Ozonolysis of 2-endo-7-anti-Diacylnorbornenes. A New Entry for the Synthesis of 2,4,6,13-Tetraoxapentacyclo[5.5.1.0^5.8.0^5.0^12]tridecanes

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Abstract: A new route for the synthesis of the title compounds 4a, 4b, 10a, and 10b has been developed via ozonolysis of 2-endo-7-anti-diacylnorbornenes 3a, 3b, 9a, and 9b. The synthesis of the unsubstituted (parent) compound 4a of tetraacetal tetraoxa-cages has been accomplished for the first time by this new entry. Ozonolysis reactions of 3a, 3b, and 9a were also performed in CDCl₃ for understanding the final ozonide structures and the ozonation chemistry. Ozonolysis of 3a, 3b, and 9a in CH₂Cl₂ at -78 °C followed by treatment with triethylamine provided an indirect support for the structures of the final ozonides 11a, 11b, and 14. © 1997, Elsevier Science Ltd. All rights reserved.

Introduction

The synthesis and chemistry of polycyclic cage compounds have attracted considerable attention in recent years. The vast majority of the work reported in this area has dealt with carbocyclic cage compounds. On the other hand, the synthesis and chemistry of heterocyclic cage compounds have received less attention. However, there are some reports regarding the chemistry and synthesis of oxa-cage compounds in the literature. This class of heterocyclic cages is synthesized by intramolecular alkene-oxirane (2c-2x) photocycloaddition, transannular cyclization of suitable compounds, tandem cyclization, dehydration of diols having the proper stereochemistry, base-promoted rearrangement, and intramolecular etherification of an alkene bond with organoselenium reagents.

Recently, we visualized that the "creation" of tetraacetal tetraoxa-cages from homopentaprismane might be achieved by replacing the skeletal carbon atoms with oxygen atoms at the proper positions and by extending the skeletal backbone. From the standpoint of retro-synthetic analysis, 2,3-bis-endo-diacylnorbornenes were chosen as the starting material for the synthesis of tetraoxa-cages by ozonolysis reaction. Therefore, we accomplished the synthesis of a series of oxa-cages along with this sequence. Afterward, we realized that 2-endo-7-anti-diacylnorbornenes might be chosen as an alternative starting material for the synthesis of tetraoxa-cages (Scheme 1). As part of a program that involves the synthesis and chemistry of new heterocyclic cage compounds, we report here the first synthesis of the unsubstituted (parent)
compound of tetraacetal tetraoxa-cages and its methyl derivatives by this new entry. We also wish to demonstrate the ozonation chemistry of 2-endo-7-anti-diacylnorbornenes.

**Scheme 1**

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\text{O} & \quad \text{O} \\
\end{align*}
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**Results and Discussion**

Reaction of 5-trimethylsilylcyclopentadiene with trimethylorthoformate in dichloromethane at -40 °C in the presence of catalytic amount of TMSOTf gave compound 1,\(^{11}\) which was run for the next reaction without purification. Diels-Alder reaction of the crude 1 with acrolein and methyl vinyl ketone at 0 °C for 48 h gave the cycloadducts 2a and 2b in 70% yields, respectively. Reaction of 2a and 2b with one equivalent of methanesulfonic acid in dichloromethane for 1 h gave the endo-anti isomers 3a and 3b in 90% yields, respectively. Compounds 3a and 3b can be directly obtained by reaction of the crude 1 with acrolein and methyl vinyl ketone in the presence of Cu(BF\(_4\))\(_2\) in dichloromethane at 0 °C for 24 h in 80% yields. Ozonolysis of the endo-anti isomers 3a and 3b in dichloromethane at -78 °C followed by reduction with dimethyl sulfide gave the tetraoxa-cage 4a and its 3-methyl derivative 4b in 80% yields, respectively (Scheme 2). Thus, we have accomplished for the first time the synthesis of the unsubstituted (parent) tetraoxa-cage 4a via ozonolysis of the endo-anti isomer 3a, a new entry for the synthesis of tetraacetal tetraoxa-cages.

