

Unexpected dual orbital effects in radical addition reactions involving acyl, silyl and related radicals†

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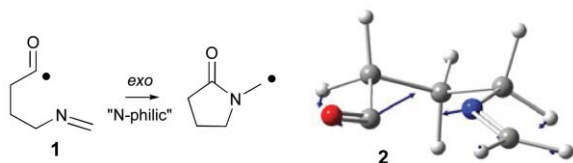
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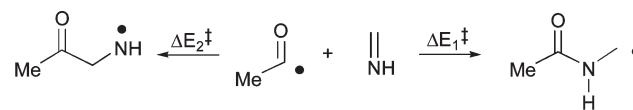
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Molecular orbital calculations reveal that acyl and silyl radicals add to numerous types of π -systems through simultaneous SOMO–LUMO and LUMO–HOMO interactions of the radical with the radicalophile respectively.

Recently, we reported that 5-azahexenoyl radicals (**1**) cyclize *via* nucleophilic addition to the acyl carbon rather than by 5-*exo* homolytic addition at the imine.¹ This conclusion was based primarily on the geometry of the ring-closure transition state (**2**) in which the acyl radical SOMO is clearly not orientated toward the imine π -system.



Scheme 1



Since this initial report, it became clear to us that not only was the geometry of **2** unusual, but so also was the motion associated with the transition state imaginary frequency (transition state vector). When animated, the acyl carbon in **2** appears to swing above the imine nitrogen during bond formation, as indicated by the motion arrows in the structure of **2**.[†] These unusual observations prompted us to investigate further the homolytic addition chemistry of acyl radicals and led us to discover a previously unreported dual orbital effect that operates in systems in which the participating radical can also act as an electrophile.

In order to provide reliable computational data, we chose to examine in detail the parent system, namely the reaction of acetyl radical with methanimine (Scheme 1). Searching of the C_3H_6NO potential energy surface located structures **3** and **4** as the lowest energy transition states for reaction of the acetyl radical at the nitrogen and carbon ends of the imine respectively. Selected energy

barriers (ΔE_1^\ddagger , ΔE_2^\ddagger , Scheme 1) are listed in Table 1, a complete listing is provided as part of the Electronic Supplementary Information (ESI)[†] together with Gaussian Archive Entries for all transition states in this study at all optimised levels of theory.

The data in Table 1 clearly indicate that the acetyl radical has a slight preference for addition to the carbon end of the imine, with the highest level of theory employed in good agreement with BHLYP/6-311G**. It is interesting to note that B3LYP, as we have observed for other radical systems,² performs poorly in both its ability to predict the regiochemistry and energy barriers for these reactions.

The transition states for attack to both ends of the imine are displayed in Fig. 1, along with motion arrows for the transition state vector. The “rolling motion” observed in **2** is clearly evident in transition state **3**.[†] On the other hand, **4** looks much more like a “traditional” transition state for homolytic addition to a π -system.

Visualisation of the Kohn–Sham orbitals generated at the BHLYP/6-311G** level of theory reveals the origin of the unexpected motion in transition state **3**. Not unexpectedly, the transition state “SOMO” comprises interaction of the unpaired electron in the acetyl radical with the imine π^* orbital. Somewhat surprisingly however, of similar energy is a second orbital

Table 1 Selected energy barriers (ΔE_1^\ddagger , ΔE_2^\ddagger , Scheme 1) for the reaction of acetyl radical with methanimine

Method	ΔE_1^\ddagger / kJ mol ⁻¹	ΔE_2^\ddagger / kJ mol ⁻¹
QCISD/aug-cc-pVDZ//MP2/aug-cc-pVDZ	28.8	23.9
CCSD(T)/aug-cc-pVDZ//MP2/aug-cc-pVDZ	23.0	19.2
BHLYP/6-311G**	22.6	19.5
B3LYP/6-311G**	7.6	11.8

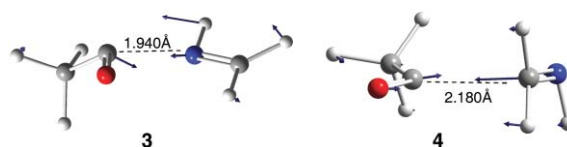


Fig. 1 BHLYP/6-311G** calculated structures **3** and **4**, and motion arrows corresponding to the transition state vector.

