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SYNTHESIS AND SPECTRAL PROPERTIES OF 1-ARYL-2-FORMYLPYRROLES

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UDC 547.745'554.01'724.1.07

Various 1-aryl-2-formylpyrroles were synthesized by reaction of furfurol with substituted anilines. For p-bromo- and p-chlorophenylsubstituents, the intermediate Schiff bases were isolated.

Recently it was shown that in contrast to the Yur'ev reaction conditions [1], 1-(p-nitrophenyl)-2-formylpyrrole can be synthesized from furfurol under mild conditions with 70% yield [2]. This work extends that synthetic method to other 1-arylpyrroles.

The reaction of furfurol with aromatic amines is known to occur differently depending on the conditions [3, 4]: in acidic media, besides the pyrrole derivatives, the formation of pyridine salts is possible [3, 5], the acidity of the medium having a significant role [2]; in neutral media, cyclopentenones are formed [5]; and the nature of the substituent on the benzene ring of the amine also is important [6].

We found the optimal conditions for synthesis of p- and m-nitrophenyl-2-formylpyrroles at a ratio of pyrrole:amine:acid of 1:2:1. The purity of the starting materials and the constant addition of acid to the reaction mixture are important.

Application of the conditions to other anilines showed that in spite of a decrease in nucleophilicity, the best results are obtained for anilines with acceptor substituents (Table 1).

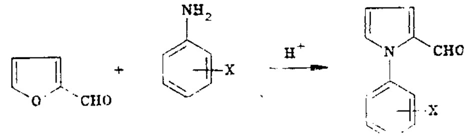

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TABLE 1. Data for the Synthesized 1-Aryl-2-formylpyrroles

X	Method	mp, °C, Lit. data	IR spectrum cm^{-1} (pyrrole)	λ_{max}, nm (log ε)	Yield, %
p-NO_2	A	170...171 169...170 [3]	1190	203 (4,12), 221 sh. (3,98), 279 (4,26)	90
m-NO_2	A	151...152 151...152 [6]	1180	217 (4,21), 263 (4.28)	95
p-CO_2Et	Б	70...72	1180	230 (4,17), 268 (4.35)	60
p-Cl	Б	96...98 96...97 [6]	1195	227 (4.19), 293 (4,22)	45
m-Cl	Б	58...60	1200	214 (4,34), 291 (4,43)	41
o-Cl	Б	90...92	1155	212 (4,66), 289 (4,66)	38
p-Br	A	93...94 94 [7]	1190	237 (4,25), 294 (4,09)	31
p-SO_2NH_2	A	193...194 197...198 [8]	1150	241 (4,03), 269 (4,07), 294 (4,07)	41
p-CH_3	Б	48...50 55 [7]	1170	221 (4.44), 297 (4,46)	10
p-OCH_3	Б	42...44 46 [7]	1180	227 (4,31), 287 (4,26)	14

TABLE 2. Data for Semicarbazones and Thiosemicarbazones of 1-Aryl-2-formylpyrroles

X	T$_{mp}$, °C	IR spectrum, ν, cm^{-1}			UV spectrum, λ_{max}, nm (log ε)	Yield, %
		C=N	C=O(S)	NH		
		Semicarbazones				
p-Cl	226...228	1590	1690	3430	309 (4,27)	63
m-Cl	178...180	1580	1680	3420	309 (4,55)	63
o-Cl	210...212	1570	1670	3430	306 (4,45)	78
p-Br	238...240	1590	1690	3420	302 (4,51)	66
p-SO_2NH_2	208...210	1580	1700	3430	302 (4,38)	82
		Thiosemicarbazones				
p-Cl	100...101	1590	1380	3390	336 (4,03)	74
m-Cl	120...121	1580	1310	3400	333 (4,42)	74
o-Cl	95...96	1550	1320	3380	330 (4,42)	54
p-Br	209...210	1550	1340	3410	333 (4,40)	64
p-SO_2NH_2	130...131	1570	1300	3450	337 (4,21)	77

The synthesized 1-aryl-2-formylpyrroles were also characterized as semicarbazones and thiosemicarbazones (Table 2).

An intense band at 1670-1650 cm^{-1} (C=O) is present in the IR spectra of the synthesized aldehydes; the lowering of the stretching frequency of the C=O group corresponds to the literature data [9] and indicates the high degree of conjugation of the carbonyl group to the electron-donating pyrrole.

Three quartets for the protons of the pyrrole ring are observed in the PMR spectra of the 1-aryl-2-formylpyrroles (Table 3), which is due to the rather large J_{35} constant (1.7 Hz). The relation known for 2-substituted pyrroles, $J_{34} > J_{45} > J_{35}$ [10] serves as the basic criterion for referencing the signals. The quartet for 5-H is additionally split because of interaction with the aldehyde proton which according to [11, 12] indicates the S-trans-position for the carbonyl group.

