INDOLE DERIVATIVES.

129.* ELECTROPHILIC-SUBSTITUTION REACTIONS IN 4,5-ETHYLENEDIOXYINDOLE

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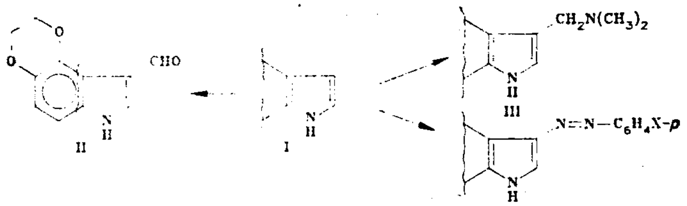
The reactivity of 4,5-ethylenedioxyindole in the Vilsmeier and Mannich reactions and in diazo coupling was studied.

It has been previously shown that the Fischer cyclization of ethyl pyruvate 3,4-ethylenedioxyphenylhydrazone leads to 5,6-ethylenedioxy-2-ethoxycarbonylindole [2]. It was subsequently established that 4,5-ethylenedioxy-2-ethoxycarbonylindole [1], which was converted to 4,5-ethylenedioxyindole (I), is also formed along with the 5,6-ethylenedioxy compound. To study its reactivity we carried out the Mannich and Vilsmeier reactions and diazo coupling.

The reaction of indole I with the Vilsmeier complex leads to the formation of 3-formyl-4,5-ethylenedioxyindole (II). The IR spectrum of aldehyde II contains a band of stretching vibrations at 1640 cm^{-1}, which is characteristic for a conjugated carbonyl group. A signal of an aldehyde proton (10.34 ppm) is observed in the PMR spectrum. The 6-H (7.03 ppm) and 7-H (6.78 ppm) protons of the benzene ring form an AB system with spin-spin coupling constant (SSCC) J_{67} = 8.77 Hz; this corresponds to an angular structure of the 3-formyl derivative [1]. 3-N,N-Di-methylaminomethyl-4,5-ethylenedioxyindole (III) was obtained in 38% yield with the use of a crystalline Mannich reagent [3]. A signal of the 3-H proton of 4,5-ethylenedioxyindole is absent in the PMR spectrum, and signals corresponding to protons of the $CH_2N(CH_3)_2$ group appear. Diazo coupling of indole I was carried out with diazonium salts obtained from aniline, p-nitroaniline, and p-chloroaniline. It was found that 4,5-ethylenedioxyindole reacts only with p-nitro- and p-chlorobenzenediazonium chlorides. A product could not be isolated in the case of diazo coupling with benzenediazonium chloride. Signals of 3-H protons are absent in the PMR spectra of 3-(p-nitrophenylazo)- and 3-(p-chlorophenylazo)-4,5-ethylenedioxyindoles (IV and V), and signals of the AB system of the protons of a p-substituted phenyl ring [8.04 and 8.41 ppm, J_0 = 9.11 Hz (IV), 7.84 and 7.52 ppm, J_0 = 8.77 Hz (V)] are observed.



IV X=NO_2; V X=Cl

The IR spectra contain absorption bands at 1430 (IV) and 1420 cm^{-1} (V), which are characteristic for an azo group. A bathochromic shift of the absorption band as compared with the spectrum of V[λ_{max} (log ε): 416 nm (4.0)] is observed in the UV spectrum of IV[λ_{max} (log ε): 442 nm (4.21)]; this is due to the presence of a nitro group in azo compound IV.

As a result of these studies, it was shown that, with respect to its reactivity, 4,5-ethylenedioxyindole resembles indole in electrophilic-substitution reactions, with orientation of the entering substituent in the 3 position of the indole ring.

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*See [1] for communication 128.

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EXPERIMENTAL

The course of the reactions and the purity of the compounds were monitored by thin-layer chromatography (TLC) on Silufol UV-254 plates in a benzene—acetone system (5:2). Silica gel (100/160 μm) was used for preparative chromatography of the compounds. The IR spectra of suspensions of the compounds in mineral oil were recorded with a UR-20 spectrometer. The UV spectra of solutions in ethanol (~10^{-4} mole/liter) were recorded with a Specord UV-Vis spectrophotometer. The PMR spectra of solutions in d_6-acetone and d_6-DMF were obtained with a Bruker WP-200SV spectrometer with tetramethylsilane (TMS) as the internal standard.