**Scheme 2**
The $^1$H NMR spectrum of the parent compound 4a showed a doublet at $\delta$ 5.84 for the acetal protons on C$_1$ and C$_7$, a doublet at $\delta$ 5.51 for the acetal protons on C$_3$ and C$_5$, a multiplet at $\delta$ 3.42 for the protons on C$_8$ and C$_{12}$, a multiplet at $\delta$ 2.82 for the protons on C$_9$ and C$_{11}$, and a multiplet at $\delta$ 2.06-1.93 for the protons on C$_{10}$. The $^{13}$C NMR spectrum of 4a revealed a peak at $\delta$ 109.6 for C$_1$ and C$_7$, a peak at $\delta$ 103.1 for C$_3$ and C$_5$, a peak at $\delta$ 53.1 for C$_8$ and C$_{12}$, a peak at $\delta$ 45.3 for C$_9$ and C$_{11}$, and a peak at $\delta$ 29.5 for C$_{10}$. The structure of these tetraacetal oxa-cage compounds was proven by X-ray analysis of the crystalline compound 4a. The conformation of the oxygen atom O-4 with respect to the apical carbon atom C-10 was proven to be boat conformation which is consistent with previous reports. The bond angles of C(3)-O(4)-C(5) and C(9)-C(10)-C(11) are 117.5° and 99.5°, respectively, remarkably different from the ordinary bond angles with sp$^3$-hybridized atoms.

![Figure 1. ORTEP diagram of the parent compound 4a.](image-url)
and 9b in a ratio of 5 : 1 in 80% yield. The stereochemistry of the formyl group on the apical carbon of compounds 8a,b and 9a,b was confirmed by the next step ozonolysis reaction. Ozonolysis of the endo-anti isomers 9a,b in dichloromethane at -78 °C followed by reduction with dimethyl sulfide gave the tetraacetal tetraoxa-cages 10a,b in 80% yields. Ozonolysis of the endo-syn isomers 8a,b under the same reaction conditions did not give any detectable amount of 10a,b.

Scheme 3

Next, we turn our attention on the ozonolysis chemistry to clarify the problem that which carbonyl group, the endo carbonyl group or the carbonyl group on the apical carbon, reacts intramolecularly with the carbonyl oxide to form the final ozonide. Ozonolysis of 3a,b in dichloromethane at -78 °C followed by removal of the solvent at room temperature without reduction gave oligomeric or polymeric products which were not soluble in CDCl₃, acetone-d₆, or methanol-d₄ for NMR spectral analysis. Ozonolysis of 3a,b in CDCl₃ at -78 °C gave the final ozonides 11a,b (≥ 90%). No detectable amount of the other isomers 12a,b was obtained. In the case of 3b, no detectable amount of of 13 was obtained. Ozonolysis of 9a in CDCl₃ at -78 °C gave the final ozonide 14 as major product in about 80% yield. The ¹H and ¹³C NMR spectra of 11a,b and 14 were taken at -30 °C right after the ozonation reaction without purification. Thus, our experimental results may indicate that it is the anti carbonyl group on the apical carbon rather
than the endo carbonyl group to react preferentially with the carbonyl oxide group to form the final ozonide.

Scheme 4

![Scheme 4](image)

The $^1$H NMR spectrum of 11a showed two singlets at δ 9.84 and 9.50 for the two aldehyde protons and two singlets at δ 6.25 and 5.77 for the 1,2,4-trioxolane ring protons. The final ozonide obtained from ozonolysis of 3a is not the structure 12a, since 12a possesses a symmetry plane. The $^1$H NMR spectrum of 11b showed a singlet at δ 9.69 for the aldehyde proton, two singlets at δ 6.16 and 5.72 for the 1,2,4-trioxolane ring protons and a singlet at δ 2.17 for the methyl ketone protons. The $^1$H NMR spectrum of 14 displayed two singlets at δ 9.97 and 9.71 for the two aldehyde protons, a singlet at δ 5.76 for the 1,2,4-trioxolane ring proton and a singlet at δ 1.68 for the angular methyl protons. The $^{13}$C NMR spectrum of 14 revealed a singlet at δ 110.2 and a peak at δ 104.6 (d) for the quaternary carbon and the tertiary carbon of the trioxolane ring, respectively.

