On the Methylation of 5-(4-Alkoxyphenyl)-15-(4-pyridyl)porphyrins

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Mixed condensation of 3,3'-diethyl-4,4'-dimethyl-2,2'-dipyrrolylmethane **1** with 4-formylpyridine **2** and 4-alkoxybenzaldehyde **3** in acid medium and subsequent oxidation of the reaction mixture with DDQ gives, among other compounds, title compound **5**. An efficient methylation procedure of the pyridyl group in 5-(4-alkyoxyphenyl)-15-(4-pyridyl)porphyrins is described. Mixed condensation of **1** with *N*-methyl-4-formylpyridinium salt **9** and **3** yields among other compounds 5-(4-*N*-methylpyridiniumiodide)porphyrin **10**.

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Introduction.

Numerous porphyrins have been synthesized with the aim to mimic the charge separation in the photosynthetic process [1,4]. The vast majority of these model systems belongs to the class of the *meso*-tetraarylporphyrins. The study of model systems like 5,15-diarylporphyrins is more restricted, since their synthesis is more cumbersome; therefore fewer investigations about this type of porphyrins have been reported.

It is well-known that organized media have a beneficial effect on the photo-chemical charge separation, since the charge recombination is retarded in these media. A certain degree of organisation of the reactants occurs in assemblies such as (reversed) micelles, microemulsions and vesicles.

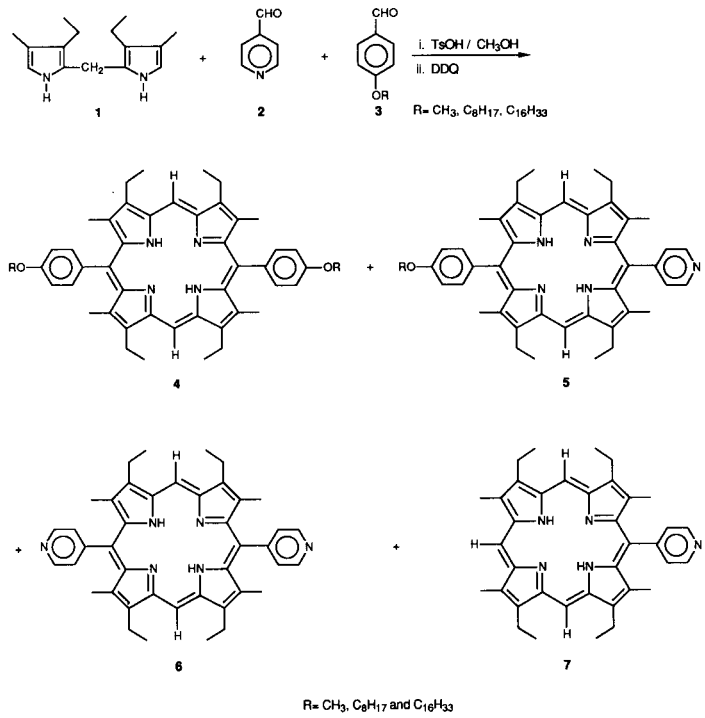
In this paper we describe the synthesis of some 5-aryl-15-pyridinium porphyrin salts **8** to investigate the photophysical properties of these charged species in reversed micelles.

Results and Discussion.

Condensation of 3,3'-diethyl-4,4'-dimethyl-2,2'-dipyrrolylmethane **1** [5,6] with 4-formylpyridine **2** and the 4-alkoxybenzaldehyde **3** (R = methyl, octyl, hexadecyl) in the solvent methanol and in the presence of the catalyst *p*-toluenesulfonic acid gave a reaction mixture which on subsequent treatment with DDQ yields a mixture of 5,15-di(*p*-alkoxyphenyl)porphyrin **4**, the 5-(*p*-alkoxyphenyl)-15(4-pyridyl)porphyrin **5**, the 5,15-di(4-pyridyl)porphyrin **6** and surprisingly (4-pyridyl)porphyrin **7**; these compounds can be separated by means of column chromatography.

Intermediates in the formation of the compounds **4-7** are the corresponding porphyrinogens (hexahydroporphyrins), which are easily oxidized by DDQ. This procedure, in which the acid catalysed condensation is combined by oxidation with DDQ, is a modification of a procedure, in which the porphyrinogens are isolated and oxidized in a separate step [5,6]. During the course of our investigations, the synthesis of 5,15-bis(4-pyridyl)-2,8,12,-18-tetraethyl-3,7,13,17-tetramethylporphyrin was described in the literature [3] using the same modification as described in this paper. It is known from the literature that the amount of catalyst in the condensation reaction is very critical [6]. Variation of the amount and kind of catalyst usually results in an increased yield of the monoarylporphyrin at the expense of the diarylporphyrin. This side reaction seems to be more pronounced in the condensation of **2** with **1**, probably due to the fact that in the acid medium **2** is protonated before condensation.

