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Further *Ab Initio* Studies on the Reactivity of Nitrosoketene

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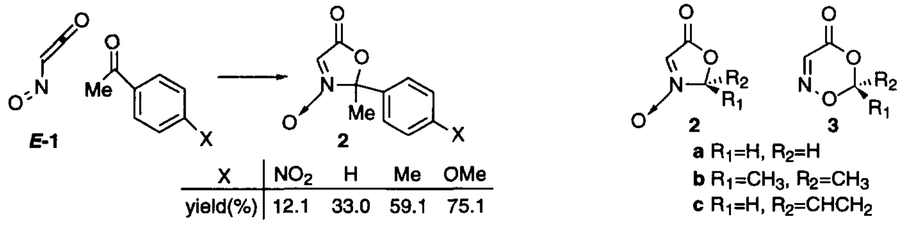
Abstract: The cycloadditions of nitrosoketene with formaldehyde, acetone and 2-propenal were calculated using *ab initio* molecular orbital theory (MP2/6-31G*). The reactions proceed by the [3+2] pathway via a concerted, planar and pseudopericyclic transition state with a significantly lower barrier rather than by the alternative [4+2]. The transition state asynchronicity can be used to explain the substituent effects on the cycloaddition of ketones with nitrosoketene. © 1997 Elsevier Science Ltd.

Nitrosoketene (**1**), formed by the pyrolysis of isonitroso Meldrum's acid, reacts with ketones to give cyclic nitrones (**2**).[1] Two pathways have been proposed for this reaction, (a) direct [3+2] cycloaddition of ***E*-1** to give **2**, or (b) initial [4+2] of **Z-1** to give dioxazinones (**3**) followed by 1,2-rearrangement. We previously calculated that the direct [3+2] pathway is favored for the reaction of **1** with formaldehyde.[2] Katagiri *et al.* pointed out that if the N-C bond leads the reaction, as we calculated, electron-withdrawing *para*-substituents on acetophenones would favor the reaction.[1b] Experimentally, however, higher yields are obtained with electron-donating groups (Scheme 1).[1b] Although other reactions may affect the isolated yields, these results suggest that either our earlier RHF calculations[2] were misleading, or formaldehyde is not a good model for acetophenone. Therefore we reexamined the cycloaddition of **1** with formaldehyde at the MP2/6-31G* level and investigated the cycloadditions of **1** with 2-propenal and acetone.

Scheme 1.



X	NO_2	H	Me	OMe
yield(%)	12.1	33.0	59.1	75.1

a R_1=H, R_2=H
b R_1=CH_3, R_2=CH_3
c R_1=H, R_2=$CHCH_2$

All calculations were carried out with Gaussian 94.[3] Geometries were optimized at the RHF/6-31G* level and characterized by vibrational frequency calculations. The structures were then reoptimized at the MP2/6-31G* level; these are shown in Figure 1.[4] Relative energies were calculated at the MP4(SDQ)/6-31G* level using the MP2/6-31G* optimized geometries with scaled zero-point energy corrections[5] from frequency calculations at the RHF/6-31G* level and are reported in Table 1. For each reactant, a significant computational preference (3.9 - 5.5 kcal/mol) for the [3+2] pathway is found at this level of theory which is consistent with our previous calculation. The lack of cyclic overlap in planar, pseudopericyclic transition states (as in Figure 2) often contribute to exceptionally low barriers, particularly when the geometry is favorable as in the [3+2] pathway.[6] Furthermore, the dioxazinones (**3**) are calculated to be more stable than the nitrones (**2**). Thus even if rearrangement from **3** to **2** occurred, the equilibrium would favor **3**. This is again consistent with the sole observed product **2** being formed via a kinetically favored [3+2] pathway, as we previously suggested.[2]

