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First Example of an Enone−Alkene [2 + 2 + 2] Photocycloaddition: 1,3-Photocycloaddition of Tetramethylethylene across 2,7-Cyclooctadienone

Albert R. Matlin,*[,†] Susanne C. Lin,[†] Hiren R. Patel,[†] and Minghui Chai[‡]

Departments of Chemistry, Oberlin College, Oberlin, Ohio 44074, and University of Akron, Akron, Ohio 44325

albert.matlin@oberlin.edu

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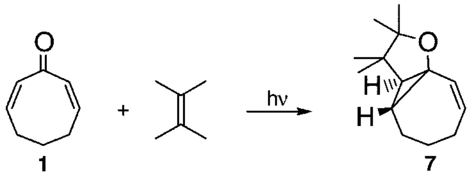
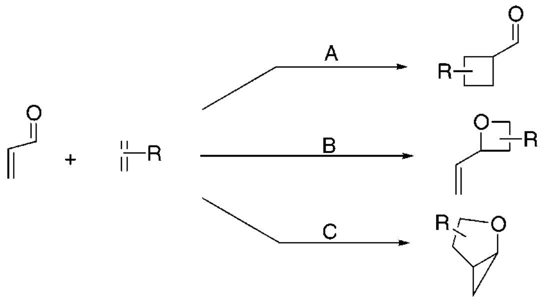
ABSTRACT



Irradiation of cyclooctadienone (1) in the presence of tetramethylethylene (TME) produces 9,10,10-tetramethyl-11-oxatricyclo[6.3.0.0^{1,7}]undec-2-ene (7) in 33% yield. This reaction is the first example of a 1,3-cycloaddition of an alkene across an enone system. This novel cycloaddition suggests that there is substantial interaction between the carbonyl carbon and the β-enone carbon in the triplet excited state of 1.

Scheme 1



The enone−alkene [2 + 2] photocycloaddition reaction is one of the most well studied[1−3] and synthetically useful organic photochemical reactions.[4−7] The cycloaddition reaction proceeds in a stepwise manner, giving cyclobutane products with the alkene adding across the α,β-positions of the excited enone (Scheme 1, path A). It is also well-known that alkenes can react in a [2 + 2] manner across the carbonyl portion of an enone to give oxetanes (path B).[8] Both of these processes involve the cleavage of two π-bonds and the formation of two σ-bonds. To date there has been no report in the literature of a 1,3-addition of an alkene across an enone system (path C). This process is formally a [2 + 2 + 2] photocycloaddition involving the breaking of three π-bonds

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[†] Oberlin College.

[‡] University of Akron.

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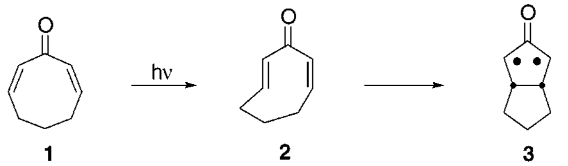
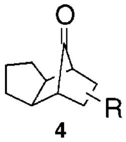
and the forming of three σ-bonds. We report the first example of this process.

In the course of a larger study on the photochemical generation of oxyallyl intermediates, we have been investigating the photochemistry of *cis*,*cis*-2,7-cyclooctadienone **1** as a potential entry to a cyclopentyl oxyallyl system.[9,10] We have found that irradiation of cyclooctadienone **1** resulted in formation of the *cis*,*trans*-isomer **2**, which thermally cyclized below room temperature to the bicyclic oxyallyl compound **3** (Scheme 2). The reactive intermediate **3** could be trapped with alkenes, dienes, and alcohols. The reaction path is highly dependent on the electron density of the alkene. Inclusion of electron-rich vinyl ethers in the photolysis mixture produced bridged **4** and fused cycloadducts **5** in good yields (50−80%) via a stepwise capture of the oxyallyl intermediate. A concerted ene reaction occurred between simple alkenes (e.g. isobutylene) and oxyallyl **3**, which produced bicyclic ketoalkenes **6**. No [2 + 2] cycloadducts corresponding to pathways A or B were observed even when ethyl vinyl ether or 2-methoxypropene was used as the solvent.[11]

Scheme 2





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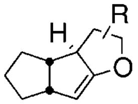

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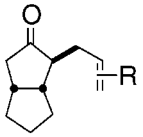

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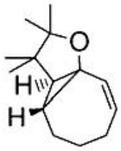
The results were quite different when **1** was irradiated in the presence of tetramethylethylene (TME). A 1:1 photoadduct was isolated in 33% yield after purification by column chromatography. Spectroscopic analysis showed that the product was clearly not related to the bridged (**4**), fused (**5**), or ene products (**6**) isolated in our previous studies nor was it a [2 + 2] cycloadduct (path A or B). ^{1}H NMR showed two vinyl protons at δ 5.90 (ddt, $J = 11.3$, 2.2, 1.1 Hz) and δ 5.43 (ddd, $J = 4.5$, 6.0, 11.3 Hz). The ^{13}C NMR showed that the molecule had no symmetry and no carbonyl and confirmed the presence of the alkene (δ 130.2, 128.9). The coupled ^{13}C NMR displayed two doublet methine carbons at δ 45.1 and δ 35.8 with heteronuclear J_{CH} values of 165 and 162 Hz, respectively. These values are consistent with cyclopropyl CH coupling.[12] The coupling constant between the cyclopropyl methines ($J = 4.5$ Hz) indicates that these protons are trans. DEPT ^{13}C NMR confirmed the presence of three quaternary carbons, four methyl groups, and three methylene carbons. The tricyclic alkene **7** is consistent with these data. Additional NMR studies (COSY, HETCOR, HMQC) supported the structural assignment.

