

Diozonides from Cozonolyses of Cyclodienes and Carbonyl Compounds

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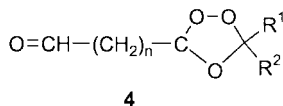
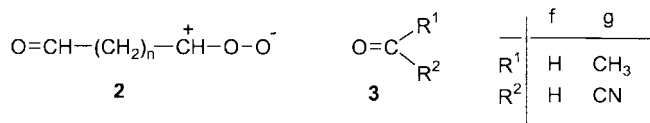
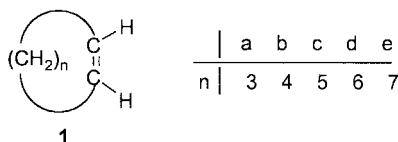
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Treatment of conjugated cyclodienes (**5a-5c**) with excess ozone in dichloromethane in the presence of added carbonyl compounds (**3**) resulted to give the corresponding diozonides **10** and cross-ozonides **14**. Similarly, ozonolysis of the nonconjugated 1,4-cyclohexadiene (**6a**) and 1,5-cyclooctadiene (**6b**) under same conditions afforded both diozonides **20** and cross-ozonides **14**. On the other hand, Ozonolysis of bicyclo[2.2.0]hepta-2,5-diene (**6c**) in the presence of **3A** provided the corresponding diozonide **19**.

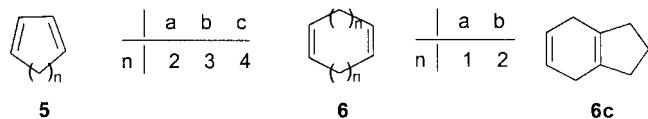
Keywords : Diozonides, Cozonolyses, Cyclodienes.

Introduction

Ozonolysis reactions of cyclodienes in nonparticipating solvents have not been studied extensively.¹⁻⁴ Ozonation of cycloalkenes in anhydrous nonparticipating solvents result in the formation of polymeric ozonides because intramolecular cycloaddition of carbonyl oxides with aldehydes are much slower than intermolecular reactions. In order to avoid the polymeric ozonides formation, a good 1,3-dipolarophile is needed to trap the carbonyl oxide intermediates. In previous work, we had shown that the carbonyl oxide intermediates **2**, generated from the ozonolysis of cycloalkenes **1** can be trapped by carbonyl compounds **3** to form the corresponding ozonides **4**.⁵⁻⁷



We have now extended this mode of reaction to the ozonolysis of conjugated cyclodienes **5a-5c** and non-conjugated cyclodienes **6a-6c** in presence of carbonyl compounds **3f** and **3g** to obtain the corresponding diozonides, respectively.



Results and Discussion

In pursuit of our goal, we have ozonized the conjugated

cyclodienes **5a-c** in dichloromethane with excess of ozone in the presence of carbonyl compounds **3f** and **3g**, respectively.

Ozonolyses of 1,3-cyclohexadiene (**5a**) and 1,3-cycloheptadiene (**5b**) and 1,3-cyclooctadiene (**5c**) in the presence of carbonyl compounds **3f** and **3g** afforded the corresponding diozonides **10c**, **10d**, **10e**, **10f**, **10g** and **10h**, which have been isolated in yields of 15.3%, 12.80%, 26.7%, 24.3%, 28.2% and 31.2%, respectively. By-products of these reactions were cross-ozonides **14c-h** in yields of 14.2-24.1%, each. Ozonolyses of **5a-c** with one equivalent of ozone under similar reaction conditions afforded the unsaturated ozonides **7** and **8** as major products.⁸ It can be concluded that ozone cleavage of the double bonds in unsaturated ozonides **7** and **8** occurs predominately in one direction only, with the formation of higher substituted carbonyl oxides **9** and **12**. The fact that no ozonides **13** have been found in ozonolyses of **5a-c** could be due to the instability of α -oxo ozonides of type **13**.^{9,10}

