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BARRIER TO INVERSION AT NITROGEN IN IMINES.

CONFIGURATIONAL STUDIES UPON S-METHYL THIOIMIDATES

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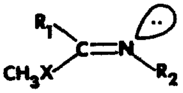
Recently we reported that linear and large-membered cyclic O-methyl imidates were configurationally homogeneous existing in the anti configuration (X=O).[1,2]

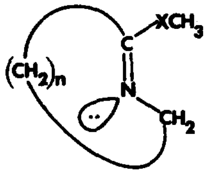


anti form

X=O, R_1=CH_3, R_2=alkyl or aryl

X=S, 1, R_1=CH_3, R_2=C_2H_5

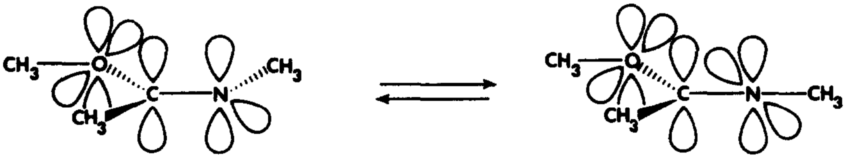
2, R_1=R_2=C_2H_5



anti form

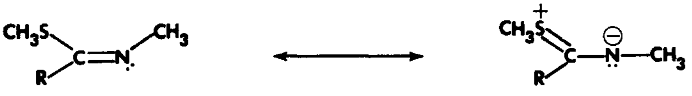
n=9-13, X=O; X=S

The preference for the anti configuration was attributed to interorbital electron repulsion in the syn form between the non-bonding electrons upon the oxygen atom and the lone pair on nitrogen localized in an sp^2 orbital. The same effect should come into play in destabilizing the transition state for stereomutation in the $sp^2 \rightleftarrows sp \rightleftarrows sp^2$ inversion process:



sp^2 sp

Substitution of sulfur for oxygen in this system, namely, comparison of S-methyl thioimidates with the O-methyl imidates, offers a test for the interorbital electron repulsion description. The Coulombic repulsion curve for the oxygen-nitrogen lone pair-lone pair interaction is steeper than the sulfur-nitrogen lone pair-lone pair interaction because: (a) the greater length of the sulfur-carbon bond relative to oxygen-carbon bond increases the distance over which the interaction takes place; (b) the reduced electronegativity of the sulfur relative to oxygen diverts increased s-character into lone pair electrons on the sulfur compared to oxygen. Since hybrid 3s orbitals are used in the sulfur example, the greater polarizability should allow the 3s wave function to deform in such a way as to decrease the Coulombic repulsion; and (c) the reduced electronegativity of sulfur should favor resonance delocalization of the lone pairs on sulfur as exemplified by dipolar form B:

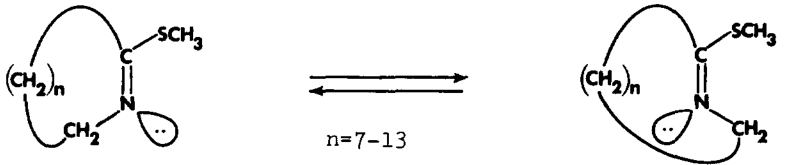


A B

We now report the first observation of the existence of interconverting diastereomers among the S-methyl thioimidates and determination of activation parameters for their exchange.[3]

The syn configuration must exist purely for steric reasons in the 5 to 9-membered rings and this is revealed by a sharp singlet peak in their nmr spectra for the S-CH_3 protons (Table I). In the 10-membered ring a new peak appears at a lowered position due to 10% of the presumably anti isomer. In the 11-membered ring, the intensity ratios are reversed with the anti isomer predominating to the extent of 80%. The 12- and 13-membered rings are chiefly anti and the 16-membered ring is 1:1.

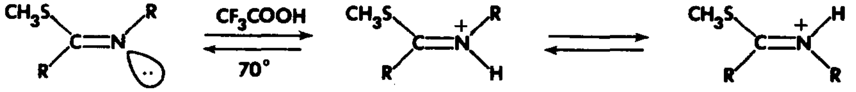
With the existence of the syn and anti conformers established, we applied the $W_{1/2}$ method for the determination of the barrier height for their interconversion.[4] The activation energies (Table II) for the cyclic compounds are in the range of barriers for rapidly interconverting diastereomers, and undoubtedly correspond to exchange between the cyclic syn and anti diastereomers.



syn form anti form

As a further area of comparison between the O-methyl imidates and S-methyl imidates, the behavior of the conjugate acids of the latter was investigated. Equilibrium concentrations of the isomers are presented in Table I. The similarity in the syn:anti ratio of the free thiomidate and conjugate acid may indicate that steric effects are the dominant factor in determining the diastereomer ratios in contrast to the behavior of the O-methyl imidates.

In summary, the existence of interconverting syn and anti diastereomers for



the large-membered cyclic and linear S-methyl thioimidates agrees with our proposal of interorbital repulsion as the governing factor in destabilizing the syn form of the O-methyl imidates.

Table I. Chemical Shifts for Proton Absorption in Cyclic and Linear S-Methyl Imidates and their Conjugate Acids

Ring Size	ppm SCH_3 syn	ppm SCH_3 anti	$C = NCH_2$	$N = CCH_2$	Diastereomer Ratio for Conjugate Acids syn	Diastereomer Ratio for Conjugate Acids anti
7	2.16	----	3.58	2.40	100	--
9	2.18	----	3.63	2.37	100	--
10	2.15	2.35	3.60	2.48	90	10
11	2.21	2.38	3.45	2.45	80	20
12	2.17	2.38	3.44	2.48	30	70
13	2.20	2.38	3.43	2.47	35	65
16	2.20	2.40	3.36	2.50	50	50

Compound	ppm SCH_3 syn	ppm SCH_3 anti	$C = NCH_2$		$N = CCH_3$		syn	anti
1	2.22	2.40	3.30	3.42	2.27	2.49	45	55
2	1.90	2.40	----	----	1.38	2.49	55	45

Table II. Activation Parameters for Cyclic and Linear S-Methyl Imidates (at 352.3°K)

Ring Size	Isomer Ratio anti	Isomer Ratio syn	$\Delta G^{\neq}$(kcal/mole)	$\Delta H^{\neq}$(kcal/mole)	$\Delta S^{\neq}$(e.u.)
7	0	100	----	----	----
9	0	100	----	----	----
10	10	90	----	----	----
11	80	20	18.8	17.9	-2.6
12	75	25	21.2	21.2	+3.8
13	75	25	19.0	19.0	+0.3
16	50	50	21.7	21.7	+3.6
Compound					
2	50	50	19.4	19.4	-2.2

References

1. R. M. Moriarty, C.-L. Yeh, K. C. Ramey, and P. W. Whitehurst, J. Am. Chem. Soc., 92, 6360 (1970).

2. For a review see C. G. McCarty in THE CHEMISTRY OF THE CARBON NITROGEN DOUBLE BOND, Ed. S. Patai, Interscience, London, 1969, p. 363; H. Kessler, Angew. Chem., 82, 237 (1970).

3. The S-methyl thioimidates used in this study were prepared by treatment of either the thioamide or thiolactam with trimethyloxonium fluoroborate. All the compounds prepared gave correct microanalyses and had consonant ms, ir, and nmr spectra.

4. K. C. Ramey, D. J. Louick, P. W. Whitehurst, W. B. Wise, R. Mukherjee, and R. M. Moriarty, Org. Magn. Res., 3, 201 (1971).