Unsaturated Ozonides from the Ozonolysis of Nonconjugated Cyclodienes in the Presence of Carbonyl Compounds

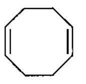
Shin Hee Park and Tae Sung Huh*

Department of Chemistry, The Catholic University of Korea, Puchon 422-743, Korea

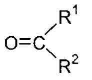
Received July 12, 2001

Keywords : Unsaturated ozonide, Ozonolysis, Nonconjugated cyclodiene, Carbonyl compound.

Ozonolysis reactions of cyclodienes in nonparticipating solvents have not been studied extensively.[1-4] Griesbaum *et al.* had shown that in methanol ozone attacks the double bond of nonconjugated cyclodienes simultaneously, in contrast to those of conjugated cyclodienes.[5-8] In previous work, we had shown that the carbony oxide intermediates, generated from the ozonolysis of 1,5-cyclooctadiene **1** can be trapped by carbonyl compounds **2** to form the corresponding unsaturated ozonide **3**, monoozonide **4**, diozonide **5** and dialdehyde **6**.[9]

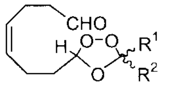


1

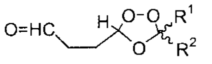


2

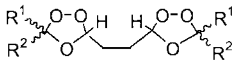
	A	B
R^1	H	CH_3
R^2	H	CN



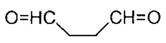
3



4

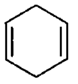


5

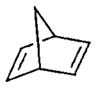


6

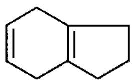
We have now tried whether this mode of reaction can be extended to ozonolyses of nonconjugated cyclodienes **7** in the presence of carbonyl compounds **2**.



7a



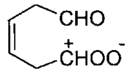
7b



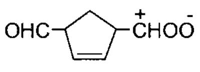
7c

In pursuit of our goal, we ozonized the noncojugated cyclodienes **7a-c** in dichloromethane with about one equivalent of ozone in the presence of carbonyl compounds **2A** and **2B**, respectively.

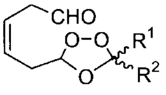
Ozonolyses of 1,4-cyclohexadiene (**7a**) and bicyclo[2.2.1]-hepta-2,5-diene (**7b**) in the presence of carbonyl compounds **2A** and **2B** afforded the corresponding unsaturated ozonides (*Z*)-**9aA**, (*Z*)-**9aB**, **9bA** and **9bB**, *via* intermediates **8a** and **8b**, which have been isolated in yields of 49.7%, 48.0%, 59.0% and 60.7%, respectively.



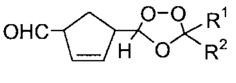
8a



8b

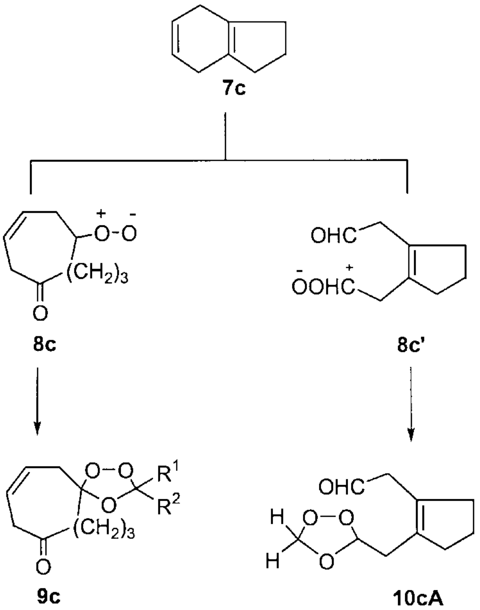


9a



9b

In the ozonolysis of bicyclo[4.3.0]nona-3,6-diene (**7c**) in the presence of **2A** and **2B** the formation of intermediated **8c** was favored over **8c'** as evidenced by the formation of 43% and 37% of ozonide **9cA** and **9cB**, yet only 21% of **10cA**.



