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o-(Bromomethyl)-Substituted Tetraarylporphyrin Building Blocks

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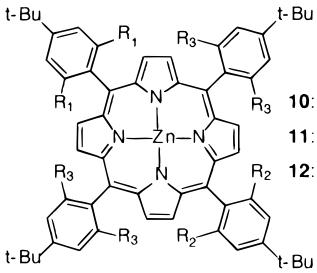
ABSTRACT



10: $R_1 = R_2 = R_3 = CH_2Br$; M = Zn

11: $R_1 = R_2 = CH_2Br$; R_3 = H; M = Zn

12: $R_1 = CH_2Br$; $R_2 = R_3$ = H; M = Zn

A series of novel poly-*o*-(bromomethyl)ated tetraarylporphyrins was synthesized. Their usefulness as building blocks for porphyrinic materials is demonstrated.

meso-Tetraphenylporphyrin (TPP) is the most commonly used porphyrinic system for the construction of photosynthetic model compounds,[1] enzyme mimetics, and artificial receptors.[2] Besides biochemical aspects, TPPs are found, for example, in dendrimers,[3] as liquid crystalline materials with discotic behavior[4] and as part of optoelectronic devices.[5] Thus, the usefulness of TPPs encompasses chemistry, medicine, biochemistry, physics, and materials sciences.[6] Since the derivatization of TPPs has been well studied, it is possible to tailor their properties, allowing adaption into the desired specific environment.

Obviously, novel materials containing porphyrins have become a major research field in porphyrin chemistry. It appears to us that by using the inherent geometry of porphyrins interesting new conjugates would be available. In this paper we introduce a series of poly-*o*-(bromomethyl)-ated tetraphenylporphyrins which are useful building blocks in this regard.

Because tetraphenylporphyrins are easy to prepare and are well studied, we decided to use these compounds as

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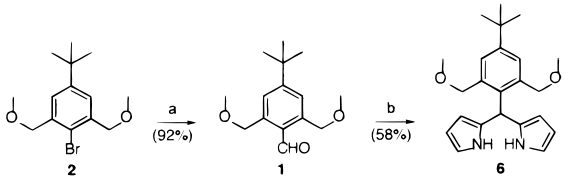
foundation for our research. Our aim was to generate porphyrins with easily modifiable groups in close proximity to the core. Therefore, these substituents had to be placed at the *ortho*-positions of the phenyl rings. TPPs with *o*-phenyl substituents are subject to extensive research[7] because *ortho*-groups prevent aggregation and protect the core of the porphyrin from side reactions. The modification of some derivatives, especially of amino and hydroxy derivatives, was extensively studied and led to beautiful molecules such as cyclam-capped porphyrins[8] and barrel-shaped systems[9] with a porphyrin center. Molecular modeling suggests that the geometric situation of substituents in the *ortho*-positions should lead to better interactions with the porphyrin core. Also, due to the size of the porphyrin the rotation of such groups will be strongly hindered.

These considerations led to the belief that a 2,6-disubstituted benzaldehyde had to be made and used in the cyclocondensation reaction with pyrrole to yield porphyrins. For synthetic reasons and to ensure good solubility the *tert*-butyl group was included as the *para*-substituent. Encouraged by recently reported improved reaction conditions for the synthesis of TPPs with sterically encumbered benzaldehydes,[10] we started by preparing 2,6-bis(methoxymethyl)-4-*tert*-butylbenzaldehyde **1** using a modified literature[11] procedure for the corresponding acid derivative.[12] **1** was obtained by reacting aryl bromide **2** with *n*-butyllithium at −78 °C and subsequent addition of dimethylformamide (Scheme 1). With aldehyde **1**, porphyrins **3**−**5** are available

Scheme 1[a]