Scheme 1

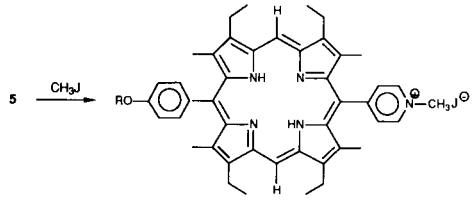


Although the desired porphyrin **5** can be obtained from the crude reaction mixture by means of column chromatography, the procedure is time consuming; moreover it is very difficult to get **5** completely pure. Even after repeated chromatography **5** is still contaminated with traces of **4** and **6**. However, the purity is found to be depending upon the length of the alkyl chain R. With R = $C_{16}H_{33}$, better separation is effected and therefore a more pure product **5**

is obtained than with R = CH_3.

Since our goal is to prepare pure *N*-methylpyridinium product **8**, the best procedure is to purify the crude porphyrin mixture containing **4-7** by means of column chromatography only one time and methylate the reasonable pure product **5** with methyl iodide in dichloromethane and methanol (10:1.5). The quaternary salt **8** is purified by means of column chromatography. After only one purification **8** is obtained in a very pure form. The much greater difference in polarity of salt **8** and the contaminants **4** and **6** makes the separation procedure very effective.

Scheme 2

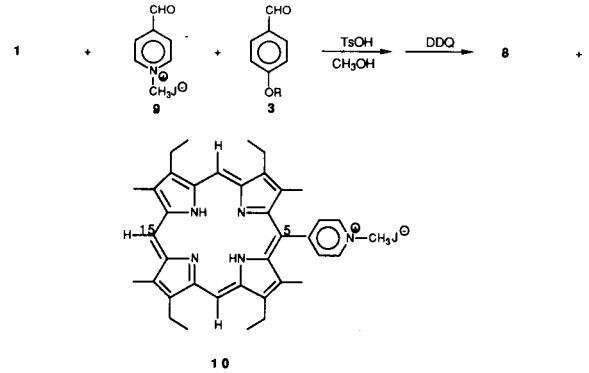


8

The methylation of **5** into **8** provided us initially with a lot of problems, though the methylation of tetraarylporphyrins that contain one or more pyridine substituents is well documentated [5,6]. Methylation of **5** with methyl iodide under conditions analogous for tetrapyridylporphyrins only yields the starting compound even after treatment for several days. The failure of methylation is due to low solubility of **5**. After we have observed that **5** is surprisingly soluble in a mixture of dichloromethane and methanol (10:1.5), methylation was found to occur very readily. The same procedure was also found to be successful for the methylation of **6** into **11**.

An alternative approach to obtain **8** by condensation of **1** with *N*-methyl-4-formylpyridinium iodide **9** and the appropriate 4-alkoxybenzaldehyde **3**, gave besides **8** the monopyridiniumporphyrin **10**. The structure of **10** could be established unequivocally by means of ^{1}H-nmr and mass spectroscopy. Compounds **8** and **10** were very difficult to separate.

Scheme 3



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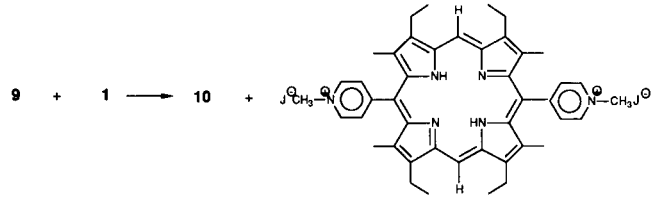
The formation of the monopyridylporphyrin **7** and of the monopyridinium porphyrin **10** is puzzling, since it is unclear how carbon atom C_{15} is incorporated in the porphyrin ring. Carrying out the reaction of **1**+**9**+**3** in different solvents (as acetonitrile or ethanol), compound **10** is still formed, which justifies the conclusion that carbon atom 15 does not originate from the solvent. The formation of a monopyridinium-porphyrin in the condensation of a quarternized pyridinium aldehyde with dipyrrolylmethanes seems to be a general phenomenon; in the synthesis of **11** by reaction of **9** with **1**, porphyrin **10** is the main product. The formation of a monoarylporphyrin as a minor reaction product in the synthesis of a mesodiarylporphyrin has been reported in the literature [6,8]. However no satisfactory explanation could be given to account for its formation in these reactions.

