Tetrahedron Letters No.3, pp. 183-188, 1965. Pergamon Press Ltd.
Printed in Great Britain.

SYNTHESIS OF DIACETYLDEUTEROPORPHYRIN IX [x]

A.F.Mironov, R.P.Evstigneeva and
N.A.Preobrazhensky

The Lomonosov Institute of Fine Chemical Technology
Malaya Pirogovskaya 1, Moscow

(Received 7 December 1964)

Protoporphyrin IX is known to be one important porphyrins. As a "key compound" for its synthesis use may be made of diacetyldeuteroporphyrin IX [1]. This communication deals with a ready synthesis of this compound.

Synthesis of the dimethyl ester of diacetyldeuteroporphyrin IX was effected starting from our two dipyrrylmethanes - 4,3',5'-trimethyl-3,4'-diacetyl-5-formyldipyrrylmethane (I) [2] and 4,4'-dimethyl-3,3'-bis-(β-carbmethoxyethyl)-dipyrrylmethane (II) [3]. Porphyrin was condensed in methanol in the presence of hydrobromic acid in catalytic amount, the reaction having been characterised by the spectral changes in the visible region and by means of thin-layer chromatography on silicagel. The cyclisation of the resulting tetrapyrrole system in the presence of cupric acetate followed

---

[x] Translated by A.L.Pumpiansky, Moscow

by oxidation with air oxygen led to a copper complex of diacetyldeuteroporphyrin IX (III,X=Cu), m.p. 229.5–231°; lit.[1] 230°. Spectrum in chloroform: I, 586; II, 546 mμ (I > II). (Found: C, 63.04; H, 5.34; N, 8.01. $C_{36}H_{36}N_4O_6Cu$ requires: C, 63.19; H, 5.30; N, 8.19%).

Metallic complex (III, X=Cu) being treated with sulphuric acid gave rise to free porphyrincarboxylic acid that led on esterification to dimethyl ester of diacetyldeuteroporphyrin IX (IV). Yield 86%, m.p. 241.5–242°.

The mixed melting point with the analytical sample produced from hemin [4] showed no depression. Paper chromatography (n-heptan-chloroform, 1.15:1) produced similar R_f for both samples and their spectra in the visible region in chloroform were also found to be identical: I, 642; II, 589; III, 554; IV, 518 mμ (I < II < III < IV). (Found: C, 69.56; H, 6.03; N, 900. $C_{36}H_{38}N_4O_6$ requires: C, 69.44; H, 6.15; N, 8.99%).

The infra-red spectrum of the synthetic compound proved to be similar to that of porphyrin from hemin (Fig.1).

In order futher to characterise diacetyldeuteroporphyrin IX its dimethyl ester was complexed with zinc and mercury under the action of the acetates of corresponding metals. The purity of the zinc complex of the dimethyl ester of diacetyldeuteroporphyrin IX (III, X=Zn) was substantiated by paper chromatography in such systems as chloroform : kerosine (1:1.15) and n-propanol : kerosine (1:5), m.p. 259-260°. (Found: C, 63.10; H, 5.35; N, 8.05. $C_{36}H_{36}N_4O_6Zn$ requires: C, 63.02; H, 5.29; N, 8.17%). Spectrum in chloroform: I,596; II, 557 mμ(I< II).

The mercury complex of the dimethyl ester of diacetyldeuteroporphyrin IX (III, X=Hg) was not stable and decomposed under the action of most organic solvents, m.p. 214-215° (with decomp.). (Found: C, 52.91; H, 4.39; N, 7.06. $C_{36}H_{36}N_4O_6Hg$ requires: C, 52.65; H, 4.42; N, 6.82%). Spectrum in pyridine: I, 616; II, 582 mμ(I< II).

