# Efficient Synthesis of *meso-meso*-Linked Diporphyrins by Nickel(0)-Mediated Ullmann Homocoupling

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**Abstract:** *meso-meso*-Linked diporphyrins have been prepared by nickel(0)-mediated Ullmann homocoupling under mild conditions.

**Key words:** diporphyrins, bromoporphyrins, dimerization, Ullmann homocoupling, debromination

Porphyrin arrays are of particular usefulness in the field of molecular electronic device and artificial photosynthetic system.[1] Among them, *meso-meso* directly linked diporphyrins are important precursors for fully conjugated triply fused porphyrins.[2] Meanwhile, *meso-meso* linkages are widely found in the construction of the multiporphyrin arrays.[3] Thus, a lot of methods for the formation of *meso-meso* covalent bond are known. Among several approaches[4–6] to the *meso-meso* diporphyrins, the oxidative dimerizations of monomeric porphorins are prevalent. The oxidants for the homocouplings are $AgPF_6$,[5a] DDQ,[3d,5b] bis(trifluoroacetoxy)iodobenzene (PIFA),[5c] and $PhIX_2$ (X = Cl or F).[5d] Under oxidative conditions, an important discovery is the dependence of the coupling products on the metals incorporated in the porphyrins. Usually, the products were mainly the coupling products when zincated porphyrins were used, whereas chlorination[5d] or *meso*-β-dimerization[2d,e,f,6a] together with homocoupling, also took place in some cases of nickel(II) porphyrin complexes, though the nickel(II) porphyrins could be oxidated by PIFA to form *meso-meso* directly linked diporphyrins. Furthermore, all the oxidative couplings of the 5,15-disubstituted porphyrins which have two free *meso* positions resulted in a mixture of oligomers except for Senge's case.[5a–5c] For example, Ag(I)-promoted oxidative coupling of a zinc(II) 5,15-diarylporphyrin provides a porphyrin dimer only in 25% isolated yield and a porphyrin trimer in 4% yield, based on the amount of the starting porphyrin used.[5a] When zincated 5,15-diphenylporphyrin was treated with PIFA, several porphyrin oligomers (dimer, 17%; trimer, 16%; tetramer, 11%; pentamer, 7%) were obtained.[5c] When $PhIX_2$ was employed as an oxidant, the coupling of zinc(II)–5,15-diphenylporphyrin gave dimer product in 15% yield, together with chlorinated products, unidentifiable oligomers, and unreacted starting porphyrin.[5d] Under electrochemical conditions, a combination of starting porphyrin (44%), porphyrin dimer (20.7%), porphyrin trimer (2.9%), and porphyrin tetramer (0.9%) was obtained, when [5,15-bis(3,5-di-*tert*-butylphenyl)porphyrinato] zinc(II) was used.[6b] Hence, the development of a new general approach to nickel(II) diporphyrins, especially without oligomers, is demanding.

Ullmann reaction is the reaction of aryl halides with stoichiometric copper to produce aryl–aryl bonds. The similarity of the aromatic properties between benzene and porphyrin encouraged us to utilize Ullmann reaction in the coupling of *meso*-bromoporphyrin. In the first several attempts to use copper to promote the coupling of nickel(II)–5,10,15-triphenylbromoporphyrin complex (**Ni1a**) in DMF at 100 °C, we found that all the starting porphyrin was debrominated. The debromination was also found in the case of 5,10,15-triphenylbromoporphyrin (**1a**) or its zinc(II) complex (**Zn1a**) under the classic Ullmann reaction conditions, to give a debrominated copper(II) complex as the final product. After that, we turned our interest into the $NiCl_2(PPh_3)_2/Zn$ system for nickel(0)-mediated Ullmann homocoupling. When the reaction of porphyrin **1a** was carried out at 60 °C in the presence of 0.2 equivalents of $NiCl_2(PPh_3)_2$/2 equivalents of zinc in DMA for one hour, a mixture of reduction product **Zn3a** (76% yield) and coupling product **Zn$_2$4a** (21% yield) was formed (Table 1, entry 1). In the same conditions, zinc(II) and nickel(II) metalloporphyrin complexes (**Zn1a** and **Ni1a**) provided a similar result (Table 1, entries 2 and 3). Interestingly, **Ni1a** gave more coupling product. The similar coupling reactivities of nickel(II) porphyrins to that of zinc(II) porphyrins have been found also under a few previous oxidative dimerization conditions.[5c,d] According to those data, PIFA and $PhIX_2$ were successful reagents used in the coupling of 5,10,15-trisubstituted nickel(II) porphyrin.[5c,d] *Meso-meso*-linked nickelated diporphyrins prepared by nickel(0)-mediated Ullmann homocoupling became another successful method used in the coupling of nickel(II) porphyrin. Unexpectedly, no coupling products were observed when iodoporphyrins (**2a**, **Zn2a**, **Ni2a**) were used under various conditions (Table 1, entries 4–6). The screening of the solvents showed that the reaction went smoothly also in DMF and pyridine and slowly in THF (Table 1, entries 7–9). The temperature played an important role in the reaction. A decrease of the temperature favored the formation of the coupling product (Table 1, entries 3, 10–12). The dimerization afforded di-

