Published in final edited form as:

Tetrahedron. 2013 June 17; 69(24): 5044–5047. doi:10.1016/j.tet.2013.03.053.

Temperature-dependent, competitive 1,3-acyl shift versus decarbonylation of a cyclopropanone intermediate

Ihsan Erden^{a,*}, Jingxiang Ma^a, Christian Gärtner^a, Saeed Azimi^a, and Scott Gronert^{b,§}

Ihsan Erden: ierden@sfsu.edu; Scott Gronert: sgronert@vcu.edu

^aDepartment of Chemistry and Biochemistry, San Francisco State University, 1600 Holloway Avenue, San Francisco, CA 94132

^bDepartment of Chemistry, Virginia Commonwealth University, 1001 West Main Street, Richmond, Virginia, 23284, Oliver Hall 3041

Abstract

Photooxygenation of 1,1,3-trimethyl-1,2-dihydropentalene gives an unstable endoperoxide which upon decomposition delivers a bicyclic cyclopropanone intermediate; this species either extrudes CO to give a cycloheptadienone or undergoes a 1,3-acyl shift, both processes occurring most likely in a stepwise manner via diradical intermediates. Alternatively, C3a-C4 cleavage in the dioxygen diradical derived from the endoperoxide yields a 2-cyclopropyl substituted cyclopentadienone epoxide.

Keywords

Fulvene; Endoperoxide; Cyclopropanone; Singlet Oxygen; 1; 2-Dihydropentalene

1. Introduction

Singlet oxygenation of fulvenes was first reported by two groups to give an unstable endoperoxide followed by rapid decomposition to mainly oxepin-2(3*H*)-one derivatives by way of postulated allene oxide and cyclopropanone intermediates^{1,2} (Scheme 1).

In subsequent work we demonstrated the intermediacy of endoperoxides in these reactions by way of selective reduction of the unstable singlet oxygen adduct with diazene,³ we also verified the allene oxide mechanism⁴ by isolation and characterization of a stable derivative. Subsequent valence isomerization to cyclopropanones was also corroborated by trapping the latter by intra- and intermolecular cycloadditions as well as cyclizations.⁵ Novel aliphatic [3.4] sigmatropic shifts of suitably substituted cyclopropanones were also observed.⁶ Since reactive intermediates such as allene oxides and cyclopropanones form in these reactions in the absence of nucleophiles or electrophiles, fulvene endoperoxides offer a unique opportunity to generate these species under neutral conditions at ambient temperatures.

© 2013 Elsevier Ltd. All rights reserved.

*Corresponding author: Tel.: +0-415-338-1627; fax: +0-415-338-2384; ierden@sfsu.edu. [§]Author to whom correspondence related to computational work should be directed; sgronert@vcu.edu.

6. Supplementary Data. Computational data, ¹H and ¹³C NMR spectra. This material is available free of charge via the Internet at <http://>

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Herein we report not only on novel decomposition pathways of endoperoxides derived from a 1,2-dihydropentalene, but also provide experimental evidence that the thermal decarbonylation of the cyclopropanone intermediate may proceed stepwise through biradical intermediates. Toward achieving our objectives we studied the photooxidation chemistry of 1,2-dihydropentalenes (1,2-DHPs), the only fulvenic DHP isomers, for whose synthesis we recently developed an efficient one-step method starting from fulvenes.^{7,8}

2. Results and Discussion

Singlet oxygenation of 1,1,3-trimethyl-1,2-dihydropentalene (**1**) in CH₂Cl₂ proved to be temperature-dependent and resulted in the formation of three major products, as shown in Scheme 2.

Based on all spectroscopic and analytical data the structures **6**, **7**, and **8** were assigned to the three products. At first glance, none of the products **6**, **7**, and **8** appeared to be typical of ordinary fulvene endoperoxide decomposition pathways. The formation of **7**- at least in the initial stage- remotely resembles that of any unstable endoperoxide **9** undergoing homolytic cleavage of the labile O-O bond.

Homolytic cleavage of C3a-C4 (pentalene numbering⁹) followed by closure of **12** to a cyclopropane would lead to the unusual cyclopentadienone monoepoxide **7** (Scheme 2).

