Communications

Sensitized Photooxygenation of Linear Monoterpenes Bearing Conjugated Double Bonds

Summary: Sensitized photooxygenation of linear monoterpenes bearing conjugated double bonds, such as α-myrcene, epoxymyrcene, and epoxyhymenthrene was found to afford the corresponding 1,4-endoperoxides, i.e., 3,6-dihydro-1,2-dioxins.

Sir: It has recently been reported that 1,4 cycloaddition of singlet oxygen ($^1O_2$) to acyclic conjugated dienes occurs readily, even if an allylic hydrogen exists in the same molecule.[1] This fact seems to show that the dienophilic reactivity of $^1O_2$ surpasses the other two modes of reaction affording hydroperoxides and 1,2-dioxetanes. Contrary to this expectation, however, β-myrcene (**1**), which has both isolated and conjugated double bonds, is known to give a mixture of hydroperoxides **2** and **3** and thus no reaction occurs on the 1,3-diene moiety of **1**.[2] To shed light on the reactivities of various double bonds toward $^1O_2$, we have now reinvestigated the sensitized photooxygenation of the monoterpene **1** and have found that the conjugated double bond in **1** is also reactive to $^1O_2$, although the isolated one is far more reactive.

A solution of **1** (0.03 mol) and Rose Bengal (2×10^{-4} mol) in dichloromethane containing 5% methanol was irradiated under an oxygen atmosphere with a halogen lamp (Toshiba JD 100V 500W) for 1.5 hr.[3] After removal of the solvent under reduced pressure, the residual liquid was fractionated by column chromatography on silica gel with *n*-hexane. The first eluate contained unreacted **1** (3%). The hydroperoxides **2** (36%) and **3** (56%) were then eluted in this order. Further elution of the column with benzene afforded a mixture of new hydroperoxides **4** and **5** (0.3%).[4] Prolonged irradiation (4.5 hr) of a solution of **1** gave a mixture of **2** and **3** in 44% total yield and a mixture of **4** and **5** in 20% total yield (Figure 1). These results clearly demonstrate that **4** and **5** are produced by further photooxygenation of **2** and **3** respectively. This conclusion was now confirmed by the following experiments. When a solution of the hydroperoxides **2** in carbon tetrachloride was irradiated for 4 hr using tetraphenylporphine as a sensitizer, the 3,6-dihydro-1,2-dioxin **4** was obtained in 35% yield.[5] Similar photooxygenation of **3** for 3 hr also afforded the cyclic peroxide **5** in 45% yield. The physical properties of these hydroperoxy 1,2-dioxins, as well as the other dioxins (vide infra), are collected in Table I (microfilm edition).

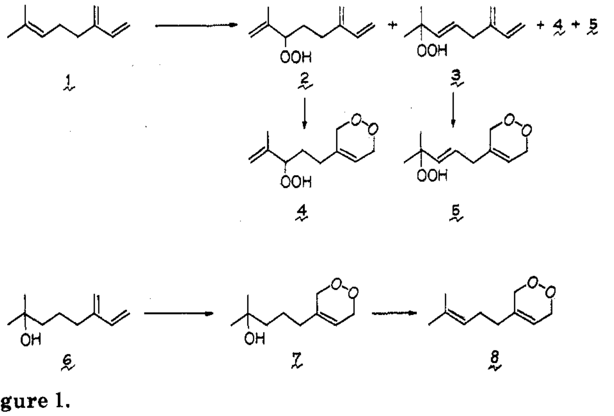

Figure 1.

One of the other possible products from **1** would be the dioxin **8** resulting from the selective oxygenation of the diene moiety in **1**. An authentic sample of **8** was prepared by dehydration of **7** with P_2O_5 in dichloromethane at room temperature in 53% yield. The dioxin **7** was synthesized from myrcenol **6**[6] in 81% yield by the sensitized photooxygenation under conditions similar to those described above. The presence of **8** could not be proved, although the NMR spectrum of the crude product obtained by the oxygenation of **1** was carefully compared with that of the authentic sample of **8**.

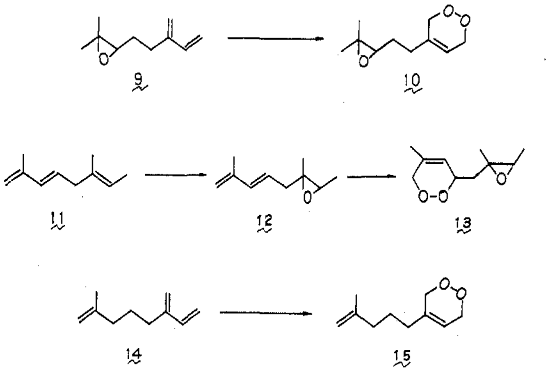

Figure 2.

