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On the Regioselectivity of Photocycloadditions of Triplet Cyclohexenones to Alkenes

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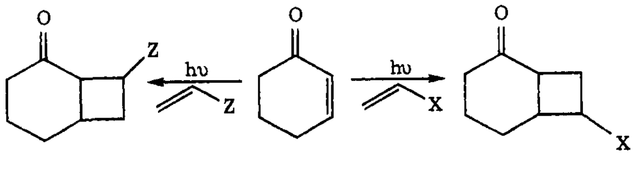
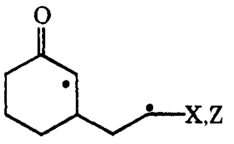
Photocycloadditions of cyclohexenones to alkenes occur with predictable regioselectivity. Electron-deficient alkenes (Z = acceptor) react with triplet cyclohexenones to yield head-to-head adducts; electron-rich alkenes (X = donor) yield head-to-tail adducts.[1]



What is the origin of the regioselectivity? All reactions would yield predominately head-to-head adducts if formation of the thermodynamically most stable diradical intermediate, **1**, controlled regioselectivity. Thirty years ago, Corey proposed a now-classic explanation.[2] He postulated that $n\pi^*$ excited enone triplets have the polarity depicted in **2**. The polarity of the enone directs electron-deficient alkenes to approach as in **2** and electron-rich alkenes as in **3**. These complexes collapse first to biradicals and then to products.



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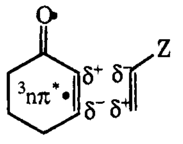

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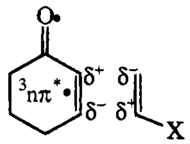

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Although Corey's model nicely rationalizes the experimental results, it is not completely concordant with experimental evidence. The π-complexes have not been observed; they may not exist.[3,4] Corey assumed that the enone reactive state is an $n\pi^*$ triplet, yet experimental studies indicate that the enone $\pi\pi^*$ triplet is involved in these reactions.[5]

We have discovered the origin of regioselectivity in the biradical-forming step. In those cases where cyclization is faster than collapse of diradicals to reactant ground state, the initial bond formation rates will determine the product regioselectivity. Agosta has found this to be the case for certain intramolecular enone photocycloadditions.[6]

Competition between cyclization of the biradicals, such as **1**, and reversion to ground-state reactants has also been postulated or found for many cases.[7−10] Weedon has provided evidence of such competition in photocycloadditions of cyclopentenones to alkenes[3,7] and the reaction of cyclohexenone with an enol ether.[8]

We have used *ab initio* theory implemented in the GAUSSIAN[11,12] programs to locate the transition states for the formation of regioisomeric biradicals and to investigate the influence of substituents on the rates. Figure 1 depicts the UMP2/6-31G* optimized planar and twisted conformers of the $n\pi^*$ and $\pi\pi^*$ triplet states of acrolein,[13] a model for the enones. UMP4-(SDTQ)/6-31G* single-point calculations on the UMP2/6-31G* geometries show that the twisted $\pi\pi^*$ triplet is the global minimum. The planar $n\pi^*$ triplet is higher by 9.9 kcal/mol, the planar $\pi\pi^*$ triplet by 13.2 kcal/mol, and the twisted $n\pi^*$ triplet by 23.4 kcal/mol. In accord with experimental observations, the lowest energy $\pi\pi^*$ triplet is more stable than the lowest energy $n\pi^*$ triplet. The 6-31G* Mulliken charges of the planar $n\pi^*$ triplet show that the β carbon, as proposed by Corey, bears more negative charge than the α carbon. The polarity of the planar $n\pi^*$ triplet fits the Corey proposal, but the polarity of the minimum energy triplet does not: the β carbon of the twisted $\pi\pi^*$ acrolein triplet bears more positive charge than the α carbon.

The twisted $\pi\pi^*$ enone triplet may be considered as an alkyl radical at the β carbon linked by a single bond to an α-acyl radical at the α carbon. Alkyl radicals are nucleophilic and add rapidly to the less substituted terminus of electron-deficient alkenes. The α-acyl radicals are more electrophilic than alkyl radicals and add rapidly to the less substituted terminus of electron-rich alkenes.[14] The enone triplet should favor β attack on the least-substituted terminus of electron-deficient alkenes and α attack on the least-substituted terminus of electron-rich alkenes. The polarity of the alkene directs the attack of the triplet and thus determines the regioselectivity of the reaction.

