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SYNTHETIC STUDIES OF PIGMENTS OF GREEN BACTERIA
II. Synthesis of Unsymmetrical Dipyrrylmethanes*

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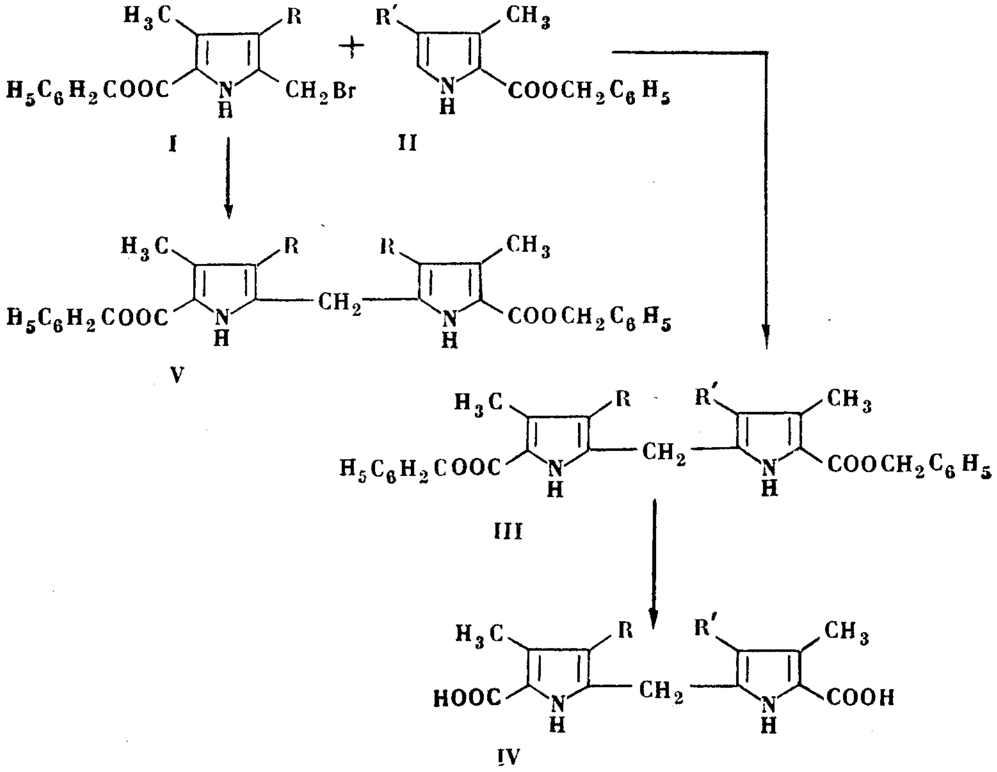
A number of symmetrical and unsymmetrical dipyrrylmethanes are synthesized. These are 4,4'-dimethyl-3-(β-carbomethoxyethyl)-3'n-propyl-5,5'-dicarbobenzoxydipyrrylmethane (III, R=$CH_2CH_2COOCH_3$, R'=n-C_3H_7); 4,4'-dimethyl-3-(β-carbomethoxyethyl)-3'-n-propyl-5,5'-dicarboxydipyrrylmethane (IV, R=$CH_2CH_2COOCH_3$, R'=n-C_3H_7); 3-bromo-3',4-dimethyl-4'-ethyl-5,5'-dicarbobenzoxydipyrrylmethane (VII, R=Br); 3,3'-dibromo-4,4'-dimethyl-5,5'dicarbobenzoxydipyrrylmethane (V, R=Br); 3',4-dimethyl-3-ethyl-4'-carboethoxy-5-carbobenzoxydipyrrylmethane (IX, R=Et).

Unsymmetrical dipyrrylmethanes can be used to synthesize porphyrins related to chlorobium chlorophyll. In the present work unsymmetrical dipyrrylmethanes were prepared by condensing α-bromomethylpyrroles with α-unsubstituted pyrroles.

Synthesis of unsymmetrical dipyrrylmethanes presents great difficulties because symmetrical dipyrrylmethanes can be formed as side products. To demonstrate the unsymmetrical nature of the structure, and to study the reactivities of pyrroles in the methane condensation as a function of β-substituents, 4,4'-dimethyl-3-(β-carbomethoxyethyl)-3'-n-propyl-5,5'-dicarbobenzoxypyrrylmethane (III, R=$CH_2CH_2COOCH_3$, R'=n-C_3H_7) was synthesized by two routes, starting from 2-bromomethyl-4-methyl-3-(β-carbomethoxyethyl)-5-carbobenzoxypyrrole (I, R=$CH_2CH_2COOCH_3$) and 4-methyl-3-n-propyl-5-carbobenzoxypyrrole (II, R'=n-C_3H_7) in the first case (30% yield), and from 2-bromomethyl-4-methyl-3n-propyl-5-carbobenzoxypyrrole (I, R=n–Pr) and 4-methyl-3-(β-carbomethoxyethyl)-5-carbobenzoxypyrrole (II, R'= =$CH_2CH_2COOCH_3$) in the second case (18.6% yield). The greater yield of III in the first case can be ascribed to the greater reactivity of compound II (R'=n–Pr) as compared with I (R'=$CH_2CH_2COOCH_3$).

