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Effect of heteroatom on tandem cycloaddition-Cycloreversion of 2-pyrone and 1,4-oxazinone with hetero alkynes: A DFT exploration

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Abstract

Reactions of 2-pyrone (2P) and 1,4-oxazinone (OXZ) with hetero alkynes *viz*., phosphines (HA1) and silanes (HA2) have been scanned at B3LYP/6-31G(d) level. NBO, FOE and variation in magnetic susceptibility isotropy have been analysed and the results have been compared with that of acetylene (Ace). On account of heteroatomic influence on frontier orbitals, hetero alkynes are faster than simple ones. The order of reactivity is observed as HA2>HA1>Ace.

Keywords: DFT, aromaticity, silanes, phosphines, heteroarenes, (2+4) cycloaddition and cycloreversion

1. Introduction

Tandem strategy has been used in the generation of sterically hindered phosphabenzene [1]. Sterically hindered pyrone reacts with phosphine to form the cycloadduct and subsequently extrudes CO_2 yielding phosphabenzene. Silyne is another interesting heteroalkyl whose (synthesis is a challenge in Organic Chemistry) properties have been theoretically probed [2, 3]. The elusiveness of triply bonded silicon compounds is due primarily to their lower thermodynamic and kinetic stability in isomerisation (unimolecular) and dimerization (bimolecular) reactions. Silyne is dissimilar to simple alkynes in many aspects. A notable feature is its geometry. It is stable in the trans bent form whose energy is 8 kcal mol^{-1} lower than its linear form (acetylene linear form is stable by 30 kcal mol^{-1} [2, 3]) which is a first order saddle. Shaik, Apeloig and coworkers explained this by VB analysis that upon bending π bonds in HSi≡CH, and HC≡CH, are destabilized by 34 and 60 kcal mol^{-1}, respectively, while the σ bonds are strengthened by 42 and 34 kcal mol^{-1} respectively. Overall bending has led to stabilization of HSi≡CH by 8 kcal mol^{-1} and destabilization by 26 kcal mol^{-1} in HC≡CH. It should be noted that the trans bent form of silyne is only a local minimum and this form is used in modelling silyne reaction, though salicylidene isomer is the most stable form. It would be interesting to study if silabenzene could be synthesized by such a tandem process. Therefore, this work focuses on exploring the relative feasibility of reactions between 2-Pyrone (2P) and 1, 4-oxazinone (OXZ) with hetero alkynes *viz*., phosphines (HA1) and silanes (HA2) along with the role of aromaticity as driving force and it is considered worthwhile here to investigate the dienophile nature of C≡Si bond. This would enable the comparison of cycloaddition Chemistry of C≡Si with C≡C and C≡P.

2. Computational Methods

In this study, all the reactions were scanned using Gaussian 98 program [4] at B3LYP [5, 6] /6-31G (d) level. To calculate magnetic susceptibility isotropy, NMR shielding tensors were computed at B3LYP/6-311+G (2d, p) using IGAIM method [7, 8[which is slightly varied from CSGT [7-9] method. Natural bond orbital (NBO) calculations have been done. Frontier orbitals analysis of both diene and dienophiles have also been performed. Along the reaction coordinate, the variation in magnetic susceptibility isotropy (χ_{iso}) (between the range (-1 to +1 (amu) $^{[1/2]}$. Bohr)) was monitored for both the cycloaddition and cycloreversion processes. Modification in aromaticity of the studied systems was computed.

