

Reactions of Acetyl Radical with Acetylene – A Computational Study[†]

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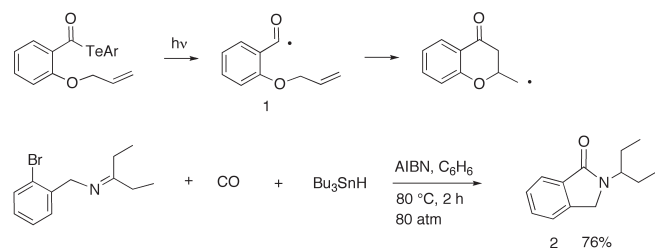
Ab initio and DFT molecular orbital calculations predict that acetyl radical reacts with acetylene through interactions primarily involving the SOMO of the radical and the in-plane π -bond of acetylene. An energy barrier (ΔE_1^\ddagger) of 39.6 kJ mol⁻¹ is predicted for the preferred *anti* arrangement of reactants at the CCSD(T)/cc-pVDZ//BHandHLYP/cc-pVDZ level of theory. NBO analysis reveals additional interactions between the radical SOMO and the nearby C-H σ -bond in acetylene worth about 10% of the total transition state interaction energy. This type of orbital interaction has not previously been observed in radical addition reactions involving C-C π -bonds.

Key Words: Acetyl radical, Acetylene, Molecular orbital calculations

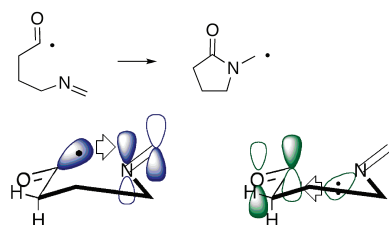
Introduction

The development of new synthetic methodology is an important endeavour in modern organic chemistry, one that relies on an understanding of the mechanistic details of the new chemistry being developed. Contributions from many leading laboratories around the world, including those of Professor Kim,[†] have been instrumental in the transformation of free radicals from mere curiosities at around the time of the Apollo 11 lunar landing,[‡] to well-understood intermediates in controlled synthetic transformations at the beginning of the 21st Century.

In recent times we,¹ and others,² have been interested in the application of acyl and related radicals to synthetic problems.



Scheme 1



Scheme 2

While radicals such as **1** can be generated from acyl selenides or tellurides³ to afford interesting carbo- and hetero-cyclic compounds, the free radical carbonylation chemistry developed by Ryu and co-workers remains an attractive protocol, and perhaps the method of choice, for the efficient and convenient preparation of cyclic molecules including lactams (**2**) (Scheme 1).⁴

During the course of this work, it was observed that acyl radicals are N-philic; in other words they attack the nitrogen-end of imine π -systems, often contrary to Baldwin's Rules.⁵ Through the use of computational techniques, we were able to explain these observations; acyl radicals enjoy the benefits of multi-orbital interactions not available to other carbon-centred radicals, allowing them to "masquerade" as electrophiles when favourable orbital opportunities arise, such as those depicted in Scheme 2.⁶

As part of our ongoing interest in the chemistry of these radicals, we have explored the additions of acyl and related radicals to numerous π -systems as well as some homolytic substitution reactions at higher heteroatoms, using computational techniques.⁷ In this paper we report our studies of reactions involving acetylene and show that along with the in-plane π -bond of the alkyne, a C-H σ -bond also becomes involved in interactions with the SOMO of the radical.

Computational Methods

Ab initio and DFT molecular orbital calculations were carried out on Dell PowerEdge 400SC and SGI Altix AC computers using the Gaussian 03 program.⁸ Geometry optimizations were performed using standard gradient techniques at HF, BHandHLYP, and B3LYP levels of theory using restricted and unrestricted methods for closed- and open-shell systems respectively. ROMP2 optimizations were carried out using the Numerical Eigenvector Following (NEF) method available within Gaussian 03. In every case, standard basis sets were used. All ground and transition states were verified by vibrational frequency analysis. Further single-point QCISD and CCSD(T) calculations were performed on some of the BHandHLYP optimized structures. When correlated methods were used, calculations

[†]This paper is dedicated to Professor Sunggak Kim on the occasion of his honourable retirement.

