Angewandte Chemie International Edition

Porphyrinoids

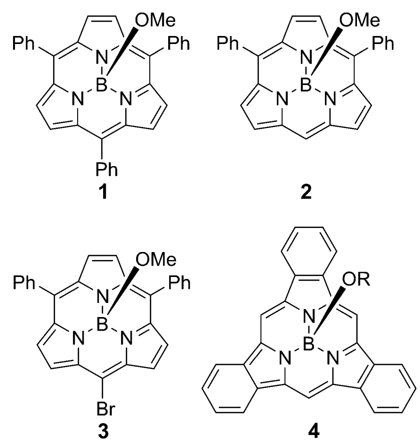
DOI: 10.1002/anie.201201853

Effective meso Fabrications of Subporphyrins**

*Masaaki Kitano, Shin-ya Hayashi, Takayuki Tanaka, Hideki Yorimitsu, Naoki Aratani, and Atsuhiro Osuka**

Subporphyrins, which are legitimate ring-contracted porphyrins in terms of the regular arrangement of three pyrrolic units and methine carbons, have emerged as a novel functional pigment since their first synthesis in 2006.[1] Interest in these macrocycles initially lay on the influence of symmetry change from D_{4h} of metalloporphyrins to C_{3v} of boron(III) subporphyrins. In the meantime however, it has turned out that subporphyrins have attractive attributes, such as a 14π-electronic aromatic circuit, bowl-shaped bent structure, and variable electronic properties that are tunable by meso-aryl substituents.[2,3] Despite these promises, the synthetic chemistry of subporphyrins lags far behind the porphyrin counterpart, since only symmetric meso-aryl-substituted subporphyrins, such as triphenyl subporphyrin **1**, can be prepared by the condensation of tri-*N*-pyrrolylborane or pyridine-tri-*N*-pyrrolylborane with aryl aldehydes in a practical sense. As has been extensively demonstrated in the porphyrin chemistry, rational synthetic routes to nonsymmetrically substituted subporphyrins are highly desirable for exploration of subporphyrin-based functional molecular systems.[4] So far, however, such a rational nonsymmetric fabrication method has been unknown for a subporphyrin except for low-yielding statistical cross-condensation reactions that entail tedious separation steps.[2c,d,f] Furthermore, there is no synthetic route to meso-alkenyl or meso-alkynyl subporphyrins despite their high promise as functional dyes, as suggested by the very rich chemistry of porphyrin counterparts that were pioneered by Therien[5] and Anderson.[6]

Herein, we present the synthesis of meso-free and meso-bromo subporphyrins **2** and **3**, which can be effective synthetic precursors for nonsymmetrically substituted subporphyrins, judging from the extensive and successful uses of meso-free[7] and meso-bromo porphyrins.[8] Tribenzosubporphines **4** were the first synthesized meso-free subporphyrins, but their meso-positions are entirely unreactive towards electrophiles such as bromine and *N*-bromosuccinimide (NBS), because they correspond to nodes in their HOMO as revealed by DFT calculations.[2a] On the other hand, meso-free subporphyrin **2**



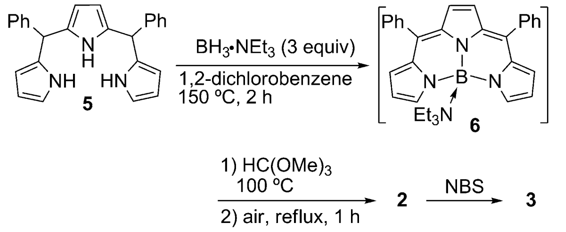
has been suggested to be a useful precursor for **3** by DFT calculations (see the Supporting Information), which predicts favorable HOMO characteristics for meso halogenation.