3-Formyl-4,5-ethylenedioxyindole (II). A 0.72-ml sample of $POCl_3$ was added at −5°C to 2.5 g (24.0 mmole) of freshly distilled DMF at such a rate that the temperature did not rise above 0°C, after which the mixture was stirred at 20°C for 1.5 h. A solution of 1.05 g (6 mmole) of I in 2.5 ml of DMF was then added, and the mixture was stirred at 20°C for 3 h. The reaction mass was then poured over 30 g of ice, the aqueous mixture was made alkaline to pH 10 with 20% NaOH solution, and the resulting suspension was extracted with three 50-ml portions of ethyl acetate. The extract was washed with water until the wash water was neutral and dried with sodium sulfate. The solvent was evaporated in vacuo to 5-10 ml, and the resulting precipitate was removed by filtration and washed with 5 ml of ethyl acetate to give 0.72 g (60%) of aldehyde II in the form of a creamish-white powder with mp 157-158°C (from ethyl acetate). IR spectrum: 3100-3210 (NH), 1640 cm^{-1} (CO). UV spectrum, λ_{max} (log ε): 221 (4.28), shoulder at 268-279 (3.72), and 334 nm (3.78). PMR spectrum (in d_6-acetone): 11.14 (NH); 7.96 (d, J_{NHCH} = 2.7 Hz, 2-H); 4.35-4.43 (m, OCH_2CH_2O): 7.03 and 6.78 (J_{67} = 8.77 Hz, AB system of 6-H and 7-H); 10.34 ppm (s, CHO). Found: C 65.2, H 4.4, N 6.7%. $C_{11}H_9NO_3$. Calculated: C 65.0, H 4.4, N 6.8%.

3-N,N-Dimethylaminomethyl-4,5-ethylenedioxyindole (III). A 0.2-g (1.14 mmole) sample of I was dissolved in 3 ml of absolute alcohol, 0.88 g (3.0 mmole) of the crystalline Mannich reagent was added, and the mixture was stirred at 75-80°C for 4 h. It was then cooled and diluted with 50 ml of water, and the aqueous mixture was made alkaline to pH 10 with 20% NaOH solution. The resulting suspension was extracted with three 100-ml portions of ether, and the extract was washed with water until the wash water was neutral and dried with sodium sulfate. The ether was evaporated in vacuo to give 0.1 g (38%) of III with mp 148-150°C (from benzene). IR spectrum: 3050-3110 cm^{-1} (NH). PMR spectrum (in d_6-acetone): 9.98 (NH); 7.04 (d, J_{NHCH} = 2.5 Hz, 2-H); 4.24-4.30 (m, OCH_2CH_2O); 6.81 and 6.60 ($J_{6,7}$ = 8.40 Hz, AB system of 6-H and 7-H); 3.71 (s, CH_2N); 2.21 ppm [s, $N(CH_3)_2$]. Found: C 68.1, H 6.6, N 12.4%. $C_{13}H_{16}N_2O_2$. Calculated: C 67.7, H 6.9, N 12.1%.

3-(p-Nitrophenylazo)- and 3-(p-Chlorophenylazo)-4,5-ethylenedioxyindoles (IV, V). A solution of p-nitrobenzenediazonium chloride, obtained from 0.34 g (2.5 mmole) of p-nitroaniline, was added at 0°C to a mixture of 0.35 g (2.0 mmole) of indole I in 15 ml of dioxane and 10 ml of water while maintaining the pH at 6.5-7.0, after which the reaction mixture was stirred at 0°C for 3 h and extracted with three 50-ml portions of chloroform. The solvent was evaporated, and the residue was subjected to column chromatography (silica gel, chloroform) to give 0.32 g (50%) of azoindole IV in the form of a dark-claret-colored powder with mp 250-252°C. IR spectrum: 3200-3280 (NH), 1520, 1330 (NO_2), 1430 cm^{-1} (N=N). UV spectrum, λ_{max} (log ε): 210 (4.22), 259 (3.95), 312 (3.85), 442 nm (4.21). PMR spectrum (in d_6-DMF): 12.37 (NH); 8.00 (d, J_{NHCH} = 2.7 Hz, 2-H); 4.41-4.49 (m, OCH_2CH_2O); 7.09 and 6.87 (J_{67} = 8.44, AB system of 6-H and 7-H); 8.04 and 8.41 ppm (J_o = 9.11 Hz, AB system of a p-substituted phenyl ring). Found: C 58.8, H 3.8, N 17.0%. $C_{16}H_{12}N_4O_4$. Calculated: C 59.2, H 3.7, N 17.2%.

