SHORT PAPER

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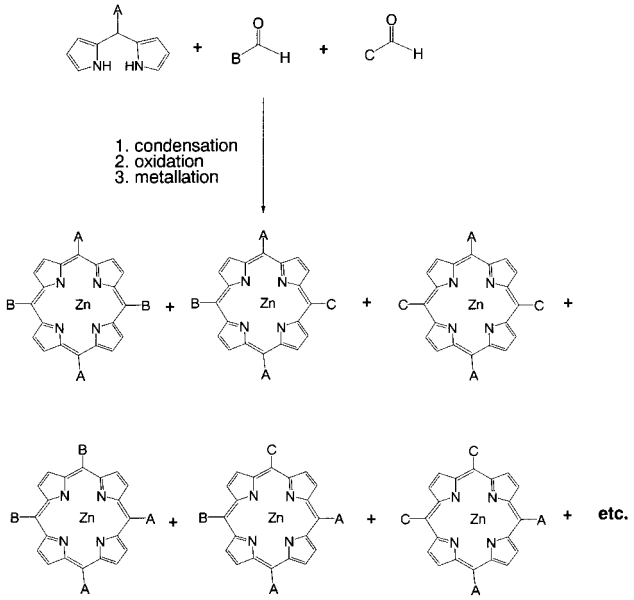
No scrambling in the synthesis of *meso*-substituted porphyrins from one dipyrromethane and aryl aldehydes†

Yasuhiro Suga[a], Takashi Arimura[a]*, Seiji Ide[a], Takuya Nishioka[a], Hideki Sugihara[a], Shigeo Murata[a] and Hirohisa Tsuzuki[b]

[a]*COE Laboratory, National Institute of Materials and Chemical Research, Tsukuba 305-8565, Japan*
[b]*Center of Environmental Analysis, Tohwa University, Fukuoka 815-8510, Japan*

The cross-condensation of dipyrromethane **1** and aryl aldehydes in the presence of trichloroacetic acid in CH_2Cl_2 afforded non-scrambled products in good yields for the first time.

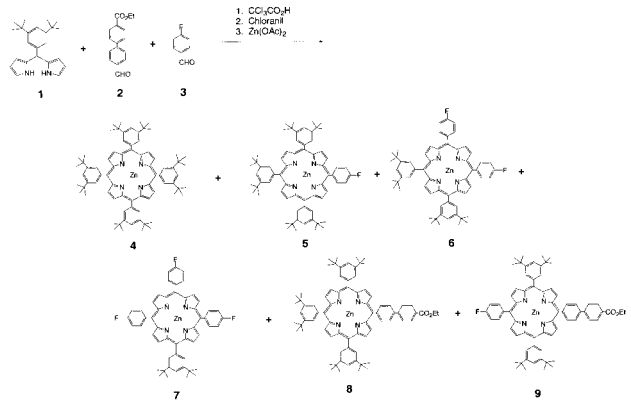
A porphyrin ligand has been demonstrated in a diverse range of metal-catalysed redox reactions. The metal redox property can be controlled by the electronic effects of the peripheral substituents of the porhyrin.[1] Applications of synthetic substituted porphyrins are, therefore, expanding. Sophisticated porphyrin derivatives are of special interest in relation with key structural moieties that include charge separation models that mimic photosynthesis,[2] long-range electron transfer reactions,[3] synthetic receptors for optoelectronic devices,[4] and potential sensitisers for synthetic porphyrins in lipid membrane assemblies.[5] As shown in Scheme 1, the MacDonald-type 2+2 cross condensation[6] of a dipyrromethane and two aldehydes has been adopted to prepare *meso*-substituted porphyrin derivatives. The product from the MacDonald-type reaction is frequently, however, a scrambled mixture of porphyrin that contains the desired porphyrins.[7] As part of our present studies in porphyrin chemistry, we have been making an effort to develop methods for the synthesis of versatile porphyrin bearing a wide range of functionality. In this paper, we describe the synthesis of *meso*-substituted porphyrins from one dipyrromethane and aryl aldehydes that gave no scrambling.



