Synthesis of a porphyrin with allyl tethers for grafting on diamond

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Abstract
The synthesis of *meso*-tetrakis(4-allyl-2,6-dimethylphenyl)porphyrin from 2,6-dimethylaniline is described.

Keywords: Porphyrin, allyl tethers, grafting on diamond, halogen-magnesium exchange

Introduction

Diamond is a particularly attractive substrate material because of its optical transparency, its chemical stability, and its biocompatibility. It can be deposited as thin film on many substrates at relatively low temperature and can be doped. Furthermore, diamond surfaces can be photochemically modified by [2+2]-addition of olefins with surface C=C dimer rows to give strong covalent molecule-substrate bonds.[1] It opens new avenues for applications, such as molecular electronics, photovoltaic conversion and chemical/biological sensing.[2] Despite their insulating character, diamond surfaces can be imaged at the atomic scale by scanning tunnelling microscopy (STM) in an unconventional resonant electron mode.[3] In the course of a study of tunnelling electrons-induced luminescence, we were interested in designing chromophores suitable for covalent coupling on a diamond surface in ultra-high vacuum (UHV). The figure 1 shows the design of the target molecule.

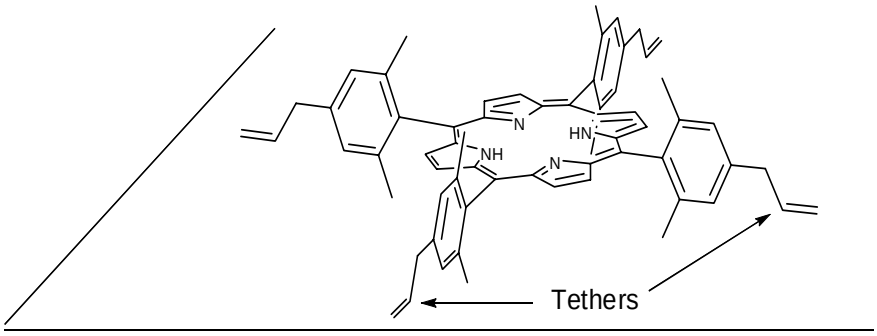
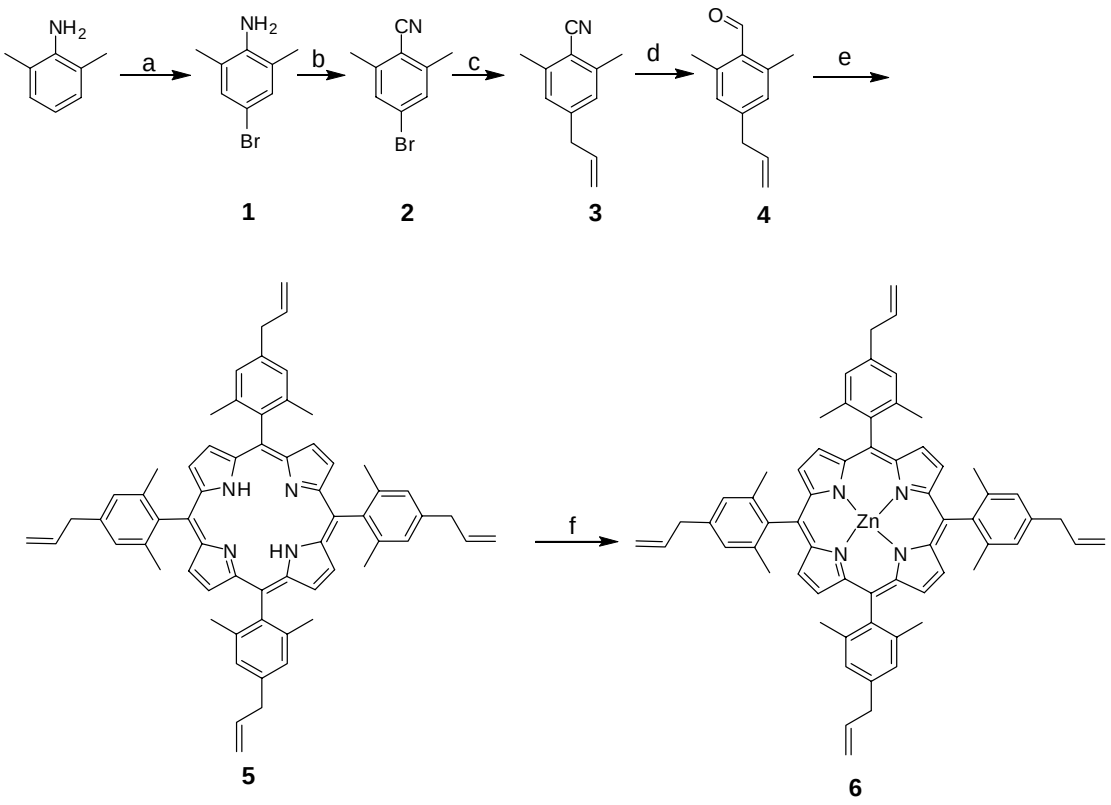