Chromatographic characteristics, melting points and mixed melting points of specimens, prepared by the two methods, proved the identity of the unsymmetrical products (III, R=$CH_2CH_2COOCH_3$, R'=n-C_3H_7 and III, R=n–C_3H_7, R'=$CH_2CH_2COOCH_3$). The dipyrrylmethane III (R=$CH_2CH_2COOCH_3$, R'=n-C_3H_7) gives a depressed mixed melting point



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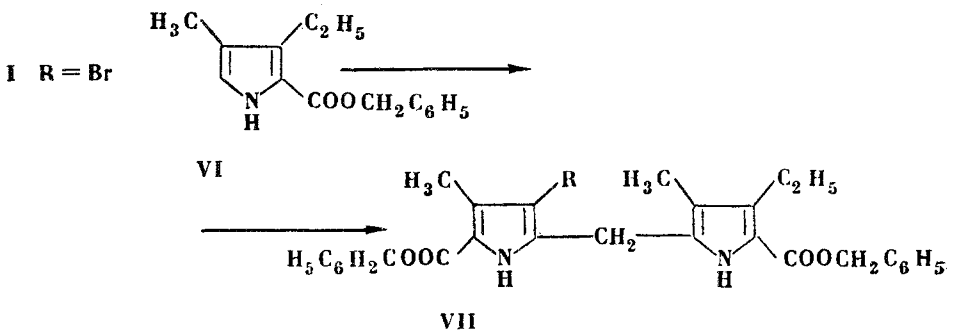
* For Part I see [1].

with the symmetrical methane V ($R=CH_2CH_2COOCH_3$), prepared from 2-bromomethyl-4-methyl-3-(β-carbomethoxyethyl)-5-carbobenzoxypyrrole [2].

Hydrogenation of the dipyrrylmethane III ($R=CH_2CH_2COOCH_3$, $R'=n\text{-}C_3H_7$) with palladium-active charcoal catalyst gave 4,4'-dimethyl-3-(β-carbomethoxyethyl)-3'-n-propyl-5,5'-dicarboxydipyrrylmethane (IV, $R=CH_2CH_2COOCH_3$, $R'=n\text{-}C_3H_7$.

Synthesis of 3-bromo-3', 4-dimethyl-4'-ethyl-5,5'-dicarbobenzoxydipyrrylmethane (VII, R=Br) was effected by condensing 3-bromo-2-bromomethyl-4-methyl-5-carbobenzoxypyrrole (I, R=Br) with 3-methyl-4-ethyl-5-carbobenzoxypyrrole (VI)

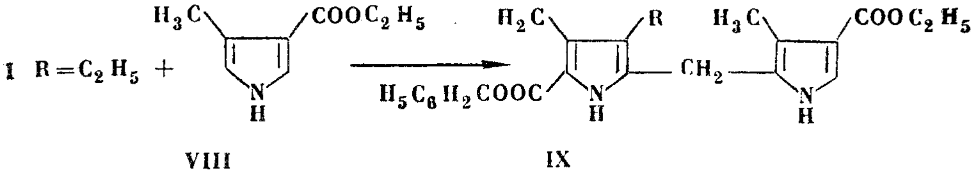

I R = Br

VI

VII

To confirm the structure of the unsymmetrical dipyrrylmethane VII, symmetrical 3,3'-dibromo-4,4'-dimethyl-5,5'-dicarbobenzoxydipyrrylmethane (V, R=Br), was synthesized from 3-bromo-2-bromoethyl-4-methyl-5-carbobenzoxypyrrole (I, R=Br). The mixed melting point of dipyrrylmethane VII (R=Br, mp 108-109°) and dipyrrylmethane V (R=Br, mp 118.5-119°) was 98-104°.

Condensation of 2-bromomethyl-4-methyl-3-ethyl-5-carbobenzoxypyrrole (I, R=Et) with 3-methyl-4-carboethoxypyrrole (VIII) gave 3',4-dimethyl-3-ethyl-4'-carboethoxy-5-carbobenzoxydipyrrylmethane (IX, R=Et) [3].


I $R=C_2H_5$ +

VIII

IX

The homogeneities of the compounds prepared were confirmed by thin-layer chromatography on silica gel in the system petrol ether – ether (for V, R=Br, VII, and IX), or on alumina, in chloroform (for III and IV, where $R=CH_2CH_2COOCH_3$, $R'=n\text{-}C_3H_7$).

