Complementary face-to-face dimer formation from *meso*-aryl subporphyrins bearing a 2-carboxyphenyl group†

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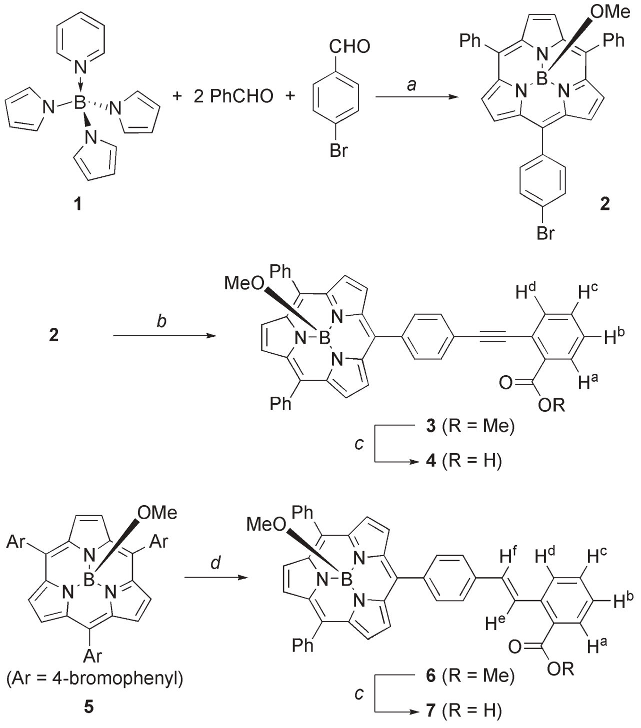
Received (in Austin, TX, USA) 1st May 2007, Accepted 20th May 2007
First published as an Advance Article on the web 12th June 2007
DOI: 10.1039/b706573f

***meso*-Aryl-substituted subporphyrins bearing a 2-carboxyphenyl group were prepared and shown to form complementary face-to-face dimers upon azeotropic removal of methanol.**

Subporphyrin, a ring-contracted porphyrin congener with cone-shaped 14π-electronic aromatic ring, has been, in spite of its important position in porphyrin chemistry, an elusive macrocycle until our first synthesis of tribenzosubporphines in 2006.[1] Shortly later, synthetic protocols for *meso*-aryl substituted subporphyrins have been developed.[2,3] This contrasts sharply with subphthalocyanines,[4] in that there have been extensive studies on this class of macrocycles since the first synthesis by Meller and Ossko in 1972.[5] Subporphyrins are attractive molecules exhibiting C_3 symmetric structure, extreme thermal stability, strong aromaticity, intense green fluorescence, and rather free rotation of *meso*-aryl substituents that allows large substituent effects on the electronic properties of subporphyrins.[1–3] Subporphyrins have been so far produced only as boron(III)-chelated forms involving a mono-anionic axial ligand such as alkoxy, hydroxy, and carboxy groups. Since these ligands can be reversibly replaced under suitable conditions,[1,3] it occurred to us that this reversible nature of axial bond would enable construction of discrete supramolecular assemblies.

Organization of supramolecular assemblies of porphyrins and related molecules is a hot current topic,[6] where metal–ligand coordination often plays a central role. Considering the rich photochemical and electrochemical properties as well as bowl-shaped structures,[1–3] subporphyrins may be a new, attractive component for such supramolecular assembly. Reported examples of supramolecular assemblies are quite limited for subphthalocyanines[7,8] and not known for subporphyrins. Herein we report the synthesis of 2-carboxyphenyl-substituted subporphyrins as the first examples of non C_3-symmetric subporphyrins and the formation of face-to-face dimers by complementary coordination of carboxylic group to the boron(III) center upon azeotropic removal of methanol.

