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SHORT COMMUNICATION

Synthesis of *trans*-substituted porphyrin building blocks containing two S-trityl or thiol groups

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Abstract−The synthesis of some linear structured *trans*-porphyrin bearing functional groups (S-trityl or thiol) was described. The rational synthetic pathway consisted of 6 reaction steps (up to S-trityl derivatized porphyrin, 5 steps), constituting a MacDonald-type 2+2 condensation and amine-carboxylic acid coupling. The completion of each step was confirmed by ^{1}H-NMR, UV/Vis adsorption, and FAM-MS. The resulting porphyrins would be applicable to the study of self-assembled gold-thiol structures, due to the reactive nature of the molecules with a gold surface.

Key words: Cross-linking, Dithiol, Porphyrin, Self-assembly, Synthesis

INTRODUCTION

Meso-substituted *trans*-porphyrins containing specific functional groups are key structural components in porphyrin-based biomimetic systems and molecular materials. A *trans*-porphyrin can be used for the construction of well-defined porphyrin-based architectures. *Trans*-A_2B_2 porphyrins, which may be employed in the preparation of one-dimensional structures, have structural specificity compared to conventional *meso*-A_4 porphyrins.

Possible applications of porphyrins include mimics of photosynthesis related to charge separation [Imahori et al., 2003], optoelectronic devices [Holten et al., 2002], molecular oxygen diffusion in the membranes [Im et al., 1993] and transmembrane artificial proton pumps [Steinberg-Yfrach et al., 1997]. Among these applications, self-assembling is a remarkable method for attaching the porphyrin moieties to a specific surface. Terminal functional groups play an important role in self-assembling on various surfaces. A number of porphyrins with a variety of functional groups have been synthesized. A bis(porphyrin) disulfide [Imahori et al., 2001] for attachment to gold surfaces, porphyrins bearing arylphosphonic acid tethers [Muthukumaran et al., 2004] for oxide surfaces, and a porphyrin-alkyl silane for ITO [Yamada et al., 2003] and silica surfaces [Gulino et al., 2004] have been reported.

Dithiols have been used in preparing cross-linked nanoparticle films. These nanostructures have attracted interest because of their potential for use in materials, whose properties can be controlled by manipulating the size of nanoparticles and their space materials [Brust et al., 1998]. However, except for saturated carbon chains, other space materials bearing redox-active molecules such as porphyrins have not been reported. In addition, dithiol terminated materials can be utilized for the measurement of single-molecule conductivity via conducting probe atomic force microscopy (CP-AFM). The measurement of a metal-molecular-metal (m-M-m) junction composed of dithiol terminated materials is highly reproducible, due to the chemically bonded contacts [Cui et al., 2001].

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In this study, we report on a method for the synthesis of a dithiol-derivatized *trans*-A_2B_2 type porphyrin, which contains two mesityl moieties and two thiol terminated chains at the meso-position. The carbon chains provide space between metals and porphyrins in cross-linked structures and m-M-m junctions. Mesityl moieties were introduced to increase the solubility of the compounds in conventional organic solvents, and their steric hinderance prevents a J-conjugation between porphyrin units, which has an effect on the electron transfer. Electron transfer greatly depends on the distance between the porphyrin unit and other components such as nanoparticles, C_{60}, organic materials. The carbon chain creates space for such applications.

EXPERIMENTAL

1. Materials

All chemicals used were reagent grade and were purchased from Aldrich Chemical Company, Inc. Pyrrole was distilled at atmospheric pressure over CaH_2. Column chromatography was performed on silica (Merck, 230-400 mesh). All proton NMR results were obtained at a frequency of 500 MHz in $CDCl_3$ with a Bruker instrument. UV-vis absorption spectra were recorded in ethanol. Mass spectra (FAB) were obtained using a Jeol, JMS-AX505WA.

