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Rational Synthesis of A_2B-type *meso*-Triarylsubporphyrins

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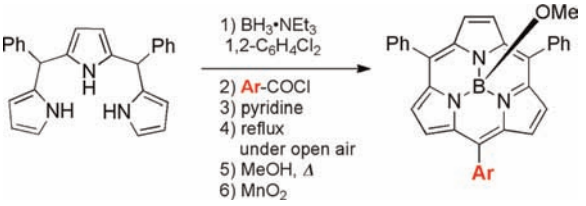
ABSTRACT



Rational synthesis of A_2B-type *meso*-arylsubporphyrins has been accomplished by the condensation of triethylamine−tri-*N*-tripyrromethene−borane with acid chlorides. These subporphyrins are useful for evaluations of the intrinsic substituent effects and the influences of substitution patterns, A_3-type versus A_2B-type substitution.

Subporphyrin, a genuine ring-contracted porphyrin, has emerged as a new functional pigment in light of its bowl-shaped curved macrocycle, distinct 14π aromatic system, strong emission, and intriguing substituent effect of *meso*-aryl groups.[1−3] The synthesis of subporphyrin was first reported as a tribenzosubporphine in 2006,[2a] which was followed by the synthesis of *meso*-aryl-substituted subporphyrins by using tri-*N*-pyrrolylborane or pyridine-tri-*N*-pyrrolylborane as templating precursors.[2b,3a] However, the chemistry of subporphyrin still remains in its infant stage mainly due to its poor synthetic accessibility, and hence, new synthetic methods to produce various subporphyrin derivatives are highly desired. In particular, there had been no rational synthetic route to subporphyrins bearing different *meso*-substituents. Quite recently, we have developed the synthesis of a *meso*-free subporphyrin by the condensation of in situ generated triethylamine−tri-*N*-tripyrromethene−borane (**2**) with trimethyl orthoformate.[4] This *meso*-free subporphyrin was smoothly transformed to *meso*-bromo subporphyrin, from which *meso*-alkynyl, *meso*-alkenyl, and *meso*-alkyl subporphyrins were prepared by metal-catalyzed reactions. We thought that the precursor **2** could be used for straightforward synthesis of A_2B-type subporphyrins by choosing an appropriate reaction partner. In this paper, we disclose our results on the direct and rational synthesis of A_2B-type subporphyrins.

By following our reported method,[4] **2** was generated from tripyrrane **1**[5] with 3 equiv of triethylamine−borane in 1,2-dichlorobenzene at 150 °C for 2 h and was used after

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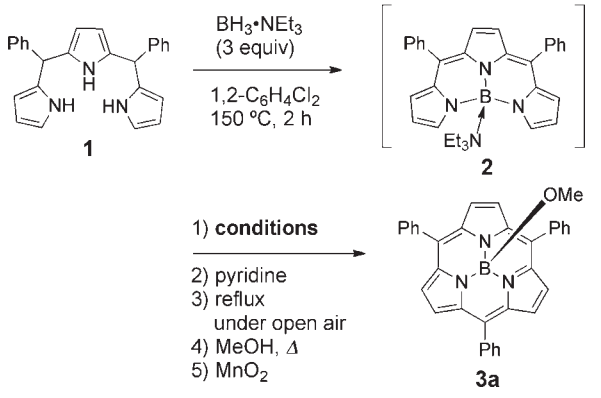
cooling without further purification. First, the condensation of **2** with 10 equiv of benzaldehyde was examined by changing acid. With trifluoroacetic acid (TFA), the reaction proceeded at 0 °C to give **3a** in 4.1% yield (Table 1, entry 1). The yield of **3a** was decreased with $BF_3 \cdot OEt_2$ (entry 2), and both methanesulfonic acid (MSA) and *p*-toluenesulfonic acid (*p*-TsOH) gave only acyclic byproducts (entries 3 and 4). In due course, we found that HCl could be used as an effective acid to produce **3a** in 4.1% yield (entry 5), and a better result was obtained at high temperature (entry 6). It occurred to us that the use of benzoyl chloride instead of benzaldehyde would work similarly or better since HCl would be released from it. This was indeed the case, as **3a** was obtained in a better yield of 6.9% (entry 7), which was drastically improved to 17.7% at 150 °C for 30 min (entry 8). Since benzoyl bromide or trimethyl orthobenzoate was not suitable for this reaction under comparable conditions (entries 9 and 10), both the high reactivity of benzoyl chloride and HCl catalysis might be crucial for the formation of subporphyrins. The reaction mechanism is unclear at this stage but probably involves first aroylation of **2** to form a ketone intermediate followed by intramolecular cyclization with the aid of acid catalysis (see the Supporting Information).[6,7]

