

A novel and facile Zn-mediated intramolecular five-membered cyclization of β -tetraarylporphyrin radicals from β -bromotetraarylporphyrins†

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Received (in Cambridge, UK) 14th July 2005, Accepted 22nd August 2005

First published as an Advance Article on the web 9th September 2005

DOI: 10.1039/b509972b

A novel and facile method for the Zn-mediated intramolecular cyclization of β -porphyrin radicals has been developed for the convenient and effective construction of newly fused five-membered porphyrin systems from readily available β -bromotetraarylporphyrins.

Porphyrins, by the nature of their electronic and redox properties, play a key role in many fields, such as oxygen activation and transfer, electron transfer, binding or transport of small molecules, light harvesting, and photosynthesis.¹ Secondary ring systems fused onto the macrocyclic core are of interest owing to their special optical, coordination and redox properties. So far, synthetic routes for these compounds mainly include the intermolecular reactions of an exocyclic double bond of the porphyrin in Diels–Alder reactions,² 1,3-dipolar cycloadditions³ and carbene additions,⁴ and the intramolecular reactions of functional groups on a porphyrin β -position attacking the *ortho*-carbon of a phenyl ring on the adjacent *meso*-position and the inverse reaction between an *ortho*-functionalized *meso*-phenyl and unsubstituted β -position.⁵ Because of the existence of functional groups such as formyl, aryl chloride groups, alkyl or nitro groups, a newly fused six-membered ring was usually formed. However, a palladium(0)-catalyzed intramolecular coupling on *ortho*-iodinated *meso*-phenyl porphyrins to form five-membered fused porphyrins has been recently reported.⁶ But this method suffered from a lack of easy availability of the starting materials. Very recently, we also discovered a facile synthesis of various *meso*-, β -perfluoroalkylated porphyrins as well as five-, six-, seven-, and eight-membered fluorinated fused porphyrins through β -perfluoroalkyl porphyrin radicals.⁷ Here, as a part of our study toward porphyrin intramolecular cyclization via a radical pathway, we wish to present a novel and facile Zn-mediated intramolecular cyclization reaction of β -porphyrin radicals for formation of newly fused five-membered porphyrin systems.

It is well known that organozinc reagents can be efficiently and rapidly prepared from organic bromine compounds by using activated metallic Zn.⁸ For generating porphyrin–Zn reagent, a first attempt to activate ZnTPP(Br) (**Zn1**), a most readily available brominated porphyrin, was carried out by treating it with metallic

zinc (activated by washing with aqueous HCl)⁹ in DMSO at 60 °C for 30 min. It was found that the starting material was consumed completely and two new products were yielded. To our surprise, no porphyrin–Zn reagent was obtained. According to spectral analysis, one was a hydrogenated product ZnTPP (**Zn3a**), the other an intramolecular cyclization product **Zn2a**, whose mass spectrometry indicated the expected mass ion with loss of the bromine atom and whose NMR spectrum revealed significant loss of symmetry as shown by an increase in the number of signals for the β -hydrogens, as opposed to the normal one singlet pattern found for tetraarylporphyrins. As expected, due to the variation of the conformation and conjugate pathway by the formation of the newly fused five-membered ring, the UV-visible spectrum exhibited a much larger bathochromic shift and broadening of the Soret band (Fig. 1).¹⁰

With these encouraging results, various brominated porphyrins H₂TAP(Br) (**1**)¹¹ and H₂TAP(Br)₄ (**4**)¹² for this reaction were then prepared by the controlled bromination of 5,10,15,20-tetraarylporphyrin (H₂TAP) (**3**) with NBS via the free-base porphyrin according to the literature procedure^{11,12} (Scheme 1), after which we turned our attention to modifying the reaction conditions for the cyclization reaction. Systematic variation of amounts of Zn, solvents and reaction temperatures revealed that the optimal condition was 50 equiv. of Zn in DMSO (the most effective solvent among the screened solvents DMSO, DMF, HMPA, CH₃CN, THF, benzene, ClCH₂CH₂Cl, dioxane) at 85 °C. The addition of

