

# Unusual endoperoxide isomerizations: a convenient entry into 2-vinyl-2-cyclopentenones from saturated fulvene endoperoxides

Ihsan Erden,<sup>a,\*</sup> Nüket Öcal,<sup>b</sup> Jiangao Song,<sup>a</sup> Cindy Gleason<sup>a</sup> and Christian Gärtner<sup>a</sup>

<sup>a</sup>San Francisco State University, Department of Chemistry and Biochemistry, 1600 Holloway Avenue, San Francisco, CA 94132, USA

<sup>b</sup>Yildiz Technical University, Faculty of Arts and Sciences, Department of Chemistry, Davutpasa Campus, 34010 Merter-Istanbul, Turkey

Received 16 June 2006; revised 12 July 2006; accepted 24 July 2006

Available online 14 September 2006

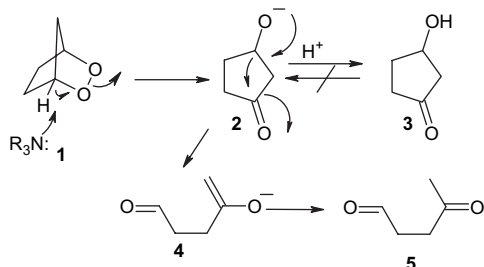
This paper is dedicated to my teacher, friend and associate, Professor Armin de Meijere

**Abstract**—An unusual peroxide base-promoted isomerization is uncovered. Saturated endoperoxides derived from fulvenes give rise to 2-vinyl-2-cyclopentenones upon treatment with DBU in CH<sub>2</sub>Cl<sub>2</sub> in a one-pot reaction. This methodology is applied to a convenient synthesis of dihydrojasnone. Moreover, functional groups placed on the side chain at C-6 participate in the base-catalyzed isomerizations via conjugate attack at the enone moiety to give 2-cyclopentenones carrying oxygen heterocycles at C-2.

© 2006 Elsevier Ltd. All rights reserved.

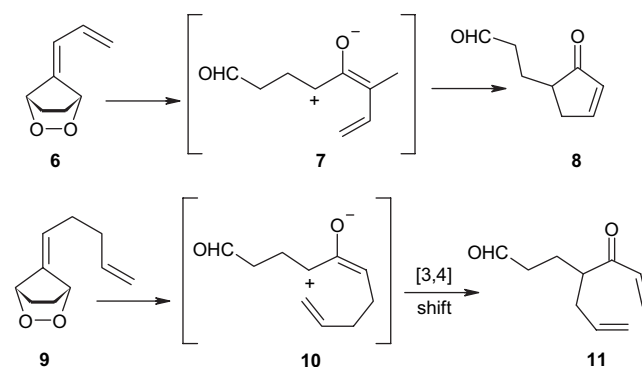
## 1. Introduction

Endoperoxides, readily available in most cases from 1,3-dienes by way of a Diels–Alder reaction with singlet oxygen,<sup>1</sup> are sensitive to thermal, photochemical, and reductive conditions.<sup>2</sup> In particular, base-catalyzed rearrangements, also known as Kornblum–De la Mare reactions are well-known.<sup>3</sup> Treatment of bridged bicyclic endoperoxides typically result in the formation of hydroxyketones. The mechanism of these reactions have been thoroughly studied. In particular, the base-catalyzed disproportionation of 2,3-dioxabicyclo[2.2.1]heptane (**1**) to 3-hydroxycyclopentanone (**3**) and levulinaldehyde (**5**) by amine catalysis has been reported by Salomon and Zagorski in an elegant study.<sup>4</sup> Isotope labeling studies show that the most likely mechanism for the disproportionation involves initial abstraction of the bridgehead proton in the rate-determining step (Scheme 1).



Scheme 1.

Previously, we studied the singlet oxygenations of fulvenes and low-temperature diazene reduction of the unstable endoperoxides<sup>5</sup> and reported on some novel mechanisms encountered during the thermal isomerizations of saturated fulvene endoperoxide, e.g., **23**, **32**, **42**, and **46**.<sup>6,7</sup> We have explored the synthetic utility of the allene oxides/cyclopropanones<sup>8</sup> to prepare functionalized cyclopentenones derived from saturated fulvene endoperoxides, e.g., **6** → **7** → **8**<sup>9</sup> and also disclosed the first aliphatic examples of [3,4]-sigmatropic shifts on suitably substituted cyclopropanones derived from the corresponding endoperoxides by thermolysis (**9** → **10** → **11**) (Scheme 2).<sup>10</sup>



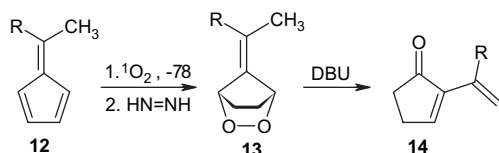
Scheme 2.