Cycloheptadienone **8** contains a mass unit of 28 less than the endoperoxide precursor **9**, indicating a CO loss during the decomposition. It appears that both **6** and **8** stem from the same intermediate, as outlined in Scheme 3. Diradical **10** suffers an alternative C-C cleavage (C3a-C6a) to give allene oxide **14**; the latter undergoes a well known valence isomerization¹⁰ to the bicyclic cyclopropanone **15** whose decarbonylation delivers **8**. A very minor product, dione **16**, formed from **13** by a 1,2-hydrogen transfer, was also isolated whose formation is informative with respect to the order of the C-C cleavage and C-O formation processes.

Though it has been established that fulvene endoperoxides isomerize to allene oxides and cyclopropanones, decarbonylation of the latter species in these reactions had not previously been observed. The strained bicyclic structure in **15** presumably encourages CO extrusion in the present case. Earlier work has established the fact that cyclopropanone intermediates carrying electron-withdrawing groups or groups capable of resonance undergo facile decarbonylations via a stepwise mechanism.¹¹⁻¹⁵ In the present case, the strained bicyclic nature of intermediate **15**, as well as the presence of a conjugated ketone moiety similarly encourages decarbonylation. The question whether the cyclopropanone decarbonylation is stepwise or concerted is answered by the fact that product **6** clearly stems from an intramolecular acyl trapping via the diradical intermediates **17** during decarbonylation, as shown in Scheme 5¹⁶.

The formation of **6** from **15** is a formal 1,3-acyl shift. 1,3-Acy shifts have been shown to proceed, at least in part, via radical pair intermediates such as **17a** and are often accompanied by decarbonylations. As to the question which cyclopropanone bond cleaves preferentially, computation at G3MP2(B3LYP) level using the Gaussian 03 program revealed that the triplet diradical **17a**, formed via C1-C8 cleavage, is more stable by 15.2 kcal/mol than the alternative diradical (from C7-C8 cleavage).

The temperature effect on the product distribution is consistent with the expectation that the intramolecular cyclization of the acyl radical **17b** leading to **6** is enthalpically favoured and dominates at -78 °C; increasing the photooxygenation temperature to -25 and 0 °C,

respectively, progressively favors the entropically favoured decarbonylation process (**17**→**8**) at the expense of product **6**.

Turro¹⁷ and Baldwin¹⁸ stated that cyclopropanone decarbonylations are expected to occur in a stepwise, nonconcerted fashion. Earlier theoretical work by Hoffmann using the extended Hückel method concluded that the thermal decarbonylation involves non-linear departure of CO, and the process -though highly unsymmetrical- was termed concerted.^{19,20} On the other hand, based on ab initio calculations Birney and coworkers argue that this prototypical nonlinear decarbonylation is an “effectively forbidden” process due to the lack of “energy of concert”.²¹ A comparative semi-empirical, ab initio and DFT study by Balcio lu and Sevin likewise casts doubts upon the asynchronous (${}_2\pi_s + {}_2\omega_a$) concerted nature of these reactions.²²

It is also worthy of note that prolonged exposure of epoxy ketone **7** to silica gel during preparative TLC resulted in partial isomerization to the hydroxy ketones **20** and **21** via the mechanism shown in Scheme 6.

The fact that only one single stereoisomer, **20** (*Z*), was formed from **3** is a result of the opening of the epoxide being coupled with the opening of the cyclopropane ring. An *anti*-relationship between the breaking bonds is preferred (this is supported by G3MP2(B3LYP) calculations) and the system adopts a conformation in which the cyclopropane CH₂ group is proximal to ring carbonyl, locking the stereochemistry of the exocyclic double bond in **20** (see transition state structure **18a** in Figure 1).

In an attempt to synthesize **20** independently, fulvene **22**²³ was photooxygenated at -78 °C in CH₂Cl₂, and the base-catalyzed isomerization affected with a few drops of DBU at low temperatures. However, the product isolated from this reaction was not **20**, but its *E*-isomer (with respect to the exocyclic double bond) **24**. The exclusive formation of **24** may be attributed to the fact that proton abstraction of the bridgehead proton in **23** by base occurred from the sterically less hindered side (proximal to the methyl group) of the bicyclic peroxide **23**.

