A Stereochemical Investigation of 1,3-Diphenyl-4-methyl-1,3-diazolidines and its Related Compounds *via* NMR

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Four 1,3-diphenyl-4-methyl-1,3-diazolidines and two isomeric 2,5-diphenyl-3-methyl-1,2,5-thiadiazolidine 2-oxides were prepared. The pmr and cmr spectra of these compounds were obtained. On the basis of the chemical shifts due to the γ- and δ-effects, the stereochemical structures are discussed.

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In a previous paper, we reported on the conformational structures of 5-substituted 3-aryl-1,2,3-oxathiazolidine 2-oxides based on the data of the γ-shifts and the δ-effects of nmr [1]. In a similar manner, the conformational analysis of five membered 1,3,2-dioxathiolane 2-oxides have been reported [2]. In connection with our previous study on five membered heterocyclic compounds, we have synthesized and examined some stereochemical structures of 1,3-diphenyl-4-methyl-1,3-diazolidines and 2,5-diphenyl-3-methyl-1,2,5-thiadiazolidine 2-oxides.

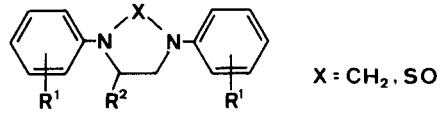


Figure 1

EXPERIMENTAL

All the melting points are uncorrected. The pmr and cmr spectra were determined at 400 and 100 MHz with JEOL GSX-400 spectrometer in deuteriochloroform. The chemical shifts were referred to with the internal tetramethylsilane as the standard. The starting *N,N'*-diphenylethylenediamine was obtained commercially. *N,N'*-diphenyl-2-methylethylenediamines used our study were prepared from the reactions of the 1,2-dibromopropane with corresponding anilines. The transformation of these 1,3-diphenylalkyldiamines to 1,3-diphenyl-4-methyl-1,3-diazolidines and 2,5-diphenyl-3-methyl-1,2,5-thiadiazolidine 2-oxides was accomplished by their reaction with paraformaldehyde and thionyl chloride, respectively. The purification of the crude product by the use of silica gel column, with hexane or hexane-benzene (1:1) mixture as an eluent, and subsequent recrystallization afforded a pure product. In case of 2,5-diphenyl-3-methyl-1,2,5-thiadiazolidine 2-oxides, two isomers of types a and b can be separated by the use of silica gel column. The products of these reactions and physical properties are summarized in Table 1.

Results and Discussion.

The ^{13}C-nmr chemical shifts for the materials examined are presented in Table 2. The cmr spectra of C-2 carbon show the same chemical shift between compound **1** without a methyl group at C-4 carbon and compounds **2-4** with a methyl group at C-4 carbon. Therefore, it can be considered that the geometrical relationship of compounds **2-4**

Table 1

Physical Properties of Compounds **1-7**

Compound No.	X	R^1	R^2	Yield %	Mp °C	C	H (Calcd.)	N
1	CH_2	H	H	41	122.0-123.0	80.05 (80.32)	7.21 (7.19)	12.34 (12.49)
2	"	"	CH_3	80	61.0- 62.5	80.28 (80.63)	7.65 (7.61)	11.65 (11.76)
3	"	*m*-Cl	"	76	[a]	62.30 (62.53)	5.19 (5.23)	9.21 (9.12)
4	"	*m*-CH_3	"	69	[a]	81.01 (81.16)	8.38 (8.32)	10.30 (9.92)
5	"	*o*-CH_3	"	5	[a]	81.13	8.27	9.92
6a	SO	*o*-CH_3	"	51	[a]	68.26	7.09	9.32
6b	"	"	"	37	[a]	(67.97)	(6.71)	(9.32)
7a	"	*m*-CH_3	"	56	99.5-100.5	67.98	6.77	9.29
7b	"	"	"	41	[a]			

[a] Liquid.

Table 2

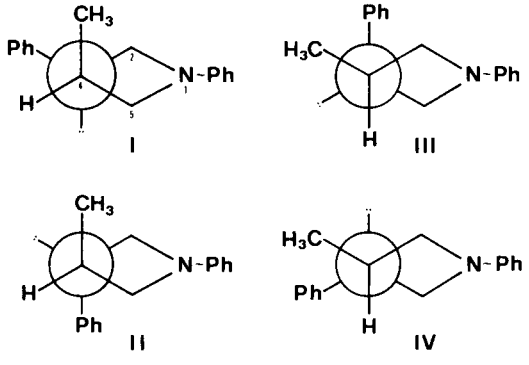
Carbon-13 Chemical Shifts (δ) of Compounds **1-7**

Compound No.	Chemical shifts, δ			
	C-2	C-4 (C-3)	C-5 (C-4)	4-CH_3 (3-CH_3) [a]
1	65.7	46.4	46.4	--
2	65.3	53.9	52.4	17.5
3	64.7	53.6	52.3	17.3
4	65.4	53.9	52.4	17.6
5	56.7	57.7	53.3	16.7
6a	--	59.0	57.3	17.3
6b	--	62.5	56.2	17.8
7a	--	54.6	54.2	17.2
7b	--	57.0	53.6	18.2

[a] For compounds **6** and **7**.

between the C-2 carbon and the methyl group attached to the C-4 carbon is γ-anti **III** or **IV** as shown in Scheme 1 viewing the Newman projection along the C-5-N-1 bond. Conformers **I** and **III** are γ-gauche and γ-anti forms between the methyl group attached to th C-4 carbon and the C-2 carbon, respectively. Similarly, conformers **II** and **IV** are γ-gauche and γ-anti forms which are interconverted inversion at N-3 of conformers **I** and **III**, respectively.

