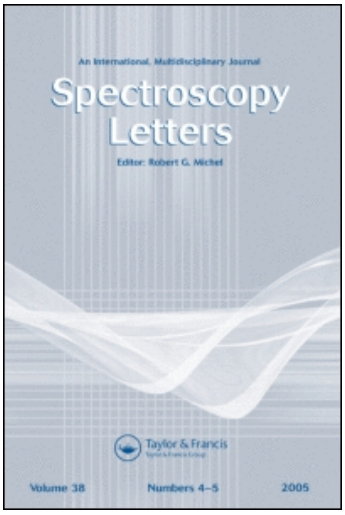

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Carbon-13 NMR Studies of Nitrogen Compounds. II.-^{13}C NMR Chemical Shifts of N-Substituted Formamides in Neutral and Acidic Solvents

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CARBON-13 NMR STUDIES OF NITROGEN COMPOUNDS. II.- ^{13}C NMR CHEMICAL SHIFTS OF N-SUBSTITUTED FORMAMIDES IN NEUTRAL AND ACIDIC SOLVENTS

^{13}C NMR, N-Substituted Formamides, SCS of the formamido group, Protonation

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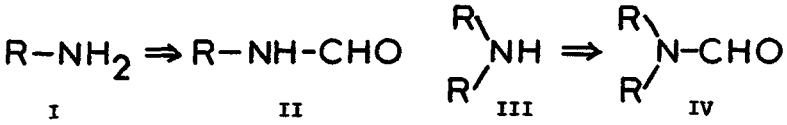
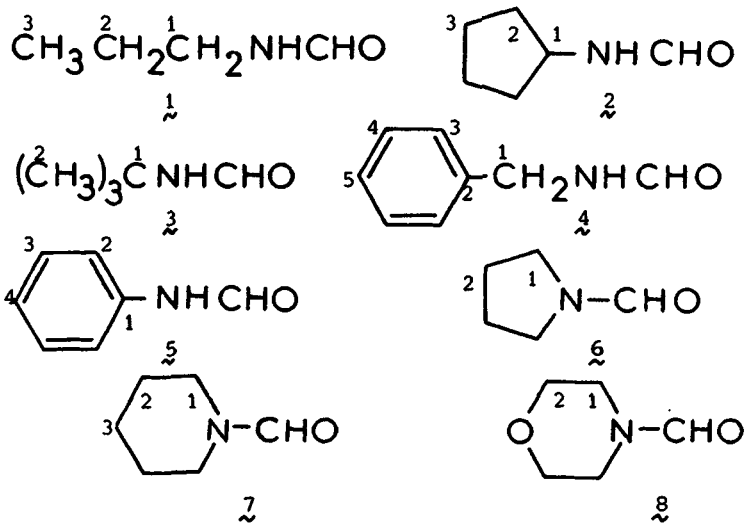
With the purpose to determine the structure of N-formyl pyrazolines[1] and their salts, we have undertaken a preliminary study of the effect produced by the replacement of an amino group by a formamido group on the carbon chemical shifts of the substituent R, both in a neutral solvent (hexadeuteriodimethylsulphoxide) and in an acidic solvent (trifluoroacetic acid).



I II III IV

The following N-substituted and N,N-disubstituted Formamides have been studied :



EXPERIMENTAL.

The ^{13}C NMR spectra were recorded at 20.0 MHz in the FT-mode on a Varian FT-80 spectrometer (spectral width = 5000 Hz; acquisition time = 0.8 s; pulse width = 8 μs). The compounds were studied at 28±2 °C. In DMSO-d_6 solutions, the chemical shifts were measured, in the noise decoupled mode, with respect to the central line of the solvent and referred to the TMS signal by the relationship $\delta_{TMS} = \delta_{DMSO} + 39.6$ (δ in ppm)[2]. In the case of trifluoroacetic acid solutions, field frequency control was effected by means of the deuterium resonance of DMSO-d_6 placed in an internal capillary tube; chemical shifts were determined with respect to TMS as an internal standard. The accuracy of the chemical shifts is better than 0.1 ppm.

Most of the samples used in this study were prepared by known methods[3,4]; the synthesis of the other compounds has been described elsewhere[5].

RESULTS AND DISCUSSION.

