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Computational study of the thermal rearrangement of acetoxy(methoxy)carbene

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ABSTRACT: Thermolysis of 2-acetoxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline affords acetoxy(methoxy)-carbene. Thermal rearrangement of acetoxy(methoxy)carbene to methyl pyruvate is a concerted 1,2-migration, avoiding a potential radical-pair mechanism. Copyright © 2005 John Wiley & Sons, Ltd.
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KEYWORDS: acetoxy(methoxy)carbene; carbene; concerted; computation; rearrangement

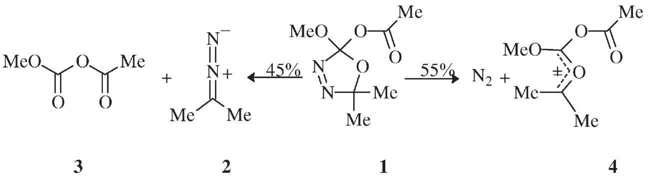
INTRODUCTION

Recently, we reported that 2-acetoxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (**1**) (also known as 2-acetoxy-2,5-dihydro-2-methoxy-5,5-dimethyl-1,3,4-oxadiazole) undergoes two competing cycloreversions upon thermolysis in benzene at 110 °C.[1] The cycloreversions were essentially balanced, affording 2-diazopropane (**2**) together with the acetic methylcarbonic anhydride **3** on the one hand, and N_2 and the carbonyl ylide **4** on the other, as shown in Scheme 1. That scheme was supported with computation of the energetics of the possible cycloreversions (W. Czardybon, J. Warkentin and N. H. Werstiuk, in preparation). The ylide was assumed to be the initial product of the extrusion of N_2; the actual materials identified were acetone and methyl pyruvate (**6**), the latter from rearrangement of acetoxy(methoxy)-carbene (**5**), presumably formed by fragmentation of ylide **4**. The carbene was also inferred from thermolysis in the presence of benzylidenemalononitrile, which gave methyl ester **7** through a sequence of reactions outlined in Scheme 2.[1]

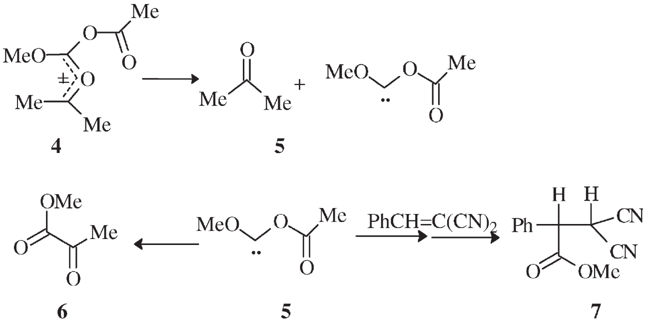
We now report computations concerning the conformational properties of carbene **5** and the mechanism of its rearrangement to methyl pyruvate (**6**). The pyruvate could arise by concerted rearrangement of **5**, or its genesis could involve the radical pair **8** (Scheme 3). The experimental results indicated the concerted pathway, for which there is precedent in the rearrangement of 1-acetoxyalkylidenes.[2–4] However, the radical pair mechanism is also known for the cases of several dioxycarbenes[5–7] and it was of interest to estimate the barrier for radical-pair formation from **5**, even though there was no direct experimental evidence for this reaction, and to compute the barriers for other potential fates of the carbene.

