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A computational study of the conformational equilibria of α-phenoxy, α-phenylthio, α-phenylseleno substituted cyclohexanones

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α-XH and α-Xφ substituted and cyclohexanones (X= O, S, Se) are studied in order to understand the nature of the stabilizing and destabilizing interactions in these compounds.

The conformational equilibium for α-XH and α-Xφ substituted cyclohexanones has been carried out for the data collected at the B3LYP/6-31G*level.

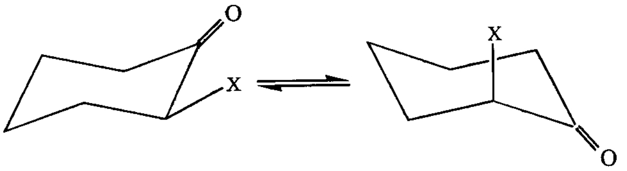

Figure 1

α-XH substituted cyclohexanones (X= O, S, Se)

All the substituents in the axial position prefer the + gauche (anticlockwise) position with respect to the ring except for OH. In the +gauche location, the dipole is minimum, the substituent points outwards the ring. In the equatorial position, the H of the XH substituents tends to be eclipsed with the carbonyl oxygen except for Se because of its large size. The OH group is almost eclipsed to the ring and one can notice the long range H bonding (2.010 Å) between the carbonyl oxygen and the hydroxyl hydrogen. The same interaction, although weaker (2.150 Å) is also present in SH substituted cyclohexanone. As the size of the heteroatom increases, long-range attractive interactions lose their priority and the H adopts the sterically less hindered position inspite of producing a high dipole moment for the molecule.

α-Xφ substituted cyclohexanones (X= O, S, Se)

The conformational behavior of α-Xφ substituted cyclohexanones is expected to mimic the trends observed for α-XH substituted cyclohexanones. When the substituent is in the axial position, all the three compounds (X= Oφ, Sφ, Seφ) adopt the +gauche orientation with respect to the ring. Comparison with the smaller analogues (X= OH, SH, SeH) shows that this angle in these compounds is slightly larger than in their small counterparts. In the equatorial position long-range stabilizing interactions between the substituent and the carbonyl group are weaker than in the small compounds because H is not attached directly to the heteroatom. Thus, instead of the eclipsed conformation adopted by the small substituent, the Xφ group prefers the staggered or anti positions with respect to the carbonyl oxygen. The –gauche positon is prefered by the -Oφ substituent. As the size of the heteroatom increases the less crowded anti position is prefered as in the case of the SH and SeH substituents.

In these compounds, the phenyl ring is perpendicular to the C–X bond and steric interactions between the hydrogens on the phenyl ring and the geminal hydrogen are minimized.

Table 1 gathers the relative energies for the conformational equilibrium for α-substituted cyclohexanones where $\Delta E°$, $\Delta H°$, $\Delta S°$ and $\Delta G°$ are differences for the total electronic energy, enthalpy, entropy and free energy betwen the axial and equatorial conformers.

Experimental free energies show an increasing preference for the axial substituent as the size of the chalcogen increases. The axial conformers of the α-XH substituted compounds have smaller dipole moments than the equatorial conformers. The OH substituent prefers largely the equatorial orientation rather than the axial orientation. The preference shifts to the axial position as the size of the substituent increases. The large preference for the equatorial conformer for α–OH in comparison to its analogues stems from the stabilization of the five membered ring formed for OH in the equatorial position. For SeH, such stabilizing interactions are not present due to the opposite orientation of the SeH substituent to the carbonyl oxygen and the equilibrium shifts towards the axial conformer with minimum dipole moment. The α–Xφ substituted compounds exhibit the same trend as their smaller counterparts *e.g.* the population of the axial conformer increases as the size of the substituent increases. B3LYP/6-31G* reproduces the experimental findings with an accuracy of 0.87 kcal/mol for α–Oφ, 0.25 kcal/mol for α–Sφ and 2 kcal/mol for α–Seφ substituted compounds. Higher level energy calculations are expected to reproduce better the experimental trend.

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Table 1 Energetics (kcal/mol) for the conformational equilibrium for α-substituted cyclohexanones. (HF/6-31G* and B3LYP/6-31G*)

Substituent	HF ΔH[a]	HF $\Delta S/10^{-3}$[b]	HF ΔG[c]	HF ΔE[d]	B3LYP ΔH[a]	B3LYP $\Delta S/10^{-3}$[b]	B3LYP ΔGc	B3LYP ΔEd	ΔGexp[e]
–OH	3.68	0.59	3.51	3.64	5.95	1.06	5.63	5.96	0.00*
–SH	0.05	–1.07	0.26	–0.25	1.12	–0.29	1.04	1.13	–1.40**
–SeH	–1.76	0.20	–1.82	–1.95	–1.59	0.65	–1.79	–1.63	—
$-OC_6H_5$	–0.98	–1.26	–0.60	–1.32	–0.94	–0.57	–0.77	–0.94	0.10
$-SC_6H_5$	0.16	1.79	–0.37	0.06	–0.67	–1.32	–0.28	–0.63	–0.55
$-SeC_6H_5$	–2.26	0.44	–2.38	–2.45	–2.34	1.10	–2.67	–2.38	–0.60

[a] ΔH= (Sum of electronic and thermal energy)$_{ax}$ – (Sum of electronic and thermal energy)$_{eq.}$ [b] $\Delta S = S_{ax} - S_{eq.}$ [c] $\Delta G = \Delta H - T\Delta S$ at 298K. [d] $\Delta E = E_{ax} - E_{eq}$. [e] R.R. Fraser and N.C. Faibish, *Can. J. Chem.*, 1995, **73**, 88. *ΔG_{exp} of α-OCH_3 substituted cyclohexanone. **ΔG_{exp} of α-SCH_3 substituted cyclohexanone.

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