Figure 2 depicts the UHF/3-21G transition structures for the α and β additions of twisted $\pi\pi^*$ acrolein triplets to ethylene. PMP3/6-31G* single-point calculations on the UHF/3-21G transition structures show that β addition of the twisted $\pi\pi^*$ acrolein triplet is 0.3 kcal/mol easier than α addition. The β addition of the planar $n\pi^*$ triplet (not pictured) is 12.8 kcal/mol more difficult. The α addition transition structure of the planar $n\pi^*$ triplet could not be located. Barring severe structural con-

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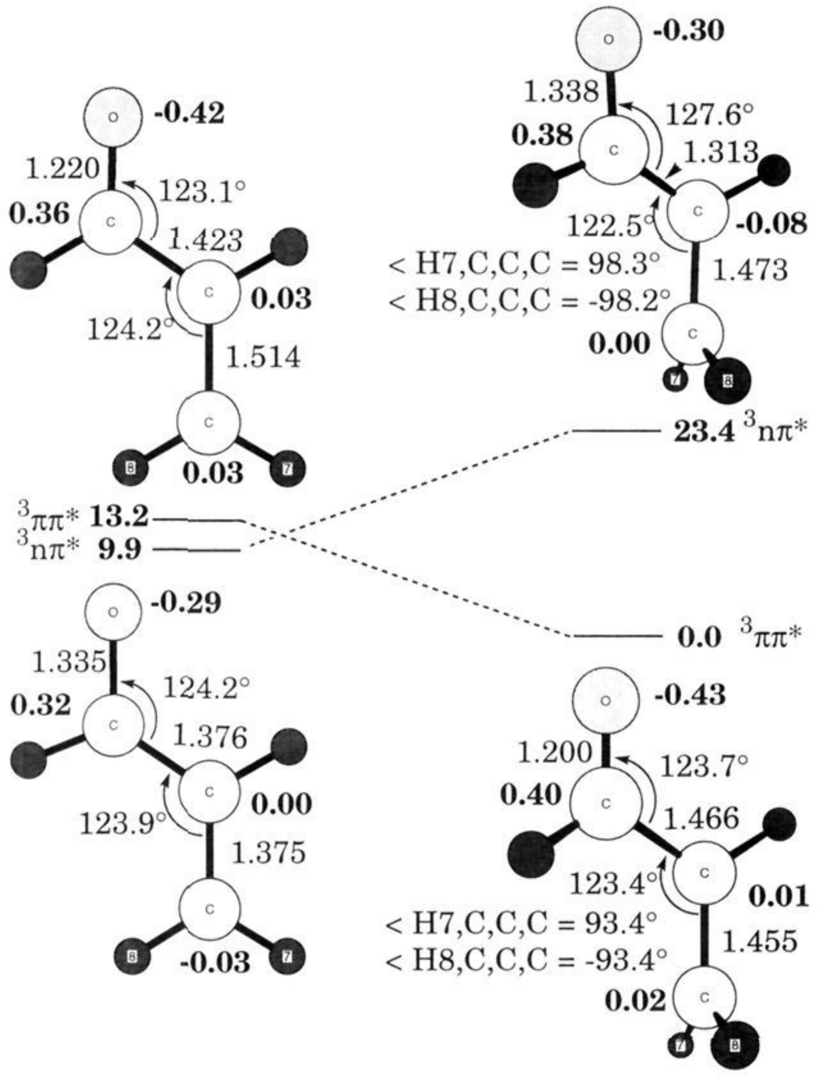

Figure 1. UMP2/6-31G* optimized planar and twisted conformers of $n\pi^*$ and $\pi\pi^*$ *s-trans*-acrolein triplets with UMP4(SDTQ)/6-31G* relative energies in kcal/mol. Boldface type depicts Mulliken charges with hydrogens summed into heavy atoms.

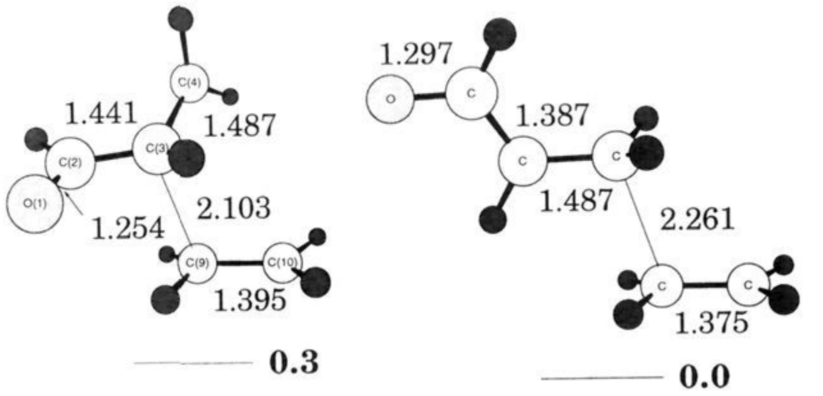

Figure 2. UHF/3-21G optimized transition structures for the α and β photocycloadditions of $\pi\pi^*$ *s-trans*-acrolein triplets to ethylene with PMP3/6-31G* relative energies (kcal/mol), given in boldface.

