Available online at www.journalijmrr.com

INTERNATIONAL JOURNAL OF MODERN RESEARCH AND REVIEWS

Int. J. Modn. Res. Revs.

Volume 6, Issue 1, pp 1-6, January, 2018

ISSN: 2347-8314

SYNTHESIS AND ^{1}H AND ^{13}C NMR SPECTRAL STUDY OF SOME 5R-ARYL-3T-CYANO-3C-METHYLCYCLOHEXANONE OXIMES

[*1]S. Kamatchi and [2]R.T.Sabapathy Mohan

[*1] Department of Chemistry.Govt arts college,C.Mutlur,Chidambaram.

[2]Department of Chemistry, Annamalai University, Annamalainagar, India

Article History: *Received 2nd March,2018, Accepted 30th March,2018, Published 31st March,2018*

ABSTRACT

Five 5r-aryl-3t-cyano-3c-methylcyclohexanone oximes **2a-e** (Ar=C_6H_5,p-FC_6H_4,p-$OMeC_6H_4$,p-ClC_6H_4,p-MeC_6H_4)have been synthesized by treating the corresponding ketones with NH_2OH in the presence of sodium acetate. ^{1}H and ^{13}C NMR spectra have been recorded in $CDCl_3$.For **2a** DMSO-d_6 has been recorded .Changeof solvent from $CDCl_3$ to DMSO-d_6 has a marked effect on the chemical shifts of the protons in the cyclohexane ring and OH proton. However,^{13}C chemical shifts are not influenced by the change of solvent.For **2a** HSQC and HMBC spectra have been recorded.Oximation shields allthe protons in cyclohexanone ring except H_{2a}.Which is deshielded by about 0.15ppm.use of ^{1}H and ^{13}C chemical shifts for determining the configuration and conformation of oximes is also discussed.

Keywords: ^{1}H NMR,^{13}C NMR,Oximes,Synthesis,Configuration, Conformation

1.INTRODUCTION

NMR spectral studies of oximes have been of constant interest. Configuration and conformation of oximes have been assigned using NMR spectra. Acetone and ethyl methyl ketone oximes have been synthesized to investigate the differences in relaxation behaviour between conformational isomers by using ^{13}C NMR spectra[1].Hawkes *et al.*[2] have used ^{13}C NMR as a tool to determine the configurations and conformations of aldoximes and ketoximes. They have distinguished the composition of the *syn* and *anti* isomers of oximes. They have confirmed that the OH group of oxime preferred its position *anti* to the □-quaternary carbon in most of the cases.

Oximation of *cis*-1-alkyl-3,5-diphenylpiperidin-4-ones has been reported by Andrisano*et al.*[3] Geneste*et al.*[4] have investigated ^{13}C chemical shifts for a number of relatively rigid ketoximes. They suggested that the chemical shift difference Δ□ (*syn-anti*) for the carbons □ to the oxime carbon, depends on the dihedral angle between the C=N and C□-H bonds. From the observed values, they determined the preferred conformation of oximes in solution. Pandiarajan and Tamilselvi[5] have studied the conformational analysis of some 3-alkyl-2,6-diphenylpiperidin-4-one oximes and 3-alkyl-2,6-diphenyltetrahydropyran-4-one oximes on the basis of ^{1}H and ^{13}C NMR spectral studies.

Pandiarajan*et al.*[6] have discussed the conformations of some 1-hetera-2,6-diarylcyclohexan-4-one oximes using NMR spectra. They have suggested that the oximes having the phenyl groups in *cis* orientation exist largely in chair conformation. Diaz *et al.*[7]have studied the conformations of 2,6-diaryl-1-hydroxypiperidin-4-one oximes using ^{1}H and ^{13}C NMRspectra.Olivato*et al.*[8] reported the X-ray diffraction analyses of 2-substituted cyclohexanone oximes and of the parent cyclohexanoneoxime and showed that their cyclohexyl rings are in a slightly distorted chair conformation. These compounds have been explained to be in the solid state with **E** configuration bearing the 2-substituents in the axial conformation.deLijser et al.[9] it has been found that oximation of2,6-diphenylcyclohexanone undergoes dehydrogenation during oximation and gives (**E**)-2,6-diphenylcyclohex-2-enone oxime. The structure has been elucidated by X-ray crystallographic study.