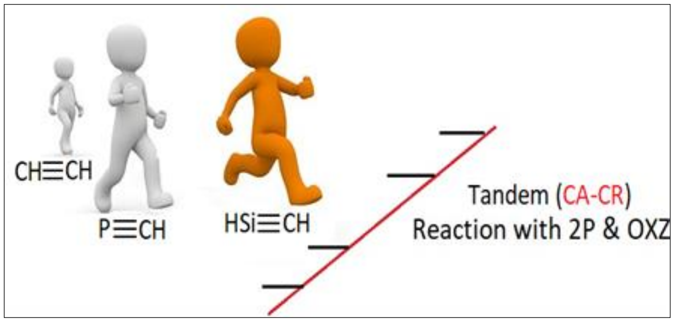

Fig 1: Graphical abstract

3. Results and Discussion

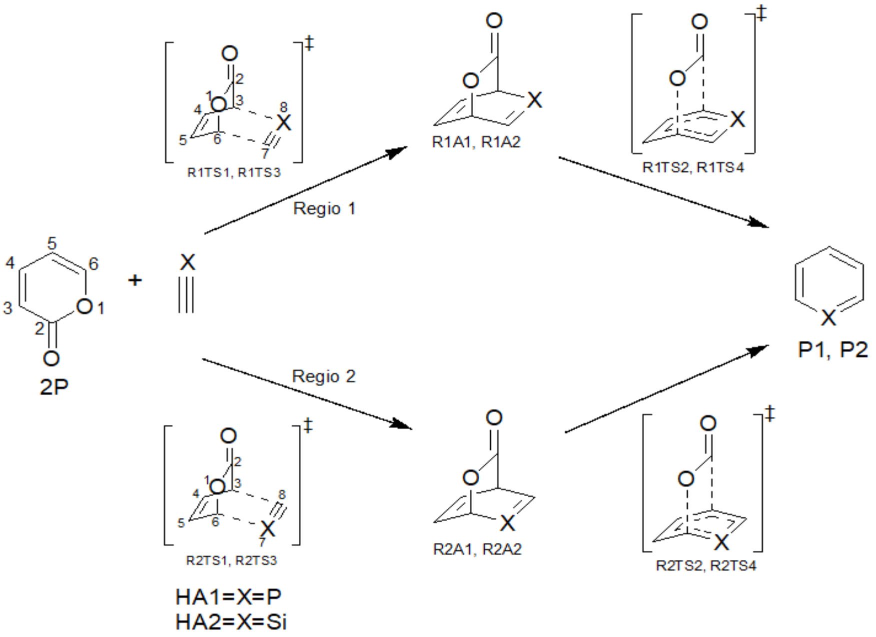

Fig 1: Reaction pathways for the Regio 1 and Regio 2 addition of 2P with HA1 and HA2.

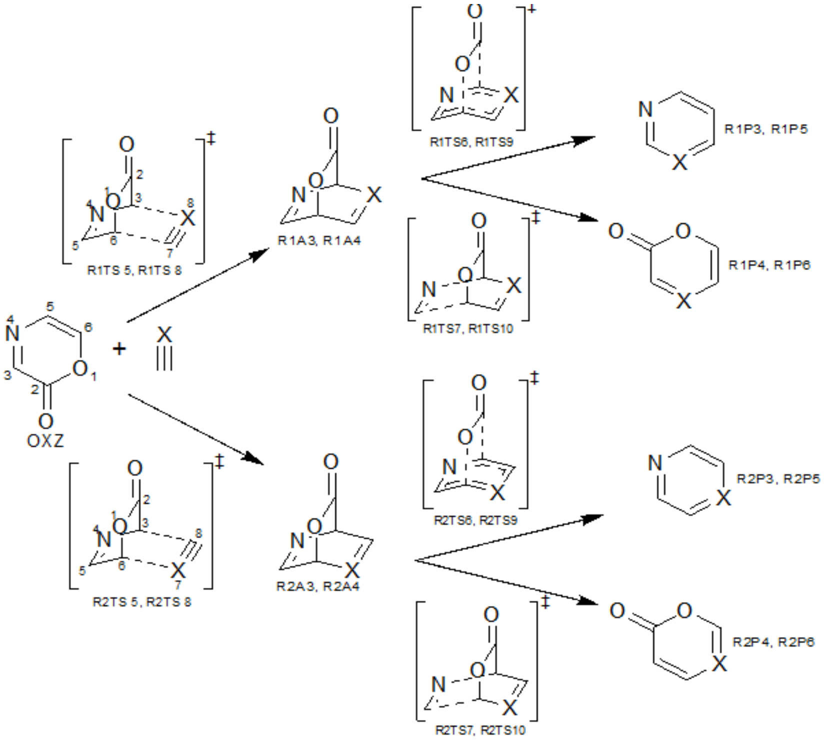

Fig 3: Reaction pathways for the Regio 1 and Regio 2 addition of OXZ with HA1 and HA2.

