A new synthesis of [2,3]naphthoporphyrins

Satoshi Ito,[a] Naoyuki Ochi,[a] Hidemitsu Uno,[b] Takashi Murashima[a] and Noboru Ono*[a]

[a] *Department of Chemistry, Faculty of Science, Ehime University, Matsuyama 790-8577, Japan. E-mail: ononbr@dpc.ehime-u.ac.jp*

[b] *Advanced Instrumentation Center for Chemical Analysis, Ehime University, Matsuyama 790-8577, Japan*

Received (in Cambridge, UK) 20th March 2000, Accepted 14th April 2000

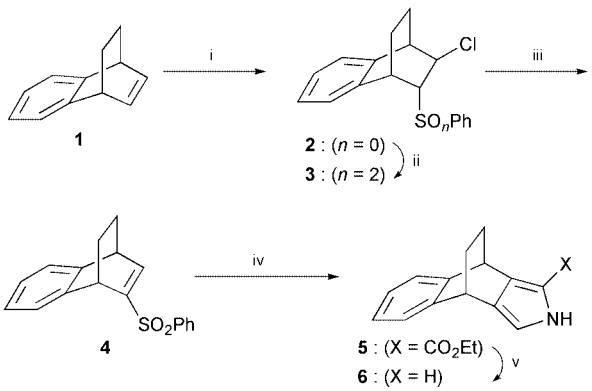
A new synthesis of [2,3]naphthoporphyrins using 4,9-ethano-*2H*-benz[*f*]isoindole as a synthon of *2H*-benz[*f*]-isoindole is described; soluble precursors of [2,3]naphthoporphyrins are converted into insoluble [2,3]naphthoporphyrins by simply heating at 290 °C.

Highly conjugated porphyrins have attracted attention as conducting materials, near-IR dyes, nonlinear optical materials,[1] or photosensitizers for photodynamic therapy (PDT) of cancer tissues on *in vivo* studies.[2] We and Lash *et al*. have reported syntheses of various highly conjugated porphyrins using pyrroles fused with polycyclic aromatic rings.[3] The requisite pyrroles are prepared by the reaction of polycyclic aromatic nitro compounds with ethyl isocyanoacetate. However, this method has a severe limitation. The reaction of nitrobenzene and nitronaphthalene with ethyl isocyanoacetate does not give the desired isoindole[4] and benz[*f*]isoindole.[5] In general, such isoindole derivatives are very difficult to prepare owing to their instability. In addition, highly conjugated porphyrins and their metal complexes are very difficult to purify, since they are insoluble in most organic solvents.[6] We have reported a simple solution of these problems using 4,7-dihydro-4,7-ethano-*2H*-isoindole as a synthon of isoindole for benzoporphyrin synthesis.[7,8] Thus, heating porphyrins fused with bicyclo[2.2.2]octadiene rings at 200–230 °C results in clean formation of benzoporphyrins *via* retro Diels–Alder reaction; the products are pure and do not require further purification. Here, we report a new synthesis of [2,3]naphthoporphyrins using a similar strategy, in which 4,9-ethano-*2H*-benz[*f*]isoindole is used as a synthon of *2H*-benz[*f*]isoindole.

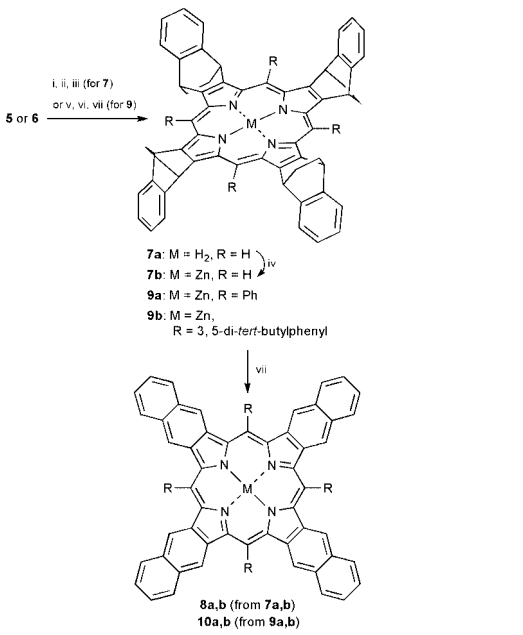
The synthesis of 4,9-dihydro-4,9-ethano-*2H*-benz[*f*]isoindole **6** is summarized in Scheme 1.† 1,4-Dihydro-1,4-ethanonaphthalene **1** was converted into sulfide **2** by reaction with PhSCl. Oxidation of **2** with *m*-CPBA followed by treatment with DBU gave α,β-unsaturated sulfone **4**. The pyrrole **5** was prepared in good yield by treatment of **4** with ethyl isocyanoacetate in the presence of 2.0 equivalents of Bu^{t}OK.[9] Deethoxycarbonylation upon heating **5** with KOH in ethylene glycol at 165 °C gave 4,9-dihydro-4,9-ethano-*2H*-benz[*f*]-isoindole **6** in 83% yield.

