Journal of the Chilean Chemical Society
On-line ISSN 0717-9707

J. Chil. Chem. Soc. vol.50 no.4 Concepción Dec. 2005

J. Chil. Chem. Soc., 50, N° 4 (2005), págs: 731-737

THEORETICAL AND CHEMOMETRIC STUDY OF SUBSTITUTED OXAZINES

J. GUILLERMO CONTRERAS[1]* , MARCIA M.C. FERREIRA[2]*, S. MARCELA HURTADO[1], LORENA GERLI[1] AND ROSARIO CASTILLO[1]

[1] Facultad de Ciencias Químicas, Universidad de Concepción, Casilla 160-C, Concepción, Chile. E-mail: gcontrer@udec.cl

[2] Physical Organic Chemistry Laboratory, Instituto de Química, UNICAMP, Caixa Postal 6154, Campinas, S.P., Brazil

---

ABSTRACT

The application of the Principal Component of Analysis (PCA) over the theoretical data of a series of substituted 1,3-oxazines helps to determine the factors that rule the conformational equilibrium. Repulsive and intertribal syn-1,3-diaxial interactions have been used as determiners for the axial structures, whereas dipolar interactions are preferred in the equatorial conformation. Theoretical variables such as hardness, charges, nuclear repulsion energy and bond order in the different nuclear sectors have been used. PCA method has been successfully used in predicting the hyperconjugative interactions that play an important role

in the conformational equilibrium between a given pair of conformers of 1,3-oxazines. The studied 1,3-oxazines belong to three different groups of structures having the heterocyclic ring as a common feature. The axial structures are stabilized by two-electron/two-orbital interactions, whereas the equatorial structures are believed to be stabilized by syn-1,3-diaxial and dipole-dipole interactions.

Keywords: PCA Analysis, Oxazines, Abinitio Methods.

INTRODUCTION

Since the decade of the 50's, oxazinic derivatives have drawn the attention because their antitumoral y antituberculostatic activities. Several analyses to determine the conformational preference have been carried out. Thus, Urbanski[1] et al.have studied the 5-nitro-5-methyl-tetrahydro-1,3-oxazines (oxazines: group 1 and 2) derivatives using dipolar moment data. They assigned a conformation with an axial N-R group when R= Methyl and Ethyl whereas a conformation with an equatorial N-R group when R= cyclohexyl and tert-butyl.. This same series of compounds along with the n-propyl and iso-propyl derivatives have been studied by Allingham and Cookson[2] , using the ^{1}H-NMR spectra. Same structures suggested by Urbanski have been proposed. Lehn and Riddell[3] analyzed the ^{1}H-NMR of oxazines belonging to group 3 of the present work and observed an equatorial conformation in those structures possessing methyl groups on C5, most likely due to the to forbidden 1,3-diaxial methyl-methyl interaction. Urbanski's oxazines without the nitro group in C5 were investigated by Jones and Katritzky[4] . In all these works a more energetic ring inversion barrier as compared with the nitrogen inversion have been implicitly assumed. This assumption seems to apply to heterocyclic six-membered rings provided that the hetero atoms are not adjacent one to another[5]. The present work uses the 1,3-oxazines as a model to rationalize the governing factors of the conformational equilibria. Considering them as a potential example of anomeric effect, it is worthy to look for a relation that could account for the stabilization of the different structures with either the presence or absence of such as effect. At the light of the models used to explain the anomeric effect that is: a) the electrostatic model and b) the double-bond/no-bond model. The former is related to an unfavorable dipole-dipole interaction between the carbon-heteroatom bonds on the ring and the C2 - equatorial electronegative substituent[5] bond.

The later treats the interaction of the heteroatom lone pair with an antibonding σ^*-orbital of the ligand bond, stabilizing the axial orientation of the anomeric substituent[6] . The several structural and electronic variables were taken in such a way that they should reflect their behavior in relation with the stability of the

molecule according to the principal component analysis (PCA)[7] . In fact, the parameters that better fit in the graphic of variance were chosen to obtain the best separation of the axial and equatorial conformers. In other words, the stable and instable structures within each conformational class. PCA was introduced by Pearson[8] in 1901. The basic concept of the method[9] can be geometrically described as a reduction of a multidimensional data sets projecting de n-dimensional sets onto a subspace of a few dimensions. These new sets are called principal components (PCs). These PCs are completely uncorrelated and built as a simple linear combination of the original variables. The first principal components PC1 is defined in the direction of maximum variance of the whole data set, PC2 is in the direction that describes the maximum variance in the orthogonal subspace to PC1, therefore the PCs were ordered in the same way the variance decreases. Mathematically, we need to decompose the data matrix X (IxJ) where I corresponds to the I molecules and J to the descriptors. Thus, **X** is split into two matrices **T** and **L** such that:

$$\mathbf{X = T L^{-1} + E}.$$

The T matrix is the "score" matrix representing the positions of the compounds in the new coordinate system whereas the PCs are the axes. E is a residual matrix and L is the "loading" matrix. Using the singular values decomposition technique, SVD, that split **X** into **U**, **S** and **V** matrices, where **U** and **V** are orthogonal eigenvector square matrices and S a diagonal matrix containing the singular values (equivalent to the square roots of the eigenvalues). The $\mathbf{U}_{*}\mathbf{S}$ product is the score matrix **T** ,whereas **V** corresponds to the loading matrix **L**. The square of each diagonal element of the **S** matrix is equal to the amount of variance in the original data described by the corresponding principal component. The original data matrix usually does not possess optimal value distribution for the analysis, requiring a pretreatment of the data. In general, the autoscale preprocessing leads to scaled variables with zero mean and unit variance is used.

