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Synthesis of Meso-Substituted Core Modified Expanded Porphyrins; Effect of Acid Catalysts on the Cyclization

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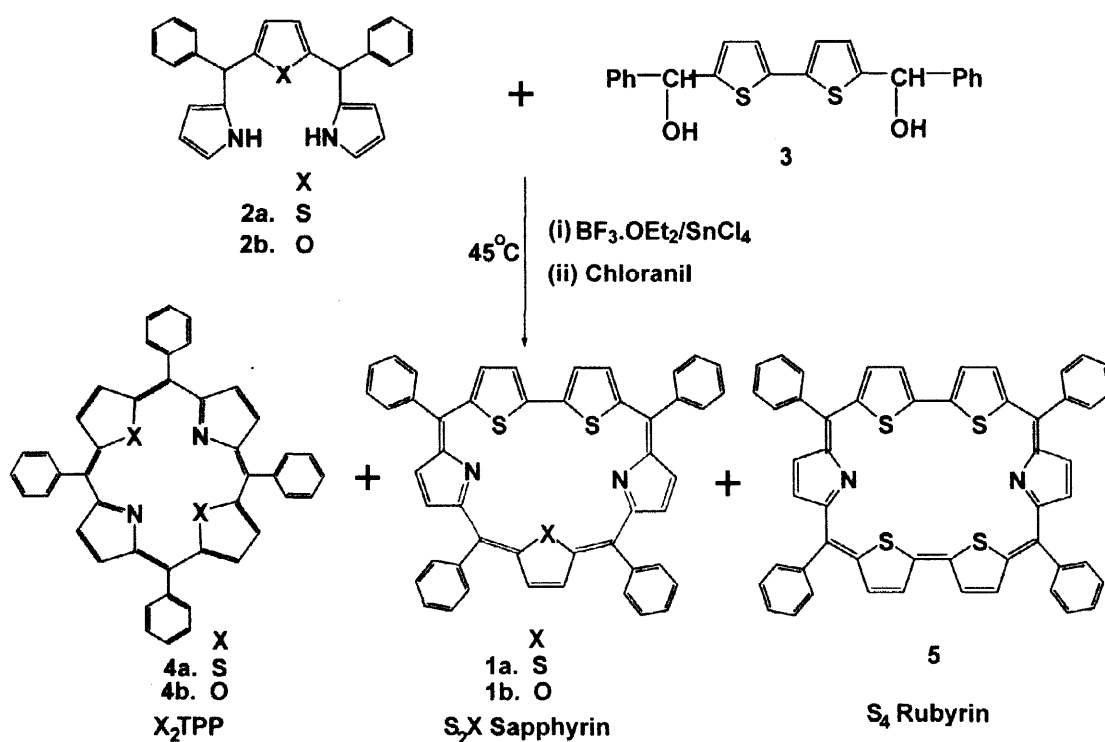
Abstract: [3+2] condensation between modified tripyrromethane and bithiophene or bifurandiols leads to the formation of 18 π , 22 π , 26 π macrocycles under Lewis acid conditions while only 22 π macrocycle is formed under protic acid conditions. © 1998 Elsevier Science Ltd. All rights reserved.

Expanded porphyrins have lately emerged as attractive target molecules because of their potential biomedical application in photodynamic therapy and as anion receptors.^{1,2} Synthetic efforts to date have resulted in characterization of diverse systems containing five to ten pyrrolic units covalently joined through methine bridges.² Core modification by replacement of one or more pyrrolic units by other heterocycles such as furan and thiophene leads to a new class of expanded porphyrins having unusual optical, electrochemical and magnetic properties due to altered electronic structure.³ A perusal of literature reveals only a few scattered reports on the synthesis of core modified expanded porphyrins probably due to non-availability of methods to prepare the heterocyclic precursors and their inherent instability relative to the pyrrolic counterpart.⁴ Herein, we wish to describe an easy and facile method for the synthesis of meso substituted core modified expanded porphyrins in which a [3+2] MacDonald type condensation between the appropriate precursors leads to the formation of expected 22 π macrocycle in addition to the unexpected 26 π and 18 π macrocycles.

