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REACTION OF THE FISCHER BASE WITH 8-HYDROXY-1-NAPHTHALDEHYDES. INVESTIGATION OF THE REACTION PRODUCTS BY ^{13}C NMR SPECTROSCOPY

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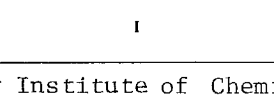
The product of the condensation of the Fischer base with unsubstituted 8-hydroxy-1-naphthaldehyde is a bisindolinespirooxepine. 5,7-Dinitro-8-hydroxy-1-naphthaldehyde reacts with the Fischer base to give a merocyanine that does not display a tendency to undergo conversion to the cyclic form. 2H-Naphtho[1,8-bc]furan derivatives are formed in the reaction of the Fischer base with 5-nitro-, 5-bromo-, and 5,7-dibromo-8-hydroxy-1-naphthaldehydes. The structures of the compounds obtained were established on the basis of data from the PMR and ^{13}C NMR spectra. It was shown by means of the ^{13}C NMR spectra that the product of the condensation of phthalic monoaldehyde with the Fischer base is not a seven-membered spirolactone, as previously assumed, but rather a phthalide derivative.

The search for photochromic substances in series of indoline spiro compounds is being conducted in various directions. One of the most important directions is the synthesis of spiro derivatives that do not contain a six-membered pyran ring as in spiropyrans but rather a seven-membered oxepine ring as, for example, in spirolactones with the I structure [1] or an eight-membered oxacine ring [2-4]. Quantum-chemical calculations [5] that showed that spirooxepine II should exist primarily in the closed form, whereas its mercyanine form should have a long-wave absorption maximum between the visible and IR regions of the spectrum, were published in 1980 for spirooxepine II, the formation of which might be expected in the reaction of the Fischer base with 8-hydroxy-1-naphthaldehyde. These calculated data indicate that it is expedient to search for new photochromic compounds among indolinespirooxepines of the II type. In the present research we made at attempt to obtain these compounds.



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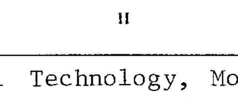

II

D. I. Mendeleev Moscow Institute of Chemical Technology, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1501-1506, November, 1982. Original article submitted November 5, 1981.

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TABLE 1. PMR Spectra of the Synthesized Compounds

Compound	δ, ppm											J, Hz							
	$C(CH_3)$	$N(CH_3)$	H^x	H^m	$H^{a,b}$	12-H	16-H	17-H	22-H	21-H	other	J_{xm}	J_{am} trans	J_{bm} cis	$J_{12,13}$	$J_{15,16}$	$J_{16,17}$	$J_{21,22}$	$J_{15,17}$
VIIIa	1,24 (A) 1,13 1,71 (B) 1,64	2,03 (A) 3,19 (B)	4,61	5,22	2,8	—	—	—	—	—	6,2—7,7	10,6	10,6	3,6	—	—	—	—	—
IXb	1,73	3,01	—	—	—	4,46	7,61	7,78	7,58	6,57	6,6—7,3	—	—	—	10,5	6,8	8,3	7,9	—
IXc	1,71	3,06	—	—	—	4,38	7,76	8,66	8,62	6,65	6,6—7,3	—	—	—	11,1	7,0	8,8	8,3	
IXd	1,73	3,02	—	—	—	4,44	7,60	7,76	7,69	—	6,6—7,3	—	—	—	10,7	6,7	8,3	—	—
Xe	1,87	4,06	—	—	—	6,94	9,49	8,97	9,15	—	7,0—7,9	—	—	—	15,5	8,1	8,1	—	1,6

