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SYNTHESIS OF PORPHYRINS WITH FOUR EXOCYCLIC RINGS FROM 4,5,6,7-TETRAHYDROINDOLES

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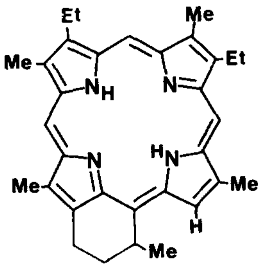
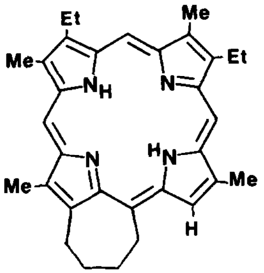
Abstract: The 3-alkyl-4,5,6,7-tetrahydroindoles 4a and 4b reacted with lead tetraacetate in acetic acid to give the corresponding 7-acetoxy derivatives; hydrolysis, followed by treatment with potassium ferricyanide in refluxing acetic acid afforded the novel porphyrins 6a and 6b.

Recently a variety of nickel and vanadyl porphyrins have been isolated from oil shales and their structures determined by nOe difference proton NMR spectroscopy[1]. Novel structures bearing five-[1], six-[2] or seven-[3] membered exocyclic rings, e.g. 1 and 2, have been characterized and these are of some interest with respect to gaining an understanding of the geochemical processes involved in the maturation of organic sediments.

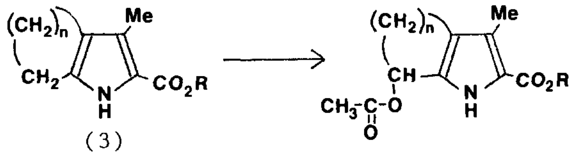


(1)

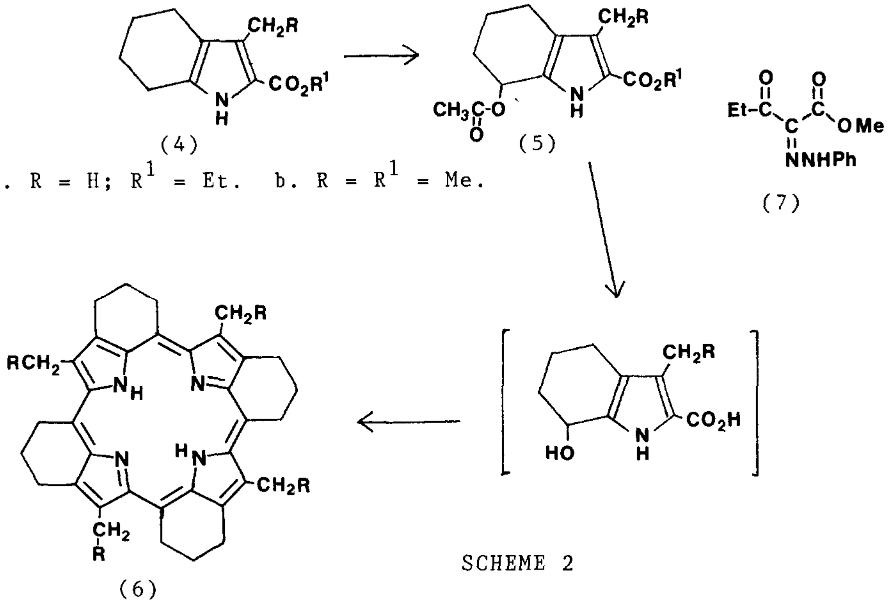


(2)

We have been interested in developing a general route to porphyrins bearing exocyclic rings of this type. Our approach[4] utilizes the incorporation of *b*-cycloalkenopyrroles 3 by derivatizing the α-methylene grouping with lead tetraacetate (Scheme 1). In this paper we report some preliminary studies[5,6], including the preparation of two novel porphyrins with four exocyclic rings.



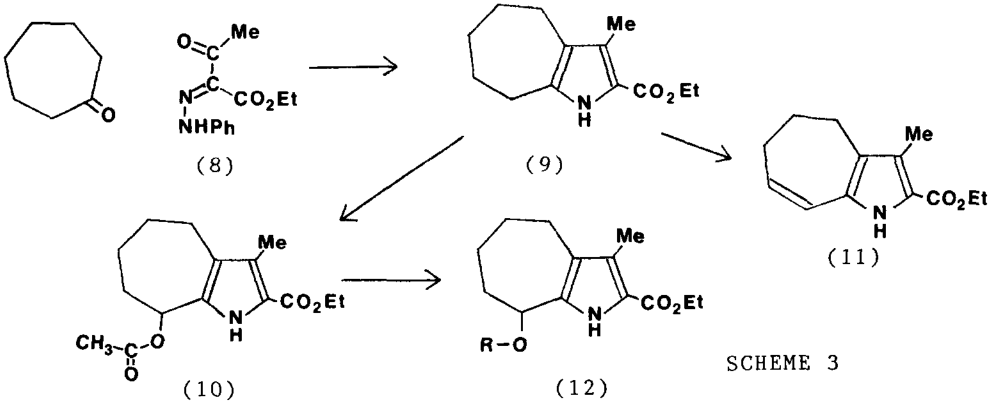
SCHEME 1



a. R = H; R^1 = Et. b. R = R^1 = Me.

