

meso-DEUTERIATION OF MAGNESIUM PORPHYRINS

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Several studies of the deuterium exchange of metalloporphyrin meso-protons have been reported.<sup>1</sup> In these investigations, the source of deuterium was usually deuterioacetic or deuteriotrifluoroacetic acid, and interpretation of the data was often complicated by demetallation of the substrates under the exchange conditions. No information on the electrophilic substitution of magnesium porphyrins has been gathered because the magnesium would be removed immediately by the acidic media. However, from simple electronic considerations,<sup>2</sup> magnesium porphyrine would be expected to be extremely susceptible to deuterium exchange. Making use of an original observation by Woodward and Škarić,<sup>3</sup> magnesium chlorins have been shown<sup>4</sup> to undergo exchange at the  $\delta$ -position under neutral conditions in deuteriomethanol. However, no exchange of the more "porphyrin-like"  $\alpha$  and  $\beta$  protons was observed, even on prolonged treatment.

We now report a simple method for the meso-deuteration (and tritiation) of magnesium porphyrins, together with preliminary results<sup>5</sup> which allow comparison of the susceptibility of magnesium and other metalloporphyrins towards electrophilic substitution.

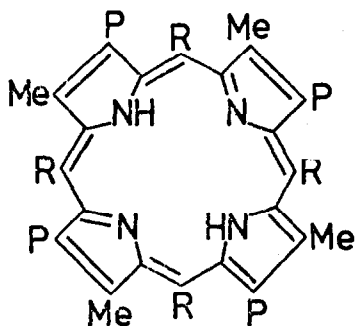
As a result of an unexpected observation<sup>6</sup> during the magnesiumation of tritium labelled porphyrins, we have found that treatment of porphyrins (e.g. coproporphyrin-I tetramethyl ester; 1a) with hexapyridyl magnesium iodide<sup>7</sup> in pyridine and deuteriomethanol or deuterium oxide, affords the magnesium chelate in which a high degree of deuteration of the meso-positions has been achieved.

A standard solution of hexapyridyl magnesium iodide was prepared as follows: A mixture of magnesium (800 mg), iodine (1.5 g), and diethyl ether (30 ml) was heated

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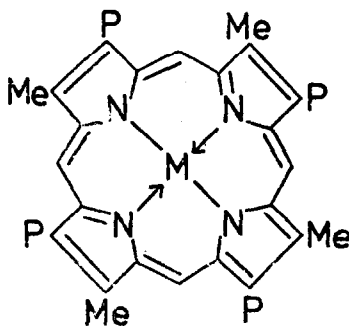
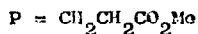
under reflux, in an atmosphere of nitrogen, until colourless (ca. 20 min), before being filtered and the filtrate evaporated to dryness. The residual yellow solid was quenched with pyridine (50 ml) and deuteriomethanol<sup>8</sup> (2 ml). In a typical deuteration experiment, 20 ml of this standard solution was added to coproporphyrin-I tetramethyl ester<sup>9</sup> (123 mg) in dry pyridine (3 ml) and the mixture was heated under reflux, in an atmosphere of nitrogen, during 4 hr. (Spectrophotometry showed that magnesianation was complete within 1 hr). The cooled solution was diluted with chloroform (50 ml) and then poured into 3% citric acid in water (200 ml). After thorough washing, the organic phase was dried ( $\text{Na}_2\text{SO}_4$ ), evaporated, and the residue was set aside overnight in 5% v/v sulphuric acid in methanol.<sup>10</sup> The solution was poured into water (250 ml) and the porphyrin was extracted into chloroform, which was washed with water, dried ( $\text{Na}_2\text{SO}_4$ ), and evaporated to dryness. The residue was chromatographed on alumina (Merck; Brockmann Grade V) and the methylene chloride eluates were evaporated; crystallization of the residue from methylene chloride - methanol gave 110 mg (90%) of (1b), having the same melting point as the undeuteriated starting material. NMR and mass spectroscopy showed that the meso-positions were deuteriated to the extent of 90-95%.



(1)

a: R = H

b: R = D



(2)

a: M = Mg

b: M = Zn

c: M = Pd

We have subsequently found<sup>11</sup> that magnesianation of porphyrins with hexapyridyl magnesium iodide in pyridine, followed by addition of a small quantity of tritiated water to the mixture before continuation of the reaction, achieves meso-tritiation with

very high radiochemical yield; we have used these tritiated porphyrins in some of our biosynthetic investigations, e.g. 11

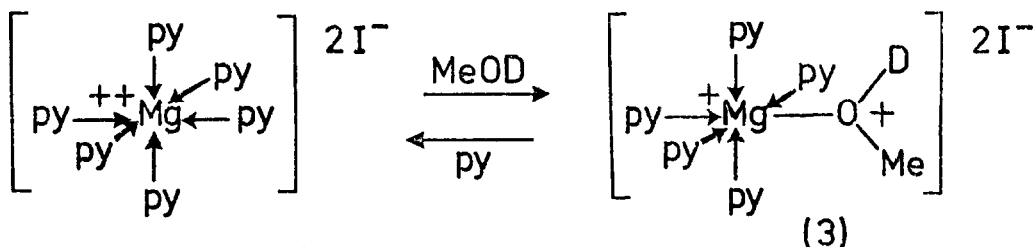
The Table shows the percentages of deuteration obtained using the procedure outlined, with coproporphyrin-I tetramethyl ester (1a) and its magnesium (2a), zinc (2b), and palladium (2c) chelates. As might be expected,<sup>2</sup> the results show the magnesium chelate to be more susceptible to deuteration than the zinc or palladium

TABLE

<u>Compound</u>	<u>Reaction Time</u>	<u>Percentage Deuteration*</u>
Coproporphyrin-I tetramethyl ester (1a)	4 hr	92
Magnesium coproporphyrin-I tetramethyl ester (2a)	80 min	68
Zinc coproporphyrin-I tetramethyl ester (2b)	80 min	25
Palladium coproporphyrin-I tetramethyl ester (2c)	20 hr	< 10

\* Estimated from both n.m.r. and mass spectra (error  $\pm 2\%$ ).

complexes. The use of aluminium dihalide catalysts in the presence of tritiated water has been shown<sup>12</sup> to be a useful method for the rapid tritium labelling of organic molecules. Garnett and co-workers<sup>12</sup> have suggested a mechanism involving a  $\pi$ -associated complex between the organic compound and the catalyst, which is hydrolysed with the tritiated water. In view of our results (Table) and since we have been unable to deuteriate simple aromatic compounds with hexapyridyl magnesium iodide (and a deuterium source), we believe that we are observing a simple electrophilic substitution of a metalloporphyrin. Magnesium iodide is a Lewis acid, and interaction of deuteriomethanol with hexapyridyl magnesium iodide might be expected to displace pyridine, giving a species (3) which would appear to be a good, "neutral" source of deuterons. Deuteration of metalloporphyrins can also be accomplished with methoxymagnesium bromide or magnesium perchlorate hydrate, in pyridine and deuteriomethanol or deuterium oxide.



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