COMPUTATIONAL METHODS

All structures were fully optimized at the HF/6-31G** level of theory using the Gaussian 03 series of programs[10]. The NBO 3.1[11] program as interfaced to Gaussian 03 package was also used. Natural Bond Orbital analysis allows the separation of the molecular energy into two fundamental contributions: the total energy (where delocalization is present), and the energy of the Lewis molecule which corresponds to the hypothetical molecule of Lewis localized hybrid orbitals. Accordingly, the electrons are strictly located in bonds and in lone pairs. The interactions between filled and antibonding (or Rydberg) orbitals represent the deviation of the molecule from the ideal Lewis structure and can be used as a measure of delocalizations. The energy of the hypothetical Lewis molecule with strictly localized bonds is obtained by removing all off-diagonal elements from

the Fock matrix and computing one SCF cycle. This information is useful in order to determine the delocalization energy: Edeloc = E_{total} -E_{Lewis}. For further details on the NBO calculations see reference 11. Principal component analysis (PCA) was carried out using pirouette package of programs[12].

RESULTS AND DISCUSSION

To visualize the interactions that govern the conformational equilibria and the stability of an allied of 1,3-oxazines, the geometry of the three groups of oxazines (see in figure1) were optimized. Frequencies and IR intensities were predicted at the equilibrium geometries (HF/6-31G**) yielding all real frequencies so that all calculated structures are local minima. The different optimized conformations were analyzed with NBO method in the aim to determine which conformations were forming a group. Accordingly, the set of conformers forming a group were introduced in the PCA data matrix. Variables representing intramolecular interactions were selected to ascribe each conformation (axial or equatorial) to the presence of a specific interaction or a combination of them. The following variables were employed:

a) **Bond Population (PE) and Bond order (BO)**: PE and BO allow to observe the electronic reordering in specific molecular sectors and its variation in conformations forming a group. Bond population and bond orders allow to infer the possible interorbital interactions. The Bond order were taken from the Wiberg bond index matrix in NBO.

b) **NRE**: the repulsion energy between nuclei, gives a measure of the syn-1,3-axial/axial interactions and the effect of the substituent over the energy.

c) **Chemical hardness (η)**[13]: is the first derivative of the electronic chemical potential with respect to the number of electrons. The global hardness is a measure of the system's resistance to change its electron density distribution. The following working formulae, based upon the finite difference approximation and Koopmans' theorem, have been used: $\eta = 1/2\ (\varepsilon_{Lumo}-\varepsilon_{Homo})$. Thus, chemical hardness determines how easily electrons are polarized or resist to deformation. Additionally the Homo and Lumo energies were analyzed as possible individual variables interpreted in terms of electronic transferences facility.

d) **Atomic charges**: CO, CC2, CN, CC4, CC5 y CC (substitution). The charges in the atomic centers specified help to predict of interactions transfer of charge involved in the stabilization of the studied systems. CC(substitution) refers to the charge en the carbon directly bonded to the oxazinic nitrogen. NBO atomic charges were used.

