INDOLOBENZO[b]FURANS.

2.* SOME INDOLO[5,6-d]- AND INDOLO[5,4-d]BENZO[b]FURANS

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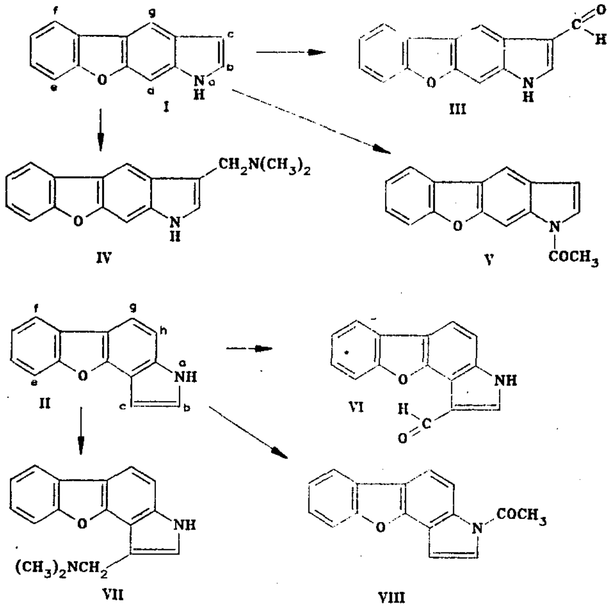
The reactivities of new heterocyclic systems, viz., indolo[5,6-d]- and indolo[5,4-d]benzo[b]furans, in several electrophilic-substitution reactions (the Mannich and Vilsmeier reactions and acylation) were studied. It was established that the indicated heterocycles, like indole, are readily formylated and aminomethylated; some anomalies are observed only in the case of acylation.

In order to study the reactivities of the previously synthesyzed four-ring pyrrole-containing condensed indolo[5,6-d]- (I) and indolo[5,4-d]benzo[b]furan (II) systems [1] we investigated some typical (for the indole series) electrophilic-substitution reactions (the Vilsmeier and Mannich reactions and acylation):



In view of the definite structural similarities of I and II with respect to indole, the indicated reactions were carried out under comparable conditions [2-5].

We found that I and II are quite readily formylated by the Vilsmeier complex to give 3-formylindolo[5,6-d]- (III) and 1-formylindolo[5,4-d]benzo[b]furan (VI). In addition to a band at 3120 cm^{-1}, which corresponds to an NH group, a band at 1630 and 1635 cm^{-1}, which is due to the stretching vibrations of the C=O bond, is noted in the IR spectra of III and VI.

In the PMR spectra of the indicated compounds one observes a significant shift of the signals of the a-H and b-H protons to weak field (see Table 1) as compared with unsubstituted

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*See [1] for Communication 1.

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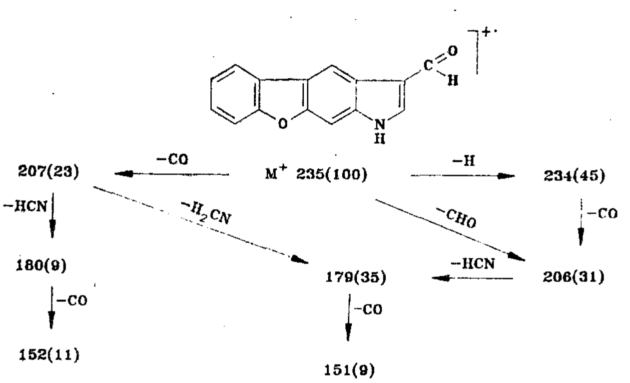
TABLE 1. Chemical Shifts and SSCC of III-VIII in d_6-DMSO at 80°C

Compound	δ, ppm											J, Hz
	a-H	b-H	c-H	d-H	e-H	f-H	g-H	h-H	CHO	CH_2	CH_3	
III	11,9*	8,24	—	7,67	7,56	8,13	8,71	—	9,96	—	—	$J_{d,g}=0{,}5$
IV	10,8	~7,3	—	7,48	7,5	8,03	8,17	—	—	3,62	2,21	$J_{d,g}<0{,}5$
V	—	7,82	6,82	8,51	†	8,06	8,22	—	—	—	2,66	$J_{d,c}=0{,}3$; $J_{b,c}=3{,}8$
VI	12,5*	8,30	—	—	7,62	8,07	7,93	7,50	10,15	—	—	$J_{g,h}=8{,}5$
VII	11,2	~7,3	—	—	7,63	7,96	7,67	7,36	—	3,87	2,26	$J_{g,h}=8{,}5$
VIII	—	7,92	7,02	—	7,68	8,06	7,96	8,38	—	—	2,70	$J_{b,c}=3{,}5$; $J_{h,c}=0{,}5$; $J_{g,h}=8{,}9$

*The NH → ND exchange is partially responsible here.
†Complex superimposition of the signals.

rings (10.3 and 11.4 and 7.36 and 7.37 ppm for rings I and II, respectively) [1]; this is due to the presence of a formyl group in the molecule. The mass spectra of III and VI contain an intense [M^+] molecular-ion peak with m/z 235, and the character of the subsequent fragmentation does not contradict the proposed structures.

