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Correlation between ^{13}C and ^{17}O chemical shifts and torsional strain in spiroacetals[☆]

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Abstract—The relationship between the ^{13}C and ^{17}O NMR chemical shifts and the dihedral energies (non-bonding interactions) of 1,4-dioxaspiro[4.4]nonane, 1,4-dioxa- and 6,10-dioxaspiro[4.5]decane, 1,4-dioxa- and 6,11-dioxaspiro[4.6]undecane, 1,5-dioxaspiro[5.5]undecane, 1,5-dioxa and 7,12-dioxaspiro[5.6]dodecane and 1,6-dioxaspiro[6.6]tridecane were analyzed. These data showed correlation of the non-bonding interactions with the chemical shift of the spiranic carbon, as well as a linear relationship between ^{13}C and ^{17}O.

1. Introduction

The correlation between the chemical shift and the molecular structure is an essential part of modern chemistry. The substituent chemical shift (SCS)[1] as well as the lone-pair are two of the most important effects used in structure elucidation.[2] These effects have been of great value to explain the change observed in the ^{13}C and ^{17}O chemical shifts of alcohols where it has been applied to the conformational[3] analyses of heterocyclic systems. Thus it has been concluded that the ^{15}N chemical shift difference between the axial–equatorial nitrogen substituents can be attributed to steric hindrance in the axial nitrogen owing to 1,3-*syn*-diaxial hydrogen interactions. The structure analyses of spiranic compounds showed an experimental linear relationship between the ^{15}N and the ^{17}O chemical shift. The *like–unlike*[4] relative configuration in substituted 1,4-diazaspiro[4.5]decanes was established by the γ-axial, γ-equatorial,[5] γ-heterocycle and β-heterocycle[6] effects.

The ^{17}O NMR data for 1,3-dioxane and 1,3-dioxolane systems have shown that there is a shift to high frequency as the ring size decreases.[7] Krivdin determined that the spiranic systems have a dependence on the one bond carbon–carbon coupling constant with respect to annular strength in spiroalkanes.[8] Theoretical calculations revealed that the $^{1}J_{C,C}$ value is directly proportional to the steric strain in this type of systems.

The annular strain of substituted dioxospiro[4.4]nonane, dioxospiro[4.5]decane, dioxospiro[5.5]undecanes, dioxospiro[4.6]undecanes, dioxospiro[5.6]dodecanes and dioxospiro[6.6]tridecane is analyzed in this Letter (Scheme 1). These compounds were prepared by condensation of cyclic ketones with the corresponding di-alcohols.[9] The ^{17}O and ^{13}C chemical shifts for the spirane carbon (carbon that is the bridge between two cyclic systems) showed important effects on the size of the system due to enhancement of the annular strain. This effect was analyzed considering the annular energy parameter due to the torsion angle estimated by molecular mechanics.[10]

2. Results and discussion

The data analyses are based on the ^{13}C and ^{17}O chemical shifts which depend on the size of the spiranic rings. It was observed that the $\delta^{13}C$ for the spiranic carbon is shifted to high frequency when the ring size decreases, while it seems to be variable for the $\delta^{17}O$.

Keywords: Dioxaspiro derivatives; Annular strength; ^{13}C and ^{17}O NMR.

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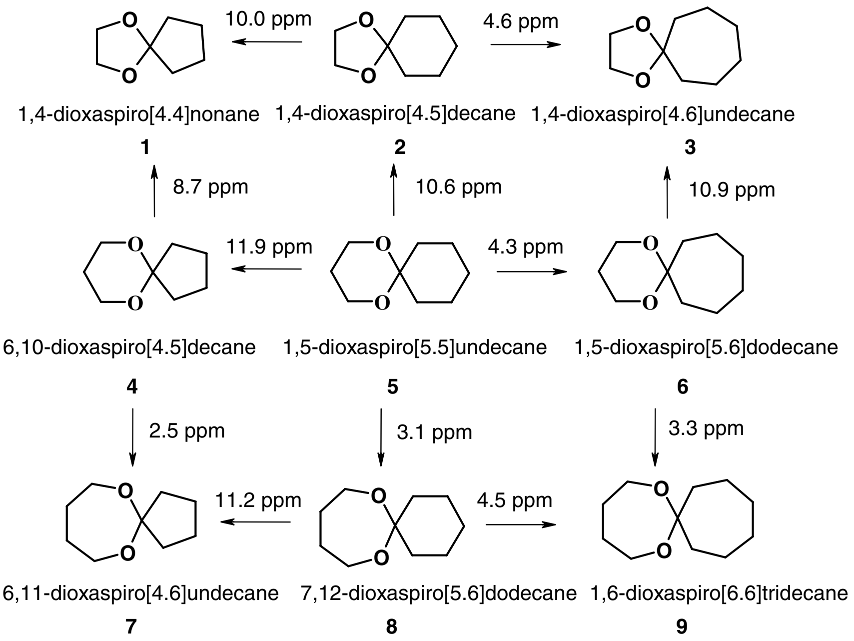
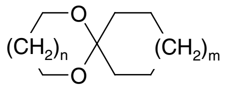


Scheme 1. Chemical shift effect of spiranic carbon taking compound **5** as reference.