The *Z* and *E* stereochemistries in **20** and **24**, respectively, were readily assigned based on the chemical shifts of the γ -H's. Whereas H_a in **16** absorbs at 6.9 ppm, the corresponding H_a in **20** absorbs at 6.1 ppm, in accord with previously reported chemical shifts for such protons in similar systems.^{24,25}

3. Conclusion

This paper describes the first photooxygenation of a bicyclic fulvene endoperoxide. Our results have shown that the incorporation of the fulvene unit in a bicyclic system, as in a 1,2-dihydropentalene has a profound effect on the fate of the dioxygen diradicals derived from the unsaturated singlet oxygen adduct. None of the products resemble those obtained from the monocyclic analogs due to constraints imposed on the structure by the bicyclic framework. The decomposition pathways of **9** leading to products **6**, **7** and **8** as well as **16** are novel in that a) the cyclopropanone intermediate **15** undergoes decarbonylation as well as a 1,3-acyl shift, both by stepwise, diradical processes; b) the bicyclic nature of the 1,2-dihydropentalene permits the observation of an alternative C-C cleavage, leading to an unusual cyclopentadienone epoxide derivative **7**; c) acid-catalyzed isomerization of the latter gives rise to the hydroxyketone **20**. Computational work indicates that this isomerization occurs by a concerted mechanism leading exclusively to the *Z* stereoisomer. Currently, studies are underway aimed at the synthesis, thermal and reagent-induced isomerizations of the saturated analog of **9**.

4. Experimental section

4.1 General

Melting points were determined in open class capillary tubes and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on 300 MHz and 500 MHz NMR spectrometers, using CDCl_3 as solvent and TMS as internal standard, unless specified otherwise. Most column chromatographic separations were carried out on a flash chromatography system using 40–60 μm silica gel columns using ethyl acetate/n-hexane solvent mixtures. For preparative TLC, Merck silica gel (grade 60 PF₂₅₄) was used. All reactions were conducted under an atmosphere of dry nitrogen or argon. Non-deuterated solvents were dried and distilled prior to use. Pyrrolidine is an exceptionally foul-smelling and toxic compound and should be handled with care in a well-ventilated hood. Fulvenes are oxygen- and heat-sensitive compounds; all reactions should be carried out under a nitrogen or argon atmosphere. 1,2-Dihydropentalene **5** used in this study was prepared by a method we recently developed.⁷ Exact masses of all new products by high resolution mass spectra (HRMS) were determined at the University of Notre Dame Mass Spectrometry Facility (<http://www.nd.edu/~massspec/>) and San Francisco State University Mass Spectrometry Facility.

4.2. General procedure for the singlet oxygenation of 2,2,3-trimethyl-1,2-dihydropentalene **5**

A stirred solution of 0.22 g (1.51 mmol) of **1** and 3 mg of TPP in 6 mL of CH_2Cl_2 was irradiated with a 400 W high pressure sodium lamp at 0 °C (or –25 °C, or –78 °C, respectively) under a positive pressure of dry oxygen. After all starting material had reacted (TLC) the solvent was rotovapped and the residue chromatographed on silica gel eluting with petroleum ether/ethyl acetate (10:1). At each temperature, the photooxygenations went to completion and the combined isolated yields in each case were >80%. The product ratios at each temperature are as follows: at –78 °C, **6:7:8** = 2.3:1:0; at –25 °C, **6:7:8** = 0.7:1:2.4; at 0 °C, **6:7:8** = 0:1:2.2. At each temperature a small amount (1.7–2%) of **16** was also isolated.

