Pergamon

Tetrahedron Letters 42 (2001) 4527–4529

TETRAHEDRON LETTERS

Unusual phlorins from the oxidative coupling of pentapyrromethanes: their facile conversion to *meso*-substituted porphyrins

Jae-Won Ka and Chang-Hee Lee*

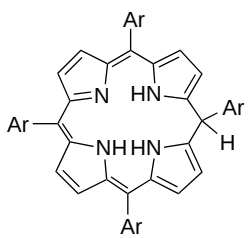
Institute of Basic Science and Department of Chemistry, Kangwon National University, Chun-Chon 200-701, South Korea

Received 27 March 2001; revised 18 April 2001; accepted 14 May 2001

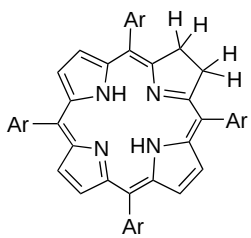
Abstract—Direct, oxidant-mediated intramolecular coupling of pentapyrromethanes afforded 5-aryl-5-(2′-pyrryl)-10,15,20-triarylporphyrin (phlorins) as single products. The outcome of the reaction is comparable with the oxidative coupling of tetrapyrromethanes. Treatment of obtained phlorins with trifluoroacetic acid resulted in exclusive elimination of the peripheral pyrrole affording *meso*-tetraarylporphyrins quantitatively. The rate of pyrrole elimination depends on the acid concentration. The selective binding with fluoride anion was also observed with a large association constant. © 2001 Published by Elsevier Science Ltd.

Phlorins, the porphyrins bearing one sp^3 hybridised *meso*-carbon, have been known to be unstable and only a few have been characterised so far.[1] Due to the air-sensitive nature of the compound, a bridging unit between N(21) and N(22) or *N*-substituents was introduced in some cases for the stabilisation of the compounds.[2] The protonation of phlorins under strongly acidic conditions gave porphodimethenes, which could be converted to the corresponding porphyrins by successive oxidation.[2] Conversion of dianionic Zn-TPP to a Zn-porphodimethene and rearrangement to Zn-(*meso*-tetraphenyl)chlorin has been demonstrated.[3] More recently, Scott et al. demonstrated the reversible conversion of porphyrin to porphodimethene.[4] Geometrically proximal nucleophiles to the *meso*-carbon alter the electrochemical behaviour of reduced porphyrins and their system could be good models of a molecular switch. The reaction of Ni(II)-porphyrins with organolithium reagent has been reported to afford the partially reduced porphyrins.[5] All of these reduced porphyrins are rather unstable due to the presence of hydrogen at the *meso*-position. The reduced porphyrins **1** and **2** are tautomers, and so are **3** and normal *meso*-tetraarylporphyrin, though the fully conjugated forms are usually more stable due to aromatic stabilisation.

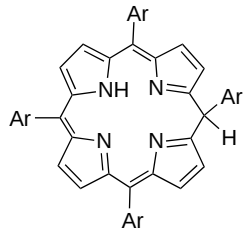
In spite of their importance in redox chemistry and biosynthetic pathway of porphyrins, the synthesis of phlorins bearing different substituents other than hydrogen at the sp^3-carbon has not been documented. This has been hampered by possible instability and difficulties in placing the desired substituents. Reduction of one or more *meso*-carbons in the porphyrin skeleton significantly alters the spectroscopic and electronic properties. The existence of different oxidation



1



2



3

Keywords: phlorin; reduced porphyrin; pentapyrromethane; oxidative coupling; molecular switch.

* Corresponding author.