Porphyrin **7a** was prepared from pyrrole **5** by reduction with $LiAlH_4$ at 0 °C followed by subsequent tetramerization and oxidation. Various metals can be introduced into **7a** by the usual method using metal acetates. Porphyrins **7a**,**b** were purified by column chromatography (alumina, $CHCl_3$) followed by washing the resulting powder with MeOH–H_2O (*ca.* 1:1). Porphyrins **7a**,**b** were converted into pure tetranaphtho[2,3-*b*;2′,3′-*g*;2″,3″-*l*;2‴,3‴-*q*]porphyrins **8a**,**b** in 100% yield by heating at 290 °C under vacuum (10 mm Hg) for 10 min. Thus, porphyrins **7a**,**b** can be regarded as soluble equivalents of the corresponding tetra[2,3]naphthoporphyrins **8a**,**b**. The reaction of **6** with benzaldehydes in the presence of $BF_3{\cdot}OEt_2$ followed by oxidation and metallation gave *meso*-tetraarylated porphyrin zinc complexes **9a**,**b**. They were also converted into the corresponding *meso*-tetraarylnaphtho[2,3-*b*;2′,3′-*g*;2″,3″-*l*;2‴,3‴-*q*]porphyrin zinc complexes **10a**,**b** in 100% yield by heating at 290 °C *in vacuo* for 10 min (Scheme 2).

Mono[2,3-*b*]naphthoporphyrin **13** was also prepared in 100% yield by heating porphyrin **12** at 290 °C (Scheme 3).† Porphyrin **12** was prepared by the well established 3 + 1 approach consisting of the reaction of tripyrrane **11** with 3,4-diethylpyrrole-2,5-dicarbaldehyde followed by oxidation.[10] The requisite **11** was prepared by the reaction of **6** with 2.0 equivalents of *tert*-butyl 5-acetoxymethyl-4-butyl-3-methyl-1*H*-pyrrole-2-carboxylate in Pr^{i}OH–AcOH.

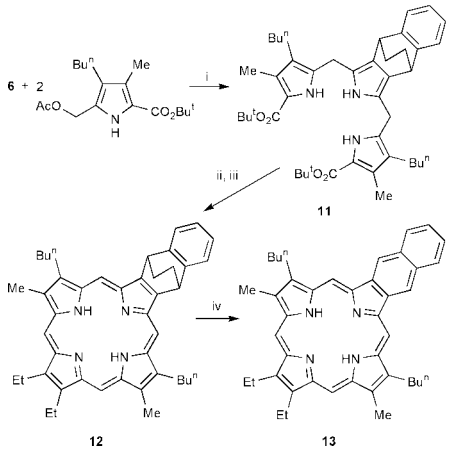


Scheme 1 *Reagents and conditions*: i, PhSCl, CH_2Cl_2, −78 °C, 1 h, 99%; ii, *m*-CPBA, $CHCl_3$, room temp., 2 h, 99%; iii, DBU, THF, 0 °C, 30 min, 99%; iv, ethyl isocyanoacetate, Bu^{t}OK, THF, 0 °C, 3 h, 91%; v, KOH, $HO(CH_2)_2OH$, 165 °C, 1.5 h, 83%.



Scheme 2 *Reagents and conditions*: i, $LiAlH_4$, THF, 0 °C, 1 h; ii, *p*-TsOH, $CHCl_3$, room temp., 15 h; iii, *p*-chloranil, room temp., 24 h, 20% (three steps from **5**); iv, Zn(OAc), $CHCl_3$–MeOH (9:1), room temp., 30 min, 95%; v, ArCHO, $BF_3{\cdot}OEt_2$, $CHCl_3$, room temp., 4 h; vi, *p*-chloranil, room temp., 4 h; vii, $Zn(OAc)_2$, $CHCl_3$–MeOH (9:1), room temp., 30 min (**9a** = 39%; **9b** = 16%, for three steps from **6**); viii, 290 °C, 10 min, 100%.

DOI: 10.1039/b002213f



Scheme 3 *Reagents and conditions*: i, AcOH–Pr^{i}OH (1 : 1), reflux, 17 h; ii, 3,4-diethylpyrrole-2,5-carbaldehyde, TFA, room temp., 2 h; iii, Et_3N, DDQ, $CHCl_3$, room temp., 1 h, 18% for three steps; iv, 290 °C, 100%.

