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The Reaction of *N*-Methyl-1,2,4-triazoline-3,5-dione with Tetracyclopropylethylene. Formation of an Unusual Meso-ionic Product and Its Rearrangement to the Diazetidine

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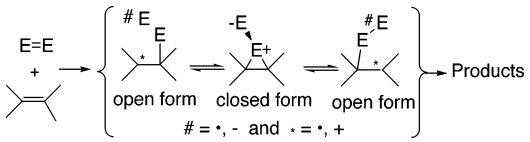
Highly electrophilic 4-substituted-1,2,4-triazoline-3,5-diones (RTADs) are known to react with olefins and dienes to give 4+2 and 2+2 cycloadducts, and ene products. The reactions of RTAD have attracted considerable interest because they exhibit a number of unusual mechanistic features, which are analogous to the reactions of singlet oxygen, $^1O_2$, and nitroso compounds, RNO. Kinetic isotope effects, solvent trapping studies, and stereochemical consequences imply the intermediacy of closed three-membered-ring zwitterions in the reactions of olefins with RTAD, singlet oxygen, and nitroso compounds.[1] Recent results have challenged the once generally accepted role and existence of the intermediate zwitterions.[2−5] The equilibrium of the proposed open and closed intermediates is illustrated in Scheme 1.

Scheme 1. Proposed Open and Closed Intermediates in the Reactions of Alkenes with $^1O_2$, RTAD, and RNO (Represented by E=E)



In the reactions of singlet oxygen with simple alkenes, computational studies and isotope effects point to the involvement of two adjacent saddle points connected through a valley-ridge inflection rather than the perepoxide (closed form).[2,3] The ene reactions of nitroso compounds are rationalized in terms of the reversible formation of an aziridine-*N*-oxide (closed form) or a similar unsymmetrical polarized diradical.[4,5] Although there is overwhelming experimental evidence for the existence of the closed form known as the aziridinium imide (AZI) in reactions of RTADs including direct spectroscopic observation,[6] Singleton recently provided arguments based on computational results and isotope effects that the AZIs are innocent bystanders and open radical intermediates are responsible for the observed reaction products.[7]

In an attempt to better understand the role and proposed equilibrium of the closed and open intermediates in the reactions of RTAD, we chose to study the reaction of tetracyclopropylethylene (TCPE), **1**, with 4-methyl-1,2,4-triazoline-3,5-dione (MTAD), **2**. Because the cyclopropyl rings provide considerable stabilization to electron-deficient centers,[8] the formation of an open intermediate may be accessible in the reaction of MTAD with TCPE. If the open form is a radical, the cyclopropyl group is expected to undergo rapid rearrangement to a characteristic ring-opened product.[9] Despite these expectations, the reaction of TCPE and MTAD yields a reaction product that based on the NMR spectra clearly does not correspond to the diazetidine, ene product, or an unusually stable AZI. Detailed analyses of proton, ^{13}C, and 2-D NMR spectra (see Supporting Information) indicate the observed product is the meso-ionic compound, 5,5,6,6-tetracyclopropyl-3-methyl-5,6-dihydro-

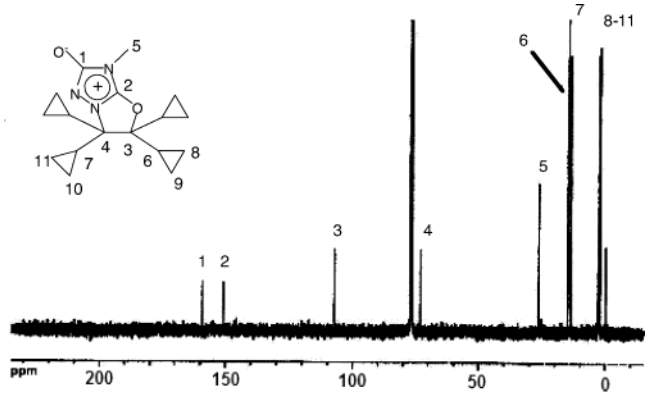


Figure 1. The ^{13}C NMR spectrum (100 MHz) of reaction product **3** in $CDCl_3$ at room temperature.

oxazolo[3,2*b*][1,2,4]-triazolium-2-olate, **3**. The assignments for the carbon NMR spectrum are illustrated in Figure 1.

We propose the unusual formation of **3** is due to constraints imposed by a bisected *s-cis* type orientation of the geminal cyclopropyl groups[10] which can lead to steric shielding of the plane perpendicular to the TCPE double bond. Computational results indicate the initial bond formation for the reactions of RTAD with simple olefins occurs at approximately 45° to the plane of the π system involving the formation of a carbon−nitrogen bond in the asymmetric approach.[7,11] While such initial bonding may be operative in the reaction of RTAD with TCPE, the subsequent reaction pathways appear to be influenced by steric factors favoring the formation of **3** with coincident geometry as compared to the perpendicular geometry of the corresponding AZI.