2P and OXZ react with phosphine (HA1) and silyne (HA2) in a fashion of tandem cycloaddition followed by cycloreversion. Two regio adducts (R1A1/R1A2 & R2A1/R2A2) are formed in both the reactions. As shown in fig 2, in 2P-HAs reactions, both the adducts (R1A1/R1A2 & R2A1/R2A2) cyclorevert to form the same product P1/P2. The cycloaddition and cycloreversion reactions are single step reactions involving concerted asynchronous transition states (TSs). Cycloadducts of OXZ-HAs reactions (R1A3/R1A4 & R2A3/R2A4) undergo extrusion of CO_2 and HCN leading to four different products shown in Fig 2. These reactions also follow single step cycloaddition involving concerted asynchronous TSs as earlier. The free energy profiles of 2P-HA1 and 2P-HA2 reactions are presented in Figs. 6 & 7. The kinetics of these reactions are discussed in terms of activation parameters.

A. Energetics

2P-HA1reaction

In 2P-HA1 reaction, Regio 1 and Regio 2 pathways shown in fig 2 are lying almost very much closer. Activation free energy to cycloaddition inRegio 1 approach ($\Delta G^{\ddagger} = 29.6$kcal mol^{-1}) is 1kcal mol^{-1} less than R2. Of the two Regio 1 adducts, cycloreversion of R1A1 is faster ($\Delta G^{\ddagger} = 15.58$ kcal mol^{-1}) than that of R2A1 whose $\Delta G^{\ddagger}$ is greater by 1.56 kcal mol^{-1}. The cycloaddition andcycloreversion TSs are more asynchronous compared to TSs obtained in reactions with simple and strained alkynes. When comparing the free energy profiles of 2P-HA1 reaction with 2P-Acetylene (2P-Ace) reaction, one can find the barrier to cycloaddition being drastically reduced by about 6-7 kcal mol^{-1} for the former. This is accordance with the literature reports that the reduction in barrier by C≡P bond would be around 10 kcal mol^{-1} with respect to C≡C[10 6-11]. Also the adducts R1A1 and R1A2 are both thermodynamically less stable than that of 2P-Ace reaction. In contrast, the computed barriers show that cycloreversion is slower than that of 2P-Ace adduct.

2P-HA2 reaction

Here also Regio 1 and Regio 2 pathways (as shown in fig 6) are followed. In this 2P-HA2 reactions, $\Delta G^{\ddagger}$for cycloaddition by both the approaches are less than that of 2P-HA1 reactions. This is almost half that of 2P-Ace reaction (reduced by 18-20 kcal mol^{-1}). Among the two regio approaches Regio 1 is low lying ($\Delta G^{\ddagger} = 16.68$ kcal mol^{-1}) than Regio 2. The thermal stability of the adducts (R1A2 and R2A2) are very high compared to that of R1A1 & R2A1 of 2P-HA1 reaction. Among the two regiomeric adducts R1A2 is more stabilized. It is interesting to note that the adduct R1A2 in spite of being more stable cyclorevert faster extruding CO_2 to form P2 (silabenzene) and the to this reaction is 9.57 kcal mol^{-1} and R2A2 requires 15.50 kcal mol^{-1} to cyclorevert. Therefore Regio 1 is an apt approach for the silyne to follow in this tandem course to form silabenzene which is thermodynamically more stable than phosphabenzene.

