SYNTHESES OF PORPHYRINS THROUGH OPEN TETRACYANETHYRROLE STRUCTURES
(REVIEW)

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Methods for the preparation of porphyrins through 1-methyl-19-formyl(H)-bil-b-enes and 1-methyl-19-H-bila-a,c-dienes are examined. Principal attention is directed to a discussion of the effect of electron-acceptor substituents on the formation of open polypyrrole compounds and cyclization of the latter to porphyrins.

Synthetic studies of porphyrins are carried out by means of investigations of the biosynthesis and catabolism of these compounds [1-5] in order to ascertain the mechanism of the action of chromoproteides [6, 7] and to create biologically active substances [8]. Porphyrins and their metal complexes are studied extensively both within a theoretical framework [9] and in order to arrive at practical applications of them [10-12]. In particular, porphyrins are used as markers in geochemistry in the determination of the level of life on the earth in various historical epochs [13, 14]; they are detected in meteorites and on the moon's surface [15].

The development of the synthesis of porphyrins began with the fundamental research of the Fischer school [16]. The culmination of this research was the synthesis of hemin. Despite the low yield of the final product (0.1%), this event was an important advance in synthetic organic chemistry. Of the later studies, one should undoubtedly note the total synthesis of chlorophyll a, accomplished by Woodward [17] in 1960.

At present, methods that include the synthesis of intermediate "linear" tetrapyrrole compounds are among the most successful of the various methods for the preparation of porphyrins. Molecular models show that such structures exist in a spiral loop conformation due to repulsion of the adjacent β substituents [18]; the extreme A and D pyrrole rings prove to be drawn together in this case, and this is an important factor in the case of closing to form macrocyclic compounds. Depending on the oxidation state of the tetrapyrrole compounds, the existing methods can be divided into two principal groups. The first group includes the synthesis of bilene structures, and the second group includes the synthesis of biladiene structures. Within each of the above-indicated groups, individual methods are in turn distinguished by the modes of construction of the polypyrrole chain and also by the presence of various substituents in the 1 and 19 positions. The latter circumstance to a considerable degree determines the method of cyclization of the bilenes and biladienes to porphyrins.

Despite undoubted advances, the synthesis of complex porphyrin structures and, in particular, porphyrins with electron-acceptor substituents has been fraught up to now with certain difficulties [19]. A number of reviews devoted to research on porphyrins has been published in recent years [18, 20-24]. However, these reviews usually encompass a broad range of problems, and this does not make it possible to consider all of the available studies in detail. The aim of the present review was a discussion of the results of a portion of our studies on the synthesis of porphyrins. We deliberately limited our examination of methods for the preparation of porphyrins, singling out a group of syntheses through linear tetrapyrrole compounds, inasmuch as this method enabled us to solve some difficult problems in the synthesis of porphyrins.

Synthesis of Porphyrins through 1-Methyl-19-formyl(H)-bil-b-enes

In developing this method we proceeded from the fact that a symmetrical dipyrrole structure (dipyrrolylmethene C-D in porphyrin molecule 1) can be isolated in most natural porphyrins of the protoporphyrin...
and coproporphyrin III types. We therefore decided to realize synthesis of bil-b-ene on the basis of
dipyrrolylmethane fragments A-B and C-D. Symmetrical dipyrrolymethanes 2a [26] and 2b [27, 28] were
the key compounds in our method for the preparation of porphyrins through bil-b-enes [29].

The most complicated problem in the preparation of dipyrrolylmethane 2a was decarboxylation of
the corresponding 5,5'-dicarboxylic acid. Only strict observance of the reaction conditions makes it pos-
sible to obtain 2a in high yield; if such conditions are not observed, the dipyrrolylmethane undergoes de-
composition, and the chief product is pyrrolecarboxylic acid 3.

Dipyrrolymethanes of the 6 type, which are considerably more accessible than the corresponding
α,α'-unsubstituted derivatives [30], were selected as the second dipyrrole fragment (A-B).

Compound 6c (R^2=R^3=Ac) and the isomeric dipyrrolymethanes were prepared by heating α-chloro-
methylpyrrole 4 with pyrrole 5 in alcohol [31]. A number of dipyrrolymethanes 6c (R^2=acyl, R^3=alkyl)
was obtained by refluxing the reagents with triethylamine in chloroform [32, 33]. In the case of 6c (R^2=Et,
R^3=Ac) better results are obtained when acetoxymethyl derivative 4 (X=OAc) and pyrrole 5 are heated in
aqueous alcohol [34]. Dipyrrolymethanes 6c (R^2=R^3=P and R^2=R^3=CH=CHOH) were obtained from
acetoxymethyl derivative 4 and pyrrole 5 in dimethylformamide (DMF) [28]. No difficulties are usually
encountered in the conversion of the resulting dipyrrolymethanes to the corresponding α-unsutituted
compounds and formylation of the latter.

In our discussion of the synthesis of dipyrrolymethanes it would be particularly desirable to dwell
on two instances. The first is associated with the preparation of dipyrrolymethanes that do not have sta-
bilizing electronegative groups and, because of this, are extremely labile. With this end in mind, we used
the accessible dipyrrolymethenes 7a,b [30], which were reduced with sodium borohydride. This method
can be used for the preparation of α-unsutituted dipyrrolymethanes, although the principle product
usually contains a small amount of pyrroles. For this reason, dipyrrolymethene carboxylie acid 7c, which
is in turn obtained in practically quantitative yield [16], was subsequently reduced. The yield of 8c was
88%. The accessibility of the starting dipyrrolymethenes and their easy reduction with sodium borohy-
dride makes it possible to hope that this method will find application in the synthesis of alkyl-substituted
dipyrrolymethanes [35].

*The nomenclature proposed by H. Fischer [16] is used for porphyrins in this review, whereas the IUPAC
system [25] is used for polypyrrole compounds.