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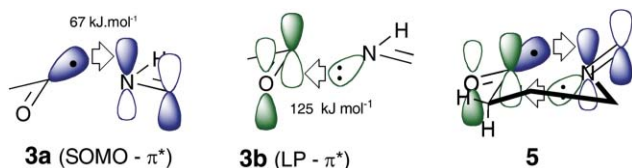
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[†] Electronic supplementary information (ESI) available: Details of computational methods used. Gaussian Archive Entries for all structures in this study at all optimised levels of theory. BHLYP/6-311G** GaussView generated animations of the transition state vectors in **2–4** and **6, 9–11**, and IRC animations for **3** and **4** as Audio Video Interleave (AVI) files. Full listings of calculated energy barriers for Scheme 1 (Table S1) and orbital evolution diagrams for **3** (Figure S1). See DOI: 10.1039/b515330a

interaction comprising interaction of the nitrogen lone pair (LP) with the acetyl radical π^* orbital (Fig. 2).

Natural Bond Orbital (NBO) analysis at the BHLYP/6-311G** level of theory reveals that the SOMO- π^* overlap depicted in **3a** is worth about 67 kJ mol⁻¹, with the LP- π^* interaction (**3b**) worth some 125 kJ mol⁻¹. Clearly then, these calculations suggest that the nucleophilic character of the imine dominates over the radical interaction in this reaction.



Intrinsic reaction coordinate (IRC) calculations provide additional insight into this phenomenon.† Fig. S1 (see ESI†) presents the evolution of the interacting orbitals for the reaction depicted in Scheme 1 and clearly shows that the LP- π^* interaction develops ahead of the SOMO- π^* interaction. NBO analyses reveal that at a distance of 2.24 Å, the former interaction is worth 49 kJ mol⁻¹, but the latter only 5 kJ mol⁻¹. As the reaction evolves, the SOMO- π^* interaction becomes more important with respect to the nucleophilic interaction. The transition state motion can now be understood as a result of orbital compromise; optimum SOMO- π^* and LP- π^* interactions result in a “dance”, with reaction partners “rocking and rolling” with each other to obtain maximum energy benefit.

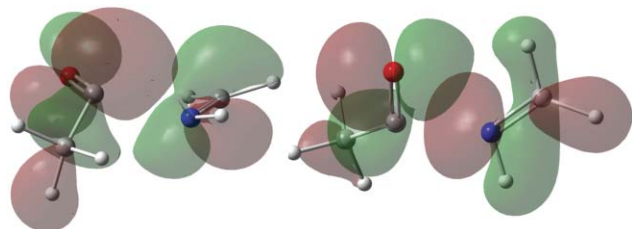


Fig. 2 Kohn-Sham SOMO- π^* (left) and LP- π^* (right) interactions in transition state **3**.

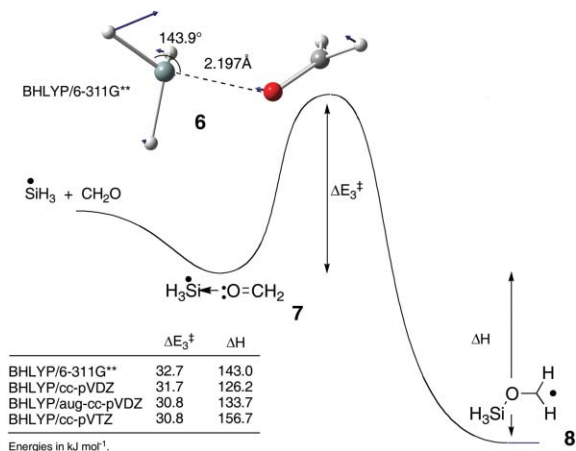
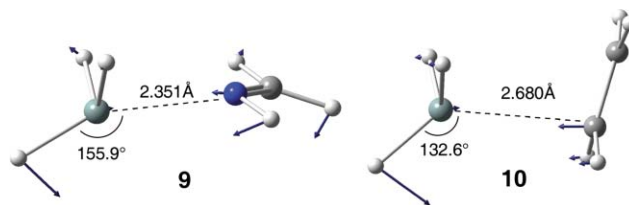


Fig. 3 Profile for reaction of silyl radical with formaldehyde; BHLYP/6-311G** calculated transition state (**6**) with transition state motion arrows.

In seemingly unrelated work we became interested in the reaction of silyl radical with formaldehyde as part of a project aimed at further exploring the self-terminating radical chemistry developed by one of us.³ As expected (Fig. 3) this reaction is calculated to be significantly exothermic, with an activation energy (ΔE_3^\ddagger) of some 31 kJ mol⁻¹ and reaction enthalpy (ΔH) in excess of 130 kJ mol⁻¹.

We became very curious about this reaction because of the unexpected geometry of the transition state (**6**) and associated transition state vector. In particular, the silyl radical component of **6** appears to be “leaning back” with one of the O-Si-H angles at about 145°, with the remaining angles at about 90°. When animated,‡ the transition state vector for **6** looks very similar to those described previously for the reactions involving acyl radicals.



