Nuclear Magnetic Resonance Study of *cis–trans*-Isomerism in Some *N*-Alkylformamides and *N*-Alkylacetamides and their *O*-Protonated Cations in Anhydrous Acids

By **M. Liler**, School of Chemistry, The University, Newcastle upon Tyne NE1 7RU

cis–trans-Isomerism has been observed in the n.m.r. spectra (at 90 MHz and 27 °C) of the *O*-protonated cations of *N*-alkylformamides (alkyl = Me, Et, or Pr^i), *N*-methylacetamide, and the corresponding *NN*-dimethyl derivatives in 100% sulphuric acid, pure fluorosulphuric acid, and 72% perchloric acid. The spectra of the unprotonated amides in water and deuteriochloroform have also been recorded for comparison. The isomer ratios have been determined and the effect of *O*-protonation on the chemical shifts and the coupling constants discussed.

N.M.R. spectra have shown amides to be *O*-protonated in concentrated and anhydrous acids.[1–5] For *N*-alkylamides *O*-protonated cations should exist in two isomeric forms (*cis* and *trans*). These have not been detected in earlier work.[4] La Planche and Rogers [6] apparently detected the existence of two isomers for *N*-alkylformamides in 100% sulphuric acid, but owing to insufficient separation of lines at 60 MHz have not been able to estimate their relative amounts (except for *N*-t-butylformamide). In the present work we have established that at 90 MHz the *cis*- and *trans*-isomers of the *O*-protonated cations of *N*-alkylamides can be observed and most spectral parameters for both isomers obtained in 100% sulphuric acid and in pure fluorosulphuric acid. In 72% perchloric acid the tautomeric equilibrium of the *N*- and *O*-protonated forms [5] is insufficiently shifted for *N*-alkylamides in favour of the *O*-protonated form and the spectra show considerable NH exchange. The *O*-protonated form of *NN*-dimethylamides is quite stable in that medium, however, and the spectra of *O*-protonated cations of *NN*-dimethylformamide and *NN*-dimethylacetamide in 72% perchloric acid are therefore also reported.

For comparison, the spectra of all the amides studied have also been recorded in aqueous solution and in deuteriochloroform. A preliminary investigation of the spectra of *N*-methylformamide in aqueous solution at various pH values was necessary in order to establish under what conditions NH exchange is absent, in view of a report [7] of exchange at pH values 2—3. No exchange was found [8] in the pH range 2—5, and the spectra of all *N*-alkylamides were therefore recorded at pH 3.

EXPERIMENTAL

Materials.—*N*-Methyl- and *NN*-dimethyl-formamide and -acetamide were B.D.H. laboratory reagents. They were vacuum-distilled before use. *N*-Ethylformamide was synthesized from pure formic acid and ethylamine by refluxing equimolar amounts. The product was distilled and the fraction of b.p. 198 °C was used. *N*-Isopropylformamide was prepared likewise (b.p. 196—199 °C).

Fluorosulphuric acid was a commercial product, supplied by the Ozark-Mahoning Co. 100% Sulphuric acid was prepared by mixing 98% acid with oleum until a maximum m.p. (+ 10·4 °C) was obtained. 72% Perchloric acid was B.D.H. AnalaR. It was diluted to 60 and 64% (w/w) for use in a few experiments. Deuteriochloroform of 99·5% isotopic purity was a product of Beta Scientific Ltd. The aqueous solution of pH 3 was a phthalate buffer solution, prepared according to Bates.[9] Solutions in all these solvents were 1M in the amide.