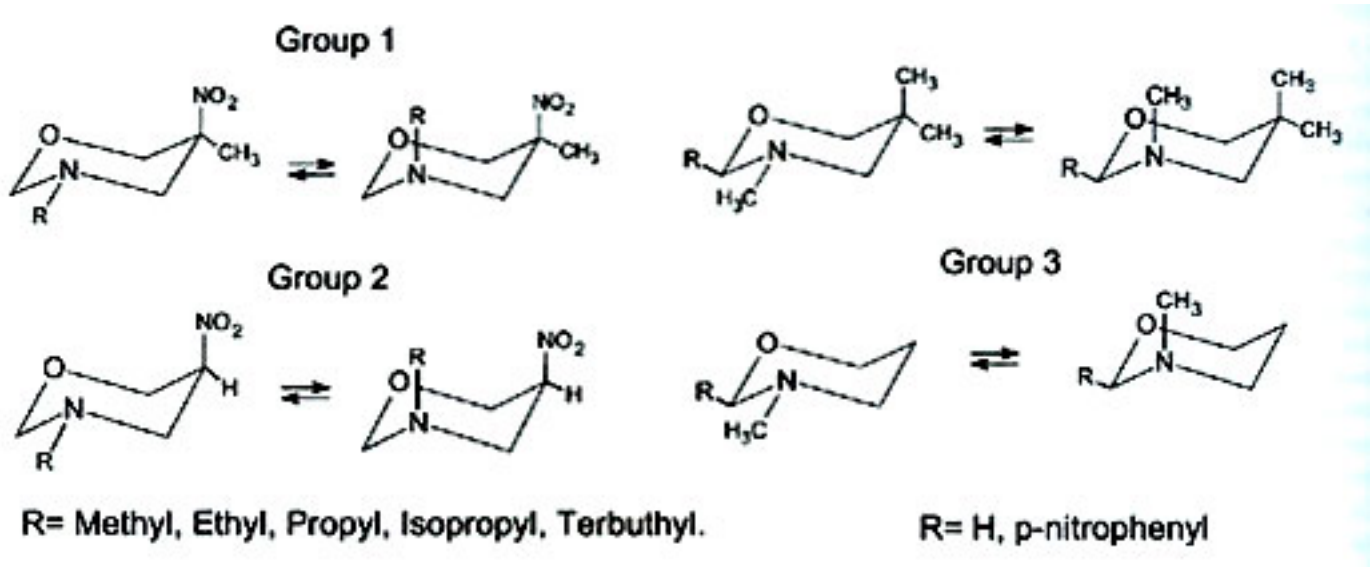

Figure 1. Optimized structures of substituted oxazines and their groups.

Principal Analysis Components (PCA): The PCA method was initially applied to 28 samples (10 oxazines from group **1**, 10 from group **2** and 8 from group **3**) trying to introduce them in a unique PCA. Twenty conformers of groups **1** and **2** were used instead and group **3** was treated separately due to its great heterogeneity that facilitates the analysis. 37 variables were used to form a 20x37 data matrix (these parameters are defined in table 1). The matrix elements are absolute values. The numbering for the bond orders and bonds population and the atomic charges are given in fig.2.

Table 1. Variables definitions in the PCA analysis

variable	Definition
NRE	nuclear repulsion energy
η	Chemical hardness
ε_{Lumo}, ε_{Homo}	Homo and Lumo energies
CO	Charge on oxygen
CC2	Charge on carbon 2
CN	Charge on nitrogen
CC4	Charge on carbon 4
CC5	Charge on carbon 5
CC(substitution)	Charge on carbon bonded to sustituent
BO1	Bond order of bonding 1
BO2	Bond order of bonding 2
BO3	Bond order of bonding 3
BO4	Bond order of bonding 4
BO5	Bond order of bonding 5
BO6	Bond order of bonding 6
BO7	Bond order of bonding 7
BO8	Bond order of bonding 8
BO9	Bond order of bonding 9
BO10	Bond order of bonding 10
BO11	Bond order of bonding 11
BO12	Bond order of bonding 12
BO13	Bond order of bonding 13
PE1	Bond Population on bonding 1
PE2	Bond Population on bonding 2
PE3	Bond Population on bonding 3
PE4	Bond Population on bonding 4
PE5	Bond Population on bonding 5
PE6	Bond Population on bonding 6
PE7	Bond Population on bonding 7
PE8	Bond Population on bonding 8
PE9	Bond Population on bonding 9
PE10	Bond Population on bonding 10
PE11	Bond Population on bonding 11
PE12	Bond Population on bonding 12
PE13	Bond Population on bonding 13

The data were scaled by subtracting column averages and dividing by column standard deviations. In this way, every variables were weighted in the same way in the principal component analysis. Data analysis was performed using the Pirouette software package[12].

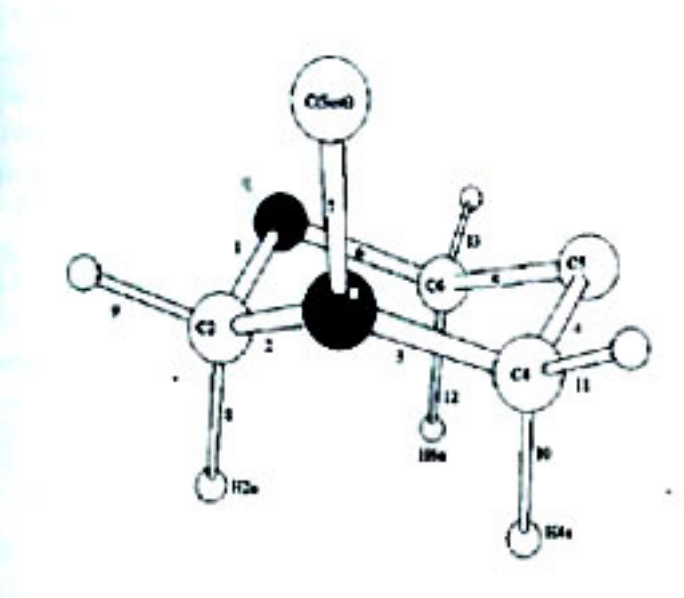

Figure 2. Numbering for the atoms and bonds used in the PCA.

The analysis shows that for axial-equatorial classification, the variables NRE, η, CC2, CN, CC5, CR, BO1, BO2, BO7, BO3, PE1, PE2, PE3 and PE7 produce a perfect separation of the samples in PC1. The equatorial conformers move towards the positive side on the PC1axis. This component describes the 58.48% of the information, with PC2 the 88.30% and with a third PC 95.15% of the information is gathered .The variables employed for separation of the axial-equatorial conformers in PC1 and PC2 have weights according to the coefficients of equations 1 and 2, respectively:

PC1=-0.03NRE+0.28η+0.34CC2-0.10CN-0.17CC5+0.01CR+0.34BO1-0.34BO2-0.33BO3 +0.13BO7+0.34PE1-0.28PE2+0.31PE7-0.32PE3 (**1**)

PC2=-0.45NRE+0.25η-0.11CC2+0.46CN-0.11CC5-0.48CR+0.05BO1-0.02BO2 +0.08BO3+0.43BO7 +0.03PE1+0.21PE2+0.07PE7+0.12PE3 (**2**)

PC3 separates group 1 from 2, but as the objective is not to visualize the differences between them, no further details will be given.