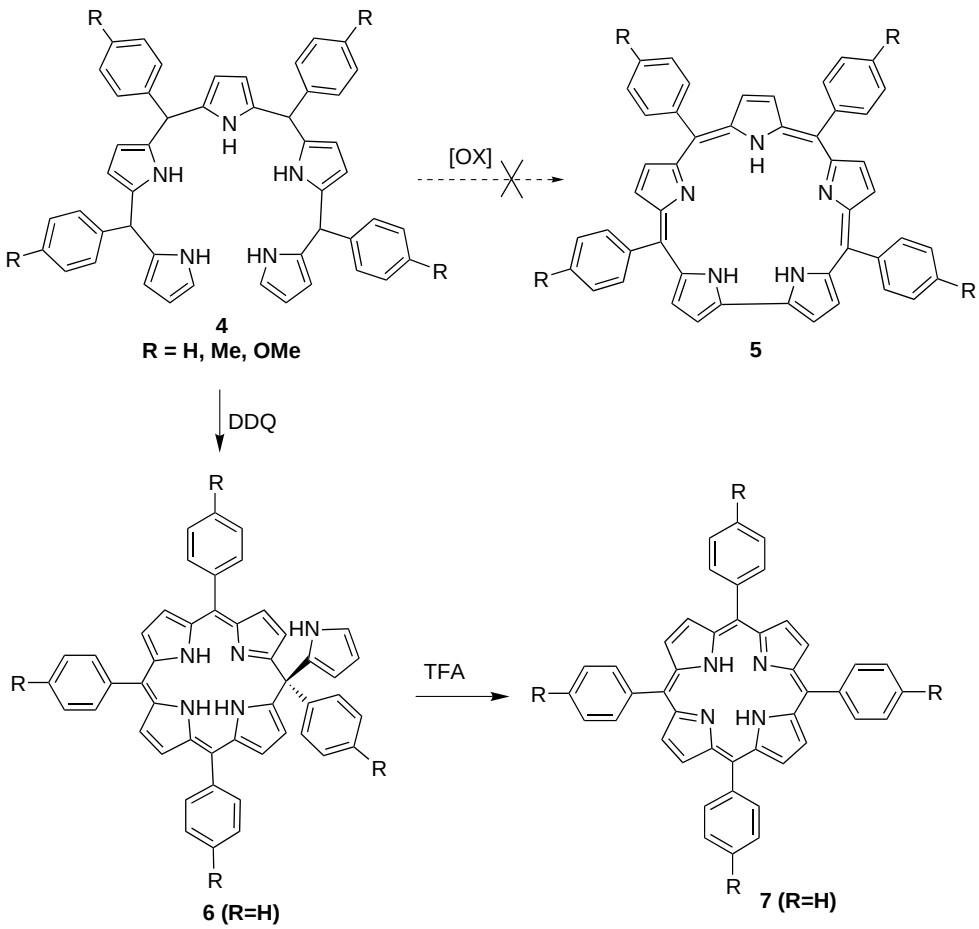
0040-4039/01/$ - see front matter © 2001 Published by Elsevier Science Ltd.
PII: S0040-4039(01)00783-3

states, the [20π] system (**1**), which is a tautomeric form of chlorin (**2**), and the fully oxidised [22π] system (**3**), indicate the complexities of the molecules.

We have been studying the transformation of linear oligopyrroles to porphyrinoid macrocycles ever since the development of a single-step synthesis for oligopyrromethanes.[6] Direct and convenient access to the functionalised porphyrins and corroles has been achieved and we have demonstrated the advantages in designing related model systems utilising oligopyrromethanes. The *meso*-aryl pentapyrromethanes **4** were routinely isolated by column chromatography from the dipyrromethane synthesis.[6] The oxidative coupling of pentapyrromethanes **4** was expected to afford sapphyrins **5**, as shown in Scheme 1. But treatment of **4** with DDQ (3 equiv.) in acetonitrile unexpectedly afforded 1-(pyrrol-2′-yl-1-aryl)-5,10,15-triarylporphyrin (a porphyrin bearing one sp^3 hybridised *meso*-carbon) **6** in 22% yield. The fast-moving dark green pigment was isolated first by silica column chromatography followed by compound **6**. We provisionally assigned the fast-moving green pigment as linearly oxidised pentapyrrolic compounds.[7]