EXPERIMENTAL AND RESULTS

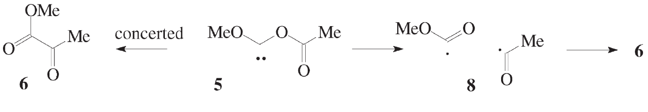
Optimized equilibrium geometries (the carbenes were not constrained to be C_s planar) and transition states were obtained at the B3PW91/6–31+G(d,p) level, which includes the three-parameter exchange functional of Becke and the gradient-corrected correlation functional of



Scheme 1



Scheme 2



Scheme 3

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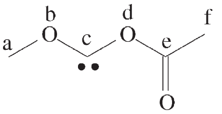


α: C^a-O^b-C^c-O^d
β: O^b-C^c-O^d-C^e
γ: C^c-O^d-C^e-C^f

Figure 1. Definition of dihedral angles α, β and γ for acetoxy(methoxy)carbene

Perdew and Wang,[8] using either Gaussian 98[9] or Gaussian 03.[10] Uncorrected total energies and *Z*-matrices for all optimized geometries and transitions states are included as Supplementary Information (available at Wiley Interscience). The ZPE-corrected energy and the enthalpy (at 298.15 K) of carbene $\mathbf{5_{W1}}$ are also included. Calculations on the dissociation of **5** to radicals were carried out at the UB3PW91/6–31+G(d,p) level. Frequency calculations were performed for all structures to characterize optimized geometries and transition states. Where necessary, uncorrected total energies, zero-point corrected energies and enthalpies at 298.15 K are presented. An IRC calculation was run for the rearrangement of carbene $\mathbf{5_{W1}}$ to methyl pyruvate (**6**).

Conformational analysis of acetoxy(methoxy)carbene (5)

To analyze possible reactions of carbene **5**, it was desirable to establish its conformational properties because the

Table 1. Selected geometric parameters of conformers of **5** optimized at the B3PW91/6–31+G(d,p) level

	Planar structure (°)			Dihedral angles found (°)			
Conformer of 5	α	β	γ	α	β	γ	Energy relative to $\mathbf{5_{W1}}$ (kcal mol^{-1})[a]
$\mathbf{5_{W1}}$	180	180	0	180	180	0.2	0.00
$\mathbf{5_{W2}}$	180	180	180	178.2	173.6	158.4	1.03
$\mathbf{5_{S1}}$	180	0	180	179.1	−4.1	101.2	5.06
$\mathbf{5_{S2}}$	0	180	0	0	180	0.1	1.40
$\mathbf{5_{S3}}$	0	180	180	−3.1	172.1	145.0	4.22
$\mathbf{5_{S4}}$	180	0	0		Not found		—
$\mathbf{5_{U1}}$	0	0	0		Not found		—
$\mathbf{5_{U2}}$	0	0	180		Not found		—

[a] 1 kcal = 4.184 kJ.