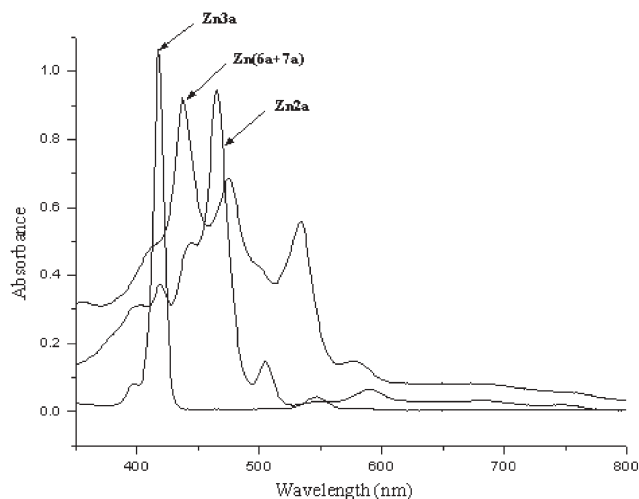
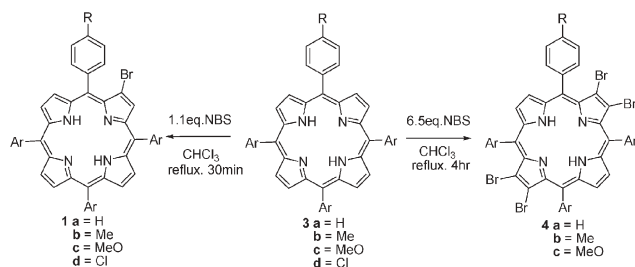


Fig. 1 The UV-visible spectrum of ZnTPP (**Zn3a**), mono-cyclization porphyrin **Zn2a** and double-cyclization porphyrin **Zn(6a+7a)**.

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† Electronic supplementary information (ESI) available: experimental details and NMR data and spectra for new compounds. See <http://dx.doi.org/10.1039/b509972b>



Scheme 1 Synthesis of various brominated porphyrins.

more reactive metal zinc–copper couples⁸ instead of zinc powder resulted in a poor yield of the cyclization product. The fact that the reaction could be completely inhibited in the presence of an electron-transfer scavenger, *i.e.*, *p*-dinitrobenzene (*p*-DNB) (20 mol%) or radical inhibitor, *i.e.*, hydroquinone (HQ) (20 mol%) indicated the radical nature of the reaction.

In order to explore the effect of the substituents on the porphyrin *meso*-aryl groups, a series of substrates with diverse steric and electronic properties were investigated. As illustrated in Table 1, under the optimal conditions, various substrates could be subjected to smooth cyclization reaction. The result that the reactivity of a substrate with an electron-withdrawing group was somewhat higher than that with an electron-donating group can probably be ascribed to the nucleophilic properties of the β -porphyrin radicals.¹³

When 2,3,12,13-tetrabromoporphyrin ZnTPP(Br)₄ (**Zn4a**)¹² was used as a substrate under similar conditions, a red band and a green band were obtained. Spectral analysis of the red band by mass spectrometry, NMR spectroscopy and elemental analysis indicated that it was a mixture of isomers **Zn6a** and **Zn7a** instead of the expected product **Zn5a**, which could not be separated by the usual flash column chromatography because of the virtually identical *R_f* values. The isomers display complicated ¹H NMR

Table 1 Zn-mediated intramolecular cyclization reaction of β -ZnTAP radicals^a

Entry	Reactant	Time (min)	Product	Yield (%) ^b
1	Zn1a	10	Zn2a	30
			Zn3a	62
2	Zn1b	20	Zn2b	23
			Zn3b	71
3	Zn1c	30	Zn2c	20
			Zn3c	72
4	Zn1d	5	Zn2d	35
			Zn3d	58

^a Reactions were carried out in 10 mL DMSO under N₂ with ZnTAP(Br) (**Zn1**) (100 mg, 1.0 equiv.) and Zn (50 equiv.) at 85 °C.
^b Isolated yields.

