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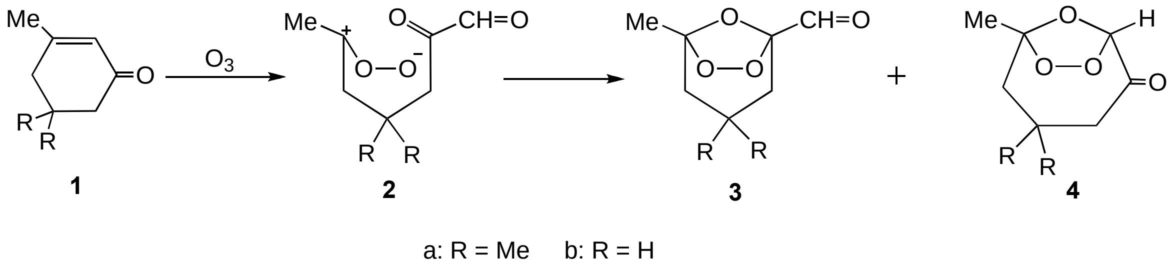
OZONOLYSES OF ISOPHORONE AND OF 3-METHYL-2-CYCLOHEXEN-1-ONE AND SUBSEQUENT REACTIONS OF THE RESPECTIVE OZONIDES TO AFFORD DI-, TRI- AND TETRAOZONIDES

In Chan Jung,* Sad Alam Sheikh, Byong-Mun Jon, Wei Li, Bon-Suk Goo, and In-Soo Jeong†

Department of Chemistry, Hanseo University, Seosan 356-706, Korea
*E-mail: icjung@hanseo.ac.kr
† Department of Housing Environmental Design, Chonbuk National University, Jeonju 561-756, Korea

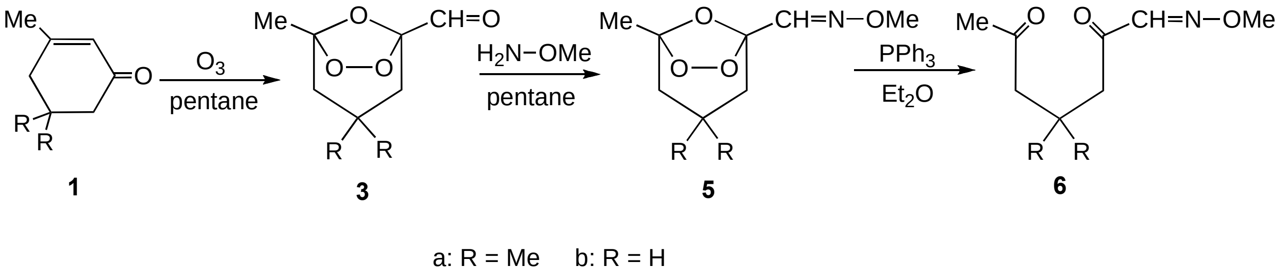
Abstract – Ozonolyses of isophorone (**1a**) and 3-methyl-2-cyclohexen-1-one (**1b**) in pentane, followed by treatment of the ozonolyses products with *O*-methyl-hydroxylamine afforded the ozonides 3,3,5-Trimethyl-6,7,8-trioxabicycle[3.2.1] octane-1-carbaldehyde-*O*-methyloxime (**5a**) and 5-Methyl-6,7,8-trioxabicyclo [3.2.1]octane-1-carbaldehyde-*O*-methyloxime (**5b**), respectively. Coozonolyses of ozonides **5** with selected carbonyl compounds resulted in the formation of diozonides (**9, 11)**, triozonides (**12)** and tetraozonides (**14**).

Ozonolyses of isophorone (**1a**) have been reported previously[1, 2] but neither the structure of peroxidic products nor the direction of cleavage have been described, since the primary reaction products were immediately converted into non-peroxidic compounds by acid catalyzed[1] or by oxidative[2] post treatment. The goal of the present investigation was the clarification of the reaction course and the identification of peroxidic products of the ozonolyses of **1a,** and subsequently also of **1b**. Based on previous experience with ozonolyses of cyclic α-oxo olefins,[3] ozone cleavage of these substrates were expected to provide intermediates of structure **2** in which the carbonyl oxide moiety has a choice to undergo cycloaddition with either one of the two carbonyl groups of **2** to give ozonides of structures **3** and **4**.



Scheme 1

Treament of **1a** with one molar equivalent of ozone in pentane at -78 °C provided a peroxidic reaction product. However, attempts at isolating the peroxidic species by chromatograpy failed because it decomposed on silica gel. Since it is known, that α-oxo-ozonides are very labile[4] but can be stabilized by converting them into the corresponding *O*-methyloximes,[5] ozonolyses of **1a** was repeated and the crude reaction product was treated with *O*-methyl hydroxylamine. From the ensuing mixture, ozonide **5a** has been isolated in a yield of 45%. In a smilar manner, ozonolyses of **1b**, provided the ozonide **5b** in a yield of 70%. Ozonides **5a** and **5b** are stable compounds. They have been characterized by their ^{1}H and ^{13}C NMR spectra and by their reaction with triphenylphosphane which, as expected, provided the corresponding diketones **6** as the sole reduction products.