[‡]2009 Marks the 40th anniversary of the Apollo 11 manned mission to the moon and is the International Year of Astronomy.

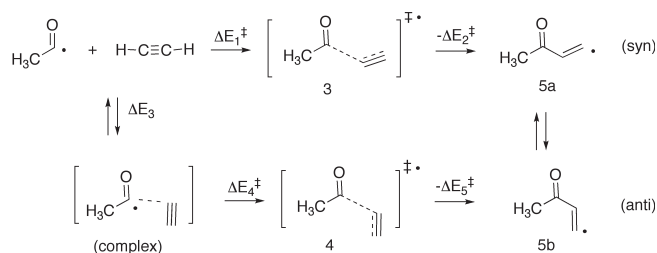
were carried out using the frozen core approximation. Where appropriate, zero-point vibrational energy (ZPE) corrections have been applied. Natural Bond Orbital (NBO) Analyses were carried out using *NBO 5.0*⁹ linked through the Gaussian 03 program.

Results and Discussion

Reaction of acetyl radical with acetylene. Extensive searching of the C_4H_5O potential energy surface located structures **3** and **4** as corresponding to stationary points; vibrational frequency analysis confirmed that these structures correspond to the transition states for the *syn* and *anti* modes[§] of attack of the acetyl radical at acetylene respectively (Scheme 3). Transition state **3** was calculated to lie some 45.4 kJ mol^{-1} above the energy of the reactants (acetyl radical + acetylene) at the BHandHLYP/6-311G** level of theory. Pleasingly, and in agreement with our previous calculations, single-point CCSD(T)/6-311G** energy correction on the BHandHLYP/6-311G** optimised structure of **3** resulted in a value for the activation energy (ΔE_1^\ddagger) of 44.1 kJ mol^{-1} , strongly suggesting that the BHandHLYP method is able to provide both energies and geometries of structures that are of reliable accuracy.⁷ Similar results are observed using other basis sets, with energy barriers of between about 40 and 45 kJ mol^{-1} calculated for ΔE_1^\ddagger at various BHandHLYP, QDISD and CCSD(T) levels. Not surprisingly the B3LYP method provided barriers some 10 kJ mol^{-1} lower, while the use of HF/6-311G** appears to significantly over-estimate this barrier.⁷ Energy data for the reactions depicted in Scheme 3 are listed in Table 1.

Inspection of Table 1 reveals that these reactions are exothermic in the direction depicted in Scheme 3, with reverse barriers that are calculated to lie in the range of $125 - 155 \text{ kJ mol}^{-1}$ at the more reliable (BHandHLYP, QCISD, CCSD(T)) levels of theory.

Interestingly, when oriented in the *anti* arrangement, most



Scheme 3

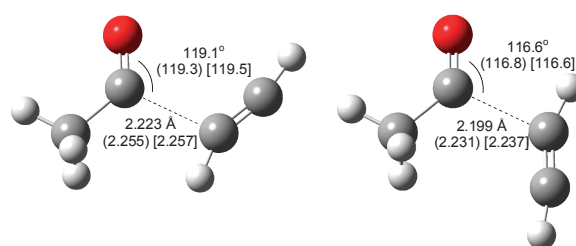


Figure 1. Selected BHandHLYP/6-311G** geometrical data for transition states **3** (left) and **4** (right). (BHandHLYP/cc-pVDZ data in parentheses) [BHandHLYP/aug-cc-pVDZ data in brackets].

computational methods in this study (Table 1) predict that acetyl radical and acetylene react to form a pre-associated complex that further reacts through transition state **4** to afford the product **5b**. (Scheme 3). Conformer **5b** is the preferred conformation of the product radical and is found to lie 4.9 (CCSD(T)/6-311G**//BHandHLYP/6-311G**) to 5.5 (BHandHLYP/6-311G**) kJ mol^{-1} below **5a**.

