_3$, followed by column chromatography, gave **27** in 67% yield (Scheme 4) (see Supporting Information for spectroscopic data).

To demonstrate energy transfer in the porphyrin dimer **27**, we recorded the emission spectrum at an excitation wavelength of 550 nm (where the Zn derivative of the N_4 porphyrin unit absorbs strongly). The emission spectrum of **27** showed bands due mainly to the N_3S unit. The emission bands of the Zn derivative of the N_4 unit in **27** were quenched to great extent, indicating that there was an efficient energy transfer from the Zn derivative of N_4 unit to the N_3S unit. Similar observations have been made for ethyne-bridged porphyrin arrays.[8]

To demonstrate the use of AB_3-type N_3S porphyrins, the non-covalently[9] linked unsymmetrical porphyrin tetramer **28** containing one N_3S unit and three N_4 units was synthesized (Scheme 5). The N_3S porphyrin **8** was treated with 3.2 equivalents of RuTPP(CO)(EtOH) in toluene at reflux overnight, to give the porphyrin tetramer **28** in 17% yield, after silica gel column chromatography and size exclusion chromatography.

Conclusion

The method reported in this communication gives access for the first time to A_3B- and AB_3-type N_3S porphyrin building blocks containing functional groups at the *meso* carbon atoms. A_3B-type 21-thiaporphyrins were also synthesized in improved yield by using unsymmetrical thiophene diols. The methods reported are simple, versatile and applicable to all N_3S porphyrins with either one or three functional groups at the *meso* positions. We have also shown that mono- and tri-functionalized N_3S porphyrin building blocks can be used to construct covalent and non-covalent unsymmetrical porphyrin arrays containing both N_3S and N_4 porphyrin units. Preliminary investigations indicate that A_3B- and AB_3-type N_3O porphyrins can also be synthesized using the mono-ol or unsymmetrical diol methods reported in this paper.

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