SYNTHESIS OF 1,4,5,8-TETRAMETHYL-2,3-DIETHOXYCARBONYLPORPHYRIN

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Khimiya Geterotsiklicheskikh Soedinenii, Vol. 4, No. 3, pp. 481–483, 1968

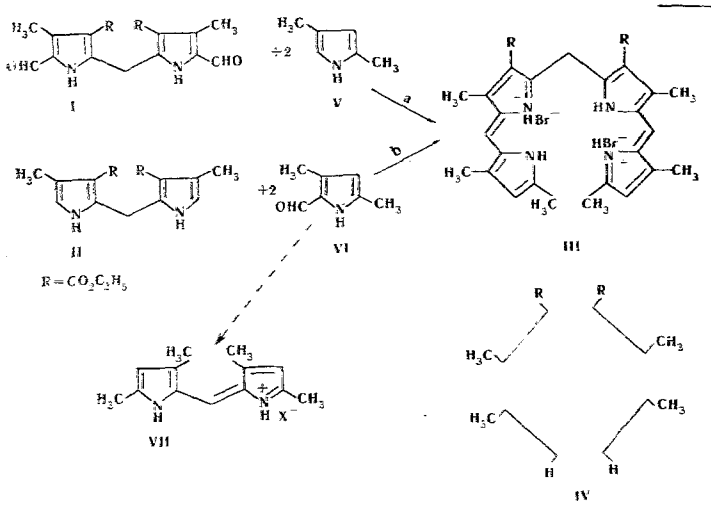
UDC 547.748

The synthesis of 1,4,5,8-tetramethyl-2,3-diethoxycarbonylporphyrin from the dihydrobromide of 1,3,7,13,17,19-hexamethyl-8,12-diethoxycarbonylbiladiene is described.

The most direct route to the synthesis of the porphyrins is the intermediate preparation of tetrapyrrole compounds—bilenes and biladienes—which are converted by oxidative cyclization into the corresponding porphyrins [1–3]. But, as in the synthesis of porphyrins by other methods, the preparation of the bilenes and biladienes is considerably complicated when electronegative groups are present in the initial pyrroles and dipyrrylmethanes.

The aim of the present work was to study the influence of the ethoxycarbonyl groups in the dipyrrylmethanes I and II on the rate of formation of the biladiene-a,c (III) and the oxidative cyclization of III into the copper complex of the diethoxycarbonylporphyrin IV by means of copper acetate.

Condensation to form the biladiene was carried out by two methods: a) from 3,3'-diethoxycarbonyl-5,5'-diformyl-4,4'-dimethyldipyrrylmethane (I) and 2,4-dimethylpyrrole (V), and b) from 3,3'-diethoxycarbonyl-4,4'-dimethyldipyrrylmethane (II) and 5-formyl-2,4-dimethylpyrrole (VI).



In both cases, substances were obtained with similar chromatographic properties and identical spectra in the visible and infrared regions. The elementary analyses of the two specimens corresponded to that of the dihydrobromide III.

The chemical activity of the initial pyrroles and dipyrrylmethanes depends greatly on the substituents which they may contain. Thus, the synthesis of the biladiene III by method (a) takes place smoothly at 0° C in two minutes with almost quantitative yield. Consequently, we conclude that the reactivity of the formyl group of a dipyrrylmethane in condensation with a pyrrole with a free α position does not depend on the presence of deactivating β-substituents. But the formation of biladiene by method (b) goes at least 60–100 times more slowly than by method (a) under comparable conditions. Here the deactivating influence of the β-ethoxycarbonyl group on the reactivity of the α position of the dipyrrylmethane II in condensation with the pyrrole aldehyde VI is expressed in full measure. In additon to this, the course of this reaction is complicated by the capacity of the pyrrole aldehyde VI for forming 3,3',5,5'-tetramethyldiprrylmethene (VII) in the presence of mineral acids [4, 5]. Although this side reaction takes place very slowly in the cold, nevertheless an acceleration of the main reaction by raising the temperature of the reaction mixture leads exclusively to the self-condensation of the pyrrole aldehyde to form dipyrrylmethene and to the complete cessation of the formation of the biladiene. The self-condensation in an acid medium of pyrryl aldehydes to dipyrrylmethenes and of dipyrrylmethanes containing an aldehyde group in the 5 or 5' positions to the corresponding bilenes or porphyrinogens is apparently a general characteristic [6–8].

