SYNTHESIS AND PROPERTIES OF AZOMETHINES BASED ON 1-NITROPHENYL-2-FORMYLPYRROLES

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Schiff bases were obtained by the reaction of 1-nitrophenyl-2-formylpyrroles with aromatic amines, and their spectral characteristics were studied.

Recently [2] we showed that 1-arylpyrrolecarbaldehydes are formed in the reactions of furfural, which is an extremely readily available raw material [1], with aromatic amines. We calculated that the Schiff bases obtained from them may exhibit pharmacological activity, like other pyrroles [3, 4]. In this connection we studied the reaction of 1-nitrophenylpyrrole-2-carbaldehydes (I, II) with aromatic amines. As a rule, such reactions are realized with equimolar ratios of the reagents in dry benzene with distillation of the water in the form of an azeotrope [5, 6]. In our case, however, a difficultly separable mixture of the azomethines (III) and (IV) and also the initial components was formed. Realization of the reaction in DMFA and sulfolane and also by the Fischer method [7] in absolute alcohol did not give good results. We obtained the best yields of the final condensation product with prolonged boiling of an equimolar mixture of the aldehyde and amine in benzene in Soxhlet apparatus with anhydrous sodium sulfate as drying agent. In this case, the azomethines (IIIa-ℓ) and (IVa, b, f, h) are formed with yields of up to 95% (Table 1). We note that not even traces of the aldehyde remained in the reaction mixture (TLC).

In the UV spectra of compounds (III) (Table 1) there are, as a rule, three absorption bands in the regions of 205-212, 227-253, and 282-298 nm. Here the substituents R^1 have the largest effect on the medium-wave band, and this makes it possible to assign it to the electronic transitions in the conjugated system of the iminomethinepyrrole fragment, which is under the influence of the p-nitrophenyl radical. Movement of the nitro group in compounds (IV) to the m position leads to leveling out of the electronic effect of the substituents R^1, so that their UV spectra become almost indistinguishable.

TABLE 1. Schiff Bases of 1-Nitrophenyl-2-formylpyrroles

Compound	Molecular formula	T_{mp}, °C	λ_{max}, nm (lg ε)	IR spectrum (KBr), C=N	Yield, %
III a	$C_{17}H_{12}BrN_3O_2$	147...148	211 (4,92), 290 (4,34)	1610	53
III b	$C_{17}H_{12}ClN_3O_2$	140...141	212 (4,68), 250 (4,41), 294 (4,49)	1615	65
III c	$C_{17}H_{12}ClN_3O_2$	87...88	212 (4,47), 253 (4,19) sh 294 (4,39)	1610	53
III d	$C_{17}H_{12}ClN_3O_2$	79...80	212 (4,40), 245 (4,30), 287 (4,05)	1615	55
III e	$C_{18}H_{15}N_3O_2$	143...144	210 (4,06), 232 (4,15), 286 (4,43)	1610	71
III f	$C_{18}H_{15}N_3O_2$	111...112	205 (4,50), 243 (4,19), 282 (4,30)	1610	71
III g	$C_{18}H_{15}N_3O_2$	83...84	242 (4,20), 290 (4,50)	1615	71
III h	$C_{18}H_{15}N_3O_3$	121...122	209 (4,30), 227 (4,01), 298 (4,10)	1610	68
III i	$C_{18}H_{15}N_3O_3$	110...111	211 (3,90), 240 (4,00), 290 (4,10)	1615	93
III j	$C_{18}H_{15}N_3O_3$	101...103	212 (3,90), 241 (3,80), 286 (4,09)	1610	93
III k	$C_{19}H_{16}N_4O_3$	95...96	208 (3,83), 267 (4,10)	1620	95
III ℓ	$C_{17}H_{13}N_3O_3$	139...140	222 (4,18), 282 (4,25)	1610	88
IV a	$C_{17}H_{12}BrN_3O_2$	145...146	241 (4,01), 270 (3,97), 285 (4,21) sh	1610	60
IVh	$C_{18}H_{15}N_3O_3$	107...108	241 (4,01), 270 (3,97), 285 (4,21) sh	1610	70
IVf	$C_{18}H_{15}N_3O_2$	110...111	209 (4,00), 294 (4,20) sh	1615	90
IVb	$C_{17}H_{12}ClN_3O_2$	105...106	209 (4,02), 270 (3,98), 292 (4,20)	1610	88

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TABLE 2. PMR Spectra of the Schiff Bases, δ, ppm (deuterochloroform)

