PROTONATION OF ACETYL AND FORMYL DERIVATIVES OF PYRROLE

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By electronic spectroscopy and PMR spectroscopy it has been shown that the protonation of derivatives of β- and α-acetylpyrroles and the corresponding formylpyrroles in 14-26 N H_2SO_4 takes place at the oxygen atom of the carbonyl group. The α derivatives substituted by an alkyl group (CH_3, C_2H_5) in position 4 have a similar structure of the conjugate acids in concentrated H_2SO_4. Under the same conditions, the α derivatives not substituted in position 4 are capable of adding a proton to C_4 of the pyrrole ring.

The study of the protonation of carbonyl derivatives of pyrrole is of considerable interest in view of the fact that these compounds are the starting materials in syntheses of dipyrrylmethanes which proceed under conditions of acid catalysis. In a preceding investigation, we studied the structure of the conjugate acids of β- and α-ethoxycarbonylpyrroles, and it was shown that the protonation of the β-ethoxycarbonyl derivatives in 22-25 N H_2SO_4 takes place at the C_5 atom of the pyrrole ring. The conjugate acid of a 2-ethoxycarbonylpyrrole unsubstituted in position 5 has a similar structure. The structure of the stable forms of the conjugate acids of the 5-alkyl-2-ethoxycarbonylpyrroles corresponds to the addition of the proton to the pyrrole nitrogen atom. A rise in the electron-accepting properties of the substituent in the pyrrole ring may lead to a change in the direction of protonation of the molecule. Thus, a study of the IR spectra of the salts of some acetyl- and formylpyrroles has shown that the structure of the conjugate acids in the crystals corresponds to the addition of the proton to the oxygen atom of the carbonyl group [2, 3]. In the present work, we have studied the protonation of β- and α-acetylpyrroles and the corresponding formylpyrroles (I-XII) in aqueous solutions of sulfuric acid by the method of electronic spectroscopy and PMR spectroscopy. As model compounds we used the corresponding β- and α-ethoxycarbonylpyrroles, which have conjugate acids of established structure. The experimental results obtained are given in Tables 1 and 2.

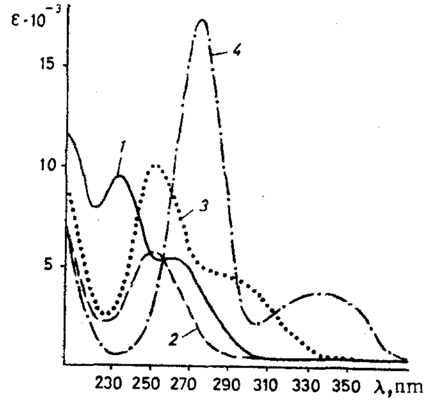

Fig. 1. UV spectra of the bases (1, 3) and of the conjugate acids (2, 4) of β-pyrrole derivatives: 1, 2) 3-ethoxycarbonyl-2,4-dimethylpyrrole; 3, 4) 3-acetyl-2,4-dimethylpyrrole (II).

β-Carbonyl Derivatives of Pyrrole. A comparison of the UV spectra of neutral molecules of acetyl-, formyl- and ethoxycarbonylpyrroles shows their considerable similarity in the 210-360-nm region, both with respect to the positions and to the intensities of the absorption bands (Table 1 and Fig. 1). In addition to this, the changes in the spectra of the compounds investigated and of model compounds on protonation proved to be opposite.

In the series of ethoxycarbonylpyrroles, on passing from the neutral molecules to the monocations, in which protonation takes place at the C_5 atom, a hypsochromic shift of the absorption bands is observed, and in the spectra of the conjugate acids

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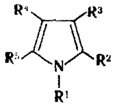
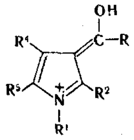
TABLE 1. UV Spectra of the Bases and of the Conjugate Acids of Acetyl and Formyl Derivatives of Pyrrole