The oxidative cyclization of the biladiene III into the copper complex of the porphyrin IV by means of copper acetate in methanol or in a mixture of methanol and acetic acid takes place with a yield of 5.2–5.5%. The reaction product, after isolation and purification by means of thin-layer chromatography on alumina (activity V) was completely identical with a sample obtained by us previously [9]. Treatment of the copper complex with concentrated sulfuric acid gave an 80% yield of the free porphyrin, which was identical with

the 1,4,5,8-tetramethyl-2,3-diethoxycarbonylporphyrin that we isolated from a mixture of porphyrins [10]. The initial pyrroles and dipyrrylmethanes required for the synthesis of the biladiene were obtained by the method of Fischer and Halbig [11].

EXPERIMENTAL

Dihydrobromide of 1,3,7,13,17,19-hexamethyl-8,12-diethoxycarbonylbiladiene (III). a) A suspension of 156 mg of 3,3'-diethoxycarbonyl-5,5'-diformyl-4,4'-dimethyldipyrrylmethane (I) of methanol was treated with 92 mg of 2,4-dimethylpyrrole (V) in 0.2 ml of methanol. The mixture was cooled to 0° C, nitrogen was bubbled through the solution and 0.2 ml of hydrobromic acid (d 1.4) was added. The solution immediately became orange and the dipyrrylmethane rapidly dissolved. After 2 min, the reaction mixture solidified. The solid matter was separated off, washed with 2 ml of isopropanol, and dried. This gave 271 mg of substance. After recrystallization from chloroform, 249 mg (86%) of the biladiene was isolated with mp 247° C (decomp.) when the sample was rapidly heated from 230° C. On slow heating, it did not melt below 300° C and gradually carbonized. Spectrum in chloroform λ_{max} nm ($\varepsilon \times 10^{-4}$): 445 (7.1), 492 (9.1). Found, %: C 50.97; H 5.71; N 7.72. Calculated for $C_{31}H_{36}N_4O_4 \cdot \cdot 2HBr \cdot 2H_2O$, %: C 51.22; H 5.82; N 7.71. A sample was dried in vacuum at 137° C for 2 hr. Found, %: Br 23.39. Calculated for $C_{31}H_{36}N_4O_4 \cdot 2HBr$, %: 23.15.

b) A mixture of 300 mg of 3,3'-diethoxycarbonyl-4,4'-dimethyldipyrrylmethane (II) and 270 mg of 5-formyl-2,4-dimethylpyrrole (VI) was carefully ground, and then 3 ml of methanol was added. The resulting suspension was treated with 0.5 ml of hydrobromic acid (d 1.4) and was stirred for 2 hr, by which time the initial dipyrrylmethane could no longer be detected in a sample. (For this test, part of the reaction mixture was diluted with water, neutralized with ammonia, and extracted with chloroform, and the chloroform extract was chromatographed on alumina (activity grade V) in chloroform with reference samples of the starting materials.) After the end of the reaction, the precipitate that had deposited was filtered off, washed with methanol, and recrystallized from chloroform. Yield 316 mg (48.3%), small orange prisms. The substance did not melt below 300° C on slow heating. The substance was chromatographically and spectrally completely identical with the biladiene obtained by method (a).

On brief heating, it was possible to isolate from the mother liquor a small amount of 3,3',5,5'-tetramethyldipyrrylmethene hydrobromide, which in its spectral and chromatographic properties was similar to the dipyrrylmethene hydrochloride obtained by other methods.

Copper complex of 1,4,5,8-tetramethyl-2,3-diethoxycarbonylporphyrin (IV). A solution of 50 mg of the biladiene III in 20 ml of methanol was treated with 100 mg of sodium acetate and 100 mg of copper acetate. The solution was boiled for 4 hr with aeration. Then the solvent was distilled off and the residue was dissolved in chloroform and a first purification of the copper complex of the porphyrin was carried out on a column of silica. The fraction containing the copper complex was evaporated in vacuum and was additionally purified by means of thin-layer chromatography on alumina (activity grade V) in chloroform. The substance was eluted from the alumina with hot chloroform; the solution, on evaporation to 5 ml, deposited 2.2 mg (5.3%) of the copper complex in the form of long needles.

The spectrum in chloroform [λ_{max} nm: 585, 542 (I > II)] was completely identical with that of a sample obtained by another method [9].

The copper complex of the porphyrin was also obtained with a yield of 5.5% by boiling in methanol without aeration for 14 hr.

1, 4, 5, 8-Tetramethyl-2, 3-diethoxycarbonylporphyrin (IV). The copper complex (30 mg) was dissolved in 5 ml of concentrated sulfuric acid, and after 5 min the solution was poured into 100 ml of water and neutralized with ammonia, and the precipitate of porphyrin that had deposited was filtered off and dried. After recrystallization from a mixture of chloroform and petroleum ether, 21 mg (80%) of the porphyrin was obtained. The spectrum in chloroform [λ_{max} nm (ε): 636 (3160); 581 (5260); 544 (6850); 510 (11900) agreed completely with that of the material described previously [10].

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15 June 1966

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