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Facile Regioselective Meso-Iodination of Porphyrins

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Abstract: Treatment of 5,15-diaryl zinc-porphyrins with $AgPF_6$ and iodine in a mixture of $CHCl_3$ and pyridine (60:1) resulted in meso-iodination of porphyrins with high regioselectivity.

Keywords: Halogenation, Porphyrins and analogues, Coupling reactions, Energy transfer

Recently, we reported the synthesis of meso-meso linked porphyrin oligomers based on Ag (I)-promoted oxidative coupling of 5,15-diaryl zinc-porphyrin.[1-3] This reaction normally needed ca. 5h with Ag (I) salt only and was markedly accelerated by a combined use of Ag (I) salt and iodine.[1] But the reaction tends to be interrupted probably due to concomitant liberation of acid that demetallates the reactant zinc-porphyrin. We thus attempted to scavenge acid by adding bases and found that in the presence of pyridine the reaction course changed from meso-meso coupling to meso-iodination. Here we report a new, facile, meso-regioselective iodination of porphyrins based on this finding. To date, there have been only a few examples of porphyrin iodinations,[4,5] while other porphyrin halogenations are rather common and widely used.[6] Recently, Dolphin *et al.* reported the meso-iodination of a 5,15-diphenyl zinc-porphyrin using bis(trifluoroacetoxy)iodobenzene-iodide.[4] Iodinations are usually quite sterically demanding and thus would be difficult for octaethyl porphyrin (OEP) derivatives owing to steric hindrance of the neighboring β-ethyl groups. In this respect, 5,15-diaryl porphyrins **1** featuring a sterically unhindered meso-position can be a good substrate for sterically demanding meso-iodination.

Synthetic procedure is quite simple, just treating a zinc-porphyrin substrate dissolved in a mixture of $CHCl_3$ and pyridine (60:1) with 1 equiv of $AgPF_6$ and iodine at room temperature. Iodination is usually completed within 15 min, and meso-iodo porphyrin products were isolated by usual work up followed by chromatography over a silica gel column. Zinc complexes of 5,15-diaryl porphyrins **1a-c** were effectively converted to the corresponding 5-iodo-10,20-diaryl porphyrins **2a-c**.[7] After complete demetallation with HCl, ^{1}H-NMR analysis of the reaction mixture revealed product distribution of the starting material **1** (10-15%), **2** (70-80%), and 5,15-diiodo-10,20-diaryl porphyrin **3** (5-10%). Interestingly meso-meso coupled porphyrin dimer was not detected at all. Although the amounts of **2** formed were comparable

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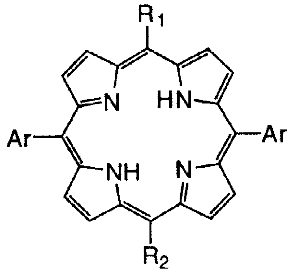
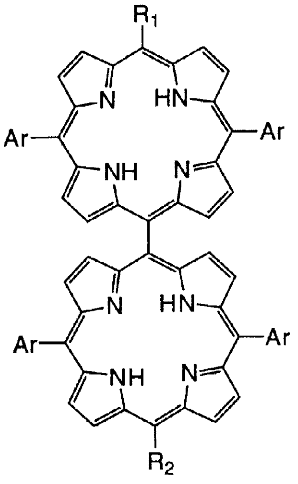
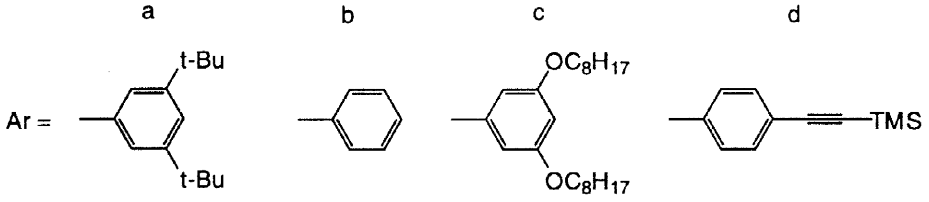
to the isolated yield (>70%) reported by Dolphin *et al.*,[4] poor solubility of **2** and **3** made their isolation quite difficult. Isolated yields in our hands that depended on solubility of porphyrins were as follows; **2a** (59%), **2b** (35%), and **2c** (51%). Zinc complex of trimethylsilyl-(TMS)-ethynylphenyl substituted porphyrin **1d** gave **2d** in 31% yield, showing the tolerance of TMS-protected triple bond in this reaction. Porphyrin meso-meso coupling reaction was effected by treating 5,15-diaryl zinc-porphyrin merely with $AgPF_6$ in $CHCl_3$. Addition of pyridine resulted in suppression of the meso-meso coupling, while the combination of $AgPF_6$, I_2, and pyridine gave rise to the efficient meso-iodination. When other aliphatic bases such as triethylamine added, neither iodination nor meso-meso coupling was effected. Although the reaction mechanism has not yet been clarified, it may involve *in-situ* formed N-iodopyridinium salt as a possible iodinating species.