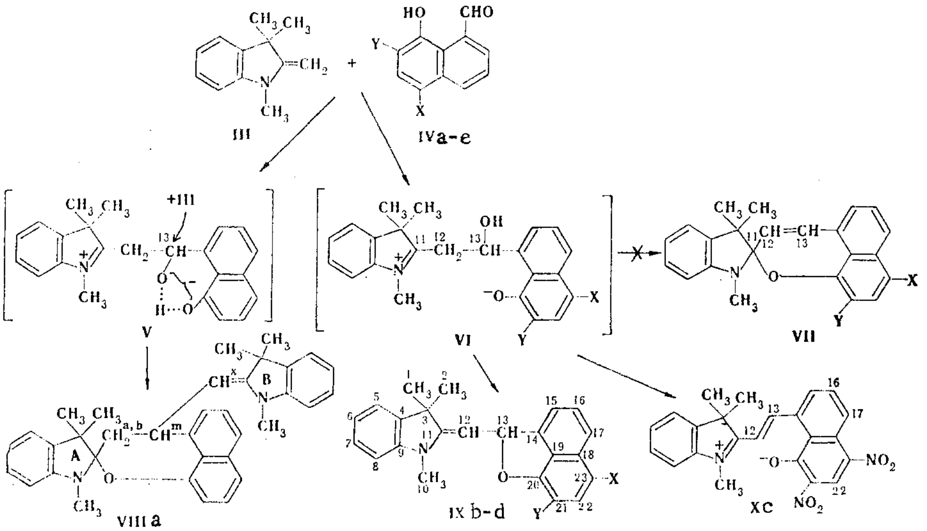
Despite our expectations, the condensation of the Fischer base with unsubstituted 8-hydroxy-1-naphthaldehyde did not lead to spirooxepine II. The reaction product was found to be a bisindoline spiro derivative of dihydrooexpine VIIIa. Since such "dicondensed" compounds in the indolinespirobenzopyran series do not have photochromic properties [6], we attempted to hinder the addition of a second molecule of the methylene base by subjecting 8-hydroxy-1-naphthaldehydes that contain electron-acceptor substituents to the reaction. In fact, in the reaction of the Fischer base with 5-nitro-, 5-bromo-, and 5,7-dibromo-8-hydroxy-1-naphthaldehydes (IVb-d) we obtained monocondensed products. However, our analysis of the ^{13}C NMR spectra showed that these compounds are not spirooxepines VII and that the IX structure corresponds to them. This structure can be regarded as being the result of splitting out of water from the intermediately formed carbinol VI [6] and nucleophilic attack of the negatively charged oxygen atom at the C_{13} atom rather than at the C_{11} atom, which would lead to the formation of the VII structure. A monocondensed product, which, however, does not display a tendency to undergo conversion to the cyclic form and exists in the form of stable merocyanine Xe, is also formed in the reaction of the Fischer base with 5,7-dinitro-8-hydoxy-1-naphthaldehyde (IVe). This is evidently explained by the significant decrease in the nucleophilicity of the negatively charged oxygen atom under the influence of two strong electron-acceptor nitro groups. The fact that the Fischer base reacts with aldehyde IVa to give only a "dicondensed" product, whereas it reacts with aldehydes IVb-e to give only monocondensed products, can be explained by the different acidities of the hydroxy aldehydes. In the reaction of the Fischer base with unsubstituted 8-hydroxy-1-naphthaldehyde (a weaker acid than aldehydes IVb-e) the intermediate form is probably the V structure, in which transfer of the proton of the phenolic group to the negatively charged oxygen atom is not realized completely, as in the VI structure, but only partially. Dehydration is therefore hindered in this case, and the nucleophilicity of the phenolic oxygen atom is decreased. Attack by a second molecule of the methylene base at the C_{13} atom, which also leads to the formation of "dicondensed" product VIIIa via the usual scheme [6], is necessary to complete the reaction.

Thus a study of the condensation of the Fischer base with various 8-hydroxy-1-naphthaldehydes showed that the formation of a seven-membered spiro ring occurs only in the reaction with unsubstituted 8-hydroxy-1-naphthaldehyde, in which case a furan derivative cannot be formed because of the addition of a second molecule of the methylene base. The presence of electron-acceptor groups in the aldehyde molecule promotes the formation of monocondensed 2H-naphtho[1,8-bc]furan derivatives. However, if the aldehyde contains two nitro groups, the reaction stops at the step involving the formation of a mercyanine.

We were unable to detect photochromic properties for IXb-d and Xe under the influence of nonpulse sources of UV light.