In Figure 3, the notation 2-i-Pr(A) refers to an oxazine of group 2 that possesses an axial isopropyl group on N3, whereas 1-t-Bu(E) refers to an oxazine of group 1 having an equatorial terbuthyl group on N3. Table 2 shows that the most stable conformations, calculated at the HF/6-31G**// HF/6-31G** level, are the axial ones for R = methyl, ethyl, or propyl. When R=iPr or tBu, the preferred conformations are oxazines substituted in an equatorial position. Accordingly, we can conclude that the principal components analysis outlined above, not only allow the separation into groups to render the common characteristics of the axial and equatorial oxazines (information given by PC1), but also permits to

establish the principal inherent characteristics of stability.

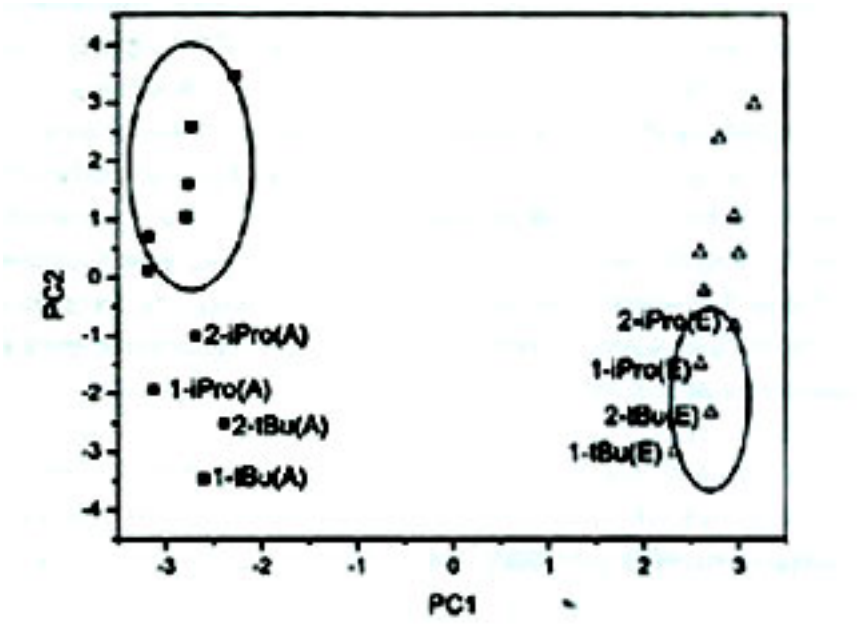

Figure 3. Scores diagram for the analysis of groups 1 and 2.

Table 2. Energies (hartrees) for the substituted oxazines

OZAXINE	ENERGY HF/6-31G**)	OZAXINE	ENERGY (HF/6-31G**)
1- Methyl-A	-567.5570883	1-Methyl-E	-567.5568529
1-Ethyl-A	-606.5957769	1-Ethyl-E	-606.5946229
1-Propyl-A	-645.6334976	1-Propyl-E	-645.6322356
1-IsopropylA	-645.6302459	1-Isopropy E	-645.6316822
1-Terbuthyl-A	-684.6622192	1-Terbuthyl-E	-684.6642173
2- Methyl-A	-528.5163075	2- Methyl-E	-528.5156971
2-Ethyl-A	-567.5549818	2-Ethyl-E	-567.5534780
2-Propyl-A	-606.5927158	2-Propyl-E	-606.5910984
2-Isopropyl-A	-606.589351	2-Isopropyl-E	-606.5905326
2-Terbuthyl-A	-645.6217536	2-Terbuthyl-E	-645.6231362
3-A	-325.0479815	3-E	-325.0474906
3-C5-A	-403.1203226	3-C5-E	-403.1242895
3-C2-A	-758.0747588	3-C2-E	-758.0735227
3-C2C5-A	-836.1464093	3-C2C5-E	-836.1499544

General speaking, we can think that the stability of the axial and equatorial structures posses opposite characteristics, i.e., they can be explained in rather different terms. In general, the equatorial structures are characterized by their hardness, to have a more positive charge on C2 and more negative charge on N3 and C5. The equatorial structures also present interactions that increase bonds 1

and 7 populations. PC2 provides information about the steric effects of the bulkier iPr and tBu substituents on N3. In fact, they increase the values of NRE, as can be expected. Moreover, these structures do not present larger differences between the interorbital interactions with respect to the rest of axial or equatorial oxazines. This implies that a low contribution of the bond orders in equation 2 is observed. In addition to the NRE, oxazines with bulky substituents show significant differences in the charges consistent with their larger hardness. This effect reflects the low trend in these conformers to experience intramolecular Homo-Lumo interactions. The better stability of the equatorial conformers over the axial ones can also be explained in terms of the electrostatic model. Keeping in mind that the ring dipole generated by the lone pairs of electrons and the approximately antiparallel polar bond or the substituent (N3-C (subst) or bond 7), is similar, thought the polarity of the bond N3-C(subst) is greater for the terbutil. In Table 3, the charges of the groups for the equatorial conformers are given in qualitative form to dimension the linkage dipole. In this way, a decrease of the electrostatic energy as a result of the less repulsive interactions (analysis carried out in gas phase) is observed.