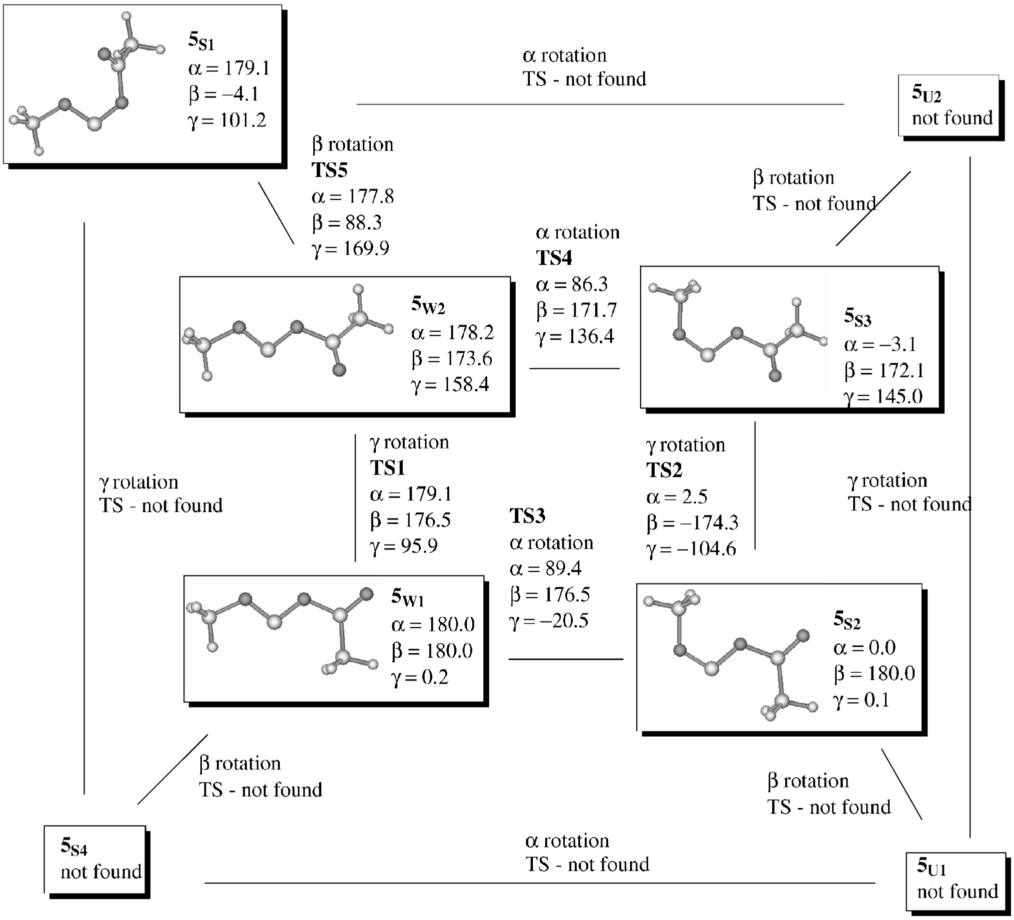


Figure 2. Conformers of **5** and transition states for their interconversion at the B3PW91/6–31+G(d,p) level

rearrangement and fragmentation of **5** might exhibit conformational dependences. It was necessary to take into consideration rotation around three bonds described by dihedral angles α, β and γ (Fig. 1). Conformers resulting from rotation of the methyl groups were omitted. The conformers found can be divided into two groups with respect to values of α and β that describe the geometry around the carbene carbon. The first group contains W-like conformers ($\alpha \approx \beta \approx 180°$) and the second group contains sickle-like (S) conformations ($\alpha \approx 180°$, $\beta \approx 0°$ or $\alpha \approx 0°$, $\beta \approx 180°$) (Table 1). Table 1 lists all conformers that were found from combinations of α, β and γ values set initially to 0 or 180°. Stable U-shaped conformations could not be located.

Values of α and β found for $\mathbf{5_{W1}}$, $\mathbf{5_{W2}}$, $\mathbf{5_{S1}}$, $\mathbf{5_{S2}}$ and $\mathbf{5_{S3}}$ are close to the values for the planar conformations (0° or 180°), varying from 0° to 4.1° and from 172.1° to 180.0°. Deviations observed for γ are significantly greater. Changes in that angle correspond to rotation around the O—C(O) (γ) single bond and have a minor influence on the energy of **5**, as will be shown below.

Figure 2 shows the angles of optimized conformations of **5** that were found, together with transition states (TSs) connecting them. The three missing conformers ($\mathbf{5_{S4}}$, $\mathbf{5_{U1}}$, $\mathbf{5_{U2}}$) are significantly more crowded than the others and the steric hindrance accounts for the fact that they are not stable structures. Optimization of those three structures, starting from ideally planar conformers, led to the more stable conformations $\mathbf{5_{S1}}$, $\mathbf{5_{S2}}$, and $\mathbf{5_{S3}}$, respectively.

