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DECARBOXYLATION OF 2-(N-PORPHYRINYL) ACETIC ACIDS . A ROUTE TO N-ALKYLPORPHYRINS

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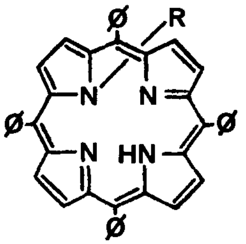
Summary. An improved preparation of N-alkylporphyrins avoiding the use of $CF_3SO_3CH_3$ is described.

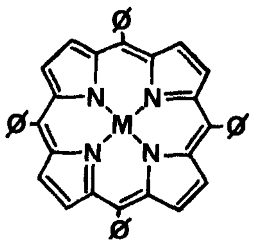
N-Alkylporphyrins have been studied in order to determine the influence of a large deformation on various properties of the macrocyclic ligand: spectra [1,2], metal coordination [3] and solvolysis [4,5], dealkylation [6] and alkyl transfer [7], redox potentials [8].

The preparation of the simplest, and widely used, N-methyl-*meso*-tetraphenylporphyrin **1** (NCH_3TPP) has been achieved *via* reaction of the free base H_2TPP **2** with $CF_3SO_3CH_3$ [4] or other methylating agents [1,9], the former being the most selective towards monomethylation.

In the present note we describe an alternative procedure avoiding the use of the very poisonous $CF_3SO_3CH_3$ and the recycling of the starting material.



1 R = CH_3
4 CH_2CO_2Et
5 CH_2CO_2H
6 Et
7 $CH(CH_3)CO_2H$
8 $CH(CH_3)CO_2Et$



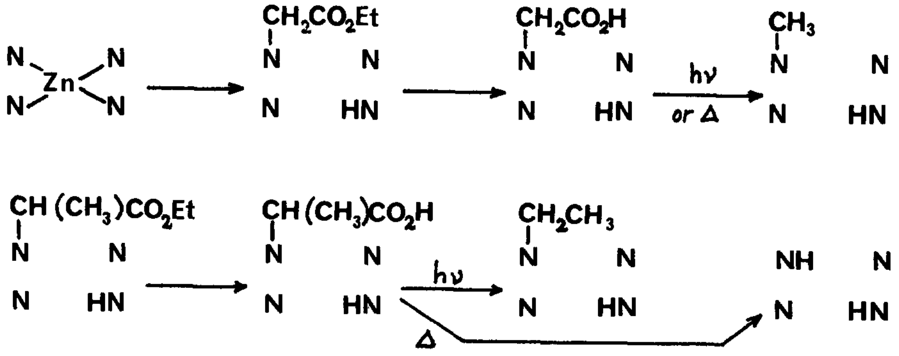
2 M = H_2
3 Zn

Free base H_2TPP 2 was quantitatively metalated to ZnTPP 3 which in turn was treated with ethyl diazoacetate to yield 4 (66% after acid removal of Zn^{++})[10]. This ester was saponified (NaOH) and the dilute solution of acid 5 in CH_2Cl_2 exposed to sunlight to effect the decarboxylation to give NCH_3TPP 1 (80% from 4; overall yield from H_2TPP 53%). Alternatively the crude acid decarboxylated in refluxing chlorobenzene (67% from 4).

A similar procedure could be used for preparing N-ethyltetraphenylporphyrin from methyl diazopropionate, although it is more convenient to react ZnTPP 3 directly with methyl pyruvate tosylhydrazone in the presence of a hindered base (iPr_2NH)[11]. NEtTPP 6 was obtained photochemically in a 25% overall yield from H_2TPP 2. In this case the thermal decomposition partly failed (25% yield) and H_2TPP was recovered.

The observed photochemical decarboxylation is not surprising in view of the examples that can be found in the literature[12]. Both hetero substitution (O,S,N) and sensitization favor the reaction, but no loss of the whole side was observed (no H_2TPP 2 detected) as described for some substituted amino-acids. We postulate that the porphyrin itself acts as a sensitizer, visible light beeing sufficient to initiate the reaction.

The low yield of the thermal decomposition of 7 may be due to an elimination reaction forming acrylic acid and H_2TPP 2.



TYPICAL PROCEDURES

1. N-methyltetraphenylporphyrin

ZnTPP 3 (500 mg) and ethyl diazoacetate (1.5 ml) in chlorobenzene (10 ml) were heated for 20 hr at 100°C. Addition of CH_2Cl_2 (100 ml), conc. HCl (3 ml) and stirring for 5 min was followed by neutralization (solid ammonium carbonate), evaporation and filtration on alumina (100 g). Toluene + 5% AcOEt eluted 4 (340 mg from MeOH; 66%) following recovered H_2TPP (55 mg)

Ester 4 (340 mg) and NaOH (1000 mg) in THF + EtOH (3:2; 150 ml) were refluxed for 3 hr. Dilution with benzene (150 ml) and AcOH (5 ml), washing with H_2O (3 times) and evaporation gave acid 5. The solution of crude 5 in CH_2Cl_2 (3000 ml) was exposed to sunlight under N_2 for 1 hr. The solvent was recovered and the residue crystallized from CH_2Cl_2-MeOH to give N-methyltetraphenylporphyrin 1 [14] (255 mg; 80% from 4).

2. N-ethyltetraphenylporphyrin

ZnTPP 3 (500 mg), methyl pyruvate tosylhydrazone (810 mg) [13] and i-Pr_2NH (0.46 ml) were heated in refluxing benzene (30 ml) for 24 hr. Work-up as above gave ester 8 (190 mg; 36.5%) and recovered H_2TPP (70 mg). Saponification and photochemical decarboxylation (as above) gave N-ethyltetraphenylporphyrin 6 [14] (120 mg; 69%; from CH_2Cl_2-MeOH; nmr: CH_3 (t) , $\delta = -1.70$ ppm; CH_2 (q) -4.45 ppm).

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