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CIS-TRANS ISOMERISM IN N-METHYL AND N-ETHYLFORMANILIDE

A. J. R. Bourn,[1] D. G. Gillies[2] and E. W. Randall
Queen Mary College, London University, Mile End Road, London

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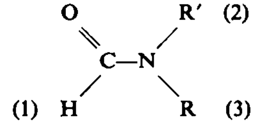
Abstract—The PMR spectra of N-methyl and N-ethylformanilide at 60 Mc/s show two isomers are present in each case in the ratio 19:1. The predominant isomers are deduced to have phenyl groups *cis* to the formyl protons from the spectra in benzene solution. Confirmation by comparison of *cis* and *trans* couplings between the formyl protons and the methyl groups for N-methylformanilide was obtained. Factors governing the shift of the formyl proton are discussed.

INTRODUCTION

Previous NMR studies of *cis-trans* isomerism in unsymmetrically N-substituted formamides have been restricted to the cases where the substituents are alkyl and



hydrogen;[3] phenyl and hydrogen;[4] both alkyls.[5] We report the case of phenyl and alkyl. The various notations used here follow those used previously.[4]

Several parameters which have been useful in the spectral and structural assignments of substituted amides are used here: (i) the coupling constants J_{12} referred to as *trans*, and J_{13} called *cis*;[4–6] and (ii) the differential effect of addition of benzene on the chemical shifts of a methyl group in positions 2 and 3.[3,7] It has also been suggested that the chemical shift of the formyl proton in N-phenyl substituted formamides is indicative of the location of the phenyl group.[4] This method of assignment, procedure (iii), is examined here.

RESULTS

The PMR spectrum at 60 Mc/s of N-methylformanilide contains peaks ascribable to two isomers: the main isomer, A, and about 5% of the subsidiary isomer, B. The chemical shifts in chloroform solution are given in Table 1.

The results for benzene dilution studies on the methyl shifts are given in Table 2.

The methyl resonance in isomer A is a 1:1 doublet with a splitting of 0·4 c/s which

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[1] Now postdoctoral Fellow at the Department of Chemistry, University of California, Los Angeles, U.S.A.

[2] Now postdoctoral Fellow at Division of Pure Chemistry, National Research Council, Ottawa 2, Canada.

[3] L. La Planche and M. T. Rogers, *J. Amer. Chem. Soc.* **86**, 337 (1964).

[4] A. J. R. Bourn, D. G. Gillies and E. W. Randall, *Tetrahedron* **20**, 1811 (1964).

[5] L. La Planche and M. T. Rogers, *J. Amer. Chem. Soc.* **85**, 3728 (1963).

[6] V. J. Kowalewski and D. G. de Kowalewski, *J. Chem. Phys.* **32**, 1272 (1960).

[7] J. V. Hatton and R. E. Richards, *Mol. Phys.* **5**, 139 (1962).

Table 1. Shifts (c/s ± 0·2 c/s) of N-methylformanilide in chloroform solution at 35° downfield from tetramethylsilane at 60 Mc/s

Vol % of amide	CHO		CH$_3$	
	A	B	A	B
100	510·0	502·9	192·9	*
80	508·2	501·1	191·7	*
50	505·7	499·7	193·2	*
20	507·3	501·4	197·5	199·5

* indistinguishable from A.

Table 2. Methyl shifts (c/s ± 0·2 c/s) of N-methylformanilide in benzene at 30°C downfield from tetramethylsilane at 60 Mc/s

Vol % amide	CH$_3$ A	CH$_3$ B
100	193·4	*
80	191·6	*
70	188·1	181·7
59	186·2	177·0
49	183·5	169·7
35	182·2	165·9
25	179·9	159·9

* overlaps with A.

