ASSOCIATION AND RELATIVE ACIDITIES OF 2-SUBSTITUTED 5-TRIFLUOROACETYLPYRROLES

N. I. Golovanova, B. A. Trofimov,
A. I. Mikhaleva, and S. E. Korostova

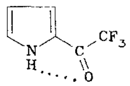
UDC 547.74:543.422.4

The acidities of 2-substituted 5-trifluoroacetylpyrroles were studied by IR spectroscopy from the shift of the frequency of the NH stretching vibration ($\Delta\nu_{NH}$) in the presence of dimethylformamide (DMF) relative to the band of vibrations of free NH. The existence of a correlation relationship between $\Delta\nu_{NH}$ and $\Sigma\sigma_I$ constitutes evidence that the acidities of pyrroles are determined primarily by the inductive effect of the substituents in the 2 and 5 positions of the pyrrole ring. The low probability of the formation of an intramolecular NH...O=C hydrogen bond in the investigated molecules was demonstrated.

The ability to form associates with various bases is an important property of pyrroles that to a great extent determines their physicochemical and biological behavior [1, 2]. 2-Substituted 5-trifluoroacetylpyrroles, which have recently become accessible [3, 4], are of promise as potentially biologically active compounds and as starting substances for the synthesis of other functionally substituted pyrroles.

In the present research we undertook a study of the association and acidic properties of the indicated group of pyrroles by IR spectroscopy. The IR spectra of 2-substituted 5-trifluoroacetylpyrroles (Table 1) in the form of KBr pellets and concentrated solutions in CCl_4 are characterized by absorption bands of associated C=O (1645 cm^{-1}) and NH (3320 cm^{-1}) groups. The bands of the associates disappear as the concentration of the pyrroles in CCl_4 decrease (Fig. 1), and only bands of the monomers (1670 and 3450 cm^{-1}) are observed. The introduction of substituents into the 2 position of the pyrrole ring does not have an appreciable effect on the frequency and integral intensity ($A_{C=O}$) of the C=O band for the unassociated compounds (Table 1).

The spin–spin coupling of the 4-H (in the 4 position) and ^{19}F nuclei through space observed for such 5-trifluoroacetylpyrroles [5] constitutes evidence for a preferred conformation with a cis orientation of the nitrogen and oxygen atoms. An intromolecular NH•••O=C hydrogen bond is possible in this sort of conformation [6, 7]:



We studied the possibility of the realization of this sort of hydrogen bond from the effect of donor solvents (acetonitrile, pyridine, and triethylamine) on the frequencies of the stretching vibrations of the C=O and NH groups. The intermolecular hydrogen bonds of pyrroles are cleaved in strong bases, and stronger NH•••B bonds with solvent molecules (B) are formed. The decrease in the νNH frequency as the basicity of the medium increases constitutes evidence for this (Table 2). In the case of cleavage of the intramolecular hydrogen bond the frequency of the stretching vibrations of the C=O group should be shifted to the high-frequency region [8]; however, $\nu_{C=O}$ remains constant on passing from acetonitrile to pyridine and triethylamine (Table 2). These data may constitute evidence for the absence of intramolecular NH•••O=C hydrogen bonds in the investigated molecules. The fact that the frequencies and integral intensities of the C=O bands have the same values as in the case of N-substituted pyrroles X-XII also serves as a confirmation of this.

Irkutsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR, Irkutsk 664033. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 772-774, June, 1984. Original article submitted September 19, 1983; revision submitted November 11, 1983.