2. Synthetic Procedures

2-1. 5-(mesityl)dipyrromethane (**1**) [Laha et al., 2003]

A solution of mesitaldehyde (7.35 mL, 50 mM) and pyrrole (139 mL, 2 mM) was degassed for 20 min and $BF_3{\cdot}O(Et)_2$ (1.845 mL, 15 mM) was then injected. The mixture was stirred for 30 min at room temperature, and treated with powdered NaOH (4 g, 0.1 M). The mixture was stirred for 1 h and then filtered. The filtrate was concentrated, and the pyrrole was recovered. The resulting solid was dissolved in ethanol/water (4 : 1) at room temperature. The suspension containing white powders was filtered, and the filtrate was set aside overnight at room temperature, affording the first crop of white crystal [6.5 g, 50% yield]; ^{1}H-NMR ($CDCl_3$) δ 7.93 (bs, 2H, NH), 6.86 (s, 2H, m-mesityl-H), 6.66 (d, J=1 Hz, 2H, α-pyrrole), 6.18 (q, J=3 Hz, 2H, β-pyrrole), 6.01 (s, 2H, β-pyrrole), 5.92 (s, 1H, *meso*-H), 2.27 (s, 3H, p-mesityl-CH_3), 2.06 (s, 6H, o-mesityl-CH_3).

2-2. H_2P-$(NHAc)_2$ (2) and H_2P-$(NH_2)_2$ (3)

A solution of **1** (1.32 g, 5 mM) and 4-acetaminophenylaldehyde (815 mg, 5 mM) in $CHCl_3$ (500 ml) was purged with N_2 for 20 min, and $BF_3{\cdot}O(Et)_2$ (0.67 mL of 2.5 M stock solution in $CHCl_3$, 67 mM) was then added. The solution was stirred for 1 h at room temperature and DDQ (861 mg, 3.79 mM) was added. The mixture was stirred at room temperature for an additional 1 h and the solvent was removed. Column chromatography (silica, CH_2Cl_2 : MeOH= 24 : 1) afforded the porphyrin as the major moving band [805 mg, 40% yield]; ^{1}H-NMR ($CDCl_3$) δ 8.80 (d, J=5 Hz, 4H, β-pyrrole), 8.68 (d, J=5 Hz, 4H, β-pyrrole), 8.17 (d, J=8 Hz, 4H, o-acetaminophenyl-H), 7.89 (d, J=8 Hz, 4H, m-acetaminophenyl-H), 7.48 (s, 2H, p-acetaminophenyl-NH), 7.27 (s, 4H, m-mesityl-H), 2.63 (s, 6H, p-mesityl-CH_3), 2.36 (s, 6H, $COCH_3$), 2.06 (s, 12H, o-mesityl-CH_3), −2.63 (bs, 2H, inner-NH); λabs (ethanol) 414(1), 514(0.126), 549(0.065), 591(0.041), 648(0.031) nm; calcd exact mass 813, obsd 813 (FAB-MS).

