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HINDERED INTERNAL ROTATION IN N-METHYLTHIOLACTAMS

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We and others have studied the barrier heights to internal rotation in thioamides.[1-13] In our investigation we compared the barriers for structurally analogous amides and thioamides using the $W_{\frac{1}{2}}$ method. It was found that almost invariably the barrier height, Ea, for the thioamide was about 3 kcal/mole higher than the amide. Now we report on the extension of this research to the cyclic analogs of the N-methylthioamide, namely, N-methylthiolactams.

Relevant nmr parameters and activation energy data are presented in Table I and Table II, respectively, for the series of N-methylthiolactams ranging in ring size from five to sixteen members.

The object of this study was to learn whether interconverting s-cis and s-trans torsional conformers could exist about the C-N bond in a sufficiently large ring example, and, corollarily, to determine the conformer ratio and barrier heights for interconversion.

Inspection of the data in Table I reveals that doublet N-methyl peaks appear in the twelve and greater membered rings. This is indicative of the existence of s-cis and s-trans conformers. The identity of the absorption peak associated with each was made on the basis of dilution shifts with benzene (e.g., for the thirteen membered the highfield component moves upfield by $\Delta\delta = 0.84$, while the low field component is shifted by $\Delta\delta = 0.22$). The highfield peak is therefore <u>trans</u> to sulfur. For a discussion of the basis of the method see the work of Walter et al.[13]

TABLE I

NMR Parameters for N-Methylthiolactams[a,c]

Ring Size	$N\underline{CH}_2$	$S{=}C\underline{CH}_2$	$N\underline{CH}_3$ Cis	$N\underline{CH}_3$ Trans	Cis: Trans[b]
5	3.81	2.92	3.22		100
7	3.71	3.07	3.47		100
9	3.85	3.02	3.32		100
12	3.72	2.76	3.37	3.33	75:25
13	3.53	2.76	3.32	3.29	65:35
16	3.57	2.76	3.36	3.27	70:30

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a) Chemical shifts are relative to TMS for dilute CCl_4 solutions.

b) The cis and trans NCH_3 peaks were identified by benzene induced chemical shifts and relative magnitude of the trans coupling constants (see text).

c) The N-methylthiolactams were prepared from the related N-methyllactam[1] by treatment with P_2S_5 in pyridine. The compounds exhibit the following:

Ring size 5, b.p. 88 - 89° (0.50mm), Lit.[2], 146 - 147° (17mm); 7, m.p. 50 - 51°, Lit.[3] 49 - 51°; 9, m.p. 47 - 48°; 12, m.p. 46 - 48°; 13, m.p. 59 - 61°; 16, b.p. 144°(0.37mm).

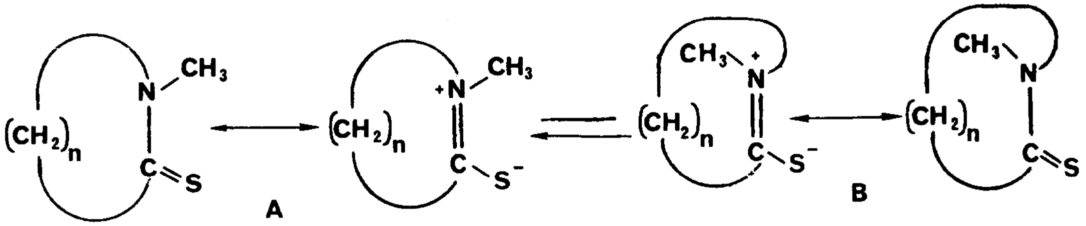
The fact that the 12 and 13 membered compounds are solids may indicate that they crystallize as single diastereomers. The solution nmr spectra of fresh samples show the presence of the two rotamers but there are distinct differences between their i.r.s. in the solid phase compared to solution.

1) R. M. Moriarty, <u>J. Org. Chem.</u>, **29**. 2748 (1964).

2) U. Berg and J. Sandström, <u>Acta Chem. Scand.</u>, **20**,689 (1966).

3) W. Walter, J. Voss, J. Curts, and H. Pawelzik, <u>Liebigs Ann. Chem.</u>, **660**, 60 (1962).

The low field peak on the other hand has a wider peak width at half height which is due to coupling of the <u>cis</u> N-methyl peak with the <u>trans</u> methylene group. It may be noticed in passing that just the opposite obtains in the case of cyclic N-methyl lactams,[14, 15] that is, the low field peak of the doublet is due the <u>trans</u> absorption. The conformer ratios listed in <u>Table I</u> show a strong preference for the s-cis form even in the sixteen membered ring. This contrasts with the N-methyllactams in which the large membered rings are predominantly in the s-trans form.[14-16] Hindered internal rotation in these systems is due to partial double bond character in the thioamido group leading to the s-cis and s-trans diastereomers A and B.



n = 3 - 7 s-cis
n = 10 - 14 s-cis + s-trans

The barrier heights, Ea, for exchange between the s-cis and s-trans forms were determined by our previously described W 1/2 method using the variation in linewidth at one-half height corrected for field inhomogeneity.[1,2] The values for Ea collected in Table II are somewhat higher than those found for open-chain thiolactams such as N,N-dimethyl thiobenzamide Ea = 19.8 kcal/mole, N,N-dimethylphenyl thioacetamide, Ea = 21.4 kcal/mole. The entropies of activation of 5.1, 6.0, and 5.8 e.u. for the twelve, thirteen, and sixteen membered rings are unusually high. We have no explanation for these high values although we must acknowledge that we have previously invoked high entropies of activation as indicative of Ea's of doubtful validity.[1,2] We claim plausibility for these high value but not necessarily significance. Of course part of the entropy of activation could be due to strong intermolecular association between these polar molecules.

TABLE II

Activation Parameters for N-Methylthiolactams[a]

Ring Size	Ea kcal/mole	ΔH kcal/mole	ΔS E.U.
12	23.7 ± 0.5	23.0 ± 0.5	5.1 ± 2
13	22.9 ± 0.5	22.1 ± 0.5	6.0 ± 2
16	22.2 ± 0.5	21.6 ± 0.5	5.8 ± 2

a) Nitrobenzene was used as solvent.

The fact that the s-cis form predominates in the large membered N-methylthiolactams while the s-trans form predominates in the related N-methyllactams[15,16] is probably due to the larger steric requirement of sulfur relative to oxygen.

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