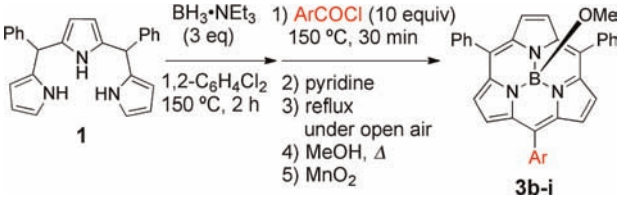
Table 1. Synthesis of 5,10,15-Triphenylsubporphyrin (**3a**)

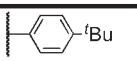
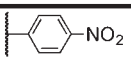
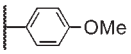
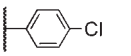
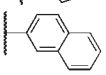
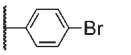
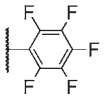


entry	reagent (equiv)	acid (equiv)	conditions	yield (%)
1	PhCHO (10)	TFA (3.3)	0 °C, 1 h	4.1[b]
2	PhCHO (10)	$BF_3 \cdot OEt_2$ (3.3)	0 °C, 1 h	1.2[b]
3	PhCHO (10)	MSA (3.3)	0 °C, 1 h	0
4	PhCHO (10)	*p*-TsOH (3.3)	0 °C, 1 h	0
5	PhCHO (10)	HCl[a] (10)	0 °C, 1 h	4.1[b]
6	PhCHO (10)	HCl[a] (10)	150 °C 30 min	4.6[b]
7	PhCOCl (10)		100 °C 30 min	6.9[c]
8	PhCOCl (10)		150 °C 30 min	17.7[c]
9	PhCOBr (10)		150 °C 30 min	trace
10	trimethyl orthobenzoate (10)		150 °C 30 min	0

[a] Et_2O solution, [b] NMR yield after MnO_2 oxidation.[7] [c] isolated yield.

Table 2. Synthesis of A_2B-Type Subporphyrins (**3b–i**)



product	Ar	yield	product	Ar	yield
3b		6.8%	**3f**		9.3%
3c		4.8%	**3g**		2.0%
3d		6.5%	**3h**		6.3%
3e		11%	**3i**		3.7%

On the basis of the optimized conditions, A_2B-type subporphyrins were prepared with various acid chlorides. The reaction with 4-*tert*-butylbenzoyl chloride afforded subporphyrin **3b** in 6.8% yield (Table 2). In this synthesis, we encountered a problem that the boiling point of the acid chloride (135 °C/20 mmHg) is too high to be completely distilled off, which made product separation quite tedious. Thus, we invented a different workup procedure that involved the addition of ethylenediamine and subsequent rough separation through a silica gel column. The decreased yield of **3b** compared with that of **3a** may be partly attributed to this problem. As a trend, electron-poor acid chlorides gave better yields than electron-rich ones, probably reflecting higher reactivities toward the condensation (Table 2). To our delight, this protocol allowed the synthesis of *meso*-(2-thienyl)subporphyrin **3g** and *meso*-(2-naphthyl) subporphyrin **3h**. Further, even *meso*-(pentafluorophenyl) subporphyrin **3i** that bears two *ortho*-substituents was prepared by this reaction. Unfortunately, this protocol was not applicable to aliphatic acid chlorides.

Figure 1 shows X-ray crystal structures of **3b**, **3c**, and **3g**.[8] The bowl depths were calculated to be 1.368, 1.338,

(6) For the examples of condensation reaction with acid chlorides affording porphyrinoids and BODIPYs, see: (a) Koszarna, B.; Voloshchuk, R.; Gryko, D. T. *Synthesis* **2007**, 1339–1342. (b) Thoresen, L. H.; Kim, H.; Welch, M. B.; Burghart, A.; Burgess, K. *Synlett* **1998**, 1276–1278.

