Tetrahedron Letters No.51, pp. 5197-5200, 1967. Pergamon Press Ltd. Printed in Great Britain.

OBSERVATION OF GEOMETRIC ISOMERISM OF ALIPHATIC AZOMETHINES BY NMR

David A. Nelson and Ronald L. Atkins
Department of Chemistry
University of Wyoming, Laramie, Wyoming 82070

(Received in USA 9 August 1967)

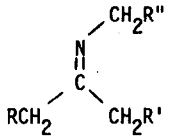
We wish to report the observation of some five-bond couplings in simple aliphatic azomethines, and the use of the coupling constants in the determination of the extent of geometrical isomerism in these compounds.

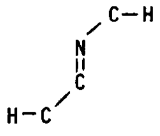
NMR spectroscopy has been used to study the isomerism of azomethines in which one or more of the groups attached to the carbon-nitrogen double bond are aromatic rings (1). Lambert, Oliver and Roberts (2) have used NMR methods to investigate the energy of rotation about the carbon-nitrogen double bond. Use of long range coupling constants has been made to study the configuration and conformations of some alkyl substituted hydrazine derivatives of ketones and aldehydes (3), and in conformational studies of some aldimines derived from isobutyraldehyde and primary aliphatic amines (4); however isomerism of simple aliphatic azomethines has not been studied. Since the factors which control the position of equilibrium of stereoisomeric aliphatic azomethines would be predicted to differ from those with aromatic rings directly attached to the carbon-nitrogen double bond, this system deserves separate study.

The 100 MHz spectrum of N-isopropylidenemethylamine in deuteriochloroform at 35° shows three resonances of equal area at $\delta = 1.80$, 1.98, and 3.06 ppm (See compound I of Table I), indicating that equilibration processes of the methyl group on nitrogen are slow on the NMR time scale and suggesting that it might be possible to study stereoisomerism about the carbon-nitrogen double bond of azomethines by NMR methods. Each of the C-methyl resonances showed coupling to the N-methyl protons, thus the two resonances appeared as distinct quartets, one with $J = 1.3$ Hz and one with $J = 0.7$Hz (five-bond coupling). Irradiation of the N-methyl resonance ($\delta = 3.06$ ppm) resulted in the collapse of the C-methyl resonances to singlets of half-height width equal to 0.7 Hz ($CHCl_3 = 0.35$ Hz) indicating a small but unresolved coupling between the C-methyl protons, but confirming the major coupling as five-

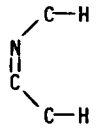
TABLE I

Methyl and Methylene Resonances and Coupling Constants of Symmetrically C-Substituted Azomethines.*





$J_{\textit{trans}}$



$J_{\textit{cis}}$

				δ, ppm. from TMS			J, hz	
Cmpd.	R	R'	R"	RCH_2	$R'CH_2$	$R''CH_2$	$J_{\textit{trans}}$	$J_{\textit{cis}}$
I	H	H	H	1.98	1.80	3.06	1.3	0.7
II	H	H	C_3H_7	2.14	1.98	3.38	1.2	0.6
III	CH_3	CH_3	C_3H_7	2.24	2.19	3.27	1.2	0.6

*Signals given are those of the methyl and/or methylene protons directly attached to the carbon-nitrogen double bond.

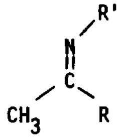
bond coupling between the C-methyl and N-methyl protons. Observation of the N-methyl resonance at a 50 Hz sweep width revealed the expected 10 line multiplet. The assumption was made that the lowest field resonance was due to the C-methyl group *cis* to the unshared pair on nitrogen (5) and thus *trans* to the N-methyl group. The observed *trans* five-bond coupling was greater than the *cis* five-bond coupling as would be expected by analogy with the coupling constants observed in simple aliphatic olefins. The spectra of two other symmetrically C-substituted azomethines were examined, and the data are given in Table I. In II, the C-methyl resonances were triplets due to five-bond coupling with the N-methylene protons of the n-butyl substituent on nitrogen, while in III the resonances of interest were those of the C-methylene protons, which appeared as a pair of overlapping quartets of triplets.

The spectra of some unsymmetrically C-substituted azomethines were then examined. Here, the potential *cis*-*trans* isomerism should be observable provided that the resonance of a group attached to the carbon-nitrogen double bond can be separately observed. In our studies to date, we have used a C-methyl group as such a probe.

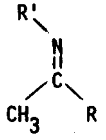
In the spectra of all the unsymmetrically C-substituted azomethines, two distinct methyl resonances could be observed, either as quartets or triplets depending on the substituent on nitrogen. The pertinent data are given in Table II.

TABLE II.

Methyl Resonances, Coupling Constants, and Isomer Populations of Some Unsymmetrically C-Substituted Azomethines.



Cis



Trans

Cmpd.	R	R'	δ, ppm. from TMS, and $J_{R'}$, hz cis CH_3	 trans CH_3	% trans
IV	C_3H_7	C_4H_9	1.97, 1.2	1.78, 0.6	77
V	$CH_2C(CH_3)_3$	C_4H_9	2.03, 1.2	1.83, 0.6	89
VI	C_3H_7	CH_3	1.98, 1.2	1.82, 0.6	72
VII	$CH_2CH(CH_3)_2$	C_4H_9	1.97, 1.2	1.77, 0.6	79

The total area of these two signals integrated for 3 protons. Irradiation at the average frequencies of the resonances of the α protons of the substituent on nitrogen resulted in the collapse of both of the C-methyl resonances to singlets. The five-bond coupling constants observed for the two methyl resonances were also consistent with those of the symmetrically C-substituted azomethines in Table I. Thus, there is little doubt that these two methyl resonances are due to cis-trans isomerism about the carbon-nitrogen double bond. By integration of the areas of the methyl signals, the percentage of trans isomer was determined. The pertinent data are given in Table II. The trans isomer, as defined, predominates, and the trend is unexceptional as the bulk of the C-substituent is increased.

All of the compounds listed in Tables I and II showed sharp resonances for the C-methyl or methylene protons of interest at the probe temperature of 35° except compound VI. In this case, the C-methyl resonance was not resolved into a quartet until the sample was cooled to 10°. Cooling below 0° did not appear to further sharpen the resonance. The percentage of trans isomer also increased as the temperature was lowered. The data are given in Table III.

TABLE III.

Percentage of Trans-N-2-Pentylidenemethylamine.

Temperature, °C	% Trans Isomer
35	72
20	76
10	81
0	86
-10	85

The reason for the temperature dependency of the C-methyl resonances of VI is not apparent in view of the behavior of other compounds in the series. We are presently investigating the temperature dependency of these and other azomethines at higher temperatures in an attempt to elucidate the processes further.

Acknowledgement

These studies were supported in part by PHS grant No. GM-13117-02.

References

1. D. Y. Curtin, E. J. Grubbs, and C. G. McCarty, J. Am. Chem. Soc., **88**, 2775 (1966), and references 4, 32, and 36 therein.
2. J. B. Lambert, W. L. Oliver, and J. D. Roberts, J. Am. Chem. Soc., **87**, 5085 (1965).
3. G. J. Karabatsos, R. A. Taller, and F. M. Vane, Tetrahedron Letters, No. 18 1081 (1964), and references therein.
4. J. Hine and C. Y. Yeh, J. Am. Chem. Soc., **89**, 2669 (1967).
5. H. A. Stabb, F. Vogtle, and A. Mannschreck, Tetrahedron Letters, No. 12, 697 (1965).