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Depending on the amount of bromine, the bromination of 1-(4-nitrophenyl)-2-formylpyrrole with bromine in chloroform without a catalyst gives 5-bromo and 4,5-dibromo derivatives. 4-Bromo-1-(4-nitrophenyl)-2-formylpyrrole is formed in the presence of excess AlCl₃, while a mixture of 3,4- and 4,5-dibromo derivatives with preponderance of the latter is formed with excess bromine. The results are compared with the literature data on the bromination of 2-formylpyrrole, 2-formylfuran, and 2-formylthiophene and are interpreted with allowance for the electronacceptor effect of the p-nitrophenyl substituent attached to the nitrogen atom of the pyrrole ring.

Formylpyrroles readily undergo substitution reactions under the influence of brominating agents, during which the meta-orienting effect of the formyl group is displayed quite distinctly [1]. Thus 2-formylpyrrole forms 4- and 5-bromo derivatives in a ratio of 96.5: 3.5 [2]. Quaternary immonium salts of 2-formylpyrrole and its complexes with AlCl₃ intensify the effect of the substituent [3, 4], and substitution takes place exclusively in the 4 position.

The aim of the present research was to investigate the bromination of 1-(4-nitrophenyl)-2-formylpyrrole (I) and to ascertain the effect of an acceptor substituent attached to the nitrogen atom of the heteroring on the reactivity and selectivity in the case of substitution. We established that bromine water oxidizes I to give dibromomaleinimide [5], and bromination was therefore carried out in dry chloroform to avoid oxidative processes.

Aldehyde I undergoes resinification when N-bromosuccinimide (NBS) is used as the brominating agent. This is apparently associated with the radical mechanism of the action of NBS [6]. In dilute solution I reacts with bromine to give substitution products in $\sim 90\%$ yield; depending on the conditions used to carry out the synthesis and the molar ratio of the reagents, the substitution products differ with respect to both the position and number of bromine atoms in the pyrrole ring. The benzene ring remains inert with respect to bromine.



Bromination was carried out in the presence of $AlCl_3$ and without it. The results are presented in Table 1. The rate of monosubstitution is somewhat higher when $AlCl_3$ is used than when it is absent.

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TABLE 1. Results of the Bromination of 1-(4-Nitropheny1)-2-formylpyrrole under Various Conditions

Molar ratio o agents, mole	of the re- /mole of I	Time, h	Temp. °C	Amounts in the reaction product, %				
В́г _г	AlCi3		Lompi, C	II	111	IV	v	
1		2	20	100				
$\frac{2}{2}$	_	4	20	- 60	40		-	
ī,	2,5	ī	20			100	_	
2	2,5	16	20		10	90	-	
2	2,5	5	61		80		20	

TABLE 2. PMR Spectra of I-V

Com - pound	δ, ppm (J, Hz)									
		benzene ri	ing							
	Сно	1-H	2-H	3-H	4-H	5-H				
I III IV V	9,62 9,34 9,33 9,31 9,44	8,32 (9) 8,33 (9) 8,23 (9) 8,29 (9) 8,30 (9)	7,51 (9) 7,42 (9) 7,33 (9) 7,45 (9) 7,39 (9)	7,19ª 7,06 (4,3) 7,17 7,18 (1)	6,48 ^b 6,50 (4,3)	7,13 ^C 7,26 (1) 7,24				

$$a_{J_{35}} = 1.7$$
 Hz. $b_{J_{34}} = 4$ Hz. $c_{J_{45}} = 3$ Hz

An inverse ratio of the rates is observed in the case of disubstitution, in which the reaction in the case of complexes of pyrrole I with AlCl₃ takes place only when the mixture is heated up to the boiling point of chloroform. Monobromo compound II, which remains in the reaction mixture (when AlCl₃ is absent), is resinified after 20 h, while dibromo compound III is resinified after 32 h; this is apparently due to the action of the liberated HBr. The complexes of pyrroles II and III with AlCl₃ are more stable: Resinification was not observed when the mixtures were refluxed for 20 h. Compound III is also formed by the action of 1 mole of bromine on monobromo compound II. The introduction of a third bromine atom in the pyrrole ring to give a tribromo-substituted aldehyde was not observed under any conditions.

