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CHIROPTICAL PROPERTIES OF N-NITROSO-2-METHYLPYRROLIDINE IN RELATIONSHIP TO THE NITROSAMINE SECTOR RULE

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Chiral N-nitrosamines give an optically active $n \rightarrow \pi^*$ transition in the 370 nm region In 1966, Snatzke *et al* proposed a sector rule which correlates the stereochemistry of nitrosamines to their $n \rightarrow \pi^*$ Cotton effects [1] They used N-nitroso-2-methylpiperidine as a model compound in designating the sector signs The rule has been used in stereochemical assignments of chiral amines, but it seemed not to be generally applicable [2] NMR studies on N-nitroso-2-methylpiperidine later revealed a conformational mobility of this compound,[3] not taken into account by Snatzke and coworkers In 1972, Gaffield *et al* , on the basis of CD data on some nitrosamino acids (e g N-nitrosoproline and N-nitrosopipecolic acid), suggested that the signs of the sectors should be reversed [4] However, they pointed out the possibility that carboxyl groups, owing to electronic interactions with the idealized nodal structure of the chromophore, might give a rotatory contribution of opposite sign to that of alkyl groups On the other hand, Maat and Beyerman have proposed that the chiroptical properties of (*R*, *R*)-2,6-dimethyl-N-nitrosopiperidine are in agreement with Snatzke's sector rule [5]

In this communication we want to report on the CD curves of the enantiomers of N-nitroso-2-methylpyrrolidine [6] This molecule should be nearly planar and relatively free from conformational mobility. The nodal properties of the N-nitroso chromophore should not be significantly altered by the perturbing influence of the methyl group

The *syn/anti* ratio of N-nitroso-2-methylpyrrolidine was determined by NMR measurements in different solvents (carbon tetrachloride, benzene and dioxan)[3,7] Integration of the methyl resonances of both isomers gave a ratio of 1/5, which was not time-dependent In this respect, the N-nitroso derivative of 2-methylpyrrolidine differs from the nitrosamino acids studied by Gaffield *et al*[8]

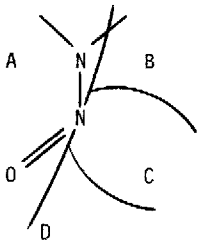
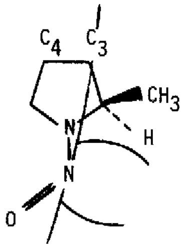
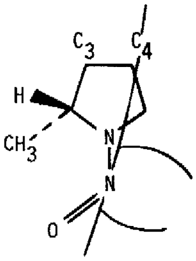


Figure 1 Modified sector rule for the $n \rightarrow \pi^*$ transition of the nitrosamino chromophore according to W Gaffield, L Keefer and W Lijinsky, *Tetrahedron Lett* 9, 779 (1972) The signs of sectors A, B, C and D (above the plane of the paper) are -, +, - and + respectively Sectors A', B', C' and D' (below the plane of the paper) have the opposite signs The N-N=O atoms and the α-carbon atoms are in the plane of the paper

The *anti* isomer of *(R)*-N-nitroso-2-methylpyrrolidine (Ia) has the methyl group in sector B, while the methyl group of the *syn* isomer (Ib) falls within sector A' In both isomers it should make a positive CD-contribution according to the modified sector rule An inspection of Dreiding's molecular models of the possible puckered conformations shows that deviation from ring planarity should have no profound effects on chiroptical properties The methyl group remains within sectors B or A' Carbon atoms C_3 and C_4 are able to deviate from the plane of the N-N=O atoms and the two α-carbon atoms. In the *anti* isomer, C_3 is close to the vertical nodal surface which separates sectors A and A' from B and B'. C_4 falls within sectors A or A' and should make only a small contribution to the overall Cotton effect[1] In the *syn* isomer, C_3 falls within sectors A or A', while C_4 is close to the vertical nodal surface



Ia



Ib

The positive Cotton effect observed for *(R)*-N-nitroso-2-methylpyrrolidine strongly suggests that the signs should be reversed in Snatzke's original sector rule As the $n \rightarrow \pi^*$ Cotton effect of *(S)*-N-nitrosoproline is also positive, it is evident that equipositioned methyl and carboxyl groups in the 2-position of N-nitrosopyrrolidine give a rotatory contribution of the same sign[9] The CD-spectra of *(R)*- and *(S)*-N-nitroso-2-methylpyrrolidine are reproduced in Figure 2[10]