(7) MnO_2 oxidation was conducted to oxidize subchlorins into corresponding subporphyrins in all cases.[2e]

(8) Crystal data for **3b**: $C_{38}H_{32}BN_3O$, 0.23 (C_6H_{14}), 1.53 (CH_2Cl_2), M_w = 707.71, triclinic, space group *P*-1 (No. 2), a = 9.8047(3) Å, b = 11.0075(4) Å, c = 16.8098(5) Å, α = 99.827(2)°, β = 96.5051(19)°, γ = 93.876(2)°, V = 1769.06(10) Å^3, T = 93 K, ρ_{calcd} = 1.329 gcm^{-3}, Z = 2, R_1 = 0.0673 ($I > 2\sigma(I)$), R_w = 0.1998 (all data), GOF = 1.002. CCDC 874758. Crystal data for **3c**: $C_{35}H_{26}BN_3O_2$, M_w = 531.40, monoclinic, space group $P2_1/c$ (No. 14), a = 7.5185(1) Å, b = 19.5104(4) Å, c = 17.6082(4) Å, β = 95.3265(13)°, V = 2571.78(9) Å^3, T = 93 K, ρ_{calcd} = 1.372 gcm^{-3}, Z = 4, R_1 = 0.0950 ($I > 2\sigma(I)$), R_w = 0.2843 (all data), GOF = 0.996. CCDC 874759. Crystal data for **3g**: $C_{32}H_{22}BN_3OS$, M_w = 507.40, monoclinic, space group $P2_1/c$ (No. 14), a = 13.4058(4) Å, b = 13.7067(4) Å, c = 14.2504(4) Å, β = 96.5051(19)°, V = 2452.45(12) Å^3, T = 93 K, ρ_{calcd} = 1.374 gcm^{-3}, Z = 4, R_1 = 0.0849 ($I > 2\sigma(I)$), R_w = 0.2857 (all data), GOF = 1.104. CCDC 874760.

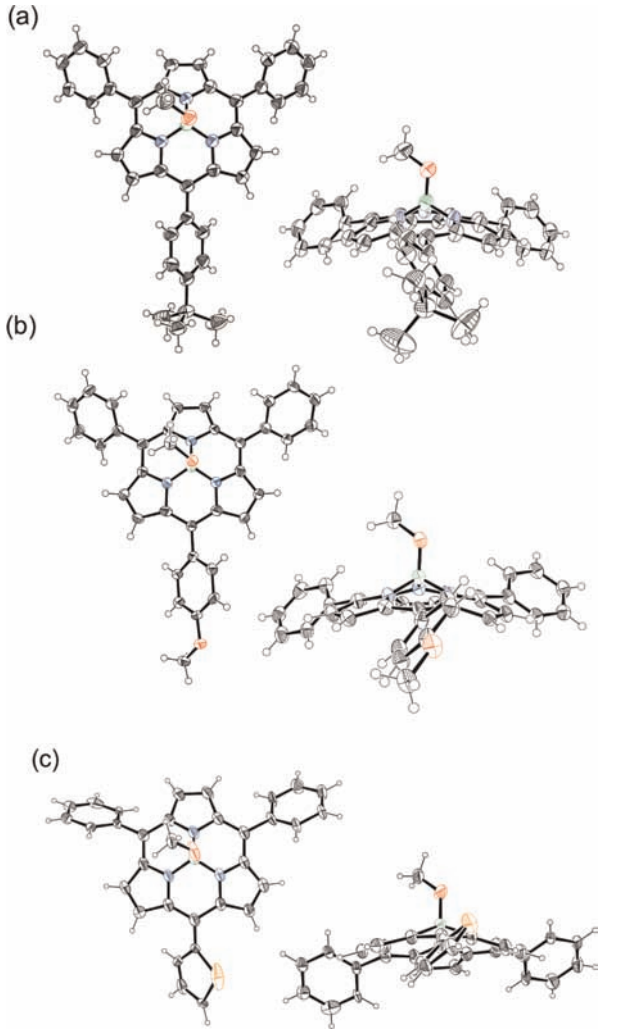


Figure 1. X-ray crystal structures of (a) **3b**, (b) **3c**, and (c) **3g** (left, top view; right, side view). Thermal ellipsoids were scaled to 25% probability. Solvent molecules and disordered parts were omitted for clarity.

and 1.318 Å for **3b**, **3c**, and **3g**, respectively, which are similar to that of **3a** (1.29 Å).[2b] The dihedral angle of thiophene ring toward subporphyrin core in **3g** is 44.10°.