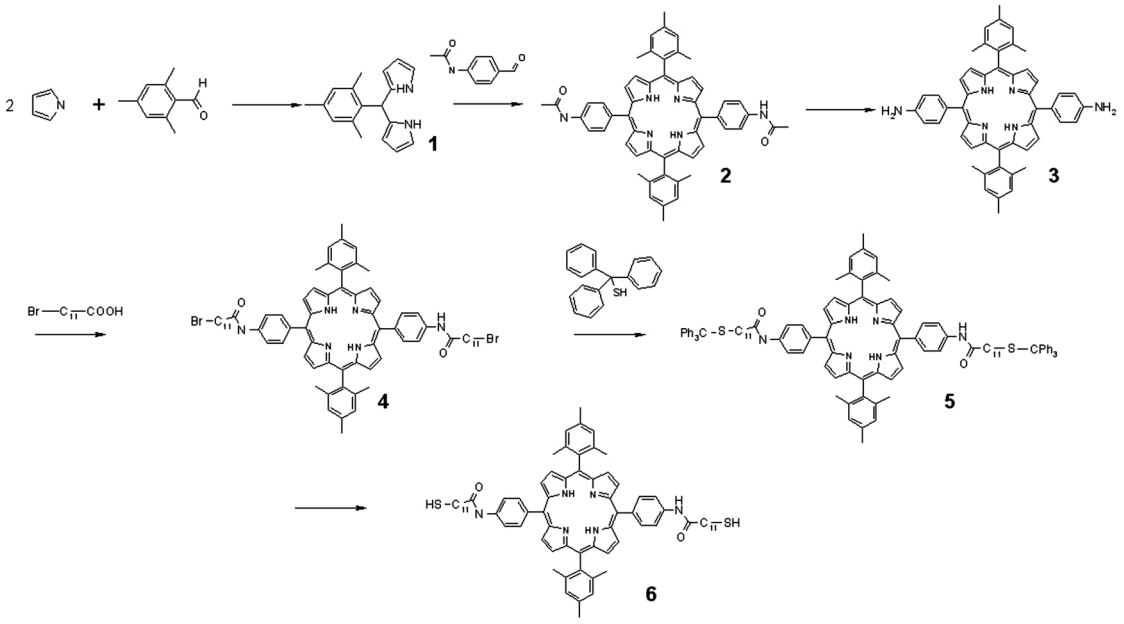
2 (500 mg, 0.615 mM) was dissolved in a mixture of ethanol (240 ml) and concentrated HCl (160 ml) and refluxed for 48 h. The mixture was poured into DI water, neutralized by the addition of $NaHCO_3$, extracted with $CHCl_3$, and then washed with aqueous $NaHCO_3$. Flash column chromatography (silica, $CHCl_3$) gave **3** [410 mg, 91% yield] as a purple solid; ^{1}H-NMR ($CDCl_3$) δ 8.86 (d, J=5 Hz, 4H, β-pyrrole), 8.66 (d, J=5 Hz, 4H, β-pyrrole), 7.99 (d, J=8 Hz, 4H, o-aminophenyl-H), 7.27 (s, 4H, m-mesityl-H), 7.05 (d, J=8 Hz, 4H, m-aminophenyl-H), 3.49 (s, 4H, p-aminophenyl-NH_2), 2.63 (s, 6H, p-mesityl-CH_3), 1.83 (s, 12H, o-mesityl-CH_3), −2.59 (bs, 2H, inner-NH); λabs (ethanol) 417(1), 517(0.116), 556(0.087), 593(0.056), 652(0.046) nm; calcd exact mass 729, obsd 729 (FAB-MS).

2-3. H_2P-$(NHCOC_{11}Br)_2$ (4)

A solution of THF (225 mL) containing 4-dimethylaminopyridine (DMAP, 552 mg, 4.5 mM) and 12-bromododecanoic acid (1.26 mg, 4.5 mM) was treated with 1-ethyl-3-(3-dimetylaminopropyl)carbodiimide hydrochloride (EDC, 863 mg, 4.5 mM) under N_2 at 0 °C. The mixture was stirred for 1 h at 0 °C. **3** (219 mg, 0.3 mM) was added to the mixture, followed be additional stirring at 0 °C for 30 min. The mixture was stirred at room temperature overnight. The mixture was concentrated in vacuo and poured into a 5% aqueous solution of HCL and extracted with $CHCl_3$. The organic layer was washed with an aqueous $NaHCO_3$ solution, dried, and evaporated. This washing with hexane was repeated 4-5 times. Column chromatography (silica, hexane : ethyl acetate=2 : 1) afforded the porphyrin as the major moving band [307 mg, 67% yield]; ^{1}H-NMR ($CDCl_3$) δ 8.81 (d, J=5 Hz, 4H, β-pyrrole), 8.68 (d, J=5 Hz, 4H, β-pyrrole), 8.16 (d, J=8 Hz, 4H, o-aminophenyl-H), 7.90 (d, J=8 Hz, 4H, m-aminophenyl-H), 7.53 (s, 2H, p-aminophenyl-NH), 7.26 (s, 4H, m-mesityl-H), 2.62 (s, 6H, p-mesityl-CH_3), 2.53 (t, J=7 Hz, 4H, carbon chain), 1.87 (q, J=7 Hz, 8H, carbon chain), 1.83 (s, 12H, o-mesityl-CH_3), 1.50-1.24 (m, 32H, carbon chain), −2.63 (bs, 2H, inner-NH); λabs (ethanol) 417(1), 514(0.058), 549(0.030), 591(0.019), 648(0.014) nm; calcd exact mass 1251, obsd 1250 (FAB-MS).