I–XII

Compound	R^1	R^2	R^3	R^4	R^5	Medium	λ_{max}, nm	ε
I	H	H	$COCH_3$	CH_3	H	H_2O 20 N H_2SO_4	280, 248 330, 275,5	3910 12600 2100 22900
II	H	CH_3	$COCH_3$	CH_3	H	H_2O 16 N H_2SO_4	290, 253 335, 276	4700 9800 2580 15900
III	H	CH_3	$COCH_3$	CH_3	CH_3	H_2O 23 N H_2SO_4	300, 254,5 360, 277,5	4100 10100 2920 18800
IV	H	CH_3	$COCH_3$	CH_3	C_2H_5	H_2O 17 N H_2SO_4	300, 254 360, 277,5	3860 9470 1580 17600
V	H	CH_3	CHO	CH_3	H	H_2O 14 N H_2SO_4	295, 257 335, 271,5	4650 12700 2300 19600
VI	C_2H_5	CH_3	CHO	H	CH_3	H_2O 16 N H_2SO_4	295, 263 335, 280	7550 12000 2860 19500
VII	H	$COCH_3$	CH_3	CH_3	CH_3	H_2O 26 N H_2SO_4	316, 265 330, 302	18600 4650 10700 13900
VIII	H	$COCH_3$	CH_3	C_2H_5	CH_3	H_2O 26 N H_2SO_4	315, 265 330, 302	19500 4950 11500 14200
IX	H	CHO	CH_3	CH_3	CH_3	H_2O 14 N H_2SO_4	315,5 270 330, 293	19200 6400 8650 15700
X	H	CHO	CH_3	CH_3	H	H_2O 16 N H_2SO_4	304, 270 340, 291,5	15100 8600 5670 18000
XI	H	$COCH_3$	CH_3	H	CH_3	H_2O 20 N H_2SO_4	305 260 319 —	20200 4480 22000 —
XII	H	CHO	CH_3	H	CH_3	H_2O 25 N H_2SO_4	309 260 298 —	21500 4120 17700 —

there is one transition at 252-255 nm (ε ~5000). The protonation of acetyl- and formylpyrroles leads to a considerable bathochromic displacement of both transitions and to a sharp rise in the intensity of the short-wave band. It must be emphasized that the spectra of the conjugate acids of all the β-acetyl and β-formylpyrroles studied, regardless of the presence or absence of substituents in the α position to the pyrrole nitrogen, are extremely similar and are characterized in each case by a strong band in the 272-280-nm region (ε ~20,000) and by a medium-intensity band in the 330-360-nm range (ε ~2000). These facts show a change in the center of protonation of the molecules investigated as compared with the model β-ethoxycarbonylpyrroles. On the other hand, the marked difference in the spectra of the conjugate acids investigated from the spectra of the N-protonated forms of 2-ethoxycarbonylpyrrole shows the absence of protonation on the pyrrole nitrogen atom. And, finally, the changes in the spectra on passing from the neutral molecules to the cations show a considerable change in the π-electronic system when the compounds investigated undergo protonation. All these facts permit the assumption that the structure of the conjugate acids of the β-acetyl- and β-formylpyrroles corresponds to the addition of a proton at the oxygen atom of the carbonyl group [structures (Ia-VIa)].



I–VIa

A consideration of the PMR spectra of compounds (I-VI) (Table 2, Fig. 2) leads to a similar conclusion. The assignment of the signals given in Table 2 follows from a comparison of the spectra of the compounds investigated. A measurement of the dependence of the chemical shifts on the concentration of sulfuric acid in the range from 10 to 35.5 N permitted the measured parameters of the spectra to be assigned to the protonated forms unambigously. The nature of the change in the PMR spectra on passing from the bases to the conjugate acids is advantageously illustrated for the case of the 5- and 4-unsubstituted compounds (II) and (VI) (Fig. 2). In the spectrum of the neutral molecule of (II) the signal of the 4-CH_3 protons appears in the form of a doublet because of spin–spin coupling (SSC) with the 5-H, the signal of which forms

TABLE 2. Chemical Shifts in the PMR Spectra of the Bases and Conjugate Acids of the Acetyl- and Formylpyrrole Derivatives (I-XII)