1; $R_1 = R_2 = H$
2; $R_1 = I$; $R_2 = H$
3; $R_1 = R_2 = I$
7; $R_1 = H$; R_2 = 3,5-di-tert-butylphenyl
8; $R_1 = I$; R_2 = 3,5-di-tert-butylphenyl
9; $R_1 = H$; $R_2 = Br$
10; $R_1 = I$; $R_2 = Br$
11; R_1 = phenylethynyl; $R_2 = Br$



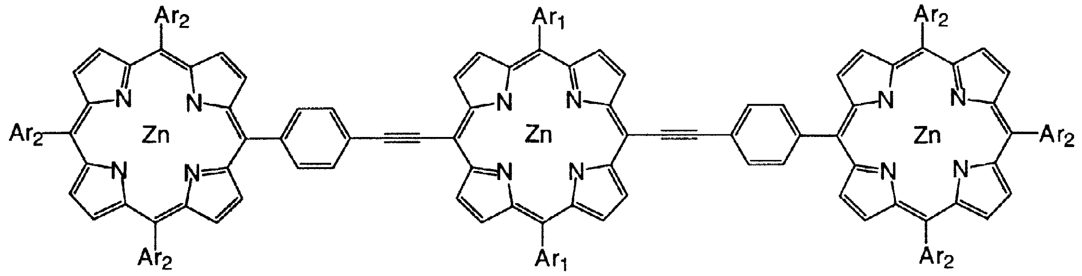
4; $R_1 = R_2 = H$
5; $R_1 = I$; $R_2 = H$
6; $R_1 = R_2 = I$



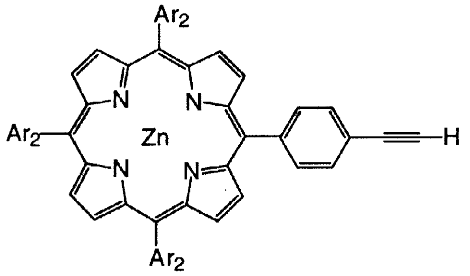
This iodination proceeds with high regioselectivity only at meso-positions both in the first and the second iodination.[8] High regioselectivity at the second iodination is in contrast to Dolphin's method.[4] Thus, upon treatment with iodine (4.1 equiv) and $AgPF_6$ (2.0 equiv), zinc complex of **1c** was smoothly converted to 5,15-diiodo porphyrin **3c** in 61 % yield. Any products iodinated at β-positions could not be detected. Under the similar conditions, zinc complexes of other porphyrins gave 5,15-diiodo porphyrins in more than 50% yields.

Bis-zinc complex of meso-meso linked diporphyrin **4a** gave monoiodo diporphyrin **5a** (46%) and diiodo diporphyrin **6a** (19%) with the recovery of the starting material (18%) under the monoiodination conditions, and gave **6a** (60%) under the diiodination conditions.

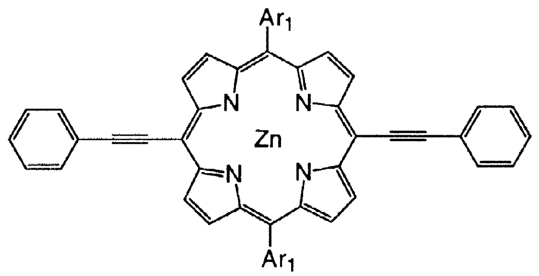
This iodination method was further applied to zinc complexes of 5,10,15-triaryl porphyrin **7a** and 5-bromo-10,20-diaryl porphyrin **9c**, giving **8a** and **10c** in 75% and 71% yields, respectively. Differently halogenated porphyrin **10c** may be an useful precursor for differently functionallized molecules. In fact, the reaction of zinc complex of **10c** with phenylacetylene under Sonogashira reaction ($Pd(PPh_3)_2Cl_2$, CuI in triethylamine/toluene) at room temperature gave coupling product **11** in 36% yield.[4,8,9]