A somewhat analogous reaction was reported in the literature in the condensation of bilabiene-ac dihydrobromide with glyoxal, which failed to yield bis-5,5′-etioporphyrin-II, but instead gave etioporphyrin-II as sole product [9]. A thorough mechanistic study revealed that the additional carbon was not derived from the solvent; no good explanation for the origin of this carbon atom could be offered to account for its formation.

Scheme 4



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EXPERIMENTAL

The ^{1}H-nmr spectra were recorded on Varian EM-390 and Bruker CXP-300 spectro-meters in deuteriochloroform. Chemical shifts are reported in ppm (δ) relative to TMS. Mass spectral data were obtained using an AEI MS-902, equipped with a VG-ZAB console, including and FD-source. Column chromatography was performed on silica gel 230-400 mesh.

Preparation of Starting Materials.

(3,3′-Diethyl-4,4′-dimethyl-2,2′-dipyrrolylmethane) [5], *p*-octyloxybenzaldehyde [11], *p*-hexadecyloxybenzaldehyde [12] and *N*-methyl-4-formylpyridinium iodide [13] were prepared according to the literature.

General Procedure for the Synthesis of Porphyrin **5**.

To 300 ml of methanol were successively added with good stirring 5 mmoles of the appropriate benzaldehyde **3**, 5 mmoles of 4-formylpyridine **2**, 10 mmoles of 3,3′-diethyl-4,4′-dimethyl-2,2′-dipyrrolylmethane **1** and **2** mmoles of *p*-toluenesulfonic acid. The mixture was stirred for 3 hours at room temperature, and then kept in the refrigerator overnight. A solution of 20 mmoles of

2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in 50 ml of THF was quickly added with stirring. The mixture was stirred for 1 hour at room temperature, and 10 ml of triethylamine was added to the mixture. The solvent was evaporated *in vacuo*. The residue was dissolved in a minimum amount of a mixture of dichloromethane and methanol (20:1) and purified by means of column chromatography, eluent dichloromethane:methanol = 20:1. The 5,15-bis(4-alkoxyphenyl)-2,8,12,18-tetraethyl-3,7,13,17-tetramethylporphyrin **4** was eluted first from the column; the second fraction was mainly 5-(4-alkoxyphenyl)-15-(4-pyridyl)-2,8,12,18-tetraethyl-3,7,13,17-tetramethylporphyrin **5**. Compound **5** was dissolved in 20 ml of a mixture of dichlormethane and methanol (10:1.5) and 15 g of methyl iodide was added. The mixture was stirred at room temperature for 2 days. The solvent was distilled off, and 20 ml of methanol was added; again the solvent was distilled off. The crude reaction mixture was dissolved in a minimum amount of a mixture of dichloromethane and methanol (10:1.5), and purified by means of column-chromatography, eluent dichloromethane:methanol = 10:1.5.

5-(4-Methoxyphenyl)-15-(4-*N*-methylpyridiniumiodide)-2,8,12,18-tetraethyl-3,7,13,17-tetramethylporphyrin (**8**, R = CH_3).

This compound was obtained in 10% yield (400 mg); ^{1}H-nmr (deuteriochloroform): δ 10.24 (s, 2H, H10, H20), 8.55 (bd, 2H, pyridinium H), 7.85 (d, 2H, aryl H), 7.63 (bd, 2H, pyridine H), 7.25 (d, 2H, aryl H), 4.51 (s, 3H, N^+-CH_3), 4.08 (s, 3H, OCH_3), 3.9 (b, 8H, CH_2CH_3), 2.51 (s, 12H, CH_3), 1.80 (b, 12H, CH_2CH_3), -2.44 (s, 1H, NH), -2.45 (s, 1H, NH); ms: m/e 661 (M^+-CH_3I).

Anal. Calcd. for $C_{45}H_{50}N_5OI$: C, 67.24; H, 6.27; N, 8.71. Found: C, 65.59; H, 6.22; N, 8.36. The microanalysis for carbon is **not** correct. It has been reported in the literature that 5,15-diarylporphyrins form solvates or include solvent molecules, which are difficult to remove [4,6].

5-(4-*n*-Octyloxyphenyl)-15-(4-*N*-methylpyridiniumiodide)-2,8,12,-18-tetraethyl-3,7,13,17-tetramethylporphyrin (**8**, R = C_8H_{17}).

