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Convenient preparation of 5-ethynyl-octaethylporphyrin free base and zinc complex

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This Letter is dedicated to the memory of Professor Guy Ourisson

Abstract—A method leading to the preparation of the free base or zinc *meso*-ethynyl functionalized octaethylporphyrin has been developed, which will open the access to various *meso*-ethynyl metalloporphyrins.

1. Introduction

In the developing field of multi-porphyrin-based materials, conjugated ethynyl linkers have been extensively used in order to enhance electronic communication between two *meso*-positions of photo- and electroactive tetrapyrrolic macrocycles.[1] Most frequently, *meso*-ethynyl linkers have been associated with porphyrin derivatives bearing aryl substituents on their remaining *meso*-positions.[2] Other than the pioneering synthetic work for the preparation of nickel octaethylporphyrin **1**(**Ni**) developed by the group of Arnold,[3] there are few reports of *meso*-linked octaethylporphyrin (OEP) derivatives. The sequence of Vilsmeier formylation to afford **2**(**Ni**), a Wittig reaction to form the *cis*/*trans*-bromovinyl derivative **3**(**Ni**), and final dehydrobromination under basic conditions seemed restricted to Ni(OEP) for almost a decade. This original strategy was later modified by the group of Higushi, to produce thiophene–diacetylene linked hetero-bis-porphyrins including two different metal centres (Ni/Pd).[4]

In our investigation of versatile synthetic approaches leading to cofacial porphyrin scaffolds built on calix[4]-arene platforms,[5] we were confronted by the lack of ethynyl OEP derivatives containing metals other than nickel. We describe hereafter a simple procedure that affords the free base and zinc derivatives of ethynyl OEP. This synthetic work paves the way towards the preparation of hetero-dimetallic species that could be of interest in the area of OEP-based materials.[6]

The initial synthetic route[3,7] (Scheme 1) involving *meso*-*trans*-bromovinyl-Ni(OEP) **3**(**Ni**) was later modified by Arnold,[8] who reported a major improvement in the formation of a *meso*-iodovinyl intermediate **4**(**Ni**) instead of the bromovinyl analog **3**(**Ni**). A Takai reaction was used for this purpose.[9] During the course of our work we fortuitously found that the yields of this reaction were temperature dependent. By performing the Takai reaction at 0 °C, instead of at room temperature, the yields were significantly improved and showed a higher reproducibility.

2. Discussion

As stated in the literature, the removal of nickel from the ethynyl NiOEP derivatives under drastic acidic conditions is precluded by the reactivity of the triple bond.[4] Milder conditions, using biphasic mixtures of organic solvents and acidic aqueous phases, have also proven unsuccessful.[10] We thus performed this demetalation step on the iodovinyl precursor **4**(**Ni**). As is the case for the bromovinyl derivative,[3] conventional treatment of **4**(**Ni**) with concentrated sulfuric acid afforded the free base **4**($\mathbf{H_2}$) in good yield (87%). From this intermediate, dehydroiodination proceeded smoothly in the presence of excess *t*-BuOK to afford the free base of ethynyl OEP **5**($\mathbf{H_2}$).

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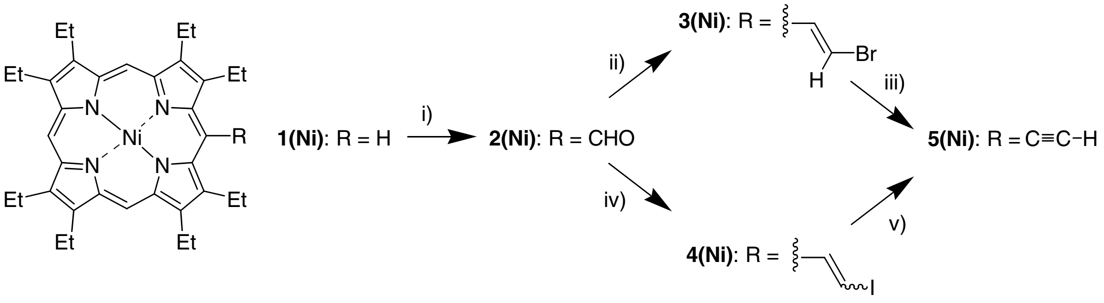
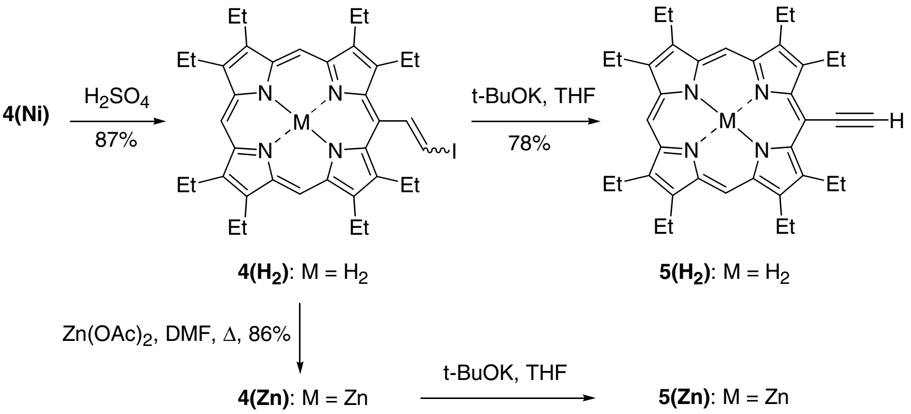