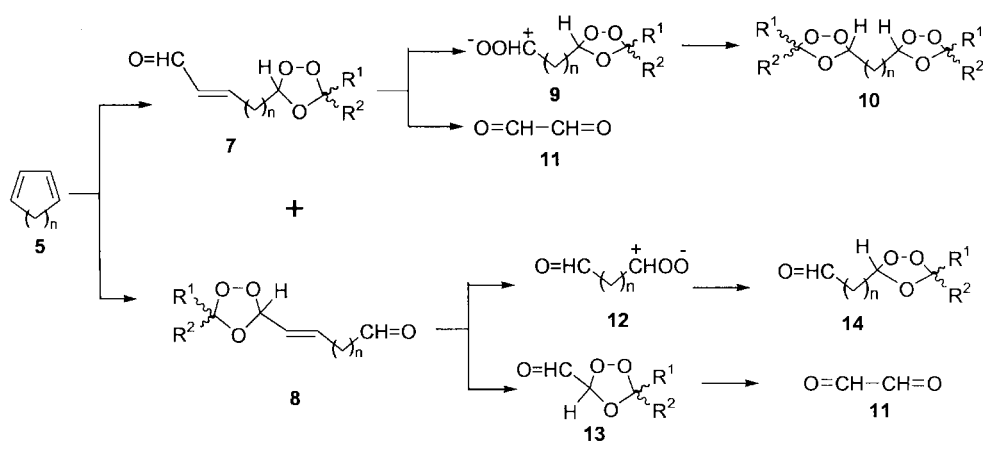
Ozonolysis of the nonconjugated 1,4-cyclohexadiene (**6a**) in the presence of carbonyl compounds **3f** provided the corresponding cross-ozonide **14a** and diozonides **10a** in yield of 8.0% and 79.3%. Ozonolysis of nonconjugated 1,5-cyclooctadiene (**6b**) in the presence of **3f** and **3g** provided the corresponding cross-ozonides **14c** and **14d** and diozonides **10c** and **10d** in yields of 25.3%, 27.3%, 30% and 28%, respectively.

Ozonolysis of bicyclo[2.2.0]hepta-2,5-diene (**6c**) in the presence of **3f** provided the corresponding diozonide **19** in yield of 58.3%. Ozonolysis of **6c** with one equivalent of ozone under same condition afforded unsaturated ozonide **17** as a major product.¹¹

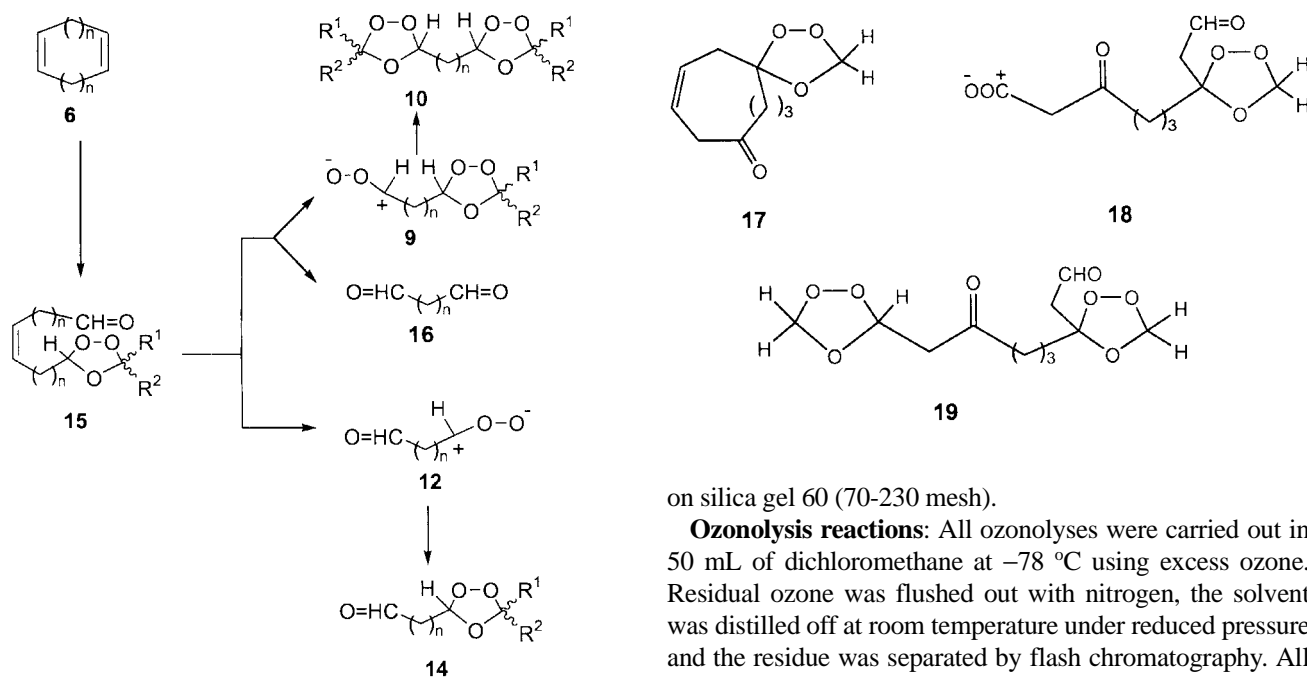
All of the ozonides have been isolated by column chromatography on silica gel. Diozonides **10d**, **10f** and **10h** were mixture of diastereoisomers at the ozonide rings.^{12,13}