12

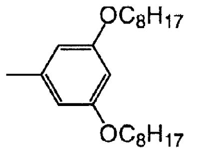


13

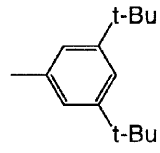


14

Ar_1 =



Ar_2 =



Utility of meso-iodo porphyrins has been shown by synthesis of porphyrin trimer **12** from zinc complex of 5,15-diiodo porphyrin **3c** and of 5-ethynylphenyl-10,15,20-tri(3,5-di-tert-butylphenyl) zinc-porphyrin **13** by Sonogashira reaction in 60 % yield. The trimer **12** consists of two peripheral 5,10,15,20-tetraaryl zinc-porphyrins and a central 5,15-diethynyl zinc-porphyrin. Since the S_1-state energy level of the central porphyrin is lower than that of the peripheral porphyrins,[9] one may expect the singlet energy transfer from the latter to the former. Figure 1 shows the absorption and fluorescence spectra of **12** along with those of the reference molecules **13** and **14**. The absorption spectrum of **12** is roughly a sum of the respective absorption spectra with some red-shifts in the absorption bands of the central diethynyl zinc-porphyrin in comparison to **14**. In contrast, the fluorescence spectrum of **12** taken for selective excitation at the peripheral porphyrins at 560 nm displays only the emission from the central 5,15-diethynyl substituted zinc-porphyrin, indicating efficient energy transfer from the peripheral porphyrin to the central porphyrin.

In summary, meso-iodinated porphyrins are obtained in an efficient manner from

5,15-diaryl zinc-porphyrins using $AgPF_6$ and iodine in $CHCl_3$ containing pyridine. High regioselective nature of the reaction makes the process attractive for modification of supramolecular porphyrin models such as meso-meso coupled porphyrin arrays[1,3] and work along this line is in pregress in our laboratory.

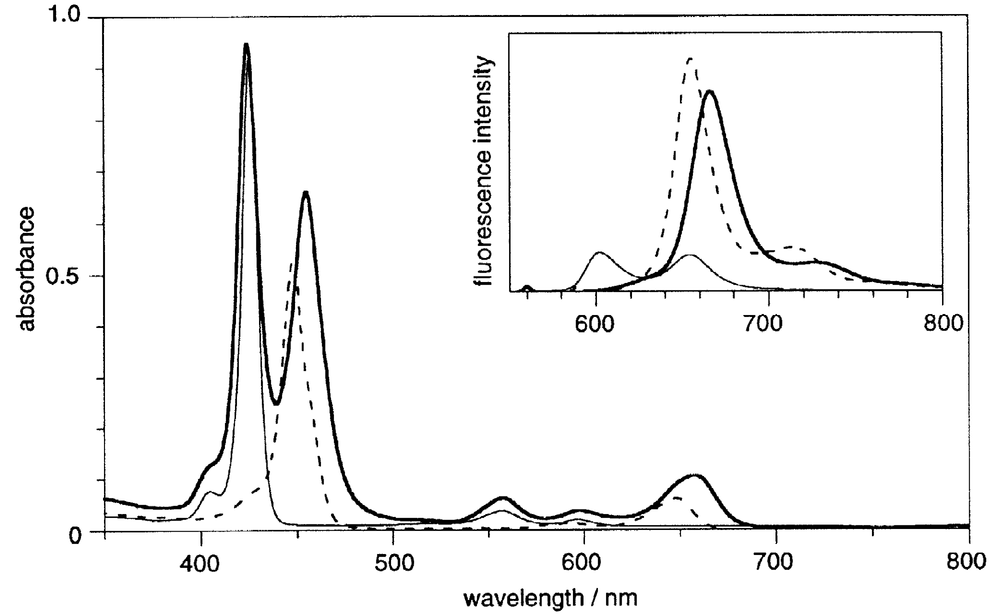


Fig. 1; The absorption spectra of trimer **12** (━━) and its reference molecules **13** (——) and **14** (- - - -) in THF. Concentrations are 1 x 10^{-6} M. Shown in inset is the fluorescence spectra of **12** (λ_{ex} = 560 nm), **13** (λ_{ex} = 560 nm) and **14** (λ_{ex} = 590 nm) in THF. The absorbances at the exciting wavelength were adjusted ca. 0.10.

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