The formation of tetrapyrrolic macrocycles seems to be more favourable over the formation of pentapyrrolic macrocycles (sapphyrinogen). These results are comparable with similar oxidative coupling of tetrapyrromethanes, which resulted in the formation of corroles exclusively.[8] The absorption spectrum of **6** (R = H) showed a Soret-like band at 417 nm ($\varepsilon = 2.4\times10^4$) and an additional band at 680 nm ($\varepsilon = 1.5\times10^4$). The proton NMR spectra clearly showed the presence of a mono-substituted pyrrolic moiety. Unlike porphyrin derivatives, a pyrrolic N–H signal was shown at 8.19 ppm as a broad singlet. The geometry of the eastern-half of the compound **6** resembles the calix[4]pyrrole and the western-half of the molecule may adapt a dipyrromethene-like conformation.[9] The bright green coloured compound **6** was stable in air for a prolonged period of time but the solution ($CHCl_3$) seems to be photosensitive and slow decomposition was observed.[10]

Quantitative conversion of **6** to porphyrin **7** was accomplished by treatment with excess trifluoroacetic acid in chloroform at room temperature (Scheme 1). Exclusive elimination of the *meso*-substituted pyrrole was observed. Preferable elimination of the pyrrolic moiety over phenyl can be explained by the fact that C(2)-protonation in the pyrrole is more favourable than in the phenyl group due to the electron-rich nature of pyrrole. The product was also easily characterised by NMR and mass spectroscopy. The progress of pyrrole elimination was monitored by UV–vis spectroscopy (Fig. 1). The



Scheme 1.

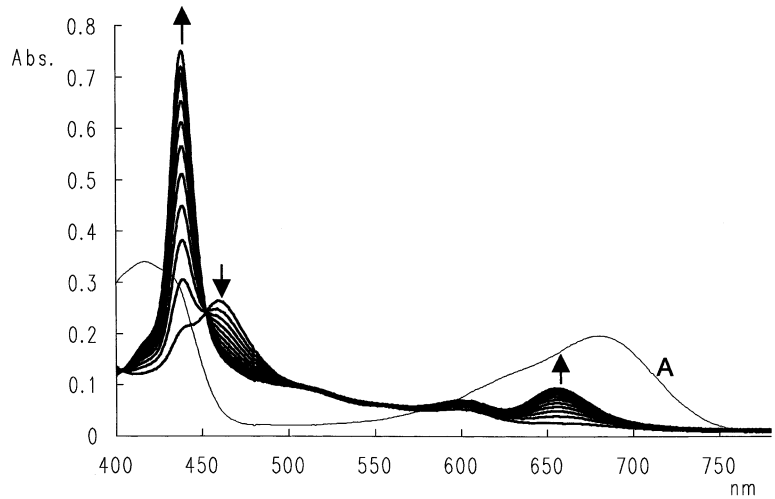


Figure 1. Time-dependent change in the UV–vis spectra of protonated **6** (2.65×10^{-5} M in $CHCl_3$) upon treatment with TFA (8.09×10^{-3} M). The arrows indicate the direction of changes. Each spectra was taken at 5 min intervals. Trace **A**: free base **6**.

acid-catalysed elimination reaction showed simple first-order kinetics and the observed pseudo first-order rate constant calculated from Fig. 1 was 0.14/min. The reaction rate was dependent on the acid concentration.

The preliminary binding behaviour of **6** toward fluoride anions was studied using UV–vis spectroscopy. In the absence of anions, **6** is characterised by a deep green colour. Upon gradual addition of F^-, the colour becomes yellowish. This colour change occurs exclusively with F^- and no detectable colour change is observed with other halogen anions (Cl^-, Br^- and I^-). The calculated association constants for fluoride were 3.4×10^4 and 1.2×10^5 M^{-1} and the Job plot indicated a 1:2 binding ratio.