We thought that meso-free subporphyrin **2** might be prepared by the condensation of pyridine tripyrromethene borane salt with trimethyl orthoformate. Along this synthetic line, we first attempted the condensation of tripyrrane **5**[9] with neat $BH_3{\cdot}NEt_3$ at 100°C for 1 h, and the resulting solution was evaporated to leave a residue, to which an equivalent amount of pyridine was added to form pyridine tripyrromethene borane precursor. This was condensed with 20 equivalents of trimethyl orthoformate in the presence of trifluoroacetic acid (TFA) to furnish **2** along with its reduced congener, meso-free subchlorins,[10] as by-products. To make the separation easier, the resultant mixture was oxidized with MnO_2 for the conversion of the meso-free subchlorins into **2**. Subsequent separation over a simple silica gel column gave **2** in 4.4% yield (method A; Supporting Information). The final oxidation step is beneficial for product separation but causes non-negligible oxidative damage to **2**. On the basis of mechanistic consideration that the subchlorin was formed by the action of acid on subporphyrinogen intermediates, which was considered for the formation of chlorins in the Adler porphyrin synthesis,[11] we thus attempted acid-free, simple thermal reaction of **6** generated in situ from **5** with $BH_3{\cdot}NEt_3$ and trimethyl orthoformate in 1,2-dichlorobenzene at various temperatures (method B; Scheme 1). Gratifyingly, the acid-free condensation reaction at 100°C furnished **2** in 9.7% yield without contamination of subchlorin by-products. The ^{1}H NMR spectrum of **2** in $CDCl_3$ exhibits a singlet at 8.89 ppm owing to the free meso proton. As expected, the bromination of **2** proceeded with NBS in $CHCl_3$ at 0°C to provide **3** quantitatively. The structures of **2** and **3**-$OCOCF_3$ were revealed by a single-crystal X-ray diffraction analysis

[*] M. Kitano, S. Hayashi, Dr. T. Tanaka, Prof. Dr. H. Yorimitsu, Dr. N. Aratani, Prof. Dr. A. Osuka
Department of Chemistry, Graduate School of Science
Kyoto University, Sakyo-ku, Kyoto 606-8502 (Japan)
E-mail: osuka@kuchem.kyoto-u.ac.jp
Dr. N. Aratani
PRESTO, Japan Science and Technology Agency (Japan)

[**] This work was supported by Grants-in-Aid (Nos. 22245006 (A) and 20108001 "pi-Space") for Scientific Research from MEXT.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201201853.



Scheme 1. Synthesis of meso-free and meso-bromo subporphyrins **2** and **3**.

(Figure 1).[12] The bowl depths are 1.460 and 1.355 Å for **2** and **3**-$OCOCF_3$, respectively. The fluorescence quantum yield Φ_F of **2** is 0.12, which is similar to that of **1**, while that of **3** is dropped to 0.004 owing to the internal heavy-atom effect.

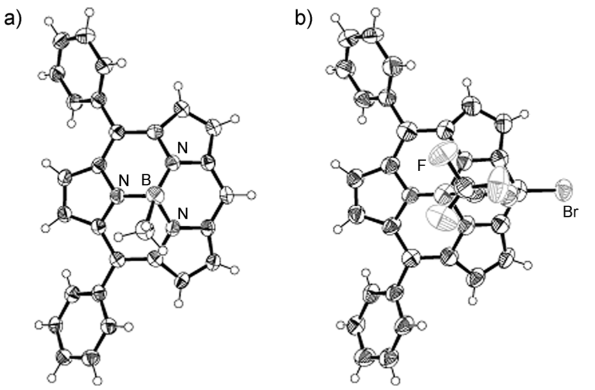
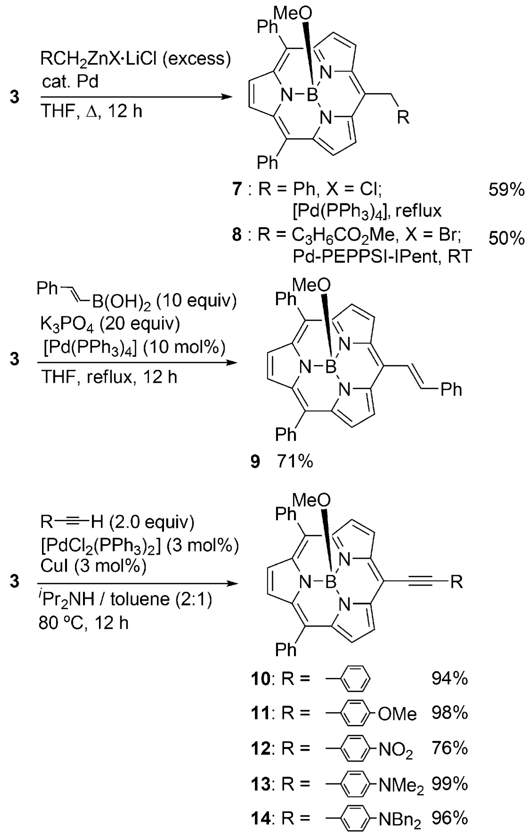


Figure 1. X-ray crystal structures of a) **2** and b) **3**-$OCOCF_3$. Ellipsoids are set to 50% probability.

