

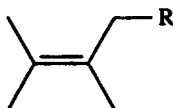
A COMPARISON OF THE ENE REACTIONS OF SINGLET OXYGEN AND TRIAZOLINEDIONES WITH ALKYL SUBSTITUTED TETRAMETHYLETHYLENES.

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Abstract: The reactions of triazolinediones and singlet oxygen are compared in their reactivity towards a series of tetrasubstituted olefins. The different regiochemistries of these reactions are discussed.

Triazolinediones (TAD)¹ and singlet oxygen (¹A_g O₂)² undergo [2 + 2], [4 + 2], and ene reactions with unsaturated substrates. In addition, isotope effect studies have led to the conclusion that intermediates of similar symmetry are found on both reaction surfaces.³ As a result of this complementary reactivity these two reactions have often been compared⁴ with the expectation that subtle differences in reactivity or regiochemistry will lead to additional insight into the intimate details of both reaction surfaces.

Orfanopoulos and co-workers⁵ have recently reported that the TAD ene reactions of unsymmetrical cis alkenes exhibit the same regioselectivity pattern as the ¹O₂ reactions. This intriguing result has prompted us to report our results that demonstrate that tetrasubstituted olefins



1a R = Me

1c R = iPr

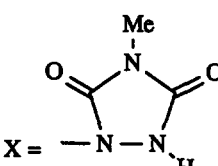
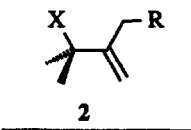
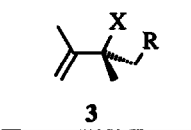
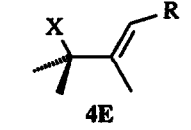
1b R = Et

1d R = tBu

1a-d exhibit different regiochemistries in these two reactions. These results are discussed and interpreted with the assistance of molecular mechanics calculations.

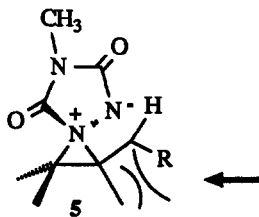
The reactions of 1a-d with TAD were conducted at -78°C in acetone-d₆ and the progress of the reactions was monitored by the disappearance of the characteristic red color of TAD and by ¹H NMR. Three of the four possible ene adducts⁶ were formed in the relative yields reported in Table I. Table II contains the MM2⁷ derived steric energies, strain energies and heats of formation for the corresponding alcohols, however, we anticipate similar energy trends in the allylic urazole and hydroperoxide series. Examination of this Table reveals that the missing adduct, 4Z, is the thermodynamically least stable allylic urazole isomer.

Table I. Relative Yields in the Ene Reactions of TAD and $^1\text{O}_2$ with 1a-d.

	Relative Yields ^a		
	 2	 3	 4E
R = Me ^b	31	44	25
R = Et	44 (41) ^c	30 (30) ^c	26 (30) ^c
R = iPr	80	0	20
R = tBu	98	0	2
X = OOH ^d			
R = Me	37	63	0
R = Et	40	60	0
R = iPr	55	45	0
R = tBu	78	22	0

a. Determined by cutting and weighing appropriate peaks from expanded portions of the NMR spectra. b. The average of two independent determinations. c. Relative yield from N-phenyl-TAD. d. The average of three independent determinations.

On the other hand, the thermodynamically most stable isomer, 4E, is not the major product.

