Some New Aspects Related to the Synthesis of *meso*-Substituted Porphyrins

A. M. d'A. Rocha Gonsalves*, Jorge M. T. B. Varejão and Mariette M. Pereira

Departamento de Química, Faculdade de Ciências e Tecnologia, Universidade de Coimbra, P-3000 Coimbra, Portugal

Received March 5, 1990

A general analysis of the steps of the Rothemund reaction, allowed for a better understanding and a significant improvement of this reaction as a synthetic method in some of the previously known difficult syntheses.

J. Heterocyclic Chem., **28**, 635 (1991).

Studies designed to find efficient conditions for the synthesis of *meso*-tetraalkylporphyrins [1] revealed that in some cases, it is necessary to perform the Rothemund reaction *via* a two-step approach. In the original publication [1] the possibilities were discussed for using this two-step approach for the generation of *meso*-tetraalkylporphyrins through preliminary cyclization of pyrrole and the acetal of the required alkyl aldehyde in a chlorinated solvent under an inert atmosphere, followed by forced oxidation of the porphyrinogen to porphyrin (which could be achieved through photochemical or purely chemical oxidation).

From a mechanistic viewpoint, we showed in that work, that the basic difference in the reaction between pyrrole and aliphatic aldehydes or benzaldehydes lies in the fact that, for the former, the resulting *meso*-tetraalkylporphyrinogens are not efficiently oxidized by oxygen to generate the corresponding porphyrins tending to form degradation products rather than porphyrins after long standing, whilst for the latter the initially formed *meso*-tetraarylporphyrinogen tends to be oxidized by oxygen to the phlorin oxidation stage under mild conditions or go efficiently to the porphyrin oxidation level under more severe conditions (Scheme 1). Therefore, in order to synthesize *meso*-tetraalkylporphyrins efficiently it is necessary to select the specific conditions for generation of the corresponding porphyrinogen followed by appropriate oxidation work up as a means of avoiding degradation of the porphyrinogen. A selection of *meso*-tetraalkylporphyrins prepared using our approach is shown in Table 1. They are either new compounds or were obtained with significantly improved yields relatively to those previously reported in the literature.

Later, Lindsey and co-workers [2] published results on studies of improved methods of some *meso*-tetraarylporphyrins closely similar to our earlier published strategy and description of reaction conditions. In a subsequent, more detailed communication [3], Lindsey showed the wide scope of the two-step method for synthesis of *meso*-substituted porphyrins and discussed a mechanistic inter-