Corresponding author:* ***Dr. S.Kamatchi, Asst. Professor,* *Department of Chemistry, Govt. Arts College, Chidambaram-608102*

Synthesis of ^{1}H and ^{13}C NMR spectral study of some 3*t*-aryl-2*r*,4*c*-dicarbalkoxy-5*c*-hydroxy-5*t*-methylcyclohexanones and their oximes have been reported by Sabapathy Mohan *et al.*[10] They have suggested chair conformation for all the compounds with axial orientations of the hydroxyl group at C-5 and equatorial orientations of all the other substituents.This paper reports the synthesis and NMR spectral study of Five 5r-aryl-3t-cyano-3c-methylcyclohexanone oximes **2a-e**.

2.RESULTS AND DISCUSSION

Synthesis and characterization of compounds

The oximes were synthesized following **scheme 1**.All compounds were characterized by their IR spectra. elemental analysis was done for **2a-e**. Mass spectrum was recorded for **2a**. Mass spectrum ofoxime**2a** reveals the molecular weight, as m/z 229 $(M + H)^+$ is predominant. This is in accordance with the molecular formula of oxime**2a** ($C_{14}H_{16}N_2O$).The physical data are given in **Table I** and the results of elemental analysis are given in **Table II.**

All compounds were purified by recrystallisation from ethanol. IR spectrum of the oxime is compared with that of the parent ketone[13]. The carbonyl frequency (C-1) is found to be absent and instead C=N frequency has been observed at 1605 cm^{-1}

^{13}C NMR spectra

Carbon-13NMR spectra of oximes **2a-e** have been recorded in $CDCl_3$. For oximes **2a** ^{13}C NMR spectra have been recorded in DMSO-d_6 also. For oxime**2a** HSQC and HMBC spectra have been recorded. C-2 and C-6 carbon resonances of oxime**2a** are assigned by comparing the corresponding resonances of the parent ketone and incorporating the effect of oximation on carbons. Among the cyclohexyl ring carbons the two ^{13}C resonances 34.7 and 38.6 ppm of the oxime considerably differ from the corresponding ketone resonances.

In ^{13}C NMR spectrum of oxime, if 34.7 and 38.6 ppm are assigned to *syn* and *anti* carbons respectively, then the *syn* and *anti* carbons are shielded by 15.6 and 8.5 ppm respectively. If 34.7 and 38.6 ppm are assigned to *anti* and *syn* carbons respectively, then the *anti* and *syn* carbons are shielded by 12.4 and 11.7 ppm respectively. The effect of oximation on *syn* and *anti* carbons is in accordance with the former argument. Hence, 34.7 and 38.6 ppm are assigned to C-2 and C-6 of the oxime respectively. Since C-2 is shielded by 15.6 ppm, C-2 must be *syn* to >C=NOH group. C-6 is shielded by 8.5 ppm and hence C-6 must be *anti* to >C=N-OH group. The above argument confirms the formation of **E**-isomer **2a**without ambiguity. The carbon-13 resonance at 155.2 ppm is assigned to C-1,sinceoximation shields C-1 by 49.7 ppm. Since other carbon-13 chemical shifts are not significantly influenced due to oximation, they are conveniently assigned by comparing carbon-13 chemical shifts of ketone and oxime.

In HSQC spectrum the ^{13}C resonance 35.8 ppm has no cross peaks and hence it is assigned to the quaternary carbon C-3. The ^{13}C resonances 34.7, 44.5 and 38.6 ppm have two cross peaks each. This reveals that the above three resonances are due to methylene carbons C-2, C-4 and C-6. The ^{13}C resonance 41.7 ppm is assigned to C-5, since it has only one cross peak. Among the aromatic carbon resonances, the ^{13}C resonance 143.4 ppm having no cross peak is assigned to C-1′. The cyano carbon resonance is distinguished from other aromatic carbon resonances based on the fact that cyano carbon has no cross peak in HSQC.