Recently, we demonstrated a new method for determining the regiochemistry of carbonyl oxide formation and hence the structure of the final ozonide.$^{10a,b}$ Now, we apply this method to support the structures of the final ozonides 11a,b and 14. Ozonolysis of 3a in dichloromethane at -78 °C followed by treatment with triethylamine gave the hydroxy lactone 15 in 85% yield (Scheme 5). Oxidation of 15 with PCC in dichloromethane gave the symmetrical bislactone 16. Ozonolysis of 3a in dichloromethane at -78 °C followed by addition of triethylamine and acetic anhydride gave the acetate 17. Ozonolysis of 3b in dichloromethane at -78 °C followed by treatment with triethylamine gave the hydroxy lactone 18 in 85% yield, which contained two stereoisomers. Acetylation of 18 with acetic anhydride and triethylamine in dichloromethane at 25 °C for 2 h gave 19 as major product and 20 as minor product. Reaction of 19 with triethylamine in dichloromethane at 25 °C for 24 h gave the thermodynamically more stable isomer 20 in 95% yield. Ozonolysis of 9a in dichloromethane at -78 °C followed by treatment with triethylamine gave the hydroxy lactone 21 in 70% yield. These results support indirectly for the structures of the final ozonides 11a,b and 14.
Conclusion

A new entry for the synthesis of the tetraacetal tetraoxa-cage compounds has been developed. The synthesis of the unsubstituted (parent) compound 4a of the tetraacetal tetraoxa-cages has been accomplished for the first time by this new route. The structure of the parent compound 4a is proven by X-ray analysis. Ozonolysis reactions of 3a, b and 9a are also performed in CDCl₃ for understanding the final ozonide structures and the ozonation chemistry. In the ozonolysis of 2-endo-7-anti-diacylnorbornenes, we found that it was the carbonyl group on the apical carbon instead of the endo carbonyl group to react intramolecularly with the carbonyl oxide group to form the final ozonides. Ozonolysis of 3a, 3b, and 9a in dichloromethane at -78 °C followed by treatment with triethylamine gave the hydroxy lactones 15, 18, and 21. This reaction gives an indirect support for the structures of the final ozonides 11a, 11b, and 14.

Experimental Section

General. Melting points were determined in capillary tubes with a Laboratory Devices melting point apparatus and uncorrected. Infrared spectra were recorded in CHCl₃ solutions or on neat
thin films between NaCl disks. 1H NMR spectra were determined at 300 MHz, and 13C NMR were determined at 75 MHz Fourier transform spectrometers. Chemical shifts are reported in ppm relative to TMS in the solvents specified. The multiplicities of 13C signals were determined by DEPT techniques. High resolution mass values were obtained with a high resolution mass spectrometer at the Department of Chemistry, National Tsing Hua University. Elemental analyses were performed at the microanalysis laboratory of National Taiwan University. X-ray analysis were carried out on a diffractometer at the Department of Chemistry, National Chung Hsing University. For thin-layer chromatography (TLC) analysis, precoated TLC plates (Kieselgel 60 F254) were used, and column chromatography was done by using Kieselgel 60 (70-230 mesh) as the stationary phase. THF was distilled immediately prior to use from sodium benzophenone ketyl under nitrogen. CH2Cl2 was distilled from CaH2 under nitrogen.

**Preparation of Compound 1 and the Diels-Alder Reaction of 1 with Acrolein and Methyl Vinyl Ketone.** To a solution of 5-trimethylsilyl cyclopentadiene (1.0 g, 7.3 mmol) in dichloromethane (20 mL) was added trimethyl orthoformate (0.85 g, 8.0 mmol) at 25 °C. The mixture was cooled to -40 °C, and a catalytic amount of TMSOTf (0.16 g, 0.73 mmol) was added at -40 °C. The reaction mixture was stirred at -40 °C for 1 h. The mixture was quenched by addition of ice. Extractive workup with dichloromethane (3 x 10 mL) followed by an ice-water wash (1 x 10 mL), drying over K2CO3, and evaporating the solvent at 0 °C afforded the crude product 1, which was kept at 0 °C without purification for the Diels-Alder reaction. To this crude product 1 in dichloromethane (20 mL) was added acrolein (0.45 g, 7.9 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 12 h and at room temperature for 36 h. The solvent was evaporated, and the crude product was purified by column chromatography to give the endo adduct 2a in 70% overall yield. The same reaction conditions and procedure were applied to the preparation of 2b in 70% yield.