Further studies on chiroptical properties of nitrosamines are in progress

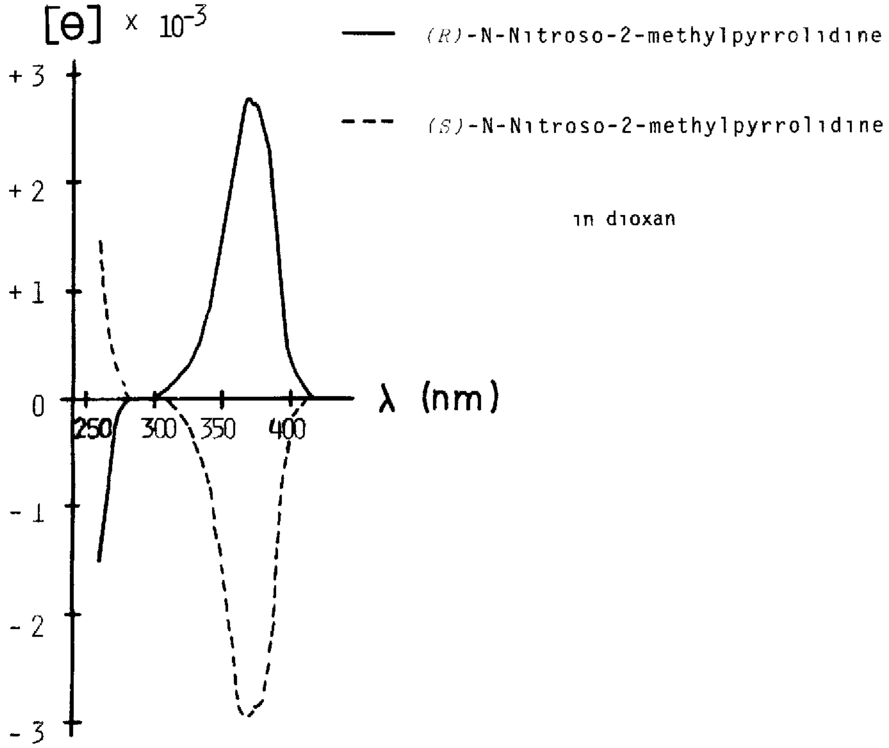


FIGURE 2

REFERENCES AND NOTES

1 G Snatzke, H Ripperger, C Horstmann and K Schreiber, *Tetrahedron* 22, 3103 (1966)

2 H Ripperger and K Schreiber, *J. Prakt Chem.* 313, 825 (1971)

3 R K Harris and R A Spragg, *J Mol Spec.* 23, 158 (1967)

4 W Gaffield, L Keefer and W Lijinsky, *Tetrahedron Lett* 9, 779 (1972).

5 L Maat and H C Beyerman, *Rec Trav Chim* 92, 156 (1973)

6 R G Kostyanovsky, I M Gella, V I Markov and Z E Samojlova, *Tetrahedron* 30, 39 (1974), have converted L-proline into (-)-2-methylpyrrolidine $\left[[\alpha]_{D}^{20}\ -31\ 2^{0}\ (c\ 1\ 0,\ \text{hexane})\right]$ thus establishing the absolute configuration of this amine We have resolved the amine into its enantiomers by fractional crystallization of its (+)- and (-)-bitartrates *(R)*-(-)-2-methylpyrrolidine $\left[[\alpha]_{D}^{22}\ -37\ 4^{0}\ (c\ 1\ 0,\ \text{hexane})\right]$ and *(S)*-(+)-2-methylpyrrolidine $\left[[\alpha]_{D}^{22}\ +38\ 4^{0}\ (c\ 1\ 8,\ \text{hexane})\right]$ thus obtained were converted to their N-nitroso derivatives according to the method described in reference 1

7 G Karabatsos and R Taller, *J Am Chem Soc* 86, 4373 (1964).

8 W Lijinsky, L Keefer and J Loo, *Tetrahedron* 26, 5137 (1970)

9 This conclusion is based on the assumption that the optical activity of the $n \rightarrow \pi^*$ transition primarily results from the perturbation of the chromophore by the substituent and not by an inherent chirality of the ring

10 CD-spectra were recorded with a Jasco J-20 automatic recording spectropolarimeter ($c = 7\ 4 \times 10^{-3}$ g/100 ml dioxan, 23^{0}C) The signs of the Cotton effects were unchanged in ethanol