N.m.r. Spectra.—All n.m.r. spectra were recorded at 27 °C on a Brüker HFX n.m.r. spectrometer, operating at 90 MHz. Tetramethylsilane was used as a reference and lock signal for solutions in deuteriochloroform. In aqueous solutions sodium 2,2-dimethyl-2-silapentane-5-sulphonate was used as internal reference and lock signal. The same compound was a suitable reference in 60—72% perchloric acid, but it proved unstable in 100% sulphuric acid and pure fluorosulphuric acid. Therefore it was thought preferable not to introduce any references into these solutions, but to use the solvent peaks as internal references and lock signals. The chemical shifts of the solvent peaks were then determined relative to water as external reference. The chemical shifts of the solvent peaks are somewhat dependent upon the solute and its concentration. For the 1M solutions of the amides studied, the solvent peaks were found to have chemical shifts in the range of $-11{\cdot}0 \pm 0{\cdot}1$ p.p.m. for sulphuric acid and $-10{\cdot}7 \pm 0{\cdot}1$ p.p.m. for fluorosulphuric acid. These mean values were used in the recalculation of the measured shifts to the δ scale (Tables). The absolute values of the shifts are not therefore highly accurate. The relative shifts in the *cis–trans* patterns and the coupling constants were obtained from expanded spectra (to 1 or 2 Hz cm^{-1}) and are accurate to $\pm 0{\cdot}1$ Hz.

The estimation of the relative amounts of the *cis*- and *trans*-isomers was carried out by three methods, depending on the degree of overlap of the lines. In cases of well separated lines (as for *N*-methylformamide) spectra were accumulated in a Fabritek 1074 signal averaging computer before integration. In *O*-protonated cations the relative shifts of the resonances of the *cis*- and *trans*-*N*-alkyl groups are as a rule smaller, and in a few instances (*e.g.*, for *N*-ethylformamide in fluorosulphuric acid) the overlap of the lines is extensive, so that an estimate of the relative amounts of the isomers was possible only by use of a Du Pont 310

[1] G. Fraenkel and C. Niemann, *Proc. Nat. Acad. Sci. U.S.*, 1958, **44**, 688.
[2] G. Fraenkel and C. Franconi, *J. Amer. Chem. Soc.*, 1960, **82**, 4478.
[3] R. J. Gillespie and T. Birchall, *Canad. J. Chem.*, 1963, **41**, 148.
[4] T. Birchall and R. J. Gillespie, *Canad. J. Chem.*, 1963, **41**, 2642.
[5] M. Liler, *Chem. Comm.*, 1971, 115.
[6] L. A. La Planche and M. T. Rogers, *J. Amer. Chem. Soc.*, 1964, **86**, 337.
[7] D. G. de Kowalewski and V. J. Kowalewski, *Arkiv Kemi*, 1960—1961, **16**, 373.
[8] M. Liler, *Spectrochim. Acta*, 1972, **28A**, 186.
[9] R. G. Bates, 'Determination of pH,' J. Wiley and Sons, New York, 1964, p. 156.

curve resolver. In most instances of overlapping multiplets the line separation was sufficient to allow integration by weighing the peaks. The agreement of this method with the curve resolver was satisfactory (to within ±2%).

RESULTS AND DISCUSSION

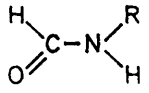
The six amides were studied in five different media. As the greatest interest attaches to the changes that the amide spectra undergo with change of medium or upon protonation, the results will be presented to highlight these points. However, some remarks, which apply to all amides, will be made first.

The *cis–trans*-patterns of *N*-alkyl- and *NN*-dialkylamides, reported here in aqueous buffer solution at pH 3, collapse in more acidic solution owing to *N*-protonation.[10-12] The *O*-protonated form is in tautomeric equilibrium with the *N*-protonated form according to equation (1) and emerges as dominant only in concentrated acids, where water is not available in sufficient

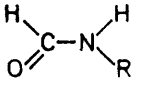
$$R{-}\overset{\overset{O}{\|}}{C}{-}\overset{+}{N}H_3,pH_2O \rightleftharpoons R{-}\overset{\overset{OH}{\|}_{+}}{C}{=}NH_2,qH_2O + (p-q)H_2O \quad (1)$$