4.3. 3,3,5-Trimethylbicyclo[3.2.1]oct-6-ene-2,8-dione (**6**)

FT-IR (neat): ν 3065, 2966, 2925, 2871, 1767, 1707, 1450, 1380, 1362, 1239, 1123, 1073, 1023, 904, 874, 783, 707 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz): δ 6.3 (d, J = 6.5 Hz, 1H); 6.2 (dd, J = 3.2 Hz, 6.5 Hz, 1H); 3.64 (d, J = 3.2 Hz, 1H); 1.90 (d, A part of an AB system, J = 13.8 Hz, 1H); 1.65 (d, B part, J = 13.8 Hz, 1H); 1.32 (s, 3H); 1.24 (s, 3H), 1.08 (s, 3H); (CDCl_3 , 125 MHz): δ 209.7, 205.4, 141.72, 127.2, 67.8, 51.6, 47.1, 45.1, 33.3, 29.9, 16.5 ppm; HRMS: calcd. for $\text{C}_{11}\text{H}_{14}\text{O}_2$: 178.0994. Found: 179.1082.

4.4. 1-(1,2,2-Trimethylcyclopropyl)-6-oxabicyclo[3.1.0]hex-3-en-2-one (**7**)

FT-IR (neat) ν 3056, 2991, 2950, 2925, 2868, 1724, 1650, 1617, 1455, 1381, 1336, 1234, 1185, 1121, 1085, 1056, 993, 907, 818, 785, 751 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz): δ 7.6 (dd, J = 1.3 Hz, 6.1 Hz, 1H); 6.05 (dd, J = 2.2 Hz, 6.1 Hz); 3.82 (dd, J = 1.3 Hz, 2.2 Hz, 1H); 1.21 (s, 3H); 1.19 (s, 3H); 1.13 (s, 3H); 0.52 (d, A part of an AB system, J = 4.2 Hz, 1H); 0.02 (d, B part, J = 4.2 Hz, 1H) ppm; ^{13}C NMR (CDCl_3 , 75 MHz): δ 199.4, 154.5, 135.0, 62.1, 56.3, 22.0, 21.1, 20.8, 20.6, 20.4, 17.4 ppm; HRMS: calcd for $\text{C}_{11}\text{H}_{14}\text{O}_2$: 178.0994. Found: 179.1074.

4.5 5,7,7-Trimethyl-2,4-cycloheptadienone (**8**)

Yellowish liquid, UV-Vis (EtOH) λ_{max} (abs): 670.0 (0.008), 510.0 (0.016), 415.0 (0.252), 300.1 (0.678), 205.0 (3.34) nm; FT-IR (neat): 3017, 2959, 2922, 2869, 1655, 1639, 1587, 1447, 1381, 1288, 1236, 1115, 1040, 833, 808 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ 6.42

(dd, $J = 10$ Hz, 5.0 Hz, 1H); 6.0 (d, $J = 10$ Hz, 1H), 5.95 (d, $J = 5$ Hz, 1H); 2.32 (s, 2H); 2.00 (s, 2H); 1.1 (s, 6H); ^{13}C NMR: δ 206.0; 149.6, 138.0, 129.5, 122.8, 46.0, 43.1, 28.7, 24.8 ppm; HRMS: calcd. for $\text{C}_{10}\text{H}_{14}\text{O}$: 150.1045. Found: 151.1067.

4.6. 6,8,8-Trimethylcycloocta-2,5-diene-1,4-dione (16)

^1H NMR (CDCl_3 , 500 MHz) δ 6.67 (d, A part of an AB system, $J = 13.5$ Hz, 1H); 6.32 (d, B part, $J = 13.5$ Hz, 1H); 5.96 (s, 1H); 2.7 (s, 2H), 1.99 (s, 3H), 1.22 (s, 6H); ^{13}C NMR (CDCl_3 , 125 MHz): δ 208.5, 191.2, 152.4, 137.8, 134.1, 129.1, 53.3, 43.2, 28.9, 23.7 ppm; HRMS: calcd. for $\text{C}_{11}\text{H}_{14}\text{O}_2$: 178.0994. Found: 179.1064.

4.7. Partial isomerization of 7 to 20 and 21

When compound **3** was purified on a preparative TLC plate on SiO_2 , eluting with petroleum ether/ethyl acetate (10:1). A small amount of a slow-moving fraction was isolated and characterized as a 6:1 mixture of hydroxyketones **20** and **21**, respectively.