Scheme 2

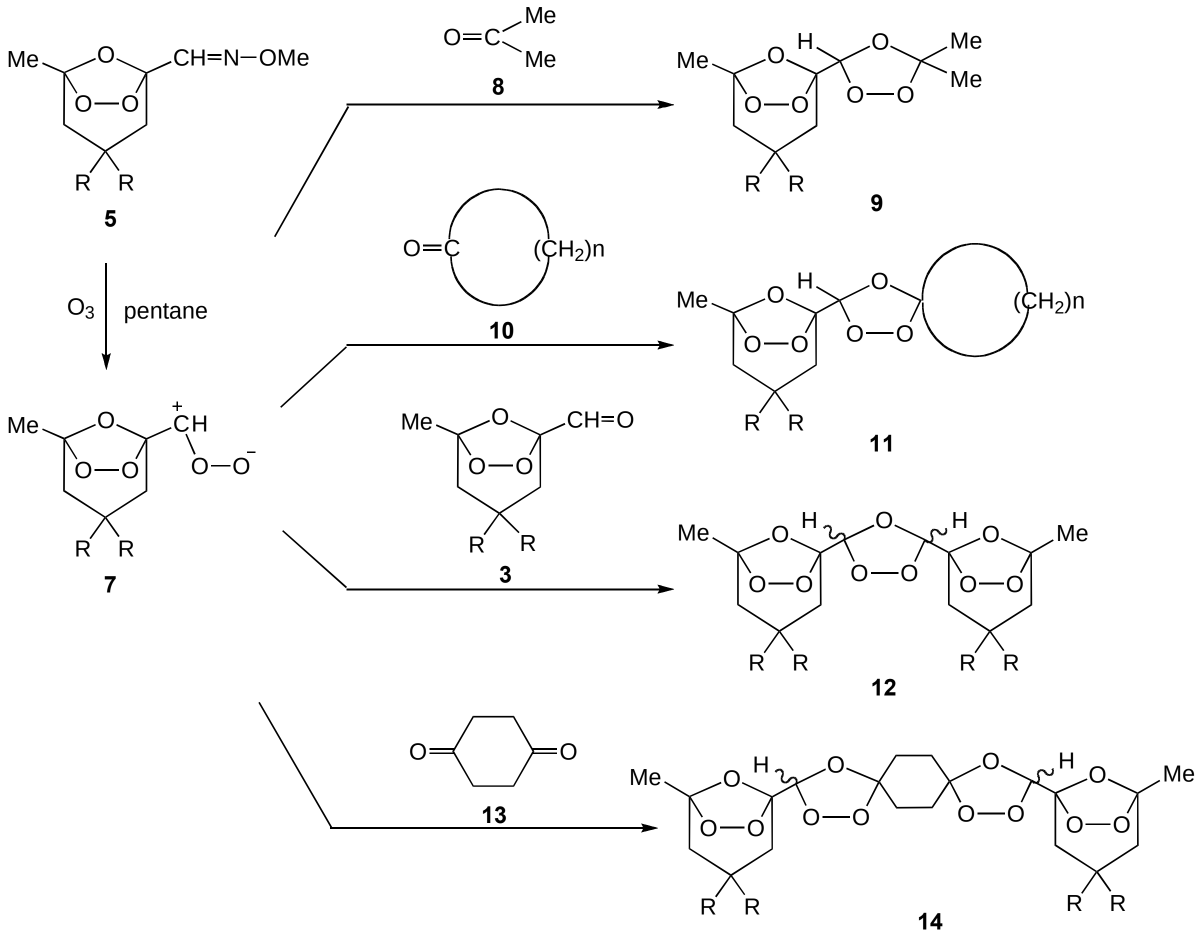
The isolation of **5a** and of **5b** proves that the corresponding ozonides **3** have been formed and persisted in the crude reaction mixture at low temperatures. On the other hand, ^{1}H NMR analyses of the crude ozonolysis products prior to their treatment with *O*-methyl hydroxylamine indicated, that ozonides of structure **4** were apparently not formed in noticeable quantities since the spectra did not exhibit any signals between 5.0 and 5.5 ppm which would be the expected range for the signals of the CH-groups in the ozonide rings of **4a** and **4b.** The preferred formation of ozonides of structure **3** is in line with the experience that the formation of cyclopentene-ozonides is favored over the formation of cyclohexene-ozonides.[3]

It has been reported that ozonolyses of *O*-methyloximes in the presence of carbonyl compounds provides an alternate access to ozonides.[6] We have applied this so-called coozonolyses reaction to ozonides **5a** and **5b**. They proceeded via the corresponding carbonyl oxide intermediates **7** and gave the results depicted in scheme 3: Coozonolyses of **5a** and of **5b** with acetone **(8)** afforded the corresponding diozonides **9**. Similarly, coozonolyses of **5a** and of **5b** with cyclopentanone (**10c**) and with cyclohexanone (**10d**) provided the corresponding diozonides **11**. Coozonolyses of **5a** and of **5b** with ozonides **3a** and **3b** provided the corresponding triozonides of structure **12**, and coozonolyses of **5a** and of **5b** with 1,4-cyclohexadiene(**13**) afforded the corresponding tetraozonides of structure **14**. All of the isolated polyozonides were stable at room temperature.