amount to stabilize the *N*-protonated form by hydrogen bonding.[5] Hydrogen-bonding stabilization of the *N*-protonated amide cations, like that of the analogous amine cations,[13] clearly decreases in the order primary > secondary > tertiary. So, although the differences in the basicity of these amides in the largely aqueous acid are relatively small,[11,12] the *O*-protonated form of primary amides is not observable in 72% perchloric acid (because the NH protons are in rapid exchange with the solvent medium [14]), while that of tertiary amides is perfectly stable under the same conditions. This is because *N*-protonated cations of tertiary amides are less solvation-stabilized in the first instance and change more readily to *O*-protonated cations in media of low water activity. The position for *N*-alkylamides in 72% perchloric acid is intermediate, the NH coupling to the *N*-methyl group being observable for *N*-methylamides, but in a state of partial collapse owing to exchange with the solvent (Figure 1, curve A). This corresponds to a lifetime of the NH protons in the *O*-protonated cation of *ca.* 0·5 s, as estimated from the intensity ratio according to Loewenstein and Meiboom.[15] By contrast, in 100% sulphuric acid and in pure fluorosulphuric acid the *O*-protonated cations of these amides are perfectly stable (Figure 1,B).

The terminology of *cis–trans* isomerism used in the Tables and in the Discussion section is the same as that of La Planche and Rogers,[6] *i.e.* (I) and (II) with the corresponding *O*-protonated cations (III) and (IV). The chemical shifts of all the resonances of the major *trans*-form have been obtainable in all cases, but some chemical shifts of the resonances of the minor *cis*-form have not, owing to overlapping lines. This is especially true of the

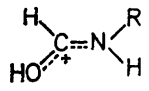


cis (I)

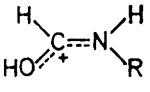


trans (II)

NH resonances, which are broadened by quadrupole relaxation of the ^{14}N nucleus, and in some instances also



cis (III)



trans (IV)

of the formyl proton resonance. The amounts of the *cis*- and *trans*- isomers have been estimated as a rule from the resonances of the *N*-alkyl groups. The resonances of the OH protons are observable only at low temperature (−90 °C),[3,4] but attempts to identify these resonances for the minor *cis*-form of the cation have failed, owing either to exchange broadening or to viscosity broadening of the resonances.

The multiplet structure of the formyl proton resonance is not resolved in some spectra. Only broadening is apparent, and therefore line widths at half-height are reported in the Tables ($w_{\frac{1}{2}}$).

N-*Methylformamide* (*Table* 1).—The *N*-methyl resonance of both isomers was observable in all media, the *cis*-form always appearing downfield from the *trans*-form. The relative shift of the two resonances ($\Delta\delta_{NMe}^{cis\text{-}trans}$) can be seen from Table 1 to be somewhat enhanced in the aqueous medium as compared with deuteriochloroform, and to be considerably reduced in the *O*-protonated cation. This fact and the smaller percentage of the *cis*-form in the cation are clearly responsible for difficulties encountered previously in attempts to observe *cis–trans* isomerism in the cation of this amide.[6,12] The percentage of the *cis*-form is especially low in pure fluorosulphuric acid (Figure 1,B). The coupling of the *N*-methyl group to the formyl proton [^4J(NMe–CH)] is enhanced by protonation. The coupling constants are in good agreement with the previously reported values.[4,6] The doublet of doublets of the *N*-methyl group of the *trans*-form shows asymmetry, both in fluorosulphuric acid (Figure 1,B) and in sulphuric acid. This second-order perturbation arises from the strong *cis*-coupling (see next paragraph) between the formyl proton and the NH proton in the *trans*-form ($J/\Delta\nu < 0{\cdot}2$). This AB part of the spectrum could not be analysed, however, because

[10] A. Berger, A. Loewenstein, and S. Meiboom, *J. Amer. Chem. Soc.*, 1959, **81**, 62.
[11] M. Liler, *J. Chem. Soc.* (*B*), 1969, 385.
[12] M. Liler, *J. Chem. Soc.* (*B*), 1971, 334.
[13] A. F. Trotman-Dickenson, *J. Chem. Soc.*, 1949, 1293.
[14] M. Liler, *J.C.S. Perkin II*, in the press.
[15] A. Loewenstein and S. Meiboom, *J. Chem. Phys.*, 1957, **27**, 1067.

of ^{14}N broadening. Coupling constants obtained by first-order rules may be inaccurate on this account by a few tenths of a Hz.