Scheme 1

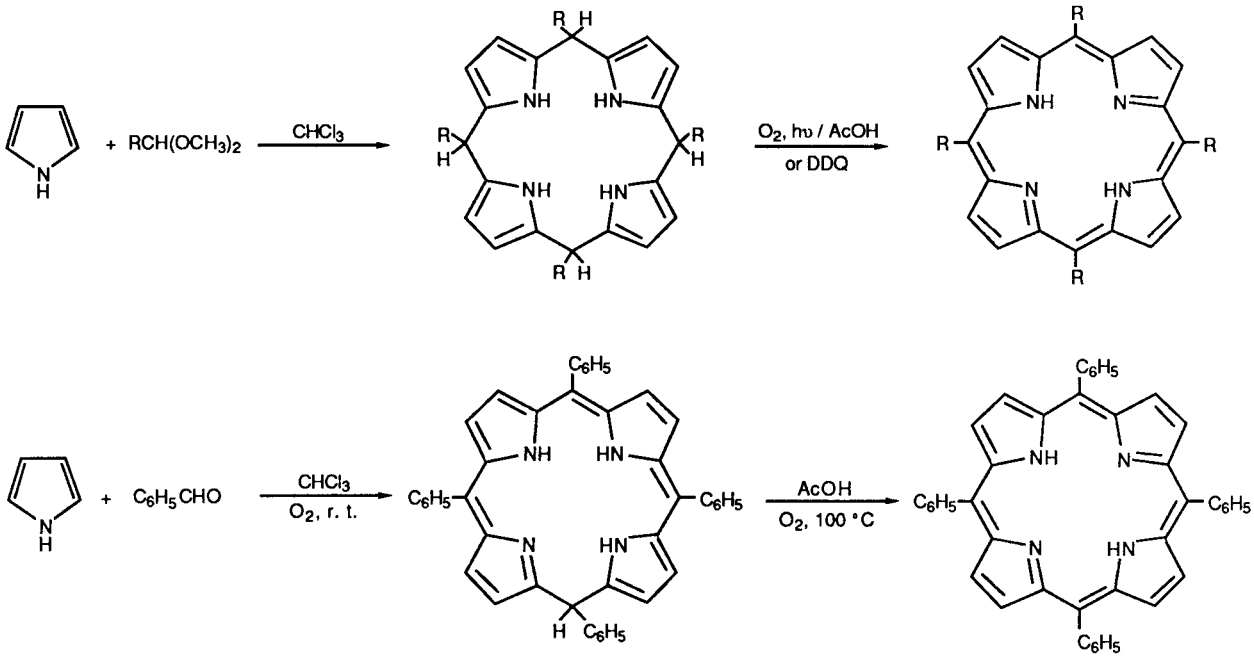


Table 1

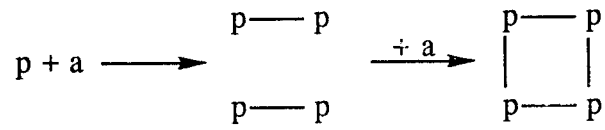
Porphyrin	Photooxidation (%)	Chemical Oxidation (%)	[Ref] (%)
meso-Tetramethylporphyrin	8	–	[6l] (1)
meso-Tetraethylporphyrin	5	11	[6j] (9)
meso-Tetra-*n*-propylporphyrin	10	18	[6h] (5.5)
meso-Tetra-*iso*-propylporphyrin	0	5	[6j]
meso-Tetra-*iso*-butylporphyrin	8	16	[6b]
meso-Tetrabenzylporphyrin	6.5	17	–
meso-Tetra-*n*-undecylporphyrin	9	8.5	[6h] (2.2)

pretation of the reaction. More recently [4], the same author claimed an extension of the synthetic use of the two-step Rothemund reaction for sterically hindered porphyrins, and Drenth [5] adapted the conditions further in order to synthesize *meso*-tetra(2,6-dichlorophenyl)porphyrin.

That the Rothemund synthesis of porphyrins is an intriguing puzzle, is clear from the 50 years of studies on this reaction which have provided adaptations of the original method, together with extensions and mechanistic studies [1-5] and [6]. Despite all efforts, wide applicability and preparative usefulness of the Rothemund reaction was not attained. Using Adler's straightforward version of "cooking" the pyrrole and aldehyde in acetic acid or propionic acid [6f], *meso*-tetraphenylporphyrin and some simple derivatives can be isolated directly in a crystalline form from the reaction medium making this route the most desirable from the preparative point of view. But relatively few *meso*-tetrasubstituted porphyrins can actually be synthesized using such a simple approach. For the majority of cases in which the aldehydes contain specific substituents, Adler's reaction conditions do not generate but traces of porphyrin or none at all. In the case of the three nitrobenzaldehydes, using the classical method we were able to obtain the porphyrin in a modest yield as reported [13] for the *ortho*-isomer but the *meta* and *para* compounds failed to yield any porphyrin. Our experience and that of others [1-5] has shown that the two-step approach can be useful in some of the difficult cases because conditions can be selected to optimize either the cyclization or oxidation steps. But although the method had allowed us to overcome the difficulties in the synthesis of some porphyrins, still it was not in itself a general answer to the synthesis of all the *meso*-substituted porphyrins in either the tetraalkyl or tetraaryl series. In our own and Lindsey's version of the reaction there are intrinsic disadvantages in the requirement for the expensive high potential quinone oxidant and in elaborate, costly purification procedures needed to isolate the porphyrin. For these reasons the method is only useful for the preparation of relatively small quantities of porphyrin. For preparative proposes, it would be more convenient if the porphyrin could be formed and directly isolated from the reaction medium through a procedure more closely fashioned to Adler's original route [6f].