Scheme 1

Results and discussion

The standard reaction conditions for MacDonald-type 2+2 cross-condensation of a dipyrromethane and two aldehydes has been used to prepare *meso*-substituted porphyrins.[8] This technique, however, gives almost a mixture of scrambled porphyrins at a low yield of the desired *trans*-porphyrin.[1] Purification of the products is also difficult. Thus far, the mechanism of the scrambling process in the condensation is poorly elucidated. It is thought that most scrambling should take place prior to the formation of porphyrinogen which is a precursor of a porphyrin. As porphyrins bearing carboxyl groups are very useful in the construction of a linear substitution patterns as photonic devices containing porphyrins joined by amino linkers, we have chosen ethyl 4′–formyl-4-biphenylcarboxylate **2**, which was synthesised according to the literature,[9] and *meso*-(3,5-di-*tert*-butylphenyl)-2,2′–dipyrromethane **1**[10] was employed as to provide enhanced solubility to the porphyrins.



Scheme 2

In principle, the condensation of dipyrromethane derivatives and two aldehydes affords a mixture of three porphyrins. The reaction of dipyrromethane **1** with **2** and 4-fluorobenzaldehyde **3** gave a mixture of six porphyrins (Scheme 2). The crude reaction mixture was purified using column chromatography technique, separated as pure compounds, afforded porphyrin derivatives **4, 5, 6, 7, 8** and **9** in 3%, 13&, 12%, trace, 10%, and 10% yields, respectively. As to the compound **6,** scrambling was observed because of recombination of 4-fluorobenzaldehyde **3.** Interestingly, the compound **7,** which can not be formed by direct condensation of **1** and **3,** was obtained as a trace yield. *Meso*-(4-flourophenyl)-2,2′-dipyrromethane **10** and 3,5-di-*tert*-butylbenzaldehyde **15** were isolated from the reaction mixture in low yields. Analytical data of **10** were

* To receive any correspondence. E-mail: takashi@home.nimc.go.jp
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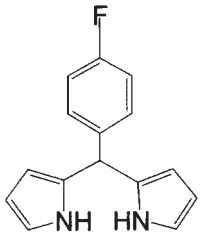
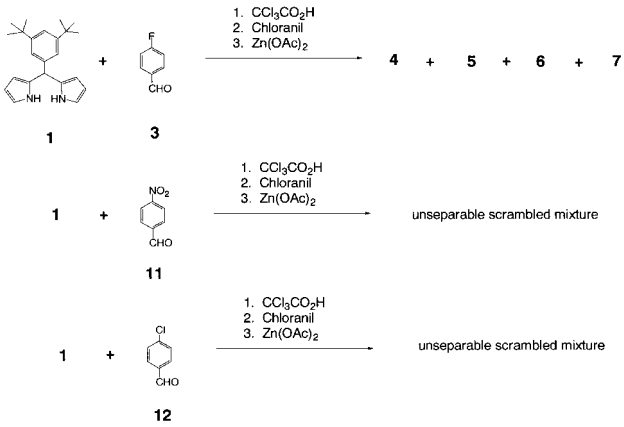
identical with the reported data.[11] Although the detailed scrambling mechanism of formation of **7** is not clear, one might assume that the condensation of 4-fluorobenzaldehyde **3,** dipyrromethanes **1,** and **10** could afford the porphyrin **7.** Strange to say, the tris- or tetrakis-biphenyl-substituted porphyrins was not detected in the reaction mixture (Scheme 2).



