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THE CONFORMATION OF α-SUBSTITUTED CYCLOHEXANONES. GROUP VI-A SUBSTITUENTS

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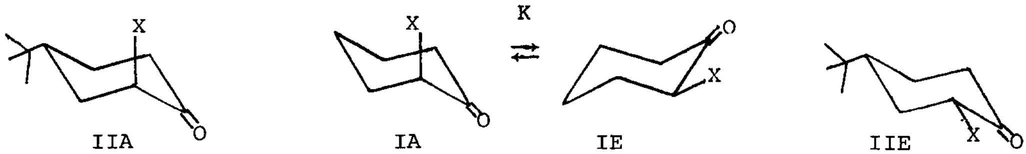
Abstract: α-Phenylthio-, α-phenylsulfono-and α-phenylseleno-cyclohexananone have the prefered conformation with the substituent axial whereas the α-phenoxy and α-phenylsulfoxo-cyclohexanones have the substituent equatorial.

The preference of a substituent to occupy the equatorial vs axial position in substituted cyclohexanes is one of the basic concepts of conformational analysis.[1] However, in six membered rings other than cyclohexane exceptions are found.[2] One of the earliest such exceptions observed was the preference for the axial position of the halogens in α-halocyclohexanones.[3] The percentage of axial conformer increases with increasing atomic number of the halogen atom (F<Cl<Br<I) and decreases with solvent polarity.[4] As part of our studies on the conformation of α-substituted cyclohexanones,[5] we wish to report our results on the conformational equilibria of cyclohexanones substituted in the α position with Group VI-A elements (O,S and Se).[6] The position of the IA ⇄ IE conformational equilibria of α-phenoxy-($X=OC_6H_5$)[7], α-phenylthio-($X=SC_6H_5$)[8], α-phenylsulfoxo-($X=SOC_6H_5$)[9], α-phenylsulfono-($X=SO_2C_6H_5$)[10], and α-phenylseleno-($X=SeC_6H_5$)[11], cyclohexanones were determined by measurement of the width of the absorption due to the α proton in ^1H nmr spectra at 90 MHz in carbon tetrachloride, chloroform,

acetone and acetonitrile.



The ΔG^o values were calculated using the following equation where W =

$$\Delta G^o = -RT\ln K = -RT\ln\{(W_A-W)/(W-W_E)\}$$

average band width and W_A and W_E are the band widths for the anancomeric[12] trans and cis - 4-t-butyl derivatives respectively (IIA and IIE).

The data and results are summarized in Tables I and II.

TABLE I: ^{1}H NMR CHEMICAL SHIFTS (ppm)[a,b] AND BANDWIDTHS (Hz)[b] OF α-PROTON

COMPOUND	δ	W	δ	W	δ	W	δ	W
I X=OC_6H_5	4.48	13.0	4.61	14.3	4.84	15.5	4.80	16.0
IIA X=OC_6H_5	4.37	7.8	4.47	8.0	4.54	8.3	4.52	8.8
IIE X=OC_6H_5	4.57	17.5	4.72	17.8	4.96	18.0	4.86	17.9
I X=SC_6H_5	3.73	11.3	3.82	12.2	4.02	13.6	4.00	14.0
IIA X=SC_6H_5	3.65	8.5	3.75	8.5	3.78	8.8	3.75	8.8
IIE X=SC_6H_5	3.83	18.5	3.93	18.6	4.24	18.7	4.15	18.6
I X=SOC_6H_5	3.24	13.7	3.42	15.4	3.78	16.5	3.57	16.7
IIA X=SOC_6H_5	3.22	9.0	3.40	9.5	3.45	9.4	3.42	9.8
IIE X=SOC_6H_5	3.83	18.4	3.83	18.4	4.00	18.7	3.84	18.2
I X=$SO_2C_6H_5$	d	—	3.95	11.4	4.21	12.9	4.14	13.7
IIA X=$SO_2C_6H_5$	d	—	3.84	9.8	3.97	9.5	3.92	9.7
IIE X=$SO_2C_6H_5$	d	—	4.02	18.0	4.35	17.9	4.22	17.7
I X=SeC_6H_5	3.82	11.4	3.92	11.9	4.08	13.5	4.02	13.5
IIA X=SeC_6H_5	3.74	8.8	3.85	8.7	3.87	8.8	3.85	8.5
IIE X=SeC_6H_5	3.95	18.4	4.05	18.7	4.30	18.0	4.22	18.4
Solvent[c]	CCl_4		$CDCl_3$		$(CD_3)_2CO$		CH_3CN	