It was clear from ours [1] and others [8-9] evidence that porphyrinogens tend to be formed in favorable amounts. In the case of *meso*-tetraalkylporphyrins, we obtain very clear evidence by nmr spectrometry [1] that the dominant route to the porphyrinogen is most likely to proceed through a "MacDonald" type cyclization step rather than *via* a linear species which later cyclizes (Scheme 2). Porphyrinogen being formed as a consequence of the high

Scheme 2



p=pyrrole

a=aldehyde

favorability of this type of cyclization is the likely explanation for the high cyclization yields so often obtained using high concentrations for the condensation step [10]. In contrast, formation of linear oligomers of pyrroles and their subsequent cyclization to porphyrinogens would be more favored under conditions of high dilution as, for example, in syntheses of macrocyclic compounds.

It was apparent that the experimental conditions we first set for the preparation of *meso*-tetraalkylporphyrinogen were more satisfactory than the conditions for subsequent oxidation to porphyrins and so we sought alternative methods of oxidation in order to overcome the following inconveniences: the instability of the porphyrin product to light irradiation when using the photooxidative method, the high cost of high potential quinones and the laborious porphyrin procedures required when such oxidants are used.

In one of our approaches, oxidation of *meso*-tetraalkylporphyrinogen was attempted in DMF solution in the

presence of zinc acetate. After extended heating, the zinc complex of the porphyrin is formed in high yields. For example, an 18% yield of *meso*-tetrakis(*n*-propyl)porphyrin zinc(II) was isolated after 24 hours at 100°, whilst a 6% yield of *meso*-tetrakis(methyl)porphyrin zinc(II) could be obtained under the same conditions (Table 2).

Table 2

Porphyrinogen	M-Acetate	Time (Hours)	M-Porphyrinate
	Zn	24	6
	Zn/Cu	0.5	7
meso-Tetra-methyl-	Cu	1	[a]
	Ni	24	[b]
	Co	24	[b]
	Mg	24	[b]
	Zn	24	15
	Zn/Cu	0.5	18
meso-Tetra-*n*-propyl-	Cu	1	[a]
	Ni	24	[b]
	Co	24	[b]
	Mg	24	[b]

[a] Visible spectrometry shows that some porphyrin metal complex is formed in the first stage of the reaction but this is quickly and fully degraded. [b] In DMF solution and presence of this salt, the porphyrinogen is recovered unaffected after 24 hours at 120°.

The preceding result led us to exploit the possibility of performing oxidative isomerizations of readily available porphyrinogens under conditions analogous to those reported by Eschenmoser [11] for octaethylporphyrinogen through proper selection of the metal cations and the reaction conditions. It was also hoped that such studies might clarify the observations reported by Ibers [12] during his studies of the Rothemund reaction with alkyl acetals and pyrrole in the presence of selected metal salts. According to Ibers, reactions performed in the presence of different metal ions lead to different oxidation levels of the porphyrinogen thereby allowing selective formation of either porphyrins or chlorins. The porphyrinogen which we have shown to yield 18% of the corresponding porphyrin zinc complex after 24 hours heating in DMF at 100° in the presence of zinc acetate, can be recovered virtually unchanged when the same treatment is done in the absence of the salts. Copper acetate is far more efficient in promoting oxidation of the porphyrinogen under similar conditions, but the porphyrin copper complex so formed does not survive the reaction conditions, being decomposed into intractable black tars. Using trace amounts of copper acetate in the presence of zinc acetate we could reduce the time length of the oxidation step from 24 hours to just a few minutes, however the work up conditions could not be made easy enough to make the process an attractive preparative method. None of the reactions done in the presence of nickel, cobalt or magnesium acetate promoted the conversion of the porphyrinogens into porphyrin. In fact all these salts appeared to stabilize the porphyrinogen oxidation level because the DMF solution of the porphyrinogen remained a pale yellow after several hours at 100°, and the porphyrinogen was easily isolated and purified after work up. In order to force the formation of metal porphyrinogenate and check its reactivity, we even tried to react the porphyrinogen solution with iodomethylmagnesium to provide a similar reaction route to that shown by the porphyrinogen solutions in the presence of magnesium acetate. The magnesium porphyrinogenate was not only stable to heating in the presence of oxygen, as it did not shown any capacity for transfer of hydride to potential hydride acceptors such as ketones or 4-benzoquinone. Another observation we have made was that solutions of the magnesium porphyrinogenate or of the porphyrinogen itself in the presence of nickel, cobalt or magnesium acetate led to fast decomposition of the porphyrinogen on irradiation by visible light to give colorless unidentified materials.