SCHEME 2

a. R = H; b. R = Me



SCHEME 3

a. R = Et; b. R = Me

The known 4,5,6,7-tetrahydroindole 4a[7] reacted with lead tetraacetate in acetic acid to give the 7-acetoxy compound 5a in 78% yield: m.p. 67.5-69.5°C; NMR ($CDCl_3$) δ 1.33(3H, t, $-CH_2C\underline{H}_3$), 1.94(4H, m, $-C\underline{H}_2C\underline{H}_2-$), 2.04(3H, s, $-OCOC\underline{H}_3$), 2.21(3H, s, pyrrolic $-C\underline{H}_3$), 2.4(2H, m, pyrrole-$C\underline{H}_2-$), 4.31(2H,q, $OC\underline{H}_2-$), 5.66(1H, m, $-C\underline{H}-O-$), 9.2(1H, b, $N\underline{H}$); IR (Nujol mull) ν 3270 (NH stretch), 1732 (acetoxy C=O), 1665 (pyrrole C=O) cm^{-1}. Compound 5a was hydrolysed with potassium hydroxide in refluxing methanol/water and carefully neutralised at 5°C with 2M hydrochloric acid. The crude hydroxy carboxylic acid (Scheme 2) was treated with refluxing glacial acetic acid containing potassium ferricyanide[8] to give an unusual porphyrin 6a bearing four exocyclic rings as small purple needles (from dichloromethane/methanol) in 15% yield: m.p. $>$300°C; NMR (50% TFA/$CDCl_3$) δ 2.69(8H, m, 4x $-CH_2C\underline{H}_2CH_2-$), 3.43(12H, s, 4x $-C\underline{H}_3$), 3.82(8H, t, 4x β-$C\underline{H}_2-$), 5.06(8H, t, 4x meso-$C\underline{H}_2-$), -3.6(4H, s, 4x $N\underline{H}$ of porphyrin dication); UV/visible (CH_2Cl_2) λ_{max} (log ϵ) 417(5.07), 516(4.01), 547(3.67), 590(3.60), 646(3.34) nm.

The 3-ethyltetrahydroindole 4b (m.p. 86.5-87.5°C) was prepared in 19% yield by a Knorr type condensation of cyclohexanone with the phenylhydrazone 7[9] in the presence of zinc dust in buffered acetic acid. Reaction of 4b with lead tetraacetate in acetic acid afforded the acetoxy derivative 5b (m.p. 88-89°C) and subsequent hydrolysis and cyclization (as above) gave the tetraethyl porphyrin 6b in 14% yield: NMR ($CDCl_3$) δ 1.65(12H, t, 4x $-CH_2C\underline{H}_3$), 2.52(8H, m, $-CH_2C\underline{H}_2CH_2-$), 3.76(16H, m, 8x β-pyrrolic $-C\underline{H}_2-$), 4.84(8H, t, 4x meso-$C\underline{H}_2-$), -2.5(2H, b, 2x $N\underline{H}$).

The *b*-cycloheptenopyrrole system has also been investigated. Reductive condensation of 8 with cycloheptanone in the presence of zinc and sodium acetate in acetic acid afforded the *b*-cycloheptenopyrrole ethyl ester 9 (m.p. 108-109°C) in 20-25% yield. Reaction with lead tetraacetate in acetic acid gave the vinylic pyrrole 11: m.p. 117-119°C; NMR ($CDCl_3$) δ 1.33(3H, t, $-CH_2C\underline{H}_3$), 1.86(2H, m, 5-$C\underline{H}_2-$), 2.23(3H, s, pyrrolic $C\underline{H}_3$), 2.43(2H, m), 2.64 (2H, m), 4.29(2H, q, $OC\underline{H}_2-$), 5.78(1H, dt, $-CH_2-C\underline{H}=$), 6.11(1H, d, pyrrole-$C\underline{H}=$), 8.57(1H, b, $N\underline{H}$); MS m/e 219. This compound presumably arises from elimination of acetic acid from the desired acetoxy derivative 10. The labile acetoxy *b*-cycloheptenopyrrole 10[10] (m.p. 90-92°C) could be isolated when the reaction of 9 with lead tetraacetate was carried out in dichloromethane; however 10 decomposed over several weeks at room temperature to give, primarily, the elimination product 11. Attempts to recrystallize 10 from hot ethanol or methanol led to the solvolysis products 12a and 12b, respectively. We also attempted to convert 10 to the corresponding tetrabutano porphyrin but these experiments resulted in the formation of intractable brown mud-like materials, presumably due to extensive polymerization, since no trace of porphyrin fluorescence could be detected, even after chromatography. It seems likely that the conformation of the cycloheptene rings does not allow the tetrapyrrolic intermediate to cyclize and further reaction leads to polymer.

In conclusion, two tetrapropanoporphyrins, 6a and 6b, have been synthesized and these unique porphyrins should be useful as model compounds. In addition acetoxy intermediates such as 5 and 11 show some promise[4] in the total synthesis of porphyrins, e.g. 1 and 2, of geochemical significance.

Acknowledgements

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5. A report on this work was presented at the Tenth International Congress of Heterocyclic Chemistry, University of Waterloo, Ontario, Canada, Aug. 1985. T. D. Lash, Book of Abstracts, P5-164.
6. All new compounds gave satisfactory NMR spectra and elemental analysis, unless otherwise stated. Porphyrin structures were further confirmed by Fast Atom Bombardment Mass Spectrometry.
7. V. I. Shvedov, L. B. Altukhova and A. N. Grinev, *Khim. Geterots. Soed.*, 1972, 8, 342.
8. Cf. "Porphyrins and Metalloporphyrins", ed. K. M. Smith, Elsevier, Amsterdam, 1975, p. 769.
9. Prepared in 98% yield by treating a buffered solution of methyl propionylacetate with benzene diazonium chloride. Crystallized as yellow needles from ethanol/water, m.p. 69-70°C.
10. Analytical data could not be obtained for 10, although the stable methoxy 12a and ethoxy 12b derivatives gave satisfactory CHN Analyses.

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