1H-N. M. R. study of the syn! anti ratio of oximes and 2,4- dinitrophenyl hydrazones determined by ASIS and LIS methods

Žinić, M.; Štromar, M .; Malnar, M.; Kolbah, D.

Source / Izvornik: **Croatica Chemica Acta, 1974, 46, 45 - 50**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:163:168186

Rights / Prava: In copyright / Zaštićeno autorskim pravom.

Download date / Datum preuzimanja: **2024-03-28**



Repository / Repozitorij:

Repository of Faculty of Pharmacy and Biochemistry University of Zagreb





CROATICA CHEMICA ACTA CCACAA 46 (1) 45—50 (1974)

CCA-817

YU ISSN 0011-1643
547.574.2
Original Scientific Paper

^{1}H-N. M. R. Study of the *Syn/Anti* Ratio of Oximes and 2,4-Dinitrophenyl Hydrazones Determined by ASIS and LIS Methods

M. Žinić, M. Štromar, M. Malnar, and D. Kolbah

Faculty of Pharmacy and Biochemistry, and Institute of Organic Chemistry and Biochemistry, University of Zagreb, 41000 Zagreb, Croatia, Yugoslavia

Received July 12, 1973

Starting from 1-chloro-butane-2-one (I) and 3-chloro-butane-2-one (II), oximes IIIa, b and IV as well as 2,4-dinitrophenyl hydrazones Va, b and VI were prepared. ^{1}H-nmr spectra show that I gives a mixture of isomeric oximes IIIa and IIIb (21 : 79) and 2,4-dinitrophenyl hydrazones Va and Vb (20 : 80). From ketone II only *anti* isomers IV and VI were obtained. Signals were assigned using ASIS method. From paramagnetic shifts obtained by LIS method it was concluded that unshared pair of nitrogen electrons participates in complex formation with rare earth atom.

INTRODUCTION

It is a matter of common knowledge that oximes occur in two forms, which are due to *cis-trans* isomerism at the carbon-nitrogen double bond. They undergo Beckmann rearrangement, resulting in amides, the structures of which depend on the starting oxime isomer. This method of structure determination of oximes can, however, fail on account of isomerisation occuring during the reaction[1].

Oxime isomerism has been recently studied by nmr spectroscopy using aromatic solvent induced shifts (ASIS)[2] and lanthanide induced shifts (LIS)[3,4].

The ASIS method is based on shilding effects caused by aromatic ring current of solvent molecules[5]. According to Karabatsos[2], benzene is attracted by the positive charge on the sp^2-hybridized carbon and is closer to the group which is *trans* to the electronegative oxygen. This causes stronger shielding and hence greater upfied shifts of *trans* protons. Hydrogen bonded complex between aromatic solvent molecules and hydroxyl proton also occurs (Fig. 1) but causes much weaker shielding effect, due to large distance from alkyl substituents. In conformation shown in Fig. 1b, *cis* protons would undergo greater upfield shift than *trans* protons, but it is well known that oximes do not exist in this conformation[2].

The LIS method is based on complexation with rare earth chelates[6]. Berlin studied the stereochemistry of methyl alkyl ketoximes using the LIS method, and observed that all protons of the *anti* form are more shifted than the corresponding protons of the *syn* form[3]. In the *anti* form there is more space available for complex formation at the unshared pair of electrons on the nitrogen, leading to a more stable complex, and hence to

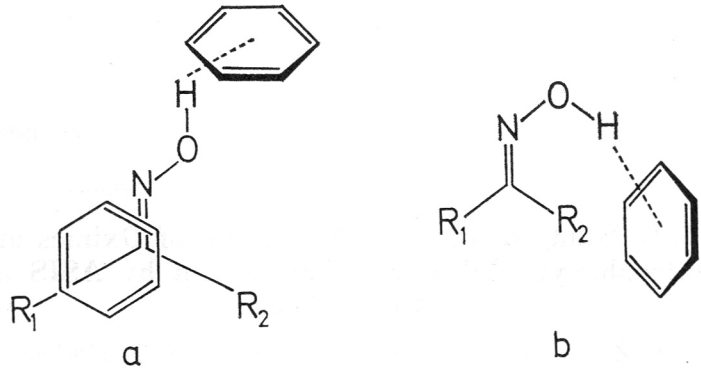
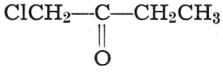


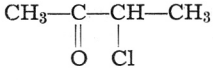
Fig. 1

greater shifts. An opposite opinion has been advanced, however, according to which coordination occurs at the oxygen lone pair of electrons[4].