The structures of all isolated ozonides were established by ¹H and ¹³C NMR spectroscopy, and their reduction with triphenylphosphine to give the expected diols and carbonyl compounds **3** in a ratio of *ca.* 1 : 1.

In the ¹H NMR spectra, the ozonide moieties of the cross-ozonides could be recognized by signals of the CH groups in the ozonide rings. They appeared in the range of $\delta = 5.03$ -



	a	b	c	d	e	f	g	h
n	1	1	2	2	3	3	4	4
R ¹	H	CH ₃	H	CH ₃	H	CH ₃	H	CH ₃
R ²	H	CN	H	CN	H	CN	H	CN



5.30. In the ¹³C NMR spectra of all ozonides, the two chemically nonequivalent carbon atoms in the ozonide ring exhibited signals in the range of $\delta = 93.82\text{--}114.04$.⁷

The successful coozonolysis of the cyclodienes in the presence of carbonyl compounds opens a convenient short-path synthesis for the types of dioxonides **10** and **17**.

Experimental Section

NMR spectra: Bruker AC-300. ¹H-NMR and ¹³C-NMR spectra were recorded in CDCl₃ with TMS as internal references. Chromatographic separations: Flash chromatography

on silica gel 60 (70-230 mesh).

Ozonolysis reactions: All ozonolyses were carried out in 50 mL of dichloromethane at -78 °C using excess 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 chromatography. All chromatography described below was carried out with dichloromethane/diethyl ether in a ratio of 15 : 1. The formaldehyde (**3f**) 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 CDCl₃ was kept at room temperature for 24 hours. The products were analyzed by ¹H NMR spectroscopy.

Caution: All ozonolysis reactions, chromatographic separations, and reductions of ozonides were carried out behind protective safety glass shields in a hood. Ozonides were invariably transported, *e.g.* to the analytical laboratory, in thick-walled steel containers. Safety glasses and gloves must

be worn.

Ozonolysis of 5a in the presence of 3f: Ozonolysis of 0.24 g (3.0 mmol) of **5a** and 1 mL of **3f** gave a liquid residue, from which 80 mg (0.46 mmol, 15.3%) of **10c** and 60 mg (0.43 mmol, 14.2%) of **14c** were isolated.

3-[2-(1,2,4-Trioxolane-3-yl)ethyl]-1,2,4-trioxolane (10c): Colorless liquid. $^1\text{H NMR}$: δ 1.89 (s, 4H), 5.07 (s, 2H), 5.14 (s, 2H), 5.27 (t, $J = 4.8$ Hz, 2H). $^{13}\text{C NMR}$: δ 25.96, 94.54, 103.10. Anal. Calcd for $\text{C}_6\text{H}_{10}\text{O}_6$ (178.1): C, 40.45; H, 5.66. Found: C, 40.32; H, 5.68. Reduction of **10c** with TPP gave butanedial.