The reaction products were analyzed from the PMR spectra. The ratio of the isomers was determined from the integral intensities of the aldehyde protons. The results show that complexing with $AlCl_3$ has a substantial effect on both the rate and the direction of substitution.

The signals of the protons of the benzene ring in the PMR spectra of II-V (Table 2) were in accordance with the chemical shifts that are characteristic for nitrobenzene derivatives and the spin-spin coupling constants (SSCC) corresponding to ortho-oriented hydrogen atoms [7]. The signals of the protons of the pyrole ring in II have SSCC that characterize them as 3-H and 4-H [7], whereas the SSCC of the 3-H and 5-H protons in the spectrum of IV is 1 Hz. We did not isolate isomer V in individual form, and its structure was established from the spectrum of the mixture obtained after the reaction. Compounds III and V differ with respect to the constant of long-range coupling of the aldehyde proton with the 5-H proton; for V this constant is 1 Hz, which is characteristic for isomers of this type [8], whereas it is absent for III. The signal of the proton of the pyridine ring in the spectrum of isomer V is found at weaker field than the signal of the proton of isomer III, which also confirms its a position. The signals of the benzene ring in the spectrum of isomer V were assigned in accordance with their intensities with respect to the 1-H and 2-H signals for isomer III.

The UV spectra of bromo compounds II-IV differ from the spectrum of pyrrole I [9] with respect to small bathochromic shifts, which is characteristic for bromo derivatives of pyrrole compounds [1]. The IR spectra confirm the presence of all of the principal fragments and functional groups. The mass spectra reveal the number of bromine atoms in the molecule, which was determined from the peaks of the molecular ions that contain ⁸¹Br [7]. The fragmentation of the molecules under the influence of electron impact proceeds in conformity with the principles established for 1-(4-nitrophenyl)pyrrole derivatives, and the spectra contain all of the characteristic peaks for compounds of this series [10].

Com-	UV spect	rum	IR spectrum, cm ⁻¹				Mass spectrum			
	λ_{max}			NO ₂			м	% of M		
F	nm	lg ε	C≈0	v _{as}	$s v_s v_s$	v_{C-N}	(1, %)	M+2	M+4	
II	289	4,459	1666	1542	1349	865	294	102,2	_	
III	287	4,408	1687	1525	1350	869	(12,1) 372	201,9	94,9	
IV	288	4,430	1669	1540	1350	864	(43,2) 294 (69,3)	101,8		

TABLE 3. Spectral Characteristics of Bromo Derivatives of 1-(4-Nitrophenyl)-2-formylpyrrole

TABLE 4. Physicochemical Characteristics of II-IV

Com - pound	°C, ℃	Found, %			Empirical	Calculated, %				Yield,	
		с	н	Br	N	formula	с	н	Br	N	%
II III IV	124 137 131	44,5 35,5 44,4	2,5 1,7 2,3	27,5 42,5 26,9	9,7 7,4 9,8	$\begin{array}{c} C_{11}H_7BrN_2O_3\\ C_{11}H_6Br_2N_2O_3\\ C_{11}H_6BrN_2O_3 \end{array}$	44,7 35,3 44,7	2,4 1,6 2,4	27,1 42,8 27,1	9,5 7,5 9,5	92 90 92

If one compares the results obtained in this study with the data for 2-formylpyrrole, it is apparent that the substituent attached to the heteroatom has a substantial effect on the selectivity of the bromination of 1-(4-nitropheny1)-2-formylpyrrole.