An intense molecular ion peak (MIP) is observed in the mass spectra of all the synthesized aldehydes (Table 4). The stability of the MIP is higher for the nitro-substituted compounds than for the halogen-containing aldehydes (Table 5), while for isomeric compounds, the para-isomers are more stable to electron impact than the meta-isomers. Apparently, this is related to the primarily localized positive charge in the molecular ion in the pyrrole part of the molecule. In this case the electron acceptor substituents probably facilitate the redistribution of electron density to the aryl group, stabilizing the heterocyclic ring. The main

TABLE 3. PMR Spectra of 1-Aryl-2-formylpyrroles

X	Solvent	δ, ppm				
		3-H	4-H	5-H	α-H	1-Ar
p-NO_2	DMSO	7,14	6.34	7,31	9.48	(*m*-H) 8.20 (*o*-H) 7,54
m-NO_2	DMSO	7,22	6,44	7,47	9.54	—
p-CO_2Et	DMSO	7,33	6,55	7,50	9,55	(*o*-H) 7,55 (*m*-H) 8,09 (Et) 1,40; 4,40
p-Cl	$CDCl_3$	7,00	6,38	7,11	9,52	(*o*-H) 7,23 (*m*-H) 7,40
m-Cl	$CDCl_3$	7.02	6.39	7.11	9,58	—
o-Cl	DMSO	7,22	6,47	*	9,49	—
p-Br	$CDCl_3$	7,00	6,38	7,10	9,55	(*o*-H) 7,20 (*m*-H) 7,56
p-SO_2NH_2	DMSO	7,29	6,55	*	9,56	(NH_2) 7,47 (*o*-H) 7,60 (*m*-H) 7,95
p-CH_3	DMSO	7,15	6,41	*	9,50	(CH_3) 2,36 (H arom.) 7,25
p-OCH_3	DMSO	*	6,40	*	9,47	(OCH_3) 3,80 (*o*-H) 7,00 (*m*-H) 7,31

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*Signal is masked by absorption of aromatic protons.

TABLE 4. Mass Spectra of 1-Aryl-2-formylpyrroles

X	*m/z* (relative intensity, %)
p-NO_2	216 (100), 217 (15), 215 (53), 214 (11), 169 (53), 141 (17), 115 (10), 93 (56), 51 (16), 50 (23)
m-NO_2	216 (100), 217 (14), 215 (70), 214 (17), 199 (16), 170 (14), 169 (70), 168 (45), 141 (24), 115 (15), 93 (57), 51 (28), 50 (39)
p-Cl	205* (77), 206* (21), 204* (32), 170 (26), 169 (18), 151 (7), 149 (12), 141 (15), 115 (18), 112 (38), 93 (100), 75 (27)
m-Cl	205* (100), 206* (34), 204* (69), 170 (36), 169 (27), 151 (11), 149 (23), 141 (25), 115 (49), 93 (97), 75 (49)
p-Br	249* (38), 250* (13), 248* (8), 170 (35), 169 (57), 158* (36), 156* (36), 141 (15), 115 (28), 93 (100), 50 (23)

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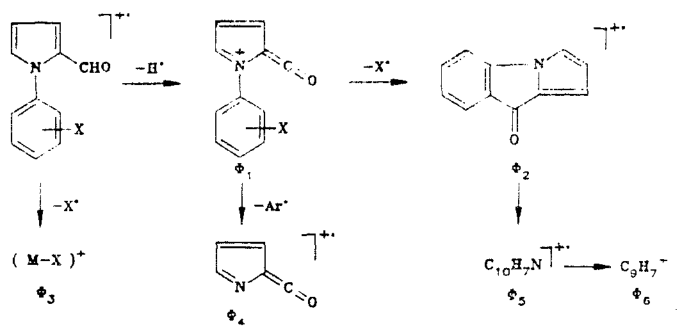
*Ions containing the isotopes ^{35}Cl and ^{79}Br.

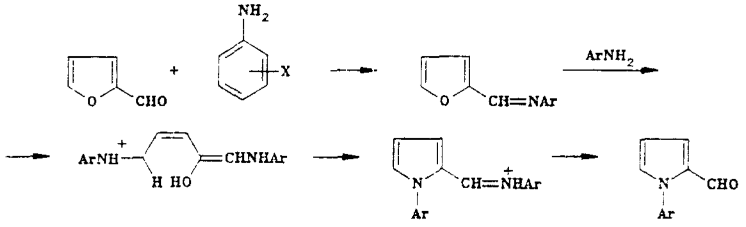
TABLE 5. Intensities of Characteristic Ion Peaks in the Mass Spectra of 1-Aryl-2-formylpyrroles (% Σ_{40})

X	W_p	Φ_1	Φ_2	Φ_3	Φ_4	Φ_5	Φ_6
p-NO_2	27,3	10,5	12,0	—	12,5	0,3	12,8
m-NO_2	17,8	10,9	11,0	2,2	10.9	—	11,0
p-Cl	17,4	4,5	2,5	3,6	14,0	2,1	2,5
m-Cl	14,8	6,1	2.3	3,2	8,6	2.2	4,4
p-Br	12,6	1,0	7,4	4,5	13,0	1,9	3,6

fragmentation path of the 1-arylpyrrole-2-aldehydes is related to the loss of a hydrogen atom with subsequent elimination by the Φ_2 ion of the X substituent and then a molecule of CO (Φ_2 and Φ_5 ions). The splitting off of an aryl residue (Φ_4) from the Φ_1 ion is also observed. An independent fragmentation path of the M^+ ion is the loss of an X substituent (Φ_3 ion). It is important to note the complete absence of rearrangement of the M − NO ion, characteristic of nitroarenes [13], and also the (M −H − CO) ions, the peak intensity of which is very great in the mass spectra of formylindoles [14]. Thus, the mass spectra confirm the structure of the formylpyrroles synthesized by us.