The data in Table 1 show that there are three different series of dioxaspiro derivatives: the 1,3-dioxolane, 1,3-dioxane and 1,3-dioxepane, where the chemical shifts of compounds **2**, **5** and **8** are less shifted in carbon, as well as in oxygen. The chemical shift difference of these compounds for each series was determined taking as reference **2**, **5** and **8**. It can be inferred from these results that the chemical shift is affected by ring size as evidenced by the spiranic carbon chemical shift.

Scheme 1 shows the chemical shift effects due to the sizes of both rings. This scheme summarizes the chemical shift effects on the spiranic carbon when the system contracts from 1,3-dioxane derivatives (**4**–**6**) to 1,3-dioxolane derivatives (**1**–**3**) where this carbon is shifted 10.0 ppm. Moreover, when the ring expands from 1,3-dioxane derivatives (**4**–**6**) to 1,3-dioxepane derivatives (**7**–**9**) it shifted 3.0 ppm in average. Furthermore, when the heterocyclic part contracts, as in compounds **2**, **5**, **8** to **1**, **4**, **7** it shifted 11 ppm, whereas expansion to **3**, **6**, **9** shifted the signal to 4.4 ppm, approximately. These results show a strong tendency of the spiranic carbon chemical shift on the annular systems. Similar tendencies have been observed in spiroalkanes such as spiro[4.5]decane,[11] where the chemical shift difference of the spiranic carbon shifted 9.9 ppm with respect to 1,5-dioxaspiro[5.5]undecane **5**.

Table 1. ^{13}C and ^{17}O chemical shifts of dioxaspiro derivatives



Compound	$\delta^{13}C$						$\delta^{17}O$
	2	3	1′	2′	3′	C_{spiro}	O
1	63.9		37.8	23.3		118.3	65.3
2	63.8		34.8	23.5	24.6	108.3	54.4
3	63.9		38.4	29.3	22.4	112.9	63.3
4	63.9	29.3	35.2	23.9		109.6	51.5
5	58.9	28.9	32.8	22.5	25.9	97.7	44.6
6	61.3	29.6	35.2	25.9	21.6	102.0	47.6
7	61.9	29.6	36.3	20.9		112.0	62.0
8	61.3	29.7	33.9	23.0	25.6	100.8	53.9
9	61.8	30.0	37.3	24.2	22.3	105.3	60.4

$n = 0$ (**1**–**3**), $n = 1$ (**4**–**6**), $n = 2$ (**7**–**9**); $m = 0$ (**1**, **4**, **7**), $m = 1$ (**2**, **5**, **8**), $m = 2$ (**3**, **6**, **9**).

Note: The $\delta^{13}C$ and $\delta^{17}O$ for compounds **1** to **3** are in agreement with the previous report[9a] and the ^{13}C for compounds **5** and **6** were reported in Ref. 9b.

As expected, the chemical shift for the carbon at the fusion of the two rings was more affected owing to the annular strain since these compounds have different cyclic systems. Pitzer[12] explained this strain in annular systems by determining that a small annular system such as cyclobutane and cyclopentane, has a strong strain relative to cyclohexane or cycloheptane.

In order to determine the effect of annular strain on the chemical shift, the different energy contributions of these structures were estimated by means of PM3 semiempirical calculations[13] which were used to optimize the geometry. A linear correlation between the chemical shift with the energy generated by dihedral angle interactions was found (Fig. 1). The structure analyses of the optimized geometries showed that the more stable conformation for five, six and seven member rings, in spirane derivatives, are the envelope, chair and half chair, respectively. A linear correlation between the chemical shift with the energy due to dihedral angle interactions generated by the MM+[14] single point, was found (Fig. 1).