Compound	Medium	δ, ppm*				
		R^1	R^2	R^3	R^4	R^5
I	$(CD_3)_2CO$	8,35 br	7,47 m	2,28	2,21 d	6,55 m
	25 *N* H_2SO_4	—	8,25 br	2,30	2,88	6,85 br
II	$(CD_3)_2CO$	8,37 br	2,43	2,28	2,17 d	6,35 q
	12—18 *N* H_2SO_4	—	2,76	2,24	2,62	6,60 br
III	$CDCl_3$	8,39 br	2,46	2,38	2,14	2,08
	12—32 *N* H_2SO_4	—	2,78	2,15	2,63	2,15
IV	$CDCl_3$	8,37 br	2,46	2,36	2,16	1,11 t 2,56 q
	25 *N* H_2SO_4	—	2,87	2,22	2,69	1,22 t 2,55 q
V	$CDCl_3$†	8,78 br	2,50	9,94	2,27 d	6,34 m
VI	CCl_4	1,32 t 3,88 q	2,49	9,59	6,06	2,22
	25 *N* H_2SO_4	1,37 t 4,13 q	2,61	8,53	6,58	2,29
VII	$CDCl_3$	9,14 br	2,38	2,16	1,89	2,24
	25 *N* H_2SO_4	—	2,38	2,45	2,01	2,70
VIII	$CDCl_3$	9,32 br	2,36	2,18	0.97 t — q	2,22
	25 *N* H_2SO_4	—	2,36	2,46	1,05 t — q	2,70
IX	$CDCl_3$	9,99 br	9,37	2,22	1,89	2,22
	23—28 *N* H_2SO_4	—	8,03	2,24	1,98	2,45
X	$CDCl_3$	9,89 br	9,54 d	2,26	1,99 d	6,86 d
	23—28 *N* H_2SO_4	—	8,30	2,32	2,08	7,90 br
XI	$CDCl_3$	9,28	2,38	2,22	5,76 d	2,32
	12—33 *N* H_2SO_4	—	2,45	2,45	6,40 br	2,66
XII	$CDCl_3$	9,99 br	9,44	2,31	5,84 d	2,31
	25 *N* H_2SO_4	—	8,18	2,41	6.51 br	2,57

*No index – singlet; d – doublet; t – triplet; q – quartet; br – broad signal; m – multiplet.

†It was impossible to measure the PMR spectrum in 25 N H_2SO_4 because of the instantaneous self-condensation of the substance.

a quartet at 6.35 ppm ($J_{4,5} = 1.3$ Hz). In the weakest field there is the broadened singlet of 2-CH_3. The width of the signal is obviously due to SSC with the proton of the heteroatom of the ring. The singlet of the acetyl group appears at 2.28 ppm. In the spectrum of the conjugate acid measured in 17 N H_2SO_4 the broadened signal of the 5-H methine proton is shifted downfield relative to the spectrum of the base by 0.25 ppm.* The signals of the methyl groups in positions 2 and 4 are also shifted downfield and appear in the form of singlets at 2.76 and 2.62 ppm. The singlet of the protons of the acetyl group is observed in a stronger field relative to the spectrum of the base ($\Delta\delta = 0.04$ ppm). On passing from the neutral molecule to the conjugate acid in compound (VI) again a downfield displacement of the signals of the 4-H and of the protons of the methyl groups in positions 2 and 5 takes place with no change in their multiplicities. Such changes in the spectra do not correspond to the protonation of the molecules investigated in the pyrrole ring. In addition to this, an upfield shift of the signal of the formyl proton ($\Delta\delta = 1.49$ ppm) into the region of aromatic protons serves as an indirect proof of the protonation of these compounds at the oxygen atom of the carbonyl group. Changes of a similar nature are observed in the PMR spectra of all the compounds of this series and correspond to structures (Ia-VIa) for the conjugate acids.

The protonation of compounds (I-VI) in concentrated acids possibly takes place at the other center. However, the determination of the structure of the cations under these conditions requires further investigation.

α-Carbonyl Derivatives of Pyrrole. With respect to the comparative proton-accepting capacity of the main centers, all the α derivatives can be divided into two groups: compounds containing an alkyl group (CH_3, C_2H_5) in position 4, and compounds unsubstituted in this position.

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*In solution in 10.3 N H_2SO_4, the 5-H signal is not observed, while the positions and multiplicities of the other signals are unchanged. This gives grounds for assuming that the absence of the 5-H signal under these conditions is due to a high rate of proton exchange.