a. TMS internal standard. b. Average value of four determinations.
c. concentration of 12 mole %, except 3 moles % for sulfoxides. d. insoluble

TABLE II: CONFORMATIONAL EQUILIBRIA IA ⇌ IE (ΔG^o in kcal/mole)

COMPOUND	K	ΔG^o	%IE	K	ΔG^o	%IE	K	ΔG^o	%IE	K	ΔG^o	%IE
I X=OC_6H_5	1.16	-0.10	54	1.80	-0.35	64	2.88	-0.63	79	3.79	-0.79	79
I X=SC_6H_5	0.39	0.55	28	0.58	0.33	37	0.94	0.03	49	1.13	-0.07	53
I X=SOC_6H_5	0.94	0.02	49	1.97	-0.40	66	3.23	-0.69	76	4.60	-0.91	82
I X=$SO_2C_6H_5$	—	—	—	0.24	0.85	19	0.68	0.23	41	1.0	0.00	50
I X=SeC_6H_5	0.37	0.58	27	0.48	0.43	32	1.04	-0.02	51	1.02	-0.02	51
Solvent	CCl_4			$CDCl_3$			$(CD_3)_2CO$			CH_2CN		

Our results show some interesting trends, some expected, other surprising. Examination of the data in Table I reveals that for each cis-trans isomeric pair the axial proton absorbs at lower field than the equatorial proton.[13] In a given solvent, for both the cis series (IIE) and trans series (IIA) the chemical shift moves to higher field as X is changed in the following order; O, SO_2, Se, S and SO, which cannot be due to a simple electronegativity effect. For the α-halocyclohexanones the chemical shifts of the α-proton move to higher field in the order F, Br, Cl and in our series the order is parallel O, Se, S. Whatever the effects are that contribute to the observed order of chemical shifts they are the same for each family of elements.

Since the equatorial conformer (IE) is more polar that the axial one (IA) it should be stabilized by polar solvents more than the axial conformer. This should lead to an increase in the amount of equatorial conformer present at equilibrium as the solvent polarity is increased. We have observed this for all the compounds studied. (See Table II).

Our results are similar to the trend observed for the α-halocyclohexanones in that as one goes from F to either Cl or Br and in our case from OC_6H_5 to either SC_6H_5 or SeC_6H_5 the % axial conformer increases[14]. A significant feature is that SC_6H_5 is so different from OC_6H_5 but so similar to SeC_6H_5. The explanation of this result appears to lie in the delicate balance between stabilization of the axial conformer as the polarizability of the atom increases and a destabilization of the equatorial conformer as the atom gets larger[15]. The conformation of the phenyl group about the XC_6H_5 bond may also play a role. Finally, the surprising results are for the sulfur compounds. We observe that as the sbustituent is changed from $SO_2C_6H_5$ to SC_6H_5 there is a decrease in the % axial conformer with SOC_6H_5 prefering the equatorial position. These results cannot be accounted for by steric effects as in cyclohexane where SCH_3, $SOCH_3$ and SO_2CH_3 are preferentially and increasingly equatorial in that order.[16] In the 5-substituted-1,3-dioxanes SCH_3 is preferentially equatorial, whereas $SOCH_3$ and SO_2CH_3 are axial with the SO_2CH_3 having a larger $-\Delta G^o$.[17] In view of this we are examining other ring systems in an effort to explain the conformational preference of sulfur substituents.

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