0009-3122/84/2006-0625$08.50

TABLE 1. Frequencies of the C=O and NH Groups and Relative Acidities (ΔνNH) of Pyrroles

Compound	R^1	R^2	νC=O, cm^{-1}		Free A C=O	ΔνNH, cm^{-1}			ΔνNH, cm^{-1}
			associate	free		free	associate	in DMF	
I	H	CH_3	1646	1669	5,5	3460	3330	3210	250
II	H	C_6H_5	1648	1672	5,8	3450	3320	3175	275
III	H	p-$C_2H_5C_6H_4$	1645	1668	5,7	3453	3320	3183	270
IV	H	p-ClC_6H_4	1647	1670	5,6	3437	3310	3147	290
V	H	p-BrC_6H_4	1646	1670	5,7	3440	3310	3150	290
VI	H	p-$CH_3OC_6H_4$	1644	1669	5,8	3455	3325	3185	270
VII	H	2-Naphthyl	1647	1669	5,7	3440	3310	3160	280
VIII	H	2-Furyl	1643	1671	5,8	3440	3305	3155	285
IX	H	2-Thienyl	1644	1670	5,7	3430	3290	3130	300
X	C_2H_5	C_6H_5	—	1674	5,6				
XI	$CH_2CH_2Si(C_2H_5)_3$	C_6H_5	—	1672	5,7				
XII	$CH_2CH_2Si(C_2H_5)_3$	2-Thienyl	—	1673	5,6				

TABLE 2. Effect of the Solvent on the νNH and νC=O Values of Pyrrole III

Solvent	νNH, cm^{-1}	νC=O, cm^{-1}
Acetonitrile	3270	1670
Pyridine	3160	1668
Triethylamine	3140	1671

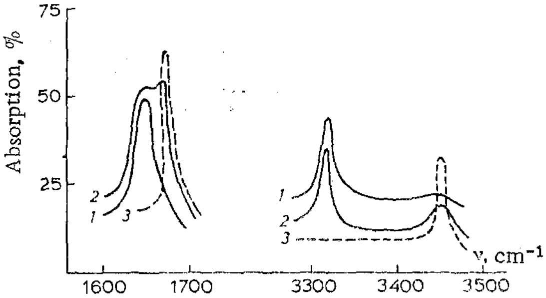


Fig. 1. Absorption bands of the C=O and NH groups in 2-phenyl-5-trifluoroacetylpyrrole: 1) in KBr; 2) in CCl_4, c = 10^{-2} mole/liter; 3) in CCl_4, c = $5 \cdot 10^{-4}$ mole/liter.

We have previously studied the hydrogen bonding of 2,3- and 2,5-substituted pyrroles with DMF and have shown that the ΔνNH value (the shift of the frequency of the NH stretching vibration relative to νNH^{free}) when DMF is added to a solution in CCl_4 is a linear function of the sum of the inductive constants of the substituents ($\Sigma\sigma_I$) [9]. Combined correlation treatment of the ΔνNH values from [9] and from Table 1, except for the data for 2-tert-butyl-5-trifluoroacetylpyrrole and 2,5-diphenylpyrrole (steric effects), leads to considerable improvement in the correlation:

$$\Delta\nu NH = (144 \pm 3) + (232 + 8)\Sigma\sigma_I,\ n = 25,\ r = 0.996,\ S_0 = 6$$

The existence of this sort of correlation (Fig. 2) confirms the conclusions that the acidities of pyrroles (ΔνNH) are determined primarily by the inductive effect of the substituents. The strength of the hydrogen bond increases as the acceptor properties of the substituents in the pyrrole ring become more pronounced. The frequency of the stretching vibration of the free NH group decreases as the –I effect of the substituents becomes more intense and is linearly related to the $\Sigma\sigma_I$ values by the equation

$$\nu NH^{free} = (3491 \pm 4.9) - (80.7 \pm 10.9)\Sigma\sigma_I,\ n = 16,\ r = 0.973,\ S_0 = 6.4$$

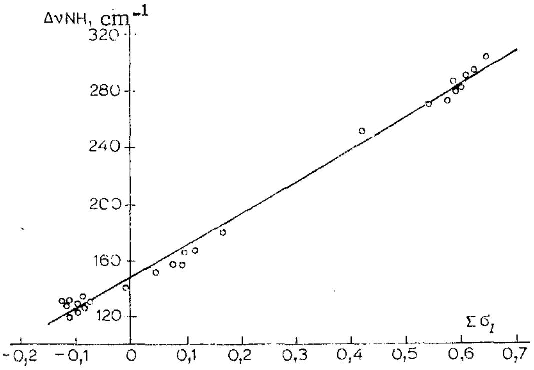
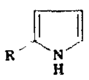
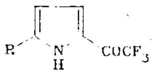


Fig. 2. Relationship between ΔνNH and $\Sigma\sigma_I$.