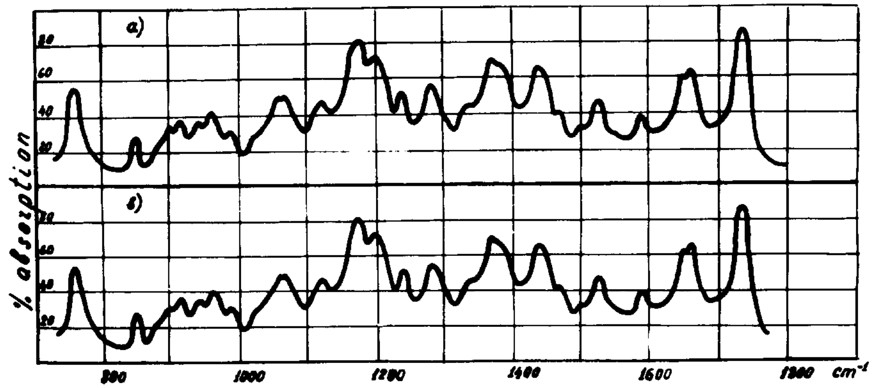
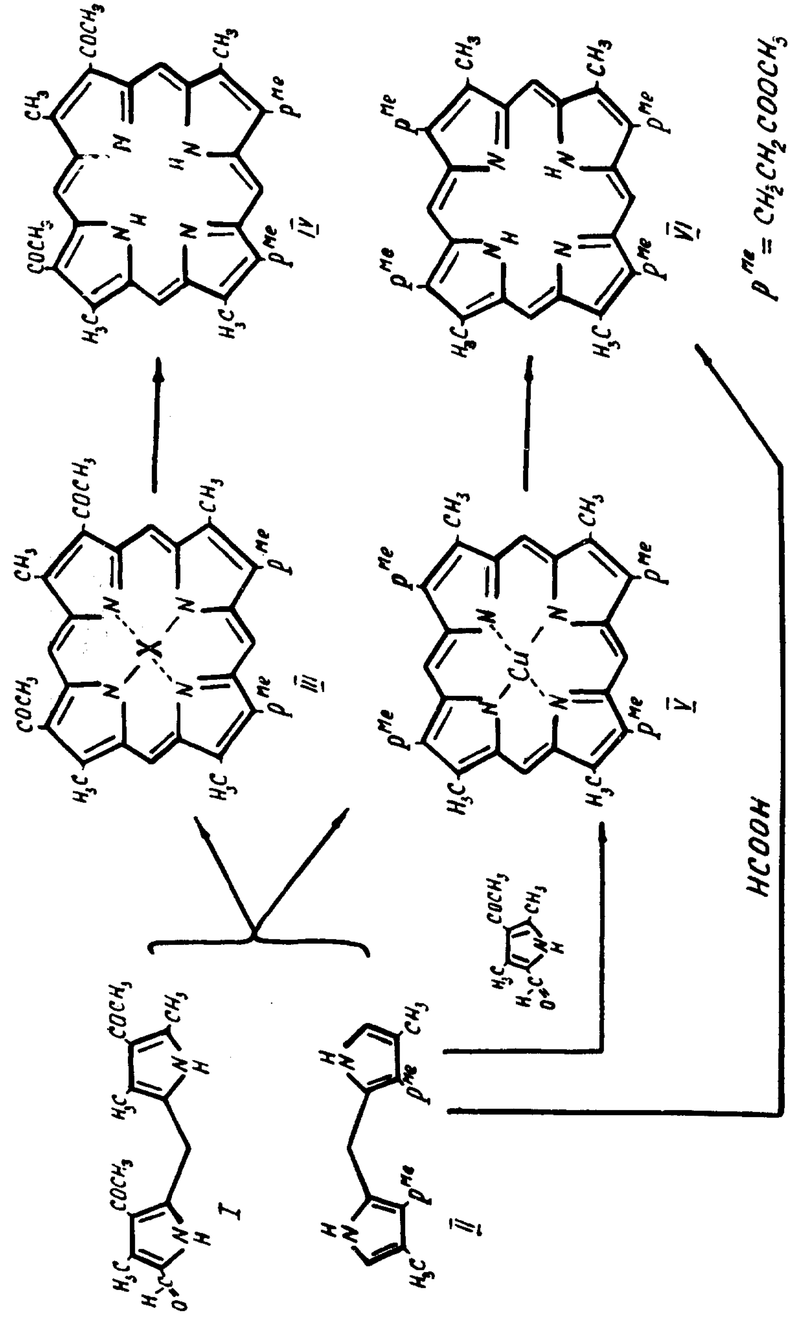