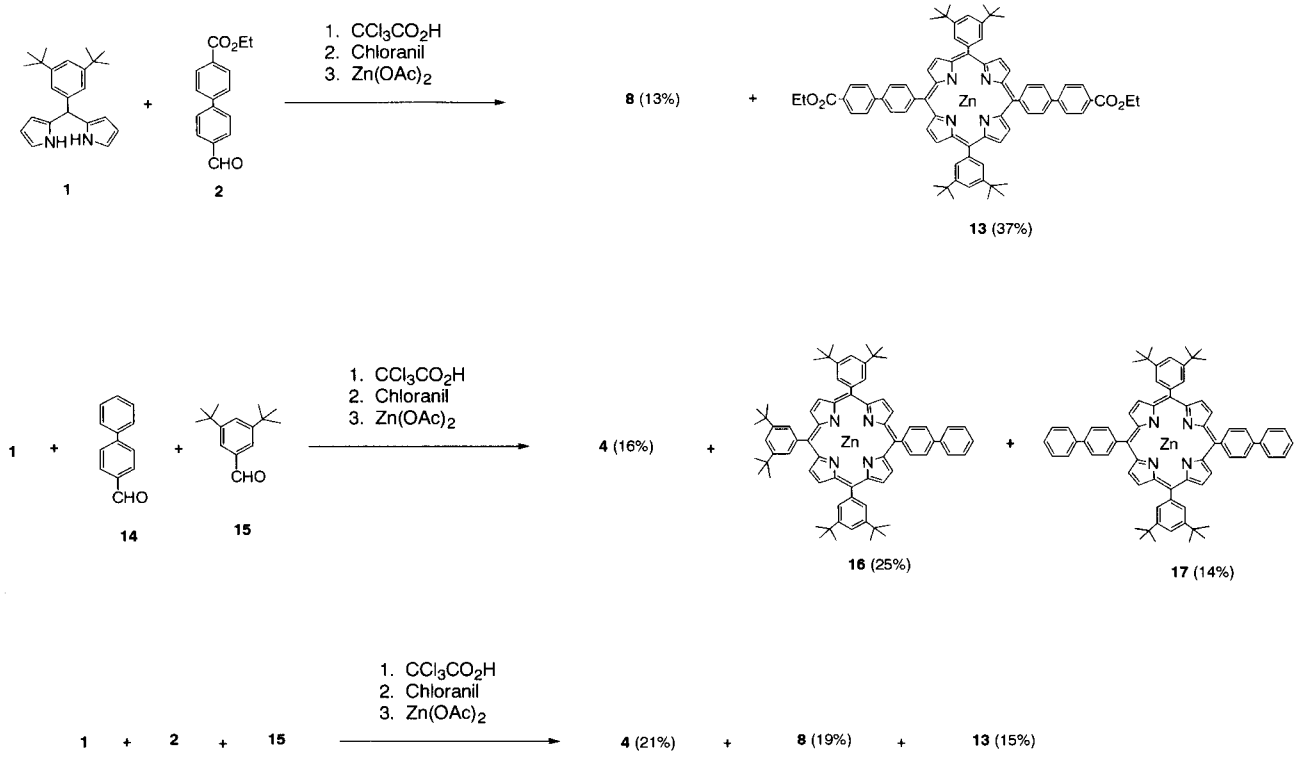
10

To find reaction conditions that give no scrambling at the maximum porphyrin yield, we examined reactions as a function of the aldehyde's substituent. In Scheme 3, the reactions of dipyrromethane **1** and three aldehydes bearing the electron-withdrawing groups are shown. The condensation of **1** with **3** gave a scrambled mixture of four porphyrins, **4, 5, 6,** and **7** in 5%, 12%, 24%, and trace yields, respectively. The reaction of **11** and **12,** having electron-withdrawing groups such as nitro and chloro, with dipyrromethane **1** also afforded a scrambled mixture of four porphyrins which could be extremely difficult to separate, even after careful column chromatography.



Scheme 3

As shown in Scheme 4, the condensation of aryl aldehydes without electron-withdrawing groups with dipyrromethane **1** afforded a mixture of two or three porphyrins. No scrambling was observed, for example, the condensation of dipyrromethane **1,** aldehyde **2,** and 3,5-di-*tert*-butylbenzaldehyde **15** afforded non-scrambled three products**, 4, 8,** and **13** in 21%, 19%, and 15% yields, respectively. Despite scrambling in the MacDonald-type condensation is very difficult to suppress, however, we demonstrated that the cross-condensation of dipyrromethane **1** and aryl aldehydes without electron-withdrawing groups in the presence of trichloracetic acid in CH_2Cl_2 afforded non-scrambled products in good yields for the first time.



Scheme 4

Experimental

Melting points were determined with an electrothermal melting point apparatus in a sealed capillary and are uncorrected. UV-visible spectra were obtained with a Shimadzu UV-3101PC spectrometer. ^{1}H NMR spectra were measured on a Varian XL-300 spectrometer, and the chemical shifts are reported as δ values in ppm. FAB mass spectra were recorded on JEOL-DX303. All chemicals were reagent grade and used without further purification. CH_2Cl_2 was distilled over calcium hydride. All reactions were carried out in an argon atmosphere.

