

# Benzoporphyrins *via* an olefin ring-closure metathesis methodology†

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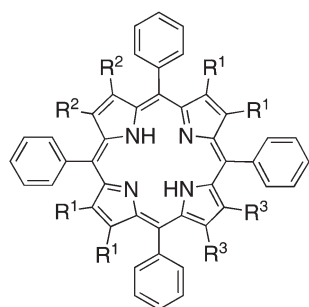
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A new route to benzoporphyrins is reported in which readily available vicinal dibromoporphyrins are bis-allylated using the Suzuki reaction, cyclized by way of olefin metathesis and finally oxidized to give mono-, di-, or tri-benzoporphyrins.

Chemical modifications of natural and synthetic porphyrin macrocycles and their peripheral substituents have been an area of intense interest for a number of years.<sup>1</sup> The development of new methodologies for the functionalization of existing porphyrinoids provides access to a variety of new, custom-designed tetrapyrrole systems that might otherwise only have been available by way of a lengthy total synthesis from monopyrroles.<sup>2</sup> The  $\beta,\beta'$ -difunctionalization of 5,10,15,20-tetra-arylporphyrins has been a particularly attractive area because of the ready availability of the appropriate porphyrin starting materials. Moreover, porphyrin derivatives with extended  $\pi$ -conjugation systems are particularly attractive because of their potential applications in medicine<sup>3</sup> (photodynamic therapy, neutron capture therapy, HIV treatment), and as electric and electro-optic materials for a number of commercial applications in materials science.<sup>4–6</sup>



- (1)  $R^1 = R^2 = R^3 = H$
- (2)  $R^1 = Br; R^2 = R^3 = H$
- (3)  $R^1 = R^2 = H; R^3 = Br$
- (4)  $R^1 = R^2 = Br; R^3 = H$
- (5)  $R^1 = CH_2CH=CH_2; R^2 = R^3 = H$
- (6)  $R^1 = R^2 = H; R^3 = CH_2CH=CH_2$
- (7)  $R^1 = R^2 = CH_2CH=CH_2; R^3 = H$

The conversion of a porphyrin into the corresponding benzoporphyrin is an obvious way to extend the  $\pi$ -conjugation of the porphyrin macrocycle.<sup>7,8</sup> However, benzoporphyrin synthesis has been limited to a small number of methods, most of which are based on the total synthesis of the tetrabenzoporphyrin from sensitive isoindoles,<sup>9</sup> self-condensation of a benzodipyrromethene to give a dibenzoporphyrin,<sup>10</sup> synthesis of (poly)butanoporphyrins (followed by DDQ oxidation),<sup>11–13</sup> or the Diels–Alder reaction on pyrrolo[3,4-*b*]porphyrins<sup>14</sup> or sulfolenoporphyrins.<sup>15,16</sup> So-called benzoporphyrin derivatives can also be prepared *via* an intramolecular cyclization methodology<sup>17</sup> or Diels–Alder reactions

on vinylporphyrins.<sup>18</sup> Total synthetic approaches to benzoporphyrins usually generate a fully symmetrical product in low yield, often following tedious separation.<sup>19,20</sup> Although monobenzoporphyrins could be obtained based on a Diels–Alder reaction, the yields are still low and the separation is difficult.<sup>21,22</sup> Regioselective syntheses of mono-, di- (two isomers) and tri-benzoporphyrins still remain a challenge.