The diozonides of structures **9** and **11** exist as mixtures of two diastereomers. These isomers have been individually isolated, but not stereochemically assigned. and, hence, denoted as isomer 1 and isomer 2. The triozonides of structures **12** exist as mixtures of cis- and trans-isomers which have been individually isolated. Their stereochemical assignment is based on the experience that in the ^{1}H NMR spectra of ozonides the signals of the hydrogen atoms attached to the ozonide rings of trans-isomers appear downfield from those of the corresponding cis-isomers.[7,8] Ozonide **14a** consisted of three diastereomers of which two, denoted as isomer 1 and isomer 2 which were individually isolated. Ozonide **14b** consisted of two diastereomers, denoted as isomer 1 and isomer 2, which were individually isolated.

Table 1. Product yields from ozonolyses and coozonolyses reactions

Substrate(s)	R	Product	Yield (%)
1a	Me	**5a**	45
1b	H	**5b**	70
5a + **8**	Me	**9a**	28
5b + **8**	H	**9b**	34
5a + **10c**	Me	**11ac**	35
5b + **10c**	H	**11bc**	19
5a + **10d**	Me	**11ad**	22
5b + **10d**	H	**11bd**	19
5a + **3a**	Me	**12a**	18
5b + **3b**	H	**12b**	31
5a + **13**	Me	**14a**	9
5b + **13**	H	**14b**	9



a: R = Me b: R = H c: n = 4 d: n = 5

Scheme 3

In summary, the present investigation has revealed the direction of ozone cleavage and the structures of the peroxidic products **5a** and **5b** from the ozonolyses of isophorone (**1a**) and of 3-methyl-2-cyclohenen-1-one (**1b**). Furthermore, coozonolyses reactions of the stable ozonides **5** and suitable carbonyl compounds have provided access to stable di-, tri- and tertaozonides, a class of compounds of which only few examples have been described.

EXPERIMENTAL

General: All reagents and solvents were of commercial grade. ^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ with TMS as internal reference on a Bruker AC-300 instrument. GC analyses were carried out on a Shimadzu GC-14B instrument using the following conditions: column J&W-DB-5, 30 m; 60-180 °C at 10 °C/min. Chromatographic separations were performed by flash chromatography on silica gel 60.

Caution: All reactions with ozone or ozonides and chromatographic separations were carried out behind protective safety-glass shiels in a hood. Safety glasses and gloves must be worn at all times when working with ozone or ozonides.

Ozonolyses of 1a: A solution of **1a** (0.50 g, 3.6 mmol) in pentane (80 mL) was treated with ozone (3.6 mmol) at -78 °C to provide a peroxidic solution. It was warmed up to room temperature and the solvent was distilled off at reduced pressure to leave 0.80 g of a colorless liquid residue. Chromatographic separation of the residue afforded no peroxidic product.

Preparation of 5a: The above described ozonolysis was repeated and the liquid residue of 0.80 g was admixed with *O*-methylhydroxylamine (360 mg, 4.32 mmol) and pyridine (341 mg, 4.32 mmol) in MeOH (20 mL). The solution was stirred for 12 h and extracted with Et_2O (20 mL). The extract was washed with an aqueous sodium hydrogen carbonate (20 mL), dried with magnesium sulfate, and filtered. The solvent was distilled off at reduced pressure at room temperature to leave 0.6 g of a yellow liquid residue from which of ozonide **5a** (348 mg, 45%) was isolated by flash chromatography (column 2.5 x 60 cm; pentane/Et_2O, 8:2).

3,3,5-Trimethyl-6,7,8-trioxabicyclo[3.2.1]octane-1-carbaldehyde-*O*-methyloxime (5a): Yellow liquid. ^{1}H NMR: δ 1.02 (s, 3H), 1.33 (s, 3H), 1.52 (s, 3H), 1.68-2.11 (m, 4H), 3.89 (s, 3H), 7.26 (s, 1H) ppm; ^{13}C NMR(BB): δ 21.47, 29.35, 31.22, 34.83, 42.24, 46.93, 62.75, 106.36, 109.84, 144.87 ppm; ^{13}C NMR (DEPT): δ 21.47, 31.22, 34.83, 42.24, 46.93, 62.75, 144.87 ppm; GC: t_R = 9.2 min.; Anal. Calcd for $C_{10}H_{17}NO_4$ (215.25): C, 55.80; H, 7.96; N, 6.51. Found : C, 55.72; H, 7.90; N, 6.69.

Reduction of 5a: A solution of **5a** (0.13 g, 0.6 mmol) in Et_2O (50 mL) was admixed with triphenylphosphane (0.21 g, 0.80 mmol) and left standing for one day. The solvent was distilled off at reduced pressure to leave 0.35 g of a colorless liquid from which **6a (**0.11 g, 92%) has been isolated by flash chromatography (column 2.5 x 60 cm; pentane/Et_2O, 7:3).

4, 4-Dimethyl-2,6-dioxoheptanal-*O*-methyloxime (6a): ^{1}H NMR δ 1.08 (s, 6H), 2.08 (s, 3H), 2.59 (s, 2H), 2.94 (s, 2H), 4.03 (s, 3H), 7.29 (s, 1H) ppm; ^{13}C NMR(BB) δ 28.86, 32.29, 33.26, 46.66, 52.91, 63.69, 148.89, 198.47, 208.67 ppm; ^{13}C NMR (DEPT) δ 28.86, 32.29, 46.66, 52.91, 63.69, 148.89 ppm.