With bromide **3** in hand, we examined its fabrications through metal-catalyzed cross-coupling reactions (Scheme 2). The first example was Negishi coupling[8b,13] with benzylzinc chloride–lithium chloride complex,[14] which allowed the synthesis of meso-benzyl subporphyrin **7** in 59% yield. The structure of **7** was confirmed by X-ray analysis of B-(3,5-dinitrobenzyloxy)subporphyrin **7**-DN (Figure 2a). Subporphyrin **7** was found to be slightly unstable in solution under the air, which is probably due to the presence of benzylic hydrogen. An alkyl group bearing an ester group was also installed by a similar coupling reaction with the corresponding functionalized organozinc reagent[15] with the aid of an NHC-Pd complex, Pd-PEPPSI-IPent,[16] to provide **8** in 50% yield. These reactions constitute the second synthetic route to meso-alkyl substituted subporphyrins,[2i] but are much more useful in terms of rational synthesis and wide functional group compatibility.

Phenylvinyl-substituted subporphyrin **9** was synthesized by Suzuki–Miyaura coupling with phenylvinylboronate in 71% yield.[17] The structure of **9** was determined by X-ray analysis; the phenylvinyl group is nearly coplanar to the subporphyrin core with a dihedral angle of 26.6° (Figure 2b). This is the first example of subporphyrin bearing a meso-alkenyl substituent.



Scheme 2. Fabrications of **3** through metal-catalyzed cross-coupling reactions.

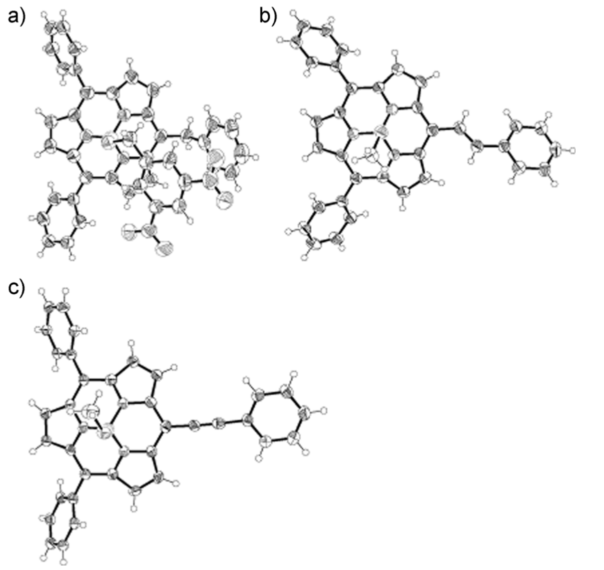


Figure 2. X-ray crystal structures of a) **7**-DN, b) **9**, and c) **10**. Solvent molecules are omitted for clarity; ellipsoids are set to 50% probability.

In the next step, we also examined meso-alkynylation of **3** by Sonogashira reaction,[2c,18] which is indeed fairly effective to produce **10**–**14** in good yields. Apart from phenylacetylene, both electron-accepting and electron-donating aryl acetylenes could be used in this coupling reaction. The crystal structures were obtained for **10**, **11**, and **12** (Figure 2c; Supporting Information).[12]

The meso-substituted subporphyrins that were thus synthesized allowed a comparison of the absorption and fluorescence spectra (Figure 3). The Soret-like band of **2** appears