Experimental

4,4'-Dimethyl-3-(β-carbomethoxyethyl)-3'-n-propyl-5,5'-dicarbobenzoxydipyrrylmethane (III, $R=CH_2CH_2COOCH_3$, $R'=n\text{-}C_3H_7$). a) 0.77 g (~0.9 mmole) 2-bromoethyl-4-methyl-3-(β-carbomethoxyethyl)-5-carbobenzoxypyrrole (I, $R=CH_2CH_2COOCH_3$) was added in small portions to a solution of 0.5 g (1.9 mmole) 3-methyl-4-n-propyl-2-carbobenzoxypyrrole (II, R=n–Pr) at 55-60°, the mixture refluxed for 1.5 hr, and left to stand for 12 hr at 0-2°. The oily material which came out was separated off, carefully triturated with 30 ml petrol ether, and recrystallized from 50 ml n-octane. Yield 0.33 g (30%), mp 91-92°, mixed mp with 4,4'-dimethyl-3,3'-di(β-carbomethoxyethyl)-5,5'-dicarbobenzoxydipyrrylmethane (mp 98-100°) 88-89°. Found: C 71.73; H 6.65; N 5.23%. Calculated for $C_{34}H_{38}N_2O$: C 71.55; H 6.71; N 4.91%.

b) 1.13 g (3.2 mmole) 2-bromoethyl-4-methyl-3-n-propyl-5-carbobenzoxypyrrole (I, R=Pr) was added in small portions to a solution of 0.97 g (3.2 mmole) 3-methyl-4-(β-carbomethoxyethyl)-2-carbobenzoxypyrrole (II, $R'=CH_2CH_2COOCH_3$) in 20 ml methanol at 50-60°. The operations which followed were the same as in a) above. Yield 0.34 g (18.6%), mp 91-92°, mixed mp with a specimen prepared as in a) above, 91-92°.

4,4'-Dimethyl-3-(β-carbomethoxyethyl)-3'-n-propyl-5,5'-dicarboxydipyrrylmethane (IV, $R=CH_2CH_2COOCH_3$, $R'=n\text{-}C_3H_7$). 1 g catalyst (nickel on chromium oxide) was added to a solution of 0.34 g (0.6 mmole) dipyrrylmethane

III ($R=CH_2CH_2COOCH_3$, $R'=n\text{-}C_3H_7$) in 50 ml methanol, and the mixture stirred for 20 min, the catalyst separated off, 0.85 g palladium-activated charcoal added, and hydrogenation carried out for 5 hr, after which the catalyst was separated off and washed with 30 ml methanol. The solvent was taken off under reduced pressure, yield 0.21 g(90.1%), mp 132-135°(decomp). Found: C 61.44; H 7.07; N 7.25%. Calculated for $C_{20}H_{26}N_2O_6$: C 61.52; H 6.71; N 7.18%.

3-Bromo-3',4-dimethyl-4'-ethyl-5,5'-dicarbobenzoxydipyrrylmethane (VII, R=Br). A solution of 0.1 g (0.4 mmole) 3-methyl-4-ethyl-5-carbobenzoxypyrrole (VI) in 2 ml methanol was added to a solution of 0.23 g(0.6 mmole) 3-bromo-2-bromomethyl-4-methyl-5-carbobenzoxypyrrole (I, R=Br) in 7 ml methanol, the mixture heated for 1 hr at 40°, and then poured into 15 ml distilled water. The gummy precipitate formed was filtered off, rubbed with petrol ether, and recrystallized from 2 ml isooctane. Yield 0.08 g (35.4%), colorless crystals, mp 108-109°. Found: C 63.48; H 5.21; Br 14.31; N 4.93%. Calculated for $C_{29}H_{29}BrN_2O_4$: C 63.39; H 5.32; Br 14.54; N 5.1%.

3,3'-Dibromo-4,4'-dimethyl-5,5'-dicarbobenzoxydiprrylmethane (V, R=Br). Two drops of 48% hydrobromic acid were added to a solution of 0.5 g(1.3 mmole) I (R = Br) in 25 ml methanol, the mixture heated for 4 hr at 60°, and poured into 25 ml distilled water. The flocculent precipitate was filtered off, and recrystallized from 10 ml heptane. Yield 0.3 g (38.6%), mp 118.5-119°, mixed mp with VII 98-104°. Found: C 54.20; H 4.22; Br 26.54; N 4.57%. Calculated for $C_{27}H_{24}Br_2N_2O_4$: C 54.03; H 4.03; Br 26.63; N 4.67%.

3',4-Dimethyl-4'-carboethoxy-5-carbobenzoxydipyrrylmethane (IX). A solution of 0.71 g (4.6 mmole) 3-methyl-4-carboethoxypyrrole in 5 ml methanol was added to a solution of 1.7 g (5 mmole) 2-bromo-methyl-4-methyl-3-ethyl-5-carbobenzoxypyrrole (I, R=Et) in 40 ml methanol, the mixture allowed to stand for 3 hr, the precipitate formed separated off, recrystallized from 8 ml methanol, and dried in a vacuum desiccator. Yield. 0.72 g (34.9%), colorless crystals, mp 167.5-168°. Found: C 70.41; H 6.74; N 6.64%. Calculated for $C_{24}H_{23}N_2O_4$: C 70.56; H 6.91; N 6.86%.

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