Once again, the calculated differences in energy between **3** and the starting materials appear to be well reproduced by the BHandHLYP method as evidenced by the CCSD(T) data.

Transition state **4** is to lie 54.5 (HF/6-311G**) to 31.7 kJ

Table 1. Calculated energies (kJ mol^{-1}) associated with the reactions depicted in Scheme 1 and transition state (imaginary) frequency of **3** and **4** (ZPE corrected energies in parentheses)

Method	3			4			
	ΔE_1^\ddagger	ΔE_2^\ddagger	ν_{TS}	ΔE_3	ΔE_4^\ddagger	ΔE_5^\ddagger	ν_{TS}
HF/6-311G**	61.2 (61.7)	171.6 (155.4)	521i	4.0 (-2.7)	58.5 (55.6)	168.3 (153.4)	569i
BHandHLYP/6-311G**	45.4 (50.9)	144.0 (130.5)	501i	6.4 (-0.4)	42.2 (41.5)	139.8 (127.2)	481i
BHandHLYP/cc-pVDZ	40.7 (45.9)	155.2 (141.0)	476i	7.5 (0.2)	38.0 (36.3)	150.7 (137.5)	457i
BHandHLYP/aug-cc-pVDZ	41.9 (47.9)	152.6 (138.3)	467i	10.0 (2.4)	42.5 (41.1)	150.3 (136.8)	450i
QCISD ^a //BHandHLYP/6-311G**	48.4	131.2		7.6	48.7	128.4	
QCISD ^a //BHandHLYP/cc-pVDZ	43.6	139.0		8.6	44.6	135.6	
QCISD ^a //BHandHLYP/aug-cc-pVDZ	37.7	137.8		11.4	41.5	136.5	
CCSD(T) ^a //BHandHLYP/6-311G**	44.1	127.7		8.4	44.8	124.9	
CCSD(T) ^a //BHandHLYP/cc-pVDZ	39.6	136.4		9.5	41.2	133.0	
B3LYP/6-311G**	33.9 (39.8)	117.9 (105.4)	386i	6.5 (-0.3)	31.8 (31.2)	115.3 (103.6)	367i
B3LYP/cc-pVDZ	28.9 (34.3)	129.8 (116.6)	359i	8.2 (0.8)	28.0 (26.3)	126.9 (114.7)	342i
ROMP2/cc-pVDZ	29.4 (35.7)	111.2 (96.2)	543i	0.0	29.4 (36.0)	116.5 (102.5)	544i

^aSingle-point calculation using the same basis set as used for the optimization.

[§]We use the terms *syn* and *anti* to refer to the alignment of the alkyne with the carbonyl unit of the acetyl radical.

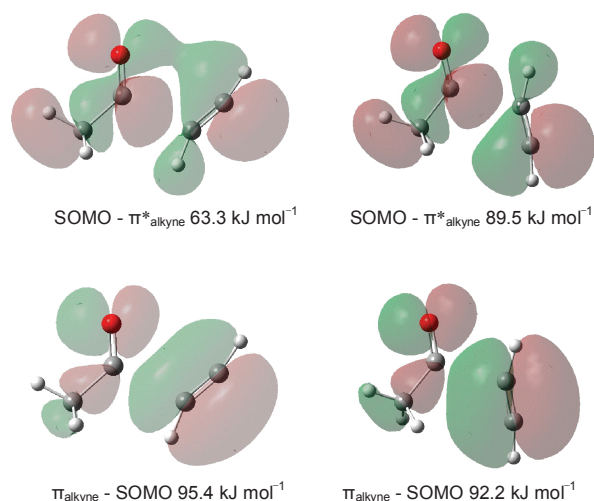


Figure 2. BHandHLYP/6-311G** generated orbitals for transition states **3** (left) and **4** (right).

mol^{-1} (CCSD(T)/cc-pVDZ/BHandHLYP/cc-pVDZ) above the energy of the starting materials, with BHandHLYP/6-311G** providing a value of 35.8 kJ mol^{-1} . By comparison with the energy barriers calculated for the reaction involving **3**, these data suggest that the *anti* pathway is preferred over the *syn* by some 5 kJ mol^{-1} . Selected BHandHLYP structural data for transition states **3** and **4** are provided in Figure 1 and reveal attack distances in the range $2.199 - 2.257 \text{ \AA}$; full geometric data are available as part of the Supporting Information.

