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Total synthesis of the porphyrin mineral abelsonite and related petroporphyrins with five-membered exocyclic rings[☆]

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Abstract—A reliable synthesis of porphyrins with five-membered exocyclic rings from *b*-bilenes has been developed. This methodology has been applied to the first total synthesis of the porphyrin mineral abelsonite, as well as the widespread petroporphyrin deoxophylloerythroetioporphyrin (DPEP) and its 3-desethyl analogue. © 2003 Elsevier Ltd. All rights reserved.

The presence of metalloporphyrins in organic-rich sediments such oil shales and petroleum, generally known as petroporphyrins or geoporphyrins, was first established in the 1930's by the pioneering efforts of Alfred Treibs.^{1,2} Treibs tentatively identified metallo-derivatives of deoxophylloerythroetioporphyrin (DPEP; 1) and etioporphyrin-III, and subsequent investigations have firmly established the structures of these geoporphyrins,³ which usually occur as the nickel(II) or vanadyl chelates.⁴ DPEP is considered to be a 'molecular fossil' of the chlorophylls due to the presence of a five-membered exocyclic ring.⁵ In the 1960's, mass spectrometric investigations demonstrated that sedimentary porphyrin fractions contain complex mixtures of metalloporphyrins.⁶ Indeed, more than eighty porphyrin structures have been identified in organic-rich sediments by mass spectrometry and NMR spectroscopy.⁴ These geoporphyrins fall into several major families, the most prevalent being the DPEP series which are structurally related to 1. The structures of the porphyrins in fossil fuels can provide insights into the origins of these materials and their sedimentary history, as well as being useful chemical markers for petroleum exploration.⁴ In addition, the porphyrins associated with a given sediment provide a unique fingerprint and may allow the origins of environmental contaminants (e.g. oil spills) to be ascertained.7 For these and other reasons, synthetic samples of sedimentary porphyrins are of value as standards in the development of new analytical meth-

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ods.^{7,8} Although a number of routes for the synthesis of DPEP have been reported,^{9–14} none of them are completely satisfactory and this has limited the availability of related *meso*, β -ethanoporphyrins.



The concentrations of metalloporphyrins in organic sediments vary considerably, but they can be as high as several parts per thousand. A particularly interesting example of this type is the mineral abelsonite, which occurs as small purple patches in fractures associated with shales from the Green River Formation of the Uinta Basin in Utah.¹⁵ Abelsonite has been analyzed by



Scheme 1.

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MS and NOE difference proton NMR spectroscopy, and its major component shown to be the nickel(II) pentamethyl DPEP-type porphyrin **2a**.¹⁶ This nickel complex is accompanied by a small amount of the C30 analogue **2b**. To date, no syntheses of this unique organic mineral have been disclosed. In relation to our efforts to develop improved routes to sedimentary porphyrins, we now report the first total synthesis of abelsonite. In addition, an improved methodology for the synthesis of DPEP-type petroporphyrins is demonstrated.

DPEP has been synthesized from chlorophyll a,⁹ and by total synthesis.^{10–14} Only the latter allows for the possibility of synthesizing related DPEP-type porphyrins. In many syntheses, the five-membered ring is introduced after the porphyrin macrocycle has been generated, but overall yields are low.¹¹ Flaugh and Rapoport introduced the five-membered carbocyclic ring prior to cyclization of a *b*-bilene intermediate 3, but this unit had a disastrous effect on porphyrin formation and DPEP was isolated in only 6% yield (Scheme 1).¹² In our studies, we have developed routes for the synthesis of cyclopenta[b]pyrroles, and related dipyrroles, and have made use of these compounds in the synthesis of naturally occurring porphyrins. The MacDonald '2+2' condensation was found to give good yields of the type II DPEPs 4 (Scheme 2),^{13,17} but attempts to carry out cyclizations of *a,c*-biladiene 5 were unsuccessful (Scheme 1).¹³ One factor that appears to aid the formation of porphyrins 4 by the 2+2 route is that the cyclizations occur while the carbon bridge linking the carbocyclic ring is sp^3 hybridized and this decreases deleterious steric interactions at this critical stage. However, the MacDonald condensation cannot be used to prepare DPEP because one of the two condensing dipyrrolic units must be symmetrical in order to avoid the formation of two isomeric porphyrin products. In an attempt to overcome this problem by carrying out a stepwise MacDonald condensation, b-bilenes 6 were generated and cyclized under mild conditions (Scheme 3).^{14,18} Although this strategy was successful,¹⁴ and a series of bacteriopetroporphyrins could be synthesized in addition to DPEP itself,¹⁹ significant difficulties were encountered. The *b*-bilene intermediates proved to be very unstable and could not be purified. Instead, the crude material was directly converted to porphyrin. Unfortunately, etioporphyrin by-products were also formed in these reactions and it was necessary to convert the porphyrin mixtures into their nickel(II) chelates and carry out extensive purification by flash chromatography. This severely limits the chemistry and does not allow the synthesis of less soluble petroporphyrins. The five-membered carbocyclic ring appears to be responsible for destabilizing the *b*-bilene intermediates and we hypothesized that this problem could be circumvented by constructing *b*-bilenes where the conjugated portion of the molecule was not directly connected to this unit.

