Available online at www.sciencedirect.com

ScienceDirect

Tetrahedron Letters 49 (2008) 3972–3975

Tetrahedron Letters

Microwave assisted synthesis of novel annealed porphyrins

Ibrahim Elghamry *, Lutz F. Tietze

Institute of Organic and Biomolecular Chemistry, Georg-August-University Göttingen, Tammannstrasse 2, D-37077 Göttingen, Germany

Received 10 January 2008; revised 28 March 2008; accepted 16 April 2008
Available online 20 April 2008

Abstract

New pyrrole derivatives (isoindoles) have been readily prepared by the reaction of an α,β-unsaturated sulfone with ethyl isocyanoacetate in the presence of *tert*-BuOK in good yields. The isoindoles are converted into new porphyrins which undergo retro Diels–Alder reactions under microwave irradiation at 250 °C for 4 min to give novel annealed porphyrins in quantitative yields.

Porphyrinoid chromophores possessing a conjugated π-electron system with a strong absorption in the far-visible/near-IR region have been the subject of numerous studies due to their potential applications in multibit molecular-based information storage arrays,[1–3] photodynamic therapy (PDT),[4–7] near-IR dyes, and nonlinear optical materials.[8,9] The extension of the π-electron system has been achieved by either peripheral changes with different chromophores at the *meso*- and β-positions or by addition of one or more fused aromatic ring systems.[10–14] Increased conjugation usually results in a red shift for a given chromophore, and it is expected that aromatic subunits fused to the porphyrin nucleus would result in the desired red shift in the electronic spectra of the chromophores.

Monobenzoporphyrin was first prepared over 30 years ago and exhibits a slight shift for both the Soret and the longest wavelength Q-band, (403 and 628 nm, respectively).[15] Further extension in mononaphthoporphyrin leads to a Soret band at 415 nm and a Q-band at 630 nm.[16] However, with di- and tetranaphthoporphyrins these values are only slightly shifted and appear at 424 and 641, and 438 and 672 nm, respectively.[17–19] The overall effects are minimal suggesting that benzenoid ring fusion does not significantly alter the porphyrin UV–vis absorption spectra. However, the ability to alter the porphyrin more profoundly remains an important goal. In this Letter, we report a microwave assisted synthesis and the UV–vis spectra of new tetranaphthoporphyrins.

5,8-Dimethoxy-1,4-dihydro-1,4-ethanonaphthalene (**1**)[20] (Scheme 1) was converted into sulfide **2a** by reaction with PhSCl. Subsequent oxidation with *m*-CPBA followed by dehydrohalogenation with DBU afforded the α,β-unsaturated sulfone **3** in an overall yield of 90%. Next, the isoindole 2-carboxylate was prepared using the Barton–Zard reaction.[21,22] Thus, treatment of sulfone **3** with ethyl isocyanoacetate in the presence of *tert*-BuOK[23] afforded isoindole 2-carboxylate **4a** in 85% yield. Porphyrin **5a** was prepared from **4a** following Lindsey condensation[24–26] which involves reduction with $LiAlH_4$ followed by tetramerization in the presence of TFA and subsequent oxidation with DDQ. Alternatively, deethoxycarboxylation of isoindole **4a** upon heating with KOH in ethylene glycol at 160–165 °C afforded isoindole **4b** in 80% yield, subsequent tetramerization in the presence of mesitaldehyde followed by oxidation with DDQ produced porphyrin **5b** in 30% overall yield.