Figure 3 shows the potential energy surfaces for all stable conformers of **5** that were found, including the transition states connecting them. It is seen that the uncorrected energies, ZPE corrected energies or enthalpies yield potential energy surfaces that differ only marginally from each other. The average barriers for rotation around dihedral angles α and β are in the regions of 20 and 8.0 kcal mol^{-1}, respectively. As can be seen in Fig. 3, both barriers for rotation γ are very small (2.6 and 4.7 kcal mol^{-1}). Detailed examination of this rotation for

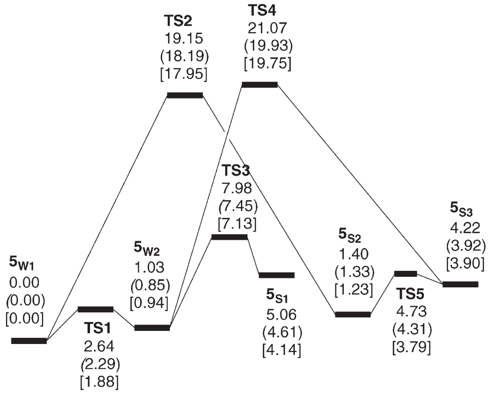
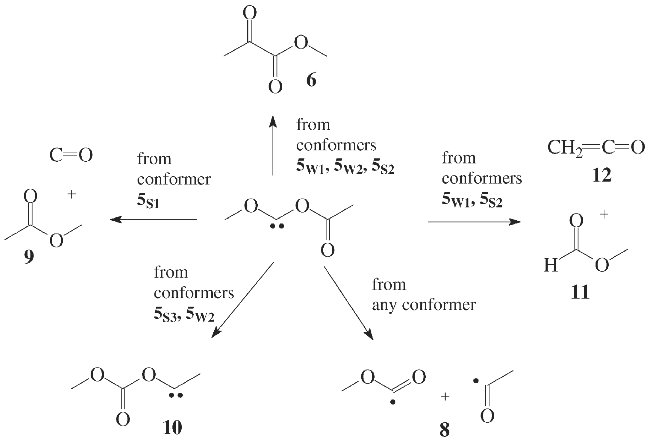


Figure 3. Potential energy surfaces (kcal mol^{-1}) for all conformers of **5**, including transition states at the B3PW91/6–31+G(d,p) level. The zero-point corrected total energies are shown in parentheses and enthalpies (at 298.15 K) in square brackets



Scheme 4

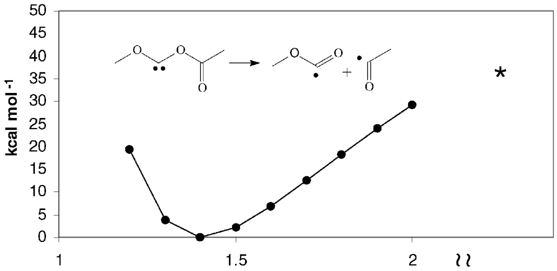


Figure 4. Plot of energy versus distance (Å) between the C and O atoms at the UB3PW91/6–31+G(d,p) level

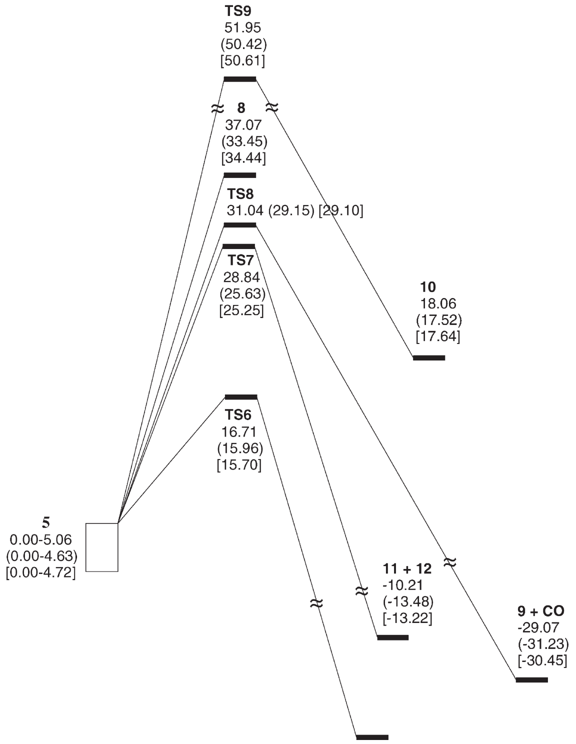


Figure 5. Potential energy surfaces (kcal mol^{-1}) for rearrangement and fragmentation of **5** at the B3PW91/6–31+G(d,p) level and, where necessary, at the UB3PW91/6–31+G(d,p) level. The values in parentheses are zero-point corrected total energies and the enthalpies (at 298.15 K) are shown in square brackets. When a product can be formed from more than one conformer, only the lowest barrier is shown