In summary, an easy conversion of porphotrimethene (phlorin) to *meso*-substituted porphyrin under moderate acidic conditions can be applied to the activation of prodrugs. Development of photosensitisers activated after in vivo elimination of a certain group would be a good example. Also, the reaction could be applicable to the synthesis whenever the controlled release of pyrrole is desired. It is also possible to conceive the use of these elimination chemistry reactions in sensing systems due to their dramatic change in colour. Synthesis of other analogues and their photochemical- and anion-binding activities are under intense investigation.

Acknowledgements

This work was supported by grants from the Korea Science and Engineering Foundation (KOSEF grant 0100044-1-1). The NMR and MS data were obtained from the Central Instrumental Facility at Kangwon National University.

References

1. (a) Setsune, J.; Yamaji, H.; Kaito, T. *Tetrahedron Lett.* **1990**, *31*, 5057–5060; (b) Setsune, J.; Ikeda, M.; Iida, T.; Kitao, T. *J. Am. Chem. Soc.* **1988**, *110*, 6572–6574.
2. (a) Ruppert, R.; Jeandon, C.; Sgambati, A.; Callot, H. J. *Chem. Commun. (Cambridge)* **1999**, 2123–2124; (b) Krattinger, B.; Callot, H. J. *Tetrahedron Lett.* **1996**, *37*, 7699–7702.
3. Dolphin, D. *J. Heterocyclic Chem.* **1970**, *7*, 275–283.
4. (a) Harmjanz, M.; Scott, M. J. *Chem. Commun.* **2000**, 397–398; (b) Harmjanz, M.; Gill, H. S.; Scott, M. J. *J. Am. Chem. Soc.* **2000**, *122*, 10476–10477.
5. Senge, M. O.; Kalish, W. W.; Bischoff, I. *Chem. Eur. J.* **2000**, *6*, 2721–2738.
6. Ka, J. W.; Lee, C. H. *Tetrahedron Lett.* **2000**, *41*, 4609–4612.
7. The FAB-MS (MW 681.28) and proton NMR spectra correspond to the mixture of linearly oxidised tetrapyrrolic pigments. Further isolation was not attempted at this point.
8. Ka, J. W.; Cho, W. S.; Lee, C. H. *Tetrahedron Lett.* **2000**, *41*, 8121–8125.
9. Bucher, C.; Seidel, D.; Lynch, V.; Kral, V.; Sessler, J. L. *Org. Lett.* **2000**, *2*, 3103–3106.
10. A typical procedure for the coupling of **4**: To a stirred mixture of pentapyrromethane (**4**, 50 mg, 0.073 mmol) and NH_4Cl (38 mg, 0.73 mmol) in acetonitrile (36 mL) was added DDQ (50 mg, 0.22 mmol). The mixture was stirred for 1 h at room temperature and the solvent was removed in vacuo. The remaining solid was purified by column chromatography on silica (CH_2Cl_2). Yield: 11 mg (22%, green solid). ^1H NMR ($CDCl_3$): δ 5.86 (m, 1H, pyrrolic-H), 6.18 (m, 1H, pyrrolic-H), 6.65 (d, $J=3.9$ Hz, 2H, pyrrolic-H), 6.78 (m, 1H, pyrrolic-H), 6.83 (d, $J=3.9$ Hz, 2H, pyrrolic-H), 6.87 (m, 2H, Ar-H), 6.94 (d, $J=5.0$ Hz, 2H, pyrrolic-H), 7.17 (m, 5H, pyrrolic-H+Ar-H), 7.41–7.49 (m, 9H, Ar-H), 7.57 (m, 2H, Ar-H), 7.65 (m, 4H, Ar-H), 8.19 (brs, NH). FAB-MS calcd for $C_{48}H_{35}N_5$: 681.29; found: 681.96.