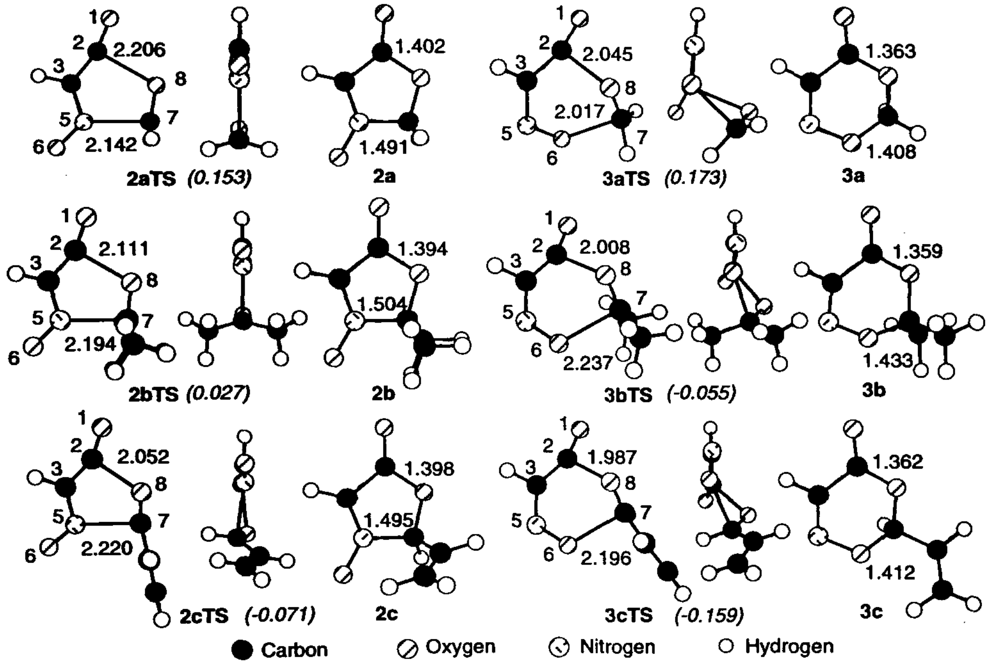
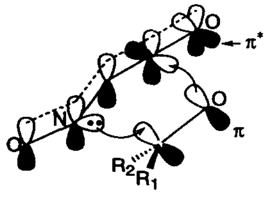


Figure 1. Geometries for [3+2] (**2TS**) and [4+2] (**3TS**) cycloadditions of nitrosoketene with formaldehyde, acetone, and 2-propenal optimized at the MP2/6-31G* level. Bond lengths are in Ånstroms. Asynchronicity (in parentheses) is defined as [C_2O_8 bond in TS - C_2O_8 bond in product] - [N_5C_7 or O_6C_7 bond in TS - N_5C_7 or O_6C_7 bond in product].



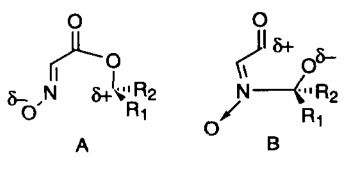


Figure 2. Pseudopericyclic Orbital Interactions in **2TS**.[7] Figure 3. Resonance Structures in **2TS**.

The new MP2/6-31G* calculation, which accounts for some electron correlation effects,[8] on the formaldehyde addition to nitrosoketene shows that the nucleophilic attack from the ketene nitrogen (N_5) leads in the planar [3+2] reaction pathway (**2aTS**), as previously calculated at the RHF level.[2] However, the [4+2] TS is qualitatively different at the two levels of theory. At the RHF/6-31G* level, the TS is close to planar, and asynchronous N_5 nucleophilic attack leads the reaction. At the MP2/6-31G* level, the formaldehyde is above the plane of the ketene (**3aTS**), and C_2O_8 bonding is more advanced. The [3+2] pathway is still calculated to be favored over the [4+2]. However, N_5C_7 bonding in **2aTS** still leads; the higher level of theory used here (MP2/6-31G*) does not resolve the discrepancy between Katagiri's experimental results and the calculated asynchronicity. Therefore, we examined the cycloaddition of nitrosoketene with acetone, the simplest ketone, which we expected would be less susceptible to nucleophilic attack than formaldehyde, for three reasons. First, steric hindrance by two methyl groups should reduce the extent of N_5C_7 or O_6C_7 bonding in both **2bTS** and **3bTS**. Secondly, stabilization of carbonyl carbon (C_7) makes it less susceptible to nucleophilic attack from N_5 or O_6 of nitrosoketene. Thirdly, considering two possible resonance structures in the TS (Figure 3), the resonance structure A is favored with R=Me over B. Indeed, C_2O_8 bond formation is increased and N_5C_7 and O_6C_7 bond formation are decreased in both **2bTS** and **3bTS**, relative to the formaldehyde reactions (Figure 1). Despite the increased steric hindrance, the barriers for the cycloadditions with acetone are lower than for formaldehyde (Table 1). This presumably reflects the additional stabilization of resonance structure A in Figure 3. The [3+2] pathway remains favored.