**2-endo-Formyl-7-anti-dimethoxymethylbicyclo[2.2.1]-5-heptene 2a:** pale yellow oil; IR (neat) 2970, 1720, 1600 cm⁻¹; 1H NMR (300 MHz, CDCl3) δ 9.47 (d, J = 2.4 Hz, 1H), 6.14 (dd, J = 5.4 Hz, J = 3.0 Hz, 1H), 5.93 (dd, J = 5.4 Hz, J = 2.7 Hz, 1H), 4.21 (d, J = 8.4 Hz, 1H), 3.30 (s, 6H), 3.25 (d, J = 1.2 Hz, 1H), 2.99-2.94 (m, 2H), 1.49 (dd, J = 12 Hz, J = 4.2 Hz, 1H); 13C NMR (75 MHz, CDCl3, DEPT) δ 203.60 (CHO), 135.45 (CH), 129.42 (CH), 102.79 (CH) 63.19 (CH), 53.25 (CH3), 53.20 (CH3), 52.35 (CH), 45.85 (CH), 44.05 (CH), 27.93 (CH2); LRMS m/z (rel inten) 196 (M+ 3), 165 (16), 75 (100); HRMS (EI) calcd for C11H16O3 196.1099, found 196.1101. Anal. Calcd for C11H16O3: C, 67.32; H, 8.22. Found: C, 67.22; H, 8.20.

**2-endo-Acetyl-7-anti-dimethoxy methylbicyclo[2.2.1]-5-heptene 2b:** pale yellow oil; IR (neat) 2970, 1710, 1600, 1370 cm⁻¹; 1H NMR (300 MHz, CDCl3) δ 6.08 (dd, J = 5.7 Hz, J = 3.0 Hz, 1H), 5.79 (dd, J = 5.7 Hz, J = 2.7 Hz, 1H), 4.19 (d, J = 8.4 Hz, 1H), 3.30 (s, 3H), 3.28 (s, 3H), 3.22 (brs, 1H), 3.07-3.02 (m, 1H), 2.85 (brs, 1H), 2.12 (s, 3H), 2.02 (d, J = 9 Hz, 1H), 1.86-1.78 (m, 1H), 1.53 (dd, J = 11.7 Hz, J = 4.2 Hz, 1H); 13C NMR (75 MHz, CDCl3, DEPT) δ 207.62 (C=O), 134.98 (CH), 128.48 (CH), 102.96 (CH), 63.34 (CH), 53.17 (CH3), 52.88 (CH3), 52.06 (CH), 46.76 (CH), 43.70 (CH), 28.66 (CH3), 27.53 (CH2); LRMS m/z (rel inten) 210 (M+ 3), 135 (22), 75 (100); HRMS (EI) calcd for C12H18O3 210.1256, found 210.1258. Anal. Calcd for C12H18O3: C, 68.55; H, 8.63. Found: C, 68.42; H, 8.51.
Hydrolysis of 2a and 2b. To a solution of 2a (1.01 g, 5.10 mmol) in dichloromethane (20 mL) was added methanesulfonic acid (CH₃SO₃H) (0.49 g, 5.10 mmol) at 25 °C. The reaction mixture was stirred at room temperature for 1 h. After addition of saturated NaHCO₃ (20 mL) and extracted with CH₂Cl₂ (2 x 30 mL), the organic layer was washed with brine, dried over MgSO₄, and evaporated, and the residue was purified by column chromatography to give 3a (0.7 g) in 90% yield. The same reaction conditions and procedure were applied to the preparation of 3b in 90% yield.