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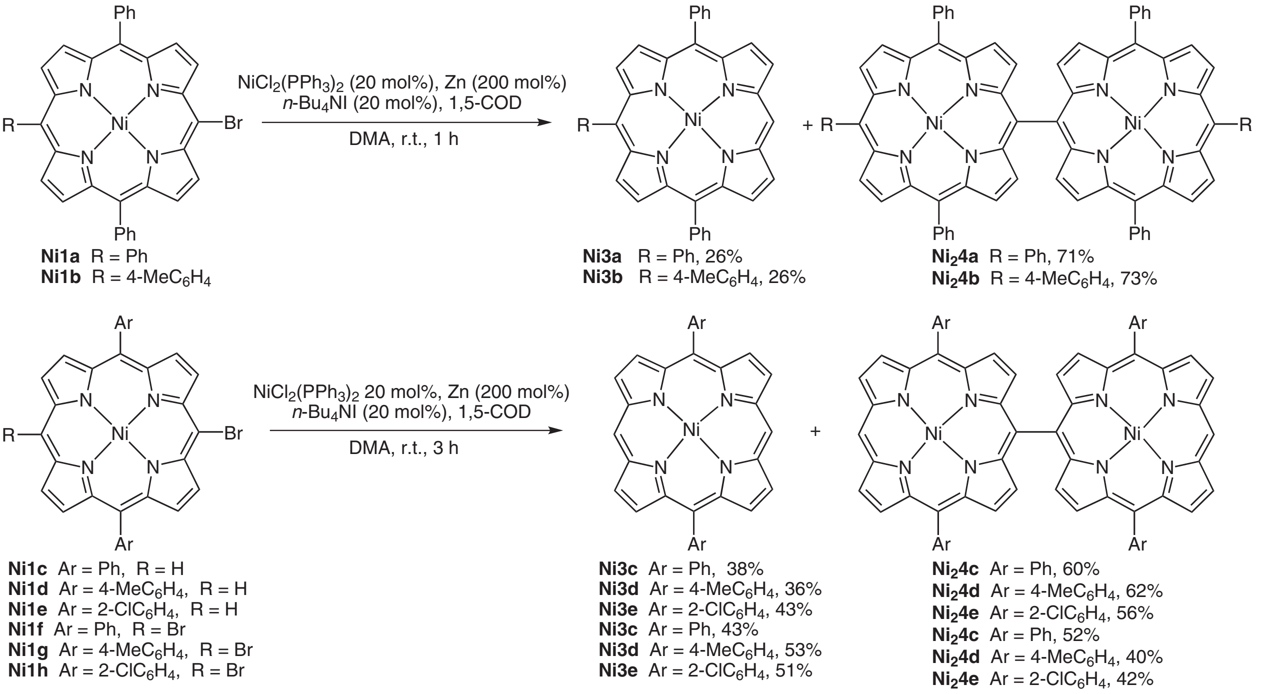
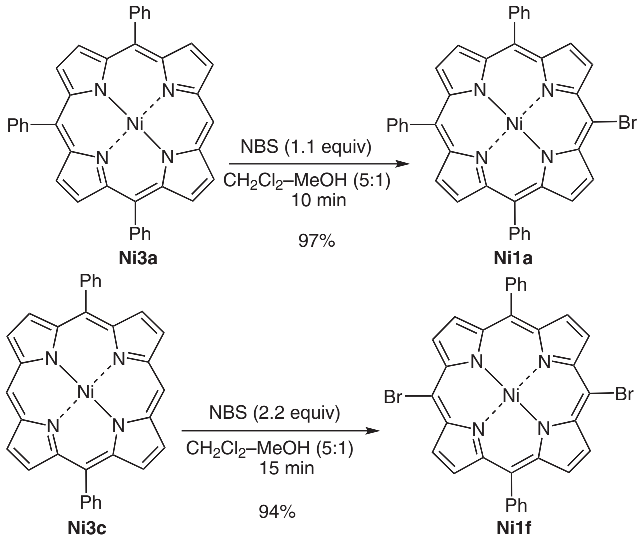