A_2B-type *meso*-aryl subporphyrins prepared in this work are useful for study on the substituent effects on the optical properties in two ways: (1) an intrinsic substituent effect of an aryl substituent and (2) substitution pattern effect, A_3 versus A_2B substitution. Large substituent effects are not observed for 4-*tert*-butylphenyl (**3b**), 4-methoxyphenyl (**3c**), 4-chlorophenyl (**3d**), and 2-naphthyl substituents (**3h**) with respect to the absorption and fluorescence spectra and fluorescence quantum yields (Figure 2, Table 3). The small fluorescence quantum yield of 4-bromophenyl-substituted subporphyrin **3e** is apparently due to internal heavy atom effect, which is smaller than tris(4-bromophenyl)-substituted subporphyrin **4e** (Φ_F = 0.008).[2b] The Soret band of 4-nitrophenyl-substituted subporphyrin **3f** is remarkably broader, and interestingly the fluorescence quantum yield

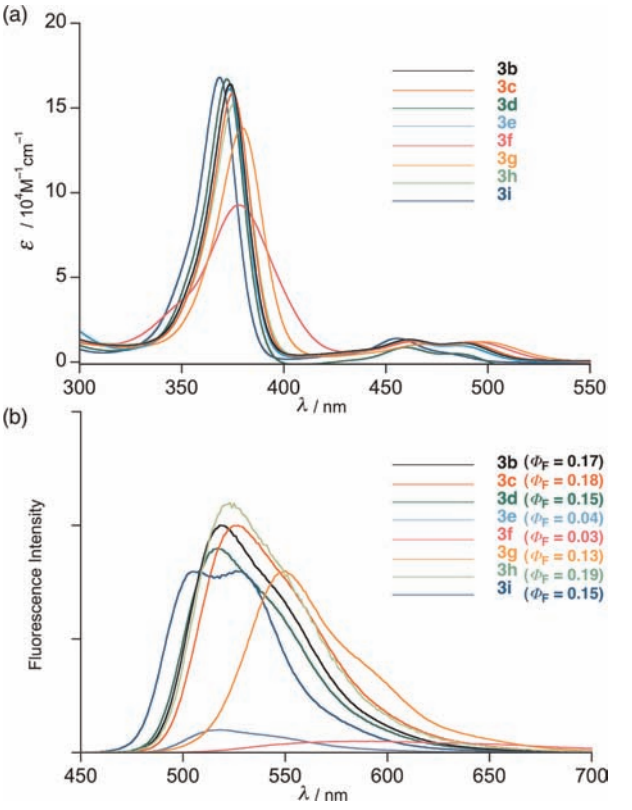


Figure 2. UV/vis absorption (a) and emission (b) spectra of **3b**−**i** in CH_2Cl_2.

of **3f** in CH_2Cl_2 is distinctly smaller than that of **4f**.[2b,9] These optical properties of **3f** may be ascribed to its A_2B-type substitution pattern, which may lead to intramolecular charge-transfer type interactions. In contrast, the substituent effect of 2-thienyl group is additive and hence larger in tris(2-thienyl) substituted subporphyrin **4g** than **3g**.[10] This is accounted for in terms of the intrinsic charge transfer interaction between the subporphyrin core and 2-thienyl substituent. *meso*-Pentafluorophenyl group causes a blue-shift of Soret band of subporphyrin as observed in tris-(pentafluorophenyl)-substituted subporphyrin **4i** (λ_{abs} = 359, 449, and 470 nm, λ_{em} = 487 and 517 nm),[11] such an effect is smaller in **3i**. It is interesting to note that single replacement by pentafluorophenyl group causes a split fluorescence spectrum which is similar to that of **4i**.[11]

The electrochemical potentials of **3a**−**i** were measured by cyclic voltammetry (CV) and differential-pulse voltammetry (DPV) experiments in CH_2Cl_2 containing 0.1 M Bu_4NPF_6 as a supporting electrolyte (Table 4). Parent subporphyrin **3a** exhibited one reversible oxidation wave at 0.71 V and one reversible reduction wave at −1.97 V.[2c]

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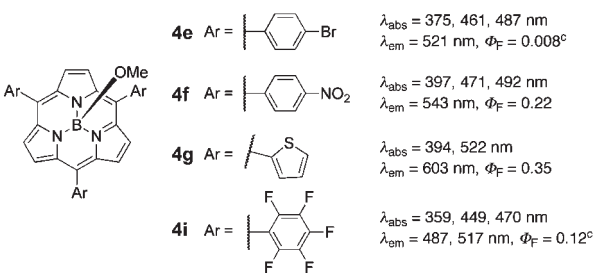
(10) Hayashi, S.; Inokuma, Y.; Osuka, A. *Org. Lett.* **2010**, *12*, 4148–4151.

(11) Saito, S.; Kim, K. S.; Yoon, Z. S.; Kim, D.; Osuka, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 5591–5593.