The cyclopenta[b]pyrrole *tert*-butyl ester 7 was prepared from cyclopentanone using Knorr-type chemistry²⁰ (Scheme 4). Reaction with lead tetraacetate



Scheme 2.



Scheme 3.

gave the acetoxy derivative 8 (quantitative) and this was condensed with α -unsubstituted pyrrole 9 in the presence of *p*-toluenesulfonic acid (*p*-TSA) in acetic acid to give the dipyrrole 10. Hydrogenolysis over 10%Pd/C gave the corresponding carboxylic acid 11. Decarboxylation with 2 equiv. of *p*-TSA, followed by formylation with benzoyl chloride-DMF under Clezy's modified Vilsmeier formylation conditions,²¹ gave the aldehyde 12. This unit represents the 'southern' half of petroporphyrins 1 and 2. The dipyrrolic precursors 13 corresponding to the 'northern' half were prepared by condensing acetoxymethylpyrroles 14 with α -free pyrrole 15 in the presence of Montmorillonite clay.²² Deprotection of the benzyl esters (H_2-Pd/C) gave the related carboxylic acids 16, and subsequent conversion to the corresponding aldehydes 17 could then be carried out under the conditions used to prepare 12. Condensation of 11 with 17a in the presence of p-TSA, followed by treatment with HCl, gave the required *b*-bilene **18a**. Alternatively, 12 could be reacted with 16a to produce the same tetrapyrrolic product. The latter route proved to give superior yields and is the recommended procedure for these syntheses. The *b*-bilene was reasonable stable and could be recrystallized from ether and fully characterized. Cyclization with TFA-trimethyl orthoformate, followed by air oxidation in the presence of zinc acetate, gave DPEP in 30% yield. Only minimal chromatography to remove polar impurities was necessary. Reaction of 12 with 16b gave the pentamethyl b-bilene 18b, and this was cyclized as previously described to give porphyrin 19 in 30% yield. Porphyrin **19** is the demetallated form of abelsonite and the synthesis was easily completed by reacting 19 with nickel(II) acetate in refluxing chloroform-methanol to give 2a in 89% yield. The related 3-unsubstituted porphyrin **20** was prepared similarly (35%).



Scheme 4.

The new syntheses afforded pure porphyrins in excellent yields. The proton NMR spectrum of **19** is well resolved and shows the presence of three *meso*-protons near 10 ppm. Carbon-13 NMR spectra of porphyrins in TFA–CDCl₃ has been used to assess their isomeric purity²³ and these data also confirm the structural identity of **19**. Of particular note, the three unsubstituted *meso*-carbons show up as 3 resonances at characteristic values of 97–100 ppm.

The construction of b-bilenes with the conjugated pyrromethene unit indirectly connected to the fivemembered carbocyclic ring greatly increases the stability of these crucial tetrapyrrolic intermediates. This consideration allows pure b-bilenes to be isolated and subsequent 'eastern' ring closure produces DPEP in the best yields ever reported. The methodology has been applied to the first total synthesis of abelsonite and the 3-desethyl DPEP **20**. This approach will be invaluable in the synthesis of many other naturally occurring DPEP-type petroporphyrins.

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References

1. (a) Treibs, A. Justus Liebigs Ann. Chem. 1934, 510, 42;

(b) Treibs, A. Angew. Chem. 1936, 49, 682.

