Synthesis of *meso*-Substituted Porphyrins

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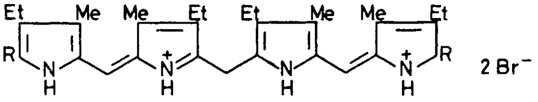
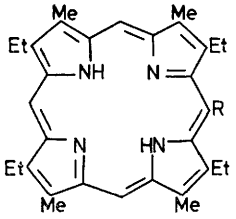
Summary Acid-catalysed condensation of 1,19-diunsubstituted biladiene-*ac* dihydrobromides with a variety of aldehydes yields *meso*-substituted porphyrins.

1,19-DIDEOXYBILADIENE-*ac*-1,19-DICARBOXYLIC ACIDS (I; R = CO_2H) were prepared originally[1] as intermediates for the synthesis of corroles, but it was also shown that condensation with formaldehyde gave the corresponding porphyrin. This method was used later for a synthesis of coproporphyrin II tetramethyl ester as well as [15-^{13}C]-protoporphyrin IX dimethyl ester required for biosynthetic studies.[2] We now report that condensation of higher aldehydes or the corresponding acetals with a 1,19-unsubstituted biladiene-*ac* dihydrobromide in presence of acid provides a useful method for the preparation of *meso*-substituted porphyrins for which a good general method of synthesis is lacking. The synthesis has been studied in the aetioporphyrin II series (II) and several examples have been provided [II; R = Ph (91%), p-$MeOC_6H_4$ (81%), p-$O_2NC_6H_4$ (40%), Me (28%) (from acetal), Pr^n (13%), and CO_2Et (68%)] using the appropriate aldehydes, RCHO. All of the products were characterised as nickel(II) complexes which were formed in high yield from the metal-free porphyrin by the action of methanolic nickel acetate. When the biladiene-*ac* dihydrobromide was condensed with terephthalaldehyde the main product was *meso*-(*p*-formylphenyl)aetioporphyrin II (89%) which, with nickel acetate in methanol, was converted (5%) into its nickel complex but mainly (65%) into the nickel derivative of *meso*-(*p*-dimethoxymethylphenyl)aetioporphyrin II [nickel complex of (II); R = $(MeO)_2CH{\cdot}C_6H_4$]. A minor product with a high R_F from the original terephthalaldehyde condensation was probably *p*-di(aetioporphyrinyl)benzene isolated, but not purified, as its nickel complex.



(I)



(II)

The porphyrin (II; R = CO_2Et) seems to be the first example of a *meso*-ethoxycarbonylporphyrin. We had earlier[3] claimed that acid hydrolysis of *meso*-cyanoaetioporphyrin I gave the *meso*-carboxy derivative but this was disputed by Clezy *et al.*[4] who showed that the product was the amide (II; R = $CONH_2$, aetio I series). The acid was not obtained by hydrolysis of the amide or the ester and Clezy *et al.*[4] failed to form the acid by oxidation of the corresponding formyl derivative, presumably for steric reasons.

(*Received*, 14*th July* 1977; *Com.* 724.)

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[4] P. S. Clezy, C. L. Lim, and J. S. Shannon, *Austral. J. Chem.*, 1974, 27, 1103.