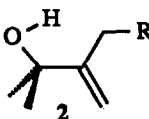
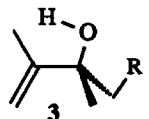
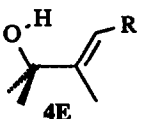
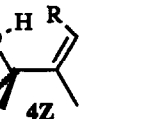


This result is consistent with a well advanced olefin-like transition state for hydrogen abstraction which is destabilized by virtue of its high strain(steric) energy content. This steric argument, depicted in 5, has previously been used in order to rationalize the product distribution in TAD ene reactions of *cis* disubstituted olefins.⁵

In the singlet oxygen ene reaction only the disubstituted olefins 2 and 3 are formed. The total absence of the most thermodynamically stable allylic hydroperoxide 4E could also be attributed to a

destabilizing steric interaction. Steric interactions in the hydrogen abstraction step have been used to rationalize the regiochemistry in the $^1\text{O}_2$ ene reactions of cis-alkenes.⁸ The large isotope effects in TAD in comparison to $^1\text{O}_2$ reactions, however, are consistent with an earlier transition state in the $^1\text{O}_2$ reaction.⁹ It is unreasonable, therefore, to suggest an even greater steric interaction in this very early transition state than in the well advanced one of the TAD reaction.¹¹

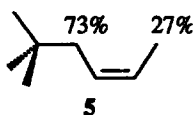
Table II. MM2 Steric(SE) and Strain(STE) Energies and Heats of Formation(ΔH_f°)^{a,b}

				
R = tBu				
SE	11.3	12.5	11.8	17.2
STE	6.7	7.8	8.0	13.4
ΔH_f°	-80.2	-79.1	-81.1	-75.7
R = Me				
SE	7.2	7.1	7.8	9.2
STE	3.9	3.8	5.4	6.8
ΔH_f°	-61.4	-61.5	-62.2	-60.7

a. in kcal/mol b. for lowest energy conformation only

Houk¹² and Clennan^{2d} have suggested that for di-, tri-, and tetra- substituted olefins that the ease of rotations of methyl and alkyl groups significantly contribute to the activation barriers of singlet oxygen ene reactions and consequently dictate regiochemistry. The rotation of the allylic hydrogen to the proper alignment for abstraction must occur earlier on the $^1\text{O}_2$ ene reaction surface than carbon-hydrogen bond cleavage and consequently plays a larger role in determining regiochemistry than developing steric interactions in the products.

Orfanopoulos¹³ has criticized the use of rotation barriers to predict regiochemistry and has pointed out that hydrogen abstraction is preferred at the neopentyl group in **5** despite its higher



rotation barrier in comparison to methyl. We point out however, that a complete 180° rotation of the neopentyl group is not necessary to place a hydrogen in the proper alignment for abstraction.

Acknowledgement. We thank the National Science Foundation and the donors of the Petroleum Research Foundation, administered by the American Chemical Society, for their generous support of this research.

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6. **2a**(MeTAD adduct) ^1H NMR(acetone- d_6) δ 1.06(t, J = 7.4Hz, 3H), 1.53(s, 6H), 2.19(m, 2H), 2.91(s, 3H), 4.90(s, 1H), 5.04(s, 1H), 8.4-8.7(bs, 1H); **3a**(MeTAD adduct) ^1H NMR(acetone- d_6) δ 0.84(t, J = 7.5Hz, 3H), 1.59(s, 3H), 1.67(s, 3H), 1.91(m, 2H), 2.90(s, 3H), 4.90(s, 1H), 4.95(s, 1H), 8.4-8.7(bs, 1H); **4Ea**(MeTAD adduct) ^1H NMR(acetone- d_6) δ 1.50(s, 6H), 1.61(d, J = 1.1Hz, 3H), 1.67(s, 3H), 2.89(s, 3H), 5.55(q, J = 8Hz, 1H), 8.4-8.7(bs, 1H).
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9. It has been pointed out that the magnitude of isotope effects in ene reactions are a function of their degree of reversibility:¹⁰ the more reversible the smaller the observed isotope effect. Foote⁴ has pointed out, however, that electron rich tetrasubstituted olefins react via an intermediate which lies in a substantial energy well and as a result are not as reversible as the reactions of less electron rich olefins. Consequently, we believe that the magnitude of the TAD and $^1\text{O}_2$ reaction truly reflect the extent of bond breakage in the hydrogen abstraction step.
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(Received in USA 15 June 1990)