## 2. Results and discussion

We here report a new and synthetically useful facet of base-catalyzed endoperoxide isomerizations that we observed in

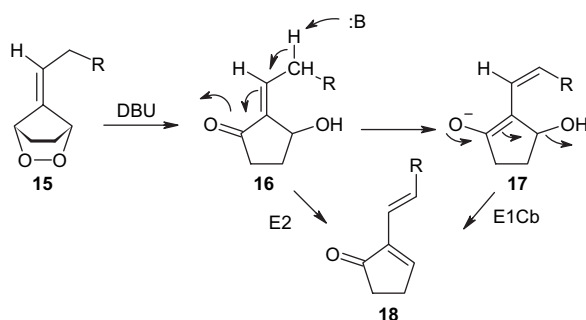
\* Corresponding author. Tel.: +1 415 338 1627; fax: +1 415 338 2384; e-mail: [ierden@sfsu.edu](mailto:ierden@sfsu.edu)

saturated fulvene endoperoxides. The outcome of these reactions has proved particular to the nature of the base. Thus, treatment of fulvene endoperoxides with triethylamine at 0 °C to rt in CH<sub>2</sub>Cl<sub>2</sub> results in the formation of the corresponding hydroxyketone as expected.<sup>5</sup> However, the use of the stronger base, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), gave 2-vinyl-2-cyclopentenones, e.g., **14**, in high yields (Scheme 3).



Scheme 3.

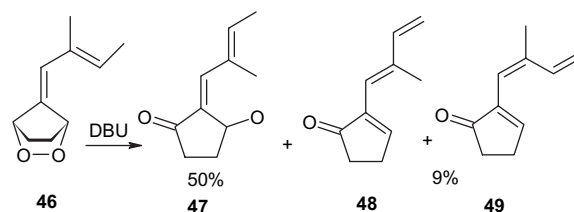
The mechanism presumably commences with initial proton abstraction at the bridgehead. However, the resulting hydroxyketone is prone to further proton abstraction at the allylic position. The timing of the proton elimination is subject to discussion and further studies, and two alternative mechanisms may be advanced for the dehydration step. One possible dehydration pathway would involve deprotonation of the  $\gamma$ -H, enolate formation, followed by hydroxide elimination (presumably via initial protonation by  $\text{BH}^+$ ), an E1Cb mechanism (Scheme 4). However, the fact that the reaction proceeds in CH<sub>2</sub>Cl<sub>2</sub>, an aprotic solvent that does not encourage ionic species, points to a concerted 1,4-elimination (E2). Regardless of the mechanism of the dehydration step, the resulting compounds from this tandem isomerization–dehydration process are 2-vinylcyclopentenones, a substance class for which there are very few synthetic methods.<sup>11–15</sup> The ease with which the 2-vinylcyclopentenones can be constructed from the readily available fulvenes in a one-pot reaction makes this approach particularly attractive. Table 1 depicts some selected systems we have prepared so far.



Scheme 4.

In one case, where the starting fulvene carried a 6-vinyl group, the reaction with DBU led to a mixture of the expected hydroxyketone **47** (50%) and a mixture of the two isomers **48** and **49** (9%). It appears that the protons at the remote methyl group are just acidic enough to permit abstraction, resulting in the formation of a highly conjugated system (Scheme 5).

In another example, we subjected the hydroxyketone **52**, obtained from **51** by treatment with DBU, to the reaction with



Scheme 5.

catalytic trifluoroacetic acid, in hopes of affecting dehydration. The product from this reaction was the alcohol **53**, obviously stemming from a process involving dehydration, double bond shift, and rehydration (Scheme 6).

The presence of functionality on side chain of the exocyclic double bond was tested in the case of **37** (entry 6). The treatment of the endoperoxide **35** with DBU delivered a 3:2 mixture of the dehydration products **36** and **37** (Scheme 7). Obviously the hydroxyl group in the side chain did not suffer elimination. The two products were identified in the mixture by means of their <sup>1</sup>H and <sup>13</sup>C NMR spectra.

When the hydroxyl group was placed at C-3 on the side chain of the exocyclic double bond in the starting fulvene (entry 7), treatment of the saturated endoperoxides **42** with DBU furnished the tetrahydrofuran derivative **40** exclusively. Compound **40** appears to be a suitable precursor of the hypotensive drug ouidenone,<sup>16</sup> and this approach is currently being explored (Scheme 8).

