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Selective Stepwise Suzuki Cross-Coupling Reaction for the Modelling of Photosynthetic Donor−Acceptor Systems

Mikhail A. Filatov, Roger Guilard,* and Pierre D. Harvey*

Institut de Chimie Moléculaire de l'Université de Bourgogne (ICMUB), UMR 5260
CNRS, 9 Avenue Alain Savary, BP 47870-21078 Dijon, France

roger.guilard@u-bourgogne.fr; pierre.harvey@u-bourgogne.fr

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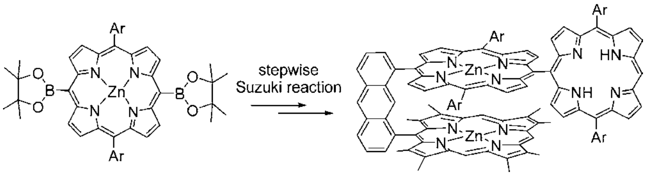
ABSTRACT



A Suzuki reaction performed as a selective stepwise substitution of two boryl groups on a diarylporphyrin precursor is reported for straightforward construction of a porphyrin trimer, modeling photosynthetic donor−acceptor systems.

The mimicry of energy and electron transfer modules of photosystems I and II is of current interest.[1] The key step in the photosynthetic conversion of light taking place in the plant and bacterial reaction centers includes an extremely rapid electron transfer (3 ps) from an excited bacteriochlorophylls "special pair" to the neighboring pheophytin.[2] Getting similar parameters for artificial systems stimulated many efforts to design multichromophore assemblies.[3] Particulary, those reported by Osuka and collaborators, comprised of a cofacial porphyrin dimer as a "special pair" linked to a corresponding electron acceptor, showed required picosecond time scale electron transfer.[4] However, further development of such perspective models requires the possibility of tuning the distances between subunits as well as their individual substitution patterns, which are strongly limited by laborious multistep synthesis. Exploration of a simple and versatile method enabling the preparation of related molecules with given structural parameters is essential.

Recent introduction of the Suzuki reaction[5] to the porphyrin chemistry has resulted in an increasing number of works describing the preparation of functionalized porphyrins as well as supramolecular assemblies that are hard to prepare using classical approaches.[6] However, so far this powerful method has been applied exclusively as a one-pot single/multiple coupling, leading from corresponding porphyrin boronates to fully substituted $A_4/A_3B/A_2B_2$-type products.[7]

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(1) Harvey, P. D. *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, 2003; Vol. 18, Chapter 113.

(2) Cogdell, R. J.; Isaacs, N. W.; Howard, T. D.; McLuskey, K.; Fraser, N. J.; Prince, S. M. *J. Bacteriol.* **1999**, *181*, 3869.

(3) (a) Wasielewski, M. R. *Chem. Rev.* **1992**, *92*, 435. (b) Harriman, A.; Sauvage, J.-P. *Chem. Soc. Rev.* **1996**, 41. (c) Guldi, D. M. *Chem. Soc. Rev.* **2002**, *31*, 22. (d) Nakamura, Y.; Aratani, N.; Osuka, A. *Chem. Soc. Rev.* **2007**, *36*, 831.

(4) Osuka, A.; Maruyama, K.; Mataga, N.; Asahi, T.; Yamazaki, I.; Tamai, N.; Nishimura, Y. *Chem. Phys. Lett.* **1991**, *181*, 413.

(5) (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147.

(6) Burrell, A. K.; Officer, D. L.; Plieger, P. G.; Reid, D. C. W. *Chem. Rev.* **2001**, *101*, 2751.

(7) (a) Hyslop, A. G.; Kellet, M. A.; Iovine, P. M.; Therien, M. J. *J. Am. Chem. Soc.* **1998**, *120*, 12676. (b) Aratani, N.; Osuka, A. *Org. Lett.* **2001**, *3*, 4213. (c) Chng, L. L.; Chang, C. J.; Nocera, D. G. *J. Org. Chem.* **2003**, *68*, 4075. (d) Dahms, K.; Senge, M. *Tetrahedron. Lett.* **2008**, *49*, 5397. (e) Aratani, N.; Osuka, A. *Chem. Commun.* **2008**, 4067. (f) Wu, C.-A.; Chiu, C.-L.; Mai, C.-L.; Lin, Y.-S.; Yeh, C.-Y. *Chem.−Eur. J.* **2009**, *15*, 4534. (g) Gotz, D. C. G.; Bruhn, T.; Senge, M.; Bringman, G. *J. Org. Chem.* **2009**, *74*, 8005. (h) Shinokubo, H.; Osuka, A. *Chem. Commun.* **2009**, 1011.