OXZ-HAs reactions

In OXZ-HA1reaction, shown in Fig 6, $\Delta G^{\ddagger}$ for cycloaddition is lower by 4 kcal mol^{-1} than that of 2P-Ace cyloaddition. This decrease is comparatively lesser in magnitude than observed between 2P-Ace and OXZ-Ace reactions. Here also the Regio 1 and Regio 2 are very closely lying and the free energy difference between both paths is less than 2 kcal mol^{-1} throughout the potential energy surface. The adducts R1A3 & R2A3 are more than non aza counter -parts (R1A1 & R2A1). These cycloadducts R1A3 & R2A3 cyclorevert by expulsion of CO_2 by crossing a barrier of 17.87 and 19.13 kcal mol^{-1} respectively.

The energy profile of OXZ-HA2 reaction (Fig 7) is very similar to the former case up to cycloaddition and then they diverge. The energy barrier for Regio 1 &Regio 2 is 13.79 and 14.77 kcal mol^{-1} respectively.$\Delta G^{\ddagger}$ for OXZ-HA2 cycloaddition is lower by 3-4 kcal mol^{-1} than 2P-HA2 cycloaddition and this is similar to OXZ-HA1 and 2P-HA1. The highly stabilized adducts cycloreverts by CO_2; R1A4 extrudes much faster ($\Delta G^{\ddagger} = 11.23$ kcal mol^{-1}) than R2A4 ($\Delta G^{\ddagger} = 18.13$ kcal mol^{-1}). This observation is quite similar to that found in 2P-HA2 reaction. R2A4 is stable and cycloreversion has a high barrier than for the cycloaddition step and hence the lactone could be isolated. The barrier to cycloreversion of R1A4is comparable to that found in pyrones. The extrusion of HCN is difficult owing to very high barrier, listed in Table 2. Hence during tandem CA-CR of 2P and OXZ with silanes, apart from silabenzene or silapyridine, the bicyclic silalactone adduct will also be obtained.

Frontier orbital energy analysis

FOE gaps for 2P-Has reactions are presented in Fig. 8 and these values indicate that 2P-HA1 and 2P-HA2 reactions are NED type and OXZ-HA1 and OXZ-HA2 reactions are IED type. The quantum of charge listed in Table 3 also supports this fact. It is noted that 2P-Ace reactions are IED type while 2P-HAs reactions are NED type since from the Fig. 8 one can observe that the HOMOs of the HAs are destabilized and LUMOs are stabilized compared to those of Ace's and the lowering of LUMO reduces the FOE gap for NED in 2P-Has reaction.

Deformation energy analysis

Deformation energy which gives the measure of the energy required to deform the dienophile and diene to form the cycloaddition TS is presented in Table 3. As Regio 1 apporaoch is the low energy path way for 2P/OXZ-HAs reactions, only the cycloaddition TS corresponding to that approach alone is taken for analysis. In 2P-HAs reaction, both diene and dienophile deform to a lower extent than observed in 2P-Ace reaction. Among 2P-HA1 and 2P-HA2 reactions, the deformation of diene and dienophile in the latter is lesser than in the former. A very similar trend is obtained with OXZ-Has reactions. This seems to indicate the cycloaddition TSs with hetero alkynesoccur much earlier than with simple alkynes. Between phosphine and silyne the latter leads to a reactant-like TS than the former. In fact, silyne fragment in the OXZ-HA2 TS stabilizes in the deformed state.

There is a gradual increase in aromaticity up to transistion state (TS) during the cycloaddition of 2P/OXZ with HA1/HA2 and thereafter steady fall in aromaticity is observed. At the same time, the partial aromaticity of 2P/OXZ ring suffers a gradual decrease throughout from reactant to product. The above two changes cumulatively reflect the total change in aromaticity during cycloaddition. Similar results are occurred in the pre and post TS phase incycloreversion, while the product fragments being phosphabenzene/silabenzene progressively gains aromaticity that shows the global trend in the cycloreversion process. This is examined by monitoring χ_{iso} values computed along IRC both for the whole reacting system and for the reactant and product fragments during both cycloaddition and cycloreversion. The changes in χ_{iso} along the reaction coordinate shown in indicate that the aromatic gain in pericyclic ring is dominant, for the whole system and the reactant fragment of 2P-HA1, than the fig. aromatic loss by the pyrone unit. In the cycloreversionstep the aromatic gain in the product fragment domininates than that of the pericyclic ring. This can be well observed in Fig. 8 with silanes as heteroalkyl the above trends are less pronounced. This observation is silmilar to that of 2P-Ace reaction. Comparison of the trend in χ_{iso} values along IRC for the reactions of 2P/OXZ with HAs and Ace also proves that dienes and dienophiles in the former reaction deformation to lower degree than in the latter. Lower degree deformation leads to a smaller change in χ_{iso} and thereby in aromaticity. Therefore monitoring the aromatic change is a good tool to quantify the deformation in embedded dienes.