Scheme 1. Conditions (i–v) previously reported by Arnold for the original synthesis of **5**(**Ni**). Reagents: (i) DMF, $POCl_3$; (ii) $[BrCH_2PPh_3]Br$, *n*-BuLi, THF; (iii) NaH, $MeOCH_2CH_2OMe$, DMSO; (iv) (1) $CrCl_2$, CH_3I, THF, 0 °C (2) $N(n\text{-}Bu)_4F$ and (v) *t*-BuOK, THF.



Scheme 2. Synthesis of free base and zinc iodovinyl- and ethynyl-octaethylporphyrins.

Coupling reactions involving ethynyl functionalized species generally require the use of reagents and (co)-catalysts such as zinc (Negishi) or copper salts (Sonogashira, Glaser-Hay). In this regard, the use of ethynyl OEP **1**(H_2) itself is rather limited due to the spontaneous in situ formation of its corresponding Zn derivative, or paramagnetic copper(II) species. Zn(II) is smoothly removed from the OEP core; therefore, it can be conveniently used to protect the porphyrin binding site, and subsequently removed after any coupling reactions that occur under basic or neutral conditions.

Even though the free base iodovinyl porphyrin **4**(H_2) (Scheme 2) is rather unstable, it is less sensitive to oxidation than the ethynyl OEP **5**(H_2) itself. Thus, it is easier to proceed with metal insertion on the iodovinyl derivative **4**(H_2). Classical zinc(II) metalation procedures ($Zn(OAc)_2$/DMF) were used to generate **4(Zn)**. From this stage on, the procedures developed by Arnold can be applied to obtain the corresponding ethynyl derivatives **5**(**Zn**), with yields similar to those reported for **5**(**Ni**) and **5**(**Pd**) obtained from the bromovinyl intermediate reported by Higushi.[4]

In conclusion, zinc(II) and free base derivatives of ethynyl OEP are available via metal replacement prior to the formation of the reactive ethynyl function. Whereas ethynyl derivatives of nickel OEP have proven to be of limited use in the generation of porphyrin-based materials due to the difficulty to incorporate various metals in the porphyrin core, the easily removable zinc(II) can be used to temporarily protect the porphyrin core. Developments in the field of porphyrin heterodyads, in particular, and porphyrin-based materials involving the OEP framework, in general, can be foreseen for these new building blocks.[11]

3. Experimental

3.1. Free base 5-iodovinyl-octaethylporphyrin: 4(H_2)

The Ni-complex of iodovinylporphyrin **4**(**Ni**) (30 mg, 0.042 mmol) was dissolved in 5 mL of sulfuric acid. The mixture was stirred at room temperature for 5 min, after which time the solution was poured into a 1/1 mixture of iced water and CH_2Cl_2, extracted with CH_2Cl_2 and washed twice with water containing three drops of NEt_3, dried over Na_2SO_4 and filtered. The solvent was removed under reduced pressure. The residue was purified by column chromatography over alumina (neutral, activities II and III), eluting with a 1:1 mixture of hexane and CH_2Cl_2. A red-brown band was collected and the solution was evaporated. Recrystallization of the residue from chloroform–methanol yielded (**4**H_2) as purple needles (24 mg, 0.037 mmol, 87%). Analytical data: $R_f = 0.37$ (Al_2O_3, CH_2Cl_2/hexane 1:3); UV–vis (toluene): λ_{max} in nm, (ε in $M^{-1}\,cm^{-1}$): 407 (178,700), 506 (19,800), 540 (16,200), 575 (16,800), 627 (10,900); ^1H NMR (300 MHz, $CDCl_3$): −3.80 (s, 2H, NH), 1.84

(m, 24H, $CH_2\mathit{CH_3}$), 4.18 (m, 16H, $\mathit{CH_2}CH_3$), 6.56 (d, 1H, CH=CHI), 9.91 (s, 1H, *meso*-H), 9.96 (s, 2H, *meso*-H), 10.13 (d, 1H, CH=CHI); HR MS [*m*/*z* (rel. intens. %)]: $C_{38}H_{47}IN_4$: 687.2902 (M+1, calcd: 687.2918, 100%).