General procedure: Dipyrromethane **1** (180 mg, 0.54 mmol), aldehyde **2** (69 mg, 0.27 mmol), and aldehyde **3** (33 mg, 0.27 mmol) were dissolved in CH_2Cl_2 (70 ml). After the addition of trichloroacetic acid (50 mg, 0.30 mmol) in 10 ml of CH_2Cl_2, the mixture was stirred for 17 h under an argon atmosphere at which time chloranil (420 mg, 1.76 mmol) in 5 ml of CH_2Cl_2 was added and the reaction allowed to stir for an additional 3 hours. This was then washed with aqueous sodium bicarbonate followed by H_2O. The organic layer was then dried over Na_2SO_4. After the solvent was removed, the residue was dissolved in 50 ml of $CHCl_3$ and 2 ml of saturated zinc acetate in methanol was added. After stirring for 1 hour, the solvent was evaporated *in vacuo*. Purification by column chromatography on silica gel (eluting with CH_2Cl_2) gave the porphyrin **(4)** (10 mg, 3%) as a purple powder; m.p.>300ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.52 (72H, s, t-*Bu*), 7.79 (4H, t, *J*=1.5 Hz, Ar*H*), 8.10 (8H, d, *J*=1.8 Hz, Ar*H*), 9.01 (8H, s, pyrrole-*H*); MS (FAB) : *m/z* 1126(M^+); absorption spectrum CH_2Cl_2, λ_{max}) 421.5 (ε = 5.1 × 10^5), 549.5, 587.5 nm. (Found: C, 76.80; H, 7.88; N, 4.35. $C_{76}H_{92}N_4Cn \cdot 2/3CHCl_3$ requires C, 76.32; H, 7.74; N, 4.64%).

Porphyrin **(5)** (40 mg 13%) as a purple powder; m.p.>300ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.53 (54H, s, t-*Bu*), 7.45 (2H, m, Ar*H*), 7.80 (3H, t, *J*=1.8 Hz, Ar*H*), 8.10 (6H, m, Ar*H*), 8.20 (2H, m, Ar*H*), 8.92 (2H, d, *J*=5 Hz, pyrrole-*H*), 9.01 (2H, d, *J*=5 Hz, pyrrole-*H*), 9.02 (4H, s, pyrrole-*H*); MS (FAB) : *m/z* 1132(M^+); HRMS *m/z*[M^+] calcd for $C_{68}H_{75}N_4FZn$ 1030.5267, found 1030.5240; absorption spectrum CH_2C1_2, λ_{max}) 421.0 (ε = 5.5 × 10^5), 549.5, 587.0 nm.

Porphyrin **(6)** (30 mg. 12%) as a purple powder; m.p.>300ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.53 (36H, s, t-*Bu*), 7.45 (4H, m, Ar*H*), 7.81 (2H, t, *J*=2 Hz, Ar*H*), 8.10 (4H, m, Ar*H*), 8.19 (4H, m, Ar*H*), 8.91 (2H, s, pyrrole-*H*), 8.93 (2H, s, pyrrole-*H*), 9.01 (2H, s, pyrrrole-*H*), 9.03 (2H, s, pyrrole-*H*); MS (FAB) : *m/z* 938(M^+); absorption spectrum CH_2Cl_2, λ_{max}) 420.0 (ε = 4.6 × 10^5), 547.5, 584.5 nm. (Found: C, 74.15; H, 5.69; N, 5.24. $C_{60}H_{58}F_2N_4Zn \cdot 1/2CH_2C1_2$ requires C, 74.07; H, 6.06; N, 5.71%).

Porphyrin **(7)** (trace) as a purple powder; m.p.>300ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.53 (18H, s, t-*Bu*), 7.45 (6H, m, Ar*H*), 7.81 (1H, t, *J*=2 Hz, Ar*H*), 8.09 (2H, m, Ar*H*), 8.19 (6H, m, Ar*H*), 8.92-9.03 (8H, m, pyrrole-*H*); MS (FAB) : *m/z* 843(M^+) ; HRMS *m/z*[M+] calcd for $C_{52}H_{41}N_4F_3Zn$ 842.2575, found 842.257; absorption spectrum (CH_2CI_2, λ_{max}) 419.5 (ε = 4.6 × 10^5), 548.0, 586 nm.

