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A NEW ROUTE FOR MESO-SUBSTITUTED PORPHYRIN

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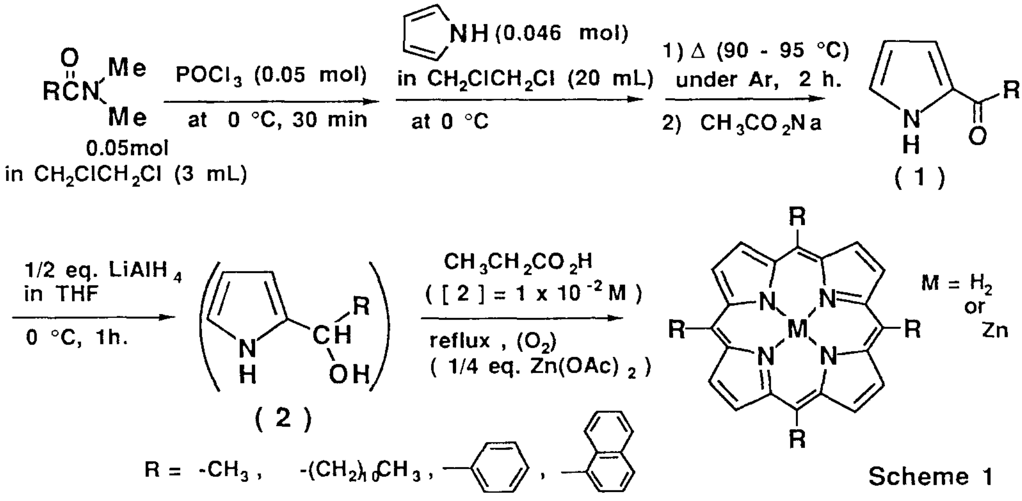
A new synthetic route of meso-substituted porphyrins was established. The method presented here shows wide applicability for the preparation of aryl and alkyl meso-substituted porphyrins.

Among the various types of the synthetic methods for porphyrins ever established, the method of the direct acid catalyzed condensation of aldehyde with pyrrole has been most frequently and widely used.1) In particular, 5,10,15,20-tetraphenyl-porphyrin derivatives thus synthesized made it possible to provide very important and useful biomimetic model compounds for hemoproteins and hemoenzymes.2) Although the original method has been improved and refined through many investigations3), there is still some basic difficulty in this method due to the fact that the condensation reaction between eight molecules (four pyrroles and four aldehydes) results in concomitant formation of many undesirable polymeric product.

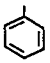
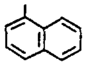
We herein report a new route for the syntheses of meso-substituted porphyrins which is applicable for both of aliphatic and aromatic substituted porphyrins. In the method described here, the porphyrin formation step is the condensation between four molecules of pyrrole derivatives.

The key intermediate for the present route is 2-acylpyrroles (**1**) which are found to be readily prepared from pyrrole and N,N-dimethylamides corresponding to the target acyl moiety by the method similar to Vilsmeier formylation.4) The typical reaction conditions were shown in Scheme 1. 2-Acylpyrroles were reduced quantitatively by the half equivalent of $LiAlH_4$ and the resultant acid sensitive alcohols (**2**) were directly used for the porphyrin



Scheme 1

Table 1. Synthetic Yields of Acylation of Pyrrole and Porphyrin Formation from **2**.

R		Yield (%)		
Reaction	$-CH_3$	$-(CH_2)_{10}CH_3$		
Acylation	64	72	69	38
Porphyrin Formation[a]				
without $Zn(OAc)_2$	15	9.2	26	16
with $Zn(OAc)_2$	21	29	34	24

a) Isolated yields based on **1**.

formation reaction in propionic acid.[5] The reaction yields of the acylations and porphyrin formations are summarized in Table 1. The most characteristic advantages of the present reactions are their wide applicabilities and relatively high yields of porphyrin formations. There are only few examples of the general synthetic methods for the preparations of meso-alkylsubstituted porphyrins but the present method can easily be applied to n-alkyl-substituted porphyrin formation in reasonable yield.[6] Furthermore, the considerable increase in the yields of porphyrins were observed by the addition of $Zn(OAc)_2$ as the template (see Table 1). The addition of the template metal is expected to be especially effective in the present case, because the coordination of four molecules of **2** on the Zn atom satisfies the necessary conditions for the condensation to afford the corresponding porphyrins, in contrast with the hitherto used method where, even after the coordination of pyrroles, other four aldehydes molecules must intermolecularly approach to this reaction center. Furthermore, the present method has marked advantage to decrease the formation of intractable by-products. Finally, it should be noted that the present method uses N,N-dimethylamides as meso-carbon source instead of aldehyde compounds which sometimes make trouble in their preparations.

References and Notes.

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2) J. P. Collman, T. R. Halpert, K. S. Suslick, Metal Ion Activation of Dioxygen (T. G. Spiro Ed.), Wiley, New York, p1, (1980).
3) B. Morgan, D. Dorphin, *Structure and Bonding*, **64**, 116, (1987).
4) R. M. Silverstein, E. E. Ryskiewics, *Org. Syn.* Coll. Vol. **4**, 831, (1963).
5) The porphyrin products were oxidized by DDQ to avoid contamination of corresponding chlorins if necessary and purified by the usual silica gel chromatography, see, for example J-H. Fuhrhop, K. M. Smith, "Laboratory Method" in Porphyrins and Metalloporphyrins (K. M. Smith Ed.), Elsevier, Amsterdam, p757, (1975).
6) 2-Isobutyryl and 2-pivaloyl pyrroles were similarly prepared and reduced in good yields. The corresponding alcohols, however, give no porphyrins under the present conditions because of their steric bulkiness.

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