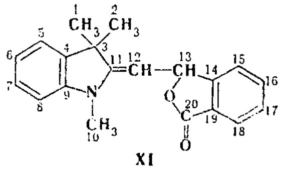
Signals of nonequivalent C- and N-methyl groups of two indoline fragments, a doublet of the H^x proton, and signals of the CH_2—CH fragments are clearly seen in the PMR spectrum (Table 1) of "dicondensed" spirooxepine VIIIa. The H^m proton shows up in the form of a multiplet with a constant of spin—spin coupling with three adjacent (H^a, H^b, and H^x) protons. Signals of methyl groups of only one indoline fragment are seen in the PMR spectrum of merocyanine Xe. The shift of the N—CH_3 signal to the weak-field region (4.06 ppm) indicates significant localization of the positive charge on the nitrogen atom [6], while the $J_{12,13}$ spin—spin coupling constant (SSCC) of 15.5 Hz constitutes evidence for the trans orientation of the

12-H and 13-H protons. In ascertaining the structures of IIb-d by PMR spectroscopy it was not possible to make an unambiguous choice between the spirooxepine (VII) and naphthofuran (IX) structures. Thus the chemical shift ($\sim$4.4 ppm) of the lone doublet with SSCC J $\sim$ 11 Hz, which is not overlapped with the aromatic-proton region, could have been assigned to both the VII structure with cis-oriented vinyl protons and to the XI structure (to its 12-H proton attached to an exocyclic double bond) [7]. For one of the synthesized compounds (IXc) we therefore studied the ^{13}C NMR spectra with total and partial suppression of the protons.



IV, VIII, IX, X a X=Y=H; b X=Br, Y=H; c X=NO_2, Y=H; d X=Y=Br; e X=Y=NO_2

Three superimposed signals from the methyl carbon atoms (which are scattered in the incompletely decoupled spectrum owing to the different $^1J_{CH}$ SSC) are observed in the proton-decoupled ^{13}C spectrum of IXc (Fig. 1a) a signal from the saturated quaternary C_3 atom and 19 signals at 88-167 ppm, eight of which belong to quaternary carbon atoms, are also seen in the spectrum. Although the magnitude of the chemical shift of the C^{13} atom (90.2 ppm) is not great enough to enable one to adopt it for the C_{12} atom of the VII structure even for sterically strained vinyl-containing fragments (110-140 ppm for styrenes [8]), the $^1J_{CH}$ value of 150.5 Hz for this signal approaches that for styrene [8] (by way of illustration, $^1J_{CH}$ = 156.0 Hz for C_{12}). The most characteristic feature that distinguishes the IX structure is therefore the presence of a signal from the quaternary C_{11} atom at very weak field (161.7 ppm). Such a weak-field shift of this signal is normal for a vinyl carbon atom bonded to an electronegative heteroatom [8], while the sp^3-hybridized C_{11} atom in the case of the VII structure should show up at stronger field (up to 100 ppm). The shifts of the aromatic atoms of the naphthalene fragment may also serve as an additional confirmation of the IX structure. Thus, taking into account only the electronic properties of the substituents in the benzene rings [8] and using an additive scheme for their effect, one cannot obtain accurate agreement between the ^{13}C chemical shifts and the shifts predicted by theory for VII. Good agreement of the data, particularly for the ortho positions, which are most sensitive to steric effects, is obtained only for the structure that reflects addition to the naphthalene ring of a sufficiently strained five-membered ring. Thus for the easily assignable signal of the C_{21} atom the shift is much more of a weak-field shift ($\sim$10 ppm) than the value expected only from the concepts of the electronic effect. The same tendency is observed when one compares the shifts of 1,8-dimethylnaphthalene with closed structures of the acenaphthene, fluoranthene, and other types [8]. The shifts of substituted indoles [9] were used as models for the assignment of the aromatic carbon atoms of IXc. The values of the observed direct and long-range SSCC are characteristic for the corresponding aromatic and vinyl fragments.