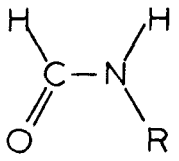
The chemical shifts in DMSO-d_6 are listed in table 1, those in trifluoroacetic acid in table 2. In open-chain N-monosubstituted formamides the *trans* (Z) conformation IIa is strongly preferred over the *cis* (E) conformation IIb, as has been shown by various analytical methods[6].

TABLE 1

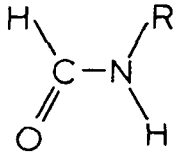
^{13}C Chemical shifts of formamides in DMSO-d_6 from internal TMS

N°	Isomer	% [a]	C-1	C-2	C-3	C-4	C-5	CHO
1	*Trans*	85	39.1	22.5	11.3			161.1
	Cis	15	42.9	24.3	10.8			164.7
2	*Trans*	88	49.1	32.4	23.5			160.45
	Cis	12	53.0	33.5	23.5			163.75
3	*Trans*	76	50.0	28.6				160.6
	Cis	24	49.5	30.5				162.7
4	*Trans*	90	40.9	138.95	127.4	128.4	127.0	161.1
	Cis	10	44.7	b	c	c	c	165.0
5	*Trans*	73	138.6	119.9	129.25	124.2		160.1
	Cis	27	138.6	118.3	129.8	124.2		163.0
6 [d]	*Trans*	--	42.4	23.6				160.3
	Cis	--	45.15	24.4				
7 [d]	*Trans*	--	39.6	24.8	24.2			160.4
	Cis	--	45.7	26.2				
8 [d]	*Trans*	--	40.0	65.9				161.1
	Cis	--	45.2	66.85				

[a] See text for the determination of these values; [b] This signal is not observed; [c] Signal overlapped by the peaks of *trans* isomer; [d] *Cis* and *trans* correspond to *cis* and *trans* carbons.



Trans IIa



Cis IIb

Assignments of chemical shifts of transoid and cisoid groups is based on the literature data[7] and on the intensity of resonance signals. In tha case of cyclic formamides, 6 to 8, our assignment

TABLE 2

^{13}C Chemical shifts of formamides in TFAA from internal TMS

N°	Isomer	%[a]	C-1	C-2	C-3	C-4	C-5	CHO
1	*Trans*	88	41.75	22.8	11.4			165.3
	Cis	12	45.7	24.4	10.9			168.1
2	*Trans*	85	54.45	33.2	24.4			165.9
	Cis	15	58.3	34.1	24.6			168.1
3	*Trans*	58	53.5	29.5				165.0
	Cis	42	53.5	30.3				166.4
4	*Trans*	80	46.4	135.2	130.8	129.5	130.5	167.0
	Cis	20	50.0	b	c	c	c	169.85
5	*Trans*	53	136.25	122.5	130.1	127.4		163.9
	Cis	47	b	120.35	130.7	127.7		163.9
6[d]	*Trans*	--	45.2	24.7				163.8
	Cis		48.3	25.4				
7[d]	*Trans*	--	43.8	25.75	24.5			163.9
	Cis		50.4	27.0				
8[d]	*Trans*	--	42.6	67.0				164.8
	Cis		48.1	67.9				

[a]See text for the determination of these values; [b] These signals are not observed; [c]Signals overlapped by the peaks of *trans* isomer; [d]*Cis* and *trans* correspond to *cis* and *trans* carbons.

is coherent with the reported[8] chemical shifts of N,N-dialkylformamides.

The relative amounts of *cis* and *trans* isomers were determined from the integrated peak intensities of selected carbons. Depending on the conformation, the mechanism of spin-lattice relaxation of the α-carbons, C_1, is different[9]; thus, this carbon has not been used in the evaluation of "conformer" ratio, except for compound 4 since for this formamide the chemical shifts of the other carbons are not available for the *cis* form (see tables 1 and 2).

The increasing proportion of the *cis* form with the increasing bulk of R-group agree with the results of a proton NMR study[10]. Moreover, the reduced percentage of *trans* isomer in N-t-butyl formamide 3 in acidic medium is consistent with the results of Laplanche and Rogers[11].

SUBSTITUENT EFFECTS DUE TO FORMAMIDO GROUP.

Substituent effects which arise from the replacement of amino protons by a formyl group are gathered in table 3.