- Baker, E. W.; Palmer, S. E. In *The Porphyrins*; Dolphin, D., Ed.; Academic Press: New York, 1978; Vol. 1, pp. 486–552.
- (a) Quirke, J. M. E.; Maxwell, J. R.; Eglinton, G.; Sanders, J. K. M. *Tetrahedron Lett.* **1980**, *21*, 2987; (b) Fookes, C. J. R. *J. Chem. Soc.*, *Chem. Commun.* **1983**, 1472; (c) Quirke, J. M. E.; Maxwell, J. R. *Tetrahedron* **1980**, *36*, 3453.
- Callot, H. J.; Ocampo, R. In *The Porphyrin Handbook*; Kadish, K. M.; Smith, K. M.; Guilard, R., Eds.; Academic Press: San Diego, 2000; pp. 349–398.
- (a) Filby, R. H.; Van Berkel, G. J. In Metal Complexes in Fossil Fuels. Geochemistry, Characterization, and Processing; Filby, R. H.; Branthaver, J. F., Eds.; American Chemical Society: Washington DC, 1987; pp. 2–39; (b) Chicarelli, M. I.; Kaur, S.; Maxwell, J. R. In Metal Complexes in Fossil Fuels. Geochemistry, Characterization, and Processing; Filby, R. H.; Branthaver, J. F., Eds.; American Chemical Society: Washington DC, 1987; pp. 40–67; (c) Ocampo, R.; Callot, H. J.; Albrecht, P. In Metal Complexes in Fossil Fuels. Geochemistry, Characterization, and Processing; Filby, R. H.; Branthaver, J. F., Eds.; American Chemical Society: Washington DC, 1987; pp. 68–73.
- (a) Baker, E. W. J. Am. Chem. Soc. 1966, 88, 2311; (b) Baker, E. W.; Yen, T. F.; Dickie, J. P.; Rhodes, R. E.; Clark, L. F. J. Am. Chem. Soc. 1967, 89, 3631.
- Cantú, R.; Stencel, J. R.; Czernuszewicz, R. S.; Jaffé, P. R.; Lash, T. D. *Environ. Sci. Technol.* 2000, 34, 192.
- (a) Rankin, J. G.; Czernuszewicz, R. S.; Lash, T. D. Inorg. Chem. 1995, 34, 3025; (b) Czernuszewicz, R. S.; Rankin, J. G.; Lash, T. D. Inorg. Chem. 1996, 35, 199; (c) Rankin, J. G.; Cantú, R.; Czernuszewicz, R. S.; Lash, T.

D. Org. Geochem. **1999**, 30, 201; (d) Boggess, J. M.; Czernuszewicz, R. S.; Lash, T. D. Org. Geochem. **2002**, 33, 1111.

- (a) Baker, E. W.; Corwin, A. H.; Klesper, E.; Wei, P. E. J. Org. Chem. 1968, 33, 3144; (b) Jeandon, C.; Ocampo, R.; Callot, H. J. Tetrahedron 1997, 53, 16107.
- (a) Fischer, H.; Hofmann, H. J. Justus Liebigs Ann. Chem. 1935, 517, 274; (b) Sugihara, J. M.; McGee, L. R. J. Org. Chem. 1957, 22, 795.
- 11. Flaugh, M. E.; Rapoport, H. J. Am. Chem. Soc. 1968, 90, 6877.
- (a) Chaudry, I. A.; Clezy, P. S.; Mirza, A. H. Aust. J. Chem. 1980, 33, 1095; (b) Smith, K. M.; Langry, K. C.; Minnetian, O. M. J. Org. Chem. 1984, 49, 4602; (c) Bauder, C.; Ocampo, R.; Callot, H. J. Tetrahedron 1992, 48, 5135.
- (a) Lash, T. D.; Catarello, J. J. *Tetrahedron* 1993, 49, 4159; (b) Lash, T. D.; Quizon-Colquitt, D. M.; Shiner, C. M.; Nguyen, T. H.; Hu, Z. *Energy Fuels* 1993, 4, 668.
- 14. Li, W.; Lash, T. D. Tetrahedron Lett. 1998, 39, 8571.
- Milton, C.; Dwornik, E. J.; Estep-Barnes, P. A.; Finkelman, R. B.; Pabst, A.; Palmer, S. E. *Am. Mineralog.* 1978, 63, 930.

- Storm, C. B.; Krane, J.; Skjetne, T.; Telnaes, N.; Branthaver, J. F.; Baker, E. W. Science 1984, 223, 1075.
- (a) Hu, Z.; Lash, T. D. Synlett 1994, 909; (b) Lash, T. D. Tetrahedron 1998, 54, 359; (c) Bastian, J. A.; Lash, T. D. Tetrahedron 1998, 54, 6299; (d) Lash, T. D. Org. Geochem. 1989, 14, 213; (e) Lash, T. D.; Balasubramaniam, R. P.; Catarello, J. J.; Johnson, M. C.; May, D. A., Jr.; Bladel, K. A.; Feeley, J. M.; Hoehner, M. C.; Marron, T. G.; Nguyen, T. H.; Perun, T. J., Jr.; Quizon, D. M.; Shiner, C. M.; Watson, A. Energy Fuels 1990, 4, 668; (f) Lash, T. D. In Advances in Nitrogen Heterocycles; Moody, C. J., Ed.; JAI Press: Stamford, CT, 1995; Vol. 1, pp. 19–51.
- Jackson, A. H.; Kenner, G. W.; Smith, K. M. J. Chem. Soc. (C) 1971, 502.
- 19. Li, W.; Lash, T.D., unpublished work.
- Quizon-Colquitt, D. M.; Lash, T. D. J. Heterocyclic Chem. 1993, 30, 477.
- 21. Chong, R.; Clezy, P. S.; Liepa, A. J.; Nichol, A. W. Austr. J. Chem. 1969, 22, 229.
- Jackson, A. H.; Pandey, R. K.; Rao, K. R. N.; Roberts, E. *Tetrahedron Lett.* 1985, 26, 793.
- 23. Lash, T. D. J. Porphyrins Phthalocyanines 1997, 1, 29.