XI

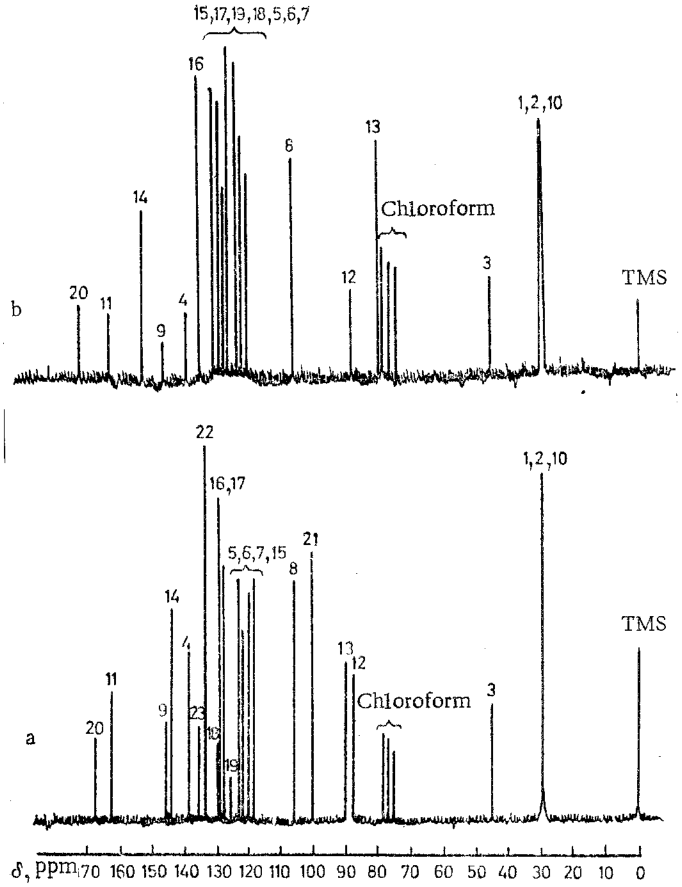


Fig. 1. ^{13}C NMR spectra: a) IXc; b) XI.

The results obtained in our research cast doubt on the correctness of the structures of the products of condensation of 2-methyleneindolines with monoaldehydes of phthalic acids, to which seven-membered spirolactone structures I were assigned in a Japanese patent [1]. We repeated the reaction of the Fischer base with phthalic monoaldehyde and thoroughly analyzed the reaction product by ^{13}C NMR spectroscopy. As expected, this compound was found to be a phthalide derivative (XI), i.e., in this case also the formation of a five-membered ring is preferable to the formation of a seven-membered ring. In addition to the signal of a carbonyl carbon atom (170.6 ppm), the ^{13}C spectrum of XI (Fig. 1b) contains yet another weak-field signal from a quaternary carbon atom (161.5 ppm), which, as in the case of IX, can belong only to an sp^1-hybridized atom attached to a nitrogen atom (C_{11}). The shifts of the atoms of the indolien fragment and the C_{12} atom of XI are close to the shifts of the signals of the corresponding atoms in IXc. A difference is observed only for the carbon atoms of the five-membered ring; the introduction of a carbonyl group leads to substantial redistribution of the electron density in it, so that the signal of the C_{13} atom is shifted ∿10 ppm to strong field, while the C_{14} signal is correspondingly shifted to weak field by approximately the same value (∿8 ppm). The incompletely proton-decoupled ^{13}C NMR spectra were used to assign the signals of the carbon atoms of XI.

EXPERIMENTAL

The PMR spectra of solutions of VIIIa and IXb,d in $CDCl_3$ and of Xe in $(CD_3)_2SO$ were recorded with a Varian XL-100A-12 spectrometer. The PMR and ^{13}C NMR spectra of IXc and the ^{13}C NMR spectrum of XI in $CDCl_3$ were recorded with a Varian CFT-20 spectrometer (80 MHz) with tetramethylsilane (TMS) as the internal standard. The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-20 spectrometer.

We described the synthesis of 8-hydroxy-1-naphthaldehydes in [10]. Phthalic acid monoaldehyde was obtained by the method in [11] by oxidation of naphthalene with potassium permanganate with subsequent decarboxylation of the phthalonic acid (mp 96°C, in agreement with the data in [11]) that was formed in the first step. The constants and yields of the compoinds obtained are presented in Table 2.