Similarly, the reaction of 0.35 g (2.0 mmole) of indole I and 0.32 g (2.5 mmole) of p-chloroaniline gave 0.15 g (24%) of 3-(p-chlorophenylazo)-4,5-ethylenedioxyindole (V) in the form of a claret-colored powder with mp 130-132°C. IR spectrum (in $CHCl_3$): 3480 (NH), 1420 cm^{-1} (N=N). UV spectrum, $_{max}$ (log ε): shoulder at 208-227 (4.21), 298 (4.00), 416 nm (4.21). PMR spectrum (in d_6-acetone): 10.97 (NH); 7.82 (d, J_{NHCH} = 2.5 Hz, AB system of 6-H and 7-H); 7.84 and 7.52 ppm (J_o = 8.77 Hz, AB system of a p-substituted phenyl ring). Found: C 61.6, H 4.0, Cl 11.4, N 13.4%. $C_{16}H_{12}ClN_3O_2$. Calculated: C 61.2, H 3.8, Cl 11.3, N 13.4%.

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PORPHYRINS.

22.* SYNTHESIS OF PORPHYRINS WITH TWO CYCLOPENTANE RINGS

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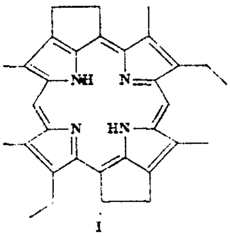
The Vilsmeier formylation of meso-methylporphyrins and a porphyrin with a cyclopentane ring was investigated. A meso substituent increases the ability of free meso positions to undergo electrophilic substitution reactions. Schiff bases of meso-formylporphyrins were subjected to thermolysis, and a porphyrin with two cyclopentane rings was synthesized for the first time.

Recent years have been marked by significant advances in the study of "geological" porphyrins isolated from petroleum oils, bitumens, shales, and sedimentary rocks [2, 3]. It has been accurately established that "geological" porphyrins are complex mixtures of compounds consisting primarily of two major and three "minor" homologous series of vanadyl and/or nickel complexes: a) the etioporphyrin series; b) the desoxophylloerythroetioporphyrin series; c) the didesoxophylloerythroetioporphyrin series; d) the rhodoetioporphyrin series; e) the rhododesoxophylloerythroetioporphyrin series (in other words, the M–, M–2, M–4, M–6, and M–8 series, respectively [3]). The structures of some porphyrins of the major series have been established [2, 4-6], but reliable information relative to the structures of porphyrins of the "minor" series, viz., M–4, M–6, and M–8, is not available in the literature. It has been suggested, for example, that compounds of the M–4 series are porphyrins with two saturated rings of the I or II type, while structures of the benzoporphyrin III and IV type correspond to porphyrins of the M–6 and M–8 series [3].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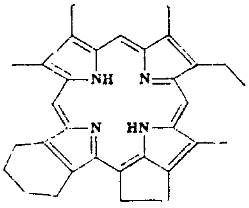
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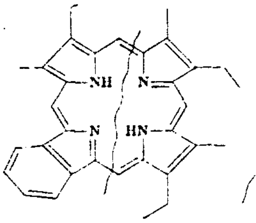
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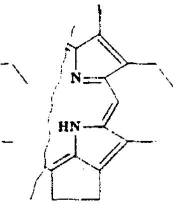
IV

To investigate the spectral and chromatographic characteristics of compounds of the M–4 series we attempted to synthesize model porphyrins containing two five-membered exocycles. We assumed that they might be synthesized by thermolysis of the corresponding Schiff bases of diformylporphyrins, for example, porphyrin V, to a mixture of porphyrins VI and VII by the method that we previously developed for the synthesis of monocyclopentanoporphyrins [7].

We found that pronounced destruction of the substance occurs in the thermoloysis of Schiff base V, and only porphyrins with one cyclopentane ring are formed in low yield. The absence in the products of thermolysis of porphyrins of the M–4 series is probably due to the formation of unstable intermediate porphyrins of the VIII type.

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*See [1] for communication 21.

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