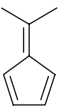

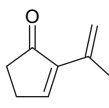
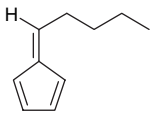
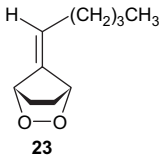
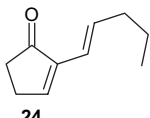
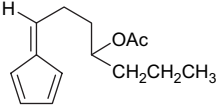
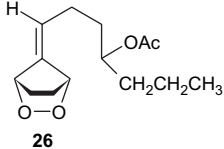
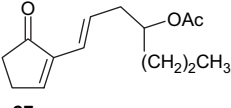
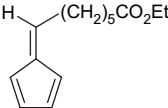
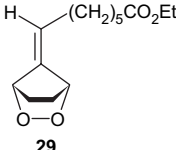
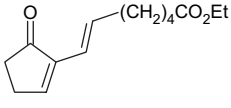
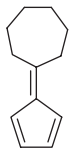
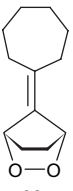
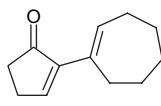
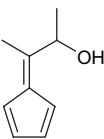
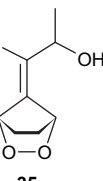
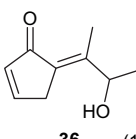
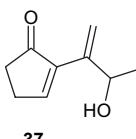
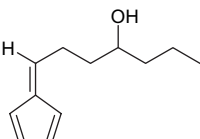
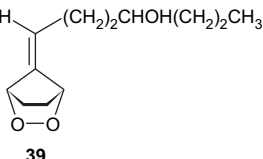
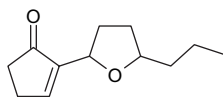
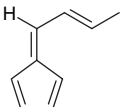
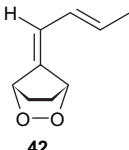
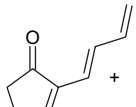
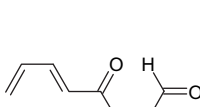
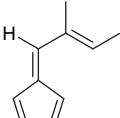
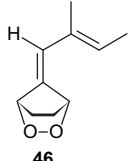
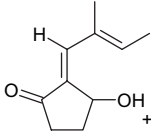
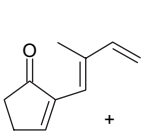
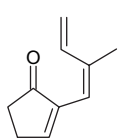
Finally, the fulvene endoperoxide–DBU isomerization–dehydration methodology was implemented in a short synthesis of the naturally occurring fragrant compound dihydrojasnone.<sup>17</sup> Starting with fulvene **22** (entry 2), readily available from valeraldehyde in 77% yield by photooxygenation in CH<sub>2</sub>Cl<sub>2</sub> at –78 °C followed by diazene reduction, (generated in situ from azodicarboxylate and acetic acid at low temperatures), endoperoxide **23** was obtained, which without isolation was treated with DBU to give the cyclopentenone **24** in 83% yield. The conversion of **24** to dihydrojasnone was achieved by the well-documented protocol<sup>18,19</sup> involving methyllithium addition to the carbonyl group and subsequent treatment with PCC in CH<sub>2</sub>Cl<sub>2</sub> to furnish **56** in 50% overall yield from **24** (Scheme 9).

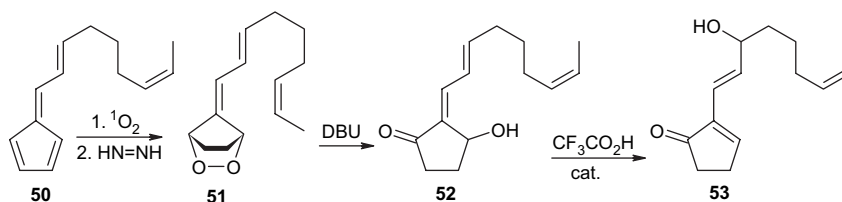
Compound **30** (entry 4) can also be obtained in this manner in a very short sequence from the readily available fulvene. The former represents an important precursor of certain prostaglandins and related compounds. These aspects are currently being explored.

It is noteworthy that the respective unsaturated fulvene endoperoxides do not suffer dehydration after base-catalyzed isomerization with DBU, presumably owing to the unstable nature of the products (cyclopentadienones). Endoperoxide **57**, derived from 6,6-dimethylfulvene for instance, gave a mixture of the hydroxyketones **58** and **59** in a ratio of 5:1 (Scheme 10).<sup>20</sup>

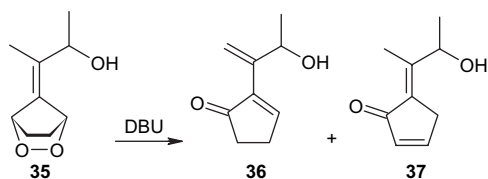
Compound **58** is the expected primary isomerization product, however, **59** is a secondary product that most likely

**Table 1.** DBU-catalyzed isomerizations–dehydrations of fulvene endoperoxides

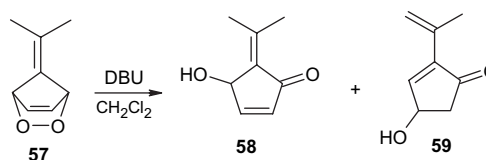
Entry	Fulvene	Endoperoxide	Cyclopentenone	Yield (%)				
1	 <b>19</b>	 <b>20</b>	 <b>21</b>	76				
2	 <b>22</b>	 <b>23</b>	 <b>24</b>	83				
3	 <b>25</b>	 <b>26</b>	 <b>27</b>	81				
4	 <b>28</b>	 <b>29</b>	 <b>30</b>	69				
5	 <b>31</b>	 <b>32</b>	 <b>33</b>	82				
6	 <b>34</b>	 <b>35</b>	 <b>36</b>	+ (1.7:1)	 <b>37</b>	66		
7	 <b>38</b>	 <b>39</b>	 <b>40</b>			68		
8	 <b>41</b>	 <b>42</b>	 <b>43</b>	+ (2.5:1)	 <b>44</b>	66		
9	 <b>45</b>	 <b>46</b>	 <b>47</b>	+ 50%	 <b>48</b>	+ 9%	 <b>49</b>	59



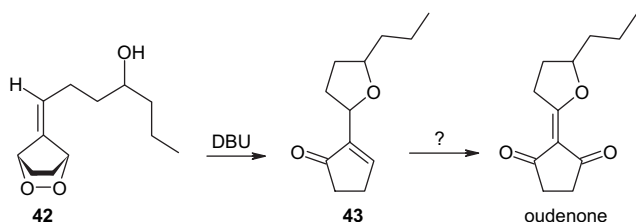
Scheme 6.



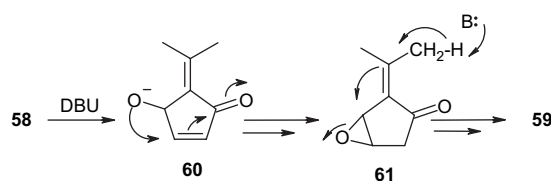
Scheme 7.