2-endo-7-anti-Diformynorbornene 3a: pale yellow oil; IR (neat) 2970, 1718, 1600, 1370 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 9.62 (d, J = 2.1 Hz, 1H), 9.52 (d, J = 1.5 Hz, 1H), 6.24 (dd, J = 6.0 Hz, J = 3.0 Hz, 1H), 6.05 (dd, J = 6.0 Hz, J = 3.0 Hz, 1H), 6.36 (brs, 1H), 3.63 (brs, 1H), 3.07-3.03 (m, 1H), 2.42 (d, J = 1.2 Hz, 1H), 2.10-2.02 (m, 1H), 1.65-1.59 (m, 1H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ 203.69 (CHO), 202.43 (CHO), 135.80 (CH), 130.41 (CH), 70.85 (CH), 51.88 (CH), 45.82 (CH), 44.51 (CH), 27.76 (CH₂); LRMS m/z (rel inten) 150 (M⁺, 7), 121 (16), 94 (100); HRMS (EI) calcd for C₉H₁₀O₂ 150.0681, found 150.0683. Anal. Calcd for C₉H₁₀O₂: C, 71.98; H, 6.71. Found: C, 71.85; H, 6.79.

2-endo-Acetyl-7-anti-formylnorbornene 3b: pale yellow oil; IR (neat) 2970, 1720, 1708, 1600, 1370 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 9.60 (d, J = 2.7 Hz, 1H), 6.19 (dd, J = 5.7 Hz, J = 3.3 Hz, 1H), 5.94 (dd, J = 5.7 Hz, J = 2.7 Hz, 1H), 3.58 (brs, 1H), 3.26 (brs, 1H), 3.13-3.10 (m, 1H), 2.41 (brs, 1H), 2.15 (s, 3H), 1.94-1.90 (m, 1H), 1.66-1.61 (m, 1H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ 207.15 (C=O), 204.27 (CHO), 135.48 (CH), 129.88 (CH), 71.20 (CH), 51.97 (CH), 46.96 (CH), 44.48 (CH), 29.07 (CH₃) 27.88 (CH₂); LRMS m / z (rel inten) 164 (M⁺), 12, 136 (18), 121 (100); HRMS (EI) calcd for C₁₀H₁₂O₂ 164.0837, found 164.0841. Anal. Calcd for C₁₀H₁₂O₂: C, 73.15; H, 7.37. Found: C, 73.02; H, 7.28.

One Pot Procedure for the Preparation of 3a and 3b from 5-Trimethylsilyl Cyclopentadiene. To a solution of 5-trimethylsilyl cyclopentadiene (1.0 g, 7.3 mmol) in dichloromethane (20 mL) was added trimethyl orthoformate (0.85 g, 8.0 mmol) at 25 °C. The mixture was cooled to -40 °C, and a catalytic amount of TMSOTf (0.144 g, 0.67 mmol) was added at -40 °C. The reaction mixture was stirred at -40 °C for 1 h. The mixture was quenched by addition of ice. Extractive workup with dichloromethane (3 x 10 mL) followed by an ice-water wash (1 x 10 mL), drying over K₂CO₃, and evaporating the solvent at 0 °C afforded the crude product 1, which was kept at 0 °C without purification for the Diels-Alder reaction. To this product 1 in dichloromethane (20 mL) was added acrolein (0.45 g, 7.9 mmol) at 0 °C. After ten minutes, to this solution was added Cu(BF₄)₂ (0.17 g, 0.73 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 12 h. The solvent was evaporated, and the crude product was purified by column chromatography to give 3a (0.76 g) in 70% overall yield. The same reaction conditions and procedure were applied for the preparation of 3b from 5-trimethylsilyl cyclopentadiene in 70% overall yield.

Ozonolysis of 3a. Synthesis of the Unsubstituted (Parent) Compound 4a. A solution of 3a (0.10 g, 0.67 mmol) in dichloromethane (20 mL) was cooled to -78 °C, and ozone was bubbled through it at -78 °C until the solution turned light blue. To this solution was added dimethyl sulfide (0.20 g, 3.3 mmol) at -78 °C. Then, the reaction mixture was stirred at room temperature for 5 h. The solvent was evaporated, and the crude product was purified by column
Ozonolysis of 2-endo-7-anti-diacylnorbornenes

chromatography to give the parent compound 4a (0.098 g, 80%). The same reaction conditions and procedure were applied to the preparation of 4b in 80% yield.