The preceding results on the behavior of porphyrinogens in the presence of metal salts cast some doubts on Ibers [12] conclusions in relation to the role of metal ions on the chlorin/porphyrin ratio in the reaction of pyrrole and alkylaldehyde acetals. Whilst Ibers points out that the presence of a copper salt leads to the selective formation of chlorin, our results indicate that the copper salt is the best promoter of oxidation of the porphyrinogen to the porphyrin stage and that cobalt and nickel salts simply impair the oxidation of the porphyrinogen for reactions done both in DMF and in acetic acid. Stronger evidence that Ibers' results correspond to vagaries in amounts associated with the extremely low yields of isolated materials and are not representative of any documented mechanism come from the fact that, in a series of experiments, only in one case could we obtain spectroscopic evidence for the presence of chlorin from the reaction of pyrrole and the butyraldehyde acetal in acetic acid in the presence of copper acetate.

Eschenmoser's [11] experiments on the isomerization or oxidation of porphyrinogens have very strong experimental support. We did not attempt to reproduce closely his results because his reported reaction conditions required an extremely specific control and high dilution which were not easily adaptable to our large scale preparative objectives. An attempt to isomerize a solution of *meso*-tetra(*n*-propyl)porphyrinogen in DMF in the presence of magnesium acetate and diazabicyclononene (DBN) under anaerobic conditions did not give any evidence for rearrangement of the type reported by Eschenmoser.

The especially demanding conditions for the oxidation of the *meso*-tetraalkylporphyrinogens led us to check their behavior in oxidizing solvents. Taking *meso*-tetra(*n*-propyl)porphyrinogen in DMSO led simply to the formation

of black precipitates without formation of any porphyrin. The same result was obtained in the presence of metal salts which, in DMF solution, had led to the porphyrinogen being converted into porphyrin. However, in a more recent development, we found that a mixtue of nitrobenzene and acetic or propionic acid was extremely efficient in promoting the oxidation of porphyrinogens to porphyrins and even allowed the preparation of porphyrins in excellent yield in a "one pot" pyrrole-aldehyde reaction in cases where the previously reported conditions of the Rothemund reaction gave either poor yields or no porphyrin. In the case of alkylaldehydes, both butyraldehyde and phenylacetaldehyde in the presence of pyrrole dissolved in acetic acid/nitrobenzene (7:3) and warmed at 120° gave, after ordinary work up, 4% yield of the corresponding porphyrins. This is a significant result, since under ordinary Rothemund reaction conditions the alkyl aldehyde and pyrrole do not give any porphyrin.

The mixture of acetic acid/nitrobenzene also proved to be highly efficient for the synthesis of some aryl porphyrins which could not be obtained or gave extremely low yields in previously reported conditions (Table 3). Significant examples from our work are found in the preparation

Table 3

R =	Isolated Product (%)	[Ref.] (%)
Phenyl	20	[6f] (20)
o-Nitrophenyl	20	[13] (12)
o-Methoxyphenyl	15	[14] (9)
o-Chlorophenyl	8.5	[15] (3)
m-Nitrophenyl	9	[17] (12)
p-Nitrophenyl	25 [a]	[18a] (24)
p-Methoxyphenyl	45 [b]	[6h] (7)
2,6-Dichlorophenyl	5	[16] (1.5)
1-Naphtyl	10	[6h] (6)