Preparation of 5b: A solution **1b (**0.50 g, 4.5 mmol) in pentane (80 mL) was treated with ozone (4.5 mmol) at -78 °C. The mixture was warmed up to room temperature and the solvent was distilled of at reduced pressure to leave 0.60 g of a colorless liquid residue. It was admixed with *O*-methylhydroxylamine (292 mg, 3.5 mmol) and pyridine (276 mg, 3.5 mmol) in MeOH (20 mL). The solution was stirred for 6 h and extracted with Et_2O (20 mL). The extract was washed with an aqueous sodium bicarbonate (20 mL), dried with magnesium sulfate and filtered. The solvent was distilled off at reduced pressure and room temperature to leave 0.75 g of a colorless liquid residue from which of ozonide **5b** (593 mg, 70%) was isolated by flash chromatography (column 2.5 x 60 cm; pentane/Et_2O, 7:3).

5-Methyl-6,7,8-trioxabicyclo[3.2.1]octane-1-carbaldehyde-*O*-methyloxime (5b): Colorless liquid .^{1}H NMR δ 1.52 (s, 3H), 1.76-1.92 (m, 4H), 2.11-2.18 (m, 2H), 3.90 (s, 3H), 7.27 (s, 1H) ppm; ^{13}C NMR(BB) δ 16.79, 21.29, 29.45, 33.83, 62.86, 106.97, 110.61, 144.71 ppm; ^{13}C NMR (DEPT) δ 16.79, 21.29, 29.44, 33.83, 62.86, 144.71 ppm; GC: t_R = 8.0 min. Anal. Calcd for $C_8H_{13}NO_4$ (187.19): C, 51.33; H, 7.00; N,7.48. Found: C, 50.58; H, 7.00; N, 7.58

Reduction of 5b: A solution of **5b** (0.10 g, 0.5 mmol) in Et_2O (50 mL) was admixed with triphenylphosphane (0.18 g, 0.70 mmol) and left standing for one day. The solvent was distilled off at reduced pressure to leave 0.30 g of a colorless liquid from which **6b (**90 mg, 90%) has been isolated by flash chromatography (column 2.5 x 60 cm; pentane/Et_2O, 7:3).

2,6-Dioxoheptanal-*O*-methyloxime (6b): ^{1}H NMR δ 1.84-1.91 (m, 2H), 2.10 (s, 3H), 2.45-2.50 (m, 2H), 2.76-2.81 (m, 2H), 3.99 (s, 3H), 7.36 (s, 1H) ppm; ^{13}C NMR(BB) δ 17.94, 30.20, 37.08, 42.79, 63.67, 147.72, 198.06, 208.40 ppm; ^{13}C NMR (DEPT) δ 17.94, 30.20, 37.08, 42.79, 63.67, 147.71 ppm.

Coozonolyses of Ozonides 5 with acetone(8), cyclopentanone(10c) and cyclohexanone (10d):

a) General procedure: A solution of one of the ozonides **5** and a ketone in pentane or in CH_2Cl_2 was treated with ozone at -78 °C until it turned slightly blue. Residual ozone was flushed off with nitrogen and the mixture was warmed up to room temperature. The solvent was distilled off at room temperature and reduced pressure and the liquid residue was separated by flash chromatography (column 2 x 55 cm; pentane/Et_2O, 9:1) to provide mixtures of the stereoisomeric ozonides in a first step and the individual isomers in a second separation step.

b) Coozonolyses of 5a with 8: Ozone treatment of **5a** (0.5 g, 2.32 mmol) and an excess of **8** (10 mL) in pentane (70 mL) provided 0.7 g of a colorless liquid residue from which diozonide **9a** (171 mg, 28%, mixture of isomer **1** and isomer **2**) and subsequently isomer **1** (21 mg, 3.4%) and isomer **2** (30 mg, 5%) were isolated.

1-(5,5-Dimethyl-1,2,4-trioxolan-3-yl)-3,3,5-trimethyl-6,7,8-trioxabicyclo[3.2.1]octane (9a, isomer 1): Colorless liquid. ^{1}H NMR δ 1.02 (s, 3H), 1.32 (s, 3H), 1.51 (s, 3H), 1.53 (s, 3H), 1.56 (s, 3H), 1.74-1.81

(m, 4H), 5.21 (s, 1H) ppm; ^{13}C NMR(BB) δ 21.24, 23.10, 24.00, 29.29, 31.56, 34.86, 38.65, 46.98, 102.08, 107.54, 109.87, 110.29 ppm; ^{13}C NMR (DEPT) δ 21.24, 23.10, 24.00, 31.56, 34.86, 38.65, 46.98, 102.08 ppm; Anal. Calcd for $C_{12}H_{20}O_6$ (260.28): C, 55.37; H, 7.74. Found: C, 55.72; H, 7.51.