The formyl proton resonance of the *cis*-form is clearly observable at high field from that of the *trans*-form, but the large splitting by the NH proton leads to overlap of one half of the doublet with the formyl proton resonance

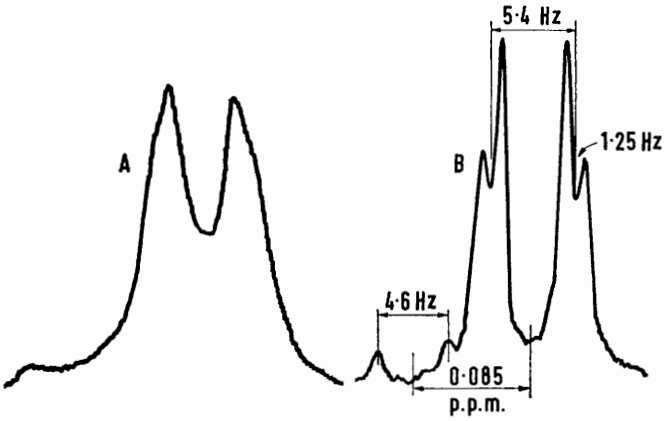


FIGURE 1 The *N*-methyl resonance of *N*-methylformamide in A, 72% perchloric acid and B, pure fluorosulphuric acid, both at 27°C and 90 MHz

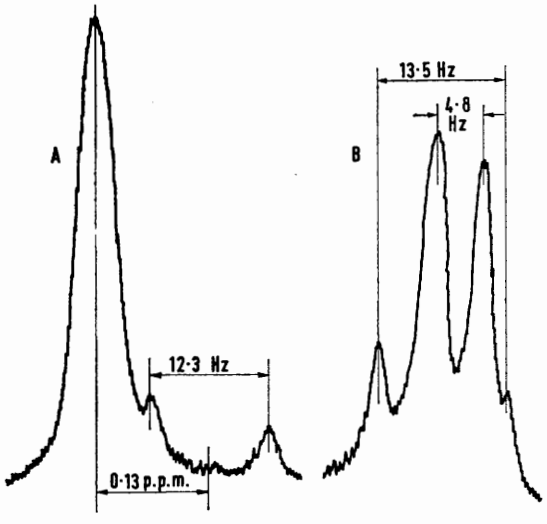
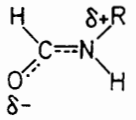


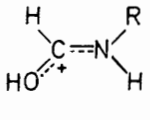
FIGURE 2 The formyl proton resonance at 27 °C and 90 MHz of A, *N*-methylformamide in deuteriochloroform and B, *N*-isopropylformamide in 100% sulphuric acid

of the *trans*-form in all media, except in deuteriochloroform (Figure 2,A). The large coupling constant of 12·3 Hz is closely similar to that in formamide.[16] The splitting of the formyl proton resonance in the *trans*-form, which was not resolvable in the unprotonated amide under the conditions of our experiments, is considerably enhanced by protonation. In the cation this resonance becomes an apparent doublet with ^3J(NH–CH) 4·5—4·6 Hz, in good agreement with the previous value [6] in 100% sulphuric acid of 5 Hz.

The reduction in the proportion of the *cis*-form in water as compared with deuteriochloroform, and the further reduction upon *O*-protonation, suggest that in the more polar, and therefore more nearly planar



(V)



(VI)

structures (V) and (VI), the non-bonded repulsions between the formyl proton and the *N*-methyl group are greater. The same trend is not so apparent when *N*-alkyl groups are larger (Et or Pr^i). The reasons for this are not clear.

N-*Ethylformamide* (*Table* 2).—*cis–trans*-Isomerism of this amide and its *O*-protonated cation is most clearly observable in the resonance of the methyl group, which shows two separate triplets in all media, except in fluorosulphuric acid, where there is some overlapping. The resonance of the *cis*-methyl group is always at lower field than that of the *trans*-group.

