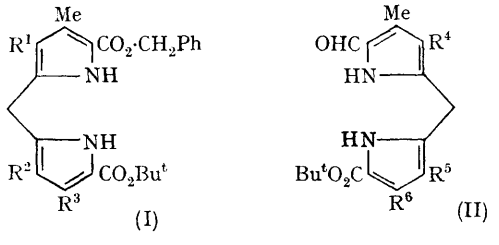
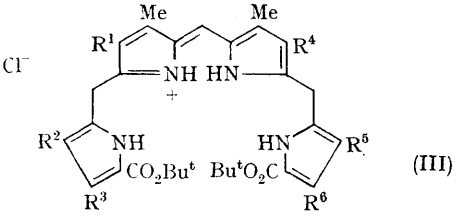
Syntheses of Porphyrins through *b*-Bilenes

By M. T. COX, R. FLETCHER, A. H. JACKSON, G. W. KENNER,* and K. M. SMITH
(*The Robert Robinson Laboratories, University of Liverpool, Liverpool 7*)

THE synthesis of porphyrins from *a*-oxobilanes[1,2] proceeds by removal of the oxo-function and dehydrogenation in the middle of the tetrapyrrole system. However, the latter process is only partially selective and the intermediate *b*-bilene dicarboxylic acids [related to the t-butyl esters (III)] are contaminated with *a*- and *c*-bilenes. A more direct route to such intermediates became apparent through our use of 5-benzyloxycarbonyl-5′-t-butyloxycarbonylpyrromethanes (I)[3] in syntheses of porphyrins, *e.g.*, protoporphyrin-IX,[4] by the *b*-oxobilane method.[1,5] Such compounds (I)



(I) (II)

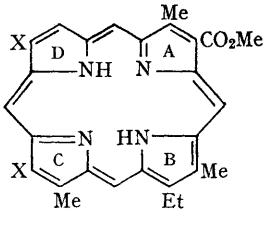


(III)

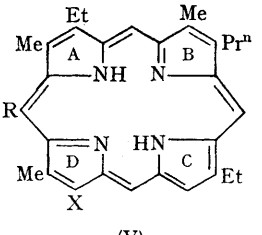
(a) $R^1 = [CH_2]_2{\cdot}CO_2Me$; $R^2 = Et$; $R^3 = Me$
(b) $R^1 = Et$; $R^2 = Me$; $R^3 = [CH_2]_2{\cdot}CO_2Me$
(c) $R^1, R^2 = Et$; $R^3 = Me$
(d) $R^4 = [CH_2]_2{\cdot}CO_2Me$; $R^5 = Et$; $R^6 = Me$
(e) $R^4 = Et$; $R^5 = Me$; $R^6 = [CH_2]_2{\cdot}CO_2Me$
(f) $R^4 = CO_2Me$; $R^5 = Et$; $R^6 = Me$

can be converted by successive hydrogenolysis, decarboxylation, and reaction with phosphoryl chloride–dimethylformamide into the corresponding 5-formyl-5′-t-butyloxycarbonylpyrromethanes (II), *e.g.*, (IId) from (Ia) and (IIe) from (Ib). The acids formed by hydrogenolysis of the benzyl esters (I) can be condensed with the formylpyrromethanes (II) under carefully controlled conditions to give the *crystalline* *b*-bilene hydrochlorides (III) in high yield. The condensation is carried out in methylene chloride–methanol at room temperature with small amounts of either hydrogen chloride or toluene-*p*-sulphonic acid, which is washed out with aqueous sodium carbonate and replaced by dry hydrogen chloride at the end of reaction. Treatment of the *b*-bilene hydrochloride (III) with cold trifluoroacetic acid removes the t-butyloxycarbonyl groups and then, after liberation of the decarboxylated *b*-bilene by evaporation and treatment with base, the macrocycle can be formed rapidly by treatment with methyl orthoformate–trichloroacetic acid.[2] Thus (IIIad) yielded mesoporphyrin-IV dimethyl ester, m.p. 236—238°, lit.,[6] m.p. 238° (39%), (IIIbe) mesoporphyrin-XIII dimethyl ester, m.p. 217°, lit.,[6] m.p. 217° (57%), (IIIbd) mesoporphyrin-X dimethyl ester,† m.p. 175—177°, (47%), and (IIIce) 3,6,7-triethyl-1-(2′-methoxycarbonylethyl)-2,4,5,8-tetramethylporphin,† m.p. 221—223° (51%). These products were not contaminated by other porphyrins, and we were encouraged to apply the method to more complex cases.

The porphyrin (IV), m.p. 216—217°† required for our studies in synthesis of porphyrin-*a*, was prepared in 18% yield by closure of the macrocycle between rings A and D of a *b*-bilene formed by condensation between a formylated AB pyrromethane and a CD pyrromethane. The cyclisation was very slow (40 hr.), doubtless owing to electron-withdrawal by the methoxycarbonyl group in ring A, and originally the alternative route through condensation between ring D and a formyl group on ring A and cyclisation between



(IV)
(X=$CH_2{\cdot}CH_2{\cdot}CO_2Me$)



(V)
(a) R=Et
(b) R=Me

rings B and C had been expected to be better. However, it gave a mixture of porphyrins and the crystalline, chromatographic fraction having the

† New porphyrin, characterized by mass and n.m.r. spectra and elemental analyses.

correct mass and electronic spectra for structure (IV) was a mixture (n.m.r. spectrum in $CDCl_3$). Again, in a simpler model system, the undoubtedly homogeneous *b*-bilene hydrochloride (IIIbf) gave a mixture of porphyrins. The origin of the by-products in these two syntheses is uncertain, but it is probably connected with the enhanced electrophilic reactivity of the pyrromethene system bearing a methoxycarbonyl substituent and redistribution of pyrrole nuclei can be visualized as proceeding through complex tripyrrylmethanes.[7]

Structures (Va) and (Vb) have been assigned to the phylloporphyrins derived from chlorobium chlorophyll (660) bands 3 and 4, respectively.[8] Syntheses of these compounds by the classical pyrromethene method afforded only minute yields and identification with the natural products was not achieved.[9] We have therefore synthesized both porphyrins (Va), m.p. 175—176°, and (Vb), m.p. 195—198°, by the *b*-bilene method employing condensation between ring A and a formyl group on ring B and closure of the macrocycle between rings C and D. The yields were only 5%, but sufficient for proper analytical and spectroscopic characterization of the products which were not contaminated with other porphyrins. We hope to report elsewhere comparisons with samples of natural origin.

From the experience gained so far, we conclude that the *b*-bilene method, although subject to important limitations, is a useful addition to existing porphyrin syntheses through well characterized open-chain tetrapyrroles. It must be emphasized that its fundamental principles are the same as those of the established MacDonald method,[10] which, however, is restricted to porphyrins with an element of symmetry. A *b*-bilene was a spectroscopically detected intermediate in the Harvard synthesis of chlorophyll.[11]

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