Table 3. Charge of the equatorial oxazines group (HF/6-31G**)

Group (R=)	Charge
Metil	0.217755
Etil	0.230173
Propil	0.241942
Isopropil	0.242175
Terbutil	0.247993

According to the information provided by PC1 and PC2 in the diagram of Scores (fig.3) and equations 1 and 2, the variables of greater importance related to the axial conformation, as well as to the stability of them are BO3, PE2 and PE3, and thereby we can expect they will be involved in attractive interactions and interorbitals delocalizations increasing bonds 2 and 3 in populations. If an analysis is performed on the principal components of the axial oxazines, we will be able to correlate the principal delocalizations directly involved with the stability. Accordingly, we have used the interorbital interactions taken from the Natural Bond Orbital analysis (NBO) as variables. These interactions are related with both $n \rightarrow \sigma^*$ N3 and O1 delocalizations and were employed, since they are always stronger than $\sigma \rightarrow \sigma^*$. This last type were also considered, in particular, those which involve delocalizations from and to the bond connecting N3 and the alkyl substituent (bond 7). The inclusion of the bonds

A 10x34 matrix was constructed with the variables given in table 4. The data were autoscaled. The PCA results show the separation the axial more stable

oxazines from the unstable ones in the first PCA collecting the 90.50% of the information. Equation 3 shows the weights of the selected variables:

PC1=0.31A + 0.33B -0.30D +0.33E +0.33Q +0.33R -0.33S -0.33T -0.31AB -0.27AC (**3**)

Table 4. Interactions employed in the PCA analysis with its corresponding PCA.

Interaction Donor / Acceptor	Notation
LP (1) N 3 / BD*(1) O 1 - C 2	A
LP (1) N 3 / BD*(1) C 2 - H 2a	B
LP (1) N 3 / BD*(1) C 2 - H 2e	C
LP (1) N 3 / BD*(1) C 4 - C 5	D
LP (1) N 3 / BD*(1) C 4 - H 4a	E
LP (1) N 3 / BD*(1) C 4 - H 4e	F
LP (1) O 1 / BD*(1) C 2 - N 3	G
LP (1) O 1 / BD*(1) C 2 - H 2a	H
LP (1) O 1 / BD*(1) C 2 - H 2e	I
LP (1) O 1 / BD*(1) C 5 - C 6	J
LP (1) O 1 / BD*(1) C 6 - H 6a	K
LP (1) O 1 / BD*(1) C 6 - H 6e	L
LP (2) O 1 / BD*(1) C 2 - N 3	M
LP (2) O 1 / BD*(1) C 2 - H 2a	N
LP (2) O 1 / BD*(1) C 6 - C 5	O
LP (2) O 1 / BD*(1) C 6 - H 6a	P
BD(1) N 3 - C(sust) / BD*(1) C2-N 3	Q
BD(1) N 3 - C(sust) / BD*(1) N3 -C 4	R
BD(1) N3 - C (sust) /BD*(1) C2-H2a	S
BD(1)N3 - C(sust)/ BD*(1) C4 – H4a	T
BD(1)N3 -C(sust)/ BD*(1)O1 – C2	U
BD(1)N3 - C(sust)/ BD*(1) C 4 – C5	V
BD(1)N3 - C(sust)/ RY*(4) C2	W
BD(1)N3 - C(sust) / RY*(3) C4	X
BD(1)N3 - C(sust)/ RY*(2) C5	Y
BD(1)N3 - C 2/ BD*(1) N3 - C(sust)	Z
BD(1)N3 - C 4/ BD*(1)N3- C(sust)	AA
BD(1)C2 - H2a / BD*(1)N3 - C(sust)	AB
BD(1)C4 - H4a / BD*(1)N3 - C(sust)	AC
BD(1)C2 - O1 / BD*(1)N3 - C(sust)	AD
BD(1)C5 - C 4/ BD*(1)N3 - C(sust)	AE
CR(1)C2 / BD*(1)N3- C(sust)	AF
CR(1)C4 / BD*(1)N3 - C(sust)	AG
LP(2)O1 / BD*(1)N3 - C(sust)	AH

The stable axial oxazines generate a compact group (see fig.4) in which the principal delocalizations are D, S, T, AB and AC; the last four are related with the delocalization from (S and T) and towards (AB and AC) bond 7., AB and AC are

of larger magnitude implying a withdrawing character for the substituent. The most important is the D interaction, since it implies the presence of a clear anomeric center. It can also be expected the A interaction to be of great significance, though its importance is clearly diminished when one sees that is approximately equal in all structures. In other words, all oxazines belonging to group 1 and 2 with axial conformation, delocalize in a larger extent the lone pair on N3 towards the orbital $\sigma^*_{O1\text{-}C2}$, avoiding to be decisive at the time of establishing a relation with the stability. So that, the axial stable oxazines belonging to groups 1 and 2 have a larger delocalizations N3$\rightarrow\sigma^*_{C4\text{-}C5}$ than the unstable axial as well as the equatorial oxazines, most likely due to an unfavored stereoelectronically favored situation. This finding could be related to the presence of a nitro group on C5, which confers strongly electron withdrawing properties to the bond under discussion.