Scheme 10.



Scheme 8.



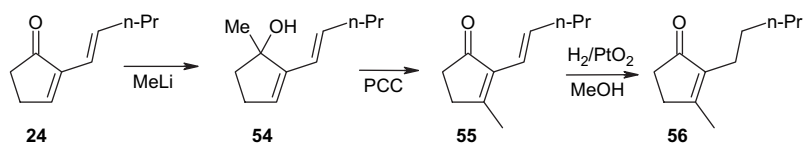
Scheme 11.

forms by further isomerization of **58** by a mechanism outlined in Scheme 11.

It is interesting to note that the base-catalyzed decomposition of unsaturated fulvene endoperoxides appears to be entirely analogous to those of the saturated counterparts, except for the dehydration step in the latter. Intermediates **16** (Scheme 2) and **61** (Scheme 11) differ only in the nature of the leaving groups (alcohol vs epoxide). The epoxide suffers ring opening to the allylic alcohol, whereas the hydroxyl group is eliminated in **16**.

### 3. Conclusion

In summary, we have uncovered a new useful facet of base-catalyzed endoperoxide rearrangements that result in a Kornblum–De la Mare isomerization followed by dehydration to give 2-vinyl-2-cyclopentenones, which are highly desirable synthetic intermediates. In cases where there are oxygen nucleophiles on the side chain, conjugate attack at the  $\beta$ -carbon of the exocyclic double bond occurs to give 2-cyclopentenones that carry a heterocycle at C-2. Implementation of this methodology in the synthesis of a variety of targets is underway.



Scheme 9.

## 4. Experimental

### 4.1. General

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a General Electric QE-Plus 300 MHz and Bruker Avance DRX 300 MHz spectrometers, using  $\text{CDCl}_3$  as solvent and TMS as internal standard, unless specified otherwise. IR spectra were obtained on a Nicolet Avance 370 DTGS FT-IR spectrometer. Column chromatographic separations were carried out with Davison 6–200 mesh silica gel. For preparative TLC, Merck silica gel (grade 60 PF254) was used. All reactions were conducted under an atmosphere of dry nitrogen or argon. Fulvenes were stored under argon in the freezer at  $-30^\circ\text{C}$ . Non-deuterated solvents were dried and distilled prior to use. All fulvenes in this study were prepared according to published procedures.<sup>21,22</sup> Signal multiplicities in the NMR spectra are reported as follows: s-singlet, d-doublet, t-triplet, dd-doublet of doublets, dt-doublet of triplets, q-quartet, quin-quintuplet, sext-sextet, m-multiplet, br-broad.

Spectroscopic data for the synthesis of those fulvenes not found in literature are described below.

**4.1.1. Fulvene 25.** It was prepared from **38** (vide infra) by stirring with acetic anhydride in the presence of pyridine

for 48 h followed by aqueous work-up in 86% yield.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  6.55 (m, 1H), 6.46 (m, 2H), 6.37 (t,  $J=8.0$  Hz, 1H), 6.12 (dt, 1H), 4.95 (m, 1H), 2.55 (m, 2H), 2.02 (s, 3H), 1.8 (m, 2H), 1.55 (m, 2H), 1.33 (m, 2H), 0.9 (t,  $J=7.2$  Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  170.8, 146.2, 141.5, 133.4, 131.1, 125.6, 118.9, 73.5, 36.3, 33.9, 27.1, 21.2, 18.7, 14.0 ppm. Anal. Calcd for  $\text{C}_{14}\text{H}_{20}\text{O}_2$ : C, 76.33; H, 9.15. Found: C, 76.28; H, 9.13.

**4.1.2. Fulvene 28.** Yield 78%.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  6.6–6.4 (m, 4H), 6.2 (m, 1H), 4.1 (q,  $J=7.5$  Hz, 2H), 2.54 (q,  $J=7.5$  Hz, 2H), 2.30 (t,  $J=7.2$  Hz, 2H), 1.65 (m, 2H), 1.50 (m, 2H), 1.4 (m, 2H), 1.25 (t,  $J=7.5$  Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  173.7, 146.1, 142.8, 133.1, 130.8, 125.6, 119.1, 60.2, 34.2, 30.9, 29.1, 28.8, 24.8, 14.3 ppm. Anal. Calcd for  $\text{C}_{14}\text{H}_{20}\text{O}_2$ : C, 76.33; H, 9.15. Found: C, 76.31; H, 9.15.

**4.1.3. Fulvene 38.** Yield 49%.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  6.53 (m, 2H), 6.45 (m, 1H), 6.40 (t,  $J=7.5$  Hz, 1H), 6.2 (m, 1H), 3.63 (m, 1H), 2.65 (q,  $J=7.5$  Hz, 2H), 1.67 (m, 2H), 1.44 (m, 2H), 1.30 (m, 4H), 0.9 (t,  $J=7.5$  Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  146.2, 142.6, 133.2, 130.8, 125.6, 119.1, 71.3, 37.6, 36.9, 31.9, 27.5, 25.3, 22.7, 14.1 ppm. Anal. Calcd for  $\text{C}_{12}\text{H}_{18}\text{O}$ : C, 80.85; H, 10.18. Found: C, 80.82; H, 10.23.