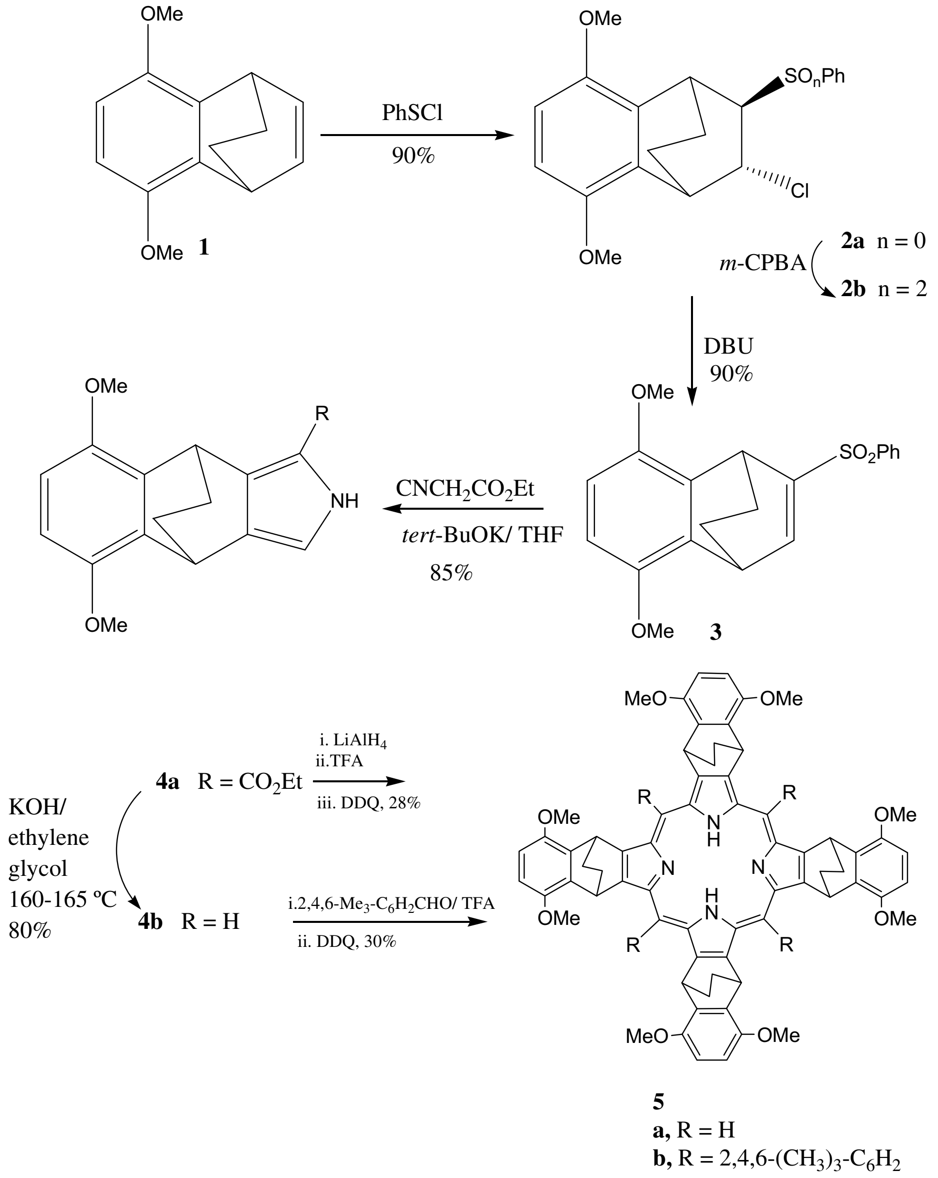
Retro Diels–Alder reactions often require severe conditions, high temperatures, and sometimes, flash vacuum thermolysis. Microwave irradiation has been used as an alternative to these harsh conditions and significant reductions in reaction times and high yields of the desired

---

* Corresponding author. Present address: Misr International University, Faculty of Pharmacy, Pharmaceutical Chemistry Department, PO Box 1, Heliopolis, Cairo, Egypt. Tel.: +20 105368228; fax: +20 2 44771566.

E-mail address: ibrahim.ghamry@miuegypt.edu.eg (I. Elghamry).

