Unusual regioselective mercuration of metalloporphyrins and its potential applications†

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The reaction of $Hg(CF_3CO_2)_2$ with metalloporphyrins produces mercurated porphyrins regioselectively, the reaction, surprisingly occurring at the most hindered β^B-position; this behavior is in marked contrast to the usual electrophilic substitution reactions of porphyrins, whose reactions produce *meso*-substituted porphyrins; the obtained mercurated porphyrins are active to transition metal-catalyzed coupling reactions, such as the Mizoroki–Heck reaction.

Organomercury compounds have long attracted much attention[1] from the viewpoint of their specific reactivity, attributable to the electropositive character of mercury (electronegativity $\chi = 2.00$),[2] despite their toxicity. The traditional and widely employed reaction is the transmetallation reaction, *i.e.*, the replacement of mercury with a more electropositive metal such as Mg ($\chi = 1.31$), Zn (1.65) and Ga (1.81); *e.g.*, the formation of $MgMe_2$, $ZnMe_2$ and $GaMe_3$ by the reactions of $HgMe_2$ with metallic Mg, Zn and Ga, respectively, for which the corresponding organometal compounds are hard to obtain by direct metallation reactions.[1] Organomercurials are also useful for the transmetallation of less electropositive metals (*e.g.*, Pd) by the substitution of halides.[1] Recent interest focuses on the aryl coupling reactions with olefins in the presence of transition metal catalysis, *i.e.*, Mizoroki–Heck reactions.[3] Contemporary interdisciplinary research on porphyrins requires advanced multi-functions, attributable to both the porphyrin and the introduced functional group(s) (FG).[4] To create novel porphyrin FG-linked systems, peripherally-metallated porphyrins (PMPs),[5] including mercury-substituted porphyrins[6] and the corresponding aryl coupling reactions, have been extensively studied. The recent wide applications of functionalized 5,15-disubstituted porphyrins (substituents = aryl or alkyl) encouraged us to study the reaction of those compounds with Hg(II) salts and the potential applications of the corresponding mercury-substituted porphyrins.

As porphyrins have a high reactivity towards electrophiles, an electrophilic substitution reaction seemed to be the best candidate for obtaining mercury-substituted porphyrins. Treatment of 5,15-bis(3,5-di-*tert*-butylphenyl)porphyrinato nickel (**1a**) with $Hg(CF_3CO_2)_2$ for 30 min smoothly produced the mercury-substituted porphyrin. Due to the instability of the initial product, the $-HgOCOCF_3$-substituted porphyrin, the replacement of $CF_3CO_2^-$ with Cl^- was required, giving the –HgCl-substituted analogue.[7,8] Mono-mercurated product **2a** was isolated as the main product, after silica gel chromatography, in an acceptable yield (33%) as a purple solid that was stable towards moisture, air and light. In marked contrast to the usual *meso*-regioselectivity for the electrophilic reactions of 5,15-disubstituted porphyrins, *e.g.*, formylation and halogenation, the main product was characterized as **2a**; *i.e.*, this mercuration reaction occurred at the more hindered β^B-position.[9] Some metal dependence was observed for this mercuration reaction, **1b** and **1c** affording **2b** and **2c** in 17 and 21% yields, respectively. The similar reaction behavior of 5,15-dialkylporphyrin **1d** to give **2d** (23%) discounts a mercury–aryl π-interaction reaction mechanism. No formation of the regio-isomers, *i.e.*, β^A-substituted porphyrins, was observed by our very careful chromatographic analyses of these four reactions.

To demonstrate the versatility of the mercury porphyrins obtained in our study, we report three types of reactions of **2a**. Firstly, protolysis with trifluoroacetic acid (TFA) quantitatively regenerates the starting material **1a**, although **2a** is stable under treatment with acetic acid or water. An experiment using TFA-*d* induced the regioselective *ipso*-substitution to give the corresponding deuterated porphyrin **3**.

Secondly, the coupling reaction with methyl acrylate in the presence of Pd catalysis, a Mizoroki–Heck reaction, was examined. Initially, we attempted to use the widely-used reaction conditions, *e.g.*, a catalytic amount of $Pd(OAc)_2$ and PPh_3 as a ligand (conditions (iv) in Scheme 1). Unexpectedly, rearrangement product **4** was obtained as a major product, along with the desired **5**. The replacement of PPh_3 with a more bulky ligand, such as P^tBu_2-biphenyl, produced only **4**, suggesting that steric repulsion in the Pd-inserted intermediate triggered the subsequent rearrangement reaction. Omission of the phosphine ligand resolved the problem, affording **5** as the sole product (conditions (v) in Scheme 1).