Table 3. Absorption and Fluorescence Data of **3a**–**i** in CH_2Cl_2 (Reference A_3-Type Molecules **4e**–**g**,**i** Shown below)

compd	absorption λ_{abs} [nm] (ε [10^4 $M^{-1}cm^{-1}$])	fluorescence λ_{em} [nm][a]	Φ_F[b]
3a	373 (16.6), 461 (1.3), 484 (0.9)	516	0.14
3b	374 (16.4), 462 (1.3), 487 (1.1)	521	0.17
3c	375 (15.9), 462 (1.2), 489 (1.1)	527	0.18
3d	372 (16.6), 460 (0.8)	517	0.15
3e	375 (16.1), 461 (1.3), 489 (1.0)	525	0.04
3f	379 (9.3), 462 (1.2), 487 (1.2)	550	0.03
3g	380 (13.8), 462 (1.1), 487 (1.2)	550	0.13
3h	376 (15.2), 462 (1.3), 488 (1.1)	527	0.19
3i	369 (16.8), 462 (1.4)	508, 526	0.15



[a] Excited at the Soret-like band except for **3f** (λ_{ex} = 462 nm). [b] Absolute fluorescence quantum yield. [c] Fluorescence quantum yields were determined with a reference to that of 8-amino-1-naphthalenesulfonic acid (Φ_F = 0.37 in ethanol).

Compounds **3b**, **3c**, and **3e** showed similar features, exhibiting one oxidation potentials at 0.63–0.73 V and one reduction potentials at −1.97–2.03 V. Curiously, the oxidation waves in **3d**, **3f**, **3g**, **3h**, and **3i** were somewhat split with ΔE_{ox} ($= E^{1/2}{}_{ox.2} - E^{1/2}{}_{ox.1}$) = 70–120 mV, while the reduction waves were only shifted. The $E^{1/2}$ potentials of *para*-substituted subporphyrins **3a**–**f** are plotted as a function of Hammett's parameter (σ) (Supporting Information). The first oxidation potentials of **3a**–**f** lie on a linear slope with ρ = 0.166 V, whereas a linear slope with ρ = 0.117 V is obtained when the first reduction potential is plotted except for **3f**. The reaction constants ρ are roughly similar to those of reported triarylsubporphyrins (ρ = 0.105 and 0.124 V for the oxidation and reduction potentials, respectively)[2b] and larger than those of tetraarylporphyrins (ρ = 0.065 and 0.073 V for the oxidation and reduction potentials, respectively),[12] indicating larger substituent effects of subporphyrins. The first reduction potential of −1.57 V in **3f** was considered to be the reduction at the nitrophenyl group ($E^{1/2}$ = −1.6 V for nitrobenzene).[13]

Table 4. Electrochemical Properties[a]

	oxidation		reduction	
compd	$E^{1/2}{}_{ox.2}$	$E^{1/2}{}_{ox.1}$	$E^{1/2}{}_{red.1}$	HOMO–LUMO gap (eV)
3a		0.71	−1.97	2.68
3b		0.69	−2.03	2.72
3c		0.63	−2.02	2.65
3d	0.83	0.76	−1.97	2.73
3e		0.73	−1.97	2.70
3f	0.92	0.82	−1.57	2.39
3g	0.69	0.57	−1.88	2.45
3h	0.81	0.71	−1.91	2.62
3i	1.00	0.88	−1.91	2.79

[a] These values were measured by cyclic voltammetry using a glassy carbon working electrode, platinum wire counter electrode, and $Ag/AgClO_4$ reference electrode. The measurements were carried out in CH_2Cl_2 solutions containing 0.1. M Bu_4NPF_6 as a supporting electrolyte. Potentials versus ferrocene/ferrocenium ion pair. Scan rate: 0.05 V/s.

In summary, we have developed the direct and rational synthesis of A_2B-type *meso*-arylsubporphyrins **3b**–**i** by the condensation of **2** with acid chlorides in 2–11% yields. This method is advantageous by circumventing the presynthesis of the *meso*-free subporphyrin, *meso*-bromination, and metal-catalyzed subsitutiton reactions. In addition, this method may be potentially more suited for achieving high yields of subporphyrins, as suggested by the yield of **3a** (17.7%) which is highest among *meso*-arylsubporphyrins so far reported. Through the examinations of the optical and electrochemical properties of **3a**–**i**, the intrinsic effects of *meso*-aryl substituents and the substituion pattern effects have been studied. This rational synthesis of A_2B-type subporphyrins will be useful for more elaborated molecular systems and is now actively in progress in our laboratory.

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Supporting Information Available. Experimental details and characterization of new compounds and crystal data. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

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