0040-4039/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2008.04.094

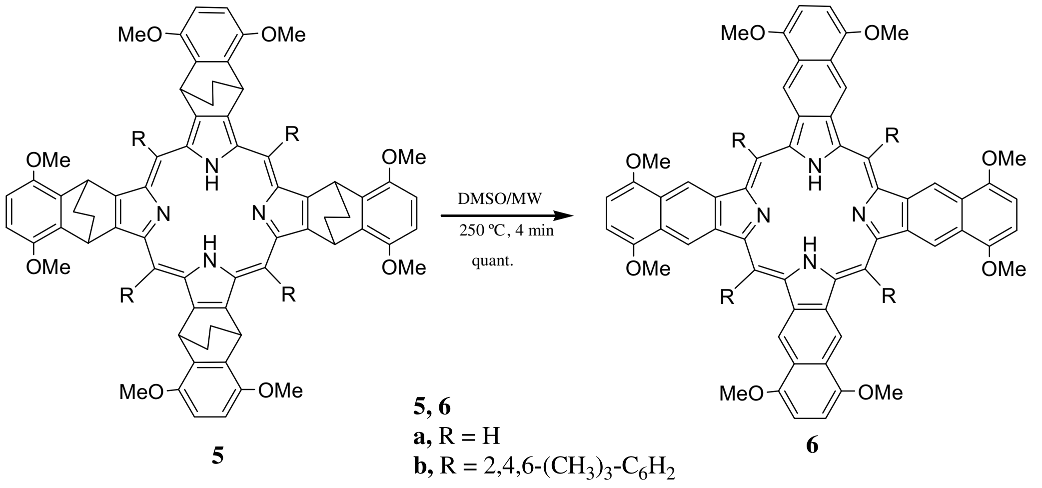


Scheme 1.

products have been observed.[27,28] Porphyrins **5a**,**b** in DMSO were subjected to microwave irradiation for 4 min at 250 °C to give a quantitative yield of porphyrins **6a**,**b** (Scheme 2). [29] It is worth mentioning that, firstly, the product annealed porphyrins **6a**,**b** do not need any further purification (just washing with methanol), and secondly, when the reaction was performed for a shorter time a mixture of porphyrins **5a**,**b** and **6a**,**b** was obtained. In order to check the role of microwave assistance of the reaction a blank experiment was performed under conventional heating (sand bath) for the same period of time and at the same temperature. The annealed porphyrin **6** was obtained but in a very low yield (25%).[29]

The UV–vis spectra ($CHCl_3$) indicated that porphyrins **5a**,**b** show intensified Soret bands at 410 and 394 nm, respectively, compared to 396 nm for the related octaethylporphyrin (OEP)[10,30] (Table 1). After fusing the naphthalene units onto the porphyrin nucleus the absorption spectra were significantly changed with **6a** while those of **6b** showed a small change in both the Soret and the longest wavelength Q bands. Moreover, **6a** exhibited a very intense and strong Soret band at 444 nm and longest wavelength Q-band at 692 nm. Similar values have been reported for similar porphyrin ring systems.[31] Surprisingly, naphthaloporphyrin **6b** also exhibited small red shifts (Table 1). In this case, the steric crowding due to the *meso*-substituents most likely leads to severe distortion of the porphyrin macrocycle, and formation of nonplanar porphyrins, a factor that is known to cause significant changes in the absorption spectra.[10,31,32]

In conclusion, novel annealed porphyrins have been prepared using a microwave assisted retro Diels–Alder reaction. The high purity of the products coupled with the quantitative yields give this method the advantage over



5

6

5, 6
a, R = H
b, R = 2,4,6-$(CH_3)_3$-C_6H_2

Scheme 2.