Thirdly, treatment with iodine achieved a perfect *ipso*-substitution, producing **6** quantitatively. The resultant β^B-iodide should

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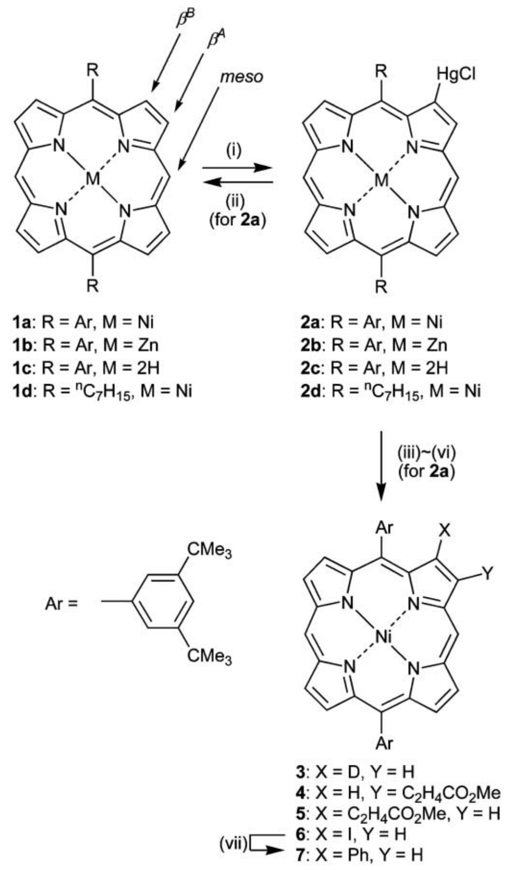

Scheme 1 *Reagents and conditions:* (i) 1.0 ∼ 1.5 equiv. $Hg(CF_3CO_2)_2$, CH_2Cl_2, r.t. for 30 min, then NaCl aq.; (ii) CF_3CO_2H, then $NaHCO_3$ aq.; (iii) CF_3CO_2D, then $NaHCO_3$ aq.; (iv) $Pd(CH_3CO_2)_2$, PPh_3 or P^tBu_2-biphenyl, K_2CO_3, methyl acrylate, THF—these conditions afforded a mixture of **4** and **5**; (v) $Pd(CH_3CO_2)_2$, K_2CO_3, methyl acrylate, THF—these conditions afforded the sole product **5**; (vi) I_2, THF; (vii) PhB(–OCMe$_2$CMe$_2$O–), $Pd^0(PPh_3)_4$, $Ba(OH)_2$ aq., diglyme.

also be useful for the functionalization of porphyrins, *e.g.*, as an important substrate for aryl coupling reactions, such as the Suzuki–Miyaura reaction. The reaction of **6** with phenylboronic acid ester in the presence of $Pd^0(PPh_3)_4$ produces the corresponding β^B-phenyl porphyrin **7**. No rearrangement was observed in this Pd-catalyzed reaction.

Although the detailed reaction mechanism of the regioselective mercuration is still unclear, the mercuration reaction of 5,15-disubstituted porphyrins selectively occurred at the β^B-position of the porphyrin. With the inclusion of our new discoveries, chemists can now regioselectively functionalize 5,15-disubstituted porphyrins at the β^B (*via* our mercuration), β^A (*via* Osuka *et al.*'s Ir-catalyzed boronation[10]) or *meso* (*via* usual electrophilic substitution) positions.

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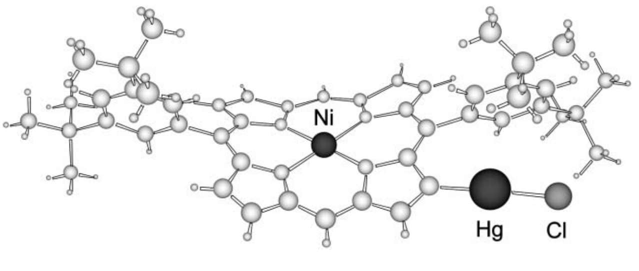
7 Experimental details including spectroscopic data are described in Electronic supplementary information (ESI†). *General procedure* of mercuration reactions: A mixture of porphyrin (*e.g.* **1a**: 0.9 mmol) and $Hg(CF_3CO_2)_2$ (0.9 mmol, 1.0 eq., Aldrich) dissolved in dry dichloromethane (170 mL) was stirred under ambient conditions for 30 min. Saturated aq. NaCl (7 mL) was added and the mixture was stirred for a further 30 min. The solution was washed with two portions of water and the organic phase was removed under reduced pressure. The residue was chromatographed on silica gel, eluting with a mixed solvent of CH_2Cl_2 and hexane (1 : 3), to give **2a**.

8 All new materials were characterized by spectroscopic methods. X-Ray photoelectron spectroscopy (XPS) also supports the formation of the mercurated porphyrins. The XPS core ionization potentials of Hg $4f_{7/2}$ for **2a**, **2b**, **2c** and **2d** are 101.6, 101.3, 101.5 and 101.8 eV, respectively (the spectrometers were calibrated such that the Au $4f_{7/2}$ peak of the clean sputtered metals appeared at 84.0 eV).

9 A preliminary single crystal diffraction study of **2a** also supports the substitution position:



Crystal data: Triclinic, $P\bar{1}$ (#2), $a = 13.224(3)$, $b = 17.378(3)$, $c = 21.090(3)$ Å, $\alpha = 69.703(9)$, $\beta = 71.092(9)$, $\gamma = 85.79(1)°$, $V = 4296.2(1)$ Å^3. CCDC 638202. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b618464b.

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