Three methylene carbon resonances (34.7, 38.6 and 44.5 ppm) have been identified in HSQC spectrum. Out of the three methylene carbons C-2 and C-4 are expected to have cross peaks with methyl protons at C-3 and C-6 methylene carbon cannot have any correlation with methyl protons at C-3.

In HMBC spectrum, the ^{13}C resonance 38.6 ppm does not show any correlation with methyl protons and hence that resonance is assigned to C-6 (38.6 ppm). ^{13}C resonances 34.7 and 44.5 ppm exhibit cross peaks with methyl protons at C-3 (34.7/1.58, 44.5/1.58 ppm). Since C-2 has been assigned based on the oximation effect, C-2 and C-4 resonances are easily distinguished.

Having assigned C-2, C-4 and C-6 resonances, the corresponding cross peaks in HSQC reveal the respective methylene protons. Hence, the proton chemical shifts of H_{4a}, H_{4e}, H_{6a} and H_{6e} are confirmed. The signal due to H_{2a} is merged with that of H_{4a}. Similarly the signal due to H_{4e} and H_{6a} are overlapped.

^{1}H NMR spectrum

In oximes from six membered saturated cyclic ketone the equatorial -proton in the *syn* side has a greater chemical shift than in the *anti* side by about 1 ppm. Also the *syn* axial proton is shielded by 1 ppm. From the above observation comparing the proton chemical shifts of ketone and oxime, the signal at 3.89 ppm is assigned to H_{2e}.

The proton resonance 1.74 ppm is assigned to H_{2a}. Based on the oximation effect on *anti* protons the proton chemical shifts 2.26 and 2.74 ppm are assigned to H_{6a} and H_{6e} respectively. Since oximation does not cause significant changes on the -proton chemical shifts, H_{4a} and H_{4e} are assigned by comparing the proton chemical shifts of the corresponding ketone.

Effect of solvent on chemical shifts

In order to study the effect of solvent on proton chemical shifts, ^{1}H and ^{13}C NMR spectra have been recorded for oximes **2a** in $CDCl_3$ and DMSO-d_6. In DMSO-d_6 the oximino proton is deshielded by 3.01 and 2.60 ppm respectively in oximes **2a** due to strong hydrogen bonding with DMSO-d_6. Change of solvent from $CDCl_3$ to DMSO-d_6 has a marked effect on the chemical shifts of *syn* (H_{2a} and H_{2e}) protons, *anti* ($H_{6a}$and H_{6e}) protons and *anti* (H_{5a}) proton. H_{2a} is deshielded by 0.15 ppm whereas H_{2e}, H_{5a}, H_{6a} and H_{6e} are shielded by 0.2 to 0.3 ppm.

A similar study has been carried out by Sabapathymohan*et al.*[10]in 3*t*-aryl-2*r*,4*c*-dicarbalkoxy-5*c*-hydroxy-5*t*-

methylcyclohexanone oximes. It has been reported that H_{6e} has a higher chemical shift than the H_{6a} in $CDCl_3$ whereas in DMSO-d_6, H_{6a} has a higher chemical shift than H_{6e}. Pandiarajan has suggested a change in conformation of the oxime in DMSO-d_6. In our present study such type of reversal of chemical shifts of *syn* protons is not observed due to change of solvent from $CDCl_3$ to DMSO-d_6.

3.CONFORMATION

Analysis of carbon-13 chemical shifts of oximes **2a** in $CDCl_3$ and DMSO-d_6 reveals that in DMSO-d_6 all the cyclohexylcarbon resonances (C-1 to C-6) are found to be shielded by 1 to 2 ppm. The structure of the compound **2a** is confirmed by X-ray crystallographic study.[11] According to the X-ray diffraction study, the cyclohexane ring adopts a chair conformation. The oxime moiety is planar and has an equatorial orientation. The cyano group has an axial orientation, whereas methyl and phenyl have equatorial orientations(**2C**).