The observed result shows that, under the reaction conditions, the conjugated double bond in **1** is significantly less reactive to $^1O_2$ than is the isolated one. Consequently, when the isolated double bond in **1** is protected by epoxidation, as in epoxymyrcene (**9**),[7] the oxygenation now occurs smoothly on the conjugated diene to afford the epoxy 1,2-dioxin **10** in 41% yield (Figure 2). The protection of the reactive double bond by epoxidation was also successful in the case of hymenthrene (**11**);[3] epoxyhymenthrene (**12**)[8] underwent 1,4 cycloaddition to $^1O_2$ to give the 1,2-dioxin **13**, mp 57–58° (colorless needles from *n*-hexane), in 59% yield, while **11** itself afforded a mixture of hydroperoxides.[9]

The selective formation of **4** and **5** from **2** and **3**, respectively, suggested that the isolated double bond with two alkyl substituents appeared to be less reactive to $^1O_2$ than the conjugated 1,3-diene. On the basis of this assumption, we then examined the oxygenation of α-myrcene (**14**).[10] Irradiation of **14** under similar conditions now produced selectively the expected 1,2-dioxin **15** in 79% yield. In conclusion, the reactivity of carbon–carbon double bonds toward $^1O_2$ follows roughly the order shown: trisubstituted monoolefin > 1,3-diene with an alkyl substituent on the 2 position > 1,1-disubstituted monoolefin.[11]

The observed selectivity as well as the oxygenation products obtained by these experiments are useful tools for the synthesis of naturally occurring furanoterpenes. These results will be presented in forthcoming communications.

Supplementary Material Available. Table I will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American

Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for $4.00 for photocopy or $2.50 for microfiche, referring to code number JOC-75-2259.

References and Notes

(1) (a) K. Kondo and M. Matsumoto, *J. Chem. Soc., Chem. Commun.*, 1332 (1972); (b) E. Demole, C. Demole, and D. Berthet, *Helv. Chim. Acta*, **56,** 265 (1973).

(2) R. L. Kenney and G. S. Fisher, *J. Am. Chem. Soc.*, **81,** 4288 (1959).

(3) Monoterpenes **1** and **11** were commercially available.

(4) All the peroxides obtained in this work were colorless oils, unless otherwise stated, and gave satisfactory analytical data.

(5) When the sensitized photooxygenation of **2** and **3** were carried out in dichloromethane–methanol mixed solvent, the peroxides **4** and **5** were also obtained, although the reaction was slow and the yield was low.

(6) G. V. Piglevskii and Z. Enebish, *Zh. Obshch. Khim.*, **30,** 1051 (1960).

(7) The epoxide **9** was prepared from **1** via the corresponding bromohydrin by a modification of the reported method: E. E. van Tamelen and T. J. Curphey, *Tetrahedron Lett.*, 121 (1962), 67%, bp 76–80° (13 mm) [lit. bp 73–75° (14 mm) reported by G. V. Pigulevskii and N. L. Prokudina, *Dokl. Akad. Nauk. SSSR*, **67,** 511 (1949)].

(8) The epoxide **12** was prepared from **11** by oxidation with *m*-chloroperbenzoic acid in dichloromethane in 48% yield: bp 78–81° (11 mm); NMR (CCl_4) δ 6.26 (d, J = 17.0 Hz, 1 H), 5.62 (d of t, J = 17.0 and 6.0 Hz, 1 H), 2.88 (q, J = 5.8 Hz, 1 H), 2.34 (br d, J = 6.0 Hz, 2 H), 1.83 (s with fine coupling, 3 H), 1.31 (d, J = 5.8 Hz, 3 H), and 1.17 (s, 3 H).

(9) The mixture (68% yield) was comprised of at least two hydroperoxides which could be assigned as 2,6-dimethyl-6-hydroperoxy-1,3,7-octatriene and 7-hydroperoxy-2-methyl-6-methylene-1,3-octadiene based on the NMR spectrum.

(10) M. Mitzner, E. T. Theimer, L. Steinbach, and J. Wolt, *J. Org. Chem.*, **30,** 646 (1965).

(11) The 1,2-disubstituted monoolefin might also be less reactive than the 1,3-diene toward $^1O_2$, as the 1,2-dioxin **5** was selectively formed from **3**.