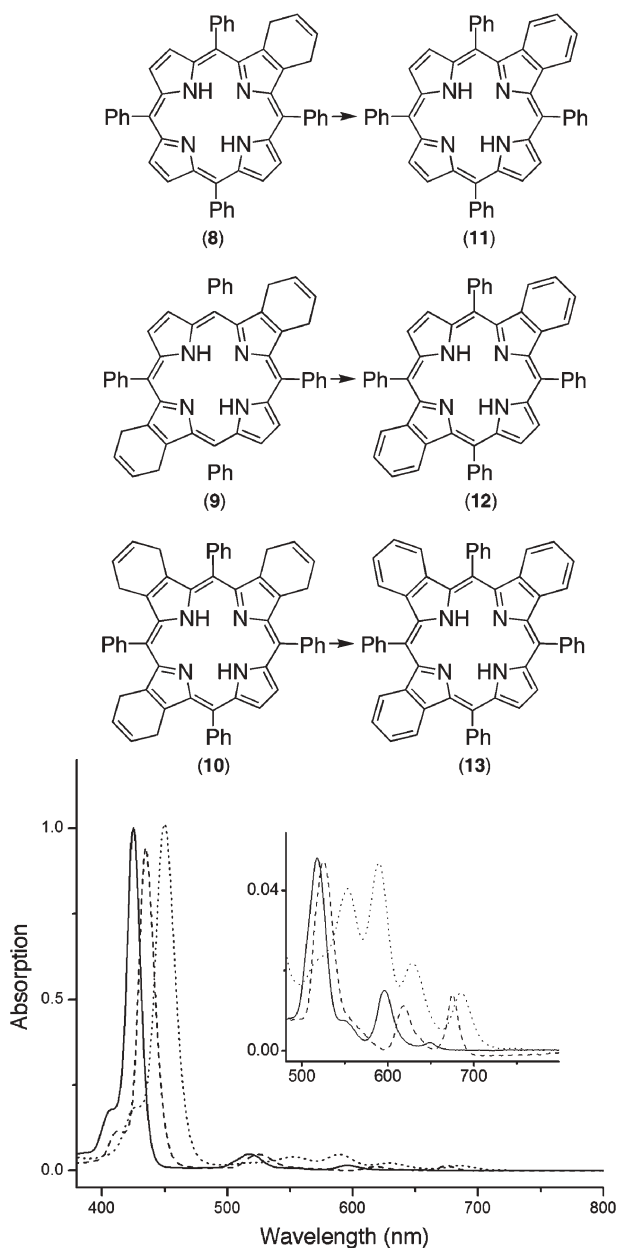
Efficient, progressive and regioselective  $\beta,\beta'$ -brominations of tetra-arylporphyrins have been reported,<sup>23–29</sup> and these make possible the selective modification of porphyrin  $\beta$ -positions through subsequent metal-catalyzed cross-coupling reactions. Among these, the Suzuki coupling reaction is a good choice in organic synthesis; it is suitable for the introduction of a variety of groups at the  $\beta$ -positions of porphyrin macrocycles by coupling halo-substituted porphyrins with the corresponding boronic acids or esters.<sup>30,31</sup> Additionally, the olefin metathesis reaction has emerged as a powerful tool for the formation of new C–C bonds, and it has excellent tolerance towards functional groups. In past decades, olefin metathesis has been widely used in advanced organic and polymer chemistry for the syntheses of both natural and non-natural products.<sup>32–34</sup> In the present paper we report the sequential application of both Suzuki and olefin metathesis reactions to eventually yield various benzoporphyrins.

5,10,15,20-Tetraphenylporphyrin (**1**) was regioselectively brominated (using NBS) to give the bromoporphyrins **2–4**, as described in the literature.<sup>23–29</sup> The Suzuki coupling reactions of bromoporphyrins **2–4** using 2-allyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane were performed in toluene at 100 °C under an argon atmosphere using anhydrous potassium carbonate as the base. Though alkyl boro-esters are known to have limited utility in Suzuki coupling reactions,<sup>35</sup> 2-allyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane gave the individual poly-allylporphyrins **5–7** in acceptable yields (**5**: 84%; **6**: 48%; **7**: 14%) after column chromatographic separation on silica gel eluted with dichloromethane/ethyl acetate mixtures. All of these reactions were monitored by TLC and MALDI-TOF mass spectroscopy. The ring-closure metathesis reaction was performed using the Grubbs' 2<sup>nd</sup> generation catalyst<sup>32–34,36</sup> at high dilution in dichloromethane to avoid any intermolecular olefin metathesis. TLC and MALDI-TOF mass spectroscopy were used to monitor reaction progress. After passing the reaction mixtures through a short silica gel plug, compounds **8–10** were obtained in 82–91% yields. Oxidation with DDQ in toluene gave the corresponding benzoporphyrins **11–13** in almost quantitative yields. Spectrophotometry in dichloromethane showed a gradual red shift of the Soret bands ( $\lambda_{max}$  **11**: 425 nm; **12**: 435 nm; **13**: 450 nm) and also of the Q bands. Fig. 1 shows the optical spectra, in dichloromethane, of the three benzoporphyrins **11–13**.