**Scheme 1** The nickel(0)-mediated Ullmann homocoupling of nickel(II) *meso*-bromoporphyrins

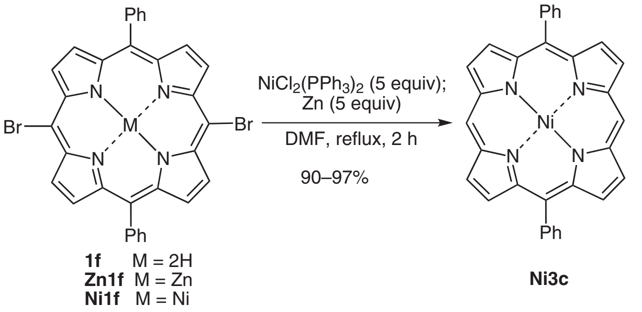
porphyrin **$Ni_2$4a** in a 55% yield at room temperature (Table 1, entry 12). The yield of **$Ni_2$4a** was optimized to 71% by adding two additives *n*-$Bu_4NI$ (0.2 equiv) and 1,5-cyclooctadiene (1,5-COD, 16 equiv).[7]

With the optimal reaction conditions, the scope of the reaction was examined (Scheme 1).[8] The dimerization of **Ni1b** proceeded smoothly affording a good yield (73%) of **$Ni_2$4b** as well as that of **Ni1a**. Porphyrins, such as **Ni1d** and **Ni1e**, which have one free *meso* position, gave less debromination products (**Ni3d**, 36%; **Ni3e**, 43%) and more dimeric porphyrin products (**$Ni_2$4d**, 62%; **$Ni_2$4e**, 56%). 10,20-Diaryldibromoporphyrins **Ni1f**, **Ni1g**, and **Ni1h**, gave a yield from 43–53% for **Ni3c**, **Ni3d**, and **Ni3e** and a yield from 40–52% for **$Ni_2$4c**, **$Ni_2$4d**, and **$Ni_2$4e**. Notably, none of the oligomers was found in these reactions. In addition, the recovered byproducts (**Ni3a** and **Ni3c**) were transformed to the corresponding bromoporphyrins easily and efficiently (Scheme 2),[9] which could be reused under the same conditions to form porphyrin dimers.

Debrominations of diaryldibromoporphyrins (**1f**, **Zn1f**, and **Ni1f**) occurred easily when excessive $NiCl_2(PPh_3)_2$ and Zn were used, affording product **Ni3c** in high yields (Scheme 3).[10] These reactions provided a facile way to debromiantions of bromoporphyrins if necessary.



