The Stereochemical Investigation of 3-Aryl-4-methyl-1,2,3-oxathiazolidine 2-Oxides Using NMR

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The title compounds were prepared by the reaction of the corresponding *N*-2-hydroxyisopropylanilines with thionyl chloride in the presence of triethylamine, and their pmr and cmr spectra were examined. On the basis of the chemical shifts due to the γ- and δ-effects, the stereochemical structures are discussed.

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In connection with our studies on the stereochemistry of 3-aryl-1,2,3-oxathiazolidine 2-oxides [1,2] and 5-substituted 3-aryl-1,2,3-oxathiazolidine 2-oxides [3], the cyclization of β-amino alcohols with thionyl chloride is now investigated to obtain the information regarding the stereochemistry of 3-aryl-4-methyl-1,2,3-oxathiazolidine 2-oxides.

EXPERIMENTAL

The pmr and cmr spectra were determined at 400- and 100 MHz JEOL GSX-400 spectrometer in deuteriochloroform. The chemical shifts were referred to with the internal tetramethylsilane as the standard. β-Amino alcohols, the precursors of the 3-aryl-4-methyl-1,2,3-oxathiazolidine 2-oxides, were prepared by the reaction of the corresponding anilines with α-chloropropionic acid methyl ether, followed by lithium aluminium hydride reduction. The transformation of these β-amino alcohols to 3-aryl-4-methyl-1,2,3-oxathiazolidine 2-oxides was accomplished by the reaction with thionyl chloride in dry benzene at room temperature. A slight excess of triethylamine was used as the hydrogen chloride acceptor.

Results and Discussion.

The 3-aryl-4-methyl-1,2,3-oxathiazolidine 2-oxides prepared are listed in Table 1. An examination of Table 1 reveals that all amino alcohols yielded a pair of isomeric

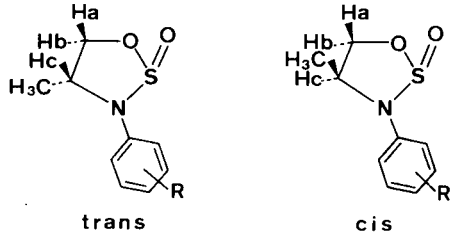
Table 1

Physical Properties of Compounds **1-5**

Compound No.	R	Yield %	*trans*/*cis*	Found/(Calcd) % C	H	N
1	H	81	1.13	54.89 (54.80)	5.65 (5.62)	7.15 (7.10)
2	*p*-Cl	58	1.08	46.79 (46.66)	4.41 (4.35)	6.19 (6.05)
3	*p*-CH_3	83	1.17	56.98 (56.85)	6.14 (6.20)	6.61 (6.63)
4	*o*-Cl	38	2.45	46.95	4.36	5.97
5	*o*-CH_3	87	2.57	56.45	6.20	6.70

cis- and *trans*-3-aryl-4-methyl-1,2,3-oxathiazolidine 2-oxides. The relative ratio of the *cis*- and *trans*-isomers as shown in Scheme 1 was determined by a capillary gas

Scheme 1. Possible Isomers of Compounds **1-5**



chromatography. The *trans*-isomer was preferentially obtained in all cases. Moreover, the product ratio depended on the position of the substituent on the aromatic ring. These differences can be considered that there are repulsive van der Waals interactions between the *ortho*-substituted group and the C-4 methyl group or the S=O group in the *cis*-form. Also yield of an *ortho*-compound is lower than those of other compounds.

The pmr chemical shift of the heterocyclic and methyl protons attached to the C-4 carbon are shown in Table 2. It is possible to assign the substituent geometry of the isomeric pairs by means of pmr spectroscopy. The sulfoxide