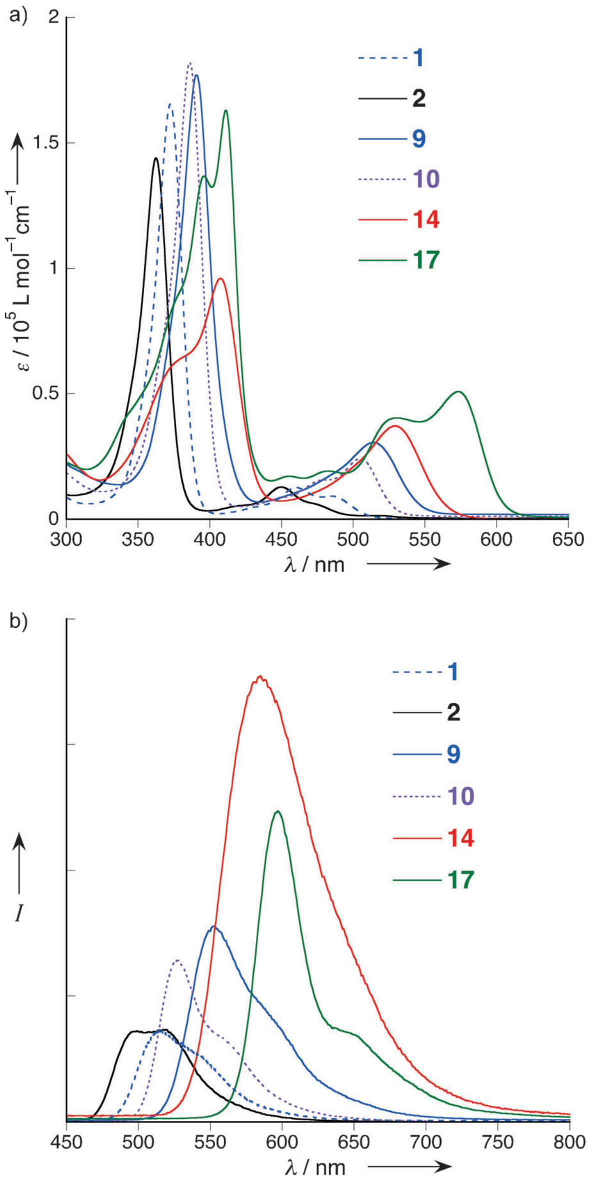


Figure 3. a) UV/Vis absorption and b) fluorescence spectra of selected subporphyrins in CH_2Cl_2.

at 362 nm, which is blue-shifted as compared with those of **1** (373 nm) and **8** (367 nm), indicating that the meso-alkyl substituent causes a slight red-shift in a Soret-like band. The fluorescence bands and quantum yields are observed for **7** (507 nm, $\Phi_F = 0.15$) and **8** (508 nm, $\Phi_F = 0.14$). The meso-alkenyl- and meso-alkynyl-substituted subporphyrins display more red-shifted Soret-like bands; **9** (391 nm), **10** (386 nm), **11** (390 nm), and **12** (396 nm), and Q-like bands: **9** (514 nm), **10** (505 nm), **11** (510 nm), and **12** (516 nm), reflecting the effective conjugation of meso substituents with subporphyrin chromophore. In the arylethynyl-substituted series, both the electron-donating and electron-accepting groups cause red-shifts in the Soret-like band as compared with **10**. A similar trend was observed for their fluorescence spectra. The fluorescence bands and quantum yields are observed as follows: **9** (552 nm, $\Phi_F = 0.26$), **10** (527 nm, $\Phi_F = 0.22$), **11** (538 nm, $\Phi_F = 0.23$), and **12** (554 nm, $\Phi_F = 0.039$). Remarkably, meso-(4-dimethylaminophenyl)ethynyl subporphyrin **13** exhibits a split Soret-like band at 376 and 406 nm and a considerably intensified fluorescence quantum yield (601 nm, $\Phi_F = 0.59$; see the Supporting Information). These optical properties are reminiscent of those of meso-(4-dibenzylaminophenyl)subporphyrin **15**,[2c] and are similarly ascribed to a HOMO that is spread over the entire dibenzylaminophenyl group and considerably destabilized relative to HOMO−1. Since subporphyrin **15** displayed the structural deformations of the meso-(4-aminophenyl) group towards the quinonoid structure, we prepared meso-(4-dibenzylaminophenyl)ethynyl subporphyrin **14** by the same Sonogashira coupling under the same conditions and succeeded in the X-ray crystal structural determination of **14**-OEt. However, the meso-alkynyl moiety does not display structural deformation towards the allene structure (Figure 4).