NBO analysis of the transition state orbitals in **6** at the BHLYP/6-311G** level reveals a similar orbital origin for the “dance” experienced by **6** to that for the other transition states in this study (Fig. 4). It is interesting to note that these calculations predict a SOMO- π^* interaction as well as an interaction between the lone pair on oxygen with the Si-H σ^* orbital; the former interaction (**6a**) is worth about 515 kJ mol⁻¹, while the LP- σ^* interaction (**6b**) is calculated to be worth some 163 kJ mol⁻¹.

The attack angle (θ) in **6** is a compromise between the two interactions described above and should be influenced by the nucleophilicity of the radicalophile, with θ increasing with stronger nucleophiles as the interaction in **6b** becomes more important. It was therefore gratifying to see that the transition state (**9**) for the reaction of silyl radical with imine (CH₂=NH) does indeed have an increased attack angle ($\theta = 155.9^\circ$) relative to **6**, as well as a reduced energy barrier for reaction ($\Delta E^\ddagger = 5.7$ kJ mol⁻¹ at BHLYP/6-311G**). The transition state motion of **9** is calculated to be almost identical to that of **6**.‡

Surprisingly, our calculations predict that even ethylene (a weak nucleophile) reacts with silyl radical *via* a transition state (**10**) that

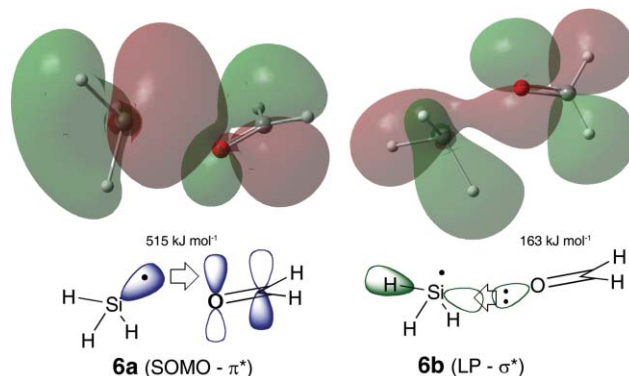


Fig. 4 Kohn-Sham SOMO- π^* (left) and LP- σ^* (right) interactions in transition state **6**.

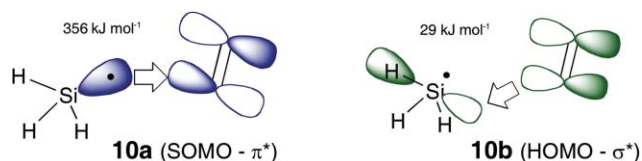


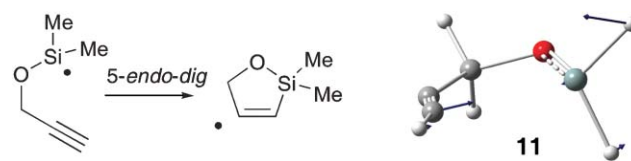
Fig. 5 Calculated orbital interactions in transition state **10**.

shows striking resemblance to the others in this study (Fig. 5). B3LYP/6-311G** calculations suggest that **10** is earlier than the other structures (**3–6**, **9**) and has a smaller (132.6°), albeit significant, attack angle, commensurate with the decreased nucleophilicity of ethylene. We conclude, therefore, that radicals such as silyl, that can also masquerade as electrophiles, will seek to capitalise on the stabilisation afforded by HOMO– σ^* overlap in addition to the conventional (radical) interaction. It should be noted that “distorted” transition states have been reported previously for reactions involving silyl radicals and alkenes, although the nature of this “distortion” was not commented on.⁴

We believe that the work described in this paper is the “tip of the iceberg” and will provide insight into a gamut of free-radical reactions whose outcomes either defy explanation, or are poorly understood. One example of this is depicted in Scheme 2 in which Amrein and Studer describe the first *5-endo-dig* cyclization involving a silyl radical (Scheme 2).⁵

Inspection of the B3LYP/6-311G** calculated transition state (**11**) for the closely-related ring-closure reveals what has now become the common rolling-motion associated with these radical addition reactions.[‡] In addition, NBO analysis suggests that the secondary π – σ^* interaction in transition state **11** contributes about 65 kJ mol^{-1} of “extra” stabilisation to this reaction. We expect, therefore, that secondary orbital interactions are very likely to be the reason for why this *5-endo-dig* reaction is possible.

Finally, using the type of dual orbital analysis that rationalises the geometries of the transition structures and the nature of the



Scheme 2

associated motion vectors that are described in this communication, it is possible to predict the regiochemistries of new radical addition reactions. Examples will be provided in future experimental and computational research from these laboratories.

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Notes and references

‡ Animations of the transition state imaginary frequency and IRC calculations are conveniently visualised using the GaussView software that complements Gaussian 03.

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