4.8. (Z)-4-Hydroxy-5-(4-methylpent-3-en-2-ylidene)cyclopent-2-enone (20)

(in the mixture of **16** and **17**): ^1H NMR (CDCl_3 , 500 MHz): δ 7.32 (dd, $J = 6.0$ Hz, 2.6 Hz, 1H); 6.30 (dd, $J = 6.0$ Hz, 1.0 Hz, 1H); 5.22 (br.s, 1H); 2.25 (s, 3H); 1.91 (d, $J = 1.2$ Hz, 3H); 1.81 (d, $J = 1.0$ Hz, 3H); ^{13}C NMR (CDCl_3 , 125 MHz): δ 195.0, 155.8, 149.2, 142.5, 138.6, 132.4, 125.4, 72.9, 28.4, 22.2, 21.6 ppm.

4.9. (Z)-4-Hydroxy-5-(4-methylpent-4-en-2-ylidene)cyclopent-2-enone (21)

(signals not coinciding with those of **20** in the mixture of **20** and **21**): ^1H NMR (CDCl_3 , 500 MHz): δ 7.35 (dd, $J = 6.0$ Hz, 2.6 Hz, 1H); 6.32 (dd, $J = 6.0$ Hz, 1.0 Hz, 1H); 4.81 (narrow m, 1H), 4.71 (narrow m, 1H); 3.64 (d, A part of an AB system, $J = 13.4$ Hz, 1H); 3.54 (d, B part, $J = 13.4$ Hz, 1H), 1.69 (s, 3H); ^{13}C NMR (CDCl_3 , 125.8 Hz): δ 155.8, 112.9, 72.6, 41.4, 22.9, 18.7 ppm; HRMS (**20+21**): calcd. for $\text{C}_{11}\text{H}_{14}\text{O}_2$: 178.0994. Found: 179.1076.

4.10. (E)-4-Hydroxy-5-(4-methylpent-3-en-2-ylidene)cyclopent-2-enone (24)

A solution of 400 mg (2.8 mmol) of 5-(4-methylpent-3-en-2-ylidene)cyclopenta-1,3-diene (**22**)²² was photooxygenated at -78 °C in 20 mL of CH_2Cl_2 for 2h, as described above. After the lamp was turned off and the solution was purged with nitrogen, two drops of DBU was added and the mixture was allowed to warm up to room temperature with stirring under nitrogen. After the solvent was rotovapped, the residue was purified by flash chromatography on silica gel, eluting with *n*-hexane/EtOAc (3:1) to yield 199 mg (40%) of **24**. ^1H NMR (CDCl_3 , 300 MHz): δ 7.34 (dd, $J = 2.6$ Hz, 6.0 Hz, 1H); 6.34 (dd, $J = 1.1$ Hz, 6.0 Hz, 1H); 6.16 (s, 1H); 5.14 (s, 1H); 2.4 (s, 3H); 1.9 (d, $J = 1.1$ Hz, 3H); 1.81 (d, $J = 0.8$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz): δ 196.0, 154.8, 148.0, 138.1, 132.7, 125.6, 71.5, 27.0, 20.6, 18.8 ppm; HRMS: calcd. for $\text{C}_{11}\text{H}_{14}\text{O}_2$: 178.0994. Found: 179.1068.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Support of this work by funds from the National Institutes of Health (Grant No. 1SC1GM082340) is gratefully acknowledged. Funding from the National Science Foundation (Grants No. DBO-0521342 and DUE-9451624) for the purchase of 300 MHz and 500 MHz NMR spectrometers is also acknowledged. S. Gronert acknowledges funding by the National Science Foundation (CHE-1011771) and the VCU Center for High-Performance Computing. *This paper is dedicated to Professor James R. Keeffe on the occasion of his 75th birthday.*