1-(5,5-Dimethyl-1,2,4-trioxolan-3-yl)-3,3,5-trimethyl-6,7,8-trioxabicyclo[3.2.1]octane (9a, isomer 2): Colorless liquid. ^{1}H NMR δ 1.02 (s, 3H), 1.32 (s, 3H), 1.51 (s, 3H), 1.53 (s, 3H), 1.56 (s, 3H), 1.74-1.82 (m, 4H), 5.21 (s, 1H) ppm; ^{13}C NMR(BB) δ 21.25, 23.17, 24.10, 29.26, 31.40, 34.91, 38.76, 46.98, 101.80, 107.64, 109.85, 110.24 ppm; ^{13}C NMR (DEPT) δ 21.25, 23.17, 24.09, 31.40, 34.91, 38.76, 46.98, 101.80 ppm; Anal. Calcd for $C_{12}H_{20}O_6$ (260.28): C, 55.37; H, 7.74. Found: C, 55.52; H, 7.71.

c) Coozonolyses of 5a with 10c: Ozone treatment of **5a (**0.50 g, 2.32 mmol) and **10c** (0.20 g, 2.32 mmol) in pentane (70 mL) provided 0.7 g of a colorless liquid residue from which diozonide **11ac (**237 mg, 35%, mixture of isomer **1** and isomer **2**) and subsequently isomer **1** (45 mg, 6.8%) and isomer **2** (40 mg, 6%) were isolated.

3-(3,3,5-Trimethyl-6,7,8-trioxabicyclo[3.2.1]oct-1-yl)-1,2,4-trioxaspiro[4.4]nonane (11ac, isomer 1): Colorless liquid. ^{1}H NMR δ 1.02 (s, 3H), 1.32 (s, 3H), 1.52 (s, 3H), 1.65-1.83 (m, 8H), 1.90-1.96 (m, 3H), 2.07-2.10 (m, 1H), 5.19 (s, 1H) ppm; ^{13}C NMR(BB) δ 21.27, 23.94, 24.42, 29.31, 31.56, 33.11, 34.89, 35.56, 38.51, 47.04, 101.94, 107.80, 109.95, 119.99 ppm; Anal. Calcd for $C_{14}H_{22}O_6$ (286.32): C, 58.73; H, 7.74. Found: C, 58.64; H, 7.68.

3-(3,3,5-Trimethyl-6,7,8-trioxabicyclo[3.2.1]oct-1-yl)-1,2,4-trioxaspiro[4.4]nonane (11ac, isomer 2): Colorless liquid. ^{1}H NMR δ 1.02 (s, 3H), 1.32 (s, 3H), 1.53 (s, 3H), 1.68-1.81 (m, 8H), 1.93-1.95 (m, 3H), 2.06-2.08 (m, 1H), 5.19 (s, 1H) ppm; ^{13}C NMR(BB) δ 21.26, 23.96, 24.40, 29.19, 31.43, 33.27, 34.91, 35.56, 38.54, 46.97, 101.69, 107.82, 109.80, 119.88 ppm; ^{13}C NMR (DEPT) δ 21.26, 23.96, 24.40, 31.43, 33.27, 34.91, 35.57, 38.53, 47.00, 101.69 ppm; Anal. Calcd for $C_{14}H_{22}O_6$ (286.32): C, 58.73; H, 7.74. Found: C, 58.59; H, 7.76.

d) Coozonolyses of 5a with 10d: Ozone treatment of **5a** (0.6 g, 2.78 mmol) and **10d** (0.5 g, 3.1 mmol) in pentane (70 mL) provided 0.76 g of a colorless liquid residue from which diozonide **11ad** (182 mg, 22%, mixture of isomer **1** and isomer **2**) and subsequently isomer **1** (37 mg, 4.4%) and isomer **2** (32 mg, 3.8%) were isolated.

3-(3,3,5-Trimethyl-6,7,8-trioxabicyclo[3.2.1]oct-1-yl)-1,2,4-trioxaspiro[4.5]decane (11ad, isomer 1): Colorless liquid. ^{1}H NMR δ 1.02 (s, 3H), 1.32 (s, 3H), 1.52 (s, 3H), 1.53-1.85 (m, 14H), 5.20 (s, 1H) ppm; ^{13}C NMR(BB) δ 21.29, 23.91, 24.26, 25.18, 29.30, 31.61, 32.98, 33.53, 34.89, 38.64, 47.03, 101.90, 107.66, 109.90, 111.09 ppm; ^{13}C NMR (DEPT) δ 21.30, 23.91, 24.26, 25.18, 31.61, 32.98, 33.53, 34.89, 38.64, 47.02, 101.90 ppm; Anal. Calcd for $C_{15}H_{24}O_6$ (300.35): C, 59.98; H, 8.05. Found: C, 60.25; H, 7.96.

3-(3,3,5-Trimethyl-6,7,8-trioxabicyclo[3.2.1]oct-1-yl)-1,2,4-trioxaspiro[4.5]decane (11ad, isomer 2): Colorless liquid. ^{1}H NMR δ 1.02 (s, 3H), 1.32 (s, 3H), 1.52 (s, 3H), 1.53-1.81 (m, 14H), 5.21 (s, 1H) ppm; ^{13}C NMR(BB) δ 21.29, 23.91, 24.26, 25.17, 29.25, 31.40, 33.04, 33.59, 34.92, 38.77, 46.99, 101.63, 107.73, 109.84, 111.02 ppm; ^{13}C NMR (DEPT) δ 21.29, 23.91, 24.26, 25.16, 31.40, 33.04, 33.59, 34.92, 38.76, 46.99, 101.63 ppm; Anal. Calcd for $C_{15}H_{24}O_6$ (300.35): C, 59.98; H, 8.05. Found: C, 60.10; H, 8.06.

e) Coozonolyses of 5b with 8: Ozone treatment of **5b** (0.50 g, 2.67 mmol) and an excess of **8** (10 mL) in pentane (70 mL) provided 0.8 g of a colorless liquid residue from which diozonide **9b** (215 mg, 34%, mixture of isomer **1** and isomer **2**) and subsequently isomer **1** (49 mg, 8%) and isomer **2** (45 mg, 7%) were isolated.