The synthesis of A_2B-type *meso*-aryl-subporphyrin was carried out according to the procedure developed in our group.[3] A solution containing pyridine–tri-*N*-pyrrolylborane (**1**), benzaldehyde and methyl 3-formylbenzoate in a ratio of 1 : 2 : 1 in *o*-dichlorobenzene was treated carefully with trifluoroacetic acid (TFA) at 0 °C. After the acid was neutralized by the addition of pyridine, the resulting mixture was refluxed for 1 h. TLC and MALDI-TOF mass analyses of the resulting mixture revealed the production of 5,10-diphenyl-15-(3-methoxycarbonylphenyl)-subporphyrin, which, however, could not be isolated due to its low yield and the presence of numerous intractable byproducts. We thus attempted cross-condensation of benzaldehyde and 4-bromobenzaldehyde with **1** under similar conditions (Scheme 1), which provided four possible subporphyrins as a non-separable mixture. Then, introduction of the alkynyl group *via* Sonogashira-coupling reaction with methyl 2-ethynylbenzoate allowed us to isolate mono-arylethynyl substituted subporphyrin **3** in 1.2% yield from **1**. High-resolution electrospray ionization (HR-ESI) mass spectrum of **3** showed the peak due to corresponding borenium cation at *m*/*z* 628.2193 (calc. for $C_{43}O_2H_{27}N_3B_1$ = 628.2198 $[\mathbf{3} - \mathrm{OMe}]^+$). The ^{1}H NMR spectrum of **3** exhibits the three β-proton signals at 8.13 ppm as a singlet and at 8.15 and 8.14 ppm as a pair of doublets in line with the structure.



Scheme 1 *Reagents and conditions*: (*a*) (1) TFA at 0 °C, (2) pyridine, (3) reflux (open air) in *o*-dichlorobenzene, (4) MeOH; (*b*) excess methyl 2-ethynylbenzoate, $PdCl_2(PPh_3)_2$, CuI, *i*-Pr_2NH, toluene at 80 °C for 12 h; (*c*) 8 M NaOH aq.–MeOH–THF at r.t., overnight; (*d*) (1) methyl 2-ethynylbenzoate (1.4 equiv.), $PdCl_2(PPh_3)_2$, CuI, *i*-Pr_2NH, toluene at 80 °C for 12 h, (2) $Pd(PPh_3)_4$, Et_3N, HCO_2H, toluene at 100 °C for 2 h.

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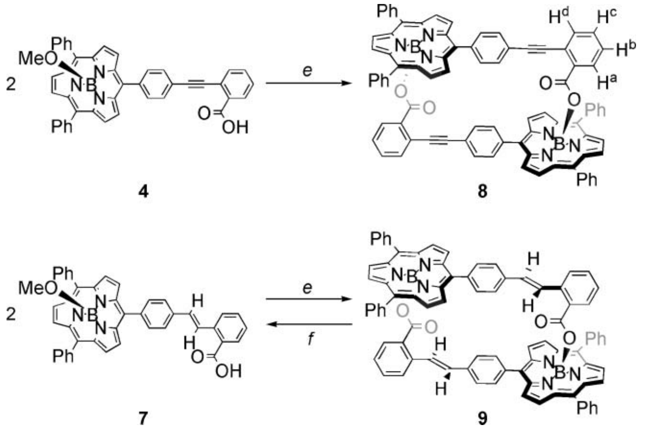
† Electronic supplementary information (ESI) available: NMR, UV-vis, and fluorescence spectra of **3**, **4** and **6–9**. See DOI: 10.1039/b706573f

As a different route, partial Sonogashira-coupling reaction of tri(4-bromophenyl)subporphyrin **5** with a 1.4 equiv. of methyl 2-ethynylbenzoate was attempted. Although the expected mono-ester subporphyrin was obtained as a major product in the coupling reaction, subsequent debromination with $Pd(PPh_3)_4$, Et_3N, HCO_2H system[9] yielded not **3** but hydrogenated product **6** in 24% yield. The HR-ESI-TOF mass spectrum of vinylene bridged subporphyrin **6** exhibited the parent borenium cation peak at *m*/*z* 630.2350 (calc. for $C_{43}O_2H_{29}N_3B_1$ = 630.2355 [**6** − OMe]$^+$). The ^1H NMR spectrum in $CDCl_3$ showed a pair of doublets at 8.22 and 7.21 ppm with *J* = 16.1 Hz due to the *trans*-vinylene protons. In addition, the ^{13}C NMR spectrum displayed peaks due to the *trans*-vinylene carbons at 131.0 and 128.5 ppm, which have correlation with the *trans*-vinylene protons H^f and H^e, respectively.

