Synthesis of Brominated Directly Fused Diporphyrins through Gold(III)-Mediated Oxidation

**Akhila K. Sahoo,[†] Yasuyuki Nakamura,[†] Naoki Aratani,[†] Kil Suk Kim,[‡]
Su Bum Noh,[‡] Hiroshi Shinokubo,*,[†] Dongho Kim,*,[‡] and Atsuhiro Osuka*,[†]**

*Department of Chemistry, Graduate School of Science, Kyoto University and CREST,
Japan Science and Technology Agency (JST), and International Innovation Center
(IIC), Kyoto University, Kyoto 606-8502, Japan, and Center for Ultrafast Optical
Characteristics Control and Department of Chemistry, Yonsei University,
Seoul 120-749, Korea*

osuka@kuchem.kyoto-u.ac.jp; hshino@kuchem.kyoto-u.ac.jp; dongho@yonsei.ac.kr

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ABSTRACT

Ar = 3,5-di-*tert*-butylphenyl
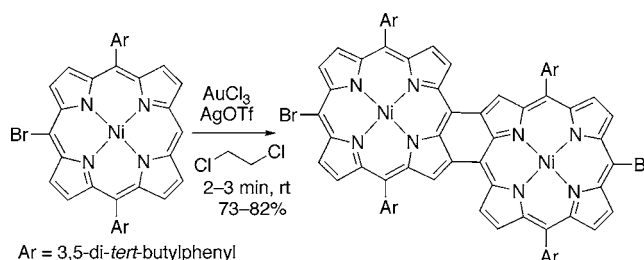
Highly efficient synthesis of *meso,meso*-dibromo doubly and triply fused diporphyrins has been achieved through a powerful oxidative coupling mediated by AuCl₃–AgOTf combination. In addition, palladium-catalyzed debromination of *meso*-bromoporphyrins has been developed. This debromination protocol enables employment of bromine as a protecting group for the reactive *meso*-position of porphyrins.

Porphyrin arrays with extensive delocalized π-conjugation are the current focus of intensive research because of their application for conductive organic materials, near-infrared dyes, NLO materials, molecular wires, molecular devices, and so forth.[1] In particular, directly fused porphyrin arrays (porphyrin tapes) have strong electronic communication between neighboring porphyrins, exhibiting the lowest energy absorption bands that reach the infrared region.[2] In addition, the triply linked porphyrin tapes exhibit exceptionally large two-photon absorption (TPA) cross sections (σ).[3] They have

also been used for the construction of functional conjugates with fullerenes due to specific supramolecular interactions.[4]

The synthesis of directly fused porphyrin arrays mostly relies on the DDQ-Sc(OTf)₃ oxidation procedure so far. This combination also induces a fusion reaction of 5,10,15-trisubstituted porphyrins to the corresponding *meso-β*, *meso-β* doubly fused or *β*−*β*, *meso*−*meso*, *β*′−*β*′ triply fused diporphyrins depending on the central metals in the porphyrin core.[5] However, electron-withdrawing substituents on the

[†] Kyoto University.

[‡] Yonsei University.

(1) (a) Chou, J.-H.; Kosal, M. E.; Nalwa, H. S.; Rakow, N. A.; Suslick, K. S. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, CA, 2000; Vol. 6, Chapter 41. (b) Schwab, P. F. H.; Levin, M. D.; Michl, J. *Chem. Rev.* **1999**, *99*, 1863. (c) Martin, R. E.; Diederich, F. *Angew. Chem., Int. Ed.* **1999**, *38*, 1351.

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starting porphyrins sometimes retard or disturb the coupling processes due to lowering of the oxidation potentials. For example, DDQ-Sc(OTf)$_3$ oxidation of *meso*-bromoporphyrins is difficult. Although a two-step synthesis of triply fused porphyrin dimers via *meso*−*meso* singly linked diporphyrins would be an alternative method, Anderson et al. reported that DDQ-Sc(OTf)$_3$ oxidation of dibromodiporphyrin **1** afforded the desired product **2** in only 9% yield (Scheme 1).[6] In view of promises of the directly fused diporphyrin