conformer 5_{S1} led to at least two more stable structures and transition states connecting them with other conformers. Differences in energy between these structures (and also transition states for their interconversions) and 5_{S1} are very small ($< 1\,kcal\,mol^{-1}$), and therefore they were not taken into consideration. Rotation around the O—C(O) (γ) single bond in **5** has a very minor influence on energy and the corresponding potential energy surface is almost flat.

Rearrangements and fragmentations of 5

The conformational preferences for several reactions of **5** that were examined are summarized in Scheme 4. Although we cannot tell which conformer is the starting point for a specific product, because some conformers are undoubtedly equilibrated, the barrier for any step of a multistep process can be calculated. Conformers $\mathbf{5_{W1}}$, $\mathbf{5_{W2}}$ and $\mathbf{5_{S2}}$ can undergo a [1,2]-acyl shift, yielding methyl pyruvate (**6**) with barriers near $17\,kcal\,mol^{-1}$. Conformers $\mathbf{5_{W1}}$ and $\mathbf{5_{S2}}$ could also fragment to methyl formate (**11**) and ketene (**12**), which might be formed through a hydrogen shift concerted with breaking of the C—O bond. The barrier for that reaction lies between about 29 (28.84 calculated) and 30 (30.18 calculated) $kcal\,mol^{-1}$.

Conformer $\mathbf{5_{S1}}$ might also fragment through concerted breaking of two C—O bonds to form carbon monoxide and methyl acetate (**9**). The barrier for this reaction is about $31\,kcal\,mol^{-1}$. Conformers $\mathbf{5_{S3}}$ and $\mathbf{5_{W2}}$ might rearrange through an oxygen shift to form carbene (**10**) with barriers near $52\,kcal\,mol^{-1}$.

The fragmentation of **5** to acetyl and methoxycarbonyl radicals (**8**) was also examined. The transition state for that reaction could not be located. Figure 4 shows a plot of energy versus C—C bond length for $\mathbf{5_{W1}}$. Stretching the C—O bond causes the energy of the system to rise but a maximum related to a transition state was not located. The sum of the energies of the free radicals, arbitrarily located along the distance axis, is indicated with an asterisk. The energetic cost of radical-pair formation was estimated as the difference between the sum of the total energies of the free radicals and the total energy of **5**. While the energy of the radical-pair remains constant, the cost of its formation varies between 32 and $37\,kcal\,mol^{-1}$, depending on the carbene conformer used. The relative energies of all stable carbene conformers studied lie in a range of about $5\,kcal\,mol^{-1}$.

