A new synthesis of benzoporphyrins using 4,7-dihydro-4,7-ethano-*2H*-isoindole as a synthon of isoindole

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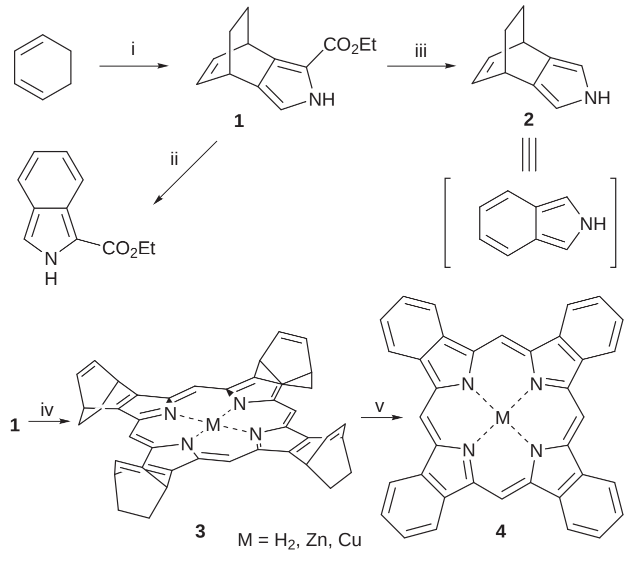
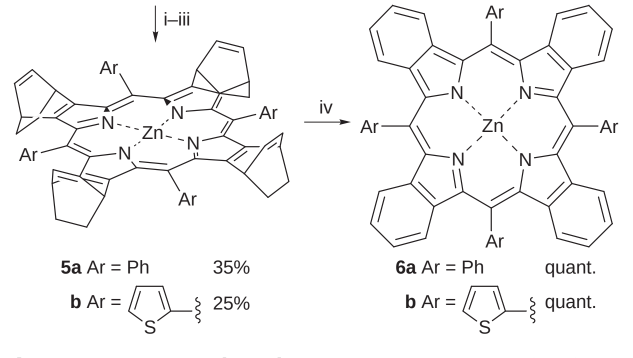
Heating 4,7-dihydro-4,7-ethano-2*H*-isoindole at 200 °C induces the retro-Diels–Alder reaction to give isoindole in essentially quantitative yield, which can be applied to a new synthesis of tetrabenzoporphyrins and monobenzoporphyrins.

Pyrroles fused with aromatic rings, namely isoindoles, may be useful as precursors of polypyrroles with low band gap[1] and benzoporphyrins.[2] However, unsubstituted isoindole is too unstable to be used directly for the preparation of such compounds.[3] Recently we have developed a new synthesis of isoindoles *via* the Barton–Zard pyrrole synthesis using aromatic nitro compounds and ethyl isocyanoacetate, from which polypyrroles and porphyrins fused with various aromatic rings have been prepared.[1,2] However, this method is not applicable to the synthesis of unsubstituted isoindole, for nitrobenzene does not react with ethyl isocyanoacetate. Here we report a very simple method for the synthesis of isoindole. Ethyl 4,7-dihydro-4,7-ethano-*2H*-isoindole-1-carboxylate **1** was prepared by the reaction of the Diels–Alder reaction of 1,3-cyclohexadiene with β-sulfonylnitroethylene followed by the treatment with ethyl isocyanoacetate.[4] De-ethoxycarbonylation by heating **1** with KOH in ethylene glycol at 170 °C gave **2**,[‡] which acted as a masked isoindole (Scheme 1). Namely, heating **2** at 200–230 °C causes a retro-Diels–Alder reaction, the product of which can be trapped in about 70% yield with reactive dienophiles such as *N*-phenylmalenimide[5] Although there are many possibilities for the use of **1** or **2** as an isoindole synthon, here we focus on the synthesis of benzoporphyrins. Porphyrin **3**,[4] which was prepared from **1** *via* reduction of the ester function with $LiAlH_4$ followed by tetramerization and oxidation, was converted into tetrabenzoporphyrin **4** in 100% yield by heating at 200 °C for 10 min. In general, it is rather difficult to handle tetrabenzoporphyrin and its metal complexes due to their low solubility in most organic solvents. This difficulty is now resolved by the use of porphyrin **3** and its metal complexes, as they are soluble in CH_2Cl_2 and can be converted into **4** in quantitative yield by simply heating at 200 °C. Various kinds of metal complexes (Zn, Cu, Ni, Fe, *etc.*) of **3** were readily prepared by the conventional method[6] and purified by column chromatography and recrystallization from CH_2Cl_2–MeOH. They were soluble in $CHCl_3$ and CH_2Cl_2. The metal complexes of porpyrin **3** were converted into the corresponding metal complexes of **4** in essentially quantitative yield by heating at 200 °C. By using this method, various materials coated with metal complexes of **4** which may be important for electronic applications are readily prepared. For example, a glass slide coated with Zn-**3** (λ_{max} 405, 525, 560 nm) was prepared using a solution of Zn-**3** in CH_2Cl_2; this was changed into a glass slide coated with Zn-**4** (λ_{max} 454, 617, 696 nm) by heating at 200 °C for 10 min.