Scheme 1. DDQ-Sc(OTf)$_3$ Oxidation of Brominated Diporphyrin

Ar = 3,5-di-*tert*-butylphenyl
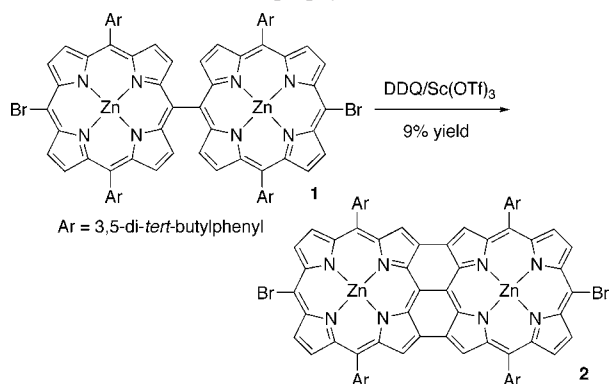
motif in various fields of material science, one can foresee the usefulness of brominated fused porphyrins as building blocks for easy installation of a variety of functionalities via transition metal catalyzed transformations.

Recently, aromatic C−H bond activation has been extensively explored in the field of organometallic chemistry, among which He et al. has reported a gold-catalyzed reaction of benzene derivatives with propiolates via C−H bond cleavage.[7] We have also reported that metalation of [26]-hexaphyrin with NaAuCl$_4$ provided a bis-Au(III) complex of hexaphyrin via four consecutive C−H bond cleavages.[8] We then explored the reaction of *meso*-free porphyrin derivatives with gold salts, and found that gold salts induced oxidative coupling of porphyrins probably via one-electron oxidation rather than the expected reaction involving C−H bond activation.[9] Herein we report an efficient and reliable method toward the synthesis of directly fused dibromodiporphyrins through the AuCl$_3$−AgOTf mediated oxidation

reaction of *meso*-bromo-substituted porphyrins. The gold-mediated oxidative coupling turned out to be more powerful and convenient than the previous protocol based on DDQ-Sc(OTf)$_3$ oxidation, enabling the synthesis of directly fused dibromodiporphyrins quickly.

We were pleased to see that treatment of 5-bromo-10,20-diaryl-Ni(II)-porphyrin **3** with a combination of AuCl$_3$ (1 equiv)−AgOTf (6 equiv) in dichloroethane at room temperature resulted in the clean formation of *meso*-β, *meso*-β doubly fused porphyrin dimer **4** exclusively, without noticeable formation of β−β, *meso*−*meso*, β'−β' triply fused porphyrin dimer **7**, in 73−82% isolated yield rapidly (2−3 min) (Scheme 2). Importantly, bromide functionality is

Scheme 2. Gold-Mediated Coupling of *meso*-Bromoporphyrin

Ar = 3,5-di-*tert*-butylphenyl
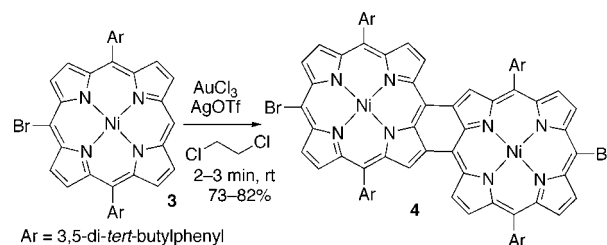
tolerant under the present reaction conditions. In addition, a simple workup procedure is beneficial and only filtration with a short pad of silica gel provided the pure product. However, excess AuCl$_3$ and longer reaction time led to the formation of polymeric residue, but lowering the catalyst amount resulted in partial transformations to the desired product. The use of silver salt as an additive is essential because reaction with only AuCl$_3$ provided a complicated reaction mixture containing chlorinated products.

Next, we turned our attention to the synthesis of β−β, *meso*−*meso*, β'−β' triply fused dibrominated Zn(II)-diporphyrin **2** on the basis of the present reaction of a 5-bromo-10,20-diaryl-Zn(II)-porphyrin. Unfortunately, however, no desired dimer was detected due to the extensive demetalation of zinc from the starting porphyrin. Instead, treatment of *meso*−*meso* singly linked bis-Ni(II) porphyrin dimer **5** with AuCl$_3$ (1 equiv)−AgOTf (6 equiv) afforded β−β, *meso*−*meso* doubly fused porphyrin dimer **6** as a predominant product beside a trace amount of triply fused diporphyrin **7**, whereas the use of AuCl$_3$ (2 equiv)−AgOTf (10 equiv) resulted in the formation of **7** in excellent yields (Scheme 3). These results suggested that the present oxidative fusion reaction proceeds in a stepwise manner via **6** to **7**.