1-(5,5-Dimethyl-1,2,4-trioxolan-3-yl)-5-methyl-6,7,8-trioxabicyclo[3.2.1]octane (9b, isomer 1): Colorless liquid. ^{1}H NMR δ 1.50-1.54 (m, 9H), 1.74-1.90 (m, 5H), 2.20-2.23 (m, 1H), 5.22 (s, 1H) ppm; ^{13}C NMR(BB) δ 16.59, 21.02, 23.01, 24.09, 25.91, 33.78, 102.02, 108.03, 110.32, 110.64 ppm; ^{13}C NMR (DEPT) δ 16.59, 21.03, 23.01, 24.09, 25.90, 33.78, 102.02 ppm; GC: t_R =10.4 min. Anal. Calcd for $C_{10}H_{16}O_6$ (232.23): C, 51.72 ; H, 6.94. Found: C, 51.75; H, 7.05.

1-(5,5-Dimethyl-1,2,4-trioxolan-3-yl)-5-methyl-6,7,8-trioxabicyclo[3.2.1]octane (9b, isomer 2): Colorless liquid. ^{1}H NMR δ 1.51-1.56 (m, 9H), 1.78-1.92 (m, 5H), 2.21-2.25 (m, 1H), 5.23 (s, 1H) ppm; ^{13}C NMR(BB) δ 16.54, 20.98, 23.04, 24.11, 26.15, 33.79, 101.65, 108.10, 110.18, 110.60 ppm; ^{13}C NMR (DEPT) δ 16.54, 21.00, 23.04, 24.12, 26.15, 33.79, 101.65 ppm; GC: t_R = 11.3 min. Anal. Calcd for $C_{10}H_{16}O_6$ (232.23): C, 51.72 ; H, 6.94. Found: C, 51.77; H, 6.98.

f) Coozonolyses of 5b with 10c: Ozone treatment of **5b** (0.6 g, 3.21 mmol) and **10c** (0.27 g, 3.21 mmol) in CH_2Cl_2 (70 mL) provided 0.9 g of a yellowish liquid residue from which diozonide **11bc** (173 mg, 19%, mixture of isomer **1** and isomer **2**) and subsequently isomer **1** (34 mg, 8%) and isomer **2** (28 mg, 7%) of were isolated.

3-(5-Methyl-6,7,8-trioxabicyclo[3.2.1]oct-1-yl)-1,2,4-trioxaspiro[4.4]nonane (11bc, isomer 1):

Colorless liquid. ^{1}H NMR δ 1.52 (s, 3H), 1.62-1.94 (m, 12H), 2.16-2.25 (m, 2H), 5.20 (s, 1H) ppm; ^{13}C NMR(BB) δ 16.23, 20.63, 23.53, 24.02, 25.38, 32.58, 33.42, 35.27, 101.46, 107.86, 110.30, 119.57 ppm; ^{13}C NMR (DEPT) δ 16.23, 20.63, 23.53, 24.02, 25.38, 32.58, 33.42, 35.27, 101.46 ppm; Anal. Calcd for $C_{12}H_{18}O_6$ (258.26): C, 55.80 ; H, 7.03. Found: C, 55.57; H, 7.28.

3-(5-Methyl-6,7,8-trioxabicyclo[3.2.1]oct-1-yl)-1,2,4-trioxaspiro[4.4]nonane (11bc, isomer 2): Colorless liquid. ^{1}H NMR δ 1.52 (s, 3H), 1.64-1.99 (m,12H), 2.05-2.26 (m,2H), 5.20(s,1H) ppm; ^{13}C NMR(BB) δ 16.12, 20.63, 23.55, 24.03, 25.51, 32.77, 33.40, 35.23, 101.14, 107.88, 110.16, 119.45 ppm; ^{13}C NMR (DEPT) δ 16.12, 20.63, 23.55, 24.03, 25.51, 32.77, 33.40, 35.23, 101.14 ppm; Anal. Calcd for $C_{12}H_{18}O_6$ (258.26): C, 55.80 ; H, 7.03. Found: C, 55.62; H, 7.27.

g) Coozonolyses of 5b with 10d: Ozone treatment of **5b** (0.6 g, 3.21 mmol) and **10d** (0.31 g, 3.21 mmol) in CH_2Cl_2 (70 mL) provided 1.0 g of a yellowish liquid residue from which diozonide **11bd** (186 mg, 19%, mixture of isomer **1** and isomer **2**) and subsequently isomer **1** (31 mg, 3.1%) and isomer **2** (30 mg, 3.0%) were isolated.

3-(5-Methyl-6,7,8-trioxabicyclo[3.2.1]oct-1-yl)-1,2,4-trioxaspiro[4.5]decane (11bd, isomer 1): Colorless liquid. ^{1}H NMR δ 1.52 (s, 3H), 1.64-1.94 (m, 12H), 2.18-2.27(m, 2H, 5.20 (s,1H) ppm; ^{13}C NMR(BB) δ 16.21, 20.64, 23.51, 23.84, 24.78, 25.50, 32.56, 33.17, 33.40, 101.43, 107.39, 110.24, 110.68 ppm; ^{13}C NMR (DEPT) δ 16.21, 20.64, 23.51, 23.84, 24.78, 25.50, 32.56, 33.17, 33.40, 101.43 ppm; Anal. Calcd for $C_{13}H_{20}O_6$ (272.29): C, 57.34 ; H, 7.40. Found: C, 57.22; H, 7.31.