The formation of oxime in which >C=N-OH is *syn* to methyl group is favoured, because of the stabilization due to the following structure before elimination of one molecule of water.

Effect of oximation

Analysis of ^{13}C chemical shifts of C-2 and C-6 confirms the formation of **E**-isomer in all cases. The *syn* and *anti*-carbon are shielded and shielding of *syn*-carbon is in the range of 15-17 ppm whereas that of *anti*-carbon is in the range of 8-10 ppm. The shielding of *syn* carbon is greater than that of *anti* carbon. The observed oximation effects are in accordance with the expected electronegativity change due to oximation.The oximation effects on , and -carbons are given in **Table V**.Oximation shields all the protons in cyclohexanone ring except H_{2e}, since the *syn* equatorial proton is deshielded by 1 ppm. The effects of oximation on proton chemical shifts are given in **Table VI**.

Experimental section

Preparation of compounds
5*r*-Aryl-3*t*-cyano-3*c*-methylcyclohexanone oximes **(2a-e)**

5*r*-Aryl-3*t*-cyano-3*c*-methylcyclohexanone oxime was prepared following the procedure of Baliah*et al.*[12] The 5*r*-aryl-3*t*-cyano-3*c*-methylcyclohexanone (0.05 mol) and sodium acetate trihydrate (0.15 mol) was dissolved in boiling ethanol and hydroxylamine hydrochloride (0.06 mol) was added. The mixture was heated under reflux for 1 h and poured into ice water. The separated solid was filtered off and the product was purified by column chromatography using silica gel (100-200 mesh) with benzene-ethyl acetate mixture (9.5:1) as eluent. By using the above procedure following fivecyanocyclohexanone oximes are prepared.

Recording of spectra

All NMR measurements were made by using 5 mm tubes. For **2a-e** on Bruker AMX 400 NMR spectrometer operating at 400.14 MHz for ^1H and 100.63 MHz for ^{13}C. For ^1H NMR spectra, solutions were prepared by dissolving 10 mg of the material in 0.5 ml of $CDCl_3$ (or) DMSO-d_6 (suitable solvent). For recording ^{13}C NMR spectra, solutions were prepared by dissolving 50 mg of the material in 0.5 ml of $CDCl_3$ or DMSO-d_6.

HSQC and HMBC spectra were recorded on a Bruker DRX 500 NMR spectrometer using standard parameters. For recording 2D spectra solutions were made by dissolving 50 mg of the material in 0.5 ml of $CDCl_3$ (or) DMSO-d_6. The number of data points was 1 K. IR spectra were recorded on AVATAR 330 FT-IR Thermo Nicolet Spectrometer in KBr pellets. Mass spectrum was recorded on a JEOL DX-303 mass spectrometer. Elemental analysis was performed on a Perkin-Elmer CHNS/O analyser.