Finally, 2-propenal, the simplest conjugated carbonyl compound, was used as a model for acetophenone. In both **2cTS** and **3cTS**, the nucleophilic attack of the ketone oxygen (O_8) leads the reaction and the electrophilic addition of the ketene (N_5 or O_6) to the carbonyl carbon (C_7) follows. This is consistent with the experimental data in which acetophenones having such an electron-donating group facilitate the cycloaddition reaction with nitrosoketene (Scheme 1). In **2cTS**, the resonance structure A (Figure 3) is stabilized by conjugation from the adjacent vinyl group, whereas resonance structure B is destabilized by loss of conjugation. The net result, as compared to both acetone and formaldehyde, is a higher barrier and more advanced C_2O_8 bonding, with the [3+2] pathway still favored. We note that the differences in asynchronicity between **2TS** and **3TS** are similar; 0.080Å, 0.082Å and 0.088Å for **a**, **b** and **c**, respectively.

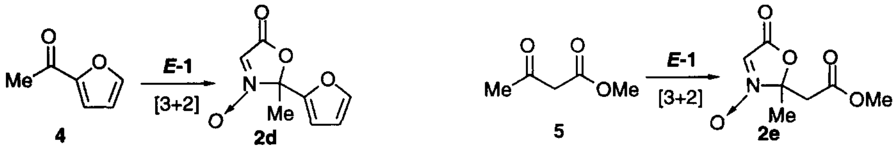
Table 1. Relative Energies (kcal/mol) of Structures Optimized at the MP2/6-31G* Level.

Structure	RHF/6-31G*[a]	MP2/6-31G*	MP4(SDQ)/6-31G*	MP4(SDQ)+ZPE[b]
		Addition of formaldehyde to *E*-**1**		
E-**1** + CH_2O	0.0	0.0	0.0	0.0
2aTS	13.3	-1.0	3.8	6.6
2a	-41.1	-53.9	-47.7	-40.9
3aTS	18.6	3.8	9.7	12.1
3a	-49.7	-51.3	-50.9	-45.0
		Addition of acetone to *E*-**1**		
E-**1** + acetone	0.0	0.0	0.0	0.0
2bTS	14.2	-2.5	2.6	4.5
2b	-36.2	-55.4	-47.5	-41.6
3bTS	16.8	2.8	7.3	9.0
3b	-41.8	-48.7	-47.3	-41.7
		Addition of 2-propenal to *E*-**1**		
E-**1** + 2-propenal	0.0	0.0	0.0	0.0
2cTS	15.3	0.0	5.2	7.3
2c	-31.1	-47.4	-40.9	-35.3
3cTS	17.9	4.6	9.5	11.2
3c	-40.7	-45.0	-44.8	-39.2

[a] Optimized at the RHF/6-31G* level. [b] Zero-point vibrational energy correction from RHF/6-31G* frequencies and scaled by 0.9135, reference 5.

An experimental comparison between conjugated and unconjugated ketones is available; Katagiri *et al.* has reported that the yield of **2d** is higher than **2e** (Scheme 2).[1b] This result appears in conflict with the calculated higher barrier for **2cTS** as compared to **2bTS**. We note, however, that **4** is very electron rich, which, in view of the asynchronicity, would be expected to give a lower barrier than 2-propenal.

Scheme 2.



In summary, the [3+2] cycloadditions of nitrosoketene (**1**) with ketones via planar, pseudopericyclic transition states are computationally preferred to the alternative [4+2] pathway. The greater stability of the [4+2] products makes 1,2-rearrangement unlikely to occur. The asynchronicity of the [3+2] reaction of **1** with 2-propenal (**2cTS**) is consistent with the experimental substituent effects in reactions of substituted acetophenones.

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7. The in-plane π-system of the ketone oxygen (O_8) adds as a nucleophile at C_2 to the in-plane π^*-orbital of the ketene to make the C_2O_8 bond. In turn, the in-plane lone pair of the nitrogen (N_5) adds as a nucleophile at C_7 to the π^* of the ketone. Those two orbital interactions are orthogonal to the out-of-plane conjugated π-system of nitrosoketene.

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