Table 1 Selected UV–VIS data for [2,3]naphthoporphyrins and their precursors

Porphyrin	λ_{max} ($CHCl_3$)/nm ($\log_{10}\varepsilon$)
7a	392 (5.20), 495 (4.14), 527 (3.66), 563 (3.69), 615 (3.12)
8a[a]	359 (0.34), 419 (0.50), 464 (1.00), 697 (0.13), 773 (0.87)
9a	349 (3.29), 426 (5.43), 549 (4.17)
10a	487 (4.96), 662 (3.73), 723 (4.87)
12	399 (5.17), 497 (4.12), 531 (3.86), 566 (3.73), 619 (3.49)
13	419 (5.34), 519 (3.92), 551 (4.53), 587 (3.75), 643 (4.34)

[a] In 5% TFA–$CHCl_3$; here relative intensities are given in parentheses.

Absorption spectrum data of [2,3]naphthoporphyrins and their precursors are summarized in Table 1. As porphyrin **8a** was insoluble in most solvents, its absorption spectrum was measured in 5% TFA-$CHCl_3$. The Soret and Q bands of the dication **8a** were observed at 464, 697 and 773 nm, respectively. The absorbance at 773 nm is unusually intense (0.87 × that of Soret band), showing behaviour reminiscent of phthalocyanines. *meso*-Tetraphenyltetra[2,3]napthoporphyrin **10a** was moderately soluble in organic solvents such as CH_2Cl_2 or $CHCl_3$. The Soret band of **10a** was rather weak compared to that of other porphyrins, owing to steric hindrance between *meso*-Ph and fused [2,3]naphthalene rings. By contrast, the intensity of the absorption at 723 nm is very strong ($\log_{10}\varepsilon$ = 4.87), this value is considerably larger than that of known π-extended *meso*-tetraphenylporphyrins.[3] The UV–VIS spectrum of **13** is rhodo-type (Q band: III > I > IV > II) which is typical for monobenzoporphyrins.[7]

In conclusion, we have succeeded in developing a new strategy for the preparation of [2,3]naphthoporphyrins using 4,9-ethano-2*H*-benz[*f*]isoindole as a synthetic equivalent of 2*H*-benz[*f*]isoindole. This strategy may extend to the synthesis of other π-extended molecules such as polypyrroles or pyrrole oligomers, which are fused with naphthalene rings.

The work was partly supported by Grants-in Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture of Japan. We are also grateful to Dr Y. Takahashi (JEOL) for recording the FAB mass spectra of porphyrins (**8a** and **10a**).