7c

8c

8c'

9c

10cA

From the results of the ozonolysis of **7a**, **7b** and **7c** it can be concluded that, in contrast to the nonconjugated cyclodienes **1**, the two double bonds in nonconjugated cyclodienes **7** are stepwise attacked by ozone to give unsaturated ozonides **9** and **10**. It can be further concluded that cleavage of the double bonds in **7c** by ozone occurs predominantly in one direction, with formation of higher substituted carbonyl oxide **8c**.

All of the ozonides have been isolated by column chromatography on silica gel. The (*Z*)-isomers were assigned by NOESY measurements. Ozonides (*Z*)-**9aB**, **9bB** and **9cB** were mixture of two diastereoisomers at the ozonide rings.[10,11]

The structures of all isolated ozonides were established by ^1H and ^{13}C NMR spectroscopy, and their reduction with triphenylphosphine to give the expected dials and carbonyl compounds **2** in a ratio of *ca.* 1 : 1.

In the ^{1}NMR spectra, the ozonide moieties of the cross-ozonides **9aA**, **9aB**, **9bA**, **9bB** and **10cA** could be recognized by signals of the CH groups in the ozonide rings. They appeared in the range of δ 5.08-5.15 as a two singlet and δ 5.23 as triplet for **9aA**, δ 5.30 as triplet for **9aB**, δ 5.07 as multiplet and δ 5.16 as doublet for **9bA** and δ 5.11-5.30 as multiplet for **9bB**, δ 5.08-5.14 as two singlet for **9cA** and δ 5.07-5.19 as two singlet for **10cA**. In addition, the double bonds and aldehyde groups in the side chains of all ozonides showed their CH=CH and CH=O signals in the range δ 5.67-5.90 as multiplet and δ 9.60-9.69 as singlet or triplet. ^{13}C NMR spectra of all ozonides, two chemically nonequivalent carbon atoms in the ozonide rings exhibited signals in the range δ 93.8-114.0. In addition, the carbon atoms of CN groups, double bonds and aldehyde groups showed signals in the range of δ 116-117, δ 123.4-134.9 and δ 198.7-202.5.[12-13]

The structural assignment of the ozonide of structure **9cA** and **9cB** are based on ^{1}H and ^{13}C NMR signals of the CH_2 groups and CH=CH in the cyclic ring systems. In the ^{1}H NMR spectra, the CH_2 groups appeared as multiplet signals, in the range of δ 1.82, 2.23-2.37, 2.47-2.53, 2.65-2.70 and 3.20 and the CH=CH groups appeared as multiplets, in the range of 5.75-5.80. In addition, CH group in the ozonide ring showed in the range of δ 5.08 and 5.14 as two singlet for **9cA** and methyl group showed at δ 1.86 as singlet for **9cB**. In the ^{13}C NMR, the signals of the C=O group, two carbon atoms in the ozonide rings and double bonds appeared in the range of δ 211.3-211.5, 93.8-110.9 and 122.1-128.4. In addition, the carbon atom of CN group for **9cB** showed at δ 116.5.

The successful coozonolysis of the nonconjugated cyclodienes in the presence of carbonyl compounds opens a convenient short-path synthesis for the hiterto unknown types of unsaturated ozonides **9** and **10**, which bear double bonds and aldehyde group at the side chains.

Experimental Section

NMR spectra. Brucker AC-300. ^{1}H-NMR and ^{13}C-NMR spectra were recorded in $CDCl_3$ with TMS as internal references. Chromatographic separations: Flash column chromatography on silica gel.

Ozonolysis Reactions. All ozonolyses were carried out in 50 mL of dichloromethane at -78 °C using one molar equivalent ozone. Residual ozone was flushed out with nitrogen, the solvent was distilled off at room temperature under reduced pressure and the residue was separated by flash column chromatography. All chromatography described below was carried out with dichloromethane/diethyl ether in a ratio of 15 : 1(v/v). The formaldehyde (2A) used in the coozonolysis was freshly prepared by pyrolysis of paraformaldehyde in each case.

Reductions of Ozonides. A solution of 20-40 mg of an ozonide and an excess of triphenylphosphine in 0.6 mL of $CDCl_3$ was kept at room temperature for 24 hours. The products were analyzed by ^{1}H NMR spectroscopy.