TABLE 2. Characteristics of the Synthesized Compounds

Compound	X	Y	mp, °C	Found					Empirical formula	Calculated					Yield, %
				C, %	H, %	N, %	Br, %	M*		C, %	H, %	N, %	Br, %	M	
VIIIa	—	—	159—160	84,0	7,0	5,6	—	500	$C_{35}H_{36}N_2O$	84,0	7,3	5,6	—	500	51
IXb	Br	H	152—154	68,1	5,0	3,4	20,1	405	$C_{23}H_{20}BrNO$	68,0	5,0	3,5	19,7	405	75
IXc	NO_2	H	208—209	74,6	5,5	7,5	—	372	$C_{23}H_{20}N_2O_3$	74,2	5,4	7,5	—	372	79
IXd	Br	Br	203—204	57,4	4,0	2,8	32,8	483	$C_{23}H_{19}Br_2NO$	56,9	4,0	2,9	32,9	483	83
Xe	—	—	>235 deg.	66,1	4,7	9,8	—	417	$C_{23}H_{19}N_3O_5$	66,2	4,6	10,1	—	417	73

*For VIIIa and Xe by mass spectrometry with a Varian MAT-112 spectrometer; for IXc-d by mass spectrometry with an MKh-1303 spectrometer.

1,3,3-Trimethyl-3',4'-dihydro-4'-[(1,3,3-trimethylindolin-2-ylidene)methyl]indoline-2-spiro-2'-naphth[1,3-bc]oxepine (VIIIa). A 0.21 g (1.21 mmole) sample of the Fischer base was added to a solution of 0.21 g (1.21 mmole) of 8-hydroxy-1-naphthaldehyde in 30 ml of absolute alcohol, and the mixture was maintained at room temperature for 2 days. The resulting precipitate was removed by filtration to give 0.16 of VIIIa. Recrystallization from ethanol—benzene gave white crystals. IR spectra: 1658 (C=C) and 980 cm^{-1}(C_{spiro}—O).

2-[(1,3,3-Trimethylindolin-2-ylidene)methyl]-6-bromo-2H-naphtho[1,8-bc]furan (IXb).* The reaction of 0.14 g (0.57 mmole) of 5-bromo-8-hydroxy-1-naphthaldehyde and 0.10 g (0.57 mmole) of the Fischer base in 10 ml of absolute alcohol gave 0.17 g of IXb. Recrystallization from acetone—ethanol gave light-yellow crystals. IR spectrum: 1648 cm^{-1} (C=C).

2-[(1,3,3-Trimethylindolin-2-ylidene)methyl]-6-nitro-2H-naphtho[1,8-bc]furan (IXc). The reaction of 0.70 g (3.22 mmole) of 5-nitro-8-hydroxy-1-naphthaldehyde and 0.56 g (3.22 mmole) of the Fischer base in 60 ml of absolute alcohol gave 0.95 g of IXc. Recrystallization from benzene—ethanol gave yellow crystals. IR spectrum: 1660 (C=C); 1510, 1348 cm^{-1} (NO_2). ^{13}C NMR spectrum: 29.5 (1, 2, 10); 45.3 (3); 88.0 (12); 90.2 (13); 100.2 (21); 105.8 (8); 118.1, 119.7, 121.5, 122.4 (5, 6, 7, 15); 125.2 (19); 127.9, 128.3 (16,17); 128.6 (18); 132.6 (22); 134.8 (23); 137.9 (4); 143.3 (14); 145.2 (9); 161.7 (11); 167.0 (20) ppm (see also Fig. 1a).

2-[(1,3,3-Trimethylindolin-2-ylidene)methyl]-6,8-dibromo-2H-naphtho[1,8-bc]furan (IXd). The reaction of 0.19 g (0.57 mmole) of 5,7-dibromo-8-hydroxy-1-naphthaldehyde and 0.10 g (0.57 mmole) of 5,7-dibromo-8-hydroxy-1-naphthaldehyde and 0.10 g (0.57 mmole) of the Fischer base in 10 ml of absolute alcohol gave 0.23 g of IXd. Recrystallization from acetone—ethanol gave light-yellow crystals. IR spectrum: 1688 cm^{-1} (C=C).