(1,2,4-Trioxolane-3-yl)propanal (14c): Colorless liquid. $^1\text{H NMR}$: δ 1.93-2.05 (m, 2H), 2.49 (t, $J = 6.1$ Hz, 2H), 4.96 (s, 1H), 5.07 (s, 1H), 5.17 (t, $J = 5.2$ Hz, 1H), 9.67 (s, 1H). $^{13}\text{C NMR}$: δ 24.31, 37.80, 94.49, 103.44, 200.96. Anal. Calcd for $\text{C}_5\text{H}_8\text{O}_4$ (132.1): C, 45.46; H, 6.10. Found: C, 45.57; H, 5.23. Reduction of **14c** with TPP gave butanedial.

3-[3-(1,2,4-Trioxolane-3-yl)propyl]-1,2,4-trioxolane (10e): Yield, 26.7%. Colorless liquid. $^1\text{H NMR}$: δ 1.56-1.64 (m, 2H), 1.75-1.81 (m, 4H), 5.03 (s, 2H), 5.14 (t, $J = 4.9$ Hz, 2H), 5.17 (s, 2H). $^{13}\text{C NMR}$: δ 18.43, 30.69, 94.43, 103.64. The data are identical to those reported.⁵

(1,2,4-Trioxolane-3-yl)butanal (14e): Yield, 24.3%. Colorless liquid. $^1\text{H NMR}$: δ 1.65-1.75 (m, 4H), 2.46 (t, $J = 6.1$ Hz, 2H), 4.99 (s, 1H), 5.08 (t, $J = 5.1$ Hz, 1H), 5.13 (s, 1H), 9.65 (s, 1H). $^{13}\text{C NMR}$: δ 16.58, 30.77, 43.60, 94.41, 103.61, 202.10. The data are identical to those reported.⁵

3-[4-(1,2,4-Trioxolane-3-yl)butyl]-1,2,4-trioxolane (10g): Yield, 28.2%. Colorless liquid. $^1\text{H NMR}$: δ 1.50 (m, 4H), 1.75 (m, 4H), 5.03 (s, 2H), 5.13 (t, $J = 5.2$ Hz, 2H), 5.18 (s, 2H). $^{13}\text{C NMR}$: δ 23.95, 31.34, 94.42, 103.86. The data are identical to those reported.⁵

(1,2,4-Trioxolane-3-yl)pentanal (14g): Yield, 26.6%. Colorless liquid. $^1\text{H NMR}$: δ 1.48 (m, 2H), 1.67-1.74 (m, 4H), 2.47 (t, $J = 6.2$ Hz, 2H), 5.02 (s, 1H), 5.13 (t, $J = 5.2$ Hz, 1H), 5.17 (s, 1H), 9.76 (s, 1H). $^{13}\text{C NMR}$: δ 21.66, 23.19, 30.84, 43.47, 93.92, 103.29, 201.94. The data are identical to those reported.⁵

Ozonolysis of 5a in the presence of 3g: Ozonolysis of 0.24 g (3.0 mmol) of **5a** and 0.41 g (6.0 mmol) of **3g** gave a liquid residue, from which 100 mg (0.38 mmol, 12.8%) of **10d** and 70 mg (0.40 mmol, 12.8%) of **14d** were isolated.

5-Cyano-5-methyl-3-[2-(5-cyano-5-methyl-1,2,4-trioxolane-3-yl)ethyl]-1,2,4-trioxolane (10d): Colorless liquid (a mixture of *cis* and *trans* isomers). $^1\text{H NMR}$: δ 1.86 (s, 6H), 1.64-2.08 (m, 4H), [5.31 (m), 5.72 (m)] (2H). $^{13}\text{C NMR}$: δ 21.11, 23.22, 23.96, 27.84, 28.39, 98.47, 99.00, 105.43, 116.21, 116.84. Anal. Calcd for $\text{C}_{10}\text{H}_{12}\text{O}_6\text{N}_2$ (256.2): C, 46.88; H, 4.72. Found: C, 46.64; H, 4.69. Reduction of **10d** with TPP gave butanedial and acetyl cyanide.

