Chemistry of Singlet Oxygen. Synthesis of Functionalized Cyclopentenones from Saturated Fulvene Endoperoxides

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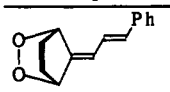
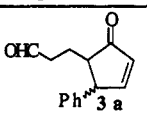
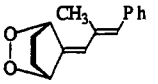
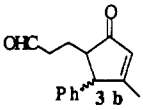
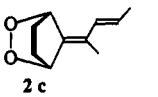
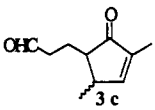
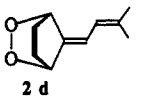
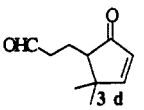
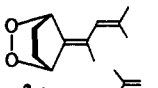
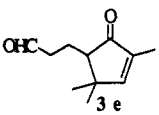
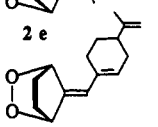
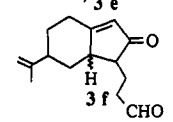
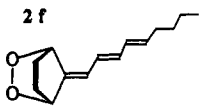
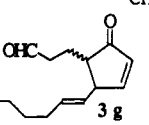
Summary: Saturated fulvene endoperoxides derived from 6-vinylfulvenes prove to be excellent precursors of 5-propylal-substituted 2-cyclopentenones; allene oxides and/or cyclopropanones are postulated as intermediates in these reactions.

The development of methods for the synthesis of cyclopentenones continues to be one of the most active areas of research[1,2] owing to the wide abundance of this structural unit in a large number of natural products such as the jasmonoids,[3] prostaglandins,[4] dicranenones,[5] and rethrolones.[6] Moreover, cyclopentanones containing a propylal substituent on the 2-position have been important targets in the synthesis of fused cyclopentanoids.[7] We report here an unconventional entry into side-chain functionalized 2-cyclopentenones. The methodology is based on an intramolecular cycloaddition of reactive intermediates which can be formally considered as vinylcyclopropanones. The latter compounds are formed during the thermal decomposition of 5,6-dihydrofulvene endoperoxides (**2**)[8-10] derived from 6-vinylfulvenes (**1**)[11] by photooxygenation[12] at −78 °C and subsequent selective diazene reduction of the unsaturated endoperoxides.[13,14] Thermolysis of the endoperoxides in refluxing CCl_4 gives the diversely substituted 2-cyclopentenones (**3**) (Table I).[15]

Table I. Cyclopentenones from Fulvene Endoperoxides

endoperoxide	product	yield (trans:cis)
 **2 a**	 **3 a**	85% (8:1)
 **2 b**	 **3 b**	83% (2:1)
 **2 c**	 **3 c**	90% (6:1)
 **2 d**	 **3 d**	68%
 **2 e**	 **3 e**	65%
 **2 f**	 **3 f**	75% (1.8:1)
 **2 g**	 **3 g**	70% (20:1)

Scheme I describes the mechanisms that satisfactorily account for our results.[16,17] Either of the three possible intermediates **4**, **5**, or **6** could serve as the precursor of the cyclopentenones **3**. In cases where more than one stereoisomer was possible (i.e., C-4 substituted derivatives), the *trans*-isomer was dominant.[18] Although the yields of **3** are modest in a few cases,[19] the present protocol offers several advantages: the starting vinylfulvenes are readily available; the photooxygenation and reduction steps are carried out in a one-pot procedure; the endoperoxides need not be isolated and can be thermolyzed in the same solvent (longer reflux in CH_2Cl_2 needed) after filtration to remove KOAc; even more importantly, this method permits the synthesis of cyclopentenones carrying a propylal group on C-5, amenable to further synthetic transformations, in-

(1) (a) Ellison, R., A. *Synthesis* **1973**, 397. (b) Bernasconi, S.; Capellini, C.; Sisti, M. *Synth. Commun.* **1978**, *8*, 71. (c) Trost, B. M.; Bogdanowicz, M. J. *J. Am. Chem. Soc.* **1973**, *95*, 5311.

(2) (a) Schore, N. *Organic Reactions*; Paquette, L. A., Ed.; Wiley & Sons: New York, 1991; Vol. 40, pp 1-90. (b) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081.

(3) Saul, E. L. *Am. Perfum. Essent. Oil Rec.* **1943**, *45*(5), 27.

(4) Bartmann, W. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 337.

(5) Ichikawa, T.; Namikawa, K.; Yamada, K.; Sakai, K.; Kondo, K. *Tetrahedron Lett.* **1985**, 2089.

(6) Bergstrom, S. *Science* **1967**, *157*, 382.

(7) Paquette, L. A. Recent Developments in Polyquinane Chemistry. In *Topics in Current Chemistry;* Springer Verlag: Heidelberg, 1984; p 119.