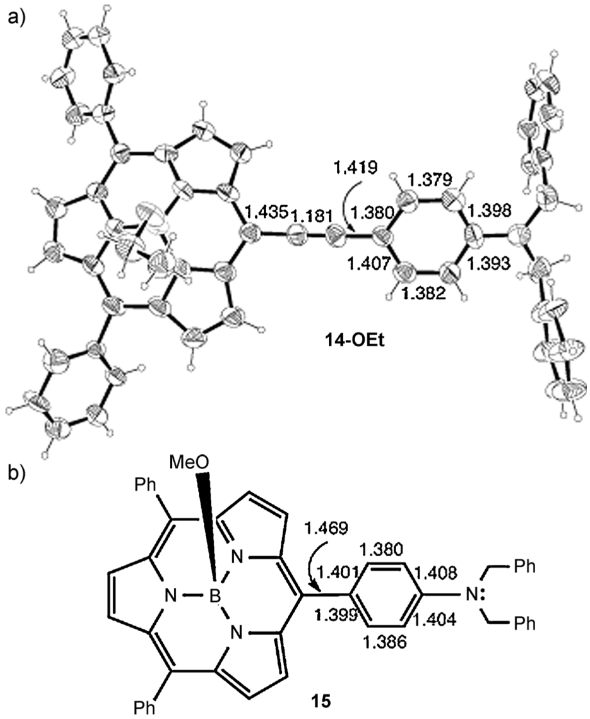
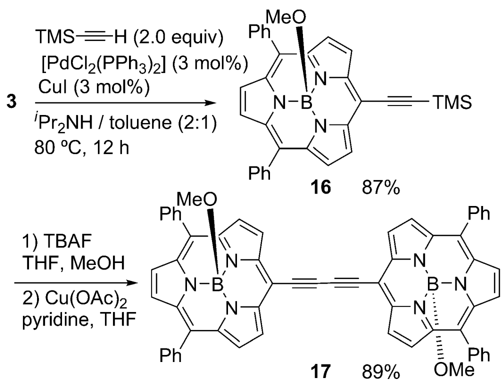


Figure 4. a) X-ray crystal structure of **14**-OEt and b) comparison of bond lengths to **15**. Solvent molecules are omitted for clarity; ellipsoids are set to 20% probability.

As an extension of this method, meso-trimethylsilylethynyl-substituted subporphyrin **16** was prepared and was transformed into 1,3-butadiyne-bridged subporphyrin dimer **17** in 89% yield (Scheme 3) by deprotection with tetrabutylammonium fluoride (TBAF) followed by dimerization under Glaser coupling conditions. The ^{1}H NMR and high-resolution



Scheme 3. Synthesis of 1,3-butadiyne-bridged subporphyrin dimer **17**.

electrospray time-of-flight mass spectra of **17** are consistent with its structure, which was confirmed by single-crystal X-ray structural analysis (Figure 5). Two subporphyrin rings are linked in an *anti* manner through a 1,3-butadiyne bridge with a center-to-center distance of 12.44 Å (B–B distance). The absorption spectrum of **17** shows multiply split Soret-like bands and red-shifted and intensified Q-band-like bands, the tail of which is at 600 nm. The fluorescence exhibits peaks at 597 and 653 nm with $\Phi_F = 0.42$. These optical properties are considered to arise from the effective conjugation.

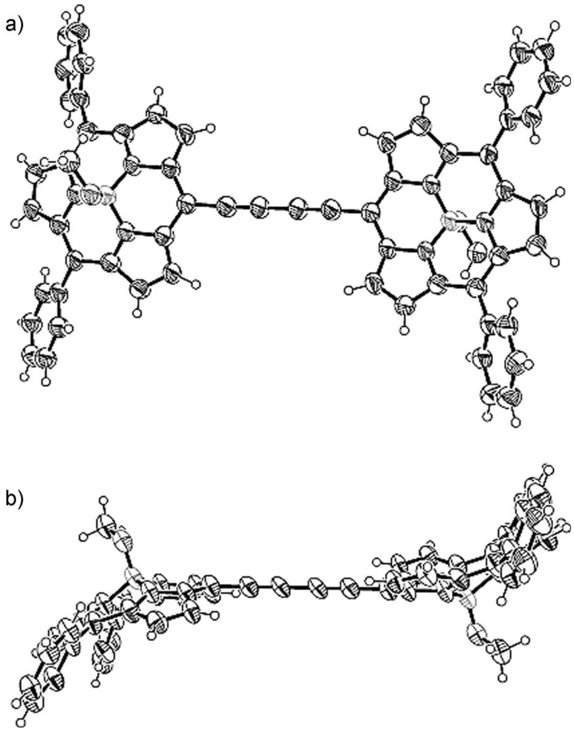


Figure 5. X-ray crystal structure of **17**. a) Top view and b) side view. Solvent molecules are omitted for clarity; ellipsoids are set to 50% probability.