4.CONCLUSION

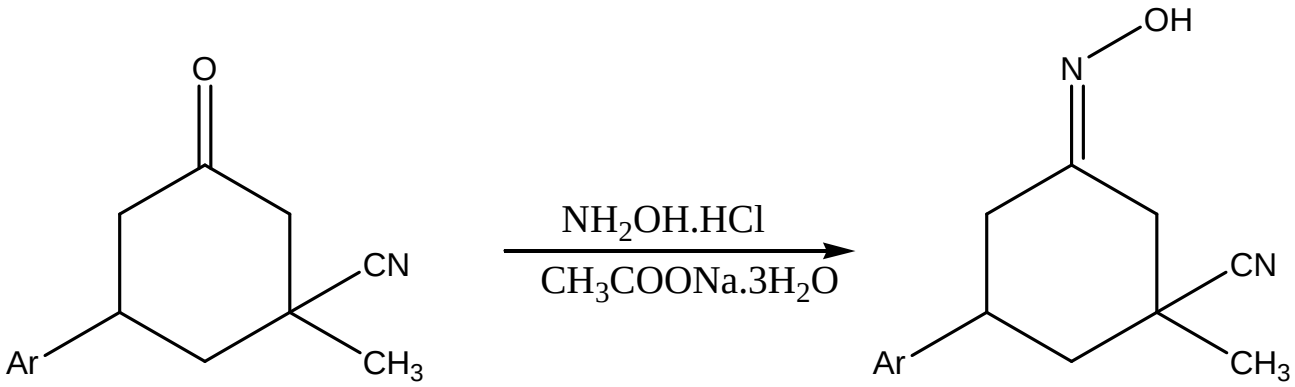
The NMR spectral data of the cyanocyclohexanone oximes suggest that these compounds exist in chair conformation with cyano group in the axial position and the aryl and methyl groups in the equatorial positions. **E**-configuration has been assigned for oximes. Effect of solvent on proton chemical shifts has been mentioned.

5.ACKNOLEDGEMENTS

Thanks are due to NMR Research Centre, IISc, Bangalore for recording the NMR spectra.

6.REFERENCES

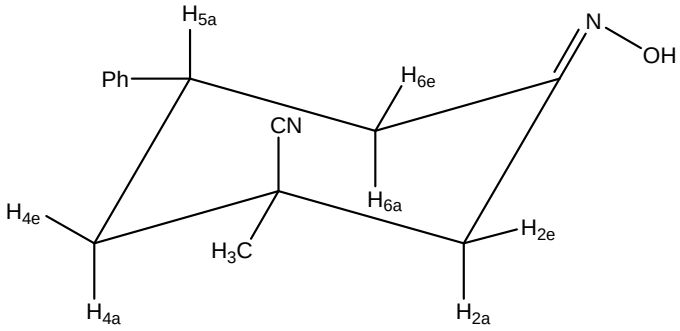
1. G.C. Levy and G.L. Nelson, *J. Am. Chem. Soc.*,**1972,** 4897.
2. G.B. Hawkes, K. Herwig and J.D. Roberts, *J. Org. Chem.*,**1974,** 39, 1017.
3. R. Andrisano, A.S. Angeloni and G. Gottarielli, *Tetrahedron*,**1974,** 30, 3827.
4. P. Geneste, R. Durrand, J.M. Kamenka, H. Beierbeck, R. Martino and J.K. Saunders, *Can. J. Chem.*,**1978,** 56, 1970.
5. K. Pandiarajan and P. Tamilselvi, *Indian J. Chem.B*,**1994,** 33, 971.
6. K. Pandiarajan, V. Gurumani and M. Swaminathan, *Bull. Chem. Soc. Jpn.*,**1997,** 70, 29.
7. E. Diaz, H. Barrios, F. del Rio Portilla, A. Guzman, J.L. Aguilera, R. Becerril, C.K. Jankowski and W.F. Reynolds, *Spectrochim. Acta A*,**2000,** 56,2191.
8. P.R. Olivato, D.S. Ribeiro, J. Schpector and G. Bombieri, *ActaCrystallogr.*,**2001,** B57, 705.
9. H.J.P. de Lijser, C.E. Dedeian, J.R. Sawyer, S.R. Herron and K.A. Kantardjieff, *J. Chem. Crystallogr.*, **2004,** 34, 103.
10. S. Amirthaganesan, R.T. Sabapathy Mohan, K. Murugavel,G. Muthukumaran and K. Pandiarajan, *Indian J. Chem. B*,**2007,** 46, 1004.
11. A. Thiruvalluvar, M. Subramanyam, R.T. Sabapathy Mohan,S. Kamatchi and K. Murugavel, *ActaCrystallogr. E*,**2007**, 63, 2780
12. V. Baliah and C.R. Noller, *J. Am. Chem. Soc.*,**1948**, 70, 3853.
13. S. Kamatchi, R.T. Sabapathy Mohan, R. Gomathi and K. Pandiarajan, *Indian J.Chem.*,***2009***, 48B, 553.