Formation of tricyclic alkene **7** represents a 1,3-cycloaddition of TME across cyclooctadienone. This novel cycloaddition reaction raises some intriguing and puzzling mechanistic questions. Unlike adducts **4**, **5**, and **6**, adduct **7** is not derived by the reaction of TME with oxyallyl **3** or *cis*,*trans*-dienone **2**. This was established by irradiating a hexane solution of **1** at −78 °C (350 nm, Rayonet Photochemical Reactor) for 55 min, turning off the lamps, and adding TME to the cold solution. GC analysis of the reaction mixture after it had warmed to room temperature showed no adducts. When the same experiment was carried out with ethyl vinyl ether instead of TME, bridged (**4**) and fused (**5**) adducts were observed.[10] Irradiation of **1** and TME at −78 °C also produces adduct **7**. These experiments indicate that TME is reacting with a transient species that can be generated, but not stored, at low temperature.



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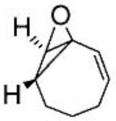

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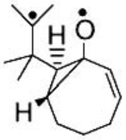

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We present two possible modes for the formation of **7**: reaction of TME with the triplet state of **1** (**1*T**) or reaction of TME with oxabicyclobutane **8**. In order for TME to react with **1*T** and not produce "normal" [2 + 2] adducts (Scheme 1, path A), the initial σ-bond formation between TME and **1*T** must be accompanied by internal σ-bond formation to give diradical **9.** Collapse of diradical **9** would then produce alkene **7**. Formation of the σ-bond between the carbonyl carbon and the β-enone carbon (establishing the cyclopropyl ring) has no precedent. The trans stereochemistry of the cyclopropyl methines in **7** (and subsequently **9**) is consistent with reaction of TME with the highly twisted double bond expected in the relaxed triplet **1*T**. However, if this mechanism is operative, it cannot be very efficient. Irradiation of **1** in the presence of varying concentrations of TME and ethyl vinyl ether indicated that TME does not effectively quench the formation of the ethyl vinyl ether derived bridged **4** and fused **5** adducts. It also is unclear how this mechanism can explain the fact that we have only observed 1,3-cycloaddition to **1** with TME and not with other alkenes (e.g. 2-methoxypropene, tetramethoxyethylene, isobutylene, allyltrimethylsilane, 1,1-dimethoxy-2-methylpropene, 2-*tert*-butylpropene).[10]

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(11) No 1:1 adducts were observed when **1** was irradiated in the presence of electron-deficient π-systems such as 1,2-dichloroethylene and dimethyl acetylenedicarboxylate. See: Haseltine, R. P. Ph.D. Thesis, University of Indiana, 1970.

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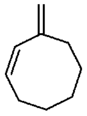
The second mechanistic proposal involves photoisomerization of **1** to produce the transient oxabicyclobutane **8** followed by reaction with TME across the C−O σ-bond to give **7**. The addition to **8** may proceed in either a stepwise (via **9**) or concerted manner to furnish **7**.[13] Recent high-level MO calculations by Dodziuk and Leszczynski on the parent oxabicyclobutane system predict that the C−O bond will be longer than the central C−C bond.[14] These results support the view that the C−O bond in **8** should have substantial π-character and be highly reactive.

To date there are no reports of the isolation, spectroscopic observation, or bimolecular trapping of an oxabicyclobutane. There have been several attempts to prepare oxabicyclobutanes by epoxidation of cyclopropenes.[15−19] The putative oxabicyclobutanes formed are unstable under these reaction conditions and undergo thermal retro [$_{\sigma}2s + {}_{\sigma}2a$] cycloadditions to produce enones.[20] Chapman and Zimmerman have considered, and ruled out, oxabicyclobutanes as reactive intermediates in photochemical reactions of *cis*-α-phenylcinnamic acid[21] and 4,4-diphenyl-2-cyclohexenone.[22] However, it is well-known that 1,3-dienes can photoisomerize to bicyclobutanes. For example, diene **10** photoisomerizes to bicyclobutane **11** in 25−35% yield.[23]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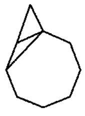
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It is possible that transient oxabicyclobutanes may be produced in other enone systems but have eluded detection. Both mechanistic proposals (capture of **1*T** or capture of oxabicyclobutane **8**) are related in that they require substantial interaction between the carbonyl carbon and the β-enone carbon in **1*T** to promote formation of the cyclopropyl ring. There may be specific geometric factors in the eight-membered ring that give rise to the 1,3-interaction.[24] Experiments directed at clarifying the mechanism of this novel cycloaddition are currently in progress.

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Supporting Information Available: Experimental procedures and tabulated spectroscopic data (NMR, IR, MS) for **7**. Copies of the 750 MHz ^{1}H NMR, COSY, and HETCOR spectra of **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[13] The reaction of TME with **8** requires a front-side attack with respect to the cleaving C−O bond. Examination of the LUMO in **8** (geometry-optimized structure, 3-21G*) shows a substantial π antibonding interaction between the bridgehead methine carbon and oxygen. Only the “front-side” lobe of the orbital on the bridgehead methine is sterically accessible for reaction with TME.

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[20] Concerted retro-cycloaddition of **8** should produce **2**. For a discussion on the stereochemistry of retro-cycloadditions in bicyclobutanes, see: Woodward, R. B.; Hoffmann, R. In *The Conservation of Orbital Symmetry*; Academic Press: Germany, 1971; pp 75−78.

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[24] Structures derived from DFT-MO calculations (see ref 9) indicate that the distance between the carbonyl and β-enone carbons is 2.609 Å in **1** and 2.429 Å in **2** (from β-carbon in *trans* double bond).