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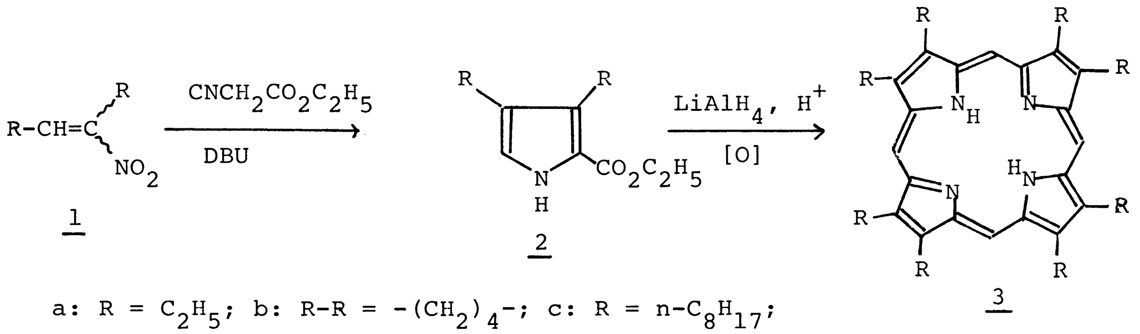
Synthesis of Octaalkyl- and Octaarylporphyrins from Nitroalkenes

Noboru ONO and Kazuhiro MARUYAMA
Department of Chemistry, Faculty of Science,
Kyoto University, Kyoto 606

Symmetrically substituted octaalkyl- and octaarylporphyrins are readily prepared by the reduction of 2-ethoxycarbonyl-3,4-diarkyl (or diaryl)pyrroles with $LiAlH_4$ followed by treatment with acetic acid and oxidizing agents.

Octaethylporphyrin (OEP) and related pophyrins have been widely exploited in the development of porphyrin model systems.1) Especially OEP is one of the most important and widely used models by reason of its symmetry and solubility. A number of methods have been devised for the synthesis of OEP so far.2) Most of them start from 2-ethoxycarbonyl-3,4-diethyl-5-methylpyrrole, which is prepared by the Knorr reaction of ethyl propionylacetate with 2,4-pentanedione. At present, the Dolphin's procedure is said to be the most reliable method among them. However, this is still not easy, for this is necessarily long and it is difficult to get pure OEP for inexperienced hands.3) Furtheremore, replacement of the ethyl group of OEP by other alkyl groups is very difficult by the conventional methods. In this paper we wish to report a simple and flexible method for the synthesis of OEP and related porphyrins starting from nitroalkenes, which may be used for the preparation of sophisticated porphyrin model systems.4)

A new method is summarized in Scheme 1. The requisite starting nitroalkenes are readily prepared either by dehydration of the corresponding β-nitro alcohols or nitration of alkenes.5) They are converted into pyrroles (2) by the reaction with ethyl isocyanoacetate in the presence of 1,8-diazabicyclo[5.4.0]undecene-7 (DBU).6) As alkyl or aryl groups of 2 are derived from nitroalkenes, various groups can be introduced at the 3- and 4-positions of pyrroles. Pyrroles having long alkyl chains at these positions such as 2c are very attractive intermediates for the synthesis of lipophilic porphyrins.[7)] The pyrroles thus obtained are ideally functionalized for the synthesis of porphyrins.[8)] If the ethoxycarbonyl group of 2 is reduced to the hydroxymethyl group, it is expected that porphyrins (3) may be formed via tetramerization of mono-pyrroles. We have studied the realization of this conversion.[9)] The conversion of 2-ethoxycarbonyl-3,4-diethylpyrrole (2a) to OEP (3a) was tried under various conditions. Reduction of 2a with $LiAlH_4$ in THF for 2 h at 0-5 °C followed by treatment with acetic acid and oxidation with oxygen in the presence of chloranil gave OEP in 40% yield. The conditions of the reduction are important to get OEP in good yield. If the reaction was carried out for longer time at higher temperature, the yield of OEP became low.[10)] The preparation of OEP is described as a typical case. Other porphyrins were prepared by the same procedure. The results are summarized in Table 1.



a: R = C_2H_5; b: R-R = $-(CH_2)_4-$; c: R = n-C_8H_{17};
d: R = Ph

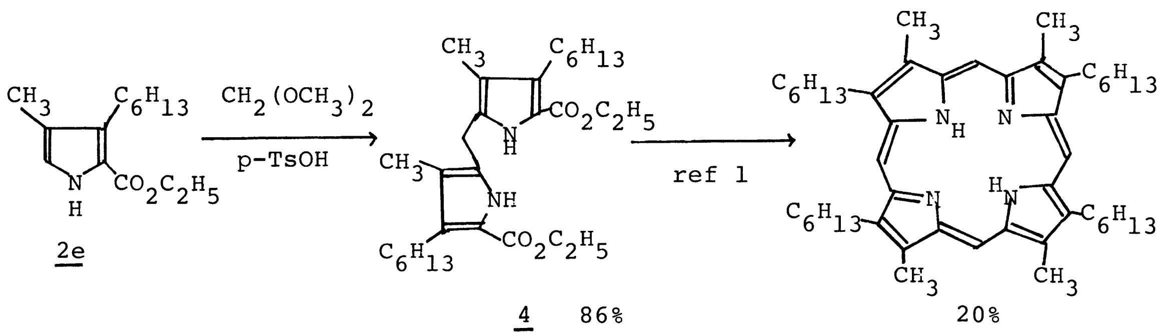
Scheme 1. Preparation of Porphyrins from Nitroalkenes.