Figure 1. Design of the target molecule. The mesityl *meso* substituents are for steric reasons perpendicular to the porphyrins ring and lift this ring above the substrate to reduce the non-radiative quenching; the alkene groups are designed for grafting on diamond surfaces.

Results and Discussion

The selected chromophores comprise a meso-substituted porphyrin core. Porphyrins are the most studied molecules in STM-induced luminescence experiments[4] because of clean emission signatures and good thermal stability required for UHV sublimation onto the substrates. To reduce non-radiative quenching, the chromophores **5** and **6** are lifted above the diamond surface by four mesityl groups. These *meso*-substituents are further functionalized by four allyl tether groups for photochemically activated cycloaddition to diamond surfaces. Indeed, the STM bias voltage, above 4 V, used for STM imaging of diamond surfaces, will require strong irreversible bonding to the surface to avoid field/tip induced diffusion of the molecules on the substrate. In order to compare metallated and non-metallated molecules in the STM experiments, we have also prepared the zinc-porphyrin complex **6**.

The synthesis of the target molecules **5** and **6** is shown on Scheme 1.



Scheme 1. (a) EtOH/HCl, cyclohexane/Br_2,NaOH. (b) $NaNO_2$/HCl, CuCN. (c) $^{i}Pr^{n}Bu_2MgLi$, THF, -30 °C/allyl bromide, CuCN·2LiCl. (d) DIBALH/DCM, 0 °C. (e) pyrrole, BF_3-etherate, chloranil, triethylamine. (f) zinc acetate, MeOH, 24 h.

The porphyrin **5** was prepared by condensation of 4-allyl-2,6-dimethylbenzaldehyde **4** with pyrrole/BF_3 etherate in chloroform containing 0.75 % of ethanol, followed by oxidation of the porphyrinogen by *p*-chloranil, according to Lindsey's procedure.[5] The aldehyde **4** was obtained from 2,6-dimethylaniline hydrochloride. After bromination,[6] Sandmeyer cyanation yielded 4-bromo-2,6-dimethylbenzonitrile **2** according to ref 7. After halogen-magnesium exchange with $^{i}Pr^{n}Bu_2MgLi$ at -30 °C,[8] the Grignard intermediate was reacted with allyl bromide in the presence of freshly prepared CuCN.2LiCl at -30°C. It must be stressed that, at this temperature, this halogen-magnesium exchange tolerates the nitrile group and that reactions at lower temperature or without copper catalyst were unsuccessful. Finally, reduction of the nitrile group of **3** gave the aldehyde **4** in 42 % yield. Other routes involving the reduction of **2** to give 4-bromo-2,6-dimethylbenzaldehyde, protection by acetals[9] and Kumada coupling were ineffective, giving inseparable mixture of compounds. Finally, the zinc porphyrin **6** was obtained in 77 % yield by metallation of **5** by zinc acetate in DCM.[10]

Experimental Section

General Procedures. The NMR spectra were recorded on 300 MHz spectrometer in the indicated solvents. Chemical shifts are expressed in parts per million using residual solvent proton and carbon as internal standards for chloroform (δ_H: 7.26 ppm, δ_C: 77.0 ppm) and dichloromethane (δ_H: 5.32 ppm, δ_C: 53.8 ppm). Mass spectra were obtained in the CI mode with a Nermag R10-R10. Elemental analyses were done by the Service d'Analyse de l'ICSN (Paris). Unless otherwise indicated, all commercially available materials were used as received. All solvents were purified before use following standard procedures. The chloroform used for the porhyrin synthesis was stabilized with ethanol (0.75 %) and distilled on potassium carbonate.