The methylene group resonance consists of two overlapping quintets under low resolution. Under high resolution (2 Hz cm^{-1}) the methylene group resonances of the unprotonated amide in both water and deuteriochloroform show a multiplet structure, which was sufficiently clear at least for the *trans*-form to enable the evaluation of both vicinal coupling constants and also of the formyl coupling constant. In the *O*-protonated amide the methylene resonance is virtually a regular quintet in both media, with some sign of formyl coupling, and therefore both vicinal coupling constants are reported as equal.

The formyl proton resonance of the *trans*-isomer of the unprotonated amide is broadened by coupling to the methylene group and to the NH proton, but protonation leads again to an apparent doublet. The formyl proton resonance of the *cis*-form is also a doublet, the low-field peak of which overlaps with the formyl proton resonance of the *trans*-form in most media.

The relative amounts of the two isomers do not show a clear trend upon *O*-protonation, but the proportion of the *cis*-form is considerably larger than for the *N*-methyl derivative. Only 12% *cis* was reported in the pure amide.[6]

N-*Isopropylformamide* (*Table* 3).—The CH*Me*$_2$ groups give doublet resonances, which are always found at lower field for the *cis*-isomer, the relative *cis–trans*-shift being noticeably reduced in water and especially upon protonation.

Owing to the relatively large amounts of the *cis*-isomer, the resonance of the C*H*Me$_2$ proton of the *cis*-form is clearly observable at 0·3—0·4 p.p.m. to high field from the resonance of the *trans*-form. This resonance is a virtual octet and therefore the coupling constant to the NH proton is closely similar to the CH–Me coupling constant.

[16] B. Sunners, L. H. Piette, and W. G. Schneider, *Canad. J. Chem.*, 1960, **38**, 681.

TABLE 1

N.m.r. spectra of the *cis*- and *trans*-isomers of *N*-methylformamide in deuteriochloroform, water, and anhydrous acids at 27 °C

	Amide				*O*-Protonated cation			
	$CDCl_3$		Water (pH 3)		Pure HSO_3F		100% H_2SO_4	
	cis	*trans*	*cis*	*trans*	*cis*	*trans*	*cis*	*trans*
% Isomer	11	89	7·8	92·2	5·3	94·7	7·7	92·3
δ_{CH}/p.p.m.	−8·03	−8·16		−8·04	(−7·8)	−7·95	(−8·2)	−8·31
δ_{NMe}/p.p.m.	−2·93	−2·81	−2·75	−2·62	−2·98	−2·89	−3·30	−3·20
$\Delta\delta_{NMe}^{cis\text{-}trans}$/p.p.m.	0·123		0·133		0·085		0·099	
δ_{NH}/p.p.m.		−7·1		−7·8		−8·20		−8·55
^3J(NH–NMe)/Hz	5·0	5·0	4·4	5·0	4·6	5·4	5·0	5·2
^4J(NMe–CH)/Hz		0·8		0·95	0·3	1·25		1·1
$w_{\frac{1}{2}}$(CH)/Hz †	d	4·5		5		d		d
^3J(NH–CH)/Hz †	12·3	(2)		(2)	(13)	4·5	(13)	4·6

The values in parentheses are uncertain, d = doublet. † Formyl proton.

TABLE 2

N.m.r. spectra of the *cis*- and *trans*-isomers of *N*-ethylformamide in deuteriochloroform, water, and anhydrous acids at 27 °C

	Amide				*O*-Protonated cation			
	$CDCl_3$		Water (pH 3)		Pure HSO_3F		100% H_2SO_4	
	cis	*trans*	*cis*	*trans*	*cis*	*trans*	*cis*	*trans*
% Isomer	18	82	16·5	83·5	21	79	15·5	84·5
δ_{CH}/p.p.m.	(−8·03)	−8·11	−7·83	−7·99	(−8·07)	−8·15	(−8·2)	−8·37
δ_{NCH_2}/p.p.m.	−3·26	−3·30	−3·26	−3·23	−3·58	−3·61 †		−3·78 †
δ_{Me}/p.p.m.	−1·18	−1·14	−1·13	−1·11	−1·31	−1·29	−1·51	−1·47
$\Delta\delta_{Me}^{cis\text{-}trans}$/p.p.m.	0·045		0·025		0·024		0·040	
δ_{NH}/p.p.m.		−6·62		−7·8		−8·4		−8·8
^3J(NH–CH_2)/Hz	*ca.* 6·5	5·7	*ca.* 5·6	5·7		7·4		7·2
^4J(CH_2–CH)/Hz		0·8		0·8		*ca.* 0·7		
^3J(CH_2–Me)/Hz	7·1	7·3	7·3	7·4	7·3	7·4	7·2	7·2
$w_{\frac{1}{2}}$(CH)/Hz ‡	d	4·4	d	6	d	d	d	d
^3J(NH–CH)/Hz ‡	(>10)		14 ± 0·5	(2)	(14)	4·6	(14)	4·6