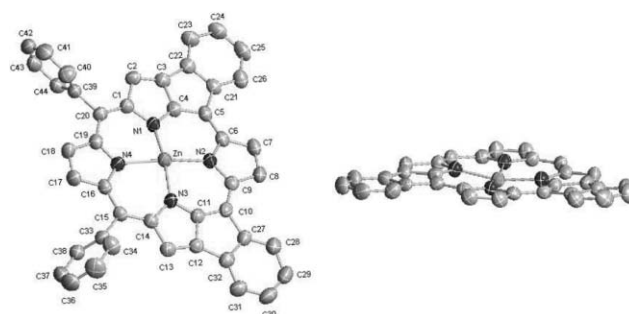
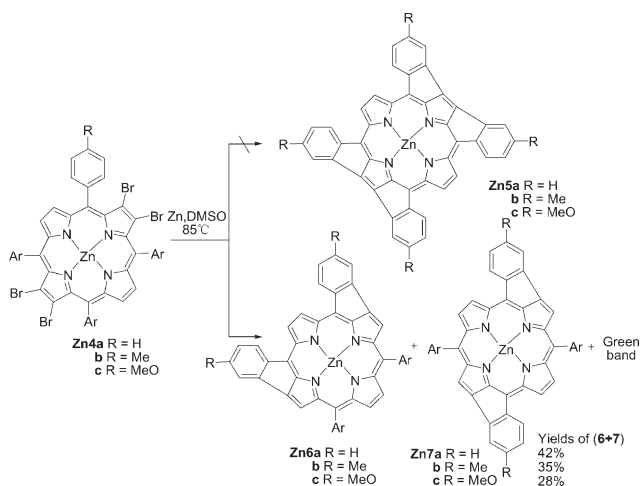


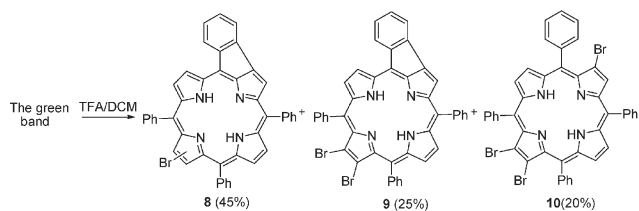
Fig. 2 Two views of the X-ray crystal structure of double-cyclization porphyrin **Zn6a** (phenyl groups, hydrogen atoms and the THF molecule coordinated to the Zn center are omitted for clarity). Representative bond lengths (Å) and angles (°) are as follows: Zn–N1 1.954(3), Zn–N2 2.157(2), Zn–N3 1.945(3), Zn–N4 2.086(3), C3–C22 1.466(4), C12–C32 1.472(4); C3–C4–C5 112.4(3), C2–C1–C20 128.4(3), C10–C11–C12 113.1(3), C13–C14–C15 128.4(3).

signals, which cannot be clearly identified. The mass spectrum gives the expected mass ion at *m/z* 672 (*M*⁺) with loss of the bromine atoms. The UV-visible spectrum for the isomers demonstrated a large bathochromic shift and broadening of the Soret band (Fig. 1). On the other hand, fortunately, one of the single crystals of the double-cyclization isomers, **Zn6a**, was obtained from THF solution of the isomers into which petroleum ether was allowed to slowly diffuse. As illustrated in Fig. 2, the X-ray structure[†] of **Zn6a** reveals a Zn(II) porphyrin skeleton that displays a mixture of the traditional ruffle/saddle distortions. The bond lengths of Zn–N(1) and Zn–N(3) are notably shorter than those of Zn–N(2) and Zn–N(4). Significant contractions of the fused C(3)–C(4)–C(5) and C(10)–C(11)–C(12) bond angles are also observed in comparisons of C(2)–C(1)–C(21) and C(13)–C(14)–C(15). All these features might be the consequence of carbon–carbon bond formation that locks the *meso*-phenyl groups into the plane of the newly formed five-membered ring. When using ZnT(*p*-Me)PP(Br)₄ (**Zn4b**) and ZnT(*p*-MeO)PP(Br)₄ (**Zn4c**) as substrates under similar conditions, similar results were obtained (Scheme 2).

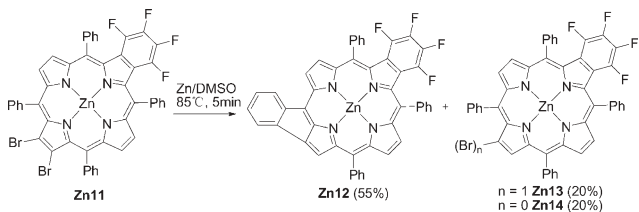
The diversity and complexity of the reaction were further indicated by demetalation of the mixture of the green band, which



Scheme 2



Scheme 3



Scheme 4

afforded three different products **8**, **9**, **10**. Their structures have been assigned by ^1H NMR, MS spectrometry, Uv-visible spectroscopy and HRMS or elemental analysis (Scheme 3).