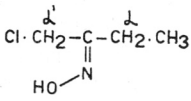
In order to clarify such controversial statements we employed both the ASIS and LIS methods in determining the *syn/anti* ratio of oximes and 2,4-dinitrophenylhydrazones of 1- and 3-chlorobutane-2-one (I, II). In these compounds the chloro and methyl substituents are either both placed on the same carbon atom or one on each carbon atom adjacent to the carbonyl double bond.



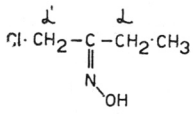
I



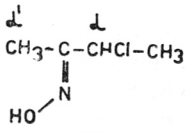
II



IIIa



IIIb

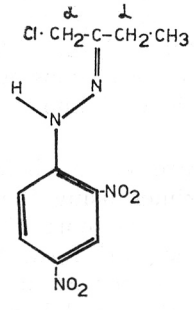


IV

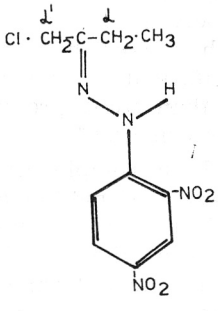
We were interested in determining the influence of these substituents on the *syn/anti* ratio of the oximes and phenylhydrazones formed.

RESULTS AND DISCUSSION

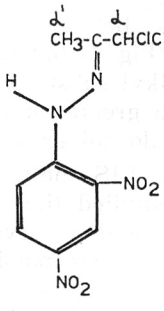
Starting from 1-chlorobutane-2-one (I) and 3-chlorobutane-2-one (II) the corresponding oximes IIIa, b and IV, as well as the 2,4-dinitrophenyl-hydrazones (Va, b and VI) were prepared.



Va



Vb



VI

Nmr spectra of the products obtained showed that both III and V consist of two isomers, while IV and VI are single compounds. The ratios obtained were 29 : 71 for IIIa : IIIb and 20 : 80 for Va : Vb. The mixture IIIa, b exhibited two separated singlets at 4.30 and 4.12 ppm belonging to α′ methylene protons of the two isomers. The peak of lower intensity belongs to the *syn* isomer IIIa, and is shifted downfield by anisotropy of the hydroxyl group[7]. Accordingly, the predominant isomer IIIb should have the *anti* configuration. This product ratio can be explained by the fact that in I each carbon atom α to the carbonyl group bears one large substituent, the chlorine atom or the methyl group, so that a mixture of oximes can be presumed. Space-filling models (CPS) show that the chlorine atom and the methyl group are approximately of the same size, hence steric reasons alone cannot account for the predominant formation of the *anti* isomer. Electrostatic repulsion of the oxime oxygen by the electronegative chlorine atom seems to be the most important factor. The mixture of dinitrophenylhydrazones Va, b was formed on account of the similar influences of the chlorine atom and the methyl group on the aromatic ring. When both large substituents are attached to the same α carbon atom as in II, the other (α′) carbon atom bears only three small hydrogen atoms, and the formation of the *anti* isomer results.

To obtain further proof for the above assignments of the signals belonging to *syn* and *anti* isomers we carried out ASIS and LIS investigations on the same set of compounds. The results obtained are given in Tables I—II.