This compound was obtained in 14% yield (650 mg); ^{1}H-nmr (deuteriochloroform): δ 10.21 (s, 2H, H10, H20), 7.93 (bd, 2H, pyridine H), 7.63 (d, 2H, aryl H), 7.06 (bd, 2H, pyr. H), 7.04 (d, 2H, aryl H), 4.16 (s, 3H, N^+-CH_3), 3.9 (b, 8H, CH_2CH_3), 2.42 (s, 12H, CH_3), 1.96 (t, 2H, OCH_2-C_7H_{15}), 1.78 (b, 12H, CH_2CH_3), 1.40 (b, 12H, OCH_2 $(CH_2)_6CH_3$), 0.90 (m, 3H, $O(CH_2)_7CH_3$, -2.43 (s, 1H, NH), -2.59 (s, 1H, NH); ms: m/e 759 (M^+-CH_3I).

Anal. Calcd. for $C_{52}H_{64}N_5OI$: C, 69.23, H, 7.15; N, 7.76. Found: C, 69.10; H, 7.23; N, 7.77.

5-(4-*n*-Hexadecyloxyphenyl)-15-(4-*N*-methylpyridiniumiodide)-2,-8,12,18-tetraethyl-3,7,13,17-tetramethylporphyrin (**8**, R = C_{16}-H_{33}).

This compound was obtained in 13% yield (950 mg); ^{1}H nmr (deuteriochloroform): δ 10.21 (s, 2H, H_{10}, H_{20}), 7.94 (bd, 2H, pyridine H), 7.63 (d, 2H, aryl H), 7.06 (bd, 2H, pyridine H), 7.04 (d, 2H, aryl H); 4.17 (s, 3H, N^+-CH_3), 3.9 (b, 8H, CH_2 CH_3), 2.42 (s, 12H, CH_3), 1.96 (t, 2H, OCH_2-$C_{15}H_{31}$), 1.78 (b, 12H, CH_2 CH_3), 1.31 (b, 28H, OCH_2-$(CH_2)_{14}$ CH_3), 0.88 (m, 3H, O $(CH_2)_{15}CH_3$), -2.43 (s, 1H, NH), -2.58 (s, 1H, NH); ms: m/e 871 (M^+-CH_3I).

Anal. Calcd. for $C_{60}H_{80}N_5OI$: C, 71.05; H, 7.95; N, 6.90. Found: C, 71.34; H, 8.11; N, 6.74.

During the course of our investigations, the synthesis of 5,15-bis(4-pyridyl)-2,8,12,18-tetraethyl-3,7,13,17-tetramethylporphyrin **6** was described in the literature [3].

The methylation of **6** into 5,15-bis(4-*N*-methylpyridiniumiodide)-2,8,12,18-tetraethyl-3,7,13,17-tetramethylporphyrin **11** occurred in a quantitative yield; ^{1}H-nmr (deuteriochloroform): 10.20 (s, 2H, H10, H20), 7.9-7.6 (b, 8H, pyridine H), 4.27 (s, 6H, N^+-CH_3), 3.9 (b, 8, CH_2-CH_3), 2.49 (s, 12H, CH_3), 1.82 (b, 12H, CH_2CH_3), -2.61 (s, 1H, NH), -3.10 (s, 1H, NH).

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REFERENCES AND NOTES

[1] A. Harriman, in Energy Resources through Photochemistry and Catalysis, M. Grätzel, ed. Academic Press, New York, 1983, Chapter 6.