In order to further explore the generality of the reaction, dibromoporphyrin **Zn11**^{7b} was then synthesized for the reaction. As expected, intramolecular cyclization product **Zn12** was obtained as the main product and debrominated porphyrins **Zn13** and **Zn14** as the minor products (Scheme 4).

Finally, an attempt to trap the β -porphyrin radicals generated from ZnTPP(Br) (**Zn1a**) with an electron-deficient alkene or alkyne (*i.e.* acrylonitrile or ethyl propiolate) under similar conditions met with failure, the intramolecular cyclization product **Zn2a** and hydrogenated product **Zn3a** still being the main products.

In conclusion, we have developed a novel and facile method for the Zn-mediated intramolecular cyclization of β -porphyrin radicals for the convenient and effective construction of newly fused five-membered porphyrin systems from readily available brominated porphyrins. Because of the ready availability of the starting material, this method might be useful for some applications in areas such as materials, biomimetics and medicine.

We thank the Natural Science Foundation of China for support of this work (No. 20272026 and D20032010).

Notes and references

‡ Crystal data. $\text{C}_{51}\text{H}_{39}\text{N}_4\text{OZn}$, $M = 789.23$, triclinic, $a = 12.6037$ (13), $b = 13.0941$ (13), $c = 13.6336$ (13) Å, $\alpha = 75.970$ (2), $\beta = 71.209$ (2), $\gamma = 63.453$ (2)°, $V = 1892.6$ (3) Å³, $T = 293$ (2) K, space group $P-1$, $Z = 2$, $D_c = 1.385$ g cm⁻³, 10463 reflections measured, 7314 unique which were used in all calculations. $R(\text{int}) = 0.0853$. The final $wR(F^2)$ was 0.0572 (all

data). CCDC 267633. See <http://dx.doi.org/10.1039/b509972b> for crystallographic data in CIF or other electronic format.

