Principal Component Analysis (PCA) of α-Substituent Effects on ^{13}C NMR Chemical Shifts of Aliphatic Compounds

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Abstract: This work presents the Principal Component Analysis (PCA) results of the effects of twelve α-substituents (Y = F, Cl, Br, I, OMe, OEt, SMe, SEt, NMe$_2$, NEt$_2$, Me and Et) on ^{1}H and ^{13}C NMR chemical shifts of carbonyl, carboxyl, and unsaturated compounds. Thus, α-monosubstituted acetones, cyclohexanones, acetophenones, camphors, acetic acids, ethyl-, methyl- and phenyl acetates, thioacetates, amides, 2-methylpropenes, cyanides, and oximes have been investigated. The main difference among classical studies, previously presented chemometric analyses on NMR substituent effects, and PCA presented here lies in the matrix construction. In this work, it consists of experimental NMR and theoretically (ab initio) obtained data. For all PCA, the compounds have been divided into the following four groups (1) parent, methyl and ethyl derivatives, (2) oxygen, (3) nitrogen, and (4) sulfur derivatives. The halogen derivatives have been analyzed separately and also grouped by heteroatom type.

Principal Component Analysis (PCA) was used to investigate the effects of twelve α-substituents (Y = F, Cl, Br, I, OMe, OEt, SMe, SEt, NMe$_2$, NEt$_2$, Me and Et) on ^{13}C NMR chemical shifts of 169 compounds. They were divided into carbonyl (acetones, cyclohexanones, acetophenones, and camphors); carboxyl (acetic acids, ethyl-, methyl- and phenyl acetates, thioacetates, and amides); and unsaturated compounds (2-methylpropenes, cyanides, and oximes).

The main difference among classical studies, previously presented chemometric analyses on NMR substituent effects, and the PCA presented here lies in the matrix construction. In this work, it consists of experimental (NMR) and theoretically (*ab initio*) obtained data. NMR data were taken at the same temperature, same concentration, and under the same solvent conditions so as to avoid the influence of these variables on substituent-induced chemical shifts (SCS) values.[1-3] The geometries of the molecules and their properties were obtained by optimizations using the *Gaussian 98* program at the 6-31g (d,p) level and electronic correlation MP2 [3,5]. Each PCA was performed by using *Pirouette* software package and autoscaling as data processing.[3-5] The results are presented in Figures 1 and 2.

In the first PCA (Figure 1), the compounds are grouped according to the differences in functional carbon NMR shifts and partial charges of the functional carbon as well as in LUMO energies (Lowest Occupied Molecular Orbital). When compared in terms of functional carbon, ^{13}C NMR shifts and by LUMO energies it is found that carbonyl and carboxyl compounds are similar. A strong grouping is observed in the second PCA (Figure 2a.), showing α-carbon chemical shift dependence on the type of heteroatom substituents. Sulfur,

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nitrogen, oxygen, and neutral groups exhibit four types of NMR effects, indicating that the heteroatom properties play a significant role in determining ^{13}C NMR chemical shifts.

We have used three variables of similar importance in PC1 with close loading values (0.5 to 0.6): α-carbon atom partial charge, its molecular orbital coefficient and α-carbon NMR chemical shift. The third PCA (Figure 2b) shows the grouping of F, Cl, Br and

I derivatives and confirms the second PCA results. Chlorine and bromine effects on ^{13}C NMR shifts are similar. However, the more pronounced effect of chlorine can be attributed to its higher electronegativity and stronger inductive effect.
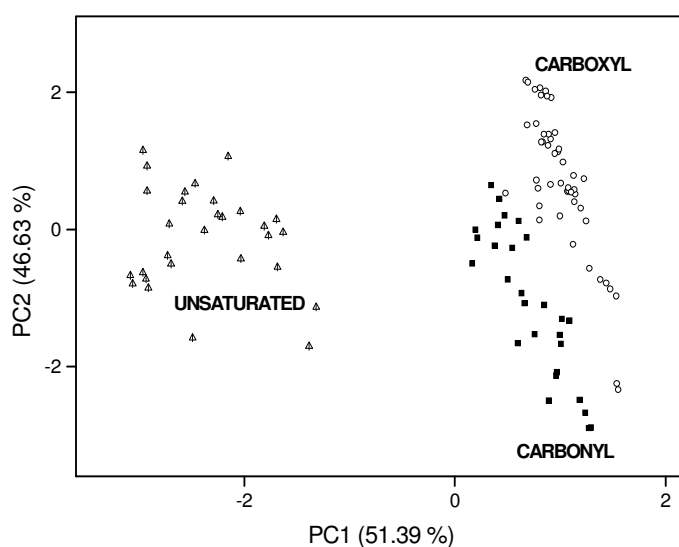

Figure 1. Graphic representation of scores in PC1xPC2 of aliphatic compounds.
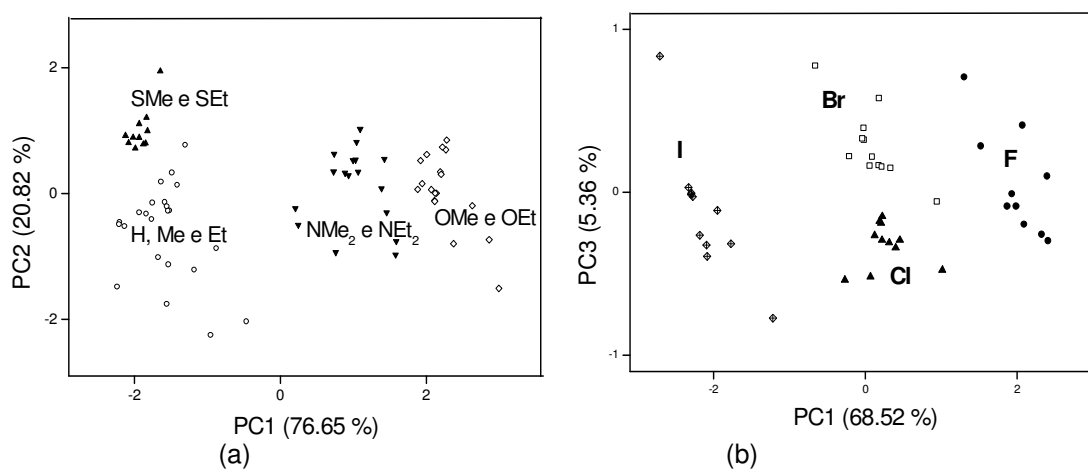

Figure 2. Graphic representations of scores in: (a) PC1xPC2 of aliphatic compounds and b) PC1xPC3 of halogen derivatives.

According to our results, α-substituents affect ^{13}C NMR chemical shifts (functional and alpha carbon atoms) of the aliphatic compounds under study by changing the carbon atom partial charges and its molecular orbital coefficients.

Acknowledgements

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