**4.1.4. Fulvene 50.** Yield 39%.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  6.75 (m, 2H), 6.5–6.2 (m, 5H), 5.4 (m, 2H), 2.3 (m, 2H), 2.2 (m, 2H), 2.05 (m, 2H), 1.0 (t,  $J=7.5$  Hz, 3H) ppm. Anal. Calcd for  $\text{C}_{14}\text{H}_{18}$ : C, 90.26; H, 9.74. Found: C, 90.25; H, 9.73.

## 4.2. Typical procedure for the preparation of the saturated endoperoxides

A solution of 6,6-dimethylfulvene (1.06 g, 10 mmol) and 5 mg of TPP (*meso*-tetraphenylporphyrin) in 200 mL  $\text{CH}_2\text{Cl}_2$  was cooled to  $-78^\circ\text{C}$  in a flat Dewar containing dry ice–acetone. The mixture was stirred while being irradiated with a 250 W high-pressure sodium lamp for 3 h under an oxygen atmosphere (a balloon filled with oxygen served this purpose). Then the lamp was turned off, 8.7 g (45 mmol) of potassium azodicarboxylate was added to the mixture in small portions, a pressure-equalizing dropping funnel fitted with a drying tube containing Drierite was attached to the flask. A solution of 5.1 g (85 mmol) of acetic acid in 20 mL  $\text{CH}_2\text{Cl}_2$  was added dropwise to the stirred slurry at  $-78^\circ\text{C}$ , and the mixture was slowly warmed up to  $-35^\circ\text{C}$  and stirred at this temperature for 1 h. The mixture was then slowly warmed up to  $0^\circ\text{C}$  for an additional 30 min. Then the salt was filtered by suction, the filtercake washed with cold  $\text{CH}_2\text{Cl}_2$ , while keeping the filter flask in an ice bath. The filtrate was washed with saturated aqueous  $\text{NaHCO}_3$ , dried over  $\text{MgSO}_4$ , filtered into a 250 mL round-bottomed flask. An aliquot was concentrated at reduced pressure (caution: saturated fulvene endoperoxides—when neat—are potentially explosive!), and dissolved in  $\text{CDCl}_3$  for NMR spectroscopy. The product was practically pure according to its  $^1\text{H}$  NMR spectrum.<sup>5</sup> For the DBU-catalyzed isomerizations, the endoperoxides need not be isolated.

## 4.3. Typical procedure for the DBU-catalyzed isomerizations

Three drops of DBU were added to a solution of endoperoxide **57**, obtained as described above, in 250 mL  $\text{CH}_2\text{Cl}_2$  at  $0^\circ\text{C}$ , and the solution was stirred at room temperature for 12–15 h. Then the mixture was concentrated at reduced pressure, and the residue chromatographed on  $\text{SiO}_2$ , eluting with hexane/ether (3:1).

**4.3.1. 2-Isopropenyl-2-cyclopentenone (21).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  7.5 (t,  $J=3.0$  Hz, 1H), 6.07 (s, 1H), 5.16 (s, 1H), 2.60 (m, 2H), 2.47 (m, 2H), 1.94 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  208.5, 158.5, 143.7, 135.1, 117.3, 36.7, 26.3, 22.0 ppm. FTIR (film): 2973, 2927, 2855, 1710, 1453, 1387, 1262, 1177, 1038, 913, 802  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_8\text{H}_{10}\text{O}$ : C, 78.65; H, 8.25. Found: C, 78.61; H, 8.24.

**4.3.2. (E)-(2)-Pent-1-enyl-2-cyclopentenone (24).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  7.4 (t,  $J=3.0$  Hz, 1H), 6.6 (dt,  $J=16.0$ , 7.0 Hz, 1H), 6.1 (d,  $J=16.0$  Hz, 1H), 2.6 (m, 2H), 2.45 (m, 2H), 2.1 (q,  $J=7.0$  Hz, 2H), 1.50 (sext,  $J=7.0$  Hz, 2H), 0.94 (t,  $J=7.0$  Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  208.3, 156.5, 141.2, 135.7, 119.8, 35.57, 35.52, 26.2, 22.2, 13.7 ppm. Anal. Calcd for  $\text{C}_{10}\text{H}_{14}\text{O}$ : C, 79.96; H, 9.39. Found: C, 79.95; H, 9.38.

**4.3.3. (E)-1-(5-Oxocyclopent-1-enyl)hept-1-en-4-yl acetate (27).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  7.3 (br s, 1H), 6.45 (dt,  $J=15.6$ , 7.2 Hz, 1H), 6.0 (d,  $J=15.6$  Hz, 1H), 4.85 (quin,  $J=6.0$  Hz, 1H), 2.5 (m, 2H), 2.35 (m, 2H), 2.26 (m, 2H), 1.94 (s, 3H), 1.45 (m, 2H), 1.24 (m, 2H), 0.82 (t,  $J=7.2$  Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  207.8, 170.4, 157.4, 157.2, 140.6, 129.9, 122.3, 72.9, 38.0, 35.3, 26.0, 20.1, 18.3, 13.7, 13.5 ppm. Anal. Calcd for  $\text{C}_{14}\text{H}_{23}\text{O}_3$ : C, 70.20; H, 9.69. Found: C, 70.17; H, 9.66.

