Dual Orbital Effects in N-Philic Cyclizations of Silyl Radicals onto Imines

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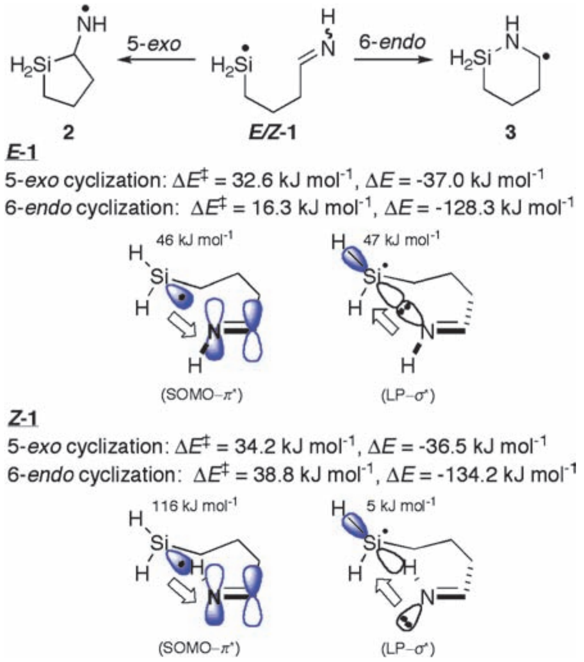
Density functional studies revealed that nucleophilic silyl radicals are able to mask as electrophiles by cyclizing with high preference onto the more electron-rich nitrogen atom of imine C=N double bonds. This remarkable behavior is a result of a combination of SOMO–π^* and lone pair (LP)–σ^* interactions during the reaction. If the LP is not available due to steric reasons, attack of the Si-radical occurs with slight preference at the carbon atom. This indicates that "dual orbital" interactions are directing the regioselectivity of silyl radical cyclizations.

Recently,[1] we reported on the results of computations performed on the reaction of silyl radicals ($SiH_3\cdot$) with various π systems as part of a project aimed at further exploring the self-terminating radical chemistry developed by us.[2] We were surprised by the unusual geometry of the transition state for the radical addition. For example, in the case of attack at N in the reaction with imine ($CH_2{=}NH$), the silyl radical component appears to be "leaning back" with one of the N–Si–H angles at about 155° and the remaining angles at about 90°. When animated, the silyl atom appears to swing in a highly unusual way above the imine nitrogen during bond formation, rather than attacking the C=N double bond with the typical angle of ca. 107°.[3] Natural Bond Orbital (NBO) analysis of the transition state orbitals revealed the origin for the unusual motion. As expected, the transition state SOMO comprises interaction of the unpaired electron at silicon with the π^* orbital of the C=N double bond. In addition to this, of even higher importance is an unexpected second orbital interaction comprising interaction of the lone pair (LP) at nitrogen with a Si–H σ^* orbital (Figure 1). These results clearly suggest that the nucleophilic character of the imine dominates over the radical interaction in this reaction: the nucleophilic Si-radical masquerades as an electrophile! Thus, the observed transition state motion can be understood as a compromise to optimize both SOMO–π^* and LP–σ^* orbital interactions.

We then became interested, how dual orbital interactions may influence the regioselectivity of Si-radical cyclizations onto imine C=N and N=C double bonds. Surprisingly, our calculations[4] reveal that the regioselectivity is strongly influenced by the stereochemistry of the imine (Scheme 1).[5]



Scheme 1. "Dual orbital" interactions in Si-radical cyclizations onto the C=N double bond in ***E/Z*-1** (BHandHLYP/6-311G**); $\Delta E^{\ddagger}$ = activation energy, ΔE = reaction enthalpy (ZPC included).

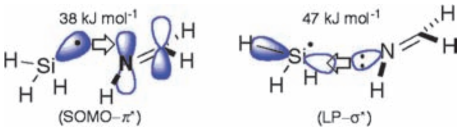


Figure 1. Calculated orbital interactions in the transition state for the addition of silyl radicals to imine.

In the case of the Si-radical possessing an *E* configurated imine, ***E*-1**, cyclization occurs with significant preference in the 6-*endo* mode ($\Delta E^{\ddagger}$ (6-*endo*) $= 16.3\,\mathrm{kJ\,mol^{-1}}$ vs $\Delta E^{\ddagger}$ (5-*exo*) $= 32.6\,\mathrm{kJ\,mol^{-1}}$ at BHandHLYP/6-311G**;[6] the energy values include zero-point vibrational correction, ZPC), to give the thermodynamically more favorable product **3** (ΔE (for **3**) $= -128.3\,\mathrm{kJ\,mol^{-1}}$ vs ΔE (for **2**) $= -37.0\,\mathrm{kJ\,mol^{-1}}$). The transition state for the 6-*endo* ring closure shows a similar unusual motion as was already observed in the intermolecular addition, with the Si-radical apparently "dancing" over the imine nitrogen (Figure 2a). The SOMO orientation is not optimum for maximal overlap with the π^* orbital, and N seems to approach Si with the LP from sideways (Figure 2b), suggesting that this radical cyclization is also governed by dual orbital