The values in parentheses are uncertain, d = doublet. † Quintet. ‡ Formyl proton.

TABLE 3

N.m.r. spectra of the *cis*- and *trans*-isomers of *N*-isopropylformamide in deuteriochloroform, water, and anhydrous acids at 27 °C

	Amide				*O*-Protonated cation			
	$CDCl_3$		Water (pH 3)		Pure HSO_3F		100% H_2SO_4	
	cis	*trans*	*cis*	*trans*	*cis*	*trans*	*cis*	*trans*
% Isomer	30	70	28	72	33	67	24	76
δ_{CH}/p.p.m.	(−8·10)	−8·06	(−8·02)	−7·91	(−7·98)	−7·96	−8·21	−8·19
δ_{NCH}/p.p.m.	−3·7	−4·14		−3·9	−3·81	−4·17	−4·03	−4·36
δ_{NH}/p.p.m.		−6·35		−7·6		−8·3		−8·66
δ_{Me}/p.p.m.	−1·22	−1·16	−1·17	−1·12	−1·21	−1·17	−1·40	−1·36
$\Delta\delta_{Me}^{cis\text{-}trans}$/p.p.m.	0·061		0·048		0·038		0·045	
^3J(NH–CH)/Hz		8·0			*ca.* 6·6 ‡	*ca.* 6·6 ‡	*ca.* 6·8 ‡	*ca.* 6·8 ‡
^4J(CH–NCH)/Hz		0·8						
^3J(CH–Me)/Hz	6·6	6·6	6·6	6·6	6·6	6·6	6·8	6·8
$w_{\frac{1}{2}}$(CH)/Hz †	d	5·2	d	d	d	d	d	d
^3J(CH–NH)/Hz †	(12)		(12)	2·0	(13)	4·8	13·5	4·8

† Formyl proton. ‡ Approx. the same as the CH–Me splitting, since the CH resonance is a virtual octet. The values in parentheses are uncertain, d = doublet.

The formyl proton resonance of this amide is different from those of the *N*-methyl and *N*-ethyl derivatives in that the resonance of the *cis*-form is on the low-field side of the resonance of the *trans*-form, the high-field peak overlapping with that of the formyl proton of the *trans*-form in most spectra. The exception was the spectrum in sulphuric acid, where the *cis*-doublet straggles the *trans*-doublet (Figure 2,B). The coupling constants found are in good agreement with those reported previously.[6] The relative shift of the formyl resonances of the *cis*- and *trans*-forms is reduced by protonation.

The proportion of the *cis*-form is higher with *N*-isopropylformamide than with *N*-ethylformamide, both in the unprotonated and in the protonated amide. In the pure amide only 12% *cis* was reported.[6]

Relative Amounts of the cis- *and* trans-*Isomers.*—In general the order of increasing proportion of the *cis*-isomer is Me < Et < Pr^i. It is thus most likely that this trend is steric in origin. On the other hand, the fact that the preference for the *trans*-configuration decreases with increasing bulk of the group means that the basic reason for the higher stability of that form is not steric in origin. It is possible that the carbonyl oxygen atom exerts some electrostatic attraction for the *N*-alkyl group in the *trans*-form.