[a] While Tsuchida [18b] was not able to obtain but a poor lower yield of porphyrin using the conditions of ref [18a] we could not obtain but traces by such traces by such method. [b] Using propionic acid instead of acetic acid.

of nitrophenyl and methoxyphenyl porphyrins. *meso*-Tetra-(2-nitrophenyl)porphyrin has been prepared by Adler's version of the Rothemund reaction with a reported best yield of 13% [7]. Somewhat surprisingly and as said before, when the same conditions are applied to the preparation of the *para* or *meta* derivatives, the results are extremely poor giving large amounts of black precipitates from which only in some cases and in relatively big scale preparations can low yields of the corresponding porphyrins be laboriously isolated. In contrast, in all these cases, when we performed the reaction of the necessary aldehydes and pyrrole in the acetic acid/nitrobenzene mixture, the corresponding porphyrins crystallized directly and very cleanly from the reaction medium; the yields were: 20% *meso*-tetra(2-nitrophenyl)porphyrin, 9% *meso*-tetra-(3-nitrophenyl)porphyrin, and 25% *meso*-tetra(4-nitrophenyl)porphyrin. Also, with the beneficial advantage of the direct isolation of the crystallized porphyrin from the reaction medium, significantly higher yields than those previously reported could be obtained as with the 15% for *meso*-tetra(2-methoxyphenyl)porphyrin and the 45% for the *meso*-tetra(4-methoxyphenyl)porphyrin.

Considering the increasing interest of *meso* substituted porphyrins as ligands of metal ions for a wide range of studies in the area of biomimetic catalysis [19], and for diagnostic and therapeutic proposes [20] advances in the knowledge of the Rothemund reaction which can broaden its applicability as an efficient preparative method were necessary.

Having been able to better pinpoint the bottlenecks in the sequence of steps from the pyrrole and aldehyde starting materials to the porphyrin product, we were able to find in the first place the advantage of separating in some cases the cyclization process to porphyrinogen and the oxidation of this to porphyrin using specific conditions which were set for each of these steps. In our original version the oxidation step was, either an oxygen promoted photochemical oxidation or required the use of high potential quinones. Subsequent studies showed that in the presence of a zinc salt, the porphyrinogen can also be efficiently oxidized by oxygen to the zinc porphyrinogenate. This observation tends to alter the classical belief about the role of zinc ions in porphyrin synthesis. It was generally taken for granted that the zinc ion has a template effect acting therefore during the cyclization process. While this interpretation was never clearly documented, our results more clearly favor the possibility for the zinc ion being effective because it favors the selective conversion of an intermediate porphomethene or porphodimethene to the porphyrin oxidation stage, and because the porphyrin zinc complex product is more stable to the reaction conditions than the free porphyrin.

The presence of cupric instead of zinc ions is far more efficient in promoting the oxidation of porphyrinogens to porphyrins, but the cupric porphyrinogenate does not stand the reaction conditions leading to degradation of the product. Even the presence of a trace of a cupric salt easily contributes to the decomposition of the usually very stable zinc porphyrinogenate which is formed in the presence of an excess of zinc salt. Magnesium, nickel and cobalt(II) ions stabilize the porphyrinogens to oxidation by oxygen.

Significant progress was made with the observation that porphyrinogens are very efficiently oxidized to porphyrins by nitrobenzene in acetic or propionic acid thus allowing to avoid the requirement for the use of the expensive high

potential quinones, and allowing for an easier work up in isolating the porphyrin. It is not unusual for the porphyrins to crystalize directly from the acetic acid/nitrobenzene mixture. The nitrobenzene/acetic acid mixture even allows to successfully synthesize in a "one pot" reaction many porphyrins which previously required the use of the cyclization-oxidation two-step approach.

We will report in due time recent results showing that nitrobenzene acts as the true oxidant of porphyrinogens. The reaction is little affected when oxygen is excluded, and nitrobenzene derivatives show a marked influence from the electron donating/withdrawing capacity of the substituents, 4-nitroaniline being highly effective.