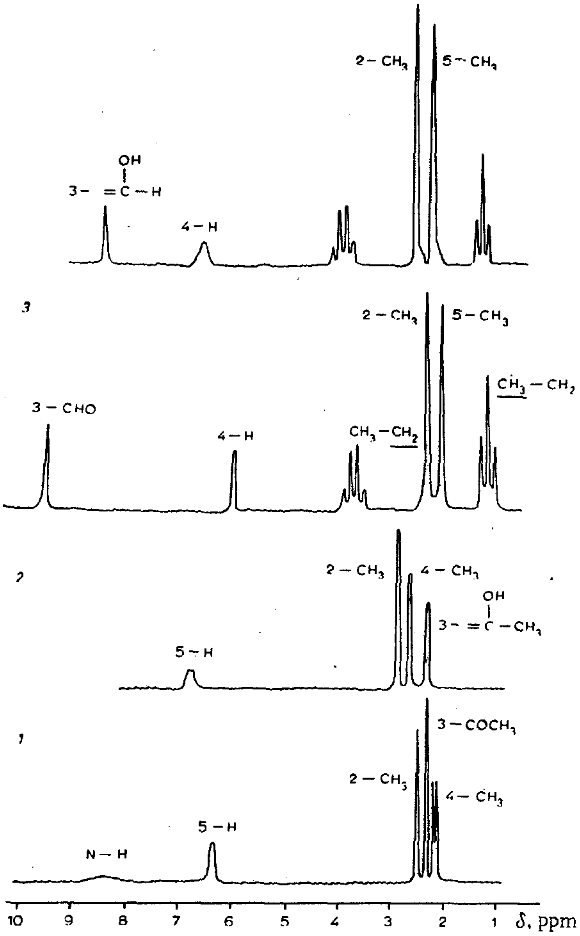


Fig. 2. PMR spectra of the bases (1, 3) and of the conjugate acids (2, 4) of β-carbonyl derivatives of pyrrole: 1, 2) 3-acetyl-2,4-dimethylpyrrole (II); 3, 4) 1-ethyl-2,5-dimethylpyrrole-3-carbaldehyde (VI).

The electronic spectra of the bases of the two groups are similar to the spectra of the corresponding model ethoxycarbonylpyrroles (Table 1, Fig. 3). They are characterized by the presence of a high-intensity band in the 304-316-nm range (ε 15,100-21,500) and of a medium-intensity band at 260-270 nm (ε 4120-8600).

The spectra of the cations of compounds substituted in position 4, regardless of the presence or absence of a substituent at C_5, differ sharply from the spectra of the conjugate acids of the corresponding ethoxycarbonylpyrroles over the whole range of concentrations of H_2SO_4. Thus, the formation of cations for the 5-alkyl-2-ethoxycarbonylpyrroles, in which protonation takes place at the nitrogen atom of the pyrrole ring, is accompanied by a hypsochromic shift and by a hypochromic effect, and in the spectra of the conjugate acids there is in each case a single transition at 253-263 nm (ε 4800-5600). The spectrum of the conjugate acid of 2-ethoxycarbonyl-3,4-dimethylpyrrole, in which the addition of the proton takes place at the unsubstituted C_5 atom, has similar parameters (λ_{max} 277 nm, ε 5000).

The electronic spectra of the cations (VII-X) are similar to one another and are characterized by two transitions – in the 302-291-nm region (ε 13,900-18,000) and the 330-340-nm region (ε 5670-11,500). Consequently, the formation of cations in acetyl- and formylpyrroles substituted in position 4 leads to a bathochromic shift, to an increase in the intensity of the short-wave band, and to a lowering of the intensity of the long-wave transition. The changes in the spectra on passing from the neutral molecules to the cations in these compounds are similar in nature to those observed in the protonation of β-acetyl- and β-formylpyrroles, which is evidence in favor of the protonation of compounds (VII-X) at the oxygen atom of the carbonyl group. A similar structure may be ascribed to the 4-unsubstituted (XI) and (XII) compounds in 20-26 N H_2SO_4. The spectra of the cations of these compounds are extremely similar to the spectra of the conjugate acids of (VII-X) and differ sharply from the spectrum of the conjugate acid of 2-ethoxycarbonyl-3,5-dimethylpyrrole.

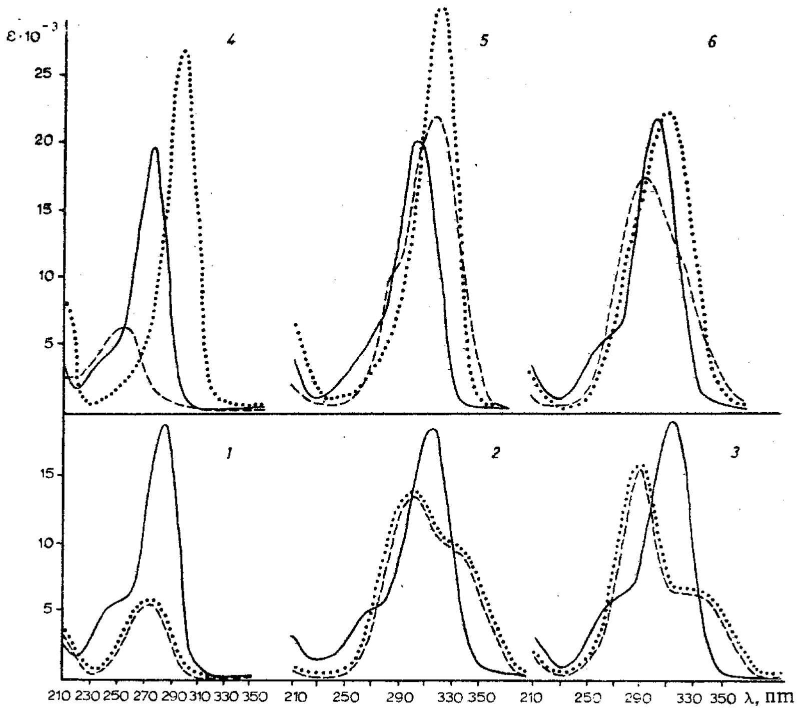
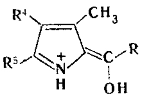