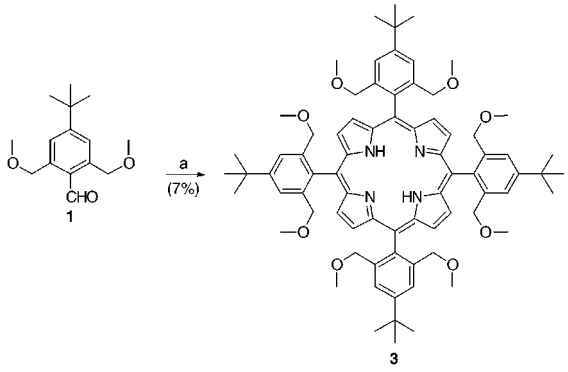


2 **1** **6**

[a] (a) i. n-BuLi, ether, −78 °C, ii. DMF, ether, −78 °C to rt, iii. NH_4Cl, H_2O, (b) pyrrole as solvent, $BF_3{\cdot}OEt_2$, rt.

by employing different strategies for their syntheses. Due to its symmetry, **3** should be the most easily accessible porphyrin in the series **3**−**5**. The cyclotetracondensation of **1** with pyrrole was achieved in methylene chloride containing about 1% ethanol as solvent and boron trifluoride−diethyl etherate as catalyst. Porphyrin **3** was obtained after oxidation with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) and repeated chromatography (silica gel, CH_2Cl_2/ethyl acetate 19:1) in a yield of 7% (Scheme 2). Identified byproducts

Scheme 2[a]



1 **3**

[a] (a) i. $BF_3{\cdot}OEt_2$, CH_2Cl_2 (+1% EtOH), rt, ii. DDQ, CH_2Cl_2, rt.

were the oxidized form of dipyrromethane **6**, a corrole derivative, and a linear tetrapyrrole.

The lower symmetries of **4** and **5** required a different approach. We decided to synthesize the porphyrin under more or less controlled conditions. Therefore, the dipyrromethane **6** was made according to a literature procedure for mesitaldehyde.[13] The formation of **6** proceeded smoothly, when aldehyde **3** was dissolved in pyrrole and boron trifluoride−diethyl etherate was used as catalyst.

The dipyrromethane **6** shows in its ^1H NMR spectrum broad signals for the methylene and methyl protons of the ether moiety. This seems to indicate a rotational constriction of the phenyl group as was expected from a crystal structure of 5-mesityldipyrromethane.[14] Temperature-dependent NMR spectroscopy will be employed to gain further insight of this phenomenon. For the synthesis of **4** dipyrromethane **6** and 4-*tert*-butylbenzaldehyde were dissolved in dry methylene chloride containing 1% ethanol. Again, boron trifluoride−diethyl etherate served as Lewis acid. After the oxidation step with DDQ, porphyrin **4** was obtained in 21% yield. No scrambling[15] of the dipyrromethane unit was observed under these conditions. Also, when ethanol was not added to the cyclization reaction the yield of product dropped well below 5%. This result is in contrast to the observations of Lindsey and co-workers,[15] who analyzed reactions of sterically hindered dipyrromethanes with sterically unhindered aldehydes and found that no ethanol was needed in such cases. The reason for this surprising behavior might be the formation of a complex of boron trifluoride and the methoxymethyl groups which is destroyed by ethanol. When

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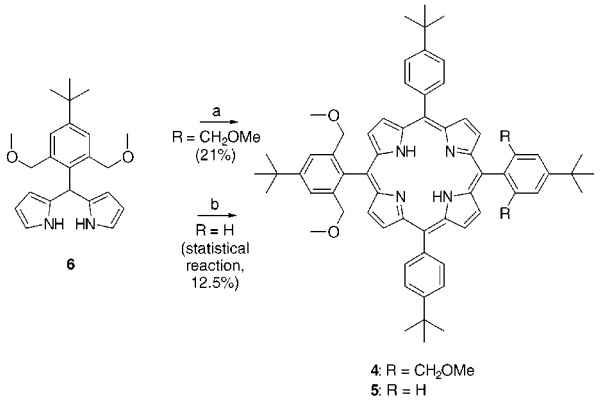
dipyrromethane **6** was reacted in a statistical way with 2 equiv of pyrrole and 3 equiv of 4-*tert*-butylbenzaldehyde using the above-mentioned conditions, porphyrin **5** was obtained in 12.5% yield. Tetrakis(4-*tert*-butylphenyl)porphyrin was found to be the major product of this reaction (24%).