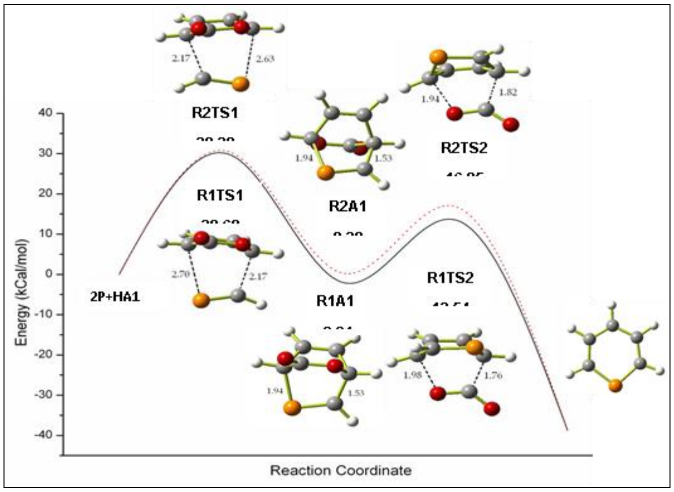

Fig 4: Schematic free energy profile of 2P-HA1 reaction computed at B3LYP/6-31G (d) level.

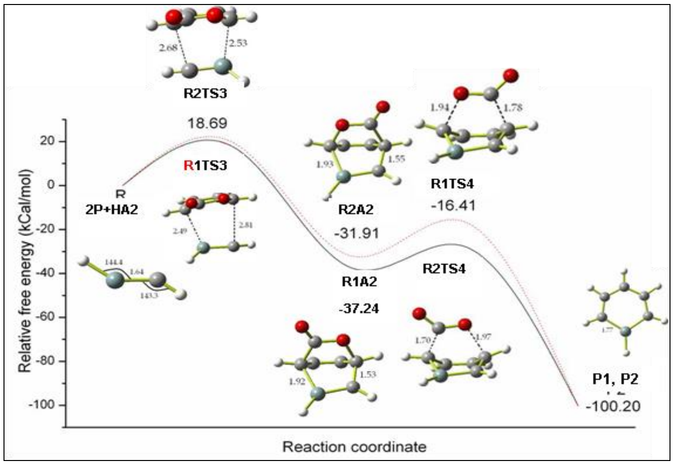

Fig 5: Schematic free energy profile of 2P-HA2 reaction computed at B3LYP/6-31G (d) level.

Table 1: Activation free energy and enthalpy (kcal mol^{-1}) and activation entropy (cal.k^{-1}.mol^{-1}) of 2P-HAs reactions

	Cycloaddition			Cycloreversion		
	ΔG‡	ΔH‡	ΔS‡	ΔG‡	ΔH‡	ΔS‡
2P-HA1						
R1	29.60	17.98	-38.99	15.58	16.04	1.54
R2	30.68	18.56	-39.33	17.14	17.06	-0.27
2P-HA2						
R1	16.68	5.01	-39.16	9.57	9.90	1.11
R2	18.69	7.21	-38.52	15.50	16.01	1.71