**4.3.4. (E)-Ethyl 7-(5-oxocyclopent-1-enyl)hept-6-enoate (30).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  7.3 (t,  $J=3$  Hz, 1H), 6.5 (dt,  $J=16.0$ , 7.2 Hz, 1H), 4.0 (q,  $J=7.2$  Hz, 2H), 2.5 (m, 2H), 2.35 (m, 2H), 2.2 (m, 2H), 2.05 (m, 2H), 1.60 (m, 2H), 1.35 (m, 2H), 1.7 (t,  $J=7.2$  Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  208.4, 173.6, 157.0, 141.0, 135.1, 120.1, 60.2, 35.6, 34.1, 33.1, 28.4, 26.3, 24.5, 14.2 ppm. Anal. Calcd for  $\text{C}_{14}\text{H}_{20}\text{O}_3$ : C, 70.20; H, 9.69. Found: C, 70.19; H, 9.66.

**4.3.5. 2-Cycloheptenylcyclopent-2-enone (33).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  7.4 (t,  $J=3.0$  Hz, 1H), 6.7 (t,  $J=6.6$  Hz, 1H), 2.56 (m, 2H), 2.45 (m, 2H), 2.37 (m, 2H), 2.25 (m, 2H), 1.8 (m, 2H), 1.55 (m, 4H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  208.2, 155.5, 145.0, 135.8, 133.0, 36.0, 32.2, 31.1, 28.4, 26.4, 26.3, 25.3 ppm. Anal. Calcd for  $\text{C}_{12}\text{H}_{16}\text{O}$ : C, 81.77; H, 9.15. Found: C, 81.77; H, 9.14.

**4.3.6. (E)-5-(3-Hydroxybutan-2-ylidene)cyclopent-2-enone (36).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  7.54 (m, 1H), 6.30 (m, 1H), 5.2 (br s, 1H, OH), 5.05 (q,  $J=7.0$  Hz, 1H), 3.2 (s, 2H), 1.32 (d,  $J=7.0$  Hz, 3H) ppm.

**4.3.7. 2-(3-Hydroxybut-1-en-2-yl)cyclopent-2-enone (37).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  7.7 (t,  $J=3.0$  Hz, 1H), 5.65 (s,



1H), 5.4 (s, 1H), 4.5 (q,  $J=6.6$  Hz, 1H), 3.9 (br s, 1H, OH), 2.7 (m, 2H), 2.5 (m, 2H), 1.26 (d,  $J=6.6$  Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , TMS, **36+37**):  $\delta$  209.1, 197.4, 160.7, 156.0, 156.4, 143.5, 142.5, 137.0, 128.5, 114.7, 68.9, 68.2, 35.2, 35.0, 26.3, 22.0, 21.0, 18.2 ppm.

**4.3.8. 2-(5-Propyltetrahydrofuran-2-yl)cyclopent-2-enone (40, both epimers).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  7.5 (t,  $J=2.7$  Hz, 1H), 4.7 and 4.61 (m, 1H), 4.1 and 3.8 (m, 1H), 2.6 (m, 2H), 2.42 (m, 2H), 2.3–1.9 (m, 2H), 1.2–1.8 (m, 6H), 0.9 (m, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  208.7, 208.5, 157.8, 157.5, 148.4, 148.2, 79.7, 79.4, 74.1, 73.8, 38.25, 38.16, 35.6, 32.0, 31.9, 31.4, 26.63, 26.6, 19.5, 14.3 ppm. Anal. Calcd for  $\text{C}_{12}\text{H}_{18}\text{O}_2$ : C, 74.19; H, 9.34. Found: C, 74.14; H, 9.33.

**4.3.9. (E)-(2-Buta-1,3-dienyl)cyclopent-2-enone (43).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  7.5 (t,  $J=3.0$  Hz, 1H), 7.16 (dd,  $J=17.0$ , 10.5 Hz, 1H), 6.2–6.5 (m, 2H), 5.35 (d,  $J=17.0$  Hz, 1H), 5.17 (d,  $J=10.5$  Hz, 1H), 2.6 (m, 2H), 2.46 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  208.6, 159.0, 141.6, 138.0, 134.3, 123.0, 120.0, 36.3, 27.2 ppm. HRMS  $m/z$  calcd for  $\text{C}_9\text{H}_{10}\text{O}$ : 134.0732. Found: 134.0733.

**4.3.10. (5E,7E)-4-Oxonona-5,7-dienal (44).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  9.8 (s, 1H), 7.35 (m, 1H), 6.4 (t,  $J=11.1$  Hz, 1H), 6.1 (m, 1H), 5.9 (d,  $J=11.1$  Hz, 1H), 2.75 (m, AA'BB' pattern, 4H), 1.8 (dd,  $J=6.6$ , 1.0 Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  201.3, 198.7, 144.2, 141.5, 130.9, 127.8, 38.3, 33.2, 19.5 ppm. HRMS  $m/z$  calcd for  $\text{C}_8\text{H}_{10}\text{O}_2$ : 138.0681. Found: 138.0677.

**4.3.11. (E)-3-Hydroxy-2-((E)-2-methylbut-2-enylidene)-cyclopentanone (47).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  7.0 (s, 1H), 6.2 (q,  $J=7.2$  Hz, 1H), 5.2 (d,  $J=4.8$  Hz, 1H), 2.6 (m, 2H), 3.3 (br s, 1H, OH), 2.23 (m, 2H), 2.0 (s, 3H), 1.8 (d,  $J=7.2$  Hz, 3H) ppm. Anal. Calcd for  $\text{C}_{10}\text{H}_{14}\text{O}_2$ : C, 72.26; H, 8.49. Found: C, 72.35; H, 8.50.