straints, the planar $n\pi^*$ triplet is unlikely to participate in these reactions. The α and β modes of addition of the twisted $\pi\pi^*$ triplet differ little in energy. Transition structures for the β addition of the triplet resemble that for addition of an alkyl radical,[15] and those of α addition resemble that for addition of an acyl-substituted alkyl radical.[16]

Table 1. PMP3/6-31G*//UHF/3-21G Relative Energies (kcal/mol) for Addition of $\pi\pi^*$ Triplet Acrolein to Substituted Alkenes

alkene	calcd $\Delta\Delta E^{\ddagger} = E(\alpha) - E(\beta)$	exptl[a,b] $\Delta\Delta G^{\ddagger}$	HH/HT ratio
acrylonitrile	0.9	>1.1	>5.7:1
allene	0.6	>2.0	≈100:0
ethylene	0.3		
isobutene	−0.5	-0.5	1:3.3
methyl vinyl ether	−1.7	<−2.0	≈0:100

[a] Experimental results (kcal/mol) are for addition of 2-cyclohexenone to the alkenes. [b] References 1 and 2.

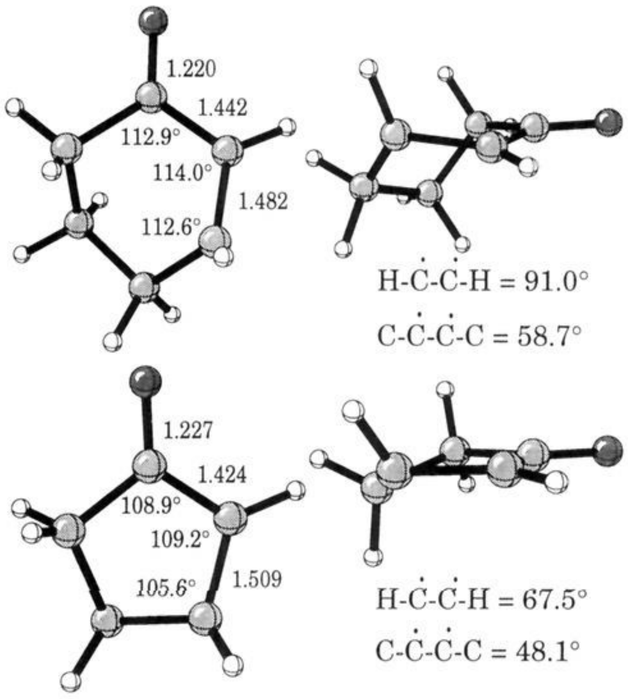

Figure 3. The UHF/6-31G* optimized structures of the $\pi\pi^*$ twisted triplet state of cyclohexenone and cyclopentenone. Top and side views are shown.

Table 1 compares the PMP3/6-31G*//UHF/3-21G head-to-tail versus head-to-head preference for addition of the acrolein $\pi\pi^*$ twisted triplet to substituted alkenes with that determined experimentally for addition of cyclohexenone to the related alkene. Progressing from ethylene to methyl vinyl ether, the preference for bond formation at the α carbon increases. As the alkene nucleophilicity increases, the preference for attack at the electrophilic radical center increases. With electron-deficient or electrophilic alkenes, reaction at the nucleophilic β center is favored. The trends computed for regioselectivities in formation of the first bond agree qualitatively with the experimentally observed regioselectivities.[1a,2] For these reactants, ratios of predicted rates of diradical formation correlate with experimental product ratios. Although the computed ratios depend upon the theory level and will be influenced by substituents on the enone, the trend in selectivity with alkene substituents is expected to survive.

These calculations used the acrolein triplet as a model. How closely do the triplets of cyclopentenone and cyclohexenone resemble those of acrolein? The optimized structures and relevant dihedral angles of the $\pi\pi^*$ twisted triplets of cyclohexenone and cyclopentenone are shown in Figure 3. Calculations on addition of these species to alkenes are in progress. The larger degree of twisting in cyclohexenone is known experimentally and affects the lifetime and energy of the triplets.[4,5c,17] Even cyclopentenone is twisted, although largely by pyramidalization of the β carbon. For cyclohexenone and cyclopentenone, the twisted $\pi\pi^*$ structures are 4.6 and 3.8 kcal/mol more stable than the planar $n\pi^*$ structures, respectively, at the PMP2/6-31G*//UHF/6-31G* level of theory.

Weedon's H_2Se diradical trapping experiments imply that there is no selectivity in α or β attack.[3,8,9] This is in contrast to the clear theoretical predictions of regioselectivity in the bond-forming step in enone photocycloadditions. Further investigations are in progress.

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