3.2. Free base 5-ethynyl-octaethylporphyrin: 5(H$_2$)

The free base 5-iodovinylporphyrin **4**(**H**$_2$) (20 mg, 0.030 mmol) was dissolved in dry THF (5 mL) under argon. Excess *t*-BuOK (0.15 mL of a 1.5 M solution in THF) was added via syringe. The solution immediately turned purple/green. After stirring for a further 10 min, the reaction was quenched by the addition of water. $CHCl_3$ was added and the organic layer was collected, washed thoroughly with water, dried over Na_2SO_4, filtered and the solvent was removed under vacuum to yield a purple residue (32 mg, 0.023 mmol, 78%). The product **5**(**H**$_2$) was used immediately in the next step without further purification. UV–vis (toluene): λ_{max} in nm: 414, 513, 551, 585, 641; ^{1}H NMR (300 MHz, $CDCl_3$): 1.88 (m, 24H, $CH_2\mathit{CH_3}$), 4.05 (m, 12H, $\mathit{CH_2}CH_3$), 4.35 (q, 4H, $\mathit{CH_2}CH_3$), 4.42 (s, 1H, C≡CH), 9.95 (s, 1H, *meso*-H), 10.10 (s, 2H, *meso*-H). FAB$^+$ MS: [*m*/*z* (rel. intens. %)]: 559.2 (M+1, calcd: 558.37, 100%).

3.3. Zinc(II) 5-iodovinyl-octaethylporphyrin: 4(Zn)

Free base iodovinylporphyrin **4**(**H**$_2$) (30 mg, 0.046 mmol) and zinc acetate (50 mg, 0.228 mmol) were added to 10 mL of DMF. The reaction mixture was refluxed under an argon atmosphere for 2 h, after which time spectrophotometry indicated that the metal insertion was complete. The solution was poured into water, and extracted with dichloromethane. The organic layer was washed twice with water, dried over Na_2SO_4, filtered and solvents were evaporated under vacuum. The resulting residue was purified by chromatography on an alumina column (CH_2Cl_2/hexane 1:1). A purple band was collected and the solution was evaporated. Recrystallisation of the residue from chloroform–methanol yielded **4**(**Zn**) as dark microcrystals (28 mg, 0.04 mmol, 86%). Analytical data: $R_f = 0.68$ (Al_2O_3, CH_2Cl_2/hexane 1:3). UV–vis (toluene): λ_{max} in nm, (ε in $M^{-1}\,cm^{-1}$): 411 (185,400), 541 (17,400), 578 (12,300). ^{1}H NMR (300 MHz, $CDCl_3$): 1.73 (t, 6 H, $CH_2\mathit{CH_3}$), 1.94 (q, 18H, $CH_2\mathit{CH_3}$), 4.10 (m, 16H, $\mathit{CH_2}CH_3$), 6.38 (d, 1H, CH=CHI), 9.95 (s, 1H, *meso*-H), 10.09 (d, H, CH=CHI), 10.14 (s, 2H, *meso*-H). HR MS [*m*/*z* (rel. intens. %)]: $C_{38}H_{45}IN_4Zn$: 749.2025 (M+1, calcd: 749.2053), 685.4270 ([M−Zn+H$_2$] +1, 100%).

3.4. Zinc(II) 5-ethynyl-octaethylporphyrin: 5(Zn)

The procedure to prepare **5**(**H**$_2$) was used, with the following quantities: **4**(**Zn**) (20 mg, 0.027 mmol), 5 mL of dry THF, *t*-BuOK (0.15 mL of a 1.5 M solution in THF) to afford **5**(**Zn**) as a purple residue (11 mg, 0.019 mmol, 69%). This product was immediately used in subsequent coupling procedures without further purification. UV–vis (toluene), λ_{max} in nm: 419, 553, 597. ^{1}H NMR (300 MH, $CDCl_3$): 1.81 (m, 24H, $CH_2\mathit{CH_3}$), 3.78 (m, 12H, $\mathit{CH_2}CH_3$), 4.21 (q, 4H, $\mathit{CH_2}CH_3$), 4.45 (s, 1H, C≡CH), 9.43 (s, 1H, *meso*-H), 9.47 (s, 2H, *meso*-H). HRMS: $C_{38}H_{44}N_4Zn$: 621.2901 (M+1, 100%, calcd: 621.2930).

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