The methoxy ethers **3**−**5** were transformed into their bromo derivatives by reaction with boron tribromide in dry methylene chloride or, with even better results, with HBr in acetic acid to give **7**−**9**. By employing the latter, the yield of the desired all-bromo compounds was usually around 85%. Depending on the quality of the BBr_3 solution, a certain amount of monohydroxylated species was always found. The porphyrins **7**−**9** were metalated quantitatively by addition of a solution of zinc acetate in methanol/1% acetic acid to a solution of the corresponding porphyrin in methylene chloride.

The new porphyrins **3**−**5** and **7**−**12** behave spectroscopically like other comparable TPPs. The ^1H and ^{13}C NMR data for the metal-free systems as well as for the zinc porphyrins point out the symmetrical situations of **3**/**7**/**10**, **4**/**8**/**11**, and **5**/**9**/**12**, respectively. The FAB mass spectra of the brominated materials **7**−**9** and their zinc complexes **10**−**12** show the expected mass distributions for Br_2, Br_4, and Br_8 compounds. UV/vis spectroscopy reveals no unusual features for all compounds.

Whereas **3**−**5** exhibit the typical porphyrin fluorescence behavior, the fluorescence diminishes on thin-layer chromatography (TLC) sheets the higher the bromine content is (**7**−**12**) and vanishes completely, as expected, when their copper derivatives (**10**−**12** with M = Cu in Scheme 4) were analyzed.

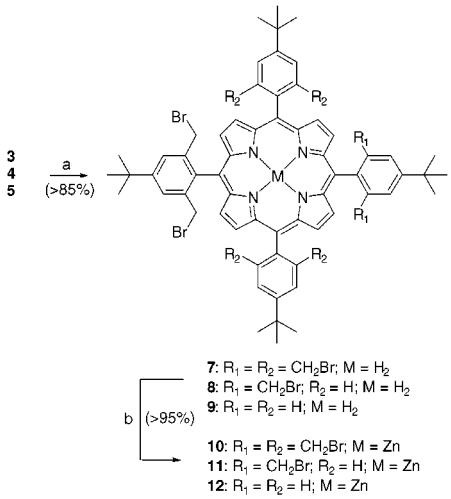
Scheme 3[a]



[a] (a) i. 1 equiv of 4-*tert*-butylbenzaldehyde, $BF_3{\cdot}OEt_2$, CH_2Cl_2 (+1% EtOH), rt; ii. DDQ, CH_2Cl_2, rt, b. 3 equiv of 4-*tert*-butylbenzaldehyde, 2 equiv of pyrrole, $BF_3{\cdot}OEt_2$, CH_2Cl_2 (+1% EtOH), rt, ii. DDQ, CH_2Cl_2, rt.

Calculations[16] of the frontier orbitals of the zinc porphyrins **10**−**12** show some remarkable differences. Whereas **11** and **12** have the typical orbital order for tetraphenyl porphyrins, i.e., a_{2u} for the HOMO and a_{1u} for the HOMO-1, like the zinc complexes of the octakis-*o*-methyl or the octakis-*o*-(methoxymethyl) porphyrin **3**, the octakis(bromomethyl)ated compound **10** has an inverse arrangement of these orbitals. This behavior is known for TPPs with electron-withdrawing groups in the *ortho*-positions.[17] Obviously, the bromine atoms have a similar effect on the electronic nature of TPP although they are not directly attached to the phenyl rings.

Scheme 4[a]



[a] (a) i. HBr, AcOH, CH_2Cl_2, rt, ii. $NaHCO_3$, H_2O; (b) $Zn(OAc)_2$, MeOH, AcOH, CH_2Cl_2, rt.