The ester groups in **3** and **6** were hydrolyzed in a mixed solvent of methanol and THF containing aqueous 8 M NaOH solution to give corresponding carboxylic acids **4** and **7** in 90 and 92% yields, respectively, after acidification with diluted hydrochloric acid. It was found that once a CH_2Cl_2 solution of **7** was evaporated to dryness, the ^1H NMR spectrum of the resulting subporphyrin exhibited a complicated feature involving an attenuated axial methoxy proton signal and new broad peaks at 8.3–8.0 and 7.2–6.5 ppm at the expense of the original spectrum, which were completely retrieved *via* a dissolution–evaporation cycle in methanol. Similar spectral changes were observed also for **4**. It is important to note that simple evaporation of solutions of **4** and **7** in CH_2Cl_2 led to complicated mixtures as judged from their ^1H NMR spectra. These ill-defined aggregation behaviors may be attributed to incomplete replacement of the axial-methoxy ligand by a carboxyl ligand.

We thus attempted to find suitable aggregation conditions by changing solvent, concentration, and temperature. A 200 μM toluene solution of **4** was refluxed with a Dean–Stark trap to remove methanol continuously and the progress of the reaction was traced by ^1H NMR spectroscopy. After 30 min, new proton peaks appeared at 8.3–8.2 and 7.2–6.8 ppm along with decrease of a set of the signals due to free carboxylic acid **4**. Prolonged refluxing for 12 h resulted in the complete conversion of **4** to dimer **8** (ESI† and Scheme 2). The solubility of **8** in toluene or CH_2Cl_2 is notably lower than **4**. The HR-ESI-TOF mass spectrum of **8** showed the parent cation peak at *m*/*z* 1249.3837, whose isotope distribution was matched well with a dimer composition $C_{84}O_4H_{48}N_6B_2Na$ = 1249.3839 [2 × **4** − 2MeOH + Na]$^+$. The ^1H NMR spectrum of **8** exhibited a single set of signals due to the subporphyrin unit without an axial-methoxy proton peak. Upon face-to-face dimerization, the proton signals due to the peripheral 2-carboxyphenyl subunit, H^a, H^b, H^c and H^d are substantially high-field shifted from 8.10, 7.45, 7.57 and 7.75 ppm in **4** to 6.84, 6.90, 7.07 and 7.18 ppm in **8**, respectively. In the ^{11}B NMR spectrum, the center boron peak of **4** was observed as a rather sharp signal, whereas that of **8** became considerably broad. These spectral changes are quite similar to those observed for conversions from axially methoxy-coordinated subporphyrin to benzoyloxy-coordinated subporphyrins,[10] thus supporting for the coordination of a carboxyl group to the boron center in **8** (Scheme 2).



Scheme 2 *Reagents and conditions*: (*e*) toluene reflux; (*f*) CH_2Cl_2–MeOH.

Dimerization of **7** in toluene was faster than that of **4**, and was completed within 3 h at 100 μM concentration to give single product **9** quantitatively. The HR-ESI-TOF mass spectrum of **9** exhibited the sodium adduct cation peak at *m*/*z* 1253.4160 (calc. for $C_{84}O_4H_{52}N_6B_2Na$ = 1253.4152 [**9** + Na]$^+$). Signals due to the peripheral protons (H^a, H^b, H^c and H^d) are high-field shifted from 7.99, 7.33, 7.52 and 7.78 ppm in **7** to 7.00, 6.90, 7.10 and 7.19 ppm in **9**, respectively (Fig. 1). It is worth noting that a doublet due to the vinylene bridge proton H^e is characteristically shifted from 8.20 ppm to 6.6–6.5 ppm as a consequence of both an attenuation of intramolecular hydrogen bonding and a diatropic ring current of the opposite subporphyrin ring.

A single crystal of **9** suitable for X-ray diffraction analysis was obtained by slow recrystallization from a CH_2Cl_2–toluene solution.‡ The solid-state structure of **9** shows a cyclic dimer structure with C_2 symmetric square (Fig. 2). Each boron atom is mutually coordinated by the terminal carboxy substituent of the opposite subporphyrin with B–O bond length of 1.50 Å. Two carbonyl groups are directed inside the square and the distance between two carbonyl-oxygen atoms is 8.41 Å. The inner cavity of the square is roughly defined with *ca.* 8 Å length and *ca.* 6 Å height. The dihedral angle between bridging *meso*-styryl unit and the mean plane of subporphyrin core defined by peripheral six β-carbons is 53.0°, which is comparable to those of other