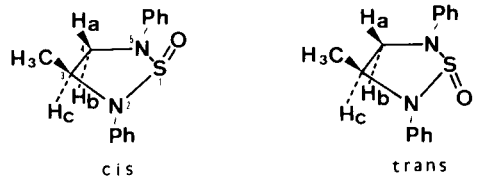
Scheme 1. Possible conformations of compounds **2-5**.



On the other hand, the chemical shift at C-2 carbon of an *ortho*-methyl compound **5** appeared higher field about 8.5 ppm than those of compounds **2-4**. These striking upfield shift can be considered that the geometrical relationship between the C-4 methyl group and the C-2 carbon is γ-gauche forms **I** or **II**. These γ-shifts have already been reported to determine a stereochemical relationships. For example, Buchanan *et al.* [3,4] 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 conformer **I**, however, there will be repulsive van der Waals interactions between the *ortho*-methyl and the C-4 methyl groups which will force the conformational equilibrium toward **II**. If the preferred conformer of the compound 5 is **II**, a δ-effect is operative to the C-4 carbon because of the *ortho*-substituted methyl group. Substituent effects over four bonds are generally negligible in open-chain compounds, since the molecules can adopt comformations which minimize steric hindrance, so that no δ-effects are detected. However, in cases in which steric interactions can not be minimized significant deshielding δ-effects have been recognized [5,6]. It has been proposed that the downfield direction of the shifts is a property of δ-interaction in general [7]. The chemical shift of the C-4 carbon in compound **5** appeared at 57.7 whereas those in compounds **2-4** appeared at about 53.8 ppm. The C-4 chemical shift of compound **5** appeared at lower field (about 3.9 ppm) than those of compounds **2-4**. Also the C-2 carbon is δ-position from the two *ortho*-methyl groups attached to the N-1 and N-3 phenyl rings. The δ-effect is expected to deshield the C-2 carbon, however, no effect is observed. From the above results, the *ortho*-methyl group attached to the N-3 phenyl group comes close to the C-4 carbon compared with the C-2 carbon, because of the steric repulsion between the *ortho*-methyl group attached to the inverting N-1 phenyl group.

The isomers of types **a** and **b** of compounds **6** and **7** indicate the possibility that the *cis* and *trans* configuration between the S=O and the methyl groups attached to the C-3 carbon as shown in Scheme 2. It is possible to assign the substituent geometry of isomers **a** and **b** by means of

Scheme 2. Possible isomers of compounds **6** and **7**.



pmr spectroscopy. The sulfoxide bond is well known to have acetylenic-like anisotropy [8]. For examples, Deyrup [9] has recorded the pmr spectra of various substituted 1,2,3-oxathiazolidines. The *trans* methyl protons of 3-*t*-butyl-4-methyl- and 3-*t*-butyl-5-methyl-1,2,3-oxathiazolidine 2-oxides appear at higher field about 0.25 and 0.16 ppm than that of the *cis* methyl protons, respectively. Similarly, the *trans* methyl protons in 3-aryl-5-methyl-1,2,3-oxathiazolidine 2-oxides appear at higher field about 0.16 ppm than that of the *cis* methyl protons [10]. In terms of our five-membered heterocyclic ring, these results in the deshielding of ring substituents which are *cis* to the sulfoxide bond. As can be seen in Table 3, the methyl signals in the compounds **6b** and **7b** appeared lower field than those of compounds **6a** and **7a**. Thus, isomers **6b** and **7b** are the *cis* form, whereas isomers **6a** and **7a** are the *trans* form.

Chemical shift nonequivalence is observed for the dia-

Table 3

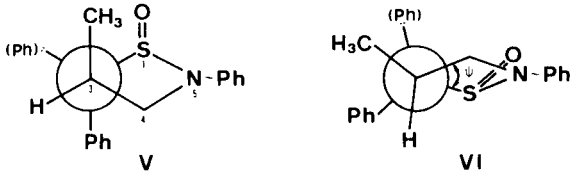
PMR Chemical Shifts and Dihedral Angle of Compounds 1-7