Interestingly, the ^{1}H NMR spectrum of **6** at room temperature does not exhibit the corresponding signals to ortho protons of the aromatic substituents, whereas those protons can be detected at −45 °C (Supporting Information). This can be accounted for by partly restricted rotation of the aromatic groups due to steric hindrance induced by the largely ruffled structure of β−β, *meso*−*meso* doubly fused diporphyrin.[5a]

With two types of fused dibromodiporphyrins **4** and **7** in our hands, we undertook their functionalization by transition

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(6) Blake, I. M.; Krivokapic, A.; Katterle, M.; Anderson, H. L. *Chem. Commun.* **2002**, 1162.

(7) (a) Shi, Z.; He, C. *J. Am. Chem. Soc.* **2004**, *126*, 13596. (b) Shi, Z.; He, C. *J. Org. Chem.* **2004**, *69*, 3669. (c) Luo, Y.; Li, C.-J. *Chem. Commun.* **2004**, 1930. (d) Alfonsi, M.; Arcadi, A.; Aschi, M.; Bianchi, G.; Marinelli, F. *J. Org. Chem.* **2005**, *70*, 2265.
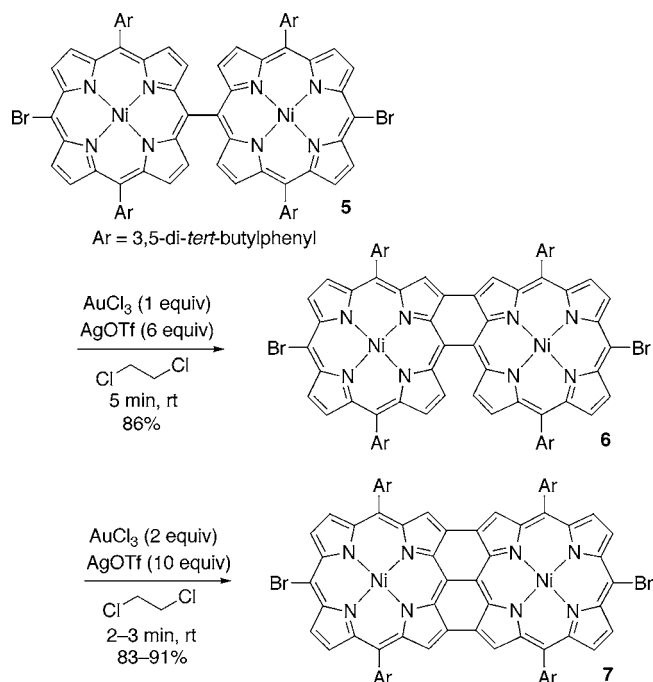
(8) Mori, S.; Osuka, A. *J. Am. Chem. Soc.* **2005**, *127*, 8030.

(9) For oxidation of porphyrins with gold salts to provide radical cation species, see: Segawa, H.; Senshu, Y.; Nakazaki, J.; Susumu, K. *J. Am. Chem. Soc.* **2004**, *126*, 1354.

Scheme 3. Gold-Mediated Fusion Reaction of Porphyrin Dimer

Ar = 3,5-di-*tert*-butylphenyl

AuCl$_3$ (1 equiv)
AgOTf (6 equiv)
5 min, rt
86%

AuCl$_3$ (2 equiv)
AgOTf (10 equiv)
2–3 min, rt
83–91%

Scheme 4. Palladium-Catalyzed Transformation of **4** and **7**

TMS≡H (10 equiv)
Pd(PPh$_3$)$_4$ (20 mol %)
CuI (40 mol %)
i-Pr$_2$NH (10 equiv)
THF, 65 °C
91%

HCO$_2$H (20 equiv)
Et$_3$N (20 equiv)
Pd(PPh$_3$)$_4$ (30 mol %)
toluene, reflux
92%

8a R = ≡TMS
8b R = H

TMS≡H (10 equiv)
PdCl$_2$(PPh$_3$)$_2$ (20 mol %)
CuI (40 mol %)
Et$_3$N (10 equiv)
THF, rt
78%

HCO$_2$H (20 equiv)
Et$_3$N (20 equiv)
Pd(PPh$_3$)$_4$ (30 mol %)
toluene, reflux
93%

9a R = ≡TMS   78%
9b R = H   93%

metal catalyzed reactions. Sonogashira coupling of **4** and **7** with trimethylsilylacetylene provided bis-alkynylated diporphyrin **8a** and **9a**[10] both in excellent yields under the standard conditions (Scheme 4).[11]