It is difficult, however, to account in these terms for the absence of consistent changes in the percentage of the *cis*-form upon protonation of *N*-ethylformamide and *N*-isopropylformamide and for the reduced percentage of the *cis*-form in the cation of *N*-methylformamide. On both steric and electrostatic grounds *O*-protonation should increase the proportion of the *cis*-form. This has

TABLE 4

N.m.r. spectra of the *cis*- and *trans*-isomers of *N*-methylacetamide in deuteriochloroform, water, and anhydrous acids at 27 °C

	Amide				*O*-Protonated cation			
	$CDCl_3$		Water (pH 3)		Pure HSO_3F		100% H_2SO_4	
	cis	*trans*	*cis*	*trans*	*cis*	*trans*	*cis*	*trans*
% Isomer	2·3	97·7	7	93	0 *	100	6	94
δ_{Me}/p.p.m.	−2·07	−2·00	−2·07	−1·98		−2·34		−2·66
δ_{NMe}/p.p.m.	−2·92	−2·79	−2·80	−2·71		−2·99	−3·34	−3·29
$\Delta\delta_{NMe}^{cis\text{-}trans}$/p.p.m.	0·129		0·088				0·056	
δ_{NH}/p.p.m.		−6·83		−7·8		−7·99		−8·53
^3J(NH–NMe)/Hz *	5·3	4·8	4·4	5·0		5·3	(5) †	5·1
^5J(Me–NMe)/Hz						0·8(q)		

q = Quartet. * Not observable, possibly owing to overlapping. † Probable value; measurement not possible owing to overlapping.

TABLE 5

N.m.r. spectra of *NN*-dimethylformamide in deuteriochloroform, water, and strongly acidic solvents at 27 °C

	Amide		*O*-Protonated cation		
	$CDCl_3$	Water	Pure HSO_3F	100% H_2SO_4	72% $HClO_4$
δ_{CH}/p.p.m.	−8·00	−7·93	−8·03	−8·35	−8·24 *
δ_{NMe}^{cis}/p.p.m.	−2·98	−3·00	−3·27	−3·57	−3·32
δ_{NMe}^{trans}/p.p.m.	−2·88	−2·84	−3·16	−3·46	−3·29
$\Delta\delta_{Me}^{cis\text{-}trans}$/p.p.m.	0·096	0·160	0·107	0·113	0·133
$^4J^{cis}$(CH–NMe)/Hz		0·5	*ca.* 0·5	0·6	0·95—1·0
$^4J^{trans}$(CH–NMe)/Hz	*ca.* 0·5	0·9	1·0	1·1	1·0
$w_{\frac{1}{2}}$(CH)/Hz	3·2	3·0	4·1	5·8	sp

sp = Septet. * In 64% $HClO_4$; in 72% $HClO_4$ the CH resonance overlaps with the solvent peak.

TABLE 6

N.m.r. spectra of *NN*-dimethylacetamide in deuteriochloroform, water, and strongly acidic solvents at 27 °C

	Amide		*O*-Pronated cation		
	$CDCl_3$	Water	Pure HSO_3F	100% H_2SO_4	72% $HClO_4$
δ_{Me}/p.p.m.	−2·07	−2·05	−2·27	−2·71	−2·52
δ_{NMe}^{cis}/p.p.m.	−3·05	−3·03	−3·07	−3·53	−3·34
δ_{NMe}^{trans}/p.p.m.	−2·95	−2·87	−3·04(q)	−3·50(q)	−3·29(q)
$\Delta\delta_{Me}^{cis\text{-}trans}$/p.p.m.	0·096	0·16	0·029	0·029	0·058
$^5J^{cis}$(Me–NMe)/Hz					*ca.* 0·5 *
$^5J^{trans}$(Me–NMe)/Hz		0·55	*ca.* 1	*ca.* 1	0·9
$w_{\frac{1}{2}}$(C–Me)/Hz	1·8	1·5	3·2 †	3·4 †	3·0 †

q = Quartet. * Estimated from the C–Me multiplet at high resolution (1 Hz cm^{-1}). † Multiplet due to unequal *cis*- and *trans*-couplings to the N–Me groups.

been found to be so only for *N*-t-butylformamide in sulphuric acid.[6] Both small increases and small decreases are found for *N*-alkylformamides studied here. The nature of the acid medium also plays a part.