Fig.1. - Infra-red spectra of the dimethyl ester of diacetyldeuteroporphyrin: a) synthetic b) from hemin


I
II
III
IV
V
VI
HCOOH
Cu
X
COCH₃
CH₃
H₃C
pᵐᵉ
pᵐᵉ = CH₂CH₂COOCH₃

The investigation of reaction products from porphyrin condensation revealed together with the compound (III, X=Cu) three more porphyrin-like compounds. One of them was found to be copper complex of the tetramethyl ester of coproporphyrin II (V), m.p. 290-291°. (Found: C, 62.01; H, 5.55; N, 7.39. $C_{40}H_{44}N_4O_8Cu$ requires: C, 62.20; H, 5.74; N, 7.25%). Spectrum in chloroform: I, 565; II, 527 mμ (I>II).

The percentage of this compound, just as that of the copper complex of diacetyldeuteroporphyrin IX depended primarily on the concentration of hydrobromic acid. It was found that increasing acidity led to a sharp decrease in (III, X=Cu) and to a considerable increase in (V). The yield of the copper complex of diacetyldeuteroporphyrin IX accounted for 8.8% at the hydrobromic acid concentration in methanol of 0.05-0.08%, whereas (V) was formed only in trace amounts. With the concentration increased up to 0.5-0.6% the condensation of porphyrin was directed to the predominant formation of coproporphyrin II (V amounted to 28.3%), a small quantity of (III, X=Cu) having been again detected by means of paper chromatography.

It seemed that the formyl group of dipyrrylmethane (I) provided the two lacking CH-groups that were necessary for the formation of coproporphyrin II from two molecules of dipyrrylmethane (II). This suggestion was proved by a similar condensation of dipyrrylmethane (II) in the presence of 2,4-dimethyl-3-acetyl-5-pyrrolaldehyde. Again porphyrin (V) was obtained, in a good yield (32.2%). Such a reaction course had been reported by Corwin for the formation of tetramethyltetracarbethoxyporphyrin [5] .

The copper complex (V) was treated with concentrated sulphuric acid and the tetracarboxylic acid formed was esterified to give the tetramethyl ester of coproporphyrin II (VI). Yield 91.3%, m.p. 287-289° , lit. [6] 288° .(Found: C, 67.82; H, 6.59; N, 7.95. $C_{40}H_{46}N_4O_8$ requires: C, 67.57; H, 6.52; N, 7.88%). Spectrum in chloroform: I, 624; II, 570; III, 534; IV, 499 mμ $(I < II < III < IV)$.

The structure of the compounds was substantiated by the synthesis of coproporphyrin II, starting from dipyrrylmethane (II) and formic acid, m.p. 287.5-288° (Found: C, 67.28; H, 6.79; N, 8.03. $C_{40}H_{46}N_4O_8$ requires: C, 67.57; H, 6.52; N, 7.88%)

We believe that our synthetic method to prepare diacetyldeuteroporphyrin IX from α-formyl-α'-methyldipyrrylmethane (I) and α,α'-free dipyrrylmethane (II) may be extended to the production of other porphyrins related to the native protoporphyrin IX.

REFERENCES

1. H.Fischer, A.Schormüller, Ann. 468, 98 (1929).
2. A.F.Mironov, R.P.Evstigneeva, A.V.Chumachenko, N.A.Preobrazhensky, Zh. Ob. khim. 34, 1488 (1964).
3. A.F.Mironov, T.R.Ovsepyan, R.P.Evstigneeva, N.A.Preobrazhensky, Zh. Ob. khim.(in the press).
4. H.Fischer, K.O.Dielmann, Ann.545, 22 (1940).
5. J.S.Andrews, A.H.Corwin, A.G.Charp, J. Amer. Chem. Soc. 72, 491 (1950).
6. H.Fischer, W.Lamatsch, Ann. 462, 240 (1928).