Competition between the α -orienting effect of the heteroatom and the meta-orienting effect of the substituent occurs in electrophilic substitution reactions in the case of fivemembered heterorings with an electron-acceptor substituent in the α position. Relatively small differences in the activities of the α and β positions are characteristic for unsubstituted pyrrole, and electrophilic substitution is directed almost exclusively to the 4 position when a meta orienter such as the CHO group is present in the 2 position [11]. In 1-(4-nitrophenyl)-2-formylpyrrole (I) the acceptor substituent attached to the nitrogen atom deactivates the pyrrole ring with respect to electrophilic reagents and, in particular, decreases the electron density on the heteroatom. As a consequence of this, the ability of the ring nitrogen atom to stabilize cationic σ complexes, which is particularly important for the formation of β -substituted compounds (see [11]), should be reduced substantially. As a result, despite the effect of the formyl group, bromination takes place in the free α position, and only an increase in the electron-acceptor capacity of the CHO group due to complexing with AlCl, makes it possible to obtain a product of substitution in the 4 position (IV). The effect of the p-nitrophenyl substituent attached to the ring nitrogen atom is also displayed in the formation of dibromo-substituted compounds (in the presence of AlCl₃): Whereas 2-formylpyrrole forms 4,5- and 3,4-dibromo derivatives in approximately equal amounts, while N-methy1-2-formy1pyrrole gives mainly the 3,4 isomer [4], in the case of aldehyde I 4,5-dibromo-substituted III predominates. 2-Formylpyrrole and its N-methylsubstituted derivative are capable of undergoing replacement of all three ring hydrogen atoms by bromine [4], but this was not observed for aldehyde I. Thus 1-(4-nitropheny1)-2formylpyrrole differs substantially from 2-formylpyrrole with respect to its regioselectivity in bromination and very much resembles furfural and 2-formylthiophene; this is due to the effect of the substituent attached to the nitrogen atom of the pyrrole ring.

EXPERIMENTAL

The PMR spectra of solutions of the compounds in CDCl₃ were recorded with a Tesla BS-497 spectrometer (100 MHz) relative to tetramethylsilane. The UV spectra of solutions in 96% ethanol were recorded with a Specord UV-vis spectrophotometer. The IR spectra of mineral oil suspensions between NaCl plates were obtained with a UR-20 spectrometer. The mass spectra were recorded with a Varian Mat CH_6 spectrometer; the source temperature was 180°C, and the emission current was 100 μA .

1-(4-Nitropheny1)-5-bromo-2-formy1pyrrole (II). A solution of 0.26 ml (0.005 mole) of Br₂ in 50 ml of chloroform was added to a solution of 1.08 g (0.005 mole) of I in 100 ml of dry chloroform, and the solution was allowed to stand at room temperature for 2-3 h. It

was then washed with 5% aqueous bisulfite solution and water, and the organic layer was separated and dried with CaCl₂. The chloroform was removed by distillation, and the precipitated crystals were reprecipitated from solution in chloroform by the addition of hexane. The yield was 2.7 g (92%).

4,5-Dibromo-1-(4-nitropheny1)-2-formy1pyrrole (III). A solution of 0.26 ml (0.005 mole) of Br₂ in 25 ml of chloroform was added to a solution of 1.08 g (0.005 mole) of I in 100 ml of chloroform, and the mixture was allowed to stand at room temperature for 3 h. The same amount of bromine dissolved in chloroform was then added, and the mixture was allowed to stand for 5 h. It was then worked up as indicated above. The yield was 3.35 g (90%).

<u>1-(4-Nitropheny1)-4-bromo-2-formy1pyrrole (IV)</u>. A 3.3-g (0.025 mole) sample of AlCl₃ was added with stirring to a solution of 2.16 g (0.01 mole) of I in 100 ml of chloroform, the mixture was stirred for 30 min, and a solution of 0.52 ml (0.01 mole) of Br_2 in 25 ml of chloroform was added dropwise. After 1 h, the reaction mixture was worked up as indicated above. The yield was 2.7 g (92%).

4,5-Dibromo-1-(4-nitropheny1)-2-formy1pyrrole (III) and 3,4-Dibromo-1-(4-nitropheny1)-2-formy1pyrrole (V). A 3.3-g (0.025 mole) sample of AlCl₃ was added with stirring to asolution of 2.16 g (0.01 mole) of pyrrole I in 100 ml of chloroform. The mixture wasstirred for 30 min, and a solution of 1.04 ml (0.01 mole) of Br₂ in 50 ml of chloroformwas added dropwise. The mixture was refluxed for 5 h, after which it was cooled and workedup as indicated above.

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