In summary, meso-free and meso-bromo subporphyrins **2** and **3** were prepared for the first time. The latter has been demonstrated to serve as an effective synthetic precursor for meso-alkyl-, meso-alkenyl-, and meso-alkynyl-substituted subporphyrins through metal-catalyzed cross-coupling reactions. 1,3-Butadiyne-bridged subporphyrin dimer **17** could be synthesized though **16**. The optical properties of subporphyrins have been modulated by meso substituents. These results now open a route to functional subporphyrins in a rational manner. Extensions of this synthetic method to other nucleophiles and further elaborated oligomeric subporphyrins are actively in progress in our laboratory.

Received: March 8, 2012
Published online: April 23, 2012

Keywords: bromination · cross-coupling · porphyrinoids · subporphyrins · substitution

[1] a) Y. Inokuma, A. Osuka, *Dalton Trans.* **2008**, 2517; b) T. Torres, *Angew. Chem.* **2006**, *118*, 2900; *Angew. Chem. Int. Ed.* **2006**, *45*, 2834; c) A. Osuka, E. Tsurumaki, T. Tanaka, *Bull. Chem. Soc. Jpn.* **2011**, *84*, 679.

[2] a) Y. Inokuma, J. H. Kwon, T. K. Ahn, M.-C. Yoon, D. Kim, A. Osuka, *Angew. Chem.* **2006**, *118*, 975; *Angew. Chem. Int. Ed.* **2006**, *45*, 961; b) Y. Inokuma, Z. S. Yoon, D. Kim, A. Osuka, *J. Am. Chem. Soc.* **2007**, *129*, 4747; c) Y. Inokuma, A. Osuka, *Chem. Commun.* **2007**, 2938; d) Y. Inokuma, S. Easwaramoorthi, Z. S. Yoon, D. Kim, A. Osuka, *J. Am. Chem. Soc.* **2008**, *130*, 12234; e) Y. Inokuma, S. Easwaramoorthi, S. Y. Jang, K. S. Kim, D. Kim, A. Osuka, *Angew. Chem.* **2008**, *120*, 4918; *Angew. Chem. Int. Ed.* **2008**, *47*, 4840; f) Y. Inokuma, A. Osuka, *Org. Lett.* **2008**, *10*, 5561; g) E. Tsurumaki, Y. Inokuma, S. Easwaramoorthi, J. M. Lim, D. Kim, A. Osuka, *Chem. Eur. J.* **2009**, *15*, 237; h) S. Hayashi, Y. Inokuma, A. Osuka, *Org. Lett.* **2010**, *12*, 4148; i) S. Hayashi, Y. Inokuma. S. Easwaramoorthi, K. S. Kim, D. Kim, A. Osuka, *Angew. Chem.* **2010**, *122*, 331; *Angew. Chem. Int. Ed.* **2010**, *49*, 321; j) S. Hayashi, E. Tsurumaki, Y. Inokuma, P. Kim, Y. M. Sung, D. Kim, A. Osuka, *J. Am. Chem. Soc.* **2011**, *133*, 4254; k) E. Tsurumaki, S. Hayashi, F. S. Tham, C. A. Reed, A. Osuka, *J. Am. Chem. Soc.* **2011**, *133*, 11956.

[3] a) N. Kobayashi, Y. Takeuchi, A. Matsuda, *Angew. Chem.* **2007**, *119*, 772; *Angew. Chem. Int. Ed.* **2007**, *46*, 758; b) Y. Takeuchi, A. Matsuda, N. Kobayashi, *J. Am. Chem. Soc.* **2007**, *129*, 8271; c) T. Xu, R. Lu, X. Liu, P. Chen, X. Qiu, Y. Zhao, *Eur. J. Org. Chem.* **2008**, 1065.