3-(5-Methyl-6,7,8-trioxabicyclo[3.2.1]oct-1-yl)-1,2,4-trioxaspiro[4.5]decane (11bd, isomer 2): Colorless liquid. ^{1}H NMR δ 1.52 (s, 3H), 1.38-1.48 (m, 2H), 1.57-1.90 (m, 13H), 2.17-2.26(m,1H), 5.22 (s, 1H) ppm; ^{13}C NMR(BB) δ 16.15, 20.66, 23.50, 23.85, 24.76, 25.77, 32.57, 33.20, 33.40, 101.08, 107.80, 110.20, 110.57 ppm; ^{13}C NMR(DEPT) δ 16.15, 20.66, 23.50, 23.85, 24.76, 25.77, 32.57, 33.20, 33.40 ppm; Anal. Calcd for $C_{13}H_{20}O_6$ (272.29): C, 57.34 ; H, 7.40. Found: C, 57.17; H, 7.29.

Coozonolyses of 5a with 3a:

A solution of **1a** (0.5 g, 3.6 mmol) in pentane (80 mL) was treated with ozone at -78 °C until it turned blue. Residual ozone was flushed off with nitrogen and the solvent was distilled off at room temperature and reduced pressure. The liquid residue was admixed with ozonide **5a (**0.78 g, 3.6 mmol) in pentane (80 mL) and the solution was treated with ozone at -75 °C until it turned blue. Residual ozone was flushed off and the solvent was distilled off to leave 0.76 g of a colorless liquid residue from which triozonide **12a**

(253 mg, 18%, mixture of cis-trans isomers) and subsequently cis-**12a** (36 mg, 2.6%) and trans-**12a** (30 mg, 2,1%) were isolated by flash chromatography (column 2.5 x 60 cm; pentane/Et_2O, 99:1).

cis-3,5-bis(3,3,5-Trimethyl-6,7,8-trioxabicyclo[3.2.1]octane-1-yl)-1,2,4-trioxolane (cis-12a): Colorless liquid. ^{1}H NMR δ 1.02 (s, 6H), 1.32 (s, 6H), 1.53 (s, 6H), 1.69-1.90 (m, 8H), 5.23 (s, 2H) ppm; ^{13}C NMR(BB) δ 21.17, 29.35, 31.57, 34.83, 39.61, 46.92, 102.38, 107.06, 110.07 ppm; ^{13}C NMR (DEPT) δ 21.17, 31.57, 34.83, 39.61, 46.92, 102.38 ppm; Anal. Calcd for $C_{18}H_{28}O_9$ (388.41): C, 55.66; H, 7.27. Found: C, 55.61; H, 7.12.

trans-3,5-bis(3,3,5-Ttrimethyl-6,7,8-trioxabicyclo[3.2.1]octane-1-yl)-1,2,4-trioxolane (trans-12a): Colorless liquid. ^{1}H NMR δ 1.02 (s, 6H), 1.32 (s, 6H), 1.53 (s, 6H), 1.69-1.82 (m, 8H), 5.25 (s, 2H) ppm; ^{13}C NMR(BB) δ 21.16, 29.36, 31.36, 34.74, 39.76, 46.94, 102.00, 107.07, 109.95 ppm; ^{13}C NMR (DEPT) δ 21.16, 31.35, 34.75, 39.76, 46.93, 102.00 ppm; Anal. Calcd for $C_{18}H_{28}O_9$ (388.41): C, 55.66; H, 7.27. Found: C, 55.55; H, 7.24.

Coozonolyses of 5b with 3b:

A solution of **1b** (0.30 g, 2.7 mmol) in pentane (80 mL) was treated with ozone at -78 °C until it turned blue. Residual ozone was flushed off with nitrogen and the solvent was distilled off at room temperature and reduced pressure. The liquid residue was admixed with ozonide **5b** (0.50 g, 2.7 mmol) in pentane (80 mL) and the solution was treated with ozone at -75 °C until it turned blue. Residual ozone was flushed off with nitrogen and the solvent was distilled off to leave 0.9 g of a yellow, viscous residue from which triozonide **12b** (275 mg, 31%, mixture of *cis-trans*-isomers) and subsequently *cis*-**12b** (37 mg, 4,2%) and *trans*-**12b** (27 mg, 3.0%) were isolated by flash chromatography (column 1.0 x 60 cm; pentane/Et_2O, 99.5:4.5).

cis-3,5-bis(5-Methyl-6,7,8-trioxabicyclo[3.2.1]octane-1-yl)-1,2,4-trioxolane (cis-12b): Yellowish liquid. ^{1}H NMR δ 1.52 (s, 6H), 1.74-2.10 (m, 12H), 5.23 (s, 2H) ppm; ^{13}C NMR(BB) δ 16.52, 20.91, 26.68, 33.70, 102.33, 107.44, 110.84 ppm; ^{13}C NMR (DEPT) δ 16.51, 20.92, 26.68, 33.70, 102.32 ppm; Anal. Calcd for $C_{14}H_{20}O_9$ (332.3): C, 50.60; H, 6.07. Found: C, 50.07; H, 6.20.