Compound	3-H*	4-H	5-H*	α-H	Compound	3-H*	4-H	5-H*	α-H
IIIa	7,12**	6,50	7,41	8,10	IIj	—	6,42	—	8,22
IIIb	7,18	6,50	7,40	8,31	IIk	7,08	6,45	—	8,22
IIIc	—	6,48	—	8,25	IIℓ	—	6,35	—	8,32
IIIe	7,00	6,42	—	8,22	IIIa	7,02	6,42	—	8,20
IIIf	7,05	6,45	—	8,20	IIIh	—	6,40	—	8,22
IIIg	—	6,48	—	8,22	IIIf	7,00	6,40	—	8,20
IIIh	7,10**	6,48	7,38	8,32	IIIb	7,02	6,45	7,22	8,18
IIIi	—	6,52	—	8,33					

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*Dashes signify that the signal is masked by the absorption of the aromatic protons.

**The spectrum was obtained in DMSO.

TABLE 3. Mass Spectra of Compounds (III, IV)

Compound	m/z (I_{rel}, %)*
IIIa	*369* (95), *368* (88), *321* (27), 243 (15), 242 (14), 199 (30), 153 (30), 121 (10), 76 (11), 75 (8)
IIIc	*325* (74), *324* (100), *278* (40), 243 (14), 242 (12), 199 (43), 187 (14), 167 (15), 153 (53), 111 (30)
IIId	*325* (100), *326* (43), *324* (82), 292 (14), 290 (68), *278* (40), 244 (60), 199 (40), 167 (11), 153 (45)
IIIe	305 (90), 306 (18), 304 (100), 258 (45), 199 (37), 167 (14), 153 (31), 128 (6), 115 (8), 91 (31)
IIIf	305 (77), 306 (16), 304 (100), 258 (37), 199 (21), 168 (12), 153 (18), 128 (4), 115 (7), 91 (19)
IIIg	305 (100), 306 (22), 304 (55), 290 (17), 258 (33), 199 (14), 168 (55), 156 (27), 153 (18), 128 (6)
IIIh	321 (100), 322 (20), 320 (62), 306 (30), 274 (13), 259 (5), 231 (12), 199 (11), 153 (13), 122 (13)
IIIi	321 (87), 322 (18), 320 (100), 274 (32), 259 (4), 231 (6), 199 (22), 153 (18), 115 (6), 92 (10)
IIIj	321 (100), 322 (20), 320 (17), 293 (20), 290 (18), 274 (15), 259 (21), 199 (13), 167 (17), 153 (17)
IIIk	348 (100), 249 (20), 347 (35), 306 (24), 305 (43), 259 (27), 199 (5), 153 (16), 107 (21), 43 (19)
IIIℓ	307 (100), 308 (17), 306 (30), 290 (12), 260 (44), 199 (47), 188 (15), 170 (53), 153 (31), 115 (11)
IVa	*369* (100), *370* (70), *368* (88), 322 (23), 243 (52), 199 (55), 167 (10), 153 (35), 121 (21), 76 (38)
IVh	321 (100), 322 (23), 320 (62), 305 (37), 273 (25), 231 (55), 230 (39), 199 (26), 167 (10), 153 (30)

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*The ions containing ^{35}Cl or ^{79}Br are given in italics.

TABLE 4. Peak Intensities of the Characteristic Ions in the Mass Spectra of Compounds (IIIa-ℓ, IVa, h) (%Σ_{40})

Compound	M^+	Φ_1	Φ_2	Φ_3	Φ_4	Φ_5
IIIa	21,8	26,2	3,9	8,0	4,1	—
IIIc	7,5	11,1	3,6	3,2	4.2	—
IIId	12,8	11,3	3,6	3,6	4,2	6,4
IIIe	13,6	13,0	3,6	5,8	4,0	—
IIf	18,0	17,0	3,6	6,6	3,1	—
IIIg	13,7	4,5	1,1	2,5	1,4	1,2*
IIIh	27,4	14,4	2,5	3,0	2,8	—
IIIi	17,9	17,0	3,8	5,4	3,3	—
IIIj	13,2	1,9	1,4	1,6	2,0	2,0**
IIIk	19,4	5,6***	0,7	0,5	2,6	—
IIIℓ	13,1	3,3	5,4	4,8	3,4	1,4
IVa	14,0	13,0	4,4	3,0	2,8	—
IVh	14,8	7,4	3,0	2,9	3,6	—

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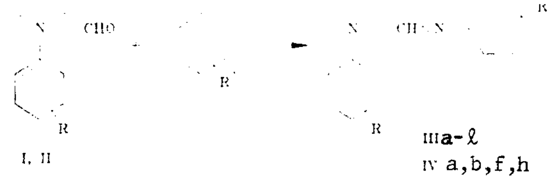
*In addition, the ion $[M - CH_3{-}C_6H_4NO_2]^+$ (4.6).