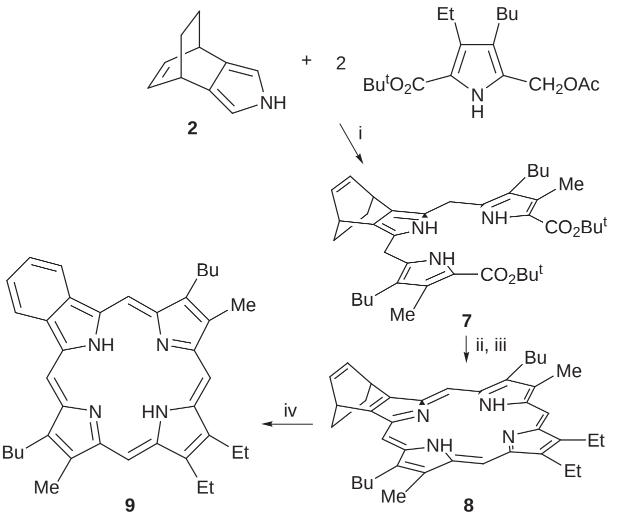


Scheme 1 *Reagents and conditions*: i, ref. 4, 60% for two steps; ii, 200 °C, 10 min; iii, KOH, $HOCH_2CH_2OH$, 170 °C, 2 h, 81%; iv, ref. 4, 30%; v, 200 °C, 10 min, quant.

Other syntheses of benzoporphyrins using **2** as an isoindole synthon are shown in Schemes 2 and 3. The reaction of **2** with aromatic aldehydes in the presence of $BF_3\cdot OEt_2$ followed by oxidation gave *meso*-tetraarylated porphyrins **5** in 25–35% yield, which were converted into the corresponding benzoporphyrins **6** in quantitative yield by heating at 200 °C for 10 min. Thus, pyrrole **2** can be used as a masked isoindole in benzoporphyrin synthesis. As pointed out by Bonnet, the chemistry of benzoporphyrins has been relatively neglected due to their synthesis being difficult, although they have potential uses as electro-optical, molecular electronic and photodynamic therapeutic materials.[7] Now various types of benzoporphyrins can be prepared *via* the use of **2** as an isoindole synthon. As a typical example, monobenzoporphyrin **9** was prepared in quantitative yield by heating porphyrin **8** at 200 °C for 10 min, as shown in Scheme 3. Porphyrin **8** was prepared by the well-established method *via* a 3 + 1 approach consisting of the reaction of tripyrrane **7** with pyrrole-2,5-dicarbaldehyde followed by oxidation.[8] The requisite **7** was readily prepared by the reaction of **2** with 2-acetoxymethylpyrroles. The UV–VIS