2-4. H_2P-$(NHCOC_{11}SPh_3)_2$ (5) and H_2P-$(NHCOC_{10}SH)_2$ (6)

Triphenylmethanethiol (102 mg, 0.5 mM) was dissolved in 5 mL of DMF. Sodiumhydride (12 mg, 0.5 mM) was added, turning the solution a golden yellow color, followed by the addition of **4** (150 mg, 0.1 mM). The reaction mixture was stirred at room temperature for 24 h. A 2 mL portion of DI water was added to quench the excess NaH, followed by the addition of 50 mL of CH_2Cl_2. The product was washed with DI water. The solvent was removed in vacuo, to give a purple solid [120 mg, 62%]. ^{1}H-NMR ($CDCl_3$) δ 8.81 (d, J=5 Hz, 4H, β-pyrrole), 8.68 (d, J=5 Hz, 4H, β-pyrrole), 8.17 (d, J=8 Hz, 4H, o-aminophenyl-H), 7.91 (d, J=8 Hz, 4H, m-aminophenyl-H), 7.64 (s, 2H, p-aminophenyl-NH), 7.31-7.16 (m, 30H, phenyl-H), 7.26 (s, 4H, m-mesityl-H), 2.63 (s, 6H, p-mesityl-CH_3), 2.53 (t, J=7 Hz, 4H, carbon chain), 1.87 (q, J=7 Hz, 8H, carbon chain), 1.83 (s, 12H, o-mesityl-CH_3), 1.51-1.24 (m, 32H, carbon chain), −2.63 (bs, 2H, inner-NH); λabs (ethanol/methylene chloride=1 : 1) 419(1), 516(0.054), 551(0.027), 591(0.017), 647(0.014) nm; calcd exact



Scheme 1. Synthesis of porphyrins bearing two S-trityl (5) and Thiol (6) Groups.

mass 1642, obsd 1641 (FAB-MS).

Trifluoroacetic acid (TFA) (5 mL) was added to **5** (50 mg, 0.026 mM), followed by the addition of triethylsilane (0.5 mL). The solvent was removed in vacuo, and the product was purified by chromatography (silica gel). The by-product was eluted with a hexane : ethyl acetate=2 : 1 solution (detection by long wave (365 nm) fluorescence on TLC). The remaining red band was eluted with elution of ethanol, resulting in **6**. [23 mg, 62%]; ^{1}H-NMR ($CDCl_3$) δ 8.81 (d, J=5 Hz, 4H, β-pyrrole), 8.68 (d, J=5 Hz, 4H, β-pyrrole), 8.17 (d, J=8 Hz, 4H, o-aminophenyl-H), 7.90 (d, J=8 Hz, 4H, m-aminophenyl-H), 7.50 (s, 2H, p-aminophenyl-NH), 7.28 (s, 4H, m-mesityl-H), 2.63 (s, 6H, p-mesityl-CH_3), 2.53 (t, J=7 Hz, 4H, carbon chain), 1.87 (q, J=7 Hz, 8H, carbon chain), 1.83 (s, 12H, o-mesityl-CH_3), 1.51-1.24 (m, 32H, carbon chain), −2.63 (bs, 2H, inner-NH); λabs (ethanol/methylene chloride=1 : 1) 418(1), 516(0.084), 551 (0.046), 591(0.030), 647(0.025) nm; calcd exact mass 1438, obsd 1438.