To further explore the reactivity of **3**, the solution was warmed to 55 °C and the structural changes were monitored by NMR. While there was no evidence for the reverse reaction of **3** leading to TCPE and MTAD, a series of new peaks appears in the ^{13}C NMR spectrum, which is assigned to the diazetidine as illustrated in Figure 2. The proton and 2-D NMR spectra confirm our structural assignments (see Supporting Information). A series of peaks in the carbon and proton NMR spectra corresponds to a methylene-cyclopropyl group and is tentatively assigned to the ene product (∼5%). Because the ene product is expected to have relatively high activation energy because of the highly strained methylene-cyclopropropyl group, it is not surprising the diazetidine is observed as the major product.

The novel rearrangement of the meso-ionic compound, **3**, likely requires homolytic or heterolytic bond cleavage of the C−O bond to form an open intermediate followed by 180° rotation around the C−N bond, and then ring closure to **4** in competition with hydrogen abstraction leading to the ene product, **5**, as illustrated in Scheme 2. Based on previous computational results, it is feasible that unsymmetrical transition structures or open intermediates could be

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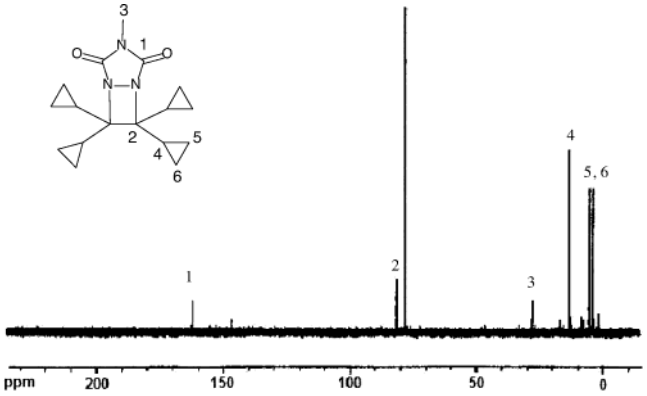
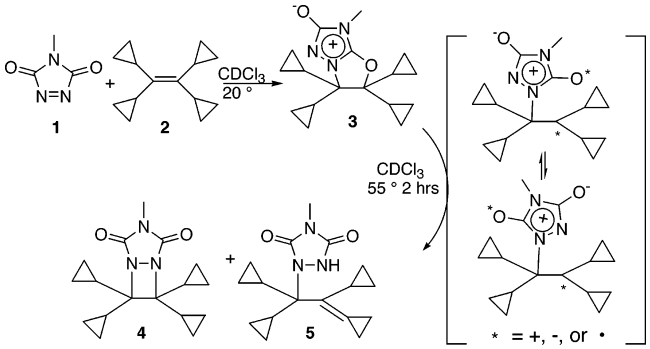


Figure 2. The ^{13}C NMR spectrum (100 MHz) of the reaction mixture from **3** after heating for 63 h at 55 °C.

Scheme 2. Formation of the Meso-ionic Compound, **3**, and the Subsequent Rearrangement to the Diazetidine and Ene Products



on the potential surface, leading to the formation of the diazetidine and meso-ionic product,[7] but it appears in our case relatively high temperatures are required to enable the molecular motions, such as rotation of the C−N bond, to afford geometries amenable to the diazetidine product.

Low-temperature NMR experiments were conducted to determine the activation energy for the formation **3**. The reaction of **1** + **2** in CD_2Cl_2 at −78 °C is exceedingly slow, and there is no indication of the presence of an AZI. Upon warming the solution to −60 °C, the starting material disappears with the simultaneous formation of **3**. Rate constants were obtained for the formation of **3** by monitoring the growth of characteristic peaks in the proton NMR spectrum as a function of temperature from −50 to −20 °C. The activation energy for the formation of **3** determined from the second order rate constant, as a function of temperature, is 8.5 kcal/mol. While the activation energy for **3** is lower than those reported for AZIs,[6] the observation of meso-ionic products from the reactions of RTAD is extremely rare.[12] It appears the meso-ionic product is less reactive than AZIs, which have only been observed at low temperatures.[6] The addition of MeOH to the solvent prior to mixing the reactants did not change the product distributions at low temperatures and 55 °C. While this does not rule out the possibility of nonconcerted reaction processes, it indicates that if reactive intermediates are involved they are too short-lived to be trapped or undergo rearrangement.

In summary, the reaction of MTAD with TCPE leads to the nearly quantitative formation of a novel meso-ionic compound that upon heating undergoes an unprecedented rearrangement to the diazetidine. While the involvement of polarized and/or diradical intermediates is general accepted in the reactions of RTAD with olefins, our results indicate that steric factors dramatically influence the reaction pathways and can promote the formation of unusual products. We are planning investigations to assess the selectivity and specificity of the reaction pathway leading to the meso-ionic compound.