Ozonolysis of 7a in the presence of 2A: Ozonolysis of 0.24 g (3.0 mmol) of **7a** and 1 mL of **2A** gave a liquid residue, from which 0.24 g (1.49 mmol, 49.7%) of (*Z*)-**9aA** was isolated.

(*Z*)-5-(1,2,4-Trioxolan-3-yl)-3-pentenal (9aA): Colorless liquid. ^{1}H NMR: δ 2.49 (m, 2H), 3.23 (d, *J* = 5.16 Hz, 2H), 5.08 (s, 1H), 5.15 (s, 1H), 5.23 (t, *J* = 2.51 Hz, 1H), 5.74 (m, 2H), 9.69 (s, 1H). ^{13}C NMR: δ 30.69, 42.92, 94.57, 102.72, 123.42, 126.59, 199.32. Anal. calcd. for $C_7H_{10}O_4$ (158.2): C, 53.15; H, 6.37. found: C, 53.48; H, 6.27.

Reduction of (*Z*)-**9aA** with TPP gave 3-hexen-1,6-dial.

(*Z*)-5-(5-Cyano-5-methyl-1,2,4-trioxolan-3-yl)-3-pentenal (9aB): Yield, 48.0%. Colorless liquid (a mixture of two diastereoisomers at the ozonide ring). ^{1}H NMR: δ 1.87 (m, 3H), [2.24 (m), 2.26 (m)] (2H), 3.26 (m, 2H), 5.30 (t, *J* = 5.30 Hz, 1H), 5.67 (m, 1H), 5.88 (m, 1H), 9.69 (t, *J* = 2.57 Hz, 1H). ^{13}C NMR: δ 20.56, 20.71, 28.28, 32.60, 42.33, 97.98, 105.04, 115.87, 116.46, 123.72, 124.16, 125.28, 198.71. Anal. calcd. for $C_9H_{11}O_4N$ (197.2): C, 54.82; H, 5.62. found: C, 54.64; H, 5.43.

Reduction of (*Z*)-**9aB** with TPP gave 3-hexen-1,6-dial and acetyl cyanide.

4-(1,2,4-Trioxolan-3-yl)-2-cyclopentenecarbaldehyde (9bA): Yield, 59.0%. Colorless liquid. ^{1}H NMR: δ 2.08-2.28 (m, 2H), 3.14 (m, 1H), 3.54 (m, 1H), 5.04 (s, 1H), 5.06 (s, 1H), 5.16 (d, *J* = 7.80 Hz, 1H), 5.90 (m, 2H), 9.60 (s, 1H). ^{13}C NMR: δ 24.00, 47.57, 58.37, 94.22, 104.36, 129.83, 132.97, 200.89. Anal. calcd. for $C_8H_{10}O_4$ (170.2): C, 56.46; H, 5.92. found: C, 56.37; H, 5.76.

Reduction of **9bA** with TPP gave 2-cyclopentene-1,4-dicarbaldehyde.

4-(5-Cyano-5methyl-1,2,4-trioxolan-3-yl)-2-cyclopentenecarbaldehyde (9bB): Yield, 60.7%. Colorless liquid (a mixture of diastereoisomers at the ozonide ring). ^{1}H NMR: δ 1.89 (m, 3H), 2.19-2.32 (m, 2H), [3.17 (m), 3.32 (m)] (1H), 3.61 (m, 1H), [5.11 (m), 5.30 (m)] (1H), 5.84 (m, 1H), 5.98 (m, 1H), 9.64 (s, 1H). ^{13}C NMR: δ 20.36, 20.89, 23.74, 24.35, 46.07, 49.89, 98.59, 107.27, 116.21, 116.84, 130.55, 130.91, 132.14, 200.34. Anal. calcd. for $C_{10}H_{11}O_4N$ (209.2): C, 57.41; H, 5.30; found: C, 57.56; H, 5.33.

Reduction of **9bB** with TPP gave 2-cyclopentene-1,4-dicarbaldehyde and acetyl cyanide.

Ozonolysis of 7c in the presence of 2A: Ozonolysis of 0.36 g (3.0 mmol) of **7c** and 1 mL of **2A** gave a liquid residue, from which 0.27 g (1.27 mmol, 42.3%) of **9cA** and 0.13 g (0.63 mmol, 21.0%) of **10cA** were isolated.