The linear correlation present in plot 1 showed that the dihedral strain energy is the result of non-bonding interactions[10] (interaction energy of the atoms that form the

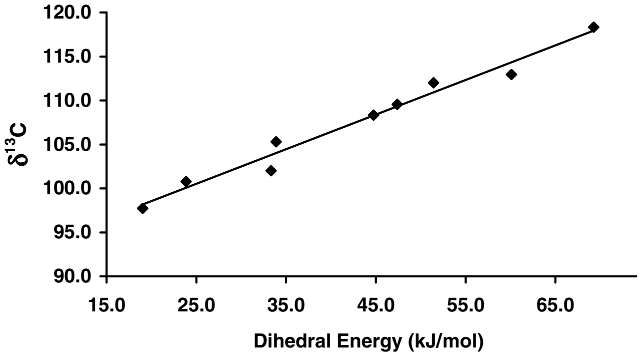


Figure 1. Relationship between the dihedral energy and the chemical shift of the spiranic carbon. $\delta^{13}C = 90.71 + 0.39$ (dihedral energy); $r^2 = 0.97$.

dihedral angles), which is the main contribution of the observed effects to the chemical shift of the spiranic carbons in this type of systems.

In addition, the contribution of the Mülliken charge in the spiranic carbon was analyzed, even though the chemical shifts do not depend linearly on this charge. This analysis is in agreement with previous works[15] where the dependence of the chemical shift on the charge density was determined; in other words, the density of the charge does not represent the main contribution to the chemical shift on the spiranic carbons in this type of systems.

A similar analysis was made for the variation of the oxygen chemical shift which showed a linear correlation with the dihedral energy (Fig. 2) when only compounds **1**–**6** were considered.

From these data it can be inferred that the oxygen chemical shift effects are due to the nature of the ring, apparently there is not a general relationship between dihedral energy and $\delta^{17}O$, therefore it is only possible to analyze it within each series of the three types of derivatives: 1,3-dioxolane, 1,3-dioxane and 1,3-dioxepane. The nature of the heterocycle is related to ring strain due to the fact that it depends on the ring size. This effect is more important in 1,3-dioxolanes than in 1,3-dioxanes. However, in the case of 1,6-dioxepanes, the seven member rings have more flexible conformations.

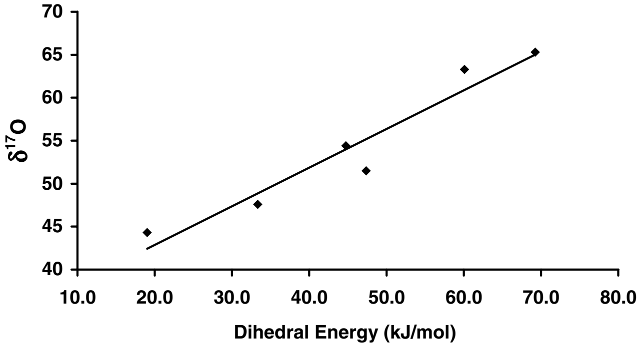


Figure 2. Relationship between the dihedral energy and the oxygen chemical shift of compounds **1**–**6**. $\delta^{17}O = 33.88 + 0.45$ (dihedral energy); $r^2 = 0.93$.

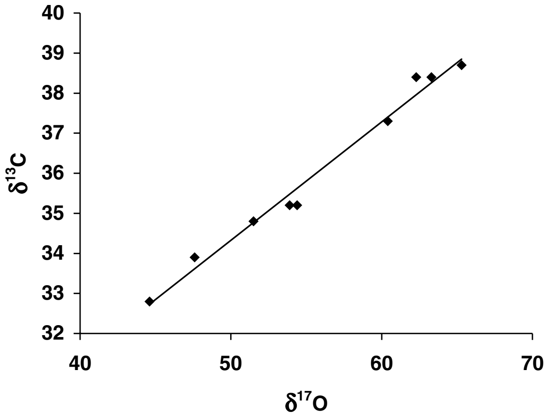


Figure 3. Correlation between ^{17}O and ^{13}C chemical shifts in equivalent positions. $\delta^{13}C = 19.56 + 0.30\delta^{17}O$; $r^2 = 0.98$.

In agreement with our previous observations, we found a linear relationship between ^{13}C and ^{17}O. As expected, the effect on the oxygen chemical shift was about three times larger than the carbon effect in the equivalent position (Fig. 3)

$$\delta^{13}C = 19.53 + 0.3\delta^{17}O \quad (r^2 = 0.98)$$

3. Conclusions

The differences observed in the linear correlations with respect to the chemical shifts of the spiranic carbon and oxygen are attributed to the fact that the spiranic carbon is affected by the strain of the two rings that form the system; whereas the oxygen is present only in the heterocyclic part.

The positive slopes in the plots of Figures 1–3 are indicative of the chemical shift effect in the spiranic carbon, as well as in the oxygen. They present similar tendencies with respect to strain. In general, these analyses show that any change in the structure affects significantly the chemical shift. In particular, when the strain in the spiranic systems increases, the signal for the atom at the fusion of the two rings shifts to high frequency.

Supplementary data

Supplementary data (experimental part, characterization and theoretical calculations) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.11.162.

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