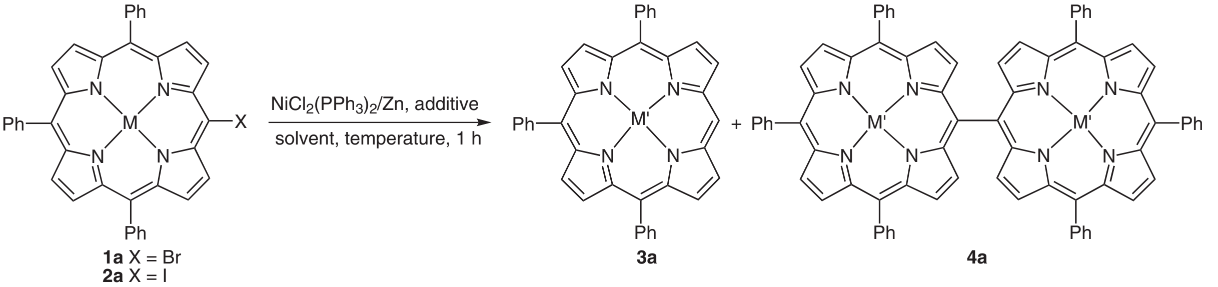
**Scheme 2** The brominations of nickel(II) *meso*-free porphyrins



**Scheme 3** Debrominations of 5,15-dibromoporphyrins

In summary, we successfully realized the nickel(0)-mediated Ullmann homocouplings of bromoporphyrins. Specifically, the dimerization of nickel(II) bromoporphyrin proceeded well without the problem of the formation of oligomers.

**Table 1** Screening of Conditions for the Nickel(0)-Mediated Ullmann Homocupling of *meso*-Bromoporphyrins



| Entry | Substrate | Solvent | Temp (°C) | Additive | Yield of **3** (%) | Yield of **4** (%) |
|---|---|---|---|---|---|---|
| 1 | **1a** M = 2 H | DMA | 60 | no | **Zn3a** M′ = Zn, 76 | **$Zn_2$4a** M′ = Zn, 21 |
| 2 | **Zn1a** M = Zn | DMA | 60 | no | **Zn3a** 75 | **$Zn_2$4a** 23 |
| 3 | **Ni1a** M = Ni | DMA | 60 | no | **Ni3a** M′ =Ni, 64 | **$Ni_2$4a** M′ = Ni, 34 |
| 4 | **2a** M = 2 H | DMA | 60 | no | **Zn3a** quant. | **$Zn_2$4a** 0 |
| 5 | **Zn2a** M = Zn | DMA | 60 | no | **Zn3a** quant. | **$Zn_2$4a** 0 |
| 6 | **Ni2a** M = Ni | DMA | 60 | no | **Ni3a** quant. | **$Ni_2$4a** 0 |
| 7 | **Ni1a** | DMF | 60 | no | **Ni3a** 70 | **$Ni_2$4a** 29 |
| 8 | **Ni1a** | pyridine | 60 | no | **Ni3a** 63 | **$Ni_2$4a** 35 |
| 9 | **Ni1a** | THF | 60 | no | **Ni3a** 10 | **$Ni_2$4a** 0 |
| 10 | **Ni1a** | DMA | 80 | no | **Ni3a** 72 | **$Ni_2$4a** 26 |
| 11 | **Ni1a** | DMA | 40 | no | **Ni3a** 50 | **$Ni_2$4a** 49 |
| 12 | **Ni1a** | DMA | 25 | no | **Ni3a** 43 | **$Ni_2$4a** 55 |
| 13 | **Ni1a** | DMA | 25 | *n*-$Bu_4$NI (0.2 equiv), 1.5-COD (0.1 mL, 16 equiv) | **Ni3a** 26 | **$Ni_2$4a** 71 |
| 14[a] | **Ni1a** | DMA | 25 | no | **Ni3a** 0 | **$Ni_2$4a** 0 |

[a] Copper was used instead of $NiCl_2$ (0.2 equiv)/Zn (2 equiv).

