Tetrahedron Letters No. 41, pp 3629 - 3632, 1974. Pergamon Press. Printed in Great Britain.

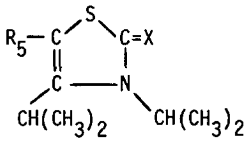
THE GEAR EFFECT IV: CONFORMATIONAL ANALYSIS OF THREE 3,4-DIISOPROPYL-5-METHYLTHIAZOLE DERIVATIVES*

A. Lidén,[a] C. Roussel,[b] M. Chanon,[c] J. Metzger[b] and J. Sandström[a]

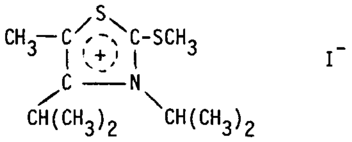
[a]Division of Organic Chemistry, Chemical Center, University of Lund,
P.O.B. 740, S-220 07 Lund 7, Sweden
[b]I.P.S.O.I., Université Aix Marseille III, St. Jérome, 13013 Marseille, France
[c]Ecole Normale Supérieure, 14 Bd de la Liberté, Le Bardo, Tunis, Tunisie

(Received in UK 8 August 1974; accepted for publication 29 August 1974)

It has been shown by strain energy calculations that 3,4-diisopropylthiazoline-2(3)-thione (I) has three energy minima with respect to the rotation of the isopropyl groups (A, B and C in the Figure). Below -10°C, distinct nmr spectra were observed for two species, which were assigned to the conformations A and B with the aid of chemical shift arguments, especially the extreme low-field resonance of the 3-methine proton in B (δ = 6.03 ppm compared to 4.70 ppm in A).



I, X = S, R_5 = H
II, X = O, R_5 = CH_3
IV, X = S, R_5 = CH_3

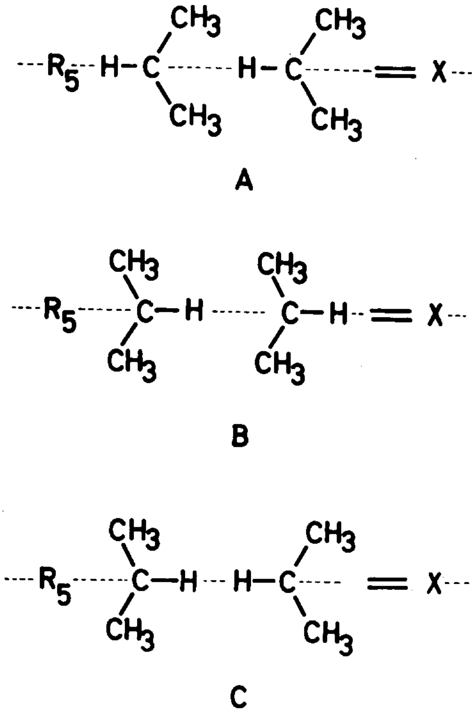


III

---

* Part III: C. Roussel, M. Chanon and J. Metzger, FEBS Letters 29, 253 (1973).

We now wish to report three cases (II-IV), where three different rotamers have been observed, which are assigned by low-temperature ^{1}H nmr to the conformations A, B and C.


A

B

C

FIGURE. Conformations of isopropyl groups viewed along the plane of the ring.

In II, the 5-methyl signal is a singlet at ambient temperature, which splits below -40°C into an unsymmetrical doublet with the stronger signal at higher field. On decreasing the temperature further, a decoalescence of the high-field signal into a doublet occurs below ca -50°C, with the low-field, low-intensity component only 0.022 ppm up-field with respect to the previous low-field component. It has been shown that conformation B leads to a less shielded 5-methyl group than conformation A,[2] and the situations in B and C with respect to the 5-methyl group should be quite similar. Thus, the two low-field signals are ascribed to conformations B and C and the high-field signal to conformation A. According to the semiquantitative calculations described in Ref. 1, the direct exchange between A and B requires much higher energy than the exchange $A \rightleftharpoons C \rightleftharpoons B$, and the temperature-dependence of the spectrum is in agreement with this picture. The barriers calculated for the shifts $B \rightleftharpoons (A + C)$ and $A \rightleftharpoons C$ are found in the Table together with chemical shifts and populations.

TABLE

Compound	ν_A Hz	ν_B Hz	ν_C Hz	p_A	p_B	p_C	$\Delta G^{\ddagger}$ kcal/mol (T K) B → (A + C)	 A → C
II	206.3	217.8	215.6	0.67	0.10	0.23	13.4 (244)	11.7 (226)
III	250.8	262.0	260.1	0.37	0.47	0.16	15.7 (298)	12.0 (226)
IV	211.7	226.3	221.6	0.12	0.82	0.06	16.5 (299)	11.9 (226)
IV	325.9[a]	355.8[a]	338.7[a]					

Spectra recorded at 100 MHz in $CHCl_2F$ with TMS as internal standard.

[a] Chemical shifts of 4-methine protons. The other shifts are of 5-methyl protons.

The nmr spectra of the 5-methyl group in the thiazolium salt III show a similar behaviour, only with rather different populations (Table). Also in this case the signals ascribed to conformations B and C appear close together ($\Delta\delta$ = 0.016 ppm) and at low field.

The 5-methyl group in the thiazoline-thione IV gives rise to a doublet below ca 26°C. In the temperature range -40°C to -70°C the high-field, low-intensity signal shows exchange broadening and splits in the same way as described before. By irradiation of the resonance frequency of the methyl protons in the 4-isopropyl group, it was possible to observe an analogous temperature-dependence of the spectrum of the 4-methine proton.

The great similarity of the $A \rightleftharpoons C$ barriers is in satisfactory agreement with the proposed process with only the 4-isopropyl group rotating. The barriers to the $B \rightleftharpoons (A + C)$ exchange process are, as expected, much more dependent on the size of the 2-substituent. The relative populations of rotamers A, B and C reflect the effective size of the 2-substituent but also the lengths of the C_2-X and C_2-N_3 bonds.

Siddall and Stewart[3] report three different signals for the cis (Z) benzhydryl methine proton in N-isopropyl-N-benzhydrylisobutyramide. However, the model used by Siddall and Stewart has been criticized,[2,4] and it is probable that the three species they observe are better described by conformations similar to A, B and C.

Acknowledgements. We are grateful to C.N.R.S. de France (International A.T.P. no 9111) and to the Swedish Natural Science Research Council for financial support.

REFERENCES

1. C. Roussel, M. Chanon and J. Metzger, Tetrahedron Letters 1971, 1861.
2. C. Roussel, M. Chanon and J. Metzger, Tetrahedron Letters 1972, 3843.
3. T.H. Siddall, III and W.E. Stewart, J. Chem. Phys. 48, 2928 (1968).
4. K.C. Ramey, D.J. Louick, P.W. Whitehurst, W.B. Wise, R. Mukherjee, J.F. Rosen and R.M. Moriarty, Org. Magn. Resonance 3, 767 (1971).