TABLE I

ASIS method. Chemical shifts δ (ppm) and $\Delta\delta = \delta_{CDCl_3} - \delta_{C_6H_6}$ *(ppm) for compounds IIIa, b, IV, Va, b, and VI*

Compd.	Solvent[a]	δ, α′	Δδ	δ, α	Δδ
IIIa	$CDCl_3$	4.30	0.30	2.43	0.29
	C_6D_6	4.00		2.14	
IIIb	$CDCl_3$	4.12	0.36	2.52	0.13
	C_6D_6	3.76		2.39	
IV	$CDCl_3$	2.00	0.20	4.66	0.26
	C_6D_6	1.80		4.40	
Va	$CDCl_3$	4.20	0.87	2.61	0.61
	C_6D_6	3.33		2.00	
Vb	$CDCl_3$	4.33	0.57	2.61	0.68
	C_6D_6	3.76		1.93	
VI	$CDCl_3$	2.20	0.70	4.83	0.47
	C_6D_6	1.50		4.36	

[a] All reported values are for 10%/v solutions in $CDCl_3$ and C_6D_6.

It is evident from Table I that the peak at 4.12 ppm, assigned to the *anti*-form IIIb, suffered a greater upfield shift than that at 4.30 ppm which belongs to the *syn*-form, because the methylene group in IIIb was more

effectively shielded by solvent molecules. Molecular models show that the α' methylene group in position *trans* to the oxime hydroxy group is better shielded by solvent molecules, and it is concluded that the peak of higher intensity at 4.12 ppm belongs to the *anti*-isomer IIIb. Opposite effects appear in the spectra of phenylhydrazones Va, b which have been discussed earlier by Karabatsos[8]: a hydrogen-bonded complex of solvent molecules with anilino hydrogen causes strong shielding of the *cis*-methylene group (Fig. 2).

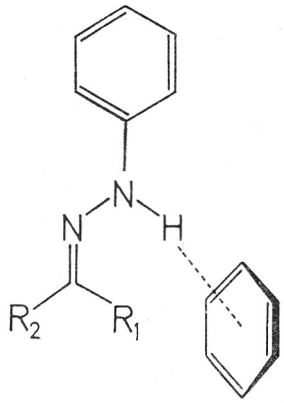


Fig. 2

Results obtained using deuterated, tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octane dionato) Eu(III), Eu(fod)$_3$, are given in Table II.

TABLE II

LIS-method. Chemical shifts δ (ppm) and $\Delta\delta$ ($\delta_{Eu} - \delta_{CDCl_3}$) (ppm) for oximes IIIa, b and IV

Compd.	Solvent[a]	δ, α'	$\Delta\delta$	δ, α	$\Delta\delta$
IIIa	$CDCl_3$	4.30	0.21	2.41	0.29
	$CDCl_3$ + Eu(fod)$_3$	4.51		2.70	
IIIb	$CDCl_3$	4.12	0.60	2.53	0.38
	$CDCl_3$ + Eu(fod)$_3$	4.72		2.91	
IV	$CDCl_3$	2.00	0.36	4.66	0.63
	$CDCl_3$ + Eu(fod)$_3$	2.36		5.29	

[a] Concn.: 0.001 mol oxime in 0.5 ml $CDCl_3$; after adding Eu(fod)$_3$ the concn. was 2.9×10^{-5} mol.

It is known that lanthanide induced shift depends on the distance between a particular proton and the centre of the complex, *i. e.* the rare earth atom, and the angle describing the position of this proton relative to the assumed symmetry axis of the europium complex[6]. If such a complex is formed at the nitrogen lone pair, the protons *trans* to the oxime hydroxy group should be more shifted than the *cis* ones. However if the oxygen lone pair participates in the complex formation, the *cis* protons should undergo

a greater shift. Table II shows that protons *trans* to hydroxyl are more shifted with the LIS method as well, meaning that they are closer to the centre of the complex*.

Our results suggest that coordination occurs at the nitrogen atom, thus confirming the results obtained by Berlin[3] at variance to those of Wolkowski[4].

EXPERIMENTAL

The melting points are uncorrected. Nmr. measurements were carried out on a Varian T-60 spectrometer at (35 ± 0.1) °C. Solvents used were chloroform-d_1, 99.8% d, and benzene-d_6 99.5% d while tetramethylsilane was employed as internal standard. Deuterated Eu(fod)$_3$ came from Stohler Isotope Chemicals, as well as the solvents and TMS.