**Supporting Information** for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

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(8) **General Procedure for Preparation of *meso-meso*-Linked Ni(II) Porphyrin Dimers**
A mixture of powdered $NiCl_2(PPh_3)_2$ (6.5 mg, 10 μmol), zinc powder (6.5 mg, 0.1 mmol), TBAI (3.6 mg, 10 μmol), and 1,5-COD (0.1 mL, 0.82 mmol) was added to a solution of *meso*-bromoporphyrin (**Ni1a**, 34 mg, 50 μmol) in *N*,*N*-dimethylacetamide (2 mL) at r.t. under nitrogen atmosphere. The reaction mixture was stirred for 1 h. The reaction was quenched immediately with $H_2O$ (10 mL) and was extracted with $CH_2Cl_2$ (40 mL). The organic layer was separated, washed with $H_2O$ (3 × 20 mL) and brine, and dried over anhyd $Na_2SO_4$. After removal of the solvent in vacuo, the residue was purified by silica column chromatography (eluent: PE–$CH_2Cl_2$, 3:1 v/v) to afford **Ni3a** (8 mg) in a 26% yield and the desired compound **$Ni_2$4a** (21 mg) in a 71% yield.
Porphyrin **Ni3a**: $^1$H NMR (300 MHz, $CDCl_3$): δ = 9.85 (s, 1 H, *meso*-H), 9.15 (d, *J* = 4.8 Hz, 2 H, β-H), 8.90 (d, *J* = 5.1 Hz, 2 H, β-H), 8.79 (s, 4 H, β-H), 8.05 (m, 6 H, PhH), 7.70 (m, 9 H, PhH). MS (MALDI): *m/z* = 594.1 [M$^+$]. HRMS (MALDI): *m/z* calcd for $C_{38}H_{24}N_4Ni$ [M$^+$]: 594.1349; found: 594.1354.
Diporphyrin **$Ni_2$4a**: $^1$H NMR (300 MHz, $CDCl_3$): δ = 8.83 (dd, *J* = 9.9, 5.1 Hz, 8 H, β), 8.57 (d, *J* = 4.8 Hz, 4 H, β), 8.12 (m, 8 H, Ph + β, overlapped), 8.04 (m, 8 H, Ph), 7.73 (m, 6 H, Ph), 7.63 (m, 12 H, Ph). UV/vis ($CH_2Cl_2$): $\lambda_{max}$ (relative intensity): 536 nm (1.0), 445 (4.3), 413 (3.6). MS (MALDI): *m/z* = 1186.3 [M$^+$]. HRMS (MALDI): *m/z* calcd for $C_{76}H_{46}N_8Ni_2$ [M$^+$]: 1186.2547; found: 1186.2555.

(9) **General Procedure for the Bromination Reaction**
*meso*-Free Ni(II) porphyrin (**Ni3c**, 26 mg, 0.05 mmol) was dissolved in $CH_2Cl_2$–MeOH (5:1 v/v, 3 mL). *N*-Bromosuccinimide (NBS, 20 mg, 0.11 mmol, 2.2 equiv) was added. The reaction mixture was stirred under air at r.t. for 15 min and quenched with acetone (1 mL). The resulting red solution was evaporated to dryness, the residue was purified by silica gel column chromatography using PE and $CH_2Cl_2$ (PE–$CH_2Cl_2$, 2:1 v/v) as eluant to provide the pure desired compound **Ni1f** in a 94% yield.

(10) **General Procedure for the Debromination Reaction**
To a solution of *meso*-dibromodiporphyrins (**Ni1f**, 34 mg, 50 μmol) in DMF (50 mL), $NiCl_2(PPh_3)_2$ (163 mg, 0.25 mmol), and zinc powder (16.3 mg, 0.25 mmol) were added sequentially under nitrogen atmosphere, and the resulting mixture was heated to reflux for 2 h. The reaction mixture was cooled down to r.t., extracted with $CH_2Cl_2$ (200 mL). The organic layer was separated, washed with $H_2O$ (3 × 200 mL) and brine, and dried over anhyd $Na_2SO_4$. After concentration in vacuo, the residue was purified by silica column chromatography (eluent: PE–$CH_2Cl_2$, 2:1 v/v) to obtain the desired compound **Ni3c** (25 mg) in a 97% yield.
Porphyrin **Ni3c**: $^1$H NMR (300 MHz, $CDCl_3$): δ = 9.94 (s, 2 H, *meso*-H), 9.19 (d, *J* = 4.5 Hz, 4 H, β-H), 8.94 (d, *J* = 4.5 Hz, 4 H, β-H), 8.07 (m, 4 H, PhH), 7.71 (m, 6 H, PhH). MS (MALDI): *m/z* = 518.1 [M$^+$]. HRMS (MALDI): *m/z* calcd for $C_{32}H_{20}N_4Ni$ [M$^+$]: 518.1036; found: 594.1037.