In a parallel series of reactions, demonstrating that functional groups provide access to, for example, chlorin chromophores,<sup>2,37,38</sup>

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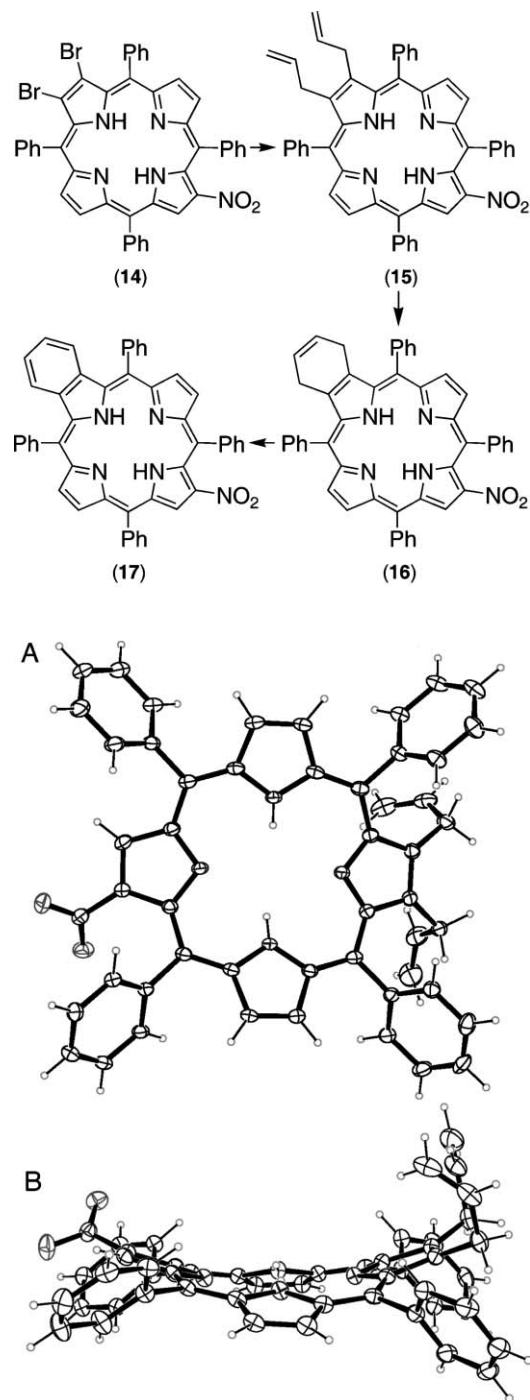
† Electronic supplementary information (ESI) available: General procedure and selected characterization data for porphyrins **11–13**, **16** and **17**. See DOI: 10.1039/b607711k



**Fig. 1** Optical spectra, in  $\text{CH}_2\text{Cl}_2$ , of **11**: full line; **12**: dashed line and **13**: dotted line.

the readily available<sup>25</sup> 2,3-dibromo-12-nitrotetraphenylporphyrin (**14**) was bis-allylated with 2-allyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane to give a 83% yield of **15**. Ring-closure metathesis, again using Grubbs' 2<sup>nd</sup> generation catalyst, gave the nitroporphyrin **16** and subsequently the nitrobenzoporphyryrin **17** in an overall yield of 93% from **15**.