4-Bromo-2,6-dimethylaniline (1).[6] To 15 ml of 2,6-dimethylaniline dissolved in 25 ml of ethanol and cooled in ice bath was added 20 ml of 1:1 HCl. White precipitate of 2,6-dimethylaniline hydrochloride was formed, filtered and washed with dry ether. The dry hydrochloride was suspended in 150 ml of cyclohexane, heated to 70°C and 12 ml of bromine was added dropwise over 3 hours with continuous stirring. The mixture was cooled to 10°C and filtered. The precipitate was washed with cyclohexane and dried in vacuum. The formed 4-bromo-2,6-dimethylaniline hydrochloride was dissolved in water (50 ml) and the insoluble materials removed by filtration. To the cooled filtrate was slowly added 20 ml of 40% NaOH solution. The pale brown crystals of 4-bromo-2,6-dimethylaniline were filtered and dried. Yield: 13 g (70 %). The compound NMR data are similar to that reported.

4-Bromo-2,6-dimethylbenzonitrile (2). This compound was prepared as reported in reference 7.

4-Allyl-2,6-dimethylbenzonitrile (3). All glassware was dried in an oven and the reaction flask was further dried in vacuum. The reaction was conducted under argon.

CuCN·2LiCl solution[8] (1.0 M/THF) was prepared by drying CuCN (869 mg, 10 mmol) and LiCl (848 mg, 20 mmol) in a Schlenk flask under vacuum for 5 h at 140 °C. After cooling to room temperature, dry THF (10 ml) was added and the mixture was stirred continuously until the salts were dissolved.

To a solution of ^{i}PrMgBr (6 ml, 2.0 M solution in THF, 12 mmol) in dry THF (7 ml), n-BuLi (15 ml, 1.6 M in hexane, 24 mmol) was added dropwise at 0°C and the mixture was stirred for 10 min. To the resulting yellow clear solution, cooled to -40°C, was added dropwise a solution of 4-bromo-2,6-dimethylbenzonitrile (**2)** (2.1 g, 10.1 mmol) in THF (15 ml). The mixture was stirred for 1 hour at -30 °C. A freshly prepared solution of CuCN·2LiCl (3 ml, 1.0 M in THF, 3 mmol) was added dropwise to the reaction mixture and stirred for 15 min. To the solution, allyl bromide was added dropwise (3.5 ml, 40 mmol) at -30°C. The temperature of the bath was slowly raised to room temperature, and the solution was stirred 1h at room temperature and quenched with saturated NH_4Cl. The contents were extracted with n-hexane (200 ml), the organic phase was dried with sodium sulfate, filtered and the solvent was removed. Then, about 15 ml of n-hexane was added to the residue and the residual solid was removed by filtration. After solvent removal, the product was purified by column chromatography (silica gel; n-hexane : ethyl acetate 9:1).

Yield: 0.82 g. (31 %). ^{1}H NMR (CD_2Cl_2): δ 6.97 (s, 2H, Ar-H), 5.88-5.97 (m, 1H, = CH), 5.12 (m, 2H, =CH_2), 3.36 (d, 2H, *J* = 6.9 Hz, CH_2), 2.48 (s, 6H, CH_3); ^{13}C NMR (CD_2Cl_2): 144.9, 142.1, 136.2, 127.6, 116.4, 40.0, 20.4; MS (ESI): m/z calcd for $C_{12}H_{13}N$: 171.1; found 171.1 [M^+]. Anal. calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18 ; Found: C, 84.13; H, 7.55; N, 8.10.

4-Allyl-2,6-dimethylbenzaldehyde (4). A solution of 4-allyl-2,6-dimethylbenzonitrile (**3**) (2.67 g, 15.59 mmol) in DCM (40 ml) was cooled to 0°C and a 1 M solution of DIBALH in hexanes (17.5 ml,17.5 mmol) was added dropwise. The mixture was allowed to warm slowly to room temperature. After 3 hours, the solution was poured into crushed ice with 6N HCl and stirred for 2h. The separated layers were extracted with DCM and washed with aqueous sodium thiosulfate. The DCM layer was dried with sodium sulfate, filtered and the solvent was removed under reduced pressure. About 15 ml of n-hexane was added to the residue, stirred and the insoluble material was filtered. The filtrate was diluted with 60 ml of n-hexane and passed through a pad of silica gel. After solvent removal, the product was obtained as pale yellow oil. Yield: 1.11 g (42 %).