We then attempted debromination of **4** and **7** by palladium-catalyzed reduction. However, the Pd-catalyzed dehalogenation reaction remains to be explored for *meso*-halogeno porphyrins. Thus, we initially optimized the reaction conditions for dehalogenation of simple 5,15-dibromo porphyrin **10** in the presence of a palladium catalyst with formic acid as a hydride source (Scheme 5).[12] After several experiments, we selected the conditions of run 5 as the optimal in terms of the desired debromination product yield as well as the amount of palladium catalyst (Scheme 5). Then, the reductions of **4** and **7** were efficiently accomplished to provide **8b** and **9b** in high yields. Here, it is worthy to note that the present protocol is particularly useful for the synthesis of *meso*-unsubstituted fused diporphyrins.[13] This feature is an apparent advantage, since DDQ-Sc(OTf)$_3$ oxidation of *meso*-unsubstituted porphyrins is known to result in extensive polymerization. This is the first application of palladium-catalyzed dehalogenation to porphyrin derivatives, to the best

of our knowledge.[14] Furthermore, bromide can be used as a removable protecting group at *meso*-positions, which is reactive toward electrophilic substitution reactions.

UV/vis absorption spectra of doubly and triply fused diporphyrins are shown in Figure 1. Incorporation of alkynyl moieties resulted in distinct red shift and enhancement of Q-bands. Since *meso*-alkynyl-conjugated porphyrins often exhibit quite large TPA cross sections,[15] we have measured the TPA cross sections (σ) of **7**, **9a**, and **9b** by an open-

Scheme 5. Optimization for Palladium-Catalyzed Debromination

Ar = 3,5-di-*tert*-butylphenyl

Pd cat
hydride source
solvent
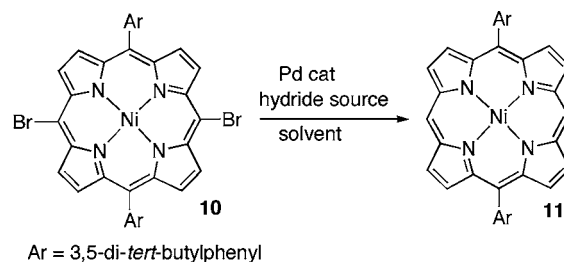
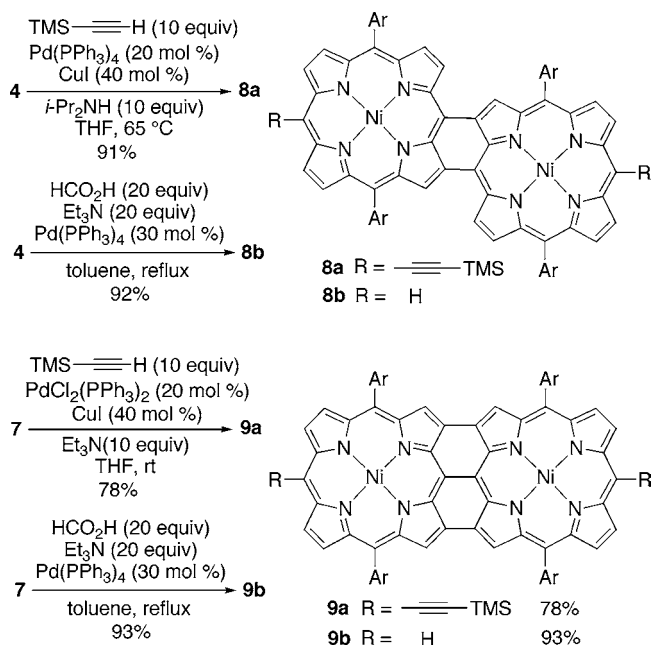| run	Pd cat	hydride source[a]	conditions	yield (%)
1	Pd/C	HCO$_2$H/Et$_3$N	THF, rt, 48 h	0
2	Pd(PPh$_3$)$_4$ (2.2 equiv)	HCO$_2$H/Et$_3$N	THF, rt, 24 h	30
3	Pd(PPh$_3$)$_4$ (1.1 equiv)	HCO$_2$NH$_4$	toluene, reflux, 2 h	93
4	Pd(PPh$_3$)$_4$ (30 mol %)	HCO$_2$NH$_4$	toluene, reflux, 12 h	8
5	Pd(PPh$_3$)$_4$ (30 mol %)	HCO$_2$H/Et$_3$N	toluene, reflux, 3 h	92

[a] 20 equiv of hydride source was employed.