trans-3,5-bis(5-Methyl-6,7,8-trioxabicyclo[3.2.1]octane-1-yl)-1,2,4-trioxolane (trans-12b): Yellowish liquid. ^{1}H NMR δ 1.52 (s, 6H), 1.77-2.12 (m, 12H), 5.25 (s, 2H) ppm; ^{13}C NMR(BB) δ 16.52, 20.87, 26.92, 33.72, 102.02, 107.49, 110.73 ppm; ^{13}C NMR (DEPT) δ 16.51, 20.86, 26.92, 33.72, 102.01 ppm; Anal. Calcd for $C_{14}H_{20}O_9$ (332.3): C,50.60; H, 6.07. Found : C, 50.42; H, 6.16.

Coozonolyses of 5a with 1,4-cyclohexanedione(13):

A solution of **5a** (0.80 g, 3.72 mmol) and **13** (0.12 g, 1.24 mmol) in CH_2Cl_2 (80 mL) was treated with ozone at -58 °C until it turned blue. Residual ozone was flushed off with nitrogen, the mixture was warmed up to room temperature and the solvent was distilled off at reduced pressure to leave 1.8 g of a yellowish liquid residue. From this residue tetraozonide **14a** (165 mg, 9%, mixture of three diastereomers) were isolated by flash chromatography (column 1 x 50 cm; pentane/Et_2O, 95:5). Subsequent chromatographic separation of this mixture of **14a**-isomers under the same conditions afforded isomer **1** (55 mg, 2.9%) and isomer **2** (35 mg, 1.8%) but not isomer **3**, probably due to its low yield.

Tetraozonide 14a (isomer 1): Yellowish liquid. ^1H NMR δ 1.02 (s, 6H), 1.32 (s, 6H), 1.53 (s, 6H), 1.68-1.84 (m, 8H), 1.99-2.07 (m, 8H), 5.25 (s, 2H) ppm; ^{13}C NMR(BB) δ 21.25, 29.32, 30.23, 31.39, 34.91, 39.15, 46.95, 101.71, 107.41, 109.35, 109.96 ppm; ^{13}C NMR (DEPT) δ 21.24, 29.83, 30.21, 31.39, 34.88, 39.13, 46.94, 101.68 ppm; Anal. Calcd for $C_{24}H_{36}O_{12}$ (516.54): C, 55.81; H, 7.02. Found: C, 55.68; H, 7.14.

Tetraozonide 14a (isomer 2): Yellowish liquid. ^1H NMR δ 1.02 (s, 6H), 1.32 (s, 6H), 1.53 (s, 6H), 1.68-1.84 (m, 8H), 1.99-2.07 (m, 8H), 5.24 (s, 2H) ppm; ^{13}C NMR(BB) δ 21.26, 29.32, 30.24, 31.39, 34.92, 39.26, 46.96, 101.72, 107.42, 109.35, 109.95 ppm; ^{13}C NMR (DEPT) δ 21.27, 30.25, 31.39, 34.92, 39.25, 46.95, 101.72 ppm; Anal. Calcd for $C_{24}H_{36}O_{12}$ (516.54): C, 55.81; H, 7.02. Found: C, 55.87; H, 7.09.

Coozonolyses of 5b with 13:

A solution of **5b** (0.50 g, 2.67 mmol) and **13** (0.10 g, 0.89 mmol) in CH_2Cl_2 (80 mL) was treated with ozone at -60 °C until it turned blue. Residual ozone was flushed off with nitrogen, the mixture was warmed up to room temperature and the solvent was distilled off at reduced pressure to leave 0.80 g of yellowish liquid residue. From this residue tetraozonide **14b** (105 mg, 9%, mixture of two diastereomers) were isolated by flash chromatography (column 1 x 50 cm; pentane/Et_2O, 95:5). Subsequent chromatographic separation of this mixture of isomers under the same conditions afforded isomer **1** (25 mg, 2.0%) and isomer **2** (20 mg, 1.6%).

Tetraozonide 14b (isomer 1): Yellowish liquid. ^1H NMR δ 1.51 (s, 6H), 1.84-2.17 (m, 20H), 5.24 (s, 2H) ppm; ^{13}C NMR(BB) δ 16.53, 20.99, 26.36, 30.23, 33.74, 101.95, 107.87, 109.25, 110.71 ppm; ^{13}C

NMR(DEPT) δ 16.53, 20.99, 26.34, 30.24, 33.73, 102.02 ppm; Anal. Calcd for $C_{20}H_{28}O_{12}$ (460.43): C, 52.17; H, 6.13. Found: C, 51.98; H, 6.15.

Tetraozonide 14b (isomer 2): Yellowish liquid. ^{1}H NMR δ 1.53 (s, 6H), 1.85-2.20 (m, 20H), 5.25 (s, 2H) ppm; ^{13}C NMR(BB) δ 16.53, 20.96, 26.49, 30.52, 33.74, 101.60, 107.86, 109.27, 110.71 ppm; ^{13}C NMR (DEPT) δ 16.54, 21.00, 26.50, 30.52, 33.74, 101.60 ppm; Anal. Calcd for $C_{20}H_{28}O_{12}$ (460.43): C, 52.17; H, 6.13. Found: C, 52.28; H, 6.18.

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