[4] a) J. S. Lindsey in *The Porphyrin Handbook*, *Vol. 2* (Eds.: K. Kadish, K. M. Smith, R. Guilard), Academic Press, San Diego, **2000**, p. 45; b) N. Aratani, A. Osuka in *Handbook of Porphyrin Science*, *Vol. 1* (Eds.: K. M. Kadish, K. M. Smith, R. Guilard), World Scientific Publishing, Singapore, **2010**, p. 1.

[5] V. S.-Y. Lin, S. G. DiMagno, M. J. Therien, *Science* **1994**, *264*, 1105.

[6] H. L. Anderson, *Inorg. Chem.* **1994**, *33*, 972.

[7] a) K. M. Smith, G. H. Barnett, B. Evans, Z. Martynenko, *J. Am. Chem. Soc.* **1979**, *101*, 5953; b) A. Osuka, H. Shimidzu, *Angew. Chem.* **1997**, *109*, 93; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 135; c) H. Hata, H. Shinokubo, A. Osuka, *J. Am. Chem. Soc.* **2005**, *127*, 8264.

[8] a) S. G. DiMagno, V. S.-Y. Lin, M. J. Therien, *J. Am. Chem. Soc.* **1993**, *115*, 2513; b) S. G. DiMagno, V. S.-Y. Lin, M. J. Therien, *J. Org. Chem.* **1993**, *58*, 5983; c) N. Aratani, A. Osuka, *Org. Lett.* **2001**, *3*, 4213; d) R. F. Kelley, M. J. Tauber, M. R. Wasielewski, *J. Am. Chem. Soc.* **2006**, *128*, 4779.

[9] a) C. Brückner, E. D. Sternberg, R. W. Boyle, D. Dolphin, *Chem. Commun.* **1997**, 1689; b) J. L. Sessler, D. Seidel, C. Bucher, V. Lynch, *Chem. Commun.* **2000**, 1473.

[10] E. Tsurumaki, S. Saito, K. S. Kim, J. M. Lim, Y. Inokuma, D. Kim, A. Osuka, *J. Am. Chem. Soc.* **2008**, *130*, 438.
[11] J. B. Kim, A. D. Adler, F. R. Longo in *The Porphyrins*, *Vol. 1* (Ed: D. Dolphin), Academic Press, New York, **1978**, p. 85.
[12] CCDC 870074 (**2**), 870073 (**3**-OCOCF$_3$), 870071 (**7**-DN), 870078 (**9**), 870075 (**10**), 870077 (**14**-OEt), and 870079 (**17**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
[13] E. Negishi, *Angew. Chem.* **2011**, *123*, 6870; *Angew. Chem. Int. Ed.* **2011**, *50*, 6738.
[14] A. Metzger, M. A. Schade, P. Knochel, *Org. Lett.* **2008**, *10*, 1107.
[15] A. Krasovskiy, V. Malakhov, A. Gavryushin, P. Knochel, *Angew. Chem.* **2006**, *118*, 6186; *Angew. Chem. Int. Ed.* **2006**, *45*, 6040.
[16] a) M. G. Organ, S. Avola, I. Dubovyk, N. Hadei, E. A. B. Kantchev, C. J. O'Brien, C. Valente, *Chem. Eur. J.* **2006**, *12*, 4749; b) S. Sase, M. Jaric, A. Metzger, V. Malakhov, P. Knochel, *J. Org. Chem.* **2008**, *73*, 7380; c) M. G. Organ, G. A. Chass, D.-C. Fang, A. C. Hopkinson, C. Valente, *Synthesis* **2008**, 2776; d) C. Valente, M. E. Belowich, N. Hadei, M. G. Organ, *Eur. J. Org. Chem.* **2010**, 4343; e) C. Valente, S. Çalimsiz, K. H. Hoi, D. Mallik, M. Sayah, M. G. Organ, *Angew. Chem.* **2012**, *124*, 3370; *Angew. Chem. Int. Ed.* **2012**, *51*, 3314.
[17] B. Shi, R. W. Boyle, *J. Chem. Soc. Perkin Trans. 1* **2002**, 1397.
[18] S. M. LeCours, S. G. DiMagno, M. J. Therien, *J. Am. Chem. Soc.* **1996**, *118*, 11854.