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Scheme 1. Donor−Acceptor Systems via Suzuki Reaction

In cases where the use of two or more coupling steps is advantageous, posterior functionalization, e.g., bromination, of the first coupling step product has been described.[7b,e,h] Evidently, such functionalization, which has to be selective for providing the construction of the target product, represents a distinct task, especially for complex aromatic molecules.

Surprisingly, Suzuki coupling on porphyrin boronates as selective stepwise substitution, i.e. introducing each boryl group to the reaction with different substrates, leading to A_2BC/ABCD-type porphyrins, has never been published, although a few examples are known for the synthesis of conjugated oligoarenes.[8]

Herein, we report the use of such modification of the Suzuki cross-coupling reaction in the synthesis of electron and energy donor−acceptor systems as illustrated by straightforward preparation of a trimeric porphyrin system, comprised of a face-to-face porphyrin dimer ("special pair" donor model D1-D2, Scheme 1) and *meso*-linked free-base porphyrin (acceptor A, Scheme 1).

The building blocks and synthetic strategy are shown in Scheme 2 (see Supporting Information for details). Two distinct opportunities for performing the stepwise reaction on porphyrin diboronate (routes A and B in Scheme 2), different in the order of assembling the building blocks, were explored to identify the most efficient route and to secure the total synthesis from possible experimental complications.

First, the anthracene bridging entity, used as a spacer in the face-to-face dimer unit, was synthesized. 1,8-Dibromoanthraquinone **1** was reduced to anthrone **2** by $NaBH_4$ in MeOH, according to a published method.[9] The following reduction by $NaBH_4$ in *n*-PrOH, described by Goichi et al.[10] for the corresponding iodo derivative, yielded 1,8-dibromoanthracene **3**. Selective monolithiation of **3** with PhLi,[11] followed by the addition of dry DMF and hydrolysis of the intermediate imidate salt, provided the aldehyde **4** in 92% yield. It was further reacted with octamethyl-a,c-biladiene dihydrobromide **5** according to the method reported by Harris et al.,[12] giving porphyrin **6a** in 35% yield, which was converted to zinc complex **6b** by a standard procedure.

Substitution of the first boryl group in **7** (steps A1, B1 in Scheme 2) gave the monoborylated face-to-face dimer **9** and *meso*−*meso* linked dimers **10a**,**b**, respectively. A mixture of toluene and DMF in the presence of a catalytic amount (10 mol %) of $Pd(PPh_3)_4$ and 1.5 equiv of Cs_2CO_3 at 90 °C, reported previously,[7b] was found to provide good yields and selectivity. Though it is known that reductive deborylation of porphyrin derivatives may occur under Pd(0) catalysis conditions,[7f] such side products were not detected by analyzing crude reaction mixtures with MALDI-TOF spectroscopy. Isolation and purification of products **9** and **10a**,**b** from the reaction mixture, usually containing small amounts of starting materials, were readily achieved by single column chromatography on silica since the incorporation of boryl groups to porphyrin derivatives was found to induce a large difference in R_f values.

A simple purification procedure for the *meso*−*meso* linked porphyrin dimers **10a**,**b** contrasts with reported syntheses of parent porphyrin dimers, lacking boryl groups, where size-exclusion (SEC) or high-performance liquid chromatography (HPLC) was applied.[7b,13] Taking into account the possibilities for further functionalization of dimers **10a**,**b** by substitution of boryl groups, this approach may serve as a convenient method for the preparation of *meso*−*meso* linked porphyrins building blocks for further synthetic applications.

Compounds **9** and **10a** were then subjected to the second coupling reaction (steps A2, B2 in Scheme 2) with the bromoporphyrins **6b** and **8a**, respectively. Despite longer reaction times (up to 48 h), incomplete conversions of the starting materials were observed, probably due to steric hindrance caused by dimer moieties. Varying other reaction conditions, such as a catalyst ($Pd_2(dba)_3$, $PdCl_2(Ph_3P)_2$) or a base ($Ba(OH)_2$, KOH) and using the 3-fold excess of the corresponding bromoporphyrins did not result in a significant increase of conversion. Therefore, the reaction was performed using the same protocol as described for the first step, contrary to previously known oligoarene syntheses,[8a,d] where different conditions were used for each step. Upon coupling of **8a** with **9** (step B2 in Scheme 2), the reaction was found to be accompanied by the formation of a small amount (3−5%) of a side product, which according to MALDI-TOF data (*m*/*z* 1411) is a corresponding deborylated face-to-face dimer. In both cases, the isolation of target trimer **11** by column chromatography did not allow for total purification, giving fractions, contaminated either by the observed side product or the starting dimer. Complete purification was achieved after applying size-exclusion chromatography on the cross-linked polystyrene. Purified trimer **11** was obtained in 35−40 and 28% yields according to routes A and B (Scheme 2), respectively, and characterized by NMR and mass spectroscopy.