EXPERIMENTAL

All solvents and reagents were purified by standard methods before use. ^{1}H-nmr spectra were recorded either on a Varian EM 360 (60 MHz) or Bruker-AC 200, 200 MHz. Mass spectra were obtained on a VG 7070 mass spectrometer.

meso-Tetramethylporphyrinogen.

Pyrrole (7.2 mmoles) was added to the required dimethylacetal (7.2 mmoles) in carbon tetrachloride (20 ml) in the presence of trifluoracetic acid (0.2 ml). The solvent was purged with argon and the reaction mixture was warmed at 60° for 16 hours. After work up, the solvent was removed and a "spongy" solid was obtained. This product was chromatographed with dichloromethane on degassed neutral alumina (Woelm, grade II). The first fraction collected gave a pale yellow solid which was recrystallized from dichloromethane *via* slow diffusion of hexane, yield 28%; ^{1}H-nmr (deuteriochloroform): δ 5.6 (d, 8, *β-H*), 3.8 (m, 4, C*H*), 1.3 (d, 12, CH_3), 6.9 (broad, 4, N*H*) (Data in agreement with Ibers' results [12]).

General Procedure for the Synthesis of *meso*-Tetraalkylporphyrins.

a) Chemical Oxidation Method.

meso-Tetrabenzylporphyrin.

Pyrrole (7.2 mmoles) was added to (7.2 mmoles) phenylacetaldehyde dimethylacetal in chloroform (20 ml) in the presence of trifluoracetic acid (0.2 ml). The solvent was purged with argon and the reaction mixture was warmed at 60° for 48 hours. A standard work up yielded the crude porphyrinogen. This product was dissolved in chloroform (100 ml) and warmed to 60°. One equivalent of DDQ or chloranil in benzene (100 ml) was added all at once. The temperature was maintained at 60° for 30 minutes. After work up the product was purified by chromatography in neutral alumina (Woelm, grade II) eluting with chloroform. The purple band was collected and after solvent removal the solid was recrystallized from chloroform/toluene to yield 212 mg of pure crystals (17%); ^{1}H-nmr (TFA): δ 9.0 (s, 8, *β-H*), 7.0 (s, 20, *o-m-p-H*), 6.4 (s, 8, CH_2), -2.5 (broad, 4, N*H*); ms: (FAB) m/e 670 (molecular ion).

Anal. Calcd. for $C_{48}H_{38}N_4$: C, 85.94; H, 5.70; N, 8.35. Found: C, 85.91; H, 5.73; N, 8.34.

b) Photochemical Oxidation.

meso-Tetra(*iso*-butyl)porphyrin.

meso-Tetra(*iso*-butyl)porphyrinogen (0.7 g, 1.3 mmoles) was dissolved in acetic acid/benzene (200:800 ml) and the solution was irradiated with visible light (8 x 8 w fluorescent lamps) during 4.5 hours. After evaporation of the solvent the residue was taken up in chloroform and washed with a saturated sodium bicarbonate solution. After chromatography with chloroform on an alumina column (Woelm, grade II) the purple fraction was collected. After crystallization from chloroform/methanol 10:1), 80 mg of *meso*-tetra(*iso*-butyl)porphyrin was obtained (8%); ^{1}H-nmr (TFA): δ 8.9 (s, 8, *β-H*), 4.9 (d, 8, CH_2), 2.7 (m, 4, C*H*), 1.3 (d, 24, CH_3), -2.3 (broad, 4, N*H*); ms: (FAB) m/e 534 (molecular ion).

Anal. Calcd. for $C_{36}H_{46}N_4$: C, 80.85; H, 8.67; N, 10.48. Found: C, 80.87; H, 8.70; N, 10.47.

meso-Tetra(*iso*-propyl)porphyrin.

This compound was obtained in 5% yield; ^{1}H-nmr (deuteriochloroform): δ 9 (s, 8, *b-H*), 4.8 (m, 4, C*H*), 1.4 (d, 24, CH_3), -2.6 (broad, 2, N*H*); ms: (FAB) m/e 478 (molecular ion).