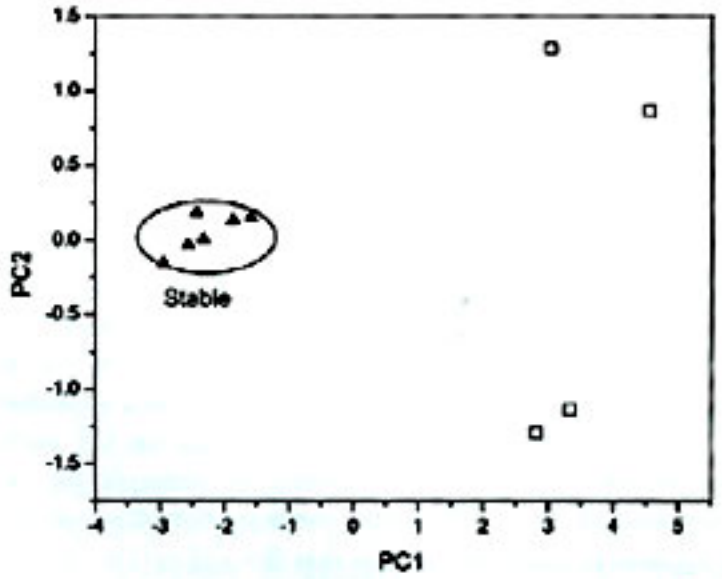

Figure 4. Scores diagram for the analysis of the interactions in the axial conformers of group 1 and 2.

Group 3 analysis: As it was mentioned in the previous section, group 3 was chosen due to its heterogeneity compared to the others group of analysis. This can be observed when performing PCA, maintaining the variables. A 8x37 matrix was worked out, the information provided by the auto-scaled data is gathered in 3 principal components, PC1 summarizes the 44,90%, PC2 the 82,38% and PC3 the 98,18% of the information. It is observed a perfect axial-equatorial separation in PC1; PC3 separates the groups that have the substitution in C5 in common (see fig.5) Table 1 shows that the energy values for group 3, are also related to the substitution in C5, so that PC3 combined with PC1 are used to establish a relation with the stability. The weights of each variable are summarized in equations 4 and 5:

PC1=-0.07NRE+0.09η+0.02CC2-0.13CN+0.01CC5-0.16CR+0.39BO1-0.37BO2-0.06BO3+0.32BO7+0.39PE1-0.39PE2+0.35PE7-0.36PE3 (**4**)

PC3=0.14NRE-0.02η+0.04CC2-0.38CN+0.66CC5+0.44CR-0.05BO1+0.02BO2+0.42BO3-0.03BO7+0.02PE1-0.09PE2-0.02PE7-0.14PE3 (**5**)

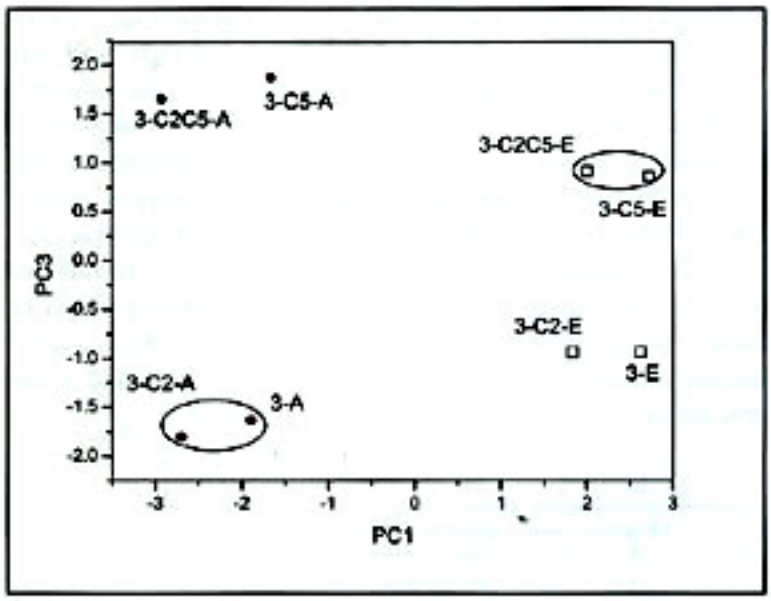

Figure 5. Scores diagram for group 3.

The notation 3-C2C5-E refers to an equatorial oxazine of group 3 that also possesses substitutions on C2 (p-nitrophenyl) and C5 (dimethyl), whereas 3-E refers to an equatorial oxazine of group 3, having no substituents on C2 and C5. 3-C2-E and3-C5-E refer to equatorial oxazines of group 3 with substitutions on C2 and C5, respectively. Methyl groups on C5 stabilize equatorial position in group 3 oxazines. Accordingly, they show high negative charges on N3, demonstrating that electrons around such nucleus is preserved and so that delocalization of the lone pair will occur to a lesser extent. Low negative charge on C5 was also found and a high population in bond 1. It can also be observed, that variables related to the stability of the equatorial group 3 oxazines are represented by some characteristics attributable to charges and bonds interactions. When the alkyl groups are in equatorial positions, the minimization of the nuclear repulsions and the total energy would help in assigning the stability of a given conformer. However, from table 5 it can be inferred that ΔNRE is larger for 3-C5 compared with 3-C2C5, where its stabilization seems to involve simultaneously delocalization and charge transfer.