Scheme 2 *Reagents and conditions*: i, $BF_3\cdot OEt_2$; ii, $Zn(OAc)_2$; iii, *p*-chloranil; iv, 200 °C, 10 min



Scheme 3 *Reagents and conditions*: i, AcOH–EtOH, reflux, 16 h; ii, 3,4-diethylpyrrole-2,5-dicarbaldehyde, TFA, room temp., 2 h; iii, DDQ, $CHCl_3$, room temp., 1 h, 11% for three steps; iv, 200 °C, 10 min, quant.

spectrum of **8** (λ_{max} 398, 497, 529, 566, 619 nm; band strength IV > III > II > I) indicated that **8** was readily converted to **9** (λ_{max} 404, 504, 541, 574, 629 nm; band strength III > I > IV > II); these were in good agreement with those reported in the literature.[7,9]

In conclusion, we have described a new synthesis of benzoporphyrins using **1** or **2** as insoindole synthons which is superior to the existing methods in its simplicity and generality. It should be emphasized that formation of benzoporphyrns **4**, **6** and **9** can be achieved by simple heating. This process is a very clean reaction and purification of products is not usually necessary if precursors **3**, **5** and **8** are pure. This method could be extended to the preparation of other π-extended molecules including polypyrroles fused with aromatic rings, which is now in progress in our laboratory.

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Notes and References

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‡ All new compounds gave satisfactory elementary analyses. *Selected data* for **2**: mp 130–131 °C, $\delta_H(CDCl_3)$ 1.54 (4 H, m), 3.85 (2 H, m), 6.45 (2 H, d, *J* 2.1), 6.50 (1 H, d, *J* 4.27), 6.52 (1 H, d, *J* 4.27), 7.53 (1 H, NH); *m/z* (EI) 145 (M^+, 7), 117 (100). For Zn-**3:** λ_{max}(solid on glass)/ nm 405, 525, 560; $\lambda_{max}(CHCl_3)$/nm 400, 534, 561. For Cu-**3**: λ_{max}(solid)/nm 402, 520, 560. For **4**: λ_{max}(solid)/nm 454, 617, 696; $\lambda_{max}[(CHCl_3+CF_3CO_2H)]$/nm 431, 605, 660 nm. For Zn-**4:** λ_{max}(solid on glass)/nm 450, 690; λ_{max}(THF–pyridine)/nm 425, 622; For Cu-**4**: λ_{max}(solid)/nm 420, 663; λ_{max}(THF–pyridine)/nm 416, 61. For Zn-**5a**: $\delta_H(CDCl_3)$ 1.44 (16 H, m), 3.39 (8 H, m), 6.45 (8 H, m), 7.78–7.8 (12 H, m), 8.24 (8 H, m); $\lambda_{max}(CHCl_3)$/nm (log ε) 425 (6.45), 550 (5.15); *m/z* (FAB) 988 (M^++1). For Zn-**6a**: $\delta_H(CDCl_3)$ 7.17 (8 H, dd, *J* 6.35, 3.42), 7.28 (8 H, dd, *J* 6.35, 2.92), 7.87 (8 H, t, *J* 7.33), 7.95 (4 H, t, *J* 7.81), 8.30 (8 H, d, *J* 6.84); $\lambda_{max}(CHCl_3)$/nm (log ε) 463 (6.44), 609 (5.09), 652 (5.68); *m/z* (FAB) 876 (M^+ +1). For **8**: $\delta_H(CDCl_3)$ −3.99 (2 H, s), 1.18 (6 H, t, *J* 7.3), 1.48 (6 H, s), 1.79 (6 H, t, *J* 7.3), 2.1–2.3 (8 H, m), 4.07 (4 H, t, *J* 7.3), 4.13 (4 H, q, *J* 7.3), 5.72 (2 H, s), 7.20 (2 H, m), 10.12 (2 H, s), 10.17 (2 H, s); $\lambda_{max}(CHCl_3)$/nm 398 (6.21), 497 (5.15), 529 (4.89), 566 (4.73), 620 (4.54); *m/z* (FAB) 585 (M^++1). For **9**: $\delta_H(CDCl_3)$ −3.64 (2 H, m), 1.14 (6 H, t, *J* 7.3), 1.52 (6 H, s), 1.80 (4 H, m), 1.89 (6 H, t, *J* 7.3), 2.30 (4 H, m), 4.02 (4 H, q, *J* 7.3), 4.16 (4 H, t, *J* 7.3), 8.08 (2 H, dd, *J* 1.1), 9.34 (2 H, dd, *J* 1.1). 10.08 (2 H, s), 10.39 (2 H, s); $\lambda_{max}(CHCl_3)$/nm (log ε) 404 (6.48), 504 (5.12), 541 (5.40), 574 (4.91), 629 (5.17); *m/z* (FAB) 557 (M^++1).