Table 3. Shifts (c/s ± 0·2 c/s) at 60 Mc/s measured downfield from tetramethylsilane of N-ethylformanilide in benzene at 30°

Vol % amide	CHO		CH$_2$		CH$_3$	
	C	D	C	D	C	D
100·0	503·5	*	229·8	*	62·8	*
77·6	502·8	*	228·4	216·9	61·7	~60
57·8	501·6	*	226·2	208·9	60·0	55·8
42·6	500·0	495·2	223·5	199·2	58·0	50·2
35·4	499·0	492·9	222·2	194·8	57·2	48·0
29·1	498·7	492·1	221·7	193·7	56·6	45·1
16·0	497·6	487·3	219·5	185·1	55·3	42·2

* overlaps with C

is removed by a proton-proton double resonance experiment involving irradiation of the formyl region. The formyl resonance is 1·5 c/s wide at half height and is sharpened by irradiation of the methyl region with the second radiofrequency.

In isomer B the methyl resonance is a single unresolved line with a width of less than 0·6 c/s. The line width of the formyl resonance which is also a singlet is less than 1·5 c/s.

In the 35 % solution in benzene the two methyl features coalesce as the temperature is raised. The process is complete at 80°. The spectra of N-ethylformanilide may be similarly assigned on the basis of two isomers: a predominant isomer, C, and 3 or 4 % of a secondary isomer, D. Each isomer gives a formyl signal, and a quartet methylene and a triplet methyl characteristic of an ethyl group with a vicinal coupling of 7 c/s. The relevant shift data are given in Table 3.

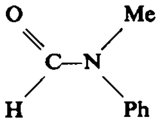
For both C and D there are no couplings visible apart from the coupling in the ethyl group either on the formyl or the methylene resonances. The line widths are approximately 1·5 c/s for the formyl resonances both C and D.

The peaks for the two isomers coalesce at about 80° to give one formyl, one methylene and one methyl peak.

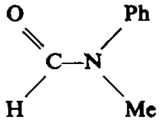
DISCUSSION

N-methylformanilide. The origin of the doublet splitting of the methyl peak in isomer A is established as a coupling with the formyl proton by the double resonance experiments. This coupling is not resolved however on the formyl resonance presumably due to the broadening effects of the nitrogen electric quadrupole relaxation.[8,9] No such coupling is evident for isomer B.

On the basis that a *trans* coupling is larger than a *cis* coupling as in other N-methylformamides,[6–8] the couplings are identified as $J_{12}(H\text{–}Me) = 0{\cdot}4$ c/s and $J_{13}(H\text{–}Me) = 0{\cdot}0$ c/s. The structural assignments are then given as



A 95%



B 5%

The behaviour of the methyl shifts when the sample is diluted with benzene is consistent with this assignment. Hatton and Richards showed that the two different methyl signals of N,N-dimethylformamide were affected differently by dilution.[7] The methyl in position (3) showed a larger shift dependence than the (2)-methyl. This argument was assumed by La Planche and Rogers to apply to the methyl resonances in the case of the *cis-trans* isomers of other N-substituted methylformamides.[5] Following this argument, the above assignment is confirmed since the methyl shift of B is affected most by the addition of benzene and hence B has the methyl in the (3) position.

We have previously suggested that the chemical shift of the formyl proton in formanilides is sensitive to the position of the phenyl group and may constitute a useful aid to structural assignment.[4] Low shifts in the region of −517 c/s were found for two amides which had a phenyl group in the (3) position; other amides, including those with a phenyl in the (2) position have shifts at higher field, viz, approximately −490 c/s. This approach may be tested in the present instance against the two procedures used above. Since the main isomer A has a formyl shift of −511·1 c/s versus the figure of −503·7 c/s of isomer B, it follows that A has the phenyl in the (3) position and B has it in the (2) position, in agreement with the deduction made above.

N-ethylformamide. Since no resolvable coupling was observed involving the formyl proton, the structural assignments of isomers C and D are accomplished solely by method (ii). The effect of dilution with benzene on the N-alkyl shifts is greater for isomer D than for isomer C both for the methylene and for the methyl groups.