(5-Cyano-5-methyl-5-1,2,4-trioxolane-3-yl)propanal (14d): Colorless liquid (a mixture of *cis* and *trans* isomers). $^1\text{H NMR}$: δ 1.86 (s, 3H), [2.01 (m), 2.61 (t, $J = 6.2$ Hz)] (2H), [2.20 (m), 2.71 (t, $J = 6.2$ Hz)] (2H), [5.32 (t, $J = 5.2$ Hz), 5.74 (t, $J = 5.2$ Hz)] (1H) 9.79 (s, 1H), $^{13}\text{C NMR}$: δ 21.07, 22.55, 26.70, 37.05, 37.76, 98.40, 98.98, 105.86, 116.29, 116.94, 200.27. Anal. Calcd for $\text{C}_7\text{H}_9\text{O}_4\text{N}$ (171.1): C, 49.14;

H, 5.30. Found: C, 48.97; H, 5.37. Reduction of **14d** with TPP gave butanedial and acetyl cyanide.

5-Cyano-5-methyl-3-[3-(5-cyano-5-methyl-1,2,4-trioxolane-3-yl)propyl]-1,2,4-trioxolane (10f): Yield, 24.3%. Colorless liquid (a mixture of *cis* and *trans* isomers). $^1\text{H NMR}$: δ 1.65-1.97 (m, 6H), 1.86 (s, 6H), [5.28 (t, $J = 5.1$ Hz), 5.64 (t, $J = 5.1$ Hz)] (2H). $^{13}\text{C NMR}$: δ 17.73, 21.30, 29.45, 29.64, 33.43, 33.71, 98.65, 98.78, 106.32, 116.73, 116.96. Anal. Calcd for $\text{C}_{11}\text{H}_{14}\text{O}_6\text{N}_2$ (270.2): C, 48.89; H, 5.22. Found: C, 48.58; H, 5.37. Reduction of **10f** with TPP gave pentanedial and acetyl cyanide.

(5-Cyano-5-methyl-1,2,4-trioxolane-3-yl)butanal (14f): Yield, 24.1%. Colorless liquid (a mixture of *cis* and *trans* isomers). $^1\text{H NMR}$: δ 1.60-1.80 (m, 4H), 1.74 (s, 3H), 2.24 (t, $J = 6.2$ Hz, 2H) [5.14 (t, $J = 5.1$ Hz), 5.52 (t, $J = 5.1$ Hz)] (1H), 9.63 (s, 1H). $^{13}\text{C NMR}$: δ 15.57, 15.78, 20.58, 20.61, 28.58, 32.67, 42.57, 42.73, 97.72, 98.16, 105.75, 115.79, 116.41, 201.05. The data are identical to those reported.⁵

5-Cyano-5-methyl-3-[4-(5-cyano-5-methyl-1,2,4-trioxolane-3-yl)butyl]-1,2,4-trioxolane (10h): Yield, 31.2%. Colorless liquid (a mixture of *cis* and *trans* isomers). $^1\text{H NMR}$: δ 1.51-1.60 (m, 4H), 1.71-1.89 (m, 4H), 1.86 (s, 6H), [5.26 (t, $J = 5.2$ Hz), 5.62 (t, $J = 5.2$ Hz)] (2H). $^{13}\text{C NMR}$: δ 21.31, 23.38, 23.68, 29.77, 33.32, 98.72, 106.72, 117.03. Anal. Calcd for $\text{C}_{12}\text{H}_{16}\text{O}_6\text{N}_2$ (284.2): C, 50.70; H 5.67. Found: C, 50.58; H, 5.58. Reduction of **10h** with TPP gave hexanedial and acetyl cyanide.