2a-2e

2a: Ar = C_6H_5
2b: Ar = *p*-FC_6H_4
2c: Ar = *p*-$OMeC_6H_4$
2d: Ar = *p*-ClC_6H_4
2e: Ar = *p*-MeC_6H_4

Scheme 1 synthesis of cyanocyclohexanone oximes



2C

Table I — Results of elemental analysis of compounds **2a-e**

Compound	Experimental			Calculated for the molecular formula		
	% C	% H	% N	% C	% H	% N
2a	73.81	7.08	12.30	73.68	7.02	12.28
2b	63.61	6.13	11.52	68.57	6.12	11.42
2c	69.83	7.01	10.87	69.77	6.98	10.85
2d	63.89	6.10	10.70	63.87	6.08	10.65
2e	75.40	8.01	11.72	74.38	7.44	11.57

Compound	Yield %	m.p. °C	Stretching frequencies (cm^{-1})		
			>C=N group	- C ≡N group	-OH group
2a	87	176	1605	2225	3381
2b	80	180	1605	2224	3380
2c	75	154	1611	2236	3281
2d	80	144	1605	2235	3281
2e	85	177	1614	2236	3270

Compound	Chemical shifts (δ, ppm)								
	C-1	C-2	C-3	C-4	C-5	C-6	CH_3 at C-3	C≡N at C-3	Aromatic [a]
2a($CDCl_3$)	155.2	34.7	35.8	44.5	41.7	38.6	27.7	123.2	127.1,128.8.129.3,143.4
2a(DMSO-d_6)	152.7	33.3	34.9	42.6	41.2	37.7	26.3	123.5	126.7,128.6,143.7
2b	154.5	34.2	35.3	44.2	40.4	38.2	26.7	123.4	115.6,128.1,139.9,161.0
2c[b]	154.8	34.2	35.3	44.4	40.5	38.4	27.3	122.8	114.1,127.6,135.1,158.5
2d	154.5	34.2	35.3	44.1	40.7	38.1	27.2	122.6	128.1,128.9,133.1,141.4
2e[c]	154.7	34.2	35.3	44.2	40.8	38.2	27.2	122.8	126.5,129.4,136.7,139.9

[a]Aromatic signals are mentioned in the order: ortho,meta,para, ipso.
[b] OCH_3 signal was observed at 55.3 ppm.
[c]CH_3 signal was observed at 20.9 ppm.

Table IV – ^{1}H NMR spectral data of cyanocyclohexanone oximes **2a-e**

Compound	Chemical shifts (δ, ppm)									
	H-2a	H-2e	H-4a	H-4e	H-5a	H-6a	H-6e	CH_3 protonsat C-3	Aromatic proton	=N-OH proton
2a($CDCl_3$)	1.74	3.89	1.74	2.26	3.23	2.26	2.74	1.58	7.69	7.34
2a(DMSO-d_6)	1.89	3.56	1.89	2.28	2.90	2.05	2.42	1.45	7.29	10.7
2b	1.69	3.85	1.69	2.19	3.17	2.19	2.69	1.54	7.20(o), 7.03(m)	8.05
2c[b]	1.67	3.84	1.67	2.17	3.15	2.17	2.69	1.53	7.16(o), 6.88(m)	7.95
2d	1.68	3.85	1.68	2.19	3.17	2.19	2.69	1.58	7.32(o), 7.18(m)	8.32
2e[c]	1.68	3.84	1.68	2.22	3.16	2.22	2.70	1.52	7.36(o), 7.13(m)	8.68

[a]In the case of aromatic protons ortho, meta, para are with respect to C-5.
[b] OCH_3 protons appeared at 3.80 ppm.
[c]CH_3 protons appeared at 2.34 ppm.