[2a] For a comprehensive list of references, see G. M. Sanders, M. van Dijk, A. van Veldhuizen and H. C. van der Plas, *J. Chem. Soc., Chem. Commun.*, 1311 (1985); [b] D. Gust, T. A. Moore, P. A. Liddell, G. A. Nemeth, L. R. Makings, A. L. Moore, D. Barrett, P. J. Pessiki, R. V. Bensasson, M. Rougee, C. Chachaty, F. C. de Schrijver, M. van der Auweraer, A. R. Holzwarth and J. S. Connolly, *J. Am. Chem. Soc.*, **109**, 846 (1987); [c] J. L. Sessler, M. R. Johnson, T.-Y. Lin and S. E. Creager, *ibid.*, **110**, 3659 (1988); [d] A. Osuka and T. Maryama, *ibid.*, **110**, 4454 (1988); [e] M. R. Wasielewski, D. G. Johnson, W. A. Svec, K. M. Kersey and D. W. Minsek, *ibid.*, **110**, 7219 (1988); [f] P. Gust, Th. A. Moore, A. L. Moore, L. R. Makings, G. R. Seely, X. Ma, T. T. Trier and F. Gao, *ibid.*, **110**, 7567 (1988); [g] P. Leighton and J. K. M. Sanders, *J. Chem. Soc., Perkin Trans. 1*, 2385 (1987); [h] J. A. Cowan and J. K. M. Sanders, *ibid.*, 2395 (1987); [i] A. Osuka, K. Maryama, I. Yamazaki and N. Tamai, *ibid.*, 1243 (1988); [j] M. Nango, H. Kryu and P. A. Loach, *ibid.*, 697 (1988); [k] C. A. Hunter, M. N. Meah and J. K. M. Sanders, *ibid.*, 692 and 694 (1988); [l] K. H. Neumann and F. Vögtle, *ibid.*, 520 (1988); [m] T. Aida, A. Takemura, M. Fuse and S. Inoue, *ibid.*, 391 (1988); [n] M. Gubelmann, A. Harriman, J. M. Lehn and J. L. Sessler, *ibid.*, 77 (1988); [o] J. Davila, A. Harriman, M. C. Richoux, L. R. Milgrom, *ibid.*, 525 (1987); [p] A. Osuka, S. Morikawa, K. Maruyama, S. Hirayama and T. Minami, *ibid.*, 359 (1987); [q] G. M. Dubowchik and A. D. Hamilton, *ibid.*, 293 (1987); [r] J. A. Cowan, J. K. M. Sanders, G. S. Beddard and R. J. Harrison, *ibid.*, 55 (1987); [s] G. M. Dubowchik and A. D. Hamilton, *ibid.*, 1391 and 665 (1986); [t] S. Gaspard, C. Giannotti, P. Millard, C. Schaeffer and T.-H. Tran-Thi, *ibid.*, 1239 (1986); [u] S. Aono, M. Koji and I. Okura, *ibid.*, 170 (1986); [v] B. Morgan and D. Dolphin, *J. Org. Chem.*, **52**, 5364 (1987); [w] G. M. Sanders, M. van Dijk. A. van Veldhuizen, H. C. van der Plas, U. Hofstra and T. J. Schaafsma, *ibid.*, **53**, 5272 (1988); [x] J. A. Schmidt, A. R. McIntosh, A. C. Weedon, J. R. Bolton, J. S. Connolly, J. K. Hurley and M. R. Wasielewski, *J. Am. Chem. Soc.*, **110**, 1733 (1988); [y] O. Wennerström, H. Ericsson, I. Raston, S. Svensson and W. Pimlott, *Tetrahedron Letters.*, **30**, 1129 (1989); [z] J. L. Sessler and S. Piering, *ibid.*, **28**, 6569 (1987); [aa] S. Noblat, C. D. Dietrich-Buchecker and J. P. Sauvage, *ibid.*, **28**, 5829 (1987).

[3] H. L. Anderson, C. A. Hunter and J. K. M. Sanders, *J. Chem. Soc., Chem. Commun.*, 226 (1989).

[4] G. M. Sanders, M. van Dijk, A. van Veldhuizen and H. C. van der Plas, *ibid.*, 1311 (1986).

[5] R. Young and C. K. Chang, *J. Am. Chem. Soc.*, **107**, 898 (1985).

[6] M. J. Gunter and L. N. Mander, *J. Org. Chem.*, **46**, 4792 (1981).

[7] J. H. Fuhrhop, U. Wanja and M. Bünzel, *Liebigs Ann. Chem.*, **426** (1984).

[8] R. F. Pasternack, P. R. Huber, P. Boyd, G. Engasser, L. Francesconi, E. Gibbs, P. Fasella, G. C. Venturo and L. deC.Hinds, *J. Am. Chem. Soc.*, **94**, 4511 (1972).

[9] D. Harris, A. W. Johnson and R. Gaete-Holms, *Bioorg. Chem.*, **9**, 63 (1980).

[10] M. Ogoshi, H. Sugimoto and T. Nishiguchi, *Chem. Letters*, 29 (1978).

[11] C. Weygand and R. Gabler, *J. Prakt. Chem.*, **155**, 332 (1940).

[12] G. W. Gray and B. Jones, *J. Chem. Soc.*, 1467 (1954).

[13] J. Tirouflet and E. Laviron, *Compt. rend*, **247**, 217 (1958).