

NON-EQUIVALENCE OF THE METHYLENE PROTONS
IN OCTAETHYLPORPHINATOTHALLIUM(III)

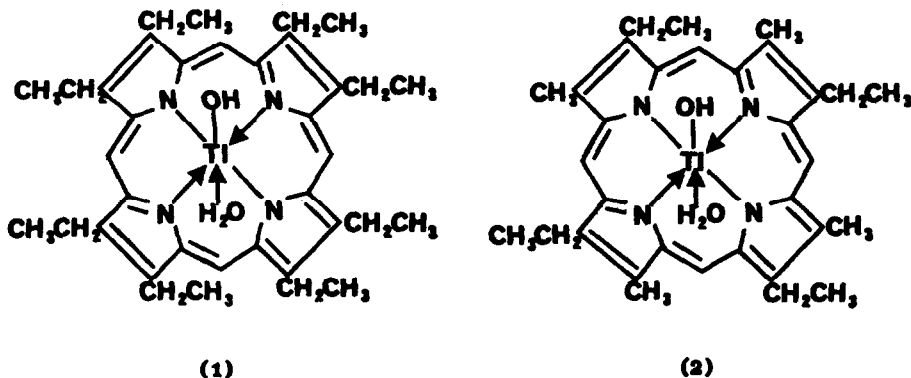
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The enzymic conversion of coproporphyrinogen-III to protoporphyrin-IX proceeds by loss of one proton from the methylene group adjacent to the macrocyclic ring¹; its removal may be specific, either due to the position of the molecule on the active site of the enzyme or because of intrinsic non-equivalence of the α -methylene protons.

We wish to report the first demonstration of non-equivalence in porphyrin α -methylene groups, using the recently reported² aquo-octaethylporphinatothallium(III) hydroxide (1)³. The n.m.r. spectrum in deuteriochloroform shows the expected doublet



for the meso- protons ($J_{Tl-H} = 45$ Hz) and triplet for the methyl protons of the ethyl groups ($J = 7.5$ Hz), but a complex pattern (Figure 1a) for the methylene protons of the ethyl side-chains. In the corresponding thallium(III) aetioporphyrin-I chelate (2)³ the thallium couples to the peripheral methyl groups ($J_{Tl-Me} = 8.2$ Hz). Thus the full description of the spin system of the methylene protons in (1) is ABR_3X . The analysis was performed by total decoupling of the methyl protons to give the five line pattern