Anal. Calcd. for $C_{32}H_{38}N_4$: C, 80.29; H, 8.00; N, 11.71. Found: C, 80.25; H, 7.97; N, 11.67.

c) Oxidation in the Presence of Metal Salts.

meso-Tetra(*n*-propyl)porphyrin.

meso-Tetra(*n*-propyl)porphyrinogen, (1.3 mmoles) in 30 ml of DMF was added to (6 mmoles) zinc acetate. This solution was maintained at 100° for 24 hours. After work up the product was chromatographed with dichloromethane on an alumina (Woelm, grade II) column. The purple fraction was collected and washed with hydrochloric acid (0.1 *M*) to remove the metal. The porphyrin was recrystallized from chloroform/methanol (5:1) to yield 112 mg of *meso*-tetra(*n*-propyl)porphyrin 18%); ^{1}H-nmr (deuteriochloroform): δ 9.5 (s, 8, *β-H*), 4.9 (t, 8, CH_2CH$_2$), 2.5 (m, 8, CH$_2$CH_2), 1.2 (t, 12, CH_3), -2.6 (broad, 2, N*H*); ms: (FAB) m/e 448 (molecular ion).

Anal. Calcd. for $C_{32}H_{38}N_4$: C, 80.29; H, 8.00; N, 11.70. Found: C, 80.30; H, 8.03; N, 11.69.

General Procedure for the Synthesis of *meso*-Tetraarylporphyrins.

meso-Tetra(4-methoxyphenyl)porphyrin.

4-methoxybenzaldehyde (10 mmoles) was mixed with propionic acid (35 ml) and nitrobenzene (15 ml). Pyrrole (10 mmoles) was added and the mixture was kept at 120° during 1 hour. On cooling, the porphyrin precipitated directly from the reaction mixture and was isolated by filtration (0.820 g, 45%); ^{1}H-nmr (deuteriochloroform + TFA): δ 8.8 (s, 8, *β-H*), 8.1 (d, 8, o-*H*), 7.3 (d, 8, m-*H*), 4.2 (s, 12, CH_3), -2.7 (broad, 4, N*H*); ms: (FAB) m/e 735 (molecular ion).

Anal. Calcd. for $C_{48}H_{38}N_4O_4$: C, 78.45; H, 5.21; N, 7.62. Found: C, 78.43; H, 5.19; N, 7.60.

Acknowledgement.

Support for this investigation by INIC and CIPAN is acknowledged. We also thank JNICT for a grant to one of us (J. M. T. B. V.); Dr. R. A. W. Johnstone and W. R. Sanderson for useful discussions and the Department of Chemistry of the University of Liverpool for mass and nmr spectra, and CHN analysis.

REFERENCES AND NOTES

[1] Results first disclosed in the 1981 Meeting of the Sociedade Portuguesa de Química and later published: A. M. d'A. Rocha Gonsalves and Mariette M. Pereira, *J. Heterocyclic Chem.*, **22**, 931 (1985).

[2] J. S. Lindsey, H. C. Hsu and I. C. Schreiman, *Tetrahedron Letters*, 4969 (1986).

[3] J. S. Lindsey, I. C. Schreiman, H. C. Hsu, P. C. Kearney and A. M. Marguerettaz, *J. Org. Chem.*, **52**, 827 (1987).

[4] R. W. Wagner, D. S. Lawrence and J. S. Lindsey, *Tetrahedron Letters*, 3069 (1987).

[5] A. W. van der Made, E. J. H. Hoppenbrouwer, R. J. M. Nolte and W. Drenth, *Rec. Trav. Chim.*, **107**, 15 (1988).

