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CONFORMATIONAL STUDIES ON N-METHYL LACTAMS. USE OF SOLVENT EFFECTS IN N.M.R.[1]

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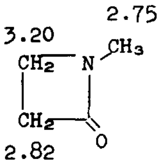
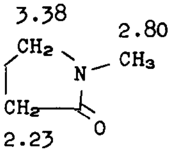
Hindered internal rotation about the carbonyl-carbon-nitrogen bond in N-methyl amides is evidenced by a doubling of the N-methyl resonance in the N.M.R.[2] Assignment of the peaks corresponding to the s-cis and s-trans to oxygen conformations has been made on the basis of solvent induced chemical shifts.[3,4] This procedure depends upon the equilibrium formation of a collisional complex between the amide and an aromatic solvent. The orientation of the solvent molecule with respect to the dipolar, planar, amide is non-random; that is, the aromatic solvent is attracted to the partial positive charge on nitrogen and repelled by the partial negative charge on oxygen.[5] The net result is that upon progressive dilution, the s-trans N-methyl group experiences the greater diamagnetic shift. Thus, observation of the relative upfield displacements of the two peaks allows assignment of the position of the s-cis and s-trans resonances.

We wish to report a study of the related phenomenon for the cyclic analog of the N-methyl amide, namely, the N-methyl lactam. Specifically, the cis N-methyl lactams, N-methylpropiolactam (I), N-methylbutyrolactam (II), N-methylvalerolactam (III), N-methylcaprolactam (IV), N-methylenantholactam (V) and N-methylcapryllactam (VI) were studied. The eleven and thirteen membered examples, N-methylcaprilactam (VII) and N-methyllauryllactam (VIII), display N-methyl doublet absorption at room temperature indicating torsional isomerism about the C-N bond of the amido group.[6] Chemical shifts for the $\underline{\mathrm{CH}}_3\mathrm{N}$, $\underline{\mathrm{CH}}_2\mathrm{N}$ and $\underline{\mathrm{CH}}_2\mathrm{CO}$ protons for dilute carbon tetrachloride solutions are shown below in p.p.m. relative to tetramethyl silane:



I



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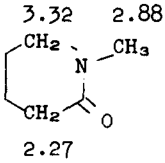

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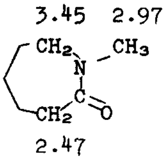

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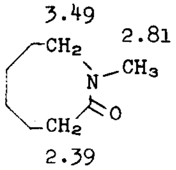
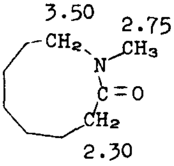
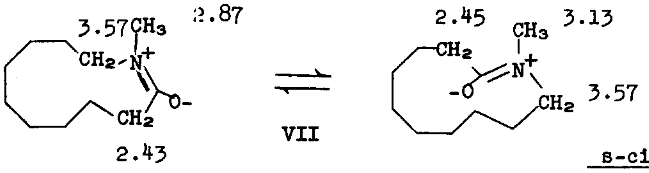


V



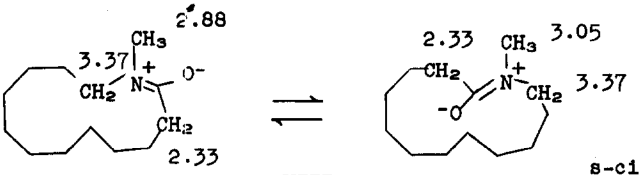
VI

Our objectives in this study were first to learn whether N-methyl lactams exhibit characteristic upfield shifts upon dilution with aromatic solvents, and, if so, possibly use such dilution behavior as a means for assignment of the s-cis and s-trans N-methyl resonance for the eleven and thirteen membered examples.



VII

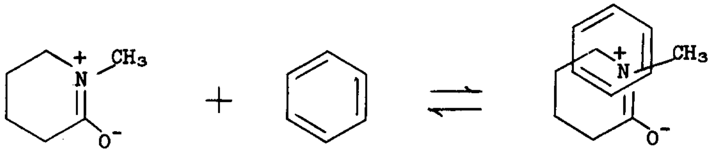
$$\frac{\text{s-cis}}{\text{s-trans}} = \frac{55}{45}$$

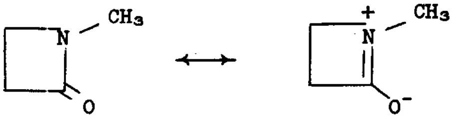


VIII

$$\frac{\text{s-cis}}{\text{s-trans}} = \frac{40}{60}$$

All the N-methyl lactams studied displayed highfield solvent shifts when diluted with aromatic solvents, either starting with the pure lactam or a dilute carbon tetrachloride solution. The dilution shifts are given in Table I. A detailed discussion of the internal magnitude variations for solute and solvent will be presented in the full report, however, the general behavior accords with the equilibrium formation of a complex[7] of the structure shown:





(A)

The behavior of N-methylpropiolactam (I) is also quite normal. The $\underline{CH_3}N$ and $\underline{CH_2}N$ protons experience diamagnetic displacements although the magnitude is smaller than that observed for the higher members. This result tends to

TABLE I

Solvent Shifts for N-Methyl Lactams of Ring Size Four to Thirteen[a]