Fig. 2 shows the X-ray crystal structure of compound **15**.<sup>‡</sup> The molecule has a saddle conformation, in which the four central N atoms are coplanar to within 0.046(2) Å. Pyrrole rings alternate in their direction of tilt out of this plane, forming dihedral angles of 17.0(2)–19.1(2)° with the  $\text{N}_4$  plane. Thus, the pyrrole ring carrying the allyl groups forms a dihedral angle of 35.6(2)° with the ring carrying the nitro group, and the other two opposite pyrrole rings form a dihedral angle of 35.7(2)° with each other. The allyl groups are folded on the same side of the porphyrin ring, facilitating the



**Fig. 2** X-Ray crystal structure of bis-allyl-nitroporphyrin **15**. A: From the top. B: End-on view showing saddled conformation. 40% ellipsoids are shown.

metathesis reaction, but have different conformations. One has a C=C–C–C torsion angle of  $-3.9(5)^\circ$ , while the other is more extended, with a torsion angle of  $-129.3(4)^\circ$ .

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## Notes and references

<sup>‡</sup> Crystal data for **15** at 115 K:  $\text{C}_{50}\text{H}_{37}\text{N}_5\text{O}_2 \cdot 2\text{CH}_2\text{Cl}_2$ , triclinic, space group  $P-1$ ,  $a = 13.497(3)$ ,  $b = 13.665(2)$ ,  $c = 13.976(3)$  Å,  $\alpha = 101.273(12)$ ,

$\beta = 92.929(9)$ ,  $\gamma = 116.774(11)^\circ$ ,  $V = 2228.2(8) \text{ \AA}^3$ ,  $Z = 2$ ,  $\mu(\text{MoK}\alpha) = 0.314 \text{ mm}^{-1}$ , 32954 reflections collected with  $\theta < 25.6^\circ$ , 8431 unique;  $R(\text{int}) = 0.036$ ;  $R1 = 0.064$ ,  $wR2 = 0.171$  refined on  $F^2$ . Both  $\text{CH}_2\text{Cl}_2$  solvent molecules are disordered, each into two orientations. CCDC 608862. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b607711k