[6a] P. Rothemund, *J. Am. Chem. Soc.*, **57**, 2010 (1935); [b] P. Rothemund, *ibid.*, **61**, 2912 (1939); [c] P. Rothemund and A. R. Menotti, *ibid.*, **63**, 267 (1941); [d] R. H. Ball, G. D. Dorough and M. Calvin, *ibid.*, **68**, 2278 (1946); [e] G. M. Badger, R. A. Jones and R. L. Laslett, *Aust. J. Chem.*, **17**, 1028 (1964); [f] A. D. Adler, F. R. Longo, J. D. Finarelli, J. Goldmacher, J. Assour and L. Korsakoff, *J. Org. Chem*, **32**, 476 (1967); [g] A. D. Adler, L. Sklar, F. R. Longo, J. D. Finarelli and M. G. Finarelli, *J. Heterocyclic Chem.*, **5**, 669 (1968); [h] A. Treibs, N. Haberle, *Liebigs. Ann. Chem.*, **183**, 718 (1968); [i] D. Dolphin, *J. Heterocyclic Chem.*, **7**, 275 (1970); [j] I. Tabushi, Ko-Ichi Sakai and K. Yamamura, *Tetrahedron Letters*, 1821 (1978); [k] B. von Maltzan, German Patent, 2,413,414 (1974), *Chem. Abstr.*, **84**, 17450 (1976); [l] U. Eisner, *J. Chem. Soc.*, 854 (1957).

[7] J. P. Collman, R. R. Gagne, C. A. Reed, T. R. Halbert, G. Lang and W. T. Robinson, *J. Am. Chem. Soc.*, **97**, 1427 (1975)..

[8] B. Franck, *Angew. Chem., Int. Ed. Engl.*, **21**, 343 (1982).

[9] B. von Maltzan, *ibid.*, **21**, 785 (1982).

[10] P. S. Clezy, A. J. Liepa and G. A. Smith, *Aust. J. Chem.*, **23**, 603 (1970).

[11a] P. Naab, R. Lattman, C. Angst and A. Eschenmoser, *Angew. Chem., Int. Ed. Engl.*, **19**, 143 (1980); [b] J. E. Johansen, C. Angst, C. Kratky and A. Eschenmoser, *ibid.*, **19**, 141 (1980); [c] V. Rasetti, K. Hilpert, A. Fassler, A. Pfaltz and A. Eschenmoser, *ibid.*, **20**, 1058 (1981); [d] C. Angst, C. Kratky and A. Eschenmoser, *ibid.*, **20**, 263 (1981); [e] J. E. Johansen, V. Piermattie, C. Angst, E. Diener, C. Kratky and A. Eschenmoser, *ibid.*, **20**, 261 (1981); [f] R. Wadischatka, E. Diener and A. Eschenmoser, *ibid.*, **20**, 631 (1983).

[12a] A. Ulman, J. Gallucci, D. Fisher and J. A. Ibers, *J. Am. Chem. Soc.*, **102**, 6852 (1980); [b] A. Ulman, D. Fisher and J. A. Ibers, *J. Heterocyclic Chem.*, **19**, 409 (1982).

[13] E. Tsuchida, E. Hasegawa and T. Kanayama, *Macromol.*, **11**, 947 (1978).

[14] B. Staubi, H. Fretz, U. Piantini and W. D. Woggen, *Helv. Chim. Acta*, **70**, 1173 (1987).

[15] J. B. Kim, J. J. Leonard and F. R. Longo, *J. Am. Chem. Soc.*, **94**, 3986 (1972).

[16] C. L. Hill and M. M. Williamson, *J. Chem. Soc., Chem. Commun.*, 1228 (1985).

[17] Tanaka Mikiaki, Nawa Hironi and Ishihara Masami (Wako Pure Chemical Industries, Ltd.) Jpn. Kokai Tokyo Koho JP, 6,267,086 (87 67086) (1987), *Chem. Abstr.*, **107**, 208858w (1987).

[18a] A. S. Semeikin, O. I. Koifman and B. D. Berezin, *Chem. Abst.*, **98**: 71769s (1983); [b] J. Gitzel, H. Ohno and E. Tsuchida, *Polym.*, **27**, 1781 (1986).

[19] Recent reviews include: [a] B. Meunier, *Bull. Soc. Chim. France*, 578 (1986); [b] I. Tabushi, *Coord. Chem. Rev.*, **86**, 1 (1988).

[20] Hubert van der Berg, *Chem. Br.*, 430 (1986).