General Procedure for Preparation of Oximes IIIa, b and IV

In a well stirred and cooled aqueous solution of hydroxylamine (1.6 g, 0.048 mol in 8.5 ml water), the corresponding chloroketone (5.0 g, 0.048 mol) was added dropwise and the stirring and cooling continued for two hours. The oximes were extracted with ether and purified by distillation *in vacuo*. IIIa,b, yield 55.1%, b. p. 80—87 °C (21 mmHg), lit. 85 °C (13 mmHg)[9]. IV, yield 53.3%, b. p. 79—80 °C (20 mmHg), lit. b. p. 70 °C (17 mmHg)[9].

Dinitrophenylhydrazones Va,b and VI were obtained by the usual procedure[10]: VI, m. p. 104—106 °C, lit. m. p. 106—107[11]; Va, b, m. p. 113—114 °C.

Anal. $C_9H_{11}O_4N$ (240.11) Calc'd.: N 19.54%
Found: N 19.48%

REFERENCES

1. L. G. Donaruma and W. Z. Heldt, *Organic Reactions*, Vol. 11, J. Wiley and Sons Inc., New York, 1960 p. 55.
2. G. J. Karabatsos and R. A. Taller, *Tetrahedron* **24** (1968) 3347.
3. K. D. Berlin and S. Rengaraju, *J. Org. Chem.* **36** (1971) 2912.
4. Z. W. Wolkowski, *Tetrahedron Lett.* (1971) 825.
5. E. D. Becker, *High Resolution NMR. Theory and Chemical Applications*, Academic Press, New York, London 1970, p. 77.
6. M. R. Peterson and G. H. Wahl, *J. Chem. Educ.* **49** (1972) 790.
7. E. D. Becker, *High Resolution NMR. Theory and Chemical Applications*, Academic Press, New York, London, 1970 p. 73.
8. G. J. Karabatsos, F. M. Vane, R. A. Taller, and N. Hsi, *J. Amer. Chem. Soc.* **86** (1964) 3351.
9. A. Dornow, H. D. Jordan, and A. Müller, *Chem. Ber.* **94** (1961) 67.
10. O. L. Brady, *J. Chem. Soc.* (1931) 756.
11. P. J. C. Fierens, *Bull. soc. chim. Belges* **64** (1955) 772.
12. A. F. Cockerill, G. L. O. Davies, R. C. Harden, and D. M. Rackham, *Chem. Rev.* **73** (1973) 553.

---

* A. F. Cockerill *et al.*[12] have recently expressed the opinion that the different conclusions reached by Berlin[3] and Wolkowski[4] could be a consequence of different oxime/shift reagent ratios used by these authors. However, using oxime IIIa,b/shift reagent mole ratios of $0.001/2.9 \times 10^{-5}$ (the result from this paper) and $3.4 \times 10^{-4}/3.4 \times^{-5}$ (unpublished result from this laboratory), the protons *trans* to the hydroxyl group were shifted in both cases more than *cis* hydrogens.

SAŽETAK

^{1}H-NMR-studija *sin/anti*-omjera oksima i 2,4-dinitrofenilhidrazona metodama ASIS i LIS

M. Žinić, M. Štromar, M. Malnar i D. Kolbah

Polazeći od 1-klorbutan-2-ona (I) i 3-klorobutan-2-ona (II), pripravljeni su oksimi IIIa, b i IV te 2,4-dinitrofenilhidrazoni Va, b i VI. NMR-spektri pokazuju da iz I nastaje smjesa izomernih oksima IIIa i IIIb (21 : 79) te 2,4-dinitrofenilhidrazona Va i Vb (20 : 80). Iz ketona II dobiveni su isključivo *anti*-izomeri IV i VI. Označavanje signala provedeno je ASIS-metodom. Iz veličine paramagnetskih pomaka dobivenih LIS-metodom zaključeno je da slobodni elektronski par oksimskog dušika sudjeluje u koordinaciji s lantanidnim kompleksom.

FARMACEUTSKO-BIOKEMIJSKI FAKULTET
41000 ZAGREB
i
INSTITUT ZA ORGANSKU KEMIJU I BIOKEMIJU
SVEUČILIŠTA U ZAGREBU
41000 ZAGREB

Primljeno 12. srpnja 1973