TABLE 3. Dependence of νNH^{free} and ΔνNH (cm^{-1}) on the Structure of the Pyrrole

R					$\Delta\nu NH^{free}$	ΔΔνNH
	νNH^{free}	ΔνNH	νNH^{free}	ΔνNH		
CH_3	3492	132	3460	250	32	118
C_6H_5	3486	156	3450	275	36	119
2-Furyl	3475	165	3440	285	35	120
2-Thienyl	3465	180	3430	300	35	120

A comparison of the data in Table 3 shows that the difference ($\Delta\nu NH^{free}$) in the frequencies of the vibrations of free NH groups and the difference (ΔΔνNH) in the acidities between pyrroles and trifluoroacetylpyrroles with identical substituents R have approximately constant values (~35 and 120 cm^{-1}, respectively). This indicates additivity of the effect of the trifluoroacetyl group on the spectroscopic acidity and νNH^{free} when there are different substituents in the 2 position of the pyrrole ring.

It is apparent from a comparison of the frequencies of the stretching vibrations of the NH groups in 2-methyl-5-acetylpyrrole (3445 cm^{-1}) (in CCl_4, $c = 10^{-4}$ mole/liter) [7] and 2-methyl-5-trifluoroacetylpyrrole (3460 cm^{-1}) that the acetyl group decreases νNH^{free} to a greater extent (by ~25 cm^{-1}) than one should have expected from its –I effect ($\sigma_I = +0.26$). The low νNH^{free} value in the case of acetylpyrrole is possibly due to the formation of an intramolecular hydrogen bond with the carbonyl oxygen atom, which should have a high basicity in this case. In an attempt to estimate the basicity of the carbonyl group in III from the shift of the band of the OH stretching vibration of the phenol we were unable to observe a band of an associated hydroxy group, and this confirms the low basicity of the oxygen atom in the investigated compounds.

EXPERIMENTAL

2-Substituted 5-trifluoroacetylpyrroles were synthesized by the method in [3]. The IR spectra were recorded with a Specord 75 IR spectrometer. The concentration of the pyrroles in CCl_4 ranged from $5 \cdot 10^{-4}$ to 10^{-1} mole/liter, and the concentration in triple solutions in CCl_4 ranged from 0.05 to 0.5 mole/liter; $c_{DMF} = 0.1$-1.0 mole/liter.

LITERATURE CITED

1. A. Gossauer, Die Chemie der Pyrrole, Berlin (1974).
2. R. A. Jones and G. P. Bean, The Chemistry of Pyrroles. Organic Chemistry. A Series of Monographs, London (1977).
3. B. A. Trofimov, A. I. Mikhaleva, S. E. Korostova, L. N. Sobenina, A. N. Vasil'ev, and L. V. Balashenko, Zh. Org. Khim., No. 15, 2042 (1979).