Table 1
UV–vis ($CHCl_3$) data for [2,3-*b*]naphthoporphyrins **6a**,**b** and their precursors **5a**,**b**

Naphthaloporphyrin	λ max (nm) (log ε)				
	Soret band	Q-bands			
5a	410 (5.21)	496 (3.73)	550 (3.96)	589 (3.46)	614 (3.14)
5b	395 (5.13)	496 (4.35)	527 (4.12)	563 (4.05)	614 (3.76)
6a	444 (4.89)	568 (4.22)	619 (4.29)	645 (4.24)	692 (4.12)
6b	372 (4.23)	410 (4.13)	440 (4.10)	580 (3.75)	633 (4.02)

other reported methods[31] for constructing similar ring systems.

Acknowledgments

This work was supported by the Fonds der Chemischen Industrie. I. Elghamry thanks the Alexander-von-Humboldt foundation for the research fellowship (Long-Term-Co-operation Program) at the Georg-August-University in Göttingen, Germany.

Supplementary data

Supplementary data (spectroscopic data and UV–vis spectral data) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.04.094.

References and notes

1. Osaka, A.; Shimidzu, H. *Angew. Chem., Int. Ed.* **1997**, *36*, 135.
2. Ogawa, T.; Nishimoto, N.; Ono, N.; Osuka, A. *Chem. Commun.* **1998**, 337.
3. Fabian, J.; Nakazumi, H.; Matsuoka, M. *Chem. Rev.* **1992**, *92*, 1197.
4. Kelly, J. F. J.; Kaufman, J. E.; Goldfarb, A.; Weishaupt, K. R.; Boyle, D.; Mittelman, A. *Cancer Res.* **1978**, *38*, 2628.
5. Milgrom, L. R.; MacRobert, S. *Chem. Br.* **1998**, *34*, 45.
6. Pandy, R. K.; Zheng, G. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, 2000; Vol. 6, pp 157–230.
7. Raymond, B. J. *J. Heterocycl. Chem.* **2002**, *39*, 455 and references cited therein.
8. Vinogradov, S. A.; Wilson, D. F. *J. Chem. Soc., Perkin Trans. 2* **1995**, 103.
9. Chen, P.; Dvornikov, A. S.; Nakashima, M.; Roach, J. F.; Nabran, D. M.; Rentzepis, P. M. *J. Phys. Chem.* **1996**, *100*, 17507.
10. Elghamry, I.; Tietze, L.-F. *J. Heterocycl. Chem.* **2005**, *42*, 503.
11. Ito, S.; Ochi, N.; Uno, H.; Murashima, T.; Ono, N. *Chem. Commun.* **2000**, 893.
12. Lash, T. D.; Chandraseker, P.; Osuma, A. T.; Chany, S. T.; Spence, J. D. *J. Org. Chem.* **1998**, *63*, 8455.
13. Fumoto, Y.; Uno, H.; Murashima, T.; Ono, N. *Heterocycles* **2001**, *54*, 705.
14. Ito, S.; Ochi, N.; Uno, H.; Murashima, T.; Ono, N. *Chem. Commun.* **2000**, 893.
15. Clezy, P. S.; Fookes, C. J. R.; Mirza, A. H. *Aust. J. Chem.* **1977**, *30*, 1337.
16. Lash, T. D.; Denny, C. P. *Tetrahedron* **1995**, *51*, 59.
17. Lash, T. D.; Roper, T. J. *Tetrahedron Lett.* **1994**, *35*, 7715.
18. Ono, N.; Hironaga, H.; Ono, K.; Kaneko, S. *J. Chem. Soc., Perkin Trans. 1* **1996**, 417.
19. Rein, M.; Hannack, M. *Chem. Ber.* **1988**, *121*, 1601.
20. Smith, W. B.; Stock, L.; Cornforth, J. *Tetrahedron* **1983**, *39*, 1379.
21. Barton, D. H. R.; Zard, S. *J. Chem. Soc., Chem. Commun.* **1985**, 1098.
22. Barton, D. H. R.; Kervagort, J.; Zard, S. *Tetrahedron* **1990**, *46*, 7587.
23. Abel, Y.; Montfront, F.-P. *Tetrahedron Lett.* **1997**, *38*, 1745.
24. Lihhler, B. J.; Ciringh, Y.; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 2864.
25. Rao, P. D.; Dhanalekshmi, S.; Lihler, B. J.; Lindsey, J. S. *J. Org. Chem.* **2000**, *65*, 7323.
26. Lee, C. H.; Lindsey, J. S. *Tetrahedron* **1994**, *50*, 11427.
27. Giguere, R. J.; Bray, T. L.; Duncan, S. M.; Majetich, G. *Tetrahedron Lett.* **1986**, *27*, 4945.
28. Bortolussi, M.; Bloch, R.; Loupy, A. *J. Chem. Res. (S)* **1998**, 34.