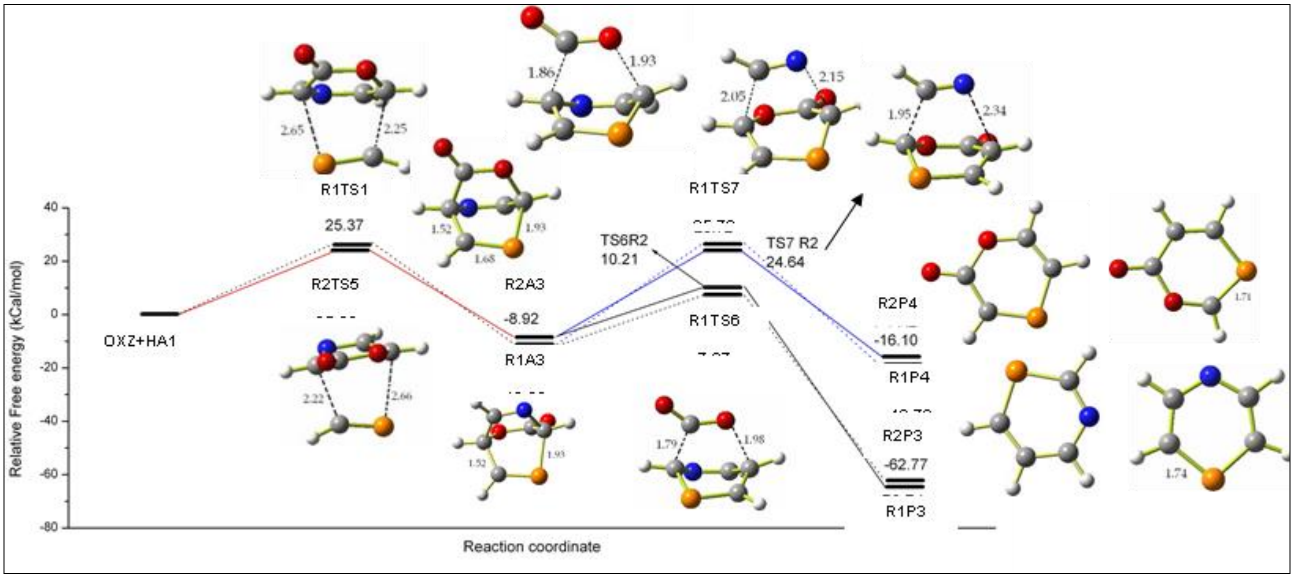

Fig 6: Schematic free energy profile of OXZ-HA1 reaction computed at B3LYP/6-31G (d) level.

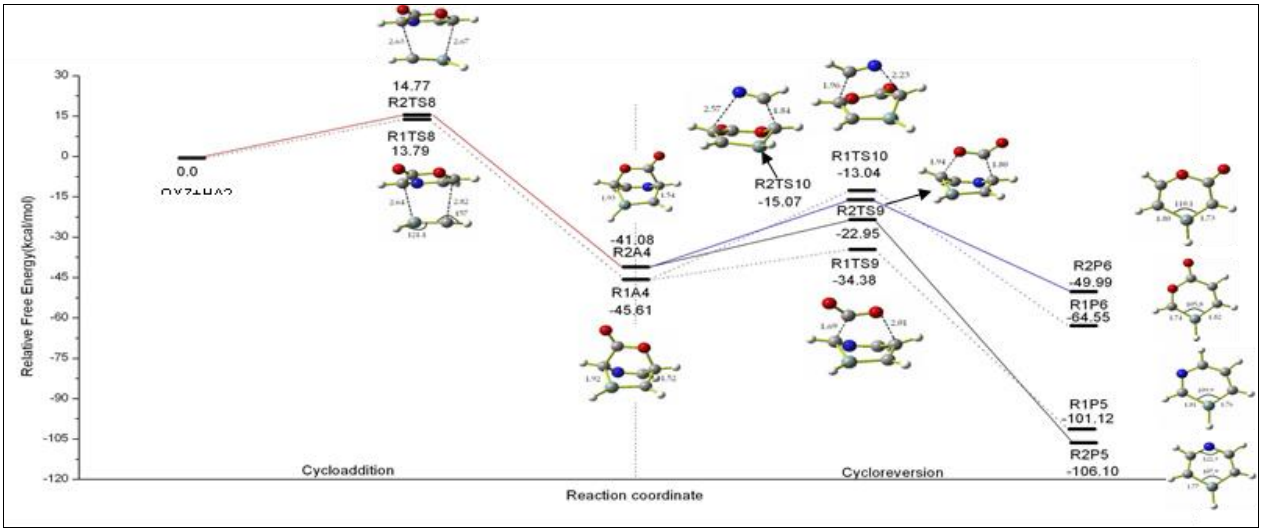

Fig 7: Schematic free energy profile of OXZ-HA2 reaction computed at B3LYP/6-31G (d) level.