The optical spectra of dimers **9** and **10a** and trimer **11** are shown in Figure 1. The absorption spectrum of **9** comprises

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(8) (a) Iovine, P. M.; Kellett, M. A.; Redmore, N. P.; Therien, M. J. *J. Am. Chem. Soc.* **2000**, *122*, 8717. (b) Smet, M.; Metten, B.; Dehaen, W. *Tetrahedron. Lett.* **2001**, *42*, 6527. (c) Paliulis, O.; Ostrauskaite, J.; Gaidelis, V.; Jankauskas, V.; Strohriegl, P. *Macromol. Chem. Phys.* **2003**, *204*, 1706. (d) Ott, S.; Borgstrom, M.; Hammarstrom, L.; Johansson, O. *Dalton Trans.* **2006**, 1434.

(9) Perez-Trujillo, M.; Maestre, I.; Jaime, C.; Alvarez-Larena, A.; Piniellab, J. F.; Virgili, A. *Tetrahedron: Asymmetry* **2005**, *16*, 3084.

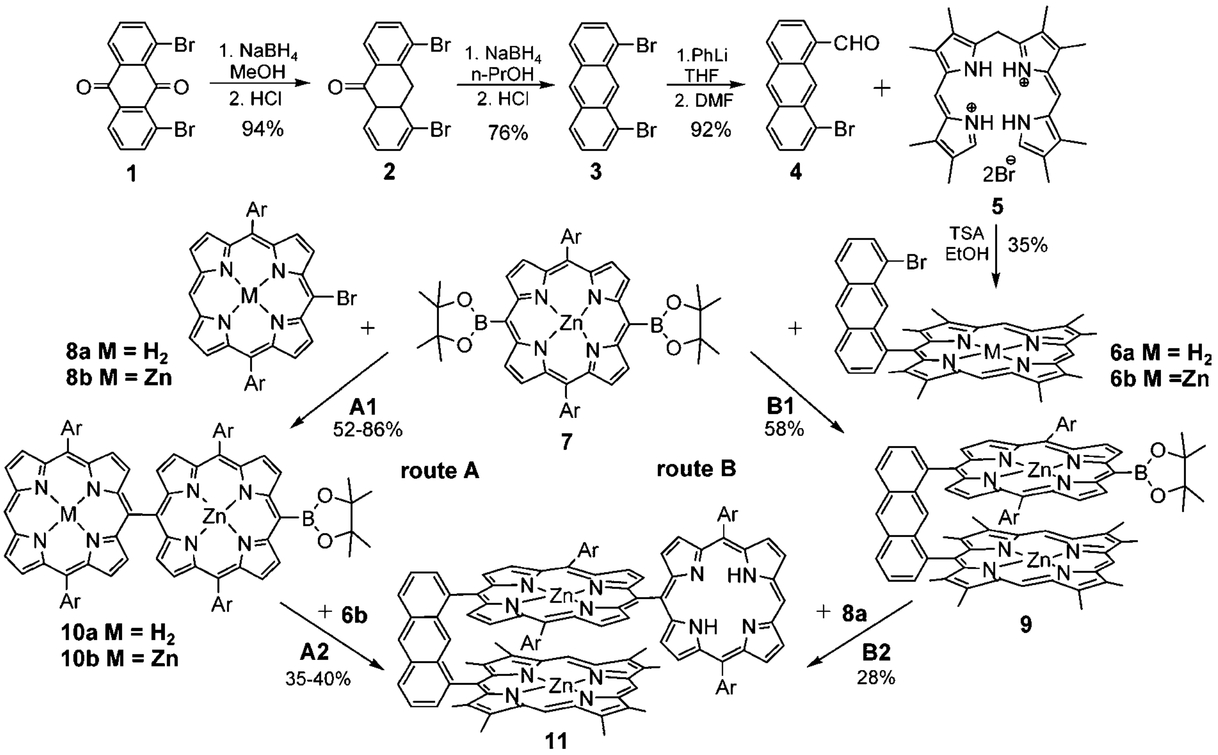
(10) Goichi, M.; Segawa, K.; Suzuki, S.; Toyota, S. *Synthesis* **2005**, 2116.