- 1 K. M. Smith, in *Rodd's Chemistry of the Carbon Compounds*, ed. M. Sainsbury, Elsevier, Amsterdam, 1997, supplement to vol. **IVB**, ch. 12, pp. 277.
- 2 K. M. Shea, L. Jaquinod and K. M. Smith, *J. Org. Chem.*, 1998, **63**, 7013.
- 3 R. K. Pandey and G. Zheng, in *The Porphyrin Handbook*, ed. K. M. Kadish, K. M. Smith and R. Guilard, Academic Press, San Diego, 2000, vol. **6**, pp. 157–230.
- 4 B. M. Hoffman and J. A. Ibers, *Acc. Chem. Res.*, 1983, **16**, 15.
- 5 W. A. Nevin and G. A. Chamberlain, *J. Appl. Phys.*, 1991, **69**, 4324.
- 6 D. V. G. L. N. Rao, F. J. Aranda, J. F. Roach and D. E. Remy, *Appl. Phys. Lett.*, 1991, **58**, 1241.
- 7 T. D. Lash, in *The Porphyrin Handbook*, ed. K. M. Kadish, K. M. Smith and R. Guilard, Academic Press, San Diego, 2000, vol. **2**, pp. 125–199.
- 8 M. O. Senge, in *The Porphyrin Handbook*, ed. K. M. Kadish, K. M. Smith and R. Guilard, Academic Press, San Diego, 2000, vol. **1**, pp. 284–287.
- 9 D. E. Remy, *Tetrahedron Lett.*, 1983, **24**, 1451.
- 10 R. Bonnett and K. A. McManus, *J. Chem. Soc., Perkin Trans. 1*, 1996, 2461.
- 11 L. T. Nguyen, M. O. Senge and K. M. Smith, *J. Org. Chem.*, 1996, **61**, 998.
- 12 T. D. Lash, *J. Porphyrins Phthalocyanines*, 1997, **1**, 29.
- 13 O. S. Finikova, A. V. Cheprakov, Z. P. Beletskaya, P. J. Carroll and S. A. Vinogradov, *J. Org. Chem.*, 2004, **69**, 522.
- 14 M. G. H. Vicente, L. Jaquinod, R. G. Khoury, A. Y. Madrona and K. M. Smith, *Tetrahedron Lett.*, 1999, **40**, 8763.
- 15 M. G. H. Vicente, A. C. Tomé, A. Walter and J. A. S. Cavaleiro, *Tetrahedron Lett.*, 1997, **38**, 3639.
- 16 S. H. Lee and K. M. Smith, *Tetrahedron Lett.*, 2005, **46**, 2009.
- 17 S. Ito, T. Murashima and N. Uno, *Chem. Commun.*, 1998, 1661.
- 18 A. R. Morgan, V. S. Pangka and D. Dolphin, *J. Chem. Soc., Chem. Commun.*, 1984, 1047.
- 19 K. Ichimura, M. Sakuragi, H. Morii, M. Yasuike, M. Fukui and O. Ohno, *Inorg. Chim. Acta*, 1991, **182**, 83.
- 20 K. Ichimura, M. Sakuragi, H. Morii, M. Yasuike, Y. Toba, M. Fukui and O. Ohno, *Inorg. Chim. Acta*, 1991, **186**, 95.
- 21 A. C. Tomé, P. S. S. Lacerda, M. G. P. M. S. Neves and J. A. S. Cavaleiro, *Chem. Commun.*, 1997, 1199.
- 22 A. M. G. Silva, A. C. Tomé, M. G. P. M. S. Neves, J. A. S. Cavaleiro and C. O. Kappe, *Tetrahedron Lett.*, 2005, **46**, 4723.
- 23 L. Jaquinod, in *The Porphyrin Handbook*, ed. K. M. Kadish, K. M. Smith and R. Guilard, Academic Press, San Diego, 2000, vol. **1**, pp. 201–237.
- 24 H. J. Callot, *Bull. Soc. Chim. Fr.*, 1974, 1492.
- 25 L. Jaquinod, R. G. Khoury, K. M. Shea and K. M. Smith, *Tetrahedron*, 1999, **55**, 13151.
- 26 M. J. Crossley, P. L. Burn, S. S. Chew, C. F. Cuttance and I. A. Newsom, *J. Chem. Soc., Chem. Commun.*, 1991, 1564.
- 27 P. K. Kumar, P. Bhyrappa and B. Varghese, *Tetrahedron Lett.*, 2003, **44**, 4849.
- 28 C. Liu, D.-M. Shen and Q.-Y. Chen, *Chem. Commun.*, 2006, 770.
- 29 D. Mandon, P. Ochsenbein, J. Fischer, R. Weiss, K. Jayaraj, R. N. Austin, A. Gold, P. S. White, O. Brigaud, P. Battioni and D. Mansuy, *Inorg. Chem.*, 1992, **31**, 2044.
- 30 K. S. Chan, X. Zhou, B.-S. Lou and T. C. W. Mak, *J. Chem. Soc., Chem. Commun.*, 1994, 271.
- 31 X. Zhou, Z.-Y. Zhou, T. C. W. Mak and K. S. Chan, *J. Chem. Soc., Perkin Trans. 1*, 1994, 2519.
- 32 A. Fürstner, *Angew. Chem., Int. Ed.*, 2000, **39**, 3012.
- 33 T. M. Trnka and R. H. Grubbs, *Acc. Chem. Res.*, 2001, **34**, 18.
- 34 R. H. Grubbs, *Tetrahedron*, 2004, **60**, 7117.
- 35 E. G. Occhiato, A. Trabocchi and A. Guarna, *J. Org. Chem.*, 2001, **66**, 2459.
- 36 Q. Yang, X.-Y. Li, H. Wu and W.-J. Xiao, *Tetrahedron Lett.*, 2006, **47**, 3893.
- 37 M. J. Crossley and L. G. King, *J. Org. Chem.*, 1993, **58**, 4370.
- 38 M. J. Crossley and L. G. King, *J. Chem. Soc., Perkin Trans. 1*, 1996, 1251.