Table 5. ΔNRE for equilibrium Axial⇔Equatorial of group 3 oxazines.(HF/6-31G)**

Equilibrium	-ΔNRE	ΔCO
3-A ⇔ 3-E	3.6921	$2.27 * 10^{-3}$
3-C5-A ⇔ 3-C5-E	3.5433	$4.27 * 10^{-3}$
3-C2-A ⇔ 3-C2-E	2.3403	0.021
3-C2C5-A ⇔ 3-C2C5-E	0.7657	0.021

Group 3 oxazines having no methyl groups on C5 are stabilized in axial positions. They display low negative charges on N3, high negative charges in C5 and high electronic population of bonds 2 and 3. One can assume that large delocalization of the N3 lone pair of electrons to the σ^*_{C2-O1} or σ^*_{C4-C5} orbitals (stereoelectronically favored) will occur and thereby the population of bonds 2 and 3 will be increased. Methyl groups on C5 decrease the negative charge in C5 and the hydrogen in the same position perform the opposite process. With the aim to visualize in a unified way the principal interactions for each conformation and see if a relation between the main delocalizations and the stability of each conformer, a new PCA was applied over the three groups of oxazines. A 28x34 matrix was used, the variables are found referenced in table 3. The new PCA indicates that 2 principal components gather the 99,25% of the information. Equations 6 and 7 show (in fig.6) the loadings of each PC.

PC1=0.289A-0.291B+0.287D-0.288E+0.289S+0.285T-0.285U-0.287V+0.292AB +0.291AC-0.291AD-0.288AE (**6**)

PC2=0.328A+0.191B+0.304D+0.333E-0.283S-0.402T-0.413U-0.362V+0.013AB +0.059AC-0.053AD+0.321AE (**7**)

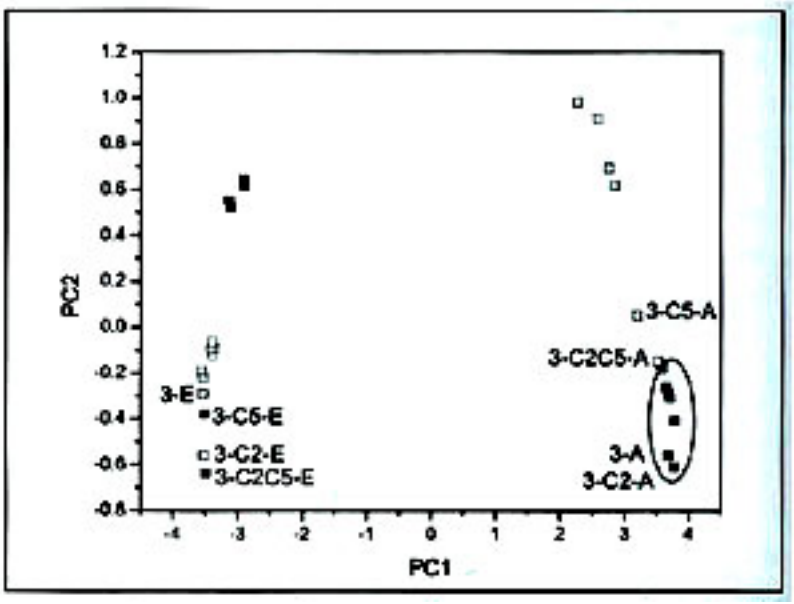

Figure 6. Scores diagram for all oxazines studied here. The dark spots correspond to stable oxazines.

As it can be observe in the graphic of scores, that the variables employed to separate the axial from the equatorial conformation work reasonably well. Within the axial group the selected variables relates the stability of the oxazines very well, separating the stable group form the unstable one, as it can be observed in PC2. However, the equatorials are not so easily related, basically because the moving away of groups 3 (3-C5-E and 3-C2C5-E) equatorial stable oxazines from the equatorial stable oxazines of group 1 and 2. Accordingly, it is plausible to think that the stability of the axial structures is directly related to the delocalization process of the lone pair of electrons on nitrogen and to the delocalization of the bond from and towards the substituent group on nitrogen. Unfortunately, a similar argument for equatorial oxazines does not work and we need to introduce delocalizations in other molecular sectors. Analysing the charge on the oxygen atom (see table 5 a noticeable difference for the oxazines 3C2C5E and 3C5E and thereby if oxygen electron delocalizations would have been introduced in this analysis is likely that the separation of the equatorial structures would have been greatly improved

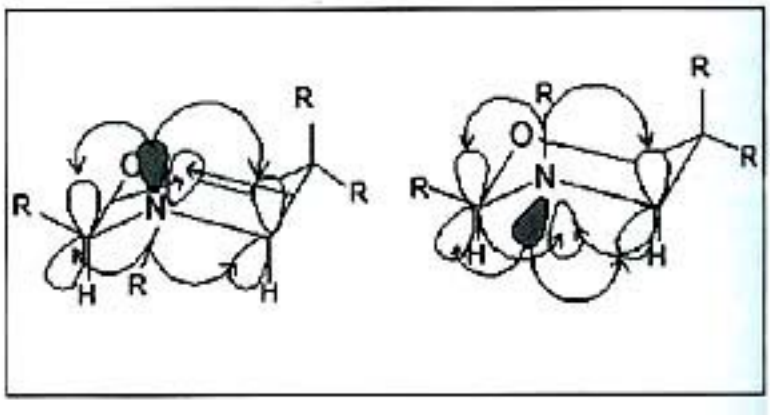

Figure 7. Principal interactions for each conformation according to the variables introduced into the analyses of the principal components

CONCLUSIONS

1.- Principal Component Analysis (PCA) allow to predict the interactions that govern the conformational equilibria of couples of 1,3-oxazines pertaining to three different groups of structures.