4. B. A. Trofimov, S. E. Korostova, A. I. Mikhaleva, R. N. Nesterenko, M. V. Sigalov, V. K. Voronov, and R. I. Polovnikova, Khim. Geterotsikl. Soedin., No. 8, 1058 (1981).
5. B. A. Trofimov, M. V. Sigalov, S. N. Tandura, G. A. Kalabin, A. I. Mikhaleva, and S. E. Korostova, Izv. Akad. Nauk SSSR, Ser. Khim., No. 5, 1122 (1979).
6. L. V. Kazanskaya, T. A. Melent'eva, and V. M. Berezovskii, Zh. Obshch. Khim., 38, 2020 (1968).
7. R. W. Guy and R. A. Jones, Aust. J. Chem., 19, 107 (1966).
8. G. C. Pimentel and A. L. McClellan, The Hydrogen Bond, Freeman, San Francisco (1960).
9. B. A. Trofimov, A. I. Shatenshtein, É. S. Petrov, M. I. Terekhova, N. I. Golovanova, A. I. Mikhaleva, S. E. Korostova, and A. N. Vasil'ev, Khim. Geterotsikl. Soedin., No. 5, 632 (1980).

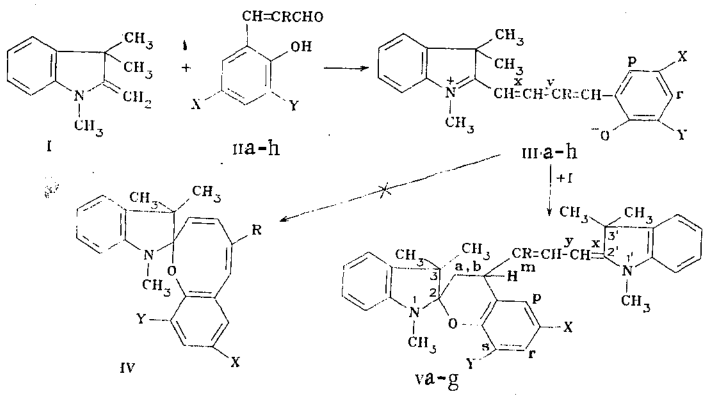
REACTION OF THE FISCHER BASE WITH NITRO- AND BROMO-SUBSTITUTED o-HYDROXYCINNAMALDEHYDES

Yu. M. Chunaev, N. M. Przhiyalgovskaya,
M. A. Gal'bershtam, L. N. Kurkovskaya,
and M. V. Karpova

UDC 547.441:547.754

The Fischer base reacts with α-ethyl-5-nitro-, 5-bromo-, and 3,5-dibromo-2-hydroxycinnamaldehydes to give bisindoline spirochromans, with 3-bromo-5-nitro-2-hydroxycinnamaldehyde to give a mixture of a spirochroman and a monoindoline merocyanine, and with 3,5-dinitro-2-hydroxycinnamaldehyde to give only a merocyanine. The monoindoline merocyanines obtained do not display a tendency to undergo intramolecular cyclization to give spiro-2H-oxocines.

It is well known that the first attempt [1] to obtain new photochromic compounds, viz., indoline spiro-2H-oxocines (IV), by the reaction of the Fischer base (I) with o-hydroxycinnamaldehydes (IIa, b) was unsuccessful. It was recently shown [2] that the indicated reaction proceeds through a step involving the formation of merocyanine structure III; however, instead of the desired spirocyclization to give an eight-membered ring (IV), the next step involves the addition of a second molecule of the methylene base, as a consequence of which the final products are bisindoline spirochromans V, which do not have photochromic properties.



a $X=Y=R=H$; b $X=NO_2$, $Y=R=H$; c $X=NO_2$, $Y=H$, $R=CH_3$; d $X=NO_2$, $Y=H$, $R=C_2H_5$; e $X=Y=Br$, $R=H$; f $X=Br$, $Y=R=H$; g $X=NO_2$, $Y=Br$, $R=H$; h $X=Y=NO_2$, $R=H$

In the present research we continued our study of the reaction of the Fischer base with various substituted o-hydroxycinnamaldehydes in order to search for conditions under which the formation of spiro-2H-oxocines becomes possible. It is known that the formation of "di-

---

D. I. Mendeleev Moscow Chemical Technology Institute, Moscow 125047. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 775-778, June, 1984. Original article submitted May 19, 1983.