We next turned our attention to whether the acetyl radical was acting as a nucleophilic or electrophilic radical in its reaction with acetylene. To that end the orbital interactions in transition states **3** and **4** were subjected to Natural Bond Orbital (NBO) analysis at the BHandHLYP/6-311G** level as described previously.⁶ The α -spin set reveals a SOMO $\rightarrow \pi^*$ interaction in structure **3** worth some 63.3 kJ mol^{-1} , while a value of 95.4 kJ mol^{-1} is found in the β -spin set for the complementary $\pi \rightarrow \text{SOMO}$ interaction. These data indicate that the acetyl radical is behaving predominantly as an electrophilic radical during the *syn* addition reaction.

In the case of the *anti* addition transition state **4**, the analogous SOMO $\rightarrow \pi^*$ and $\pi \rightarrow \text{SOMO}$ interactions are calculated to be worth 89.5 and 92.2 kJ mol^{-1} , indicative of a radical reacting in an ambiphilic manner. GaussView-generated orbital images are found in Figure 2.

It should be noted that these NBO calculations reveal that the acetyl radical reacts almost exclusively with the alkyne π -system that lies in the plane of the SOMO, with no appreciable contributions from the orthogonal π -bond. Interestingly, but not surprisingly in light of the known acidity of alkynes,¹⁰ our NBO studies reveal additional SOMO $\rightarrow \sigma_{\text{CH}}^*$ and $\sigma_{\text{CH}} \rightarrow \text{SOMO}$ interactions[†] worth 7.0 and 12.9 kJ mol^{-1} respectively in the case of **3**, and 9.2 (SOMO $\rightarrow \sigma_{\text{CH}}^*$) and 18.4 kJ mol^{-1} ($\sigma_{\text{CH}} \rightarrow \text{SOMO}$) in the case of **4**. Unlike other systems that we have examined, it would appear that during the addition of the acetyl radical to acetylene, the reaction is assisted through additional orbital interactions involving the nearby C-H σ -bond and that this interaction is worth about 10% of the total orbital interaction en-

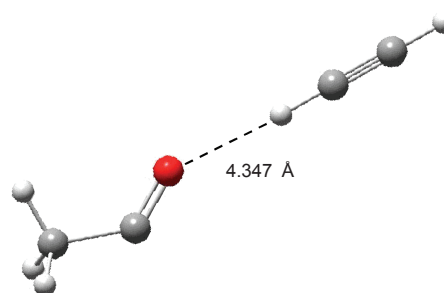


Figure 3. BHandHLYP/aug-cc-pVDZ calculated structure of the hydrogen-bonded intermediate in Scheme 3.

ergy in the transition state.

Finally, it should be noted that while at some levels of theory the complex effectively disappears when zero-point energy (ZPE) correction is applied (Table 1), using the BHandHLYP/aug-cc-pVDZ method, this complex is predicted to be moderately stabilised by about 2.4 kJ mol^{-1} through hydrogen bonding not evident at the other levels of theory when ZPE correction is applied (Figure 3). Correction for possible basis set superposition error (counterpoise correction)¹¹ reduces this barrier to only 0.6 kJ mol^{-1} (with ZPE).

Conclusion

Using computational techniques, we have shown that acetyl radical reacts with acetylene through orbital interactions involving the radical SOMO with one of the acetylene π -bonds, as well as the nearby C-H σ -bond. The second interaction has not been observed in other systems studies. NBO calculations on the transition states involved in this chemistry reveal that the acetyl radical reacts predominantly in an ambiphilic manner in its preferred *anti* approach to acetylene.

Supporting Information. Gaussian Archive Entries for transition states **3** and **4**, and the hydrogen-bonded complex are available on request from the corresponding author (carlhs@unimelb.edu.au; +61 3 9347 8189).

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