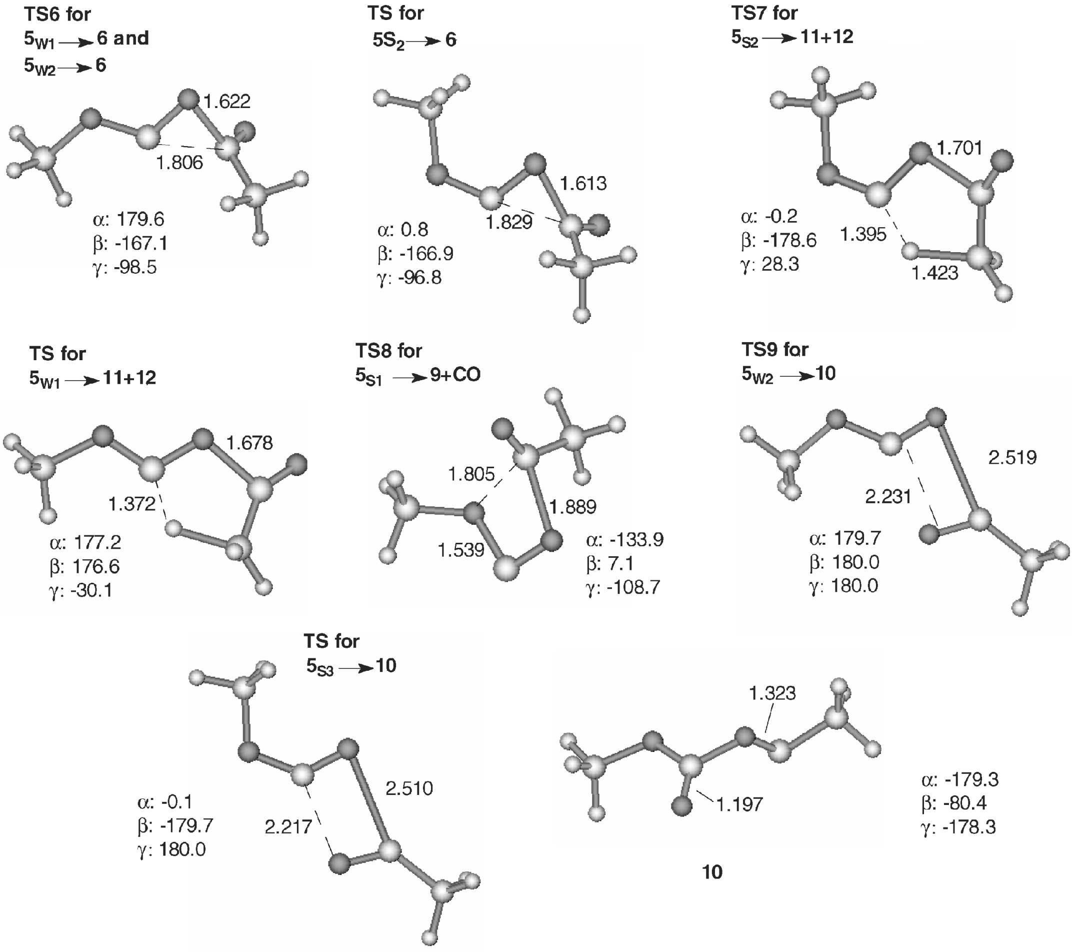


Figure 6. Geometries of transition states for rearrangements and fragmentations of **5** (Scheme 4) and the optimized geometry of carbene **10** at the B3PW91/6–31+G(d,p) and, where necessary, UB3PW91/6–31+G(d,p) levels

Figure 5 shows potential energy surfaces for rearrangements and fragmentations of **5**. The conformers of **5** shown previously are not differentiated in energy, but are represented as a box for clarity. The preferred reaction of **5** is predicted to be concerted rearrangement to methyl pyruvate, with a barrier near 17 kcal mol^{-1} for different conformers. This result and the fact that the fragmentations to radicals have barriers that range from 32 to 37 kcal mol^{-1} are nicely in accord with our experimental study showing that **5** does rearrange to methyl pyruvate (**6**) without the intermediacy of radicals.[1] Additionally, an IRC calculation clearly established that **TS6** connects **5** with methyl puruvate (**6**).

Figure 6 shows selected geometric parameters of transition states for reactions and rearrangements of **5** and the optimized geometry of **10**.

CONCLUSIONS

A computational study of the chemistry of acetoxy (methoxy)carbene indicates that it rearranges to methyl pyruvate via a concerted, 1,2-acyl group migration rather than fragmentation to a radical-pair and coupling of the latter. Other potential fates of the carbene involve higher barriers. Our work indicates calculations at the B3PW91/6–31+G(d,p) level are suitable for studying reactions of heteratom-substituted carbenes.

Acknowledgements

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