Table 1. Preparation of Pyrroles (2) and Porphyrins (3)

R	R	2, yield/%	3, yield/%
C_2H_5	C_2H_5	2a, 86	3a, 40
$-(CH_2)_4-$		2b, 90	3b, 35
n-C_8H_{17}	n-C_8H_{17}	2c, 85	3c, 25
Ph	Ph	2d, 45	3d, 15

Preparation of OEP: A mixture of 3-nitro-3-hexene (1.3 g, 10 mmol), ethyl isocyanoacetate (1.13 g, 10 mmol), and DBU (1.52 g, 10 mmol) in THF (10 ml) was stirred at room temperature for 10 h. The usual work-up followed by column chromatography (silica gel/benzene) gave 2a, 1.68 g (86%). To a stirred mixture of $LiAlH_4$ (0.2 g, 5 mmol) in THF (10 ml) was added a solution of 2a (0.84 g, 5 mmol) in THF (5 ml) at 0 °C. The resulting mixture was stirred at 0 °C for 2 h, and poured into CH_2Cl_2 (100 ml). The mixture was shaked with 1 *M*-HCl, and washed with water. The organic layer was dried with anhydrous magnesium sulfate and acetic acid (10 ml) was added to the reaction mixture, which was heated at reflux for 10 h. Then, chloranil (0.3 g) was added to the reaction mixture and oxygen was passed through it. After boiling for 1 h, the solvent was removed. The residue was subjected to column chromatography (silica gel/CH_2Cl_2) to give OEP, 0.30 g (40%). Mp 320 °C . UV-Vis (CH_2Cl_2): 620, 594, 567, 498, 400 nm. NMR ($CDCl_3$) δ -3.73 (NH, 2H, s), 1.92 (CH_3, 24 H, t), 4.10 (CH_2, 16 H, q), 10.10 (4H, s). The spectral data of other porphyrins are summarized.[11]

This approach can only be used satisfactorily if the pyrrole 3 and 4 substituents are identical. If they are different, polymarization leads to a statistical mixture of all four possible isomers. For example, the reduction of 2-ethoxycarbonyl-3-hexyl-4-methylpyrrole (2e) with $LiAlH_4$ followed by treatment with acetic acid and oxidation gave the porphyrin in 45% yield. However, this porphyrin consisted of four isomers. One isomer could be prepared via pyrromethane (4), which was obtained by the reaction of 2e with methylal in the presence of p-toluenesulfonic acid.



The direct synthesis of unsymmetrically substituted porphyrins via the controlled polymerization of mono-pyrroles is currently underway.

References

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7) It requires several steps to prepare pyrroles having long alkyl chains, see, K. M. Smith and G. M. F. Bisset, J. Org. Chem., 44, 2077 (1979); B. Morgan and D. Dolphin, ibid., 52, 5364 (1987).
8) The Knorr reaction gives the pyrrole having the methyl group at the 5-position, which can be converted into 2 via multi steps, see, T. P. Wijesekera, J. B. Paine III, and D. Dolphin, J. Org. Chem., 50, 3832 (1985).
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10) For example, the yield of OEP was 1% when the reduction was carried out at room temperature for 10 h.
11) 3b: Mp 295-300 °C. NMR (CDCl$_3$) δ -3.70 (2 H, s), 2.50 (16 H, m), 4.17 (16 H, m), 9.85 (4 H, s). Vis (CH$_2$Cl$_2$) 393, 497, 532, 566, 619 nm. 3c: oil. NMR (CDCl$_3$) δ -3.70 (2 H, s), 0.88 (24 H, t), 1.25 (48 H, m), 1.59 (16 H, m), 1.72 (16 H, m), 2.28 (16 H, m), 4.02 (16 H, t), 10.06 (4 H, s). Vis (CH$_2$Cl$_2$) 403, 503, 534, 534, 568, 620 nm. Vis (hexane) 392, 499, 528, 570, 624 nm. 3d: Mp 290-294 °C. NMR (CDCl$_3$) δ -3.10 (2 H, s), 7.80-8.10 (40 H, m), 10.10 (4 H, s). Vis (CH$_2$Cl$_2$) 383, 499, 533, 568, 621 nm.

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