Table 2: Activation free energy and enthalpy (kcal mol^{-1}) and activation entropy (cal.k^{-1}.mol^{-1}) of OXZ-HAs reactions

	Cycloaddition			**Cycloreversion**		
	ΔG‡	**ΔH‡**	**ΔS‡**	**ΔG‡**	**ΔH‡**	**ΔS‡**
OXZ -HA1						
R1	25.37	13.76	-38.96	17.87	18.40	1.77
				(35.72)	(36.91)	(3.99)
R2	25.02	13.34	-39.19	19.13	119.69	1.88
				(33.56)	(34.90)	(4.50)
OXZ -HA2						
R1	13.79	2.20	-38.89	11.23	11.66	1.44
				(32.57)	(33.66)	(3.66)
R2	14.77	2.99	-35.53	18.13	18.69	1.88
				(26.01)	(27.51)	(5.03)

The values in the parenthesis denote the thermochemical parameters for HCN elimination pathway.

Table 3: Deformation energy of dienes (2P & OXZ) (DE1) and dienophile (Ace, HA1, HA2) (DE2) components in the concerted cycloaddition transition states in (kcal mol^{-1})

Diene	**DE1**	**Dienophile**	**DE2**	**Q_{CT} at the dienophile (eV)**
	19.79	Ace	11.74	0.024
2P	15.89	HA1	7.17	-0.010
	10.68	HA2	-1.89	-0.021
	16.86	Ace	9.33	0.052
OXZ	13.60	HA1	5.61	0.030
	7.06	HA2	-2.00	0.033

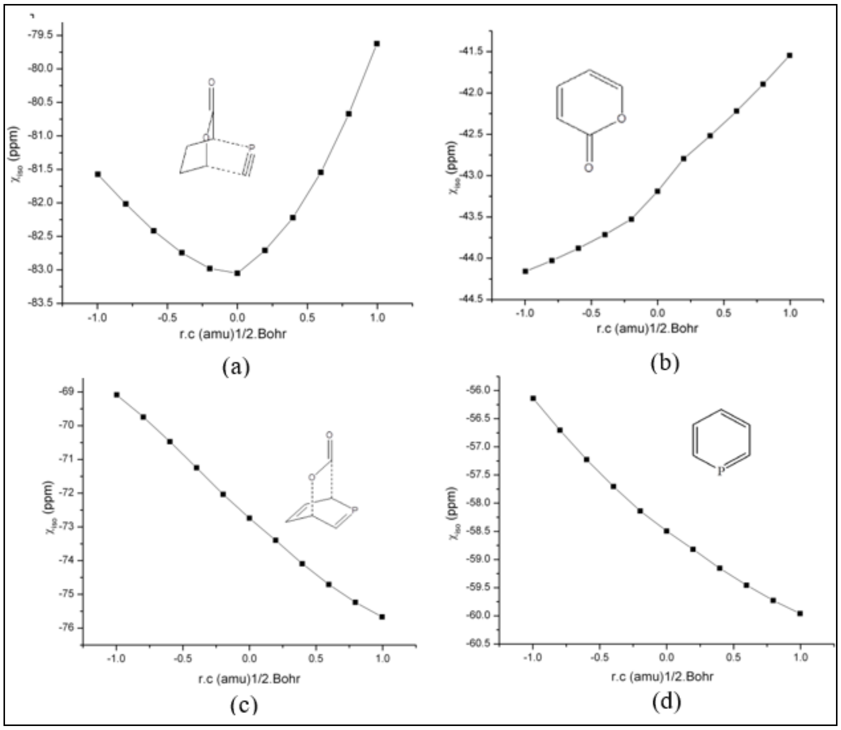

Fig 8: Variations of magnetic susceptibility along the IRC of (a) R1TS1 (b)pyrone rinR1TS1 (c) R1TS2 (d) Phosphabenzene ring of R1TS2 in 2P-HA1 reaction