(11) Chang, C. J.; Yeh, C.-Y.; Nocera, D. G. *J. Org. Chem.* **2002**, *67*, 1403.

(12) Harris, D.; Johnson, A. W.; Gaete-Holmes, R. *Bioorg. Chem.* **1980**, *9*, 63.

(13) Aratani, N.; Osuka, A.; Kim, Y. H.; Jeong, D. H.; Kim, D. *Angew. Chem., Int. Ed.* **2000**, *39*, 1458.

Scheme 2. Synthesis of Trimer **11**[a]



[a] A1-2, B1-2: Pd(PPh$_3$)$_4$, Cs$_2$CO$_3$, toluene, DMF, 90 °C, 3−24 h; Ar = 3,5-di-*tert*-butylphenyl.

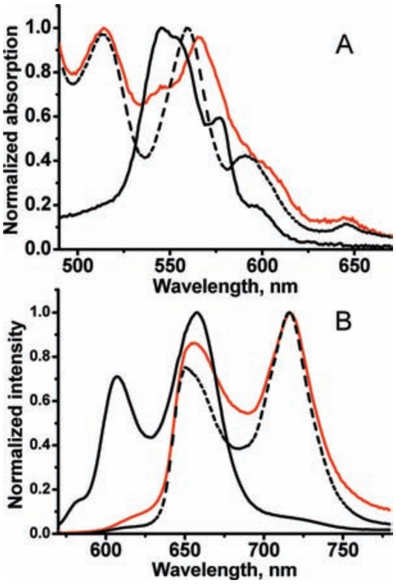


Figure 1. Absorption (A, Q-bands region) and emission (B) spectra of the porphyrins **9** (black solid line), **10a** (black dashed line), and **11** (red line) in THF at 298 K.

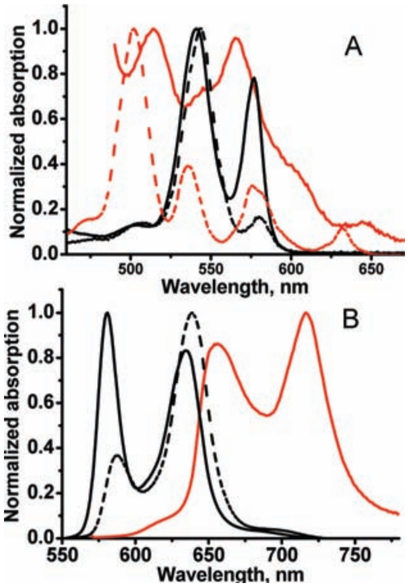


Figure 2. Absorption (A, Q-bands region) and emission (B) spectra of **6b** (black solid line), **11** (red solid line), 5,15-di-(3,5-di-*tert*-butylphenyl)porphyrin, and its zinc complex (red and black dashed lines, respectively) in THF at 298 K.

a sum of the spectra of the porphyrin subunits (see Supporting Information for the details), while its emission originates mainly from borylated diarylporphyrin as is clear from the comparison with the spectra of the corresponding compounds (Supporting Information). Both dimer **10a** and trimer **11** show common features in the observed emission ($\Phi_F = 0.062$ and 0.07, $\tau_F = 6.1$ and 7.1 ns, respectively) which obviously comes from the free base unit, even upon irradiation at wavelengths corresponding to Zn^{II}-porphyrins. Indeed, the excitation spectra registered at any wavelength of the resulting fluorescence of the free base residue match the absorption spectra in all cases, confirming the presence of singlet energy transfers. These observations corroborate those previously reported for *meso*−*meso* linked hybrid dimers.[7b] While in dimer **10a** energy transfer takes place from the adjacent Zn^{II}-porphyrin, in trimer **11** a similar process involves both Zn^{II}-porphyrin in the face-to-face dimer entity, that is seen from the comparison of its optical spectra with those of model porphyrins comprising the subunits, shown in Figure 2. No traces of octamethyl-substituted porphyrin emission can be observed in the fluorescence spectra of **11**, whereas diaryl-substituted porphyrin emission arises as a minor component seen at ∼610 nm as a weak shoulder.

In summary, we have performed the first selective stepwise Suzuki reaction on a porphyrin diborane allowing effective two-step construction of an energy transfer donor−acceptor system, mimicking the natural bacteriochlorophyls "special pair"-pheophytin module. Further investigations of this apparently very versatile method by using different types of spacers in the "special pair" unit, both energy and electron donors and linked acceptors, as well as a detailed study of the system's photophysical properties are now being conducted and will be reported in due course.

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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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