**In addition, the ion $[M - CH_3{-}C_6H_4NO_2]^+$ (1.2).

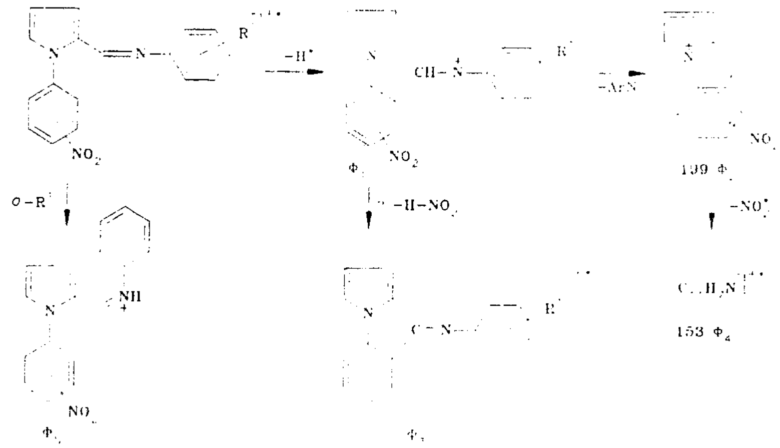
***In addition, $[M - CH_2CO]$ (5.4), $[\Phi_1{-}CH_2CO]$ (6.8).



I, III R=*p*-NO_2, II, IV R=*m*-NO_2; III, IV **a** R^1=*p*-Br; **b** R^1=*p*-Cl, **c** R^1=*m*-Cl; **d** R^1==*o*-Cl; **e** R^1=*p*-CH_3; **f** R^1=*m*-CH_3; **g** R^1=*o*-CH_3; **h** R^1=*p*-OCH_3; **i** R^1=*m*-OCH_3; **j** R^1=*o*-OCH_3; **k** R^1=*p*-$NHCOCH_3$; **ℓ** R^1=*o*-OH

In the IR spectra of all the obtained compounds a characteristic strong band is observed for the stretching vibrations of the C=N bond in the region of 1610-1615 cm^{-1} [8]. Here both substituents R and substituents R^1 have practically no effect on it.

In the PMR spectra of the investigated azomethines (Table 2) a distinct singlet for one proton of the azomethine group appears in the region of 8.1-8.3 ppm, and the substituents R and R^1 also do not have a clearly defined effect on its chemical shift. Of the other signals it is necessary to mention the doublets for the 5-H and 3-H protons in the regions of 7.4-7.38 and 7.08-7.18 ppm, respectively (J_{54} = 3.0 and J_{34} = 3.5 Hz) and also the doublet of doublets for the 4-H proton in the upfield region of 6.35-6.52 ppm.



In the mass spectra of (III, IV) (Table 3) there is a strong molecular ion peak, the stability of which (W_M) is due appreciably to the electronic characteristics of the substituents R and R^1. The molecules of the p-nitro-substituted derivatives (IIIa, h) are somewhat more stable than the analogous m-substituted azomethines (IVa, h) (Table 4). As a rule, the molecular ions of the o-substituted compounds are the least stable in the series of compounds (III), whereas the stability of the p-substituted compounds to electron impact is appreciably higher.

Like 1-nitrophenylpyrrole-2-carbaldehydes, the initial fragmentation of the M^+ ions of their azomethines (scheme 2) involves primarily the loss of a hydrogen atom ($Φ_1$), and this is followed by the loss of arylnitrene ($Φ_2$) or a nitro group ($Φ_3$). The loss of a nitro group also occurs from the $Φ_2$ ($Φ_4$) ion. Dissociation of such a type can be explained on the assumption of the initial loss not of the azomethine but of the aromatic o-hydrogen atom with cyclization of the obtained $Φ_1$ ion at the methine carbon atom. In fact, the molecular ions of the m-nitro isomers (IVa, h), in which the nitro group stabilizes the ortho–para positions of the phenyl ring, lose the hydrogen atom with appreciably lower probability than in the case of the para isomers (IIIa, h). The formation of the cyclic ion $Φ_1$ also makes it possible to explain the subsequent loss of the arylnitrene.