The complete formation scheme of 2-formylpyrroles can be represented based on known literature data [2, 5, 6] as follows:



In the case of p-bromo- and p-chloroanilines, besides the final products, formylpyrroles, we isolated the intermediate Schiff bases with yields of 32 and 9%, respectively. According to the given formation scheme for pyrroles, the effect of the amine is determined by the presence of acceptor substituents on the benzene ring leading to stabilization of both the intermediate Schiff base and the final 1-aryl-2-formylpyrroles.

EXPERIMENTAL

IR spectra were recorded on a SP-1000 instrument as KBr tablets, UV spectra on a Specord spectrophotometer in ethanol. PMR spectra were taken on a FX-90Q instrument in DMSO-D_6 and $CDCl_3$. Mass spectra were taken on a IMS-DX 300 instrument at a temperature of 250°C and an ionization energy of 70 eV. Column chromatography was done on Merck-60 silica gel, monitoring of the reaction and purity of the synthesized compounds by TLC on plates of UV-254 Silufol.

1-Aryl-2-formylpyrroles. A. With heating on a boiling water bath, 50 mmole of amine were dissolved in 100 ml ethanol, 2.5 g (25 mmole) of furfurol was added at once, and 12 ml 2 N HCl was added dropwise. The mixture was boiled for 2 h and diluted with 100 ml water. The precipitate was filtered and washed on the filter with alcohol.

B. A mixture of 50 mmole amine and 70 ml ethanol was heated on a water bath until complete dissolution, 2.5 g (25 mmole) of furfurol was added at once, and 2 ml 2 N HCl was added dropwise. The mixture was heated 5 h, the organic layer was separated, the aqueous was extracted with benzene, and the combined extracts were thoroughly washed with 10% HCl and water. The resulting benzene solution was filtered through a small layer of silica gel for separation of tars and dried over $CaCl_2$. A small quantity of silica gel was added to the dried solution and the solvent was removed in vacuum. The solid residue was extracted with hexane in a Soxhlet extractor. The precipitate which formed in the extract was filtered and an additional quantity of product was obtained from the filtrate.

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SPATIAL STRUCTURE OF DERIVATIVES OF 1-NITROPHENYLPYRROLES

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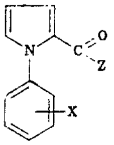
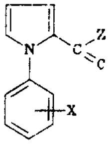
Combined ^{1}H and ^{13}C NMR data were used to show that 2-carbonyl derivatives of 1-nitrophenylpyrroles (aldehydes, acids, esters, and amides) have primarily the S-trans-configuration. Oximes of 1-nitrophenyl-2-formylpyrroles exist as a mixture of S-trans-syn- and S-cis-anti-isomers.

Lowered IR frequencies for the carbonyl groups in 2-substituted 1-nitrophenylpyrroles suggest strong conjugation of the substituent to the pyrrole ring (Table 1). This raises the barrier to rotation around the single bond between the substituent and the heterocycle. Such conjugation is strongest in the two steric conformations S-cis- and S-trans-.



S-cis



S-trans

This work studies the spatial structure of 2-substituted carbonyl derivatives of 1-nitrophenylpyrroles such as acids, esters, amides, and oximes. 1-Nitrophenyl-2-formylpyrroles are the starting materials for synthesis of all these compounds.

The classical method for oxidation of a carbonyl group to a carboxylate is the reaction with silver ions [1, 2]. In the case of 1-nitrophenyl-2-formylpyrrole this method does not give positive results because of the slight solubility of the aldehyde in water. Use of other stronger oxidants leads to polymerization or decomposition of the pyrrole ring [3]. We were able to oxidize the aldehyde group to the carboxylate with potassium permanganate in sulfolane; the reaction in acetone requires too great a volume of solvent. Esters and amides which can be used for identification were synthesized based on these acids. The acids themselves are extremely easily decarboxylated (heating for 15-20 min at the melting point), which is a convenient method for synthesis of the 2-substituted 1-arylpyrroles.

The question of the spatial structure of carbonyl compounds more often than not is decided using ^{1}H NMR spectra and dipole moments. Thus, it was found in [4, 5] that 2-formyl-, 2-acetyl-, and 2-benzoylpyrroles have dipole moments near to those calculated for the S-trans-position of the carbonyl group. Besides this, it is known [6] that for an S-trans-position of

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*Deceased.

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