Table V-Effect of oximation on ^{13}C chemical shifts (ppm) of **2a-e**

Compound	α-Carbon		β-Carbon		γ-Carbon		C-1 carbon
	syn C-2	*anti* C-6	*syn* C-3	*anti* C-5	C-4	CH_3 at C-3	
2a ($CDCl_3$)	-15.6	-8.5	-0.4	+1.2	+1.8	+0.9	-49.7
2a(DMSO-d_6)	-17.0	-9.4	-1.3	+0.7	-0.1	-0.5	-52.2
2b ($CDCl_3$)	-16.4	-9.4	-1.2	+0.2	+1.0	-0.5	-50.6
2c	-16.1	-9.0	-0.8	+0.7	+1.3	+0.4	-50.5
2d	-16.4	-9.2	-1.0	+0.6	+1.0	-0.1	-49.8
2e	-16.8	-9.7	-1.3	+0.2	+0.3	+0.5	-50.3

(-) Shielding; (+) Deshielding

Table VI -Effect of oximation on ^{1}H chemical shifts (ppm) of **2a-e**

Compound	*syn*		*anti*		*anti*			
	H_{2a}	H_{2e}	H_{6a}	H_{6e}	H_{5a}	H_{4a}	H_{4e}	CH_3 at C-3
2a($CDCl_3$)	-0.67	+1.17	-0.24	+0.08	-0.13	-0.21	-0.04	+0.04
2a (DMSO-d_6)	-0.52	+0.84	-0.45	-0.24	-0.46	-0.06	-0.02	-0.09
2b($CDCl_3$)	-0.72	+1.09	-0.30	+0.01	-0.21	-0.23	-0.14	-0.03
2c	-0.71	+1.09	-0.28	+0.02	-0.19	-0.22	-0.14	-0.03
2d	-0.68	+1.08	-0.24	+0.0	-0.23	-0.20	-0.13	+0.01
2e	-0.66	+1.08	-0.23	+0.01	-0.21	-0.20	-0.09	-0.03

(-) Shielding; (+) Deshielding

Table V-Effect of oximation on ^{13}C chemical shifts (ppm) of **2a-e**

Compound	-Carbon		-Carbon		-Carbon		C-1 carbon
	syn C-2	*anti* C-6	*syn* C-3	*anti* C-5	C-4	CH_3 at C-3	
2a ($CDCl_3$)	-15.6	-8.5	-0.4	+1.2	+1.8	+0.9	-49.7
2a(DMSO-d_6)	-17.0	-9.4	-1.3	+0.7	-0.1	-0.5	-52.2
2b ($CDCl_3$)	-16.4	-9.4	-1.2	+0.2	+1.0	-0.5	-50.6
2c	-16.1	-9.0	-0.8	+0.7	+1.3	+0.4	-50.5
2d	-16.4	-9.2	-1.0	+0.6	+1.0	-0.1	-49.8
2e	-16.8	-9.7	-1.3	+0.2	+0.3	+0.5	-50.3

(-) Shielding; (+) Deshielding

Table VI -Effect of oximation on ^{1}H chemical shifts (ppm) of **2a-e**

Compound	*syn*		*anti*		*anti*			
	H_{2a}	H_{2e}	H_{6a}	H_{6e}	H_{5a}	H_{4a}	H_{4e}	CH_3 at C-3
2a($CDCl_3$)	-0.67	+1.17	-0.24	+0.08	-0.13	-0.21	-0.04	+0.04
2a (DMSO-d_6)	-0.52	+0.84	-0.45	-0.24	-0.46	-0.06	-0.02	-0.09
2b($CDCl_3$)	-0.72	+1.09	-0.30	+0.01	-0.21	-0.23	-0.14	-0.03
2c	-0.71	+1.09	-0.28	+0.02	-0.19	-0.22	-0.14	-0.03
2d	-0.68	+1.08	-0.24	+0.0	-0.23	-0.20	-0.13	+0.01
2e	-0.66	+1.08	-0.23	+0.01	-0.21	-0.20	-0.09	-0.03

(-) Shielding; (+) Deshielding