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1,3-Dipolar Cycloadditions of Azomethine Imines and Sulfenes

Summary: The first examples of a new heterocyclic ring system (**2**) have been prepared by the 1,3-dipolar cycloaddition of azomethine imines **1** and sulfenes.

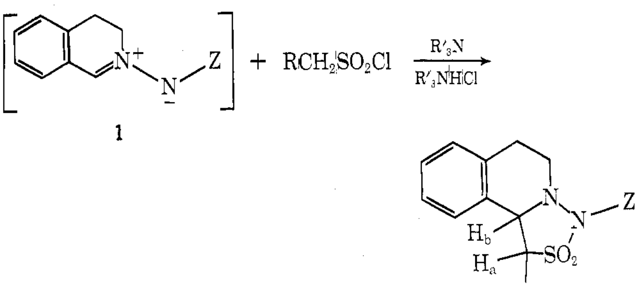
Sir: Although numerous examples of 1,2 and 1,4 cycloaddition reactions of sulfenes to yield four- and six-membered-ring heterocycles, respectively, are known,[1] only two examples of the formation of five-membered rings by cycloaddition reactions of sulfenes have been reported.[2,3] Reactions of other 1,3 dipoles under sulfene-generating conditions have led to products other than those expected from 1,3-dipolar cycloaddition reactions.[1] To further define the reactivity of sulfenes and dipolarophiles, the reactions of sulfenes with highly reactive azomethine imines of the 3,4-dihydroisoquinoline type (**1**)[4] have been explored.

The brightly-colored dipoles **1** were prepared in situ by the thermal dissociation of their respective dimers[4-6] in aromatic hydrocarbon solvents. Dropwise addition of a solution of the alkanesulfonyl chloride to the hot mixture containing the azomethine imine and an excess of trialkylamine led to the formation of adducts **2** (Table I; also, see supplementary material). Derivatives of this ring system have not previously been described. The structural assignments of **2** were based primarily on spectral and elemental analysis data. Further support for these assignments was obtained through the dehydrogenation of three of the adducts (**2a, 2b,** and **2i**) to compounds **3** by 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ).

Table I
Preparation of 1,2,3-Thiadiazolidine Derivatives

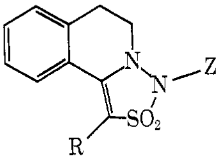
2[a]	Z	R	R′	Conditions[b]	Yield,[c] %
a	C_6H_5	H	Et	A	92
b	C_6H_5	C_6H_5	Et	A	77
c	C_6H_5	Cl	Et	A	29
d	C_6H_5	C_6H_5CO	Et	A	31
e	*p*-$NO_2C_6H_4$	H	*n*-Pr	B	86
f	*p*-$NO_2C_6H_4$	C_6H_5	*n*-Pr	B	88
g	EtO_2C	H	*n*-Pr	C	51
h	EtO_2C	C_6H_5	*n*-Pr	C	61
i	C_6H_5CO	H	Et	D	43
j	C_6H_5CO	C_6H_5	Et	D	57
k	*p*-$CH_3C_6H_4SO_2$	H	*n*-Pr	B	29
l	*p*-$CH_3C_6H_4SO_2$	C_6H_5	*n*-Pr	B	58

[a] Satisfactory elemental analysis data were obtained for compounds **2a** through **2l** (see supplementary material). [b] (A) In benzene at 70°; (B) in toluene at 100°; (C) in mesitylene at 155°; (D) in benzene at 80°. [c] Isolated yields of purified product.



1

2



3

The reactions of substituted sulfenes with the dipoles **1** could lead to the formation of two possible stereoisomers of **2** (i.e., H_a and H_b may be cis or trans). The stereoselectivity with which adducts **2b, 2h, 2j,** and **2l** were formed was studied in some detail by observing the splitting patterns of H_a and H_b in the δ 6.5–4.5 region of their NMR spectra.[7] The NMR spectrum of the crude product isolated from the reaction in which **2b** was formed indicated that the two possible isomers were present in approximately equal amounts.[8] These two isomers were separated by column chromatography and were shown to be noninterconvertible under the conditions leading to their formation.

In contrast to **2b**, adduct **2f** was formed with a high degree of stereoselectivity. Within the limits of detection of the NMR spectrometer, only one isomer of **2f** was observed in the crude product. The NMR spectra of crude adducts **2j** and **2l** showed a great preponderance of one isomer, although small amounts (<10% and <20%, respectively) of the second isomers may have been formed.[10] Purification of crude adducts **2f, 2j,** and **2l** led to the isolation of a single isomer of each adduct.