^{1}H NMR ($CDCl_3$): δ 10.57 (s, 1H, -CHO), 6.91 (s, 2H, Ar-H), 5.88 (m, 1H, =CH), 5.08-5.13 (m, 2H, =CH_2), 3.33-3.35 (d, 2H, *J* = 12 Hz, -CH_2), 2.59 (s, 6H, CH_3); ^{13}C NMR (CD_2Cl_2): 192.8, 145.6, 141.5, 136.5, 129.9, 127.6, 116.1, 40.0, 20.2; MS (ESI): m/z calcd for $C_{12}H_{14}O$: 174.1; found 173.1 [M^+-1]; UV-vis (CD_2Cl_2) λ_{max} (ε) : 514 (702730); 547 (23780); 590 (23250); Anal. calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10; Found: C, 82.67 ; H, 8.05.

Synthesis of porphyrin (5). In a three necked 500 ml round bottomed flask, a mixture of chloroform (250 ml), **4** (435 mg, 2.5 mmol) and pyrrole (167.5 mg, 2.5 mmol) was purged with argon for 10 min. To the mixture, BF_3-etherate (117.1 mg, 0.105 ml, 0.825 mmol) was added and the solution was stirred for 1 hour at room temperature. Then p-chloranil (0.461 g, 1.875 mmol) was added to the reaction mixture which was then heated to 61° C for 90 minutes. The solution was cooled to room temperature and neutralized with triethylamine (0.115 ml, 0.825 mmol). The solvent was removed from the reaction mixture. The precipitate was transferred into a filtering funnel and washed with methanol, until the filtrate was clear. TLC on silica gel, using n-hexane: ether (9:1) as eluent, showed a single spot with Rf: 0.75. Yield: 143 mg (50 %). ^{1}H NMR (CD_2Cl_2): δ 8.60 (s, 8H), 7.30 (s, 8H), 6.29 (m, 4H), 5.21-5.36 (m, 8H, merged with solvent peak), 3.65-3.67 (d, *J*= 6 Hz, 8H), 1.86 (s, 24H); ^{13}C NMR (CD_2Cl_2): 140.1, 139.5, 138.8, 138.0, 127.1, 117.4, 115.5, 40.3, 21.4; m/z calcd for $C_{64}H_{60}N_4Zn$: 948.41; found 949.41 [M^++1]; UV-vis (CD_2Cl_2) λ_{max} (ε) : 514 (702730); 547 (23780); 590 (23250); Anal. calcd for $C_{64}H_{62}N_4.2H_2O$: C, 83.26; H, 7.21; Found: C, 83.04; H, 7.28.

Zinc Insertion in Porphyrin (6). A solution of **5** (44 mg, 0.0496 mmol) in DCM (20 ml) was treated with zinc acetate (1.106 g, 5.03 mmol) in methanol (20 ml) and stirred for 24 hours at room temperature. The suspension was passed through a pad of silica gel to remove zinc acetate and other baseline impurities. Solvent removal left a purple coloured solid. TLC with n-hexane : diethylether (9:1) gave single spot with same Rf value that of the starting material. Yield: 32 mg (77 %). ^{1}H NMR (CD_2Cl_2): δ 8.66 (s, 8H), 7.29 (s, 8H), 6.29 (m, 4H), 5.22-5.35 (m, 8H, merged with solvent peak), 3.65-3.67 (d, 8H), 1.84 (s, 24H); ^{13}C NMR (CD_2Cl_2) 149.7, 139.4, 138.2,

127.1, 111.3, 40.3, 21.4; MS (CI, NH_3): m/z calcd for $C_{64}H_{60}N_4Zn$: 948.41; found 949.41 [M^++1]; UV-vis (CD_2Cl_2) λ_{max} (ε) : 550 (89390); Anal. calcd for $C_{64}H_{60}N_4Zn$ $2H_2O$: C, 76.83; H, 8.11. Found: C, 76.89 ; H, 7.28.

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