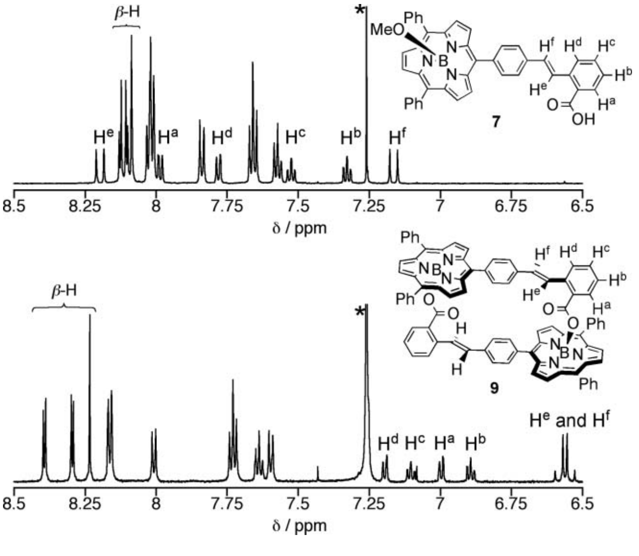


Fig. 1 ^1H NMR spectra of **7** and **9** in $CDCl_3$ (*: solvent peak).

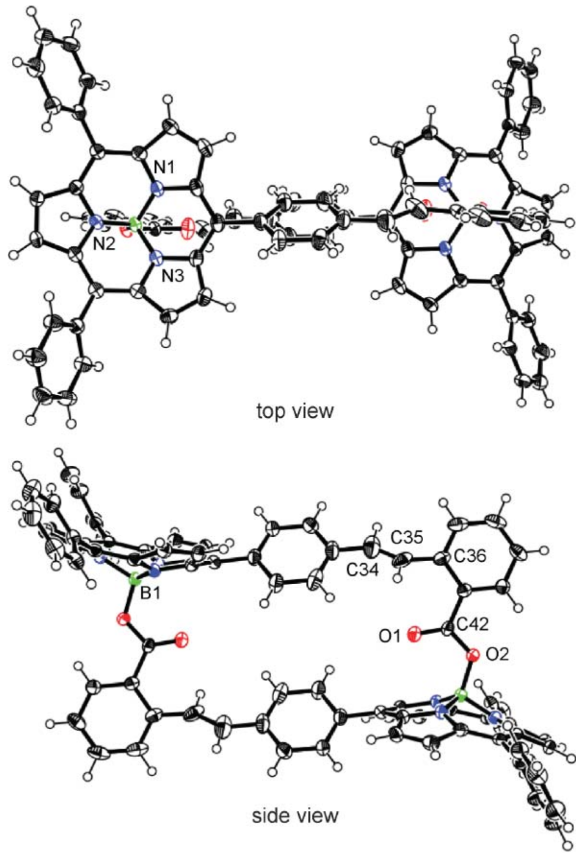


Fig. 2 X-Ray crystal structure of **9** at 50% ellipsoid probability.

subporphyrins possessing *ortho*-H aryl substituents. Interestingly, the 2-carboxyphenyl group is tilted by 27.5° from the *meso*-styryl plane, whereas it coordinates to the boron atom roughly in a perpendicular manner with a dihedral angle of 80.7°. The distortion of stilbene subunit is in line with the observation of weakening of hydrogen bonding interaction between the vinyl C–H^e and carboxyl group in the ^{1}H NMR spectrum.

UV-vis absorption spectra of dimers **8** and **9** are almost the same as those of the monomers **4** and **7**, respectively. The Soret-bands of **4**, **7**, **8** and **9** were observed at 379, 381, 379 and 382 nm, respectively, in CH_2Cl_2. The absorption coefficients of the dimers **8** and **9** are nearly twice larger than those of **4** and **7**, indicating that the electronic interaction between two chromophores is negligible in the ground state. There is no significant difference between the dimer and ester-monomer in fluorescence quantum yield (Φ_F = 0.20, 0.20, 0.21 and 0.20 for **3**, **6**, **8** and **9**, respectively), although slight sharpening was observed in the fluorescence spectra of **8** and **9**.

As reported previously, simply coordinated axial-alkoxy or carboxy ligand of subporphyrin is susceptible to hydrolysis in the presence of water. Thus, we examined the stability of cyclic dimers **8** and **9** toward hydrolysis. A CH_2Cl_2 solution of **9** was washed three times with water, dried over anhydrous sodium sulfate, and the solvent was evaporated. ^{1}H NMR analysis of the residue revealed no fragmentation of **9**. Treatment of **9** with a mixture of CH_2Cl_2 and methanol at 40 °C resulted in complete recovery of the monomer **7**. Thus, these subporphyrins **7** and **9** are quantitatively interconvertible to each other *via* simple azeotropic reflux in toluene and heating in the presence of methanol without tedious procedures. Although **8** has comparable moisture-stability, **4** could not be quantitatively recovered from **8** under the similar conditions, presumably due to the isomerization of a 2-tolancarboxylic acid subunit under the alcoholic conditions.[11] Nevertheless thermal and moisture stable assembly through boron-coordination is an attractive building block for the organization of large discrete subporphyrinic constructions.