References

1. Harada N, Suzuki S, Uda H, Ueno H. *J Am Chem Soc.* 1972; 94:1777–1778.
2. (a) Skorianetz W, Schulte-Elte KH, Ohloff G. *Angew Chem Int Ed Engl.* 1972; 11:304–305. [PubMed: 4626425] (b) Skorianetz W, Schulte-Elte KH, Ohloff G. *Helv Chim Acta.* 1971; 54:1913–1922.
3. Adam W, Erden I. *Angew Chem Int Ed Engl.* 1978; 17:210–211.
4. Erden I, Drummond J, Alstad R, Xu F. *Tetrahedron Lett.* 1993; 34:1255–1258.
5. (a) Erden I, Amputch M. *Tetrahedron Lett.* 1987; 28:3779–3782.(b) Erden I, Drummond J, Alstad R, Xu F. *Tetrahedron Lett.* 1993; 34:1255–1258.(c) Erden I, Drummond J, Alstad R, Xu F. *J Org Chem.* 1993; 58:3611–3612.(d) Erden I, Gärtner C. *Tetrahedron Lett.* 2009; 50:2381–2383. [PubMed: 20161263]
6. Erden I, Xu F, Cao W. *Angew Chem Int Ed Engl.* 1997; 36:1516–1518.
7. Coskun N, Ma J, Erden I. *Org Lett.* 2011; 13:5952–5955. [PubMed: 22029269]
8. Erden, I.; Coskun, N. 43rd IUPAC World Chemistry Congress; San Juan, PR. Aug. 1, 2011; paper # 589
9. Patterson, AM. *ACS.* 2. 1960. The Ring Index; p. 137
10. (a) Camp RL, Greene FD. *J Am Chem Soc.* 1968; 90:7349.(b) Crandall JK, Machleder WH. *J Am Chem Soc.* 1968; 90:7347–7349.
11. Starnes WH Jr, Plank DA, Floyd JC. *J Org Chem.* 1975; 40:1124–1127.
12. (a) Güsten H, Kirsch G, Schulte-Frohlinde D. *Angew Chem Int Ed Engl.* 1967; 6:948–949.(b) Güsten H, Kirsch G, Schulte-Frohlinde D. *Tetrahedron.* 1968; 24:4393.
13. Kende, AS. *Chem Ind. London:* 1956. p. 1053
14. Büchi G, Hochstrasser U, Pawlak W. *J Org Chem.* 1973; 38:4348. and references cited therein.
15. Shurygina MP, Kurskii YA, Druzhkov NO, Chesnokov SA, Abakumova LG, Fukin GK, Abakumov GA. *Tetrahedron.* 2008; 64:9784–9788.
16. (a) Chatgililoglu C, Crich D, Komatsu M, Ryu I. *Chem Rev.* 1999; 99:1991–2069. [PubMed: 11849018] (b) Yoshikai K, Hayama T, Nishimura K, Yamada K, Tomiako K. *Chem Pharm Bull.* 2005; 53:586–588. [PubMed: 15863938]
17. Turro NJ. *Acc Chem Res.* 1969; 2:25–32.
18. Baldwin JE. *Can J Chem.* 1966; 44:2051–2055.
19. Hayes DM, Zeiss CA, Hoffmann R. *J Phys Chem.* 1971; 75:340–344.
20. Woodward RB, Hoffmann R. *Angew Chem Int Ed Engl.* 1969; 8:781–932.
21. Birney DM, Ham S, Unruh GR. *J Am Chem Soc.* 1997; 119:4509–4517.
22. Balciro lu N, Sevin F. *J Mol Model.* 2000; 6:48–54.
23. Erden I, Xu FP, Sadoun A, Smith W, Sheff G, Ossun M. *J Org Chem.* 1995; 60:813–820.
24. Erden I, Öcal N, Song J, Gleason C, Gärtner C. *Tetrahedron.* 2006; 62:10676–10682. [PubMed: 17998948]
25. Gaudiana RA, Graf JF, Lillya CP. *J Org Chem.* 1979; 44:646–648.

Figure 1.
TS **18a**: Preferred conformation for the epoxide ring opening

Scheme 1.
Fulvene endoperoxide rearrangements

Temperature	Product ratios		
-78 °C	2.3	1	0
-25 °C	0.7	1	2.4
0 °C	0	1	2.2

Scheme 2.
Products from singlet oxygenation of **5**

Scheme 3.
Decomposition mechanism leading to **7**

Scheme 4.
Allene-oxide-cyclopropanone isomerization mechanism

Scheme 5.
Stepwise decarbonylation vs. 1,3-acyl shift

Scheme 6.
Acid-catalyzed isomerization of 7 via 18

Scheme 6.
Attempted independent synthesis of **20** from **22**