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Supporting Information Available: Experimental procedures, ^1H, ^{13}C, and 2-D NMR spectra (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) For representative papers, see: (a) Cheng, C. C.; Seymour, C. A.; Petti, M. A.; Greene, F. D.; Blount, J. F. *J. Org. Chem.* **1984**, *49*, 2910. (b) Orfanopoulos, M.; Foote, C. S.; Smonou, I. *Tetrahedron Lett.* **1987**, *28*, 15. (c) Jensen, F.; Foote, C. S. *J. Am. Chem. Soc.* **1987**, *109*, 6376. (d) Orfanopoulos, M.; Smonou, I.; Foote, C. S. *J. Am. Chem. Soc.* **1990**, *112*, 3607. (e) Adam, W.; Bottke, N.; Krebs, O.; Lykakis, I.; Orfanopolous, M.; Stratakis, M. *J. Am. Chem. Soc.* **2002**, *124*, 14403. (f) Frimer, A. A.; Bartlett, P. D.; Boschung, A. F.; Jewett, J. G. *J. Am. Chem. Soc.* **1977**, *99*, 7977. (g) Orfanopoulos, M.; Grdina, M. B.; Stephenson, L. M. *J. Am. Chem. Soc.* **1979**, *101*, 275. (h) Jefford, C. W.; Rimbault, C. G. *J. Am. Chem. Soc.* **1978**, *100*, 295. (i) Orfanopoulos, M.; Stephenson, L. M. *J. Am. Chem. Soc.* **1980**, *102*, 1417. (j) Poon, T. H. W.; Pringle, K.; Foote, C. S. *J. Am. Chem. Soc.* **1995**, *117*, 7611. (k) Seymour, C. A.; Greene, F. D. *J. Org. Chem.* **1982**, *47*, 5226. (l) Leach, A. G.; Houk, K. N. *Chem. Commun.* **2002**, *12*, 1243.

(2) Singleton, D. A.; Hang, C.; Szymanski, M. J.; Meyer, M. P.; Leach, A. G.; Kuwata, K. T.; Chen, J. S.; Greer, A.; Foote, C. S.; Houk, K. N. *J. Am. Chem. Soc.* **2003**, *125*, 1319.

(3) Singleton, D. A.; Hang, C.; Szymanski, M. J.; Greenwald, E. E. *J. Am. Chem. Soc.* **2003**, *125*, 1176.

(4) Adam, W.; Krebs, O.; Orfanopoulos, M.; Stratakis, M.; Vougioukalakis, G. C. *J. Org. Chem.* **2003**, *68*, 2420.

(5) Houk, K. N.; Leach, A. G. *J. Am. Chem. Soc.* **2002**, *124*, 14820.

(6) (a) Poon, T. H. W.; Par, S. H.; Elemens, Y. E.; Foote, C. S. *J. Am. Chem. Soc.* **1995**, *117*, 10468. (b) Squillacote, M.; Mooney, M.; De Fillippis, J. *J. Am. Chem. Soc.* **1990**, *112*, 5364. (c) Nelsen, S. F.; Kapp, D. L. *J. Am. Chem. Soc.* **1995**, *117*, 5548.

(7) Singleton, D. A.; Hang, C. *J. Am. Chem. Soc.* **1999**, *121*, 11885.

(8) (a) Deno, N. C.; Richey Jr., H. G.; Liu, J. S.; Hodge, J. D.; Houser, H. J.; Wisotsky, M. J. *J. Am. Chem. Soc.* **1962**, *84*, 2016. (b) Pittman, C. U., Jr.; Olah, G. A. *J. Am. Chem. Soc.* **1965**, *87*, 2998.

(9) The rapid rearrangement of the cyclopropylcarbinyl radicals to a butenyl radicals is well established by picosecond radical kinetics. For examples, see: (a) Engel, P. S.; He, S.-L.; Banks, J. T.; Ingold, K. U.; Lusztyk, J. *J. Org. Chem.* **1997**, *62*, 1210. (b) Choi, S.-Y.; Newcomb, M. *Tetrahedron* **1995**, *51*, 657. (c) Choi, S.-Y.; Toy, P. H.; Newcomb, M. *J. Org. Chem.* **1998**, *63*, 8609.

(10) Campredon, M.; Kanabus-Kaminska, J. M.; Griller, D. *J. Org. Chem.* **1988**, *53*, 5393.

(11) Chen, J. S.; Houk, K. N.; Foote, C. S. *J. Am. Chem. Soc.* **1997**, *119*, 9852.

(12) (a) Lehr, K.-L.; Werp, J.; Bingmann, H.; Kruger, C.; Prinzbach, H. *Chem. Ber.* **1982**, *115*, 1835. (b) Prinzbach, H.; Weidmann, K.; Trah, S.; Knobe, L. *Tetrahedron Lett.* **1981**, 22, 2541.

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