We targeted the synthesis of **1a** and **1b** by an acid catalysed condensation between modified tripyrrane **2a** or **2b** and bithiophene diol **3** [scheme]. This strategy was based on the method used for the synthesis of mono and dithiaporphyrins by Ulman and coworkers.⁵ This method makes use of bithiophene diol **3** instead of diformylbipyrrole which is commonly used for [3+2] or [4+2] condensations. Thus, the condensation⁶ resulted in the formation of **4a** or **4b** and **5** in addition to the expected **1a** or **1b**. The product distribution and the yields were found to be dependent on the nature of the Lewis acid or protic acid used and their concentration. Use of BF₃·OEt₂ or SnCl₄ as a Lewis acid resulted in the formation of all the three products and the yields were dependent on the concentration of the Lewis acid used. However, in TFA or p-TsOH, exclusively **1a** or **1b** is formed in moderately good yields.⁷ Table summarizes the conditions of the reaction along with the isolated yields.

The success of the cyclization depends on the effective generation of carbocation in **3** by protic or Lewis acid. In protic acids, the sole formation of expected **1a** or **1b** clearly suggests protonation followed by elimination of water from **3** generating a carbocation. However, the formation of **4a** or **4b** and **5** in addition to **1a** or **1b** in presence of Lewis acids indicate partial acidolysis of **2a** or **2b** on the time scale of porphyrin formation in addition to carbocation generation. It is possible that the metal on the Lewis acid coordinates to the heteroatom of the tripyrrane triggering its slow acidolysis. The observed increase in the yields of **4a** or **4b** and **5** at the expense of **1a** or **1b** on increasing the Lewis acid concentration supports such a possibility. Evidence

Scheme



for the acidolysis comes from the following observations; (a) Stirring of **2a** with benzaldehyde in CH_2Cl_2 under N_2 atmosphere for 15 minutes followed by addition of $\text{BF}_3 \cdot \text{OEt}_2$ (6.09×10^{-5} mol) and subsequent oxidation with chloranil under reflux temperature for 1 hour resulted in the formation of ~2% meso-tetraphenyl porphyrin and mono thia tetraphenyl porphyrin. (b) The gradual decrease in the absorbance of tripyrrane in CH_2Cl_2 in the UV-Visible spectrum upon addition of $\text{BF}_3 \cdot \text{OEt}_2$ with time and subsequent TLC analysis (Silica gel-G, Ethyl acetate : Pet. Ether [1:9]) of the mixture indicated decrease in the concentration of tripyrrane and a new purple

spot (R_f : 0.23). It is pertinent to point out here that Lindsey and coworkers have recently observed the partial acidolysis of dipyrromethanes under Lewis acid condition and have concluded that the extent of the acidolysis depends on the nature of the meso substituent.⁸ The higher yields of products in SnCl_4 relative to $\text{BF}_3\cdot\text{OEt}_2$ suggests more formation of desired cyclic porphyrinogen relative to open chain polypyrrolyl methenes.⁹

Table

Lewis Acid/ Protic Acid (Dry CH_2Cl_2)	Amount Taken (mol)	Isolated Yield (%)		
		1a(1b)	5(5)*	4a(4b)
$\text{BF}_3\cdot\text{Et}_2\text{O}$	3.05×10^{-5}	30(13)	2(3)	4(1)
$\text{BF}_3\cdot\text{Et}_2\text{O}$	6.09×10^{-5}	7(5)	5(14)	15(3)
SnCl_4	3.26×10^{-5}	35	7	3
SnCl_4	4.33×10^{-5}	20	11	4
TFA	3.25×10^{-4}	45(25)	-	-
TFA	9.75×10^{-4}	35(22)	-	-
p-TsOH	3.78×10^{-4}	63	-	-

The numbers in parantheses indicate the yields corresponding to the condensation between **2b** and **3**.