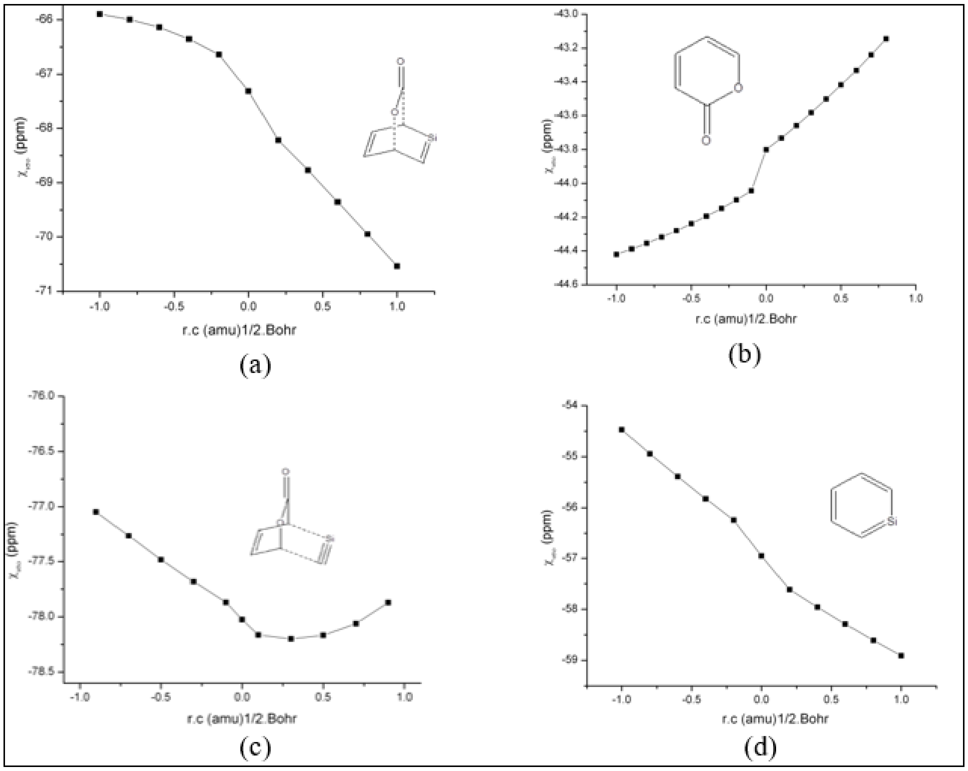

Fig 9: Variations of magnetic susceptibility along the IRC of (a) R1TS3 (b) pyrone ring of R1TS3 (c) R1TS4 (d) Silabenzene ring of R1TS4 in 2P-HA2 reaction

4. Conclusions

Heteroalkyl reacts faster than simple alkyne due to the heteroatomic influence on the frontier orbitals of alkyne, especially P and Si have substantially lowered the LUMO which facilitated the reaction. Of them, 2P-HA2 has a very low barrier similar to cyclohexyne owing to its low thermodynamic stability. Comparitively one of the regioisomericsilalactone reacts faster than the normal adduct. In the OXZ reactions CO_2 elimination is preferred over HCN extrusion. FOE analyses reveal 2P-HAs reaction follows NED while OXZ-HAs reactions follow IED. Less degree deformation trend of diene and dienophile is reflected in χ_{iso} values. Aromatic gain dominates over the loss in the pericyclic ring and reactant fragments. Moreover, silanes are more reactive than phosphines which are in turn more reactive than acetylene. The observed trend in silalactone stability indicates that by suitable substituitionsilabenzenes and silalactones can be conveniently synthesized by tandem process.

5. Acknowledgements

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