1 N. Ono, H. Hironaga, K. Simidzu, K. Ono and T. Ogawa, *J. Chem. Soc., Chem. Commun.*, 1994, 1019; N. Ono, C. Tsukamura, Y. Nomura, H. Hironaga, T. Murashima and T. Ogawa, *Adv. Mater.*, **9**, 1997, 149. Polypyrroles fused with aromatic rings have been little studied, while the corresponding polythiophenes have been well-studied, see F. Wudl, M. Kobayashi and A. J. Heager, *J. Org. Chem*., 1984, **49**, 3382; M. Hanack, U. Schmid, S. Echingerr, F. Teichert and J. Heiber, *Syntheis*, 1993, 634.

2 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 and B. H. Novak, *Angew. Chem., Int. Ed. Engl*., 1995, **34**, 683; P. Chandrasekar and T. D. Lash, *Tetrahedron Lett.*, 1996, **28**, 4873 and references cited therein.

3 R. Bonnett and R. C. Brown, *J. Chem. Soc., Chem. Commun*., 1972, 393; R. Bonnett and S. A. North, in *Advances in heterocyclic chemistry*, ed. A. R. Katritzky and A. J. Boulton, Academic Press, New York, 1981, vol. 29, pp. 341–399; R. Kreher, N. Kohl and G. Use, *Angew. Chem., Int. Ed. Engl*, 1982, **21**, 621; M. Lee, H. Morimoto and K. Kanematsu, *J. Chem. Soc., Chem. Commun*., 1994, 1535.

4 S. Ito, T. Murashima and N. Ono, *J. Chem. Soc., Perkin Trans. 1*, 1997, 3161.

5 The retro-Diels–Alder reaction of **1** or **2** takes place at 200–230 °C, the bridged moiety of **1** and **2** being stable during de-ethoxycarbonylation of **1** at 170 °C. The formation of isoindoles from **1** or **2** by heating was monitored *via* NMR spectroscopy.

6 K. M. Smith, *Porphyrins and Metalloporphyrins*, Elsevier, Amsterdam, 1975.

7 Existing methods for benzoporphyrin synthesis are summarized in R. Bonnett and K. A. McManus, *J. Chem. Soc., Perkin Trans. 1*, 1996, 2461; for a recent synthesis of benzoporphyrins, see M. G. H. Vicente, A. C. Tome, A. Walter and J. A. S. Cavaleiro, *Tetrahedron Lett*., 1997, **38**, 3639 and references cited therein.

8 T. D. Lash, *Chem. Eur. J*., 1996, **2**, 1197; A. Boudif and M. Momenteau, *J. Chem. Soc., Perkin Trans. 1*, 1996, 1235; L. T. Nguyen, M. O. Senge and K. M. Smith, *J. Org. Chem*., 1996, **61,** 998 and references cited therein.

9 P. S. Clezy and A. H. Mirza, *Aust. J. Chem.*, 1982, **35**, 197; T. D. Lash, *Energy Fuels*, 1993, **7**, 166.

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