**4.3.12. (E)- and (Z)-2-(2-Methylbuta-1,3-dienyl)cyclopent-2-enone (48 and 49).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  7.6 (t,  $J=3.0$  Hz, 1H), 7.5 (t,  $J=3.0$  Hz, 1H), 6.8 (dd,  $J=17.1$ , 10.8 Hz, 1H), 6.5 (dd,  $J=17.4$ , 10.8 Hz, 1H), 6.2 (s, 1H), 6.13 (s, 1H), 5.4 (dd,  $J=17.4$ , 10.8 Hz, 1H), 5.2 (dd,  $J=17.1$ , 10.8 Hz, 1H), 2.7 (m, 2H), 2.4 (m, 2H), 1.97 (s, 3H), 1.95 (s, 3H) ppm.

**4.3.13. (E)-3-Hydroxy-2-((2E,6Z)-octa-2,6-dienylidene)-cyclopentanone (52).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  7.0 (d,  $J=11.4$  Hz, 1H), 6.5 (m, 1H), 6.3 (m, 1H), 5.3 (m, 2H), 5.1 (m, 1H), 2.6 (m, 2H), 1.9–2.4 (m, 8H), 0.9 (t,  $J=7.5$  Hz, 3H) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  206.8, 149.4, 137.3, 137.2, 133.5, 128.0, 126.8, 70.2, 36.4, 34.3, 31.0, 26.9, 21.2, 15.0 ppm. Anal. Calcd for  $\text{C}_{14}\text{H}_{20}\text{O}_2$ : C, 76.33; H, 9.15. Found: C, 76.36; H, 9.12.

**4.3.14. 2-((1E,6Z)-3-Hydroxyocta-1,6-dienyl)cyclopent-2-enone (53).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  7.5 (t,  $J=3.0$  Hz, 1H), 6.8 (dd,  $J=16.0$ , 8.0 Hz, 1H), 6.4 (d,  $J=16$  Hz, 1H), 5.4 (m, 2H), 5.3 (m, 1H), 2.64 (m, 2H), 2.5 (m, 2H), 1.7–2.2 (m, 6H), 0.9 (t,  $J=7.5$  Hz, 3H).

Anal. Calcd for  $\text{C}_{14}\text{H}_{20}\text{O}_2$ : C, 76.33; H, 9.15. Found: C, 76.29; H, 9.14.

#### 4.4. (E)-1-Methyl-2-(pent-1-enyl)cyclopent-2-enol (54)

To a stirred solution of 1.00 g (6.66 mmol) of **24** in 50 mL of dry ether at  $-78^\circ\text{C}$  was added dropwise through a syringe 5.23 mL of an ethereal solution of methyllithium (1.4 M). The reaction mixture was allowed to warm up to room temperature and stirred for 1 h. A saturated aqueous solution of  $\text{NH}_4\text{Cl}$  solution (10 mL) was added dropwise, the layers separated, and the aqueous layers extracted twice with 10 mL portions of ether. The combined organic layers were washed twice with 10 mL of brine each, and the organic layer dried over anhydrous  $\text{MgSO}_4$ . The solvent was removed at reduced pressure and the residue chromatographed on  $\text{SiO}_2$  (3:1 hexanes/EtOAc), providing 0.8 g (72% yield) of **54**.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  6.15 (dt,  $J=16.2$ , 6.6 Hz, 1H), 5.95 (d,  $J=16.2$  Hz, 1H), 5.6 (narrow m, 1H), 2.4–1.9 (m, 6H), 1.45 (sext,  $J=7.2$  Hz, 2H), 1.40 (s, 3H), 0.91 (t,  $J=7.2$  Hz, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  146.6, 132.1, 127.5, 123.2, 83.2, 42.5, 35.5, 28.5, 25.8, 22.5, 13.7 ppm.

#### 4.5. (E)-3-Methyl-2-(pent-1-enyl)cyclopent-2-enone (55)

A solution of 1.0 g (6 mmol) of the tertiary alcohol **54** in 5 mL of  $\text{CH}_2\text{Cl}_2$  was added dropwise to a stirred suspension of 2.58 g (12.0 mmol) of pyridinium chlorochromate (PCC) in 20 mL  $\text{CH}_2\text{Cl}_2$  at  $0^\circ\text{C}$ . The mixture was stirred at room temperature for 1 h, and was diluted with 25 mL of ether. The ethereal solution was decanted from the solid, which was washed with three 20 mL portions of ether. The combined ethereal phases were washed successively with two 25 mL portions of 5% NaOH, 5% HCl, and two 10 mL portions of saturated aqueous  $\text{NaHCO}_3$ , and dried over  $\text{MgSO}_4$ . The solvent was removed at reduced pressure and the residue purified by column chromatography on  $\text{SiO}_2$ , eluting with 3:1 hexanes/EtOAc, to give 0.74 g (69% yield) of **55** as a pale yellow oil.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  6.7 (dt,  $J=16.0$ , 7.2 Hz, 1H), 6.06 (d,  $J=16$  Hz, 1H), 2.55 (m, 2H), 2.35 (m, 2H), 2.12 (s, 3H), 2.0 (m, 2H), 1.5 (m, 2H), 0.9 (t,  $J=7.2$  Hz, 3H). These data are almost identical to those reported for **55**.<sup>13</sup>

**4.5.1. 4-Hydroxy-2-(propen-1-en-2-yl)cyclopent-2-enone (59).**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  7.3 (d, 1H), 6.1 (s, 1H), 5.2 (s, 1H), 4.9 (m, 1H), 3.4 (br, OH), 2.9 (dd, B part of an ABX system,  $^2J=18.6$  Hz, 1H), 2.38 (d,  $^2J=18.6$  Hz, 1H), 1.93 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , TMS):  $\delta$  204.9, 156.2, 144.3, 134.4, 119.9, 68.0, 48.9, 22.5 ppm.