- 1 *The Porphyrin Handbook*, ed. K. M. Kadish, K. M. Smith and R. Guilard, Academic Press, San Diego, 2000–2003, Vol. 1–20.
- 2 (a) A. C. Tomé, P. S. S. Lacerda, M. G. P. M. S. Neves and J. A. S. Cavaleiro, *Chem. Commun.*, 1997, 1199; (b) A. M. G. Silva, A. C. Tomé, M. G. P. M. S. Neves and J. A. S. Cavaleiro, *Tetrahedron Lett.*, 2000, **41**, 3065.
- 3 (a) X. G. Liu, Y. Q. Feng, X. Chen, F. Li and X. G. Li, *Synlett*, 2005, **6**, 1030; (b) A. M. G. Silva, A. C. Tomé, M. G. P. M. S. Neves, A. M. S. Silva and J. A. S. Cavaleiro, *J. Org. Chem.*, 2005, **70**, 2306; (c) J. A. S. Cavaleiro, M. G. P. M. S. Neves and A. C. Tomé, *Arkivoc*, 2003, xiv, 107; (d) A. M. G. Silva, A. C. Tomé, M. G. P. M. S. Neves, A. M. S. Silva, J. A. S. Cavaleiro, D. Perrone and A. Dondoni, *Tetrahedron Lett.*, 2002, **43**, 603; (e) A. M. G. Silva, A. C. Tomé, M. G. P. M. S. Neves and J. A. S. Cavaleiro, *Synlett*, 2002, 1155; (f) A. M. G. Silva, A. C. Tomé, M. G. P. M. S. Neves, A. M. S. Silva and J. A. S. Cavaleiro, *J. Org. Chem.*, 2002, **67**, 726; (g) A. Desjardins, J. Flemming, E. D. Sternberg and D. Dolphin, *Chem. Commun.*, 2002, 2622; (h) J. Flemming and D. Dolphin, *Tetrahedron Lett.*, 2002, **43**, 7281; (i) A. M. G. Silva, A. C. Tomé, M. G. P. M. S. Neves, A. M. S. Silva and J. A. S. Cavaleiro, *Chem. Commun.*, 1999, 1767.
- 4 H. J. Callot, *Tetrahedron Lett.*, 1972, **11**, 1011.
- 5 (a) S. Richeter, C. Jeandon, J. P. Gisselbrecht, R. Graff, R. Ruppert and H. J. Callot, *Inorg. Chem.*, 2004, **43**, 351; (b) S. Richeter, C. Jeandon, N. Kyriakos, R. Ruppert and H. J. Callot, *J. Org. Chem.*, 2003, **68**, 9200; (c) S. Richeter, C. Jeandon, J. P. Gisselbrecht, R. Ruppert and H. J. Callot, *J. Am. Chem. Soc.*, 2002, **124**, 6168; (d) S. Richeter, C. Jeandon, R. Ruppert and H. J. Callot, *Chem. Commun.*, 2001, 91; (e) K. Henrick, P. G. Owston, R. Peters, P. A. Tasker and A. Dell, *Inorg. Chim. Acta*, 1980, **45**, L161–163; (f) H. J. Callot, E. Schaeffer, R. Cromer and F. Metz, *Tetrahedron*, 1990, **46**, 5253; (g) Y. V. Ishkov and Z. I. Zhilina, *Zh. Org. Khim.*, 1995, **31**, 136; (h) S. Richeter, C. Jeandon, R. Ruppert and H. J. Callot, *Tetrahedron Lett.*, 2001, **42**, 2103; (i) L. Barloy, D. Dolphin, D. Dupré and T. P. Wijesekera, *J. Org. Chem.*, 1994, **59**, 7976; (j) G. L. Li, A. Graham, W. Potler, Z. D. Grossman, A. Oseroff, T. J. Dongherty and R. K. Padey, *J. Org. Chem.*, 2001, **66**, 1316; (k) M. Nath, M. Pink and J. M. Zaleski, *J. Am. Chem. Soc.*, 2005, **127**, 478; (l) H. Aihara, L. Jaquinod, D. J. Nurco and K. M. Smith, *Angew. Chem., Int. Ed.*, 2001, **40**, 3439; (m) M. Nath, J. C. Huffman and J. M. Zaleski, *Chem. Commun.*, 2003, 858; (n) M. Nath, J. C. Huffman and J. M. Zaleski, *J. Am. Chem. Soc.*, 2003, **125**, 11484.
- 6 S. Fox and R. W. Boyle, *Chem. Commun.*, 2004, 1322.
- 7 (a) C. Liu and Q. Y. Chen, *Synlett*, 2005, **8**, 1306; (b) Z. Zeng, C. Liu, L. M. Jin, C. C. Guo and Q. Y. Chen, *Eur. J. Org. Chem.*, 2005, 306; (c) L. Chen, L. M. Jin, C. C. Guo and Q. Y. Chen, *Synlett*, 2005, **6**, 963; (d) C. Liu and Q. Y. Chen, *Eur. J. Org. Chem.*, 2005, 3680; (e) L. M. Jin, L. Chen, C. C. Guo and Q. Y. Chen, *J. Porphyrins Phthalocyanines*, 2005, **9**, 109; (f) L. M. Jin, Z. Zeng, C. C. Guo and Q. Y. Chen, *J. Org. Chem.*, 2003, **68**, 3912.
- 8 E. Erdik, *Tetrahedron*, 1987, **43**, 2203.
- 9 M. S. Newman and F. J. Arens, *J. Am. Chem. Soc.*, 1955, **77**, 946.
- 10 K. M. Kadish, E. Van Caemelbecke and G. Royal, in *The Porphyrin Handbook*, ed. K. M. Kadish, K. M. Smith, R. Guilard, Academic Press, Boston, MA, 2000, Vol. 8, p. 3.
- 11 H. J. Callot, *Bull. Soc. Chim. Fr.*, 1974, 1492.
- 12 D. K. Kumar, P. Bhyrappa and B. Varghese, *Tetrahedron Lett.*, 2003, **40**, 4849.
- 13 (a) D. P. Curran, in *Comprehensive Organic Synthesis*, ed. B. M. Trost, I. Fleming, Pergamon Press plc, Oxford, 1991, Vol. 4, p. 715–831; (b) B. Giese, *Angew. Chem., Int. Ed.*, 1983, **22**, 753.