(8) Erden, I.; Amputch, M. *Tetrahedron Lett.* **1987**, *28*, 3779.

(9) Erden, I.; Drummond, J.; Alstad, R.; Xu, F. P. *Tetrahedron Lett.* **1993**, *34*, 1255.

(10) Erden, I.; Drummond, J.; Alstad, R.; Xu, F. P. *Tetrahedron Lett.* **1993**, *34*, 2291.

(11) (a) Stone, K.; Little, R. D. *J. Org. Chem.* **1984**, *49*, 1849. (b) Griesbeck, A. *J. Org. Chem.* **1989**, *54*, 4981. (c) Neuenschwander, M.; Meuche, D.; Schaltegger, H. *Helv. Chim. Acta* **1963**, *46*, 1760.

(12) *Singlet Oxygen*; Wasserman, H. H., Murray, R. W., Eds.; Academic Press: New York, 1979.

(13) Coughlin, D. J.; Salomon, R. G. *J. Am. Chem. Soc.* **1977**, *99*, 655. Coughlin, D. J.; Brown, R. S.; Salomon, R. G. *J. Am. Chem. Soc.* **1979**, *101*, 1533.

(14) (a) Adam, W.; Erden, I. *Angew. Chem.* **1978**, *90*, 223. (b) Little, R. D.; Dang, L. L.; Venegas, M. G.; Merlic, C. *Tetrahedron Lett.* **1983**, *24*, 4499.

(15) Products of intramolecular 1,3-dipolar cycloaddition of the cyclopropanones to the aldehyde group were also formed as minor byproducts which were readily separated from the cyclopentenones by chromatography.

(16) A similar cyclization during the epoxidation of vinylallenes has previously been observed by two groups: (a) Bertrand, P. M.; Dulcere, J. P.; Gil, G. *Tetrahedron Lett.* **1977**, 4403. (b) Kim S. J.; Cha, J. K. *Tetrahedron Lett.* **1988**, *29*, 5613. The latter chemists propose an *antarafacial* pericyclic ring closure of a vinylcyclopropanone (or the corresponding zwitterion) as the mechanism responsible for the stereoselective cyclopentenone formation.

(17) The reason(s) for the observed stereochemical preferances and the variations in isomer ratios are subject to speculation at this time. It is evident that the (*Z*)-alkenyl-substituted allene oxides exhibit less stereoselectivity than the (*E*)-alkenyl analogs, suggesting that the 3 + 2 cycloaddition is not entirely concerted. A detailed discussion of the cycloaddition mechanisms and the consequences for the product stereochemistry are reserved to a full account of this subject.

(18) The *trans/cis* assignments to the products **3a-g** were based on the more upfield shift (~0.5 ppm) of the protons on C4 in the *trans*-products relative to those in the *cis*-products; see: Anteunis, M; Danneels, D. *Org. Magn. Res.* **1975**, *7*, 345.

(19) The product yields and the isomer ratios in each entry in Table I are the averages from at least two trials.

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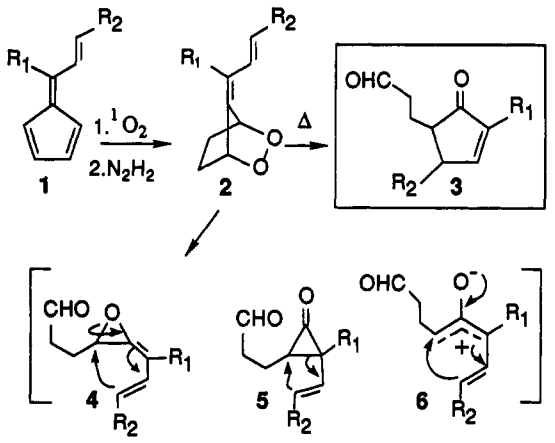
Scheme I



cluding cyclopentene (or cyclopentanone) annulation by way of the McMurry reaction[20] and intramolecular lactol or lactone annulation. Moreover, intramolecular aldol reaction of the corresponding cyclopentanones would lead to bicyclo[3.2.1]octan-8-ones.

In summary, we have uncovered a new, synthetically useful facet of the "fulvene endoperoxide → allene oxide/cyclopropanone" rearrangements in the form of a short, versatile approach to 2-cyclopentenones bearing a functional group on the side chain. We are presently exploring applications of this methodology to obvious natural targets and/or their precursors.

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Supplementary Material Available: Typical experimental procedures and spectral data and physical constants for **1a–g**, **2a–g**, and **3a–g** (5 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(20) McMurry, J. E.; Lectka, T.; Rico, J. G. *J. Org. Chem.* **1989**, *54*, 3748 and references cited therein.