Compound No.	Chemical shifts, δ						Dihedral angle
	Ha	Hb	Hc	CH_3	H-2		(ψ)
1	3.57 (s)	3.57 (s)	3.57 (s)	–	–	–	–
2	3.35 (q)	3.55 (q)	4.22 (m)	1.27 (d)	4.51 (d)	4.78 (d)	15
3	3.36 (q)	3.59 (q)	4.23 (m)	1.28 (d)	4.49 (d)	4.72 (d)	15
4	3.35 (q)	3.55 (q)	4.22 (m)	1.27 (d)	4.50 (d)	4.75 (d)	15
5	3.10 (q)	3.41 (q)	3.49 (m)	1.04 (d)	4.04 (d)	4.25 (d)	26
6a	3.34 (q)	4.31 (q)	4.66 (m)	1.19 (d)	–	–	47
6b	3.71 (q)	4.24 (t)	4.08 (m)	1.30 (d)	–	–	35
7a	3.46 (q)	4.12 (q)	4.70 (m)	1.27 (d)	–	–	48
7b	3.97 (q)	4.03 (t)	4.44 (m)	1.51 (d)	–	–	40

stereotopic methylene protons Ha and Hb. Anteunis *et al.* [11] 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 appeares at higher field about 0.61, 0.46 and 0.74 ppm than that of pseudoequatorial hydrogen, respectively. This difference in chemical shift has been attributed to shielding of the axial hydrogen by the adjacent *cis*-methyl group. If this consideration can be extended to the methylene protons of Ha and Hb for the compounds **6** and **7**, the following considerations are possible. The Ha proton of the *trans* form expects higher field shift than that of the Hb proton because of the shielding effect by adjacent *cis* methyl group and anisotropic effect of the sulfoxide bond. Similarly, the Ha proton of the *cis* form expects higher field shift than that of the Hb proton since the Ha proton is the *cis* to the adjacent methyl group. But chemical shift differences between Ha and Hb protons can be assumed smaller than that of *trans* form since Hb proton of the *cis* form is *trans* to the S=O bond. Therefore, higher field signal of the *trans* and *cis* was assigned to Ha proton.

The ^{13}C-nmr chemical shifts for the compounds **6** and **7** are listed in Table 2. For the *cis* and *trans* which have an *ortho*-methyl group, the C-3 chemical shift appeared at 62.5 and 59.0 ppm, whereas those of *meta*-substituted compounds **7** at 57.0 and 54.6 ppm, respectively. For **7b**, having the C-3 methyl *cis* to the S=O, the preferred conformation is suggested to be that depicted as **VI** in which

Scheme 3. Possible conformations of *cis* compound **7b**.

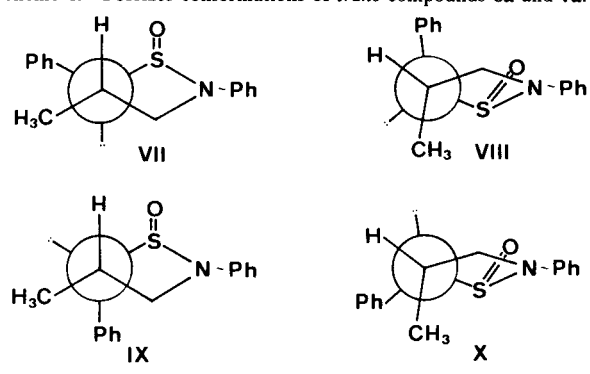


relationship between the C-3 carbon and the S=O function close to γ-anti as is shown in Scheme 3. In conformer **V** there are a gauche CH_3...S=O interaction about 1.1 Kcal/mol [12] and also inverting two aromatic rings.

The preferred conformation of **7b** is further illustrated by means of dihedral angle (ψ). Lambert [13,14] reported that the ratio (R) of the average J_{trans} to the average J_{cis} in a six-memebered ring has been found to be nearly independent of the electronegativity of substituent. Therefore, R becomes a direct measure of conformational effects. The dihedral angle of the conformer **V** can be estimated as about 60°, whereas the conformer **VI** is smaller than **V** from molecular model. The dihedral angle of compound **7b** calculated from Lambert equation is about 40°. Therefore, it can be considered that preferred conformation of **7b** exists in conformer **VI**.

For *trans* compound **7a**, again viewing the Newman projection along the C-3-N-2 bond, the preferred conformation should be **VII** or **IX** in which the methyl group has no steric interaction with the S=O bond. The high field shift at C-3 carbon compared with compound **7b** is in agreement with these conformational arguments. That is, it can be consider that the relationship between the C-3 carbon and S=O bond is γ-gauche.

Scheme 4. Possible conformations of *trans* compounds **6a** and **7a**.



In the *trans* form having an *ortho*-methyl compound **6a**, the C-3 carbon is deshielded by 4.4 ppm relative to compound **7a**. On the other hand, dihedral angle of compound **6a** is almost same value compared with compound **7a**. In conformer **VII**, there will be steric interactions between the *ortho*-methyl and the S=O groups which will force the conformational equilibrium toward **IX**. Therefore, the downfield shift at C-3 carbon may arise from the δ-effect of the *ortho*-methyl group and the deshielding δ-effects is consistent with earlier arguments for compound **5** having an *ortho*-methyl group.

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