Because of the identical character of the fragmentation of the molecular ions of III and VI, we present the scheme of the fragmentation of only 3-formylindolo[5,6-d]benzo[b]furan (III):



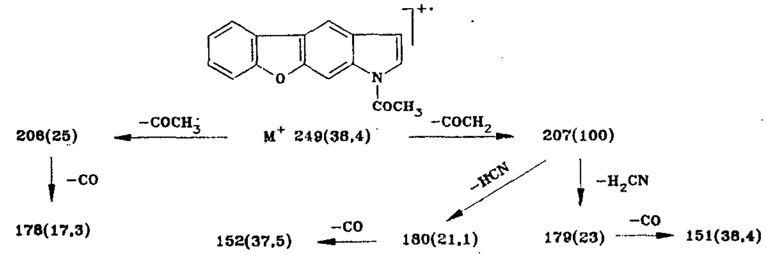
Compounds I and II undergo the Mannich reaction quite readily to give 3-(N,N-dimehtylaminomehtyl)indolo[5,6-d]- (IV) and 1-(N,N-dimethylaminomethyl)indolo[5,4-d]benzo[b]furan (VII) in quantitative yields.

The PMR spectra of IV and VII confirm that the aminomethyl group is attached to the carbon atom in the 3 position of the pyrrole ring (Table 1). In the spectra one observes the signal of an NH proton at 10.8 and 11.2 ppm, respectively; the signal of a 3-H proton is absent. Simultaneously, one observes signals at 3.62 and 2.21 ppm for IV and at 3.87 and 2.26 ppm for VII; these were assigned to the CH_2 and CH_3 groups, respectively.

The band (3410-3420 cm^{-1}) of stretching vibrations of an NH group is retained in the IR spectra of the indicated compounds, and a band at 1380-1410 cm^{-1}, which is probably due to the vibrations of the C—N < bonds, appears.

Acylation was carried out with acetic anhydride (method A) and in acetic anhydride—acetic acid (method B) (see the Experimental section) under the conditions described for indole. In contrast to indole, which, under similar conditions, forms a mixture of 3- and 1-acetylindoles with 1,3-diacetylindole as the principal product (method A) or a mixture of 3-acetyl- and 1,3-diacetylindoles (method B),in all of the cases that we examined only N-acyl derivatives V and VIII, respectively, the identical character of which, regardless of the preparative methods, raises no doubts, are formed unambiguously. The absence of a weak-field signal of the protons of an NH group in V and VIII indicates the presence of acetyl groups attached precisely to the nitrogen atom of the indicated heterocycles. The significant anisotropic shift of the signal of the close-lying d-H protons in V and the h-H protons in VIII (see Table 1) as compared with the unsubstituted ring (7.55 and 7.31 ppm, respectively) also confirms the presence of an acetyl group attached to the nitrogen atom.

In the IR spectra of V and VIII the absence of bands of stretching vibrations of an NH group and the observed narrow intense band at 1700 and 1710 cm^{-1} and at 1710 and 1715 cm^{-1}, respectively, which is due to the stretching vibrations of the C=O group, also confirm the proposed structures. No melting-point depressions were observed for mixtures of the indicated compounds. The molecular masses of all the synthesized compounds, which were determined by mass spectrometry, are equal to the calculated values and correspond to monosubstituted compounds. The character of the fragmentation of the molecular ions of the N-acyl-substituted compounds with both linear and angular structures is fundamentally similar, and we therefore present the scheme of the fragmentation only for V:



The UV spectra of solutions of III-VIII in ethanol indicate the similarity in the conjugation in isomeric structures III and VI and IV and VII.

EXPERIMENTAL

Monitoring of the course of the reactions and the purity of the compounds was carried out on plates with a fixed layer of Silufol UV-254 silica gel. The UV spectra of solutions of the compounds in ethanol were recorded with a Specord spectrophotometer. The IR spectra of mineral oil suspensions of the compounds were obtained with a UR-20 spectrometer with NaCl and LiF prisms; the scanning rate was 160 at a spectral slit width of 4 cm^{-1}. The mass spectra were recorded with an MKh-1303 spectrometer with direct introduction of the samples into the ion source at a cathode emission current of 1.5 μA and an ionizing voltage of 50 eV. The PMR spectra were recorded with a Varian CFT-20 spectrometer (80 MHz); the chemical shifts were measured relative to tetramethylsilane (TMS) as the internal standard with an accuracy of 0.01 ppm, as compared with an accuracy of 0.1 Hz in the measurement of the spin—spin coupling constants (SSCC).