5-Cyano-5-methyl-1,2,4-trioxolane-3-yl)pentanal (14h): Yield, 36.8%. Colorless liquid (a mixture of *cis* and *trans* isomers). $^1\text{H NMR}$: δ 1.37-1.81 (m, 6H), 1.79 (s, 3H), 2.42 (t, $J = 6.2$ Hz, 2H), [5.19 (t, $J = 5.1$ Hz), 5.55 (t, $J = 5.1$ Hz)] (1H), 9.70 (t, $J = 1.59$ Hz, 1H). $^{13}\text{C NMR}$: δ 20.72, 20.81, 21.30, 21.52, 22.84, 23.03, 29.27, 33.32, 43.27, 97.85, 98.27, 106.19, 116.00, 116.63, 202.14. The data are identical to those reported.⁵

Ozonolysis of 6a in the presence of 3f: Ozonolysis of 0.24 g (3.0 mmol) of **6a** and 1 mL of **3f** gave a liquid residue, from which 390 mg (2.35 mmol, 79.3%) of **10a** and 30 mg (0.24 mmol, 8.0%) of **14a** were isolated.

3-(1,2,4-Trioxolane-3-yl)methyl-1,2,4-trioxolane (10a): Colorless liquid. $^1\text{H-NMR}$: δ 2.18 (m, 2H), 5.14 (s, 4H), 5.39 (t, $J = 2.87$ Hz, 2H). $^{13}\text{C NMR}$: δ 35.37, 94.45, 100.28. Anal. Calcd for $\text{C}_5\text{H}_8\text{O}_6$ (164.1): C, 36.60; H, 4.91. Found: C, 36.87; H, 5.11. Reduction of **10a** with TPP gave propanedial.

(1,2,4-trioxolane-3-yl)ethanal (14a): Colorless liquid. $^1\text{H NMR}$: δ 2.90 (m, 2H), 5.13 (s, 1H), 5.19 (s, 1H), 5.67 (t, $J = 7.12$ Hz, 1H), 9.77 (t, $J = 1.05$ Hz, 1H). $^{13}\text{C NMR}$: δ 46.31, 94.56, 99.99, 197.68. Anal. Calcd for $\text{C}_4\text{H}_6\text{O}_4$ (118.1): C, 40.68; H, 5.12. Found: C, 40.34; H, 5.31.

Reduction of **14a** with TPP gave propanedial.

Ozonolysis of 6b in the presence of 3f: Ozonolysis of 0.32 g (3.0 mmol) of **6a** and 1 mL of **3f** gave a liquid residue, from which 160 mg (0.45 mmol, 30%) of **10c** and 100 mg (0.76 mmol, 25.3%) of **14c** were isolated.

Ozonolysis of 6b in the presence of 3g: Ozonolysis of 0.32 g (3.0 mmol) of **6b** and 0.62 g (9.0 mmol) of **3g** gave a

liquid residue, from which 120 mg (0.86 mmol, 28.4%) of **10d** and 140 mg (0.85 mmol, 27.3%) of **14d** were isolated.

Ozonolysis of 6c in the presence of 3f: Ozonolysis of 0.36 g (3.0 mmol) of **6c** and 1 mL of **3f** gave a liquid residue, from which 510 mg (1.75 mmol, 58.3%) of **19** was isolated.

3-Formylmethyl-3-[5-(1,2,4-trioxolan-3-yl)-4-oxopentyl-1,2,4-trioxolane (19): Colorless liquid. ^1H NMR : δ 1.79 (m, 2H), 1.90 (m, 2H), 2.54 (t, $J = 4.4$ Hz, 2H), 2.84 (m, 4H), 5.08 (s, 1H), 5.15 (s, 1H), 5.29 (m, 2H), 5.63 (t, $J = 3.12$ Hz, 1H), 9.73 (s, 1H). ^{13}C NMR : δ 16.75, 34.78, 43.02, 45.22, 50.06, 93.74, 94.71, 99.83, 108.38, 198.18, 204.93. Anal. Calcd for $\text{C}_{11}\text{H}_{18}\text{O}_8$ (276.2): C, 47.83; H, 5.84, Found: C, 48.21; H, 5.47.

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