Synthesis of Some Tetradehydrocorrins and 1,19-Dideoxybilanes Related to 12-Decarboxyuroporphyrin III

By Jürgen Engel and Albert Gossauer*

(*Institut fur Organische Chemie der Technischen Universität D-33-Braunschweig, Schleinitzstrasse*)

Summary Some new 10,24-dihydro-(21*H*)-bilins bearing acetic and propionic acid residues at the β-positions have been prepared and transformed into macrocyclic tetrapyrroles as well as hydrogenated to the corresponding 1,19-dideoxybilanes.

Protonated 10,24-dihydro-(21*H*)-bilins (1,19-dideoxybiladienes-*a,c* salts) and their corresponding metal chelates are very useful intermediates for the synthesis of porphyrins[1] and corroles,[2] and tetradehydrocorrin metal complexes[3,4] respectively. Their transformation to 5,10,15,22,23,24-hexahydro-(21*H*)-bilins (1,19-dideoxybilanes) has not been reported hitherto, probably because of the well known[5] lability of these compounds towards oxygen and acids. However, we felt that 1,19-dideoxybilanes carrying acetic and propionic residues at the β-positions, by analogy with the corresponding dipyrrylmethanes,[6] should be stable enough to be isolated, and should provide interesting compounds associated with the biosynthesis of cobyric acid. In this connection we contemplated the synthesis of the corresponding derivatives related to 12-decarboxyuroporphyrin III (**9**) which have been postulated as possible precursors of vitamin B_{12}.[7]

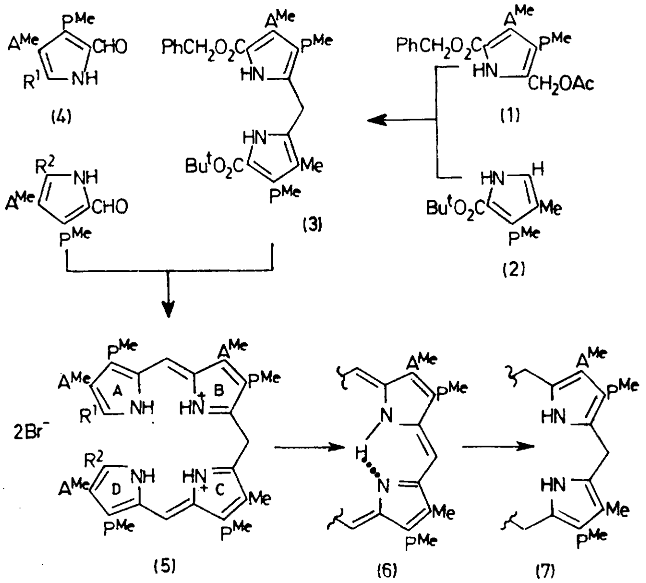
With this aim we have prepared some new 10,24-dihydro-(21*H*)-bilin dihydrobromides of the type represented by (**5**) starting from the unsymmetrically substituted dipyrrylmethane (**3**)† which is readily accessible by condensation of the known pyrroles (**1**)[8,9] and (**2**)[10] in methylene chloride containing a catalytic amount of toluene-*p*-sulphonic acid. The dibenzyl ester analogue of (**3**) has recently been synthesised independently, by Battersby *et al.*[11]

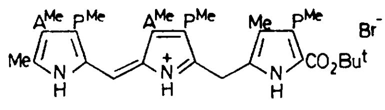
The advantage of having two different ester groups at both outer α-positions of (**3**) is to enable stepwise synthesis of 10,24-dihydro-(21*H*)-bilins such as (**5a**)† carrying different pyrrole rings A and D. In this case, the intermediate pyrrylmethylpyrromethene hydrobromide (**8**)† could be obtained, after hydrogenation of the benzyl ester group of (**3**) and decarboxylation of the resulting half-acid, by reaction with 1 mol. equiv. of the pyrrole aldehyde (**4**; $R^1 = Me$).[9] A similar approach to the synthesis of unsymmetrically substituted porphyrins has been reported recently by Kenner *et al.*[12]

When the same pyrrole aldehyde is to be attached at both end α-positions of the dipyrrylmethane (**3**) the t-butoxycarbonyl group of the latter is cleaved by treatment with trifluoracetic acid, the benzyl ester hydrogenolysed over palladised charcoal, and the resulting carboxylic acid condensed, after decarboxylation, with 2 mol. equiv. of the pyrrole aldehyde (**4**).[9] Thus, the 10,24-dihydro(21*H*)-bilins (**5b**—**e**)† have been prepared in 40—50% overall yields.

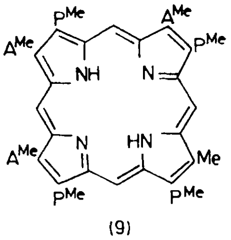
By similar methods we have synthesized some analogues of (**5**) related to uroporphyrin III, *i.e.* bearing an acetic ester chain at C-12 instead of a methyl group. Their synthesis will be reported shortly, elsewhere.

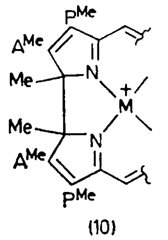
Some of the synthesized 10,24-dihydro-(21*H*)-bilin dihydrobromides could be transformed into macrocyclic tetrapyrroles, thereby confirming their structures assigned on the basis of analytical data. Thus, (**5b**) yields, on treatment with copper(II) acetate (*cf.* ref. 1) and successive demetallation, the porphyrin (**9**) which is also obtained by

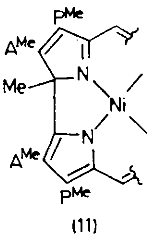



(**8**)

a; $R^1 = Me$, $R^2 = H$
b; $R^1 = R^2 = Me$
c; $R^1 = R^2 = H$
d; $R^1 = R^2 = CO_2Me$
e; $R^1 = R^2 = CO_2CH_2Ph$
f; $R^1 = R^2 = CO_2H$


(**9**)


(**10**)


(**11**)

$A^{Me} = CH_2CO_2Me$ $P^{Me} = CH_2CH_2CO_2Me$

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† New compound(s) which gave satisfactory elemental analysis, and mass, electronic, and n.m.r. spectra compatible with the formulation shown.

reaction of (**5c**) with formaldehyde (*cf.* ref. 2), by thermal cyclisation of (**5a**) in *o*-dichlorobenzene[13] or by heating (**5a**) in dimethylformamide in the presence of copper(II) acetate and successive demetallation. The porphyrin (**9**) has been recently shown to be an isomer of the metabolically interesting phyriaporphyrin III.[11]‡

The tetradehydrocorrin salts (**10**; M = Ni^{II})† and (**10**; M = Co^{II})† are obtained by base-catalysed cyclisation of (**5b**) with nickel or cobalt acetate respectively (*cf.* ref. 3). Accordingly, (**5a**) affords the 1-methyltetradehydrocorrin (**11**)† when treated with nickel acetate in methanol.[13]

The 10,24-dihydro-(21*H*)-bilin dihydrobromides (**5a**—**d**) could be catalytically hydrogenated (PtO_2, 1 atm., 20°C), after transformation into their corresponding green free bases [formulated as 22,24-dihydro-(21*H*)-bilins (**6**)[14]], to the corresponding 1,19-dideoxybilanes (**7a**—**d**).† On catalytic reduction (**5e**) yields the corresponding dicarboxylic acid (**7f**)† which can be decarboxylated thermally in *vacuo* to (**7c**).

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