Porphyrin **(8)** (30 mg 10%) as a purple powder; m.p.>300ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (3H, t, *J*=7.3 Hz, –CH_2Cl_3), 1.53 (54H, m, t-*Bu*), 4.45 (2H, q, *J*=7.3 Hz, –C*H*$_2$Cl$_3$), 7.80 (3H, t, *J*=2 Hz, Ar*H*), 8.02 (4H, m, biphenyl-*H*), 8.10 (6H, m, Ar*H*), 8.25 (2H, d, *J*=8.4 Hz, biphenyl-*H*), 8.35 (2H, d, *J*=8.1 Hz, biphenyl-*H*), 9.02 (8H, m, pyrrole-*H*); MS (FAB) : *m/z* 1162(M^+); absorption spectrum CH_2C1_2, λ_{max}) 422.5 (ε = 5.0 × 10^5), 549.5, 588.5 nm. (Found: C, 78.06; H, 7.57; N, 4.30. $C_{77}H_{84}N_4O_2Zn \cdot H_2O$ requires C, 78.32; H, 7.34; N, 4.74%).

Porphyrin **(9)** (30 mg. 10%) as a purple powder; m.p.>300ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (3H, t, *J*=7.3 Hz, –CH_2Cl_3), 1.53 (36H, s, t-*Bu*), 4.44 (2H, q, *J*=7.3 Hz, –CH_2Cl_3), 7.45 (2H, m, Ar*H*), 7.81 (2H, t, *J*=2 Hz, Ar*H*), 8.03 (4H, m, biphenyl-*H*), 8.10 (4H, m, Ar*H*), 8.19 (6H, m, Ar*H*), 8.24 (2H, d, *J*=8.7 Hz, biphenyl-*H*), 8.33 (2H, d, *J*=8.1 Hz, biphenyl-*H*), 8.93–9.05 (8H, m, pyrrole-*H*); MS (FAB) : *m/z* 1068(M^+); absorption spectrum CH_2C1_2, λ_{max}) 420.5 (ε = 5.8 × 10^5), 549.5, 588.0 nm. (Found: C, 74.93; H, 5.68; N, 5.15. $C_{69}H_{67}FN_4O_2Zn \cdot 1/3CHCl_3$ requires C, 75.13; H, 6.12; N, 5.05%).

Meso-(4-fluorophenyl)-2,2′-dipyrromethane **10** was prepared by published procedure.[11] Compound **(10)**: colourless prisms; m.p. 80-81 ºC (lit[11], 81 ºC).

3,5-di-*tert*-butylbenzaldehyde **15** was prepared by published procedure.[12] Compound **(15)**: colourless prisms; m.p. 81–83 ºC (lit[12], 82–83 ºC).

To a stirred solution of aldehydes **2** (115 mg, 0.45 mmol) and **15** 98 mg, 0.45 mmol) in 50 ml of CH_2Cl_2 was added a solution of dipyrromethane **1** (300 mg, 0.91 mmol) in 50 ml of CH_2Cl_2. After the mixture was stirred at room temperature under argon for 30 min, a solution of trichloroacetic acid (85 mg, 0.53 mmol) in 10 ml of CH_2Cl_2 was added. The mixture was treated and worked up as described above, to afford three porphyrins **4** (70 mg, 21%), **8** (100 mg, 19%), and **13** (80 mg, 15%).

Porphyrin **(13)**: a purple powder; m.p.>300ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (6H, t, *J*=7.2 Hz, –CH_2Cl_3), 1.55 (36H, s, t-*Bu*), 4.48 (4H, q, *J*=7.2 Hz, –C*H*$_2$Cl$_3$), 7.81 (2H, m, Ar*H*), 8.06 (8H, m, biphenyl-*H*), 8.11 (4H, m, Ar*H*), 8.28 (4H, d, *J*=8.1 Hz, biphenyl-*H*), 8.35 (4H, d, *J*=8.7 Hz, biphenyl-*H*), 9.04 (8H, m, pyrrole-*H*); MS (FAB) : *m/z* 1198(M^+); absorption spectrum CH_2Cl_2, λ_{max}) 422.5 (ε = 4.9 × 10^5), 550.0, 590.0 nm. (Found: C, 75.86; H, 5.87; N, 4.40. $C_{78}H_{76}N_4O_4Zn \cdot 1/3CHCl_3$ requires C, 75.96; H, 6.21; N, 4.52%).