In general, shieldings of carbons α and β to the nitrogen atom are observed, like those produced by the acetamido group[12]. Moreover α carbons *syn* to the carbonyl oxygen are more shielded than

TABLE 3

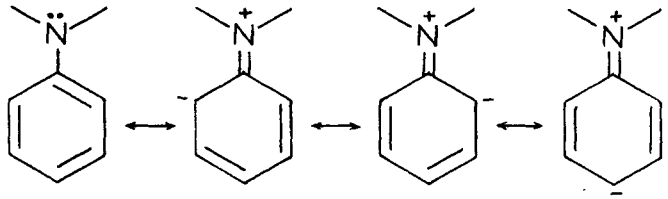
Substituent chemical shifts due to N-formylation[a]

N°	Isomer	C-1	C-2	C-3	C-4	C-5
1	*Trans*	-4.65	-4.1	0.2		
	Cis	-0.85	-2.3	-0.3		
2	*Trans*	-3.7	-3.4	0.1		
	Cis	0.2	-2.3	0.1		
3	*Trans*	3.35	-3.7			
	Cis	2.85	-1.8			
4	*Trans*	-5.0	-5.35	0.3	0.3	0.8
	Cis	-1.2	--	--	--	--
5	*Trans*	-9.9	5.6	0.2	7.9	
	Cis	-9.9	4.0	0.75	7.9	
6	*Trans*	-4.2	-1.7			
	Cis	-1.45	-0.9			
7	*Trans*	-7.4	-2.0	-0.9		
	Cis	-1.3	-0.8			
8	*Trans*	-6.3	-1.6			
	Cis	-1.1	-0.65			

[a] $\Delta\delta = \delta_{Formamide} - \delta_{Amine}$; amines chemical shifts[12].

the *anti* ones. This fact has been attributed to the two following reasons: electric-field associated with the carbon-oxygen bond[13] and, more recently, steric compression[9]. Whatever the origin of this effect, its magnitude and direction are depending on the steric hindrance around the nitrogen atom; thus for 3, the β effect is deshielding (+ 5 ppm). We explain this result by strong steric interactions leading either to a distorsion of the nitrogen bond angles or to the predominance of energetically more stable non-planar rotamers.

For compound 5, the *ortho* and *para* carbons are more deshielded than in aniline. It can be assumed that the canonical structures B, C and D are disfavoured by the formyl group on the nitrogen, thus the non-conjugative interactions (inductive effects) became the most important; these conclusions agree with the values of σ_R and σ_I for the amino and the formamido groups[14].



A B C D

EFFECTS DUE TO THE PROTONATION.

In trifluoroacetic acid there is an equilibrium between the neutral molecula and the protonated species (O- and N-protonation). The displacements of ^{13}C chemical shifts due to protonation are shown in table 4: all the signals are deshielded save those of *ipso* aromatic carbons in compounds 4 and 5. Furthermore, carbonyl shift in the *trans* isomer is more deshielded relative to the *cis* form.

The comparison between these values and those obtained from the protonation of amines[12] suggest the predominance of the O-protonation in formamides, a result in agreement with other observations[15].

TABLE 4

Changes in chemical shifts in formamides due to the "protonation"[a]

N°	Isomer	C-1	C-2	C-3	C-4	C-5	CHO
1	*Trans*	2.65	0.3	0.1			4.2
	Cis	2.8	0.1	0.1			3.4
2	*Trans*	5.35	0.8	0.9			5.45
	Cis	5.3	0.6	1.1			4.35
3	*Trans*	3.5	0.9				4.4
	Cis	4.0	-0.2				3.7
4	*Trans*	5.5	-3.75	3.4	1.1	3.5	5.9
	Cis	5.3	---	---	---	---	4.85
5	*Trans*	-2.35	2.6	0.85	3.2		3.8
	Cis	---	2.05	0.9	3.5		3.6
6	*Trans*	2.8	1.1				3.5
	Cis	3.15	1.0				
7	*Trans*	4.2	0.95	0.3			
	Cis	4.7	0.8				
8	*Trans*	2.6	1.1				
	Cis	2.9	1.05				

[a] $\Delta\delta = \delta_{TFAA} - \delta_{DMSO\text{-}d_6}$

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