1,3,3-Trimethyl-2-[(5,7-dinitro-8-oxido-1-naphthyl)vinyl]indolenium Betaine (Xe). The reaction of 0.15 g (0.57 mmole) of 5,7-dinitro-8-hydroxy-1-naphthaldehyde and 0.10 g (0.57 mmole) of the Fischer base in 70 ml of absolute alcohol gave 0.18 g of Xe in the form of black crystals, which were converted to a dark-red powder by tritration. IR spectrum: 1540, 1342 cm^{-1} (NO_2).

3-[(1,3,3-Trimethylindolin-2-ylidene)methyl] Phthalide (XI). This compound was obtained by the method of [1] by condensation of the Fischer base with phthalic monoaldehyde in alcohol. The product had mp 188-190°C (mp 189-190°C [1]). ^{13}C NMR spectrum: 29.5 (1,2,10); 45.1 (3); 79.3 (13); 88.0 (12); 105.6 (8); 119.5, 121.5, 122.7, 125.2, 127.8, 129.0 (5-7, 15, 17, 18); 126.5 (19); 133.9 (16); 137.9 (4); 145.2 (9); 151.1 (14); 161.5 (11); 170.6 (20).

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PORPHYRINS.

15.* EFFECT OF STERIC FACTORS ON THE ORIENTATION OF meso SUBSTITUTION IN THE FORMYLATION OF PORPHYRINS. FIRST EXAMPLE OF THE CHROMATOGRAPHIC IDENTIFICATION OF ISOMERS OF PORPHYRINS OF THE I AND II TYPES

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UDC 547.979.733.07:543.422'51

The Cu and Ni complexes of etioporphyrin II were subjected to Vilsmeier formylation, and a steric effect of the peripheral substituents on the direction of electrophilic meso substitution in the porphyrins was observed. The corresponding meso-N,N'-dimethylaminomethyl derivatives, which were separated by thin-layer chromatography (TLC) on silica, gel, were obtained. Their structures were proved by means of the IR, PMR, electronic, and mass spectra.

We have already observed [2] that the chromatographic mobilities of meso-dimethylaminomethylporphyrins depend on the shielding effect of the β-pyrrole substituents adjacent to the meso position. We used this property of meso-dimethylaminomethylporphyrins in the present research to study the influence of steric effects of the substituents in the porphyrin ring on the orientation of meso formylation via the Vilsmeier reaction. Studies of this sort have not been made because of the difficulty or impossibility of separation of isomers of meso-formylporphyrins into individual compounds for the unambiguous interpretation of their structures by physicochemical methods.

As the subject of the investigation we selected etioporphyrin II (I), in which, in the case of monoformylation, electrophilic substitution either in the 5 (15) position between two ethyl groups or in the 10 (20) position between two methyl groups is possible. In order to ascertain the possibility of the effect of the central metal atom on the orientation of meso substitution we carried out the reaction with copper (II) and nickel (III) complexes of porphyrin I. The use of the cobalt complex (IV) led to a mixture of polysubstituted products, and the results of its formylation are therefore not examined in the present paper.

Starting complex II was obtained in 50% yield by cyclization of the corresponding biladiene-a,c dihydrobromide (V) by refluxing in dimethylformamide (DMF) in the presence of copper acetate. After demetallation, complexes III and IV were obtained from porphyrin I by treatment with nickel and cobalt acetates.

The Vilsmeier reaction was carried out by the method that we developed in [3]. Compounds II and III were heated with the Vilsmeier complex (DMF/$POCl_3$) until the starting compounds disappeared completely in the reaction mixtures, while the intermediate "phosphorus complexes" VI and VII were reduced with sodium borohydride in alcohol and the corresponding meso-dimethylaminomethyl (DMAM) derivatives were isolated in 85-91% overall yields.

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*See [1] for Communication 14.

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