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CYCLOPROPANONES DERIVED FROM SATURATED FULVENE ENDOPEROXIDES: SYNTHESIS OF HIGHLY OXYGENATED ORGANIC COMPOUNDS[1]

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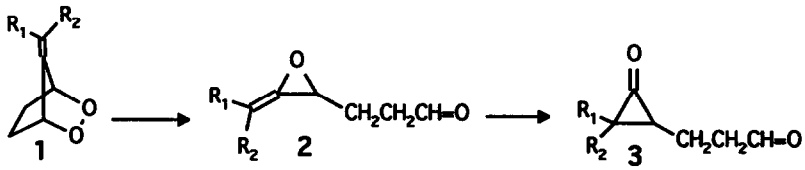
Abstract: Saturated fulvene endoperoxides give highly oxygenated compounds upon thermolysis in the presence of acetic acid. Depending on whether the fulvene precursor is 6-mono or 6,6-disubstituted, one obtains either lactol acetates or 1,5-dicarbonyl compounds, respectively.

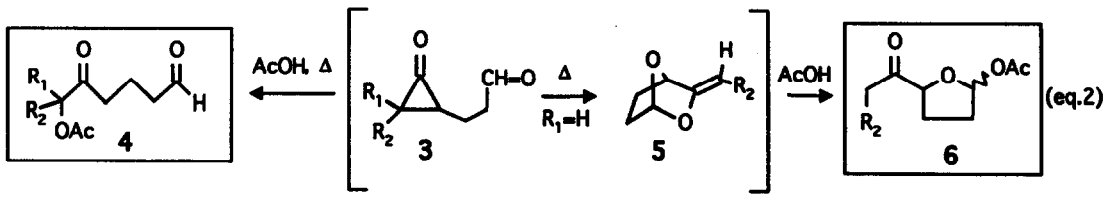
Recently we reported that saturated fulvene endoperoxides give, upon thermolysis, products that stem from allene oxide and/or cyclopropanone intermediates.[2] Cyclopropanone 3 (R_1,R_2=CH_3) was trapped by Diels-Alder reactions; allene oxide 2 (R_1= H, R_2= *t*-Bu) was isolated and observed di-



(eq.1)

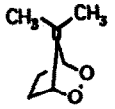
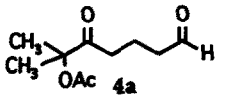
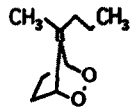
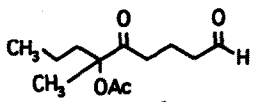
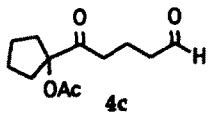
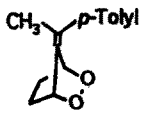
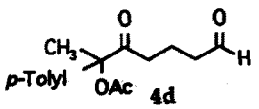
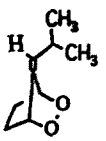
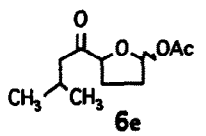
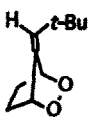
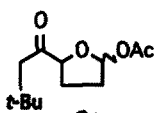
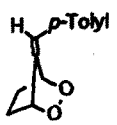
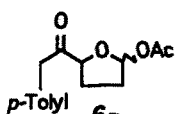
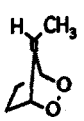
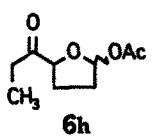
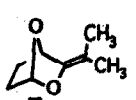
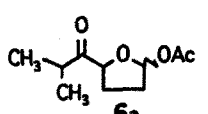
rectly by spectroscopy.[3] While the mechanistic aspects of these reactions are intriguing, and deserve future attention, the synthetic potential of the reactive intermediates 2 and 3 was explored, in hopes of developing synthetic entries into some highly oxygenated organic molecules. Our results show that functionalized 1,5-dicarbonyl compounds and tetrahydrofurans can be obtained by a relatively simple protocol, involving thermolysis of saturated fulvene endoperoxides in the presence of acetic acid.

The requisite endoperoxides were prepared from 6-mono and 6,6-disubstituted fulvenes by singlet oxygenation at -78° C, followed by selective diazene reduction[4] of the resulting unsaturated cycloadducts at low temperature.[5] The peroxides (1a-h) so obtained exhibit moderate stability, enough to permit isolation (caution!) and spectroscopic identification. The yields of the endoperoxides are excellent (~90%), and it is not necessary to isolate them, except for characterization purposes.[6] Thus, addition of an excess of glacial acetic acid to methylene chloride



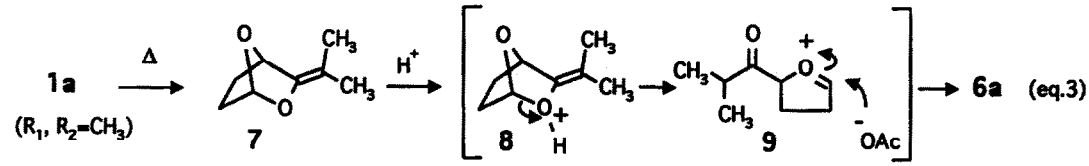
(eq.2)

Table 1. Thermolysis of Saturated Fulvene Endoperoxides in the Presence of AcOH

Substrate	Product	Yield (%)
 1a	 4a	72
 1b	 4b	76
 1c	 4c	67
 1d	 4d	73
 1e	 6e	64
 1f	 6f	78
 1g	 6g	58
 1h	 6h	80
 7	 6a	86