RESULTS AND DISCUSSION

Scheme 1 shows the overall synthetic pathway. In general, *trans*-*meso*-A_2B_2 porphyrins can be prepared by a MacDonald-type 2+2 condensation. This route involves meso-substituted dipyrromethane, which can be prepared from the acid-catalyzed reaction of an aldehyde with an excess of pyrrole. When 5-(acetaminophenyl)dipyrromethane (A-DP) is used, the pathway is not suitable, because of the difficulty of separating A-DP. In spite of the careful chromatographic separation, the yield is very poor due to scrambling. An appropriate solution could not be found for the crystallization of A-DP. Therefore, a rational synthesis could be achieved with 5-(mesityl)dipyrromethane, which could be easily separated (Must be kept it at 0 °C under nitrogen in the absence of light, or it degenerates. The yield in the porphyrin formation is influenced by degeneration of dipyrromethanes.).

The porphyrin **2** was produced by the condensation of **1** with 4-(acetaminophenyl)aldehyde and could be isolated easily by chromatography. Only one red band was found during silica gel column chromatography. Thus, mesityl substituents were advantageous in the synthetic procedures. In the synthetic procedure involving the porphyrin bearing phenyl substituents instead of mesityl substituents, a by-product bearing four phenyl substituents was observed, due to the rearrangement of the 5-phenyldipyrromethane during the condensation reaction. Sterically hindered dipyrromethanes, such as 5-mesityldipyrromethane are useful in the preparation of pure *trans*-porphyrins in good yield with minimal chromatography without any detectable acid catalyzed scrambling [Littler et al., 1999]. The proof that the product consisted only of the *trans*-isomer instead of a mixture of by-products was obtained by the ^{1}H NMR spectrum, in which the signal for the β-pyrrole protons appeared as two separated peaks at 8.80 and 8.68 ppm that were mutually spin-coupled (J=5 Hz, 8 Hz), as shown in Fig. 1 (inset).

The deprotection of **2** by treatment with HCl produced **3** in 91% yield. When the deprotection was incomplete, only one acetyl group was removed. In this case, a mass spectrum peak at m/z=770 indicating incomplete deprotection can be found as well as a 729 peak indicating the complete deprotection. Deprotection was complete by an additional treatment.

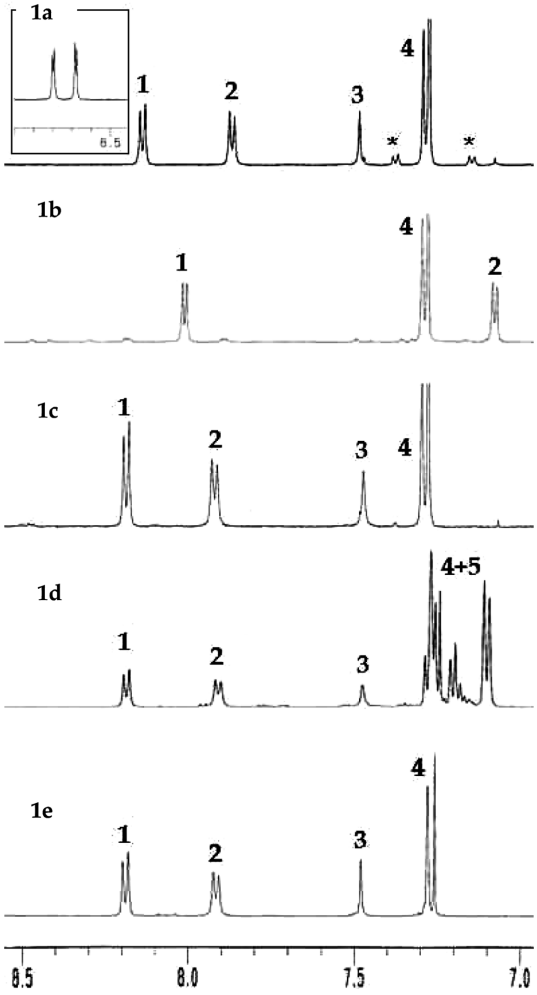


Fig. 1. ^{1}H-NMR spectra. the proton of the β-pyrrole of H_2P-(NHAc)$_2$ (inset); *otho*-amino(or akylamino)phenyl ring (1); *meta*-amino(or akylamino)phenyl ring (2); amine (3); *meta*-mesityl ring (4); trityl ring (5).