N-*Methylacetamide* (*Table* 4).—Only 3% of the *cis*-isomer was reported [17] in water. Our results show that the percentage of the *cis*-form is very low in deuteriochloroform, but is almost as high as that of *N*-methylformamide in aqueous solution. The *cis*-form appears at low field from the *trans*-form.

The *N*-methyl resonances are doublets, with ^3J(NH–Me) coupling constants somewhat different in the two forms. In aqueous solution the high-field peak of the *cis*-isomer almost overlaps with the low-field peak of the *trans*-isomer, and does so fully in the spectrum of the cation in 100% sulphuric acid. Complete overlapping may be the reason why the *cis*-form of the cation is not observable in pure fluorosulphuric acid. The *trans*-*N*-methyl resonance in fluorosulphuric acid is in fact a doublet of quartets (Figure 3), because of coupling across five bonds to the *C*-methyl group.

Concluding Remarks on N-*Alkylamides*.—The general observation in the media studied here, that the resonances of the methyl groups of *cis*-*N*-alkyl groups appear at lower field than those of *trans*-groups, contrasts with the findings on *N*-t-butylformamide.[6] The relative chemical shift of the *cis*- and *trans*-groups is usually reduced by protonation, the exception being *N*-ethylformamide. Medium effects on these shifts appear to

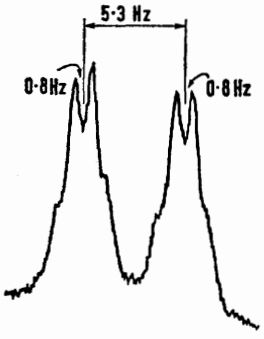


FIGURE 3 The *N*-methyl proton resonance of the cation of *N*-methylacetamide in pure fluorosulphuric acid at 27 °C and 90 MHz

be more important than protonation effects. This is in accord with a recent claim that these shifts are entirely medium-induced.[18]

NN-*Dimethylformamide* (*Table* 5).—As with *N*-methylformamide, the relative chemical shift of the methyl groups in the *cis*- and *trans*-positions is considerably enhanced in water as compared with deuteriochloroform, but is reduced compared with the value in water in the *O*-protonated cations in strongly acidic solvents. The enhancement of the coupling of the *N*-methyl groups to the formyl proton caused by protonation is minimal for the group in the *trans*-position, but considerable for the group in the *cis*-position, so that in 60—72% perchloric acid the two coupling constants are almost equal. Correspondingly, the formyl proton resonance is virtually a regular septet in these media (Figure 4).

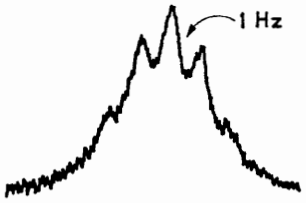


FIGURE 4 The formyl proton resonance of the *O*-protonated cation of *NN*-dimethylformamide in 60% perchloric acid at 27 °C and 90 MHz

NN-*Dimethylacetamide* (*Table* 6).—The relative shift of the resonances of the *N*-methyl groups in the *cis*- and *trans*-positions is enhanced in water compared with deuteriochloroform, in close analogy with the spectra of *NN*-dimethylformamide, but is then much more reduced upon protonation (*cf.* Table 5). The resonance of the *trans*-methyl group is clearly resolved into a quartet in water, whereas the resonance of the *cis*-methyl group is only broadened by coupling to the *C*-methyl group. This coupling is considerably enhanced in the *O*-protonated cation.

Concluding Remarks on Coupling Constants.—The enhancement of couplings across the C–N bond caused by *O*-protonation, usually ascribed to the greater double-bond character of this bond in the cation, has been generally found. The *cis*-couplings are as a rule enhanced much more than *trans*-couplings, usually by factors of the order of two, *e.g.*, $^3J^{cis}$(NH–CH) (formyl proton), which changes from about 2 Hz in the unprotonated amides to 4·5—4·8 Hz in the cation.

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