Notes and references

† New compounds gave satisfactory elementary analyses. *Selected data*: for **5**: white plates, mp 144–145 °C, ^{1}H NMR ($CDCl_3$, *J*/Hz) δ 1.39 (3H, t, *J* 7.08), 1.58–1.80 (4H, m), 4.28 (1H, m), 4.33 (2H, q, *J* 7.33, 14.16), 4.79 (1H, m), 6.66 (1H, d, *J* 2.44), 7.04–7.13 (2H, m), 7.16–7.32 (2H, m), 8.41 (1H, br s); *m/z* 267 (M^+, 9), 239 (95), 193 (100). For **6**: white needles, mp 182–183 °C, ^{1}H NMR ($CDCl_3$) δ 1.65–1.83 (4H, m), 4.26 (2H, m), 6.53 (2H, d, *J* 2.44), 7.03–7.07 (2H, m), 7.18–7.22 (2H, m), 7.53 (1H, br s); *m/z* (EI) 195 (M^+, 14), 167 (100). For **7a** (a mixture of four isomers): ^{1}H NMR ($CDCl_3$) δ −4.66 (2H, br s), 2.15–2.52 (16H, m), 6.18 (8H, m), 7.25 (8H, m), 7.80 (8H, m), 10.52 (4H, m); *m/z* (FAB) 823 (M^+ + 1). Calc. for $C_{60}H_{46}N_4{\cdot}0.5H_2O$: C, 86.61; H, 5.69; N, 6.73. Found: C, 86.49; H, 5.71; N, 6.53%. For **8a**: *m/z* (FAB) not assigned. Calc. for $C_{52}H_{30}N_4{\cdot}H_2O$: C, 85.69; H, 4.43; N, 7.69. Found: C, 85.92; H, 4.31; N, 7.62%. For **9a** (a mixture of four isomers): ^{1}H NMR ($CDCl_3$) δ 1.0–2.2 (16H, m), 3.77 (8H, m), 6.9–7.2 (16H, m), 7.9–8.6 (20H, m); *m/z* (FAB) 1189 (M^+). Calc. for $C_{84}H_{60}N_4{\cdot}3.5H_2O$: C, 80.47; H, 5.39; N, 4.47. Found: C, 80.44; H, 5.35; N, 4.21%. For **10a**: ^{1}H NMR ($CDCl_3$) δ 7.48 (8H, m), 7.67 (8H, s), 7.69 (8H, m), 7.98 (8H, m), 8.11 (4H, m), 8.39 (8H, m); *m/z* (FAB) 1076 (M^+). Calc. for $C_{76}H_{44}N_4{\cdot}2.5H_2O$: C, 81.24; H, 4.40; N, 4.99. Found: C, 81.53; H, 4.58; N, 4.84%. For **12**: ^{1}H NMR ($CDCl_3$) δ −3.95 (2H, br s), 1.15 (6H, t, *J* 7.33), 1.81 (4H, m), 1.92 (6H, t, *J* 7.33), 2.21 (2H, m), 2.28–2.39 (4H, m), 2.31 (2H, m), 3.63 (6H, s), 4.09–4.14 (8H, m), 6.07 (2H, m), 7.25 (2H, m), 7.78 (2H, m), 10.11 (2H, s), 10.23 (2H, s); *m/z* (FAB) 635 (M^+ + 1). Calc. for $C_{44}H_{50}N_4{\cdot}CH_3OH$: C, 81.04; H, 8.16; N, 8.40. Found: C, 81.38; H, 8.18; N, 8.11%. For **13**: ^{1}H NMR ($CDCl_3$) δ −3.52 (2H, br s), 1.14 (6H, t, *J* 7.32), 1.78 (4H, m), 1.89 (6H, t, *J* 7.32), 2.29 (4H, m), 3.63 (6H, m), 3.93–4.12 (8H, m), 7.80 (2H, m), 8.51 (2H, m), 9.56 (2H, s), 9.96 (2H, s), 10.18 (2H, s); *m/z* (FAB) 607 (M^+ + 1). Calc. for $C_{42}H_{46}N_4{\cdot}0.5H_2O$: C, 81.91; H, 7.69; N, 9.10. Found: C, 81.78; H, 7.64; N, 8.78%.

1 S. A. Vinogradov and D. F. Wilson, *J. Chem. Soc., Perkin Trans. 2*, 1995, 103; P. Chen, A. S. Dvornikov, M. Nakashima, J. F. Roach, D. M. Alabran and P. M. Rentzepis, *J. Phys. Chem.*, 1996, **100**, 17 507.
2 R. Bonnett, *Chem. Soc. Rev.*, 1995, **24**, 19 and references therein.
3 N. Ono, H. Hironaga, K. Ono, S. Kaneko, T. Murashima, T. Ueda, C. Tsukamura and T. Ogawa, *J. Chem. Soc., Perkin Trans. 1*, 1996, 417; T. D. Lash, P. Chandrasekar, A. T. Osuma, S. T. Chaney and J. D. Spence, *J. Org. Chem.*, 1998, **63**, 8455.
4 R. Bonnett and S. A. North, *Adv. Heterocycl. Chem.*, 1981, **29**, 341.
5 J. E. Shields and J. Bornstein, *Chem. Ind. (London)*, 1967, 1404; W. Rettig and J. Wirz, *Helv. Chim. Acta*, 1976, **59**, 1054; D. E. Remy and F. H. Bissett, *J. Org. Chem.*, 1978, **43**, 4469.
6 M. Rein and M. Hanack, *Chem. Ber.*, 1988, **121**, 1601; A. M. Vorotnikov, V. N. Kopranenkov and E. A. Lukyanets, *J. Gen. Chem., USSR*, 1991, **61**, 1128; N. Kobayashi, W. A. Nevin, S. Mizunuma, H. Awaji and M. Yamaguchi, *Chem. Phys. Lett.*, 1993, **205**, 51; A. C. Tome, P. S. S. Lacerda, M. G. P. M. S. Neves and J. A. S. Cavaleiro, *Chem. Commun.*, 1997, 1199.
7 S. Ito, N. Ochi, T. Murashima, H. Uno and N. Ono, *Heterocycles*, 2000, **52**, 399 and references therein.
8 S. Ito, T. Murashima and N. Ono, *J. Chem. Soc., Perkin Trans. 1*, 1997, 3161.
9 Pyrrole synthesis from α,β-unsaturated sulfones; Y. Abel and F.-P. Montforts, *Tetrahedron Lett.*, 1997, **38**, 1745.
10 T. D. Lash, *Chem. Eur. J.*, 1996, **2**, 1197 and references therein.