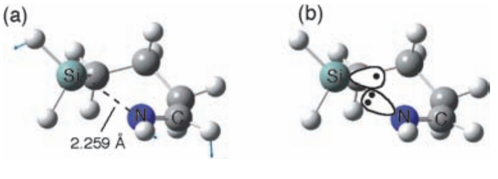
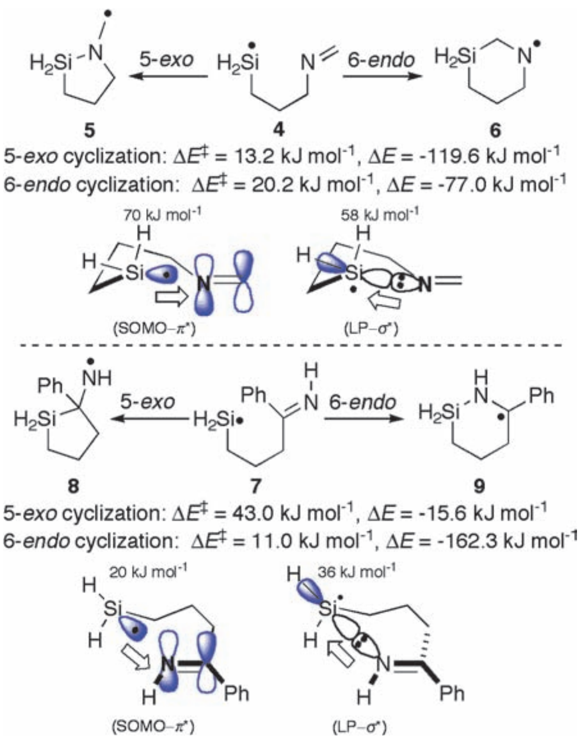


Figure 2. Calculated transition state for the 6-*endo* ring closure in ***E*-1**, (a) motion vectors, (b) orientation of the SOMO and LP.



Scheme 2. Examples for "dual orbital" interactions in Si-radical cyclizations.

interactions. Indeed, NBO analysis at the BHandHLYP/6-311G** level of theory revealed that the SOMO–π^* and LP–σ^* interactions are of equal importance (ca. 47 kJ mol^{-1}) in the transition state of the 6-*endo* cyclization.

On the other hand, because of the different orientation of the LP at nitrogen in the Z configured imine **Z-1**, virtually no stabilization can be derived from LP–σ^* interactions in the transition state for the 6-*endo* cyclization. This results in a significant increase of $\Delta E^{\ddagger}$ for this pathway by ca. 23 kJ mol^{-1}, thus making it kinetically slightly less favorable than the 5-*exo* pathway. As expected, the activation barrier for the 5-*exo* cyclization onto the carbon atom is effectively unchanged by the stereochemistry of the C=N bond.

As a consequence of the directing effects caused by dual orbital interactions, cyclizations of Si-radicals onto imine N=C double bonds, as for example in **4** (upper half in Scheme 2), occur preferably in 5-*exo* fashion ($\Delta E^{\ddagger}$ (6-*endo*) = 20.2 kJ mol^{-1} vs $\Delta E^{\ddagger}$ (5-*exo*) = 13.2 kJ mol^{-1} at BHandHLYP/6-311G**). In the transition state for the 5-*exo* cyclization, the contribution of the SOMO–π^* interaction is worth 70 kJ mol^{-1}, whereas the LP–σ^* interaction accounts for 58 kJ mol^{-1}.

The magnitude of the nucleophilic LP–σ^* interaction to the overall energy contribution is increased by electron-donating substituents at the carbon site of the C=N double bond, as is shown in the lower half of Scheme 2. Thus, the presence of the phenyl substituent in the imine **7** leads to a dramatic reduction of the activation barrier for the 6-*endo* cyclization ($\Delta E^{\ddagger}$ = 11.0 kJ mol^{-1} at BHandHLYP/6-311G**), compared to ***E*-1**. The increased nucleophilicity of the imine nitrogen leads to a LP–σ^* interaction, which impressively outweighs the SOMO–σ^* interaction by more than 50%! Compared to imine ***E*-1** (see Scheme 1), the activation barrier for the 5-*exo* cyclization of **7**, however, is higher by some 10 kJ mol^{-1}. This difference may be attributed to an increase in steric hindrance at the imine carbon in **7**, which is also reflected by the lower exothermicity for the cyclization to give **8** (ΔE (for **8**) = -15.6 kJ mol^{-1} vs ΔE (for **2**) = -37.0 kJ mol^{-1}). It should be noted that very similar results were also found for the Si-radical cyclizations onto C=O double bonds.[7]

To conclude, this type of orbital analysis that rationalizes transition state geometries and the nature of the motion vectors, enables us to predict regioselectivities of unknown radical cyclizations and assists in designing new reactions.

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References and Notes

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