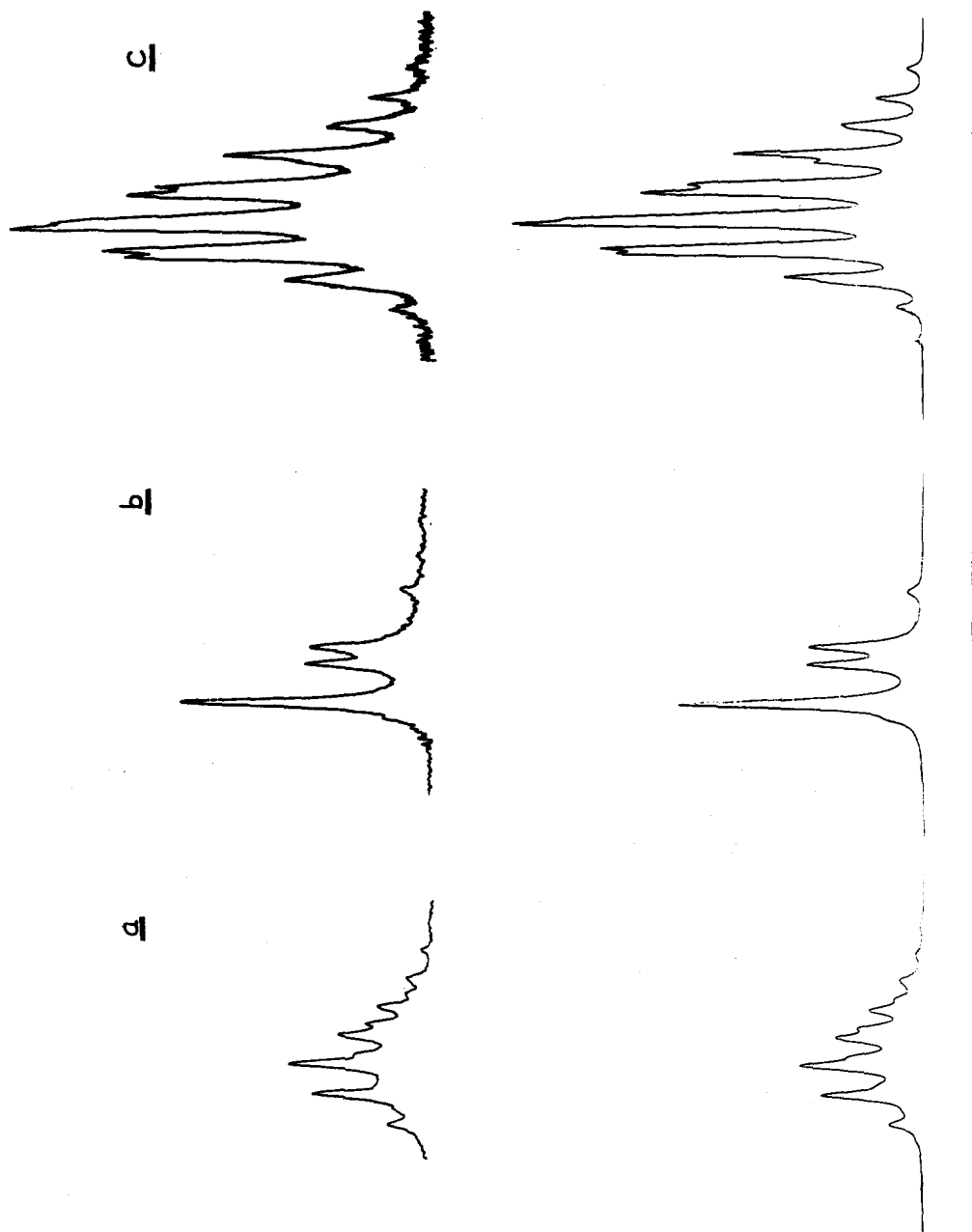


Figure 1: Observed (Upper) and Calculated (Lower) n.m.r. spectra of the methylene protons in (1):
(a) at 100 MHz (b) at 100 MHz (decoupled) (c) at 220 MHz.

shown in Figure 1**b**, corresponding to the AB part of an ABX system; this was analysed in the normal manner⁴. Confirmation of this was obtained using this data plus the CH₂-CH₃ coupling to analyse the 100 MHz and 220 MHz spectra of (1) as ABR₃X systems. The observed and calculated plotted spectra are shown in Figures 1**a**, 1**b**, and 1**c**.

The parameters obtained from these analyses are $J_{A-B}(J_{H-H}) = -13.9$ Hz; $J_{A-X}(J_{H-Tl}) = 6.1$ Hz; $J_{B-X}(J_{H-Tl}) = 18.1$ Hz; $J_{A-R} = J_{B-R}(J_{CH_2-CH_3}) = 7.5$ Hz and at 100 MHz, $\nu_A = 422.80$ Hz; $\nu_B = 416.80$ Hz; $\nu_R = 195.50$ Hz. The analysis gives the relative sign of the two Tl-H couplings, but not the signs relative to the other couplings.

Of particular interest is the marked non-equivalence of the methylene protons with respect to both their chemical shifts and thallium couplings. The spectrum was unchanged by dilution, indicating that the asymmetry cannot be ascribed to aggregation or complex formation⁵. There are two likely interpretations of these results:

- a) Inversion of the methyl groups is slow on the n.m.r. time-scale and this results in an intrinsic asymmetry of the porphyrin molecule, or
- b) The asymmetry introduced into the porphyrin ring by the metal atom and its ligands may be sufficient to cause the observed spectra even with rapid inversion of the methyl groups. This would be particularly so if the thallium were situated out of the plane of the porphyrin ring^{3,6}.

We favour the former explanation, since it is unlikely that a rapidly inverting methyl group would give two very different α -methylene Tl-H couplings. On this basis it also follows that if the thallium atom is in the plane of the porphyrin ring there must be slow rotation of the ethyl groups on the n.m.r. time-scale.

Non-bonded interaction calculations using the program MODELS⁸ and previously published porphyrin geometry⁹ show that the minimum energy conformation of the ethyl groups in (1) is that with the methyl groups almost vertically out of the plane of the porphyrin ring, slightly inclined away from each other with the two methyl groups on each pyrrole ring on opposite sides of the ring plane, (Figure 2). Furthermore, the energy barrier to rotation, (which must be a cog-wheel effect) is high. Our calculations give a value of ca. 20 kcal/mole over that of the ground state (Figure 2)

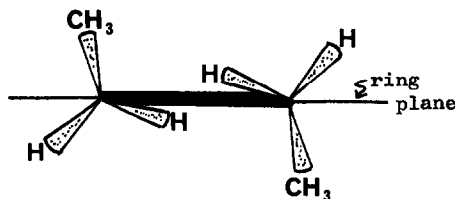


Figure 2

for the conformation with both ethyl groups in the plane. This value is large enough to produce slow rotation on the n.m.r. time-scale. (For a two site exchange with $\delta\nu = 6$ Hz, an activation energy of 15.7 kcal/mole is required to produce coalescence at room temperature.)

Assuming no great distortion of the macrocycle by the metal ion, the steric requirements of the ethyl groups in (1) will be very similar to those in octaethylporphyrin itself, since the thallium and ligands are far removed from the side-chains. Our results therefore suggest that the ethyl groups in the free ligand could be slowly rotating on the n.m.r. time-scale. The room temperature n.m.r. spectrum of octaethylporphyrin shows no evidence of non-equivalence in the methylene groups. However, a decrease in the methylene chemical shift separation could easily account for this.

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