***5** was formed in both the condensations.

In conclusion, this communication describes facile synthesis of core modified expanded porphyrins by a relatively simple but efficient method in which the product distribution can be controlled by the reaction conditions. Also, this synthetic method allows synthesis of both 22π and 26π heterocyclic expanded porphyrins in the same reaction which to the best of our knowledge has no precedence in literature. Further studies are in progress to apply this method to other expanded porphyrins containing selenophene and tellurophene and to explore their chemistry as anion receptors.

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6. A typical procedure for the condensation involves stirring of 5,5'-bis (phenylhydroxymethyl)-2,2'- bithiophene (0.150g, 3.97×10^{-4} mol) and 16 thiatripyrrin (0.156 g, 3.97×10^{-4}) in dry dichloromethane (200ml) under nitrogen atmosphere for 15 minutes at room temperature. Then freshly distilled $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (3.05×10^{-5} mol) in dry CH_2Cl_2 was added to the above mixture. The solution was stirred for further one hour under dark conditions. The resulting solution was opened to air and chloranil (0.293g, 1.19×10^{-3} mol) was added and the mixture was heated to reflux in a preheated oil bath at 50°C . After the removal of the solvent, the crude product was purified by column chromatography (basic alumina). The brown fraction eluted with $\text{CH}_2\text{Cl}_2 : \text{CCl}_4$ (40:60) was identified as **4a** in 4% yield. The second fraction eluted with $\text{CH}_2\text{Cl}_2 : \text{CCl}_4$ (50:50) was identified as **1a** in 30% yield and the final violet fraction was eluted with only CH_2Cl_2 and identified as **5** in 2% yield. Similar procedure was followed for **2b**.
7. Spectroscopic data for the new compounds are given below:
 (1a) : $\text{C}_{48}\text{H}_{30}\text{S}_3\text{N}_2$: FAB MS : m/z : 732 (100%) [$\text{M}+1$]⁺], $^1\text{HNMR}$: (300 MHz, CDCl_3) : δ = 10.27 (d, 4H, $J=3\text{Hz}$), 9.82 (d, 4H, $J=6\text{Hz}$), -0.73 (s, 2H), 8.67 (d, 2H, $J=3\text{Hz}$), 8.57 (d, 2H, $J=3\text{Hz}$), 8.39 (m, 8H), 7.91 (m, 12H); UV-Vis (CH_2Cl_2) : λ nm ($\epsilon \times 10^{-4}$) : Soret 507 (8.3) , Q-bands 581 (0.33), 622(0.51), 675(0.86), 777 (0.10), 874(0.25).
 (1b) : $\text{C}_{48}\text{H}_{30}\text{N}_2\text{S}_2\text{O}$: FAB MS : m/z 715(25%) [M^+], ^1NMR : (300 MHz, CDCl_3) : δ = 9.75(d, 4H, $J=3\text{Hz}$), 9.41 (d, 4H, $J=3\text{Hz}$), 0.61 (s, 2H), 8.57 (d, 2H, $J=3\text{Hz}$), 8.49 (d, 2H, $J=3\text{Hz}$), 8.28 (m, 8H), 7.86 (m, 12H); UV-Vis (CH_2Cl_2) : λ nm ($\epsilon \times 10^{-4}$) : Soret 511(16.6) , Q- bands 625(1.09), 681(1.93), 786(0.12), 884(0.44).
 (5) : $\text{C}_{52}\text{H}_{32}\text{N}_2\text{S}_4$: FAB MS : m/z 813 (100%) [M^+], $^1\text{HNMR}$: (300 MHz, CDCl_3) : δ = 11.66 (d, 4H, $J=6\text{Hz}$), 10.50 (d, 4H, $J=3\text{Hz}$), 9.06 (s, 4H), 8.55(m, 8H), 7.98 (m, 12H); UV-Vis (CH_2Cl_2) : λ nm ($\epsilon \times 10^{-4}$) : Soret 523(7.98) , Q- bands 659(0.49), 717(1.02), 837(0.05), 958(0.06). Combustion analysis of **1a**, **1b**, and **5** gave satisfactory data.
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