Porphyrin **(16)**: a purple powder; m.p.>300ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.56 (54H, m, t-*Bu*), 7.61 (2H, m, biphenyl-*H*), 7.80 (3H, t, *J*=2 Hz, Ar*H*), 8.00 (5H, m, biphenyl-*H*), 8.10 (6H, m, Ar*H*), 8.32 (2H, d, *J*=8.1 Hz, biphenyl-*H*), 9.02 (8H, m, pyrrole-*H*); MS (FAB) : *m/z* 1090(M^+); absorption spectrum CH_2C1_2, λ_{max}) 422.5 (ε = 5.2 × 10^5), 549.5, 588.5 nm. (Found: C, 75.75; H, 7.05; N, 4.30. $C_{74}H_{80}N_4O_2Zn \cdot 4/5CHC1_3$ requires C, 75.73; H, 6.86; N, 4.72%).

Porphyrin **(17)**: a purple powder; m.p.>300ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.56 (36H, s, t-*Bu*), 7.61 (4H, m, biphenyl-*H*), 7.80 (2H, m, Ar*H*), 8.00 (10H, m, biphenyl-*H*), 8.10 (4H, m, Ar*H*), 8.32 (4H, d, *J*=8.1 Hz, biphenyl-*H*), 9.05 (8H, m, pyrrole-*H*); MS (FAB): *m/z* 1054(M^+); absorption spectrum CH_2Cl_2, λ_{max}) 423.0 (ε = 5.0 × 10^5), 549.5, 590.0 nm. (Found: C, 75.98; H, 5.98; N, 4.50. $C_{72}H_{68}N_4Zn \cdot 4/5CHCl_3$ requires C, 76.02; H, 6.03; N, 4.87%).

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References

1 D. Dolphin, ed. *The Porphyrins*, Academic, New York, 1978.
2 (a) D. Gust, T.A. Moore and A.L. Moore, *Acc. Chem. Res.*, 1993, **26,** 198; (b) J.-P. Collin, A. Harriman, V. Heitz, F. Odobel and J.-P. Sauvage, *Coord. Chem. Rev.*, 1996, **148,** 63.
3 (a) M.R. Wasielewski, *Chem. Rev.*, 1992, **92**, 435; (b) J.L. Sessler, B. Wang, S.L. Springs and C.T. Brown, *Electron and Energy Transfer Reactions in Non-covalently Linked, Supramolecular Model Systems in Comprehensive Supramolecular Chemistry*, Y. Murakami ed., Pergamon Press Ltd, Oxford, 1996, vol. 4, Ch. 9, pp. 311–335 and references therein; (c) T. Arimura, S. Ide, H. Sugihara, S. Murata and J.L. Sessler, *New J. Chem*., 1999, **23,** 977.
4 R.W. Wagner, J.S. Lindsey, J. Seth, V. Palaniappan and D.F. Bocian, *J. Am. Chem. Soc.*, 1996, **118**, 3996 and references therein.
5 A.P.H.J. Schenning, J.H.L. Spelberg, M.C.P.F. Driessen, M.J.B. Hauser, M.C. Feiters and R.J.M. Nolte, *J. Am. Chem. Soc.*, 1995, **117**, 12655 and references therein.
6 P. Arsenault, E. Bullock and S.F. MacDonald, *J. Am. Chem. Soc.*, 1960, **82**, 4384.
7 K.M. Smith, *In Porphyrins and Metalloporphyrins;* K.M. Smith, ed.; Elsevier, Amsterdam, 1975, pp 29-58.
8 J.S. Lindsey, I.C. Schreiman, H.C. Hsu, P.C. Kearney and A.M. Marguerettaz, *J. Org. Soc.*, 1987, **52**, 827.
9 J.C. Craig and J.W. Loder, *J. Chem. Soc.*, **1965,** 100.
10 N. Yoshida, H. Shimidzu and A. Osuka, *Chem. Lett.*, **1998,** 55.
11 B.J. Litter, M.A. Miller, C.-H. Hung, R.W. Wagner, D.F. O'Shea, P.D. Boyle and J.S. Lindsey, *J. Org. Chem.*, 1999, **64,** 1391.
12 W.M. Schubert and R.G. Minton, *J. Am. Chem. Soc.*, 1960, **82,** 6188.