29. *A typical procedure:* A mixture of porphyrin **5** (200 mg) and DMSO (1 mL) was placed in a 5 mL Smith Creator Vial, equipped with a magnetic stirring bar. The vial was sealed with a Teflon septum and an alumina crimp top. The vessel was inserted into the cavity of a Smith Creator microwave reactor, irradiated at 250 °C for 4 min and subsequently cooled by rapid gas-jet cooling. The vessel was removed from the cavity and excess pressure released by piercing the Teflon septum with a needle. The Teflon septum was removed and 3 mL of methanol was added. The product was collected by filtration and washed three times with methanol to give porphyrin **6** in quantitative yield.

    Porphyrin **6a** was obtained as dark violet crystals, mp >300 °C. ν_{max} (KBr)/cm^{-1} 3448 (br, NH). ^{1}H NMR (CDCl$_3$, 300 MHz): δ −3.41 (s, 2H), 3.72 (s, 24H), 6.63 (d, $J = 7.32$ Hz, 8H), 8.62 (m, 8H), 10.51 (s, 4H). Mass (EI) (m/z): (M+1) 951.13. Anal. Calcd for $C_{60}H_{46}N_4O_8 \cdot CH_3OH$: C, 74.52; H, 5.13; N, 5.70. Found C, 74.38; H, 4.97; N, 5.65.

    Porphyrin **6b** was obtained as dark violet crystals, mp >300 °C. ν_{max} (KBr)/cm^{-1} 3425 (br, NH). ^{1}H NMR (CDCl$_3$, 300 MHz): δ −2.21 (s, 2H), 2.42 (br s, 36H), 3.68 (s, 24H), 6.64–6.85 (m, 16H), 8.51 (m, 8H). Mass (EI) (m/z): 1423.42. Anal. Calcd for $C_{96}H_{86}N_4O_8 \cdot CH_3OH$: C, 80.03; H, 6.23; N, 3.85. Found C, 79.87; H, 6.03; N, 3.67.

    A blank control experiment: A mixture of porphyrin **5a** (200 mg) and DMSO (1 mL) was placed in a 5 mL Smith Creator Vial and sealed with a Teflon septum and an alumina crimp top. The vessel was inserted into a sand bath (preheated and the temperature was kept at 250 ± 2 °C) and heated for 4 min. Following the same workup as mentioned above, porphyrin **6a** was obtained in a low yield (50 mg, 25%).
30. Vicente, M. G. H.; Jaquinod, L.; Khoury, R. G.; Madrona, A. Y.; Smith, K. M. *Tetrahedron Lett.* **1999**, *40*, 8763.
31. Lash, T. D. *J. Porphyrins Phthalocyanines* **2001**, *5*, 267.
32. Jentzen, W.; Simpson, M. C.; Hobbs, J. D.; Song, X.; Ema, T.; Nelson, N. Y.; Medforth, C. D.; Smith, K. M.; Veyrat, M.; Mazzanati, M.; Ramasseul, R.; Marchon, J. C.; Takeuchi, T.; Goddard, W. A.; Shelnutt, J. A. *J. Am. Chem. Soc.* **1995**, *117*, 11805.