(10) A similar silylethynyl-substituted fused diporphyrin has been reported, see: McEwan, K. J.; Fleitz, P. A.; Rogers, J. E.; Slagle, J. E.; MxLean, D. G.; Akdas, H.; Katterle, M.; Blake, I. M.; Anderson, H. L. *Adv. Mater.* **2004**, *16*, 1933−1935. This paper also includes nonlinear optical behavior of fused dibromo diporphyrin.

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(12) (a) Cortese, N. A.; Heck, R. F. *J. Org. Chem.* **1977**, *42*, 3491.

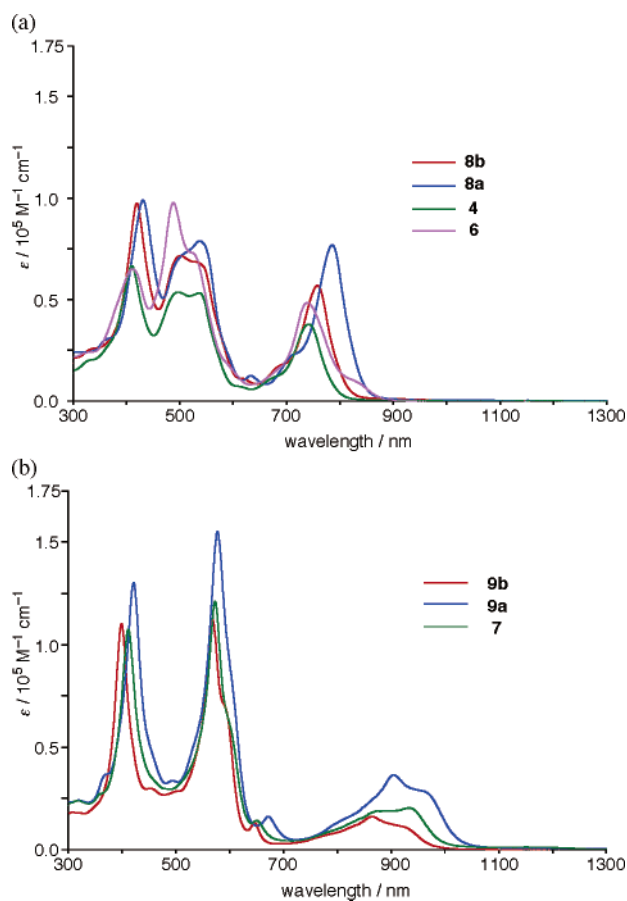(13) Ikeda, T.; Aratani, N.; Tsuda, A.; Osuka, A. *Chem. Lett.* **2006**, *35*, 946−947.

Figure 1. UV−vis absorption spectra of (a) doubly linked diporphyrins **4**, **6**, **8a**, and **8b** and (b) triply linked diporphyrins **7**, **9a**, and **9b** in dichloromethane.

Table 1. TPA Cross-Sections of Triply Lined Porphyrin Dimers

sample	$\sigma^{(2)}$ (GM)	concn (mM)	wavelength (nm)
9a	11 300	0.15	1 200
9b	10 500	0.15	1 200
7	9 980	0.14	1 200

and **6** and triply fused diporphyrin **7** through AuCl₃−AgOTf mediated oxidation in high yields. Debromination of **4** and **7** allows the synthesis of *meso*-free doubly fused and *meso*-free triply fused diporphyrins in good yields, hence opening a convenient way to use a bromine substituent as a protecting group for the reactive *meso*-position of porphyrins. Further investigations to expand the scope of the present reaction and utilize the bromo functionality at the *meso*-position of the fused diporphyrins for many transition metal-catalyzed transformations are ongoing and will be reported in due course.

Supporting Information Available: Experimental procedures and compound data. This material is available free of charge via the Internet at http://pubs.acs.org.

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aperture Z-scan method with ∼130 fs laser pulses (5 kHz repetition rate) at 1200 nm in toluene (Table 1). Disappointingly, however, the enhancement of the TPA value by introduction of the alkynyl moiety was found to be only marginal.[3b]

In summary, we have explored a practical and simple synthesis of *meso*-brominated doubly fused diporphyrins **4**

(14) A similar stoichiometric debromination reaction was reported, see: Kato, A.; Hartnell, R. D.; Yamashita, M.; Miyasaka, H.; Sugiura, K.-i.; Arnold, D. P. *J. Porphyrins Phthalocyanines* **2004**, *8*, 1222.

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