In summary, non-C_3-symmetric subporphyrins bearing a 2-carboxyphenyl group have been synthesized by Sonogashira-coupling reaction of *meso*-(4-bromophenyl)-substituted subporphyrin with arylethyne. Quantitative dimerization of **4** and **7** into **8** and **9**, and cleavage from **9** to **7** have been accomplished by simple toluene reflux and methanolysis protocols. Moisture-stable cyclic structures of **8** and **9** would be a promising platform for cyclic, bowled, polyhedral, and sphere-like subporphyrin complexes. Further research on larger subporphyrin supramolecular oligomers using this strategy is now in progress in our laboratory.

This work was partly supported by a Grants-in-Aid (A) (No. 19205006) for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology, Japan. Y. I. appreciates the JSPS Research Fellowships for Young Scientists.

Notes and references

‡ *Crystal data* for **9**: $C_{84}H_{52}B_2N_6O_4{\cdot}2CH_2Cl_2$, M = 1400.79, monoclinic, space group $P2_1/c$ (no. 14), a = 15.823(3), b = 12.328(4), c = 18.763(4) Å, β = 112.961(7)°, V = 3370.0(14) Å^3, T = 123(2) K, Z = 2, D_c = 1.380 g cm^{-3}, μ(Mo-Kα) = 0.237 mm^{-1}, 25828 reflections measured, 5920 unique (R_{int} = 0.069) which were used in all calculations, $R(F^2)$ = 0.0962 (all data), R_1 = 0.0643 ($I > 2\sigma(I)$), GOF = 1.066. CCDC 644925. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b706573f

1 Y. Inokuma, J. H. Kwon, T. K. Ahn, M.-C. Yoon, D. Kim and A. Osuka, *Angew. Chem., Int. Ed.*, 2006, **45**, 961.
2 N. Kobayashi, Y. Takeuchi and A. Matsuda, *Angew. Chem., Int. Ed.*, 2007, **46**, 758.
3 Y. Inokuma, Z. S. Yoon, D. Kim and A. Osuka, *J. Am. Chem. Soc.*, 2007, **129**, 4747.
4 (*a*) C. G. Claessens, D. González-Rodríguez and T. Torres, *Chem. Rev.*, 2002, **102**, 835; (*b*) T. Torres, *Angew. Chem., Int. Ed.*, 2006, **45**, 2834.
5 A. Meller and A. Ossko, *Monatsh. Chem.*, 1972, **103**, 150.
6 (*a*) T. Imamura and K. Fukushima, *Coord. Chem. Rev.*, 2000, **198**, 133; (*b*) J. Wojaczyński and L. Latos-Grażyński, *Coord. Chem. Rev.*, 2000, **204**, 113; (*c*) E. Iengo, E. Zangrando and E. Alessio, *Eur. J. Inorg. Chem.*, 2003, 2371; (*d*) A. Satake and Y. Kobuke, *Tetrahedron*, 2005, **61**, 13.
7 C. G. Claessens and T. Torres, *J. Am. Chem. Soc.*, 2002, **124**, 14522.
8 N. Kobayashi, T. Ishizaki, K. Ishii and H. Konami, *J. Am. Chem. Soc.*, 1999, **121**, 9096.
9 N. A. Cortese and R. F. Heck, *J. Org. Chem.*, 1977, **42**, 3491.
10 Chemical shifts of the axial ligand and center boron for benzoyloxo(5,10,15-triphenylsubporphyrinato)boron(III): ^{1}H NMR δ(ppm) 6.87 (d, J = 6.9 Hz, 2H, benzoate-*o*-H), 6.90 (t, J = 7.2 Hz, 2H, benzoate-*m*-H) and 7.09 (t, J = 7.3 Hz, 1H, benzoate-*p*-H); ^{11}B NMR δ(ppm) −15.4 (br s, 1B).
11 R. L. Letsinger, E. N. Oftedahl and J. R. Nazy, *J. Am. Chem. Soc.*, 1965, **87**, 742.