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[8] E. W. Randall and J. D. Baldeschwieler, *J. Mol. Spectroscopy* **8**, 365 (1962).

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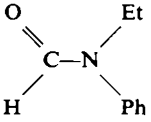
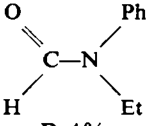
This favours the main isomer C having the alkyl group *trans* to the formyl proton.


C 95%


D 4%

Procedure (iii) in this case breaks down since in the neat liquid at least (although not in benzene solution) the two isomers have practically identical formyl shifts. Possible explanations of this fact are discussed below.

Formyl shifts. It is tempting to speculate in more detail on the factors governing the isomeric shift difference, Δ, of the formyl groups. It was shown for *cis*- and *trans*-formanilide that Δ was invariant of concentration of amide in deuterochloroform solution, and it was suggested that Δ is large because of the proximity of the formyl proton to the ring current of the phenyl group in position (3).[4]

The detailed model required to support this contention has a nearly coplanar arrangement of the phenyl ring and the amide skeleton. This coplanarity could be justified theoretically, for example, by the calculation of Baba and Suzuki.[10] Choosing reasonable values for the bond lengths and assuming that all bond angles are 120°, the distance from the formyl proton to the centres of the phenyl rings at the (2) and (3) positions are 3·61 Å and 4·65 Å respectively. Using the treatment of Johnson and Bovey,[11] Δ is then calculated to be 18 c/s. The modified ring current of Pople reduces the difference to 12 c/s.[12] The measured Δ for formanilide is approximately 20 c/s. This discrepancy could be used to justify either rejection or modification of the model. It could be accounted for by a different substituent effect of the N–H proton at positions (2) and (3) or by consideration of the orientation of the phenyl rings. Rotation of the phenyl ring around the N-phenyl bond would reduce Δ. In the case that the phenyl rings were at 90° to the skeleton Δ changes sign and the formyl proton would be at lower field for *cis*- compared with *trans*-formanilide.

For N-methyl and N-ethyl formanilides either pure or in chloroform solution Δ is 6 c/s and O c/s respectively, i.e. is smaller than for formanilide. On the above modified model the required twist around the N-phenyl bond is about 40° and 53° respectively. This increase in the angle could be rationalized by a steric interaction between the phenyl and the ethyl groups.

cis-trans Ratios. For both R = Me and R = Et the predominant isomer has the phenyl group in the (3) position. The ratio is independent of concentration unlike the situation for formanilide where hydrogen bond effects on the ratio are important. For N,N-disubstituted formamides the *cis-trans* ratios have been rationalized on purely steric grounds: the bulkier group is *trans* to the carbonyl in the preferred orientation.[5,13] If this argument is applied to the formanilides studied here, the results require that both the methyl and the ethyl groups are smaller than the phenyl. It is unlikely, however, that differential steric and conjugative effects may be neglected where phenyl is one of the substituents.

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[11] C. E. Johnson and F. A. Bovey, *J. Chem. Phys.* **29**, 1012 (1958).

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[13] C. Franconi, *Z. Electrochem.* **65**, 645 (1961).

EXPERIMENTAL

Single resonance spectra at 35° (±1°) were obtained on a Varian A60 spectrometer. Calibration was checked by the audio sideband technique[14] using a Solartron audio oscillator (type CO 546) and a Venner transistorised counter (type TSA 3336). Single and double resonance spectra employing proton-proton decoupling were taken on a Varian HR 60 spectrometer. For the single resonance spectra the field was locked by means of an audio sideband at frequency ν_1 to tetramethylsilane. The spectrum was swept by variation of ν_1 and recorded with the aid of a second audio modulation at 2000 c/s and the Varian integrator.

N-methylformanilide was supplied by the Aldrich Chemical Company. N-methylformanilide was prepared by the method of Roberts and Vogt.[15]

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[14] J. T. Arnold and M. E. Packard, *J. Chem. Phys.* **19**, 1608 (1951).

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