2.- The axial stable structures are firmly stabilized by interorbital delocalizations.

3.- The equatorial structures stabilization take place via the syn-1,3-diaxals. and dipoles.

4.- In the equatorial stabilization a process involving both the charge transfer and interorbitals interactions like observed for group 3 oxazines, is also possible .

5.- The principal components analysis outlined above not only allow the separation into groups to render the common characteristics of the axial and equatorial oxazines but also permits to establish the principal inherent characteristics of stability

ACKNOWLEDGMENTS

This work was partially supported by an operating grant (No 203.021.019-1.0) from Universidad de Concepcion, Chile. S.M.H thanks CONICYT for a scholarship.

REFERENCES

1.- (a) Gürne D. and Urbanski T., J. Chem.Soc. (1959) 1912. (b) Gürne D.,

Stefaniak L., Urbanski T. and Witanowski M., Tetrahedron supplement, **6** (1963) 211.

2.- Allingham Y., Cookson R.C., Crabb T.A., and Vary S. Tetrahedron **24** (1968) 4625.

3.- (a) Lehn J.M. and Ridell F.G., J.Chem.Soc. (B) (1968) 1224 (b) Lehn J.M., Ridell F.G. and Linscheid P. Bull. Soc. Chim. France N°3. (1968) 1172.

4.- Jones Richard A.Y., Katritzky A.R., Trepanier D.L. J. Chem. Soc(B) (1971) 1300.

5.- Edward,J.T., Chem. Ind.(London), (1955) 1102.

6.- Romers C.,Altona C., Buys H.R., Havinga E., Topics Stereochem, **4**(1969) 39.

7.- Beebe K.R. , Pell R.J., Seasholtz M.B., Chemometrics: A Practical Guide, Wiley, New York, 1998.

8.- Joliffe I.T., "Principal Component Analysis" , Springer Series in Statistics, Springer- Verlag, New York, 1986

9.- Ferreira Marcia M.C., J. Braz. Chem. Soc. 13 (2002) 742

10.- Gaussian 03, Revision B.03, Frisch M. J, Trucks G. W, Schlegel H. B., Scuseria G. E., Robb M.A., Cheeseman J. R.,. Montgomery, Jr. J. A,. Vreven T, Kudin K. N, Burant J. C., Millam J. M., Iyengar S. S.,. Tomasi J, Barone V., Mennucci B., Cossi M., Scalmani G., Rega N., Petersson G. A., Nakatsuji H., Hada M., Ehara M, Toyota K., Fukuda R., Hasegawa J., Ishida M., Nakajima T., Honda Y., Kitao O., Nakai H., Klene M., Li X, Knox J. E., Hratchian H. P., Cross J. B., Adamo C., Jaramillo J., Gomperts R., Stratmann R. E., Yazyev O., Austin A. J., Cammi R., Pomelli C., Ochterski J. W., Ayala P. Y., Morokuma K., Voth G. A., Salvador P., Dannenberg J. J., Zakrzewski V. G., Dapprich S., Daniels A. D., Strain M. C., Farkas O., Malick D. K., Rabuck A. D., Raghavachari K., Foresman J. B., Ortiz J. V., Cui Q., Baboul A. G., Clifford S., Cioslowski J., Stefanov B. B., Liu G., Liashenko A., Piskorz P., Komaromi I., Martin R. L., Fox D. J., Keith T., Al-Laham M. A., Peng C. Y, Nanayakkara A., Challacombe M., Gill P. M. W., Johnson B., Chen W., Wong M. W., Gonzalez C., and Pople J. A., Gaussian, Inc., Pittsburgh PA, 2003.

11.- Carpenter J.E., Weinhold F.T., Theoretical Chemistry Intitute, University of Wisconsin, Madison, WI , (1996)

12.- Pirouette, Infometrix , Washington, DC, (1996)

13.- Parr G.R., Pearson R.G., J. Am. Chem. Soc., **105** (1083) 7512.

14.- a) AllinghamY., Cookson R.C., Crabb T.A., Tetrahedron **24** (1968)4625. (b) Riddell F.G., Lehn J.M., J.Chem.Soc.(B), (1968)1224. (c) J.M.Lehn, Linscheid P., Riddell F.G., Bulletin Société Chimique France, (1968)1172. (d) D.Gürne, T. Urbanski, J.Chem.Soc, (1959)1912.

Paicaví 170, Depto. 19
P.O. Box 2613, Concepción, Chile
Phone 41-227815, Fax 41-235819

e-Mail
schqjournal@entelchile.net.