N-Methyl Lactam	Solvent	$\underline{CH_2}N$ $\Delta\delta$ppm	$\underline{CH_2}CO$ $\Delta\delta$ppm	$\underline{CH_3}N$ $\Delta\delta$ppm	
Propiolactam[b] (I)	benzene	0.57	——[b]	0.33	
Butyrolactam (II)	CCl_4[c]	-0.12	-0.16	-0.18	
	benzene-CCl_4	1.05	0.65	0.62	
	pyridine-CCl_4	0.85	0.60	0.62	
Valerolactam (III)	CCl_4	-0.13	-0.16	-0.14	
	benzene-CCl_4	1.08	0.52	0.62	
	pyridine-CCl_4	0.80	0.60	0.56	
Caprolactam (IV)	benzene-CCl_4	1.12	0.60	0.66	
	pyridine-CCl_4	0.78	0.52	0.35	
Enantholactam (V)	benzene	0.72	0.14	0.14	
Capryllactam (VI)	benzene-CCl_4	0.85	0.41	0.47	
	pyridine-CCl_4	0.84	0.55	0.62	
				s-cis	s-trans
Caprilactam (VII)	benzene-CCl_4	1.05	0.62	0.77	1.10
Lauryllactam (VIII)	benzene-CCl_4	0.90	0.45	0.47	0.80
	pyridine-CCl_4	0.83	0.70	0.63	0.88

(a) Spectra were measured on an A-60 spectrometer. The value $\Delta\delta$ is the maximum upfield shift from either the pure lactam or a dilute carbon tetrachloride solution. Only II and III showed downfield shifts upon dilution with carbon tetrachloride. The negative sign indicates downfield displacement. In all cases a dilution study was carried out starting with a 10% solution in carbon tetrachloride. (b) The $\underline{CH_2}CO$ resonance was obscured under the $\underline{CH_3}N$ peak. (c) CCl_4 = carbon tetrachloride.

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suggest the importance of a dipolar contributor such as A.

Further information about the charge character on the nitrogen atom of the lactams was obtained by measuring the C^{13}-H coupling constant for the N-methyl group throughout the series. The partial positive charge on nitrogen in the dipolar resonance structure would tend to increase the electronegativity of the nitrogen relative to the uncharged state. This difference in electronegativity should induce greater p-character in the carbon-nitrogen bond and greater s-character in the carbon-hydrogen bond of the methyl group. The C^{13}-H coupling constant is sensitive to such a change in s-character[8], although other factors such as the effective nuclear charge are important contributors to the magnitude of J.[9] Reference to Table II reveals the interesting fact that the value for the C^{13}-H coupling constant is about the same for all the members of the cis-N-methyl series. Furthermore the average value of 138 cps. is the same as that observed for N,N-dimethylacetamide and this corresponds to about 40% double bond character for the C-N bond of the amido group.

TABLE II

C^{13}-H Coupling Constants for N-Methyl Lactams[a]

Compound	J
N-Methylpropiolactam (I)	138
N-Methylbutyrolactam (II)	137
N-Methylvalerolactam (III)	138
N-Methylcaprolactam (IV)	138
N-Methylenantholactam (V)	138
N-Methylcapryllactam (VI)	137
Trimethylamine	134
N,N-Dimethylacetamide	138

(a) All samples were measured neat. Coupling constants were determined on an A-60 spectrometer at 100 cps. sweep width. Several compounds were measured using a frequency counter and acceptable internal agreement was attained. Values are considered to be within ± 0.20 cps.

In the case of the eleven and thirteen membered systems, VII and VIII respectively, N-methyl doublets were observed. Dilution with benzene (Table I) for each compound caused upfield shifts for each component of the doublet, however, the lowfield peak was shifted by approximately a factor of two greater amounts than the highfield peak. Invoking a solvent-solute complex, we identify the lowfield peak with the s-trans conformation and the highfield peak with the s-cis conformation. The conformation populations, based upon these assignments, are s-cis : s-trans ~55 : 45 for the eleven membered lactam and s-cis : s-trans ~40 : 60 for the thirteen membered ring. This change in the relative ratio with increasing ring size is in agreement with expectation. Presumably if the ring size were further increased, the s-cis : s-trans ratio would approach that of a comparably substituted open-chain analog.

Acknowledgement

The authors are in the debt of Dr. K. Surve for the preparation of N-methylenanthollactam (V), and to Dr. J. Kim for the measurement of several spectra.

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1. Presented in part at the 8th European Congress on Molecular Spectroscopy, Copenhagen, Denmark, August 14th-20th, 1965.

2. J. A. Pople, W. G. Schneider and H. J. Bernstein, High Resolution Nuclear Magnetic Resonance, McGraw-Hill, New York, N. Y. (1958) p. 365.

3. For a discussion of this procedure see N. S. Bhacca and D. H. Williams, Applications of NMR Spectroscopy in Organic Chemistry, Holden-Day Inc., San Francisco, Calif., (1964) chapter 7.

4. For an interesting criticism of the use of solvent effects for the assignment of conformation for mesityl oxide see J. E. Baldwin, J. Org. Chem., 30, 2433 (1965).

5. This description was first formulated explicitly by J. V. Hatton and R. E. Richards, Mol. Phys., 5, 153 (1962).

6. The term cis refers to the configurational cis relationship of the N-methyl group with respect to the carbonyl oxygen. A sharp N-methyl singlet is observed even at low temperatures. The terms s-cis and s-trans refer to the existence of observable (N-methyl doublet resonance) torsional isomers.

7. Complex in the present context implies an association between solvent and solute resulting in a discrete polymolecular assemblage which exists at least for the duration of the experiment used for its detection.

8. N. Muller and D. E. Pritchard, J. Chem. Phys., 31, 768 (1959), N. Muller and D. E. Pritchard, ibid., 31, 1471 (1959).

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