Fig. 3. UV spectra of the bases (——) and of the conjugate acids of α-carbonyl derivatives of pyrrole in 14-26 N H_2SO_4 (– – – –) and in 35.5 N H_2SO_4 (. . . .): 1) 2-Ethoxycarbonyl-3,4,5-trimethylpyrrole; 2) 2-acetyl-3,4,5-trimethylpyrrole (VII); 3) 3,4,5-trimethylpyrrole-2-carbaldehyde (IX); 4) 2-ethoxycarbonyl-3,5-dimethylpyrrole; 5) 2-acetyl-3,5-dimethylpyrrole (XI); 6) 3,5-dimethylpyrrole-2-carbaldehyde (XII).

A consideration of the PMR spectra gives additional information on the structure of the conjugate acids of the series of compounds studied. In the first place, in the spectra of the cations of (VII-IX) the signals of the methyl protons in positions 3, 4, and 5 and in the case of (X) those in positions 3 and 4 are shifted downfield relative to the spectra of the bases and consist of singlets. In the second place, the signal of the methine proton in the spectrum of the conjugate acid of (X) is shifted downfield by 1.04 ppm. In the third place, the signal of the formyl proton in the spectra of the cations of compounds (IX) and (X) is shifted upfield by 1.24-1.34 ppm as compared with its position in the spectra of the bases. Thus, the PMR spectra do not correspond to protonation in the pyrrole ring. At the same time, the latter fact shows the addition of the proton to the oxygen atom of the carbonyl group [structures (VIIa-Xa)]. A similar tendency in the change in the PMR spectra on passing from the bases to the cations is observed for compounds (XI) and (XII) in 12-33 N H_2SO_4.



VII-X a

On passing to concentrated acids, no changes whatever are observed in the UV spectra of the cations of the 4-alkyl-2-acetylpyrroles and 4-alkyl-2-formylpyrroles. At the same time, in the spectra of the 4-unsubstituted compounds (XI) and (XII) investigated and those of the model 2-ethoxycarbonyl-3,5-dimethylpyrrole a considerable change takes place: a strong band appears in the 290-325-nm region (ε 22,000-26,000). Similar changes have been described previously for a number of β-unsubstituted phenylpyrroles to which, on this basis, a β-pyrroleninium structure was ascribed [5]. This gives grounds for assuming the possibility of the protonation of the compounds studied at the C_4 atom or the presence of an equilibrium of the two protonated forms in concentrated acids.

So far as can be judged from the results of measurements of the UV spectra in time, the stability of the proposed β form falls in the sequence of the 2-formyl > 2-acetyl > 2-ethoxycarbonyl derivatives symbatically with the fall in the electron-accepting properties of the substituent in the pyrrole ring.

EXPERIMENTAL

The UV spectra of compounds (I-XII) were measured on a Hitachi EPS-3T spectrophotometer. Weighed samples of the substances were dissolved in 96% ethanol and were then diluted with standardized solutions of sulfuric acid. The concentration of ethanol in the solution measured was 1%. The spectra of the bases were obtained by diluting the initial solutions with water.

The PMR spectra were measured on a JNM-C-60HL spectrometer in $CDCl_3$, $(CD_3)_2CO$, and in sulfuric acid solutions. The chemical shifts are given in the δ scale. Tetramethylsilane was used as internal standard for the solutions in $CDCl_3$ and $(CD_3)_2CO$, and sodium 4,4-dimethyl-4-silapentane-1-sulfonate for the solutions in H_2SO_4.

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