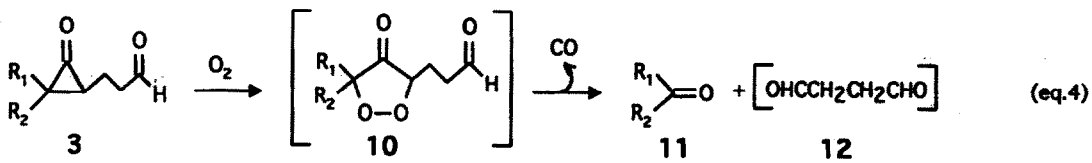
solutions of 1a-h and refluxing for 30 min gives the addition products 4 and 6 listed in Table 1. As seen in the table, the products formed are determined by the initial substrate: endoperoxides derived from 6-mono substituted fulvenes give lactol acetates (6). The 6,6-disubstituted analogs, on the other hand, lead to open chain 1,5-dicarbonyl compounds (4).

The products were isolated by preparative TLC or column chromatography on SiO_2 and identified on the basis of spectral data. The results can be rationalized (eqs.1,2) by assuming that 2-monosubstituted cyclopropanones undergo intramolecular dipolar cycloaddition faster than the acetic acid addition to form 4. The resulting bicyclic acetals (5) then suffer cleavage with acetic acid, leading to the lactol acetates (6). on the other hand, the intramolecular 1,3-dipolar cycloaddition of the 2,2-disubstituted cyclopropanones is comparatively slow, due to greater steric hindrance in the cycloaddition transition state. Thus, the result is addition of acetic acid to C2-C3 of the cyclopropanone in a regioselective manner. This hypothesis was supported by the following experiment: the bicyclic acetal (7) derived from 6,6-dimethylfulvene was first prepared by thermolysis of the respective saturated endoperoxide (1a).[2] It was then subjected to thermolysis in CH_2Cl_2 in the presence of acetic acid. From this reaction one obtained exclusively the lactol acetate (6a) (eq. 3). Thus, the preparation of the latter class of compounds is not restricted to monosubstitu-



ted analogs of 1 as peroxide precursors. In order to obtain the lactol acetates, one would have to change the order of the steps in the procedure, i.e., first thermolyze the peroxide, then treat the resulting bicyclic acetal with acetic acid.

It is worthy of note that when the thermolyses were conducted in the presence of oxygen,, considerable amounts of the carbonyl compounds (11) were formed in several cases (eq.4). Presumably, the cyclopropanone intermediates (3) are trapped by triplet oxygen to give 1,2-dioxolan-4-ones (10) which decompose to 11. Succinaldehyde (12), the other carbonyl fragment from 10 was not observed. Under the reaction conditions, polymerization and loss during the aqueous work up due to its water solubility is expected.[7] Fragmentations of other cyclopropanones have been reported previously, and in each case intermediates such as 10 have been postulated. [8,9]



The identification of the products is based mainly on FT-IR, ^1H (300 MHz, $CDCl_3$) and ^{13}C NMR (75 MHz, $CDCl_3$) spectroscopy. For example, the spectral data of **4a** are characteristic of 5-oxohexanals; its IR spectrum exhibits absorptions at 1723, 1734 and 1737 cm-1 ($\nu_{C=O}$); the ^1H NMR spectrum of **4a** displays a singlet at 9.70 ppm for the aldehyde proton, the CH_2 groups α to the carbonyl groups give rise to triplets centered at δ 2.45 (which in this case overlap and in some cases coincide), the acetyl-CH_3 absorbs at δ 2.0 as a singlet, the *gem*-dimethyl group gives a singlet at 1.4 ppm. There are nine lines in the ^{13}C NMR spectrum at δ 208, 202, 170.5, 83.5, 42.7, 34, 23.7, 21, and 16 ppm. The spectral data for **6h** are characteristic of lactol acetates: FT-IR: 1750, 1730 cm^{-1} ($\nu_{C=O}$); ^1H NMR (both epimers, **6h** and **6h'**): δ 6.45 and 6.38 (s, 1H); 4.6 and 4.45 (m, 1H); 2.4-2.7 (m, 2H); 2.0 (2H); 2.05 and 2.06 (s, 3H); 1.6 (m, 2H); 0.9 (2 overlap. t, 3H); ^{13}C NMR: δ 211.5 (211), 170.6, 99.7, 85.8 (84.5), 41.2 (40.5), 32.9 (31.8), 26.6 (26.4), 21.8 (17.2), 14.4 (14.3) ppm.

Even though the yields of **4** and **6** are moderate, the fact that these highly functionalized compounds can be obtained from readily available fulvene precursors in a short sequence makes the methodology described herein attractive. This is important, since suitably substituted derivatives of **6** could serve as precursors of various natural products which contain a tetrahydrofuran or γ-lactone moiety.[10,11] Moreover, for the construction of the 6,8-dioxabicyclo[3.2.1]octane ring system, common to several insect pheromones such as brevicomin, either **4** or **6** could be employed.[12] Applications to obvious targets molecules are in progress.

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References and Notes

1. Part of this work was presented at the 203rd National Meeting of the American Chemical Society in San Francisco, California, on April 8, 1992.
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7. For chemical properties of succinaldehyde (**12**), see *Beilstein*, *1*, 767, and references cited therein.
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