1,2,4-Trioxaspiro[4.8]trideca-7-en-11-one (9cA): Colorless liquid. ^{1}H NMR: δ 1.82 (m, 2H), 1.91 (m, 2H), 2.45-2.54 (m, 4H), 3.18 (m, 2H), 5.08 (s, 1H), 5.14 (s, 1H), 5.75 (m, 2H) ^{13}C NMR: δ 19.20. 33.25, 33.61, 42.59, 43.20, 93.82, 110.92, 124.61, 128.39, 211.49. Anal. calcd. for $C_{11}H_{14}O_4$ (210.3): C, 62.83; H, 6.71. found: C, 63.14; H, 6.84.

2-[(1,2,4-Trioxolan-3-yl)methyl]cyclopentenylethanal (10cA): Colorless liquid. ^{1}H NMR: δ 1.82 (m, 2H), 2.37-2.53 (m, 4H), 2.65 (m, 2H), 3.20 (m, 2H), 5.07 (s, 1H), 5.19 (s, 1H), 5.23 (t, *J* = 4.85 Hz, 1H). 9.60 (t, *J* = 1.53 Hz, 1H). ^{13}C NMR: δ 22.17, 31.70, 37.23, 44.43, 94.46, 102.46, 123.62, 131.29, 199.67. Anal. calcd. for $C_{11}H_{14}O_4$ (210.3): C, 62.83; H, 6.71. found: C, 62.62; H, 6.87.

3-Cyano-3-methyl-1,2,4-Trioxaspiro[4.8]trideca-7-en-

11-one (9cB): Yield, 36.7%. Colorless liquid (a mixture of two diastereoisomers at the ozonide ring). ^{1}H NMR: δ 1.82 (m, 2H), 1.86 (s, 3H), 2.23 (m, 2H), 2.47 (m, 2H), 2.70 (m, 2H), 3.23 (m, 2H), 5.68 (m, 1H), 5.80 (m, 1H). ^{13}C NMR: δ 18.85, 27.98, 31.18, 32.40, 34.76, 42.77, 98.04, 114.87, 116.51, 122.14, 125.09, 211.38. Anal. calcd. for $C_{13}H_{15}O_4N$ (249.3): C, 62.63; H, 6.06. found: C, 62.43; H, 6.12.

Acknowledgment. This work supported by the Catholic University of Korea Research Fund in the fiscal year of 2001.

References

1. Fata, W. I.; Erman, W. F. *J. Org. Chem*. **1968**, *33*, 1656.
2. Bailey, P. S.; Bath, S. S.; Dobinson, F.; Garcia-Sharp, F. J.; Johnson, C. D. *J. Org. Chem*. **1961**, *26*, 694.
3. Pappas, J. J.; Keaveney, W. P.; Berger, M.; Rush, R. V. *J. Org. Chem*. **1968**, *33*, 787.
4. Callighan, R. H.; Wilt, M. H. *J. Org. Chem.* **1961**, *26*, 5212.
5. Griesbaum, K.; Keul, H.; Agarwal, S.; Zwick, G. *Chem. Ber.* **1983**, *116*, 409.
6. Griesbaum, K.; Zwick, G. *Chem. Ber.* **1985**, *118*, 3041.
7. Griesbaum, K.; Mertens, H.; Jung, I.-Ch. *Can. J. Chem*. **1990**, *68*, 1369.
8. Griesbaum, K.; Jung, I.-Ch. Mertens, H. *J. Org. Chem.* **1990**, *55*, 6024.
9. Park, S. H.; Lee, J. Y.; Huh, T. S. *Eur. J. Org. Chem*. **2001**, 3083.
10. Huh, T. S. *Bull. Korean Chem. Soc*. **1998**, *19*, 1152.
11. Murray, R. W.; Youssefyeh, R. D.; Story, P. R. *J. Am. Chem. Soc*. **1967**, *89*, 2429.
12. Griesbaum, K.; Ovez, B.; Huh, T. S.; Dong, Y. *Liebigs Ann.* **1995**, 1571.
13. Shin, H. S.; Lee, C. W.; Lee, J. Y.; Huh, T. S. *Eur. J. Org. Chem*. **2000**, 335.