Table 2

PMR Chemical shifts of Compounds **1-5**

Compound No.	Configuration	Chemical shifts, δ Ha	Hb	Hc	4-Me
1	*cis*	4.77 (q)	4.79 (q)	4.24 (m)	1.41 (d)
	trans	5.04 (q)	4.25 (q)	4.45 (m)	1.26 (d)
2	*cis*	4.75 (q)	4.79 (q)	4.19 (m)	1.39 (d)
	trans	5.03 (q)	4.25 (q)	4.39 (m)	1.24 (d)
3	*cis*	4.73 (q)	4.75 (q)	4.20 (m)	1.38 (d)
	trans	5.00 (q)	4.19 (q)	4.41 (m)	1.24 (d)
4	*cis*	4.66 (t)	4.74 (q)	4.30 (m)	1.24 (d)
	trans	4.97 (q)	4.16 (t)	4.48 (m)	1.17 (d)
5	*cis*	4.69 (q)	4.71 (q)	4.02 (m)	1.25 (d)
	trans	4.97 (q)	4.09 (t)	4.45 (m)	1.13 (d)

bond is well known to have acetylenic-like anisotoropy [4]. For this reason, the deshielding of oxathiazolidine ring substituents which are *cis* to the sulfoxide bond results.

Moreover, Anteunis *et al.* [5] have reported the pmr spectra of various substituted 1,3-dioxolanes. The shifts of the pseudo-axial hydrogen of 2,2,4-trimethyl-*trans*-2,4-dimethyl- and *cis*-2,4-dimethyl-1,3-dioxolane appears at higher field about 0.61, 0.46 and 0.74 ppm than that of pseudo equatorial hydrogen, respectively. This difference in chemical shift has been attributed to shielding of the axial hydrogen by the adjacent *cis*-methyl group. If this two considerations can be extended to the methylene protons of Ha and Hb or methyl protons attached to the C-4 carbon for the compounds **1-5**. The Hb proton of the *trans*-form expects higher field shift than that of the Ha proton because of the shielding effect by adjacent *cis*-methyl group and anisotropic effect of the sulfoxide bond.

Similarly, the C-4 methyl protons of the *trans*-form expects higher field shift than that of the *cis*-methyl protons. As can be seen in Table 2, the averaged chemical shift differences between Ha and Hb protons in the *trans*-form was 0.80 ppm, whereas those of the *cis*-form was 0.04 ppm. Therefore, unequivocal assignment of both geminal protons Ha and Hb in their pmr spectra is not easily possible based on chemical shift information alone.

Previous pmr studies [2] of 3-aryl-1,2,3-oxathiazolidine 2-oxides without substituent on the C-4 and C-5 evaluated that the mean observed magnitude of anisotropic effect between the *cis*- and *trans*-protons at the C-5 to the sulfoxide bond was 0.36 ppm. Using this value and the averaged chemical shift difference (0.80 ppm) between the geminal protons, Ha and Hb, for the *trans*-compounds **1-5**, shielding effect by adjacent methyl group can be assumed about 0.44 ppm which is larger than anisotropic effect of the sulfoxide bond. From the above considerations, the Ha proton in the *cis*-form can be expected higher field shift compared with Hb proton.

The cmr chemical shifts for the materials examined are presented in Table 3. As can be seen in Table 3, for the *cis* and *trans* which have an *ortho*-substituent, the averaged C-4 chemical shift appeared at 60.0 and 54.4 ppm, whereas those of *para*-substituent and without a substituent are 55.8 and 52.7 ppm.

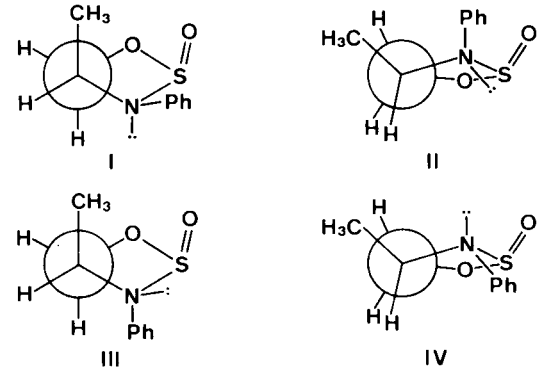
Table 3

Carbon-13 Chemical Shifts (δ) of Compounds **1-5**

Compound No.	Configuration	Chemical shifts, δ C-4	C-5	4-Me	R
1	*cis*	55.5	75.8	15.8	–
	trans	52.6	76.9	16.5	–
2	*cis*	55.6	75.9	15.6	–
	trans	52.8	77.0	16.3	–
3	*cis*	56.2	75.7	15.7	20.7
	trans	52.8	77.2	16.2	20.9
4	*cis*	58.6	75.6	16.7	–
	trans	54.3	77.1	15.6	–
5	*cis*	61.3	75.5	16.4	18.4
	trans	54.4	77.2	15.5	18.3