At this point the specific geometrical and chemical properties of the (bromomethyl)ated porphyrins should be mentioned. Due to their *ortho*-position on the phenyl rings, the bromomethyl groups sit atop of the porphyrin and also very close to the N_4 core. Because of the close proximity to the large porphyrin, the rotation of substituents will be restricted. The described situation gives rise to novel porphyrin conjugates with electro/redox-active or ion-binding substituents that are subject to conformational constraints and therefore lead to potentially better interactions between porphyrin and attached groups.

The reactive bromomethyl groups, which are in fact benzyl bromides, allow for reaction with many different nucleophiles such as azides, primary to tertiary amines, pyridines, thiols, and also carbon nucleophiles such as cyanide or malonates.

Some examples of interesting materials based on the aforementioned substances are shown in Scheme 5. Addition of sodium azide to a solution of **12** in tetrahydrofuran in the presence of [18]crown-6 gave the interesting bis-azide **13** which shows some potential for inter- and intramolecular addition reactions. As it turns out not only is it possible to substitute all of the reactive positions but in case of **12** also using only half the molar equivalents of reactant gives

(16) Calculations were performed on the PM3 level with PC Spartan Plus, Wavefunction, Inc.

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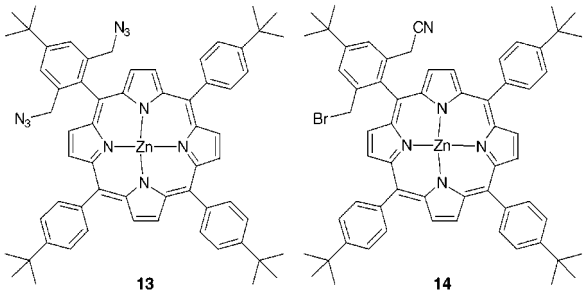
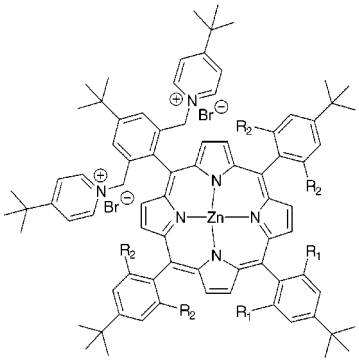
Scheme 5



13 **14**



15: $R_1 = R_2 = CH_2\text{-}(NC_5H_4\text{-}t\text{-}Bu)Br$; Octacation

16: $R_1 = CH_2\text{-}(NC_5H_4\text{-}t\text{-}Bu)Br$; $R_2 = H$; Tetracation

17: $R_1 = R_2 = H$; Dication

differentially substituted molecules. Of course, these can be modified in a second step to give even more complex compounds. As an example **12** reacts with potassium cyanide in THF (presence of [18]crown-6 required) to yield **14**. Azides give access to amino derivatives, cyanides also to amines but to carboxylates, too. Such materials allow the syntheses of peptide or carbohydrate conjugates, which create chiral environments near the metal center of the porphyrin. Reaction of **10**, **11**, and **12** with 4-*tert*-butylpyridine in refluxing toluene yielded an octa-, a tetra-, and a dipyridinium salt (**15**, **16**, **17**), respectively, which showed shifts in both their NMR and UV spectra, indicating clearly the influence of the positive charges on the porphyrin chromophore. The shift of the Soret band to longer wavelengths is (compared to zinc tetrakis[4-*tert*-butylphenyl]porphyrin; in methanol) about 5 nm for **17**, 12 nm for **16**, and 15 nm for **15**. Cyclic voltammetry is currently being performed on these species, and the results and other data will be presented elsewhere.

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Supporting Information Available: Descriptions of experimental procedures, NMR and FAB mass spectral data for **1**, **3**−**17**, and UV/vis data for **3**−**5**, **7**−**17**. This material is available free of charge via the Internet at http://pubs.acs.org.

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