It is important to emphasize that the mass spectra of the azomethines (III) and (IV) do not contain [M – NO_2] ions or, in most cases, [M – R^1] ions. The exceptions are the o-substituted compounds (IIId, g, j, ℓ). In all probability the formation of such fragments is due to cyclization at the nucleophilic β-carbon atom of the pyrrole ring, which is typical of the azomethines of many other heterocycles [9].

EXPERIMENTAL

The UV spectra were recorded on a Specord instrument in ethanol. The IR spectra were obtained on an SP-1000 instrument for tablets with potassium bromide. The PMR spectra were obtained on an FX-900 instrument. The mass-spectral investigations were conducted on a JMS-DX 300 instrument at 70 eV. The reactions and the purities of the obtained compounds were monitored by TLC on Silufol UV-254 plates in benzene with development in iodine vapor. The elemental analyses for C and H correspond to the calculated compositions.

The initial p- and m-nitrophenyl-2-formylpyrroles were obtained by the method in [10].

General Procedure for the Production of Compounds (III, IV). In a 250-ml flask fitted with a Soxhlet extractor, in which there was 10 g of anhydrous sodium sulfate, we placed 0.5 g (23 mmoles) of 1-nitrophenyl-2-formylpyrrole and 23 mmoles of the respective amine, dissolved in 100-200 ml of dry benzene. The mixture was boiled for 20 h, the solvent was evaporated, and the solid residue was recrystallized from alcohol. The properties of the obtained compounds (III, IV) are given Table 1.

LITERATURE CITED

1. A. A. Delgodo and N. J. Blanco, Revista ICIDCA La Habana, Cuba, 17, 27 (1983).
2. R. Petit and R. Palaud, Compt. Rend., 258, 230 (1964).
3. R. A. Jones and P. B. Gerritt, The Chemistry of Pyrroles, Academic Press, London (1977).
4. R. B. Moffett and W. H. Hoehn, J. Am. Chem. Soc., 69, 1792 (1947).
5. H. Saikachi and S. Shimamura, Yakugaki Zasshi, 80, 37 (1960); Chem. Abs., 54, 13092 (1960).
6. M. Dezelic and B. Bobarevic, Bull. Soc. Chim. Rep. Popul. Bosnie Herzeg., 11, 11 (1957); Chem. Abs., 52, 10054 (1958).
7. O. Fischer, A. Balling, and R. Aldinger, J. Prakt. Chem., 208, 105 (1920).
8. J. Fabian, M. Legrand, and P. Poirier, Bull. Soc. Chim. Fr., No. 5, 1499 (1956).
9. P. B. Terent'ev and A. P. Stankyavichus, Mass Spectrometry of Biologically Active Nitrogen Bases [in Russian], Mokslas, Vil'nyus (1987).
10. M. C. Pina and V. A. Budilin, 3^a Semana Cientifica del IQBE: Resumenes, La Habana Cuba (1982), p. 120.

SYNTHESIS OF DERIVATIVES OF 1,3-DIHYDROSPIRO[2H-INDOLE-2,2'-PYRROLIDINE]

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Derivatives of 1,3-dihydrospiro[2H-indole-2,2'-pyrrolidine] were synthesized by the reaction of 2-methylene-2,3-dihydro-1H-indoles with α-iodoacetamide. Treatment of the products with alkyl iodides in the presence of potassium hydroxide gave 1'-substituted spiroindole-2,2'-pyrrolidines. The 1,3-dihydrospiro[2H-indole-2,2'-pyrrolidines] were converted by the action of perchloric acid into 2-(2-carbamoylethyl)-3H-indolium perchlorates.

The alkylation of heterocyclic enamines containing an exocyclic carbon—carbon double bond and derivatives of 2-methylene-2,3-dihydro-1H-indole, in particular, has so far been studied little [1, 2]. According to data in [3], the alkylation of 2-methylene-1,3,3-trimethyl-2,3-dihydro-1H-indole with methyl iodide takes place at the β-carbon atom of the enamine group, and the corresponding 2-isopropylidene base is formed. The reaction of the above-mentioned indoline enamine with 2-halogenoalkanols or oxiranes is also accompanied by initial C-alkylation and leads finally to derivatives of spiro[indole-2,2'-furan] [4, 5]. The spiroannellation of the pyrroline ring to the indole ring by the action of 2-methylene-2,3-dihydro-1H-indole with tetracyanoethylene was described earlier [6]. It is known that

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