For compounds **1-3**, having the C-4 methyl *cis* to the S=O, there will be repulsive van der Waals interaction about 4.60 KJ mole^{-1} between the *syn*-axial methyl group and the S=O function [6], and 1.26 KJ mole^{-1} for CH_3---O gauche interaction [7] in **I** which will force the conformational equilibrium toward **II** as shown in Scheme 2 viewing the Newman projection along the C-4-C-5 bond. The methyl group of conformers **I** and **II** is essentially axial

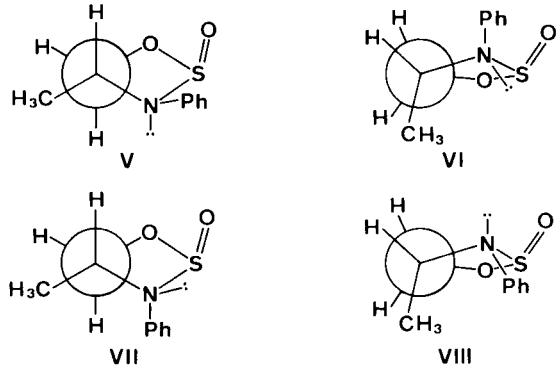
Scheme 2. Possible Conformations of *cis*-Compounds



and pseudo axial, respectively. Similarly, conformers **III** and **IV** are interconverted forms at N-3 of conformers **I** and **II**, respectively.

In the *trans*-compounds, however, the preferred conformations should be **V** or **VI** in which the methyl group is equatorial and the hydrogen on the C-4 carbon is axial as shown in Scheme 3.

Scheme 3. Possible Conformations of *trans*-Compounds



The γ-shifts for the *cis* and *trans* in compounds **1-3** are consistent with these conformational argument. That is, the highfield shift of 3.1 ppm at C-4 carbon in the *trans*-form relative to the *cis*-form is due to the hydrogen on C-4 carbon is *syn*-axial to the S=O bond in conformers **V** and/or **VII**. In conformers **VI** and/or **VIII** there is gauche CH_3---O interaction. Conversely, the minor γ-shift about 1.2 ppm for the C-5 carbon for the *cis* relative to this posi-

tion in the *trans*-form may arise from the contribution of conformers **II** and **IV** in which the hydrogen on the C-5 carbon is pseudo axial to the S=O bond. These γ-shifts have already been reported for ethylene sulfites and propylene sulfites. For example, Buchanan *et al.* [8,9] reported upfield shifts of 9.9 and 6.6 ppm at the C-4 and C-6 carbons of 4-phenyl-1,3,2-dioxathiane 2-oxides with an axial S=O bond relative to that the equatorial S=O type.

In the *cis*-compounds which has an *ortho*-substituent, there is a steric interaction between the S=O, methyl group attached to the C-4 carbon and the *ortho*-substituent in conformer **II** which will force the conformational equilibrium toward **IV**. If the preferred conformer of the *cis*-compounds **4** and **5** is **IV**, a δ-effect is operative to the C-4 carbon because of an *ortho*-substituent. Substituent effects over four bonds are generally negligible in open-chain compounds, since the molecules can adopt conformations which minimize steric hindrance, so that no δ-effects are detected. However, in the case in which steric interactions can not be minimized significant deshielding δ-effects have been recognized [10,11]. It has been proposed that the downfield direction of the shifts is a property of δ-interaction in general [12]. The shift differences of C-4 carbon between the *cis*-compounds **1-3** and the *ortho*-substituted compounds, **4** and **5**, for the *cis*-form are consistent with these conformational arguments. That is, the lowfield shift of 4.2 ppm at C-4 carbon in the compounds **4** and **5** relative to the *cis*-compounds **1-3** is due to the δ-effect of an *ortho*-substituent.

For the *trans*-compounds **4** and **5** with an *ortho*-substituent, the C-4 carbon is deshielded by 1.7 ppm relative to the *trans* compounds **1-3**. On the other hand, there is no shift difference between the C-5 carbon of the *trans*-compounds **1-5**. From above results, lowfield shift of the C-4 carbon may arise from the contribution of δ-effect of an *ortho*-substituent in conformers **V** and/or **VII**.

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