The formation of amide bonds between carboxylic acids and amines involved the use of the coupling agent, 1-ethyl-3-(3-dimetylaminopropyl)carbodiimide hydrochloride (EDC). Deprotection and protection were confirmed by the four peak changes of the protons attached to the aminophenyl functionality (Fig. 1a-1c). In some case, materials might be with the product. Repetitive washing with hexane that selectively solubilizes these the impurities was effective in solving this problem. Bond formation was vertified by thin-layer chromatography (TLC). A spot corresponding to the product **4** was observed, whereas no spot corresponding to the reactant **3** was found on a TLC plate eluted with ethyl acetate : hexane.

We refer to earlier published studies for the preparation of the protected porphyrin **5** and the deprotected porphyrin **6**. The trityl(triphenylmethane) protecting group is commonly used in the synthesis of thiol-containing monolayer precursors because it is stable in most chemical environments. The *in situ* deprotection of trityl molecules could produce self assembled monolayers (SAMs) with a quality comparable to that formed from the purified thiol [Inman et al., 2004]. The variation of the integrals of the phenyl protons in ^{1}H-NMR spectrum clearly verified that the compounds were sub-

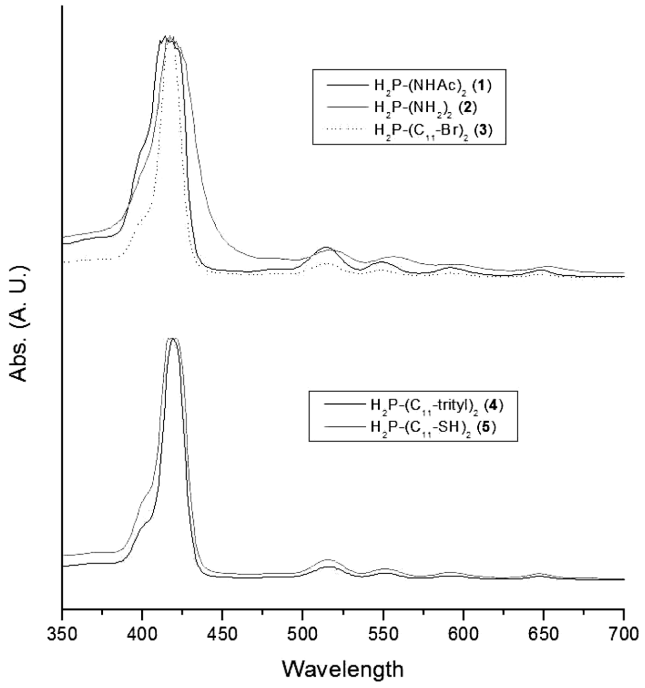


Fig. 2. UV/Vis spectra of porphyrins 1-3 (ethanol) and porphyrins 4-5 (ethanol : methylene chloride=1 : 1).

stituted with trityl groups, as shown in Fig. 1d and Fig. 1e. UV/Vis spectra of the porphyrins were consistent with the peak positions and intensities of the conventional tetraphenylporphyrins, as shown in Fig. 2.

In summary, a method for the synthesis of *trans*-substituted porphyrin building blocks bearing two S-trityl (**5**) or thiol (**6**) groups was described. The synthetic pathway involved preparing the porphyrin by a MacDonald-type 2+2 condensation. The formation of a porphyrin moiety between the carbon chain was accomplished by the amine-carboxylic acid coupling. Both the porphyrin protected by a trityl group and the deprotected porphyrin could be applied in the field of self-assembly. We expect that this synthesized material can be utilized in structural and photoelectric studies of molecular devices and cross-linked nanostructures including porphyrin moieties.

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