#### 4.6. 3-Methyl-2-pentylcyclopent-2-enone (dihydro-jasmone, 56)

Ketone **55** (0.5 g, 3.0 mmol) was dissolved in 10 mL of methanol, 2%  $\text{PtO}_2$  was added, and the mixture was hydrogenated at atmospheric pressure at room temperature. Hydrogenation was interrupted after the uptake of 1 equiv of  $\text{H}_2$ , and the catalyst filtered off, the residue concentrated at reduced pressure to give **56** in quantitative yield. Its physical and spectroscopic data were identical in all respects with the reported values in literature.

### Acknowledgements

This work was supported by funds from the National Science Foundation (CHE-9729001), the National Institutes of Health, MBRS-Score Program-NIGMS (Grant No. GM52588), and in part from a grant (P20 MD) from the Research Infrastructure in Minority Institutions Program, NCMHD, NIH.

### References and notes

1. *Singlet Oxygen*; Wasserman, H. H., Murray, R. W., Eds.; Academic: New York, NY, 1979.
2. Balci, M. *Chem. Rev.* **1981**, *81*, 91.
3. Kornblum, N.; De La Mare, H. E. *J. Am. Chem. Soc.* **1951**, *73*, 880.
4. Zagorski, M. G.; Salomon, R. G. *J. Am. Chem. Soc.* **1980**, *102*, 2501.
5. Adam, W.; Erden, I. *Angew. Chem.* **1978**, *90*, 223; *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 210.
6. Erden, I.; Amputch, M. *Tetrahedron Lett.* **1987**, *28*, 3779.
7. Erden, I.; Drummond, J.; Alstad, R.; Xu, F. *Tetrahedron Lett.* **1993**, *34*, 1255.
8. Erden, I.; Drummond, J.; Alstad, R.; Xu, F. *Tetrahedron Lett.* **1993**, *34*, 2291.
9. Erden, I.; Xu, F.; Drummond, J.; Alstad, R. *J. Org. Chem.* **1993**, *58*, 3611.
10. Erden, I.; Xu, F.; Cao, W. *Angew. Chem.* **1997**, *109*, 1557; *Angew. Chem., Int. Ed.* **1997**, *36*, 1516.
11. Ishihara, H.; Inomata, K.; Mukaiyama, T. *Chem. Lett.* **1975**, 531.
12. Funel, J.-A.; Prunet, J. *J. Org. Chem.* **2004**, *69*, 4555.
13. Shimada, J.; Hashimoto, K.; Kim, B. H.; Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1984**, *106*, 1759; Nakamura, E.; Shimada, J.; Kuwajima, I. *J. Chem. Soc., Chem. Commun.* **1983**, 498.
14. Stetter, H.; Leinen, H. T. *Chem. Ber.* **1983**, *116*, 254.
15. Johnson, C. R.; Adams, J. P.; Braun, M. P.; Senayake, C. B. W. *Tetrahedron Lett.* **1992**, *33*, 919.
16. For a recent synthesis of ouidenone, see: Flynn, B. L.; Silveira, C. C.; de Meijere, A. *Synlett* **1995**, 812.
17. For a review on Jasmonoids, see: Ho, T.-L. *Synth. Commun.* **1974**, *4*, 265.
18. Dauben, W. G.; Michno, D. M. *J. Org. Chem.* **1977**, *42*, 682.
19. Seo, J.; Fain, H.; Blanc, J.-B.; Montgomery, J. *J. Org. Chem.* **1999**, *64*, 6060.
20. Though 2(3*H*)-oxepinones are the sole products from thermal isomerizations of unsaturated fulvene endoperoxides in aprotic, non-nucleophilic solvents, **57** has been reported to give rise to considerable amounts of **58** in methanol; see Refs. **23** and **24**.
21. Stone, K. J.; Little, R. D. *J. Org. Chem.* **1984**, *49*, 1849.
22. Erden, I.; Xu, F.; Sadoun, A.; Smith, W.; Sheff, G.; Ossun, M. *J. Org. Chem.* **1995**, *60*, 813.
23. Harada, N.; Suzuki, S.; Uda, H.; Ueno, H. *J. Am. Chem. Soc.* **1971**, *94*, 1777; Harada, N.; Uda, H.; Ueno, H.; Utsumi, S. *Chem. Lett.* **1973**, 1173.
24. (a) Skorianetz, W.; Schulte-Elte, K. H.; Ohloff, G. *Angew. Chem.* **1972**, *84*, 3111; *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 330; (b) Skorianetz, W.; Schulte-Elte, K. H.; Ohloff, G. *Helv. Chim. Acta* **1971**, *54*, 1913.