3-Formylindolo[5,6-d]benzo[b]furan (III). A 0.15-ml sample of phosphorus oxychloride was added slowly at 0°C to 0.6 ml of freshly distilled dimethylformamide (DMF), after which the Vilsmeier complex was maintained at room temperature for 1 h, and a solution of 0.3 g (1.4 mmoles) of I in 3 ml of DMF was added. The mixture was heated to 60-70°C for 1 h, after which it was cooled, treated with crushed ice, and heated up rapidly. The precipitate was removed by filtration, washed with water, and dried to give 0.3 g (88%) of a product with mp 276-278°C. IR spectrum: 1630 (C=O) and 3120 cm^{-1} (NH). UV spectrum, λ_{max} (log ε): 204 (4.59), 222 (4.64), 247 (4.73), 288 (4.28), 315 (4.50), and 327 nm (4.49). Found: C 76.9; H 3.8; N 5.9%. $C_{15}H_9NO_2$. Calculated: C 76.6; H 3.8; N 6.0%.

1-Formylindolo[5,4-d]benzo[b]furan (VI). This compound, with mp 244-246°C, was obtained in quantitative yield by a method similar to that used to prepare III by heating the reaction mixture at 80-100°C for 2 h. IR spectrum: 1635 (C=O) and 3120 cm^{-1} (NH). UV spectrum, λ_{max} (log ε): 204 (5.38), 247 (5.51), 283 (5.16), 310 (4.99), and 320 nm (5.02). Found; C 76.6; H 3.9; N 6.4%. $C_{15}H_9NO_2$. Calculated: C 76.6; H 3.8; N 6.0%.

3-(N,N-Dimethylaminomethyl)indolo[5,6-d]benzo[b]furan (IV). A 1.2-ml sample of acetic acid was added slowly with cooling to 1.2 ml (1 mmole) of a 33% aqueous solution of dimethylamine, after which 0.6 ml of 40% formalin and 0.3 g (2 mmoles) of I were added, and the mixture was maintained at room temperature for 2 h. It was then poured into water, and the aqueous mixture was made alkaline with 10% KOH solution. The precipitate was removed by filtration, washed with water, and dried in a vacuum desiccator over KOH to give a product with mp 158-160°C in quantitative yield. IR spectrum:1380 (C—N<) and 3420 cm^{-1} (NH). UV spectrum, λ_{max} (log ε): 209 (5.37), 233 (5.24), 244 (5.38), 280 (4.74), 310 (5.09), and 320 nm (5.14). Found: C 77.3; H 6.2; N 10.6%. $C_{17}H_{16}N_2O$. Calculated: C 77.3; H 6.1; N 10.6%.

1-(N,N-Dimethylaminomethyl)indolo[5,4-d]benzo[b]furan (VII). This compound, with mp 162-164°C, was obtained in quantitative yield by a method similar to that used to prepare IV. IR spectrum: 1410 (C—N<) and 3410 cm^{-1} (NH). UV spectrum, λ_{max} (log ε): 212 (4.00), 250 (4.51), 296 (3.90), and 315 nm (3.50). Found: C 7.0; H 6.0; N 11.0%. $C_{17}H_{16}N_2O$. Calculated: C 77.3; H 6.1; N 10.6%.

1-Acetylindolo[5,6-d]benzo[b]furan (V). A) A mixture of 0.1 g (0.5 mmole) of I and 15 ml of acetic anhydride was refluxed for 23 h, after which it was cooled and poured into water. The precipitate was removed by filtration, washed with water, dried, and purified with a column packed with silica gel (100/400 μ) by elution with ether–hexane (1:3) to give 0.04 g (33%) of a product with mp 158-160°C. IR spectrum: 1710 cm^{-1} (C=O). UV spectrum, λ_{max} (log ε): 200 (5.23), 217 (5.28), 262 (5.55), 272 (5.66), 290 (5.32), 302 (5.23), 315 (4.59), and 328 nm (4.32). Found: C 77.1; H 4.4; N 5.9%. $C_{16}H_{11}NO_2$. Calculated: C 77.1; H 4.4; N 5.6%.

B) A compound, which, with respect to all of its parameters, was identical to V, was obtained by refluxing a mixture of heterocycle I with acetic anhydride in the presence of acetic acid. Workup gave 0.029 g (24%) of a product with mp 158-160°C. No melting-point depression was observed for a mixture of the samples obtained by methods A and B.

3-Acetylindolo[5,4-d]benzo[b]furan (VIII). This compound, with mp 137-139°C, was obtained in a yield of 0.025 g (21%) by a method similar to that used to prepare V. IR spectrum: 1700 cm^{-1} (C=O). UV spectrum, λ_{max} (log ε): 208 (4.68), 243 (4.99), 248 (5.08), 262 (4.55), 287 (4.44), 292 (4.50), 296 (4.52), 302 (4.44), 312 (4.35), and 325 nm (3.99). Found: C 77.4; H 4.4; N 5.9%. $C_{16}H_{11}NO_2$. Calculated: C 77.1; H 4.4; N 5.6%.

A compound, which, with respect to all of its parameters, was identical to VIII, was obtained by method B. Workup gave 0.031 g (26%) of a product with mp 137-139°C. No melting-point depression was observed for a mixture of samples obtained by methods A and B.

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