2,4,6,13-tetraoxapentacyclo[5.5.1.0S'lX.05's.0s'12]tridecane 4a: white waxy solid; IR (CHCl₃) 2980, 2880, 1060 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.84 (d, J = 5.1 Hz, 2H), 5.51 (d, J = 5.7 Hz, 2H), 3.43-3.39 (m, 2H), 2.82 (brs, 2H), 2.06-1.93 (m, 2H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ 109.60 (2CH), 103.05 (2CH), 53.14 (2CH), 45.27 (2CH), 29.48 (CH₂); LRMS m/z (rel inten) 182 (M⁺, 56), 108 (100); HRMS (EI) calcd for C₉H₁₀O₄ 182.0579, found 182.0579. Anal. Calcd for C₉H₁₀O₄: C, 59.34; H, 5.53. Found: C, 59.30; H, 5.51.

3-Methyl-2,4,6,13-tetraoxapentacyclo[5.5.1.0a'11.05's.08'12]tridecane 4b: white waxy solid; IR (CHCl₃) 2980, 2880, 1060 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.81 (d, J = 5.1 Hz, 1H), 5.77 (d, J = 6.6 Hz, 1H), 3.51-3.38 (m, 2H), 2.87-2.78 (m, 1H), 2.70-2.62 (m, 1H), 1.95-1.93 (m, 2H), 1.46 (s, 3H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ 109.34 (C), 109.17 (CH), 108.44 (CH), 102.73 (CH), 54.30 (CH), 53.17 (CH), 49.44 (CH), 49.78 (CH), 29.89 (CH₂), 25.81 (CH₃); LRMS m/z (rel inten) 196 (M⁺, 12), 99 (76), 79 (100); HRMS (EI) calcd for C₁₀H₁₂O₄ 196.0736, found 196.0731. Anal. Calcd for C₁₀H₁₂O₄: C, 61.22; H, 6.16. Found: C, 61.20; H, 6.14.

Diels-Alder Reaction of Compound 6 with Acrolein and Methyl Vinyl Ketone. To a solution of 613 (2.0 g, 13 mmol) in dichloromethane (10 mL) was added acrolein (0.83 g, 14.3 mmol) at 25 °C. The reaction mixture was stirred at 25 °C for 48 h. The solvent was evaporated, and the crude product was purified by column chromatography to give the endo adduct 7a (50%), which was a mixture of two regioisomers without further separation. The same reaction conditions and procedure were applied to the preparation of 7b in 50% yield.

2-endo-Formyl-7-(a-acetoxyethylidene)bicyclo[2.2.1]-5-heptene 7a: pale yellow oil; IR (neat) 2960, 1750, 1720, 1190 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 9.51 and 9.49 (s, 1H), 6.34-6.28 (m, 1H), 6.15-6.05 (m, 1H), 3.67-3.60 (m, 1H), 3.35-3.29 (m, 1H), 3.08-2.98 (m, 1H), 2.17 and 2.14 (s, 3H), 2.08-1.98 (m, 1H), 1.81 and 1.77 (s, 3H), 1.65-1.53 (m, 1H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ 203.54 (CHO), 202.75 (CHO), 168.90 (2CO), 139.82 (C), 139.70 (C), 137.46 (CH), 136.88 (CH), 131.86 (CH), 131.25 (CH), 125.11 (C), 124.99 (C), 51.36 (CH), 50.54 (CH), 44.08 (CH), 43.23 (CH), 42.27 (CH), 41.48 CH), 27.85 (CH₂), 27.18 (CH₂), 27.03 (CH₂), 20.45 (CH₃), 15.90 (CH₃), 15.76 (CH₃); LRMS m/z (rel inten) 206 (M⁺, 11), 93 (17), 108 (100); HRMS (EI) calcd for C₁₂H₁₄O₃ 206.0943, found 206.0930.

2-endo-Acetyl-7-(a-acetoxyethylidene)bicyclo[2.2.1]-5-heptene 7b: pale yellow oil; IR (neat) 2960, 1750, 1720, 1190 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.30-6.21 (m, 1H), 6.06-5.97 (m, 1H), 3.59-3.52 (m, 1H), 3.27-3.22 (m, 1H), 3.15-3.03 (m, 1H), 2.15 and 2.13 (s, 3H), 2.07 and 2.05 (s, 3H), 2.02-1.87 (m, 1H), 1.81 and 1.76 (s, 3H), 1.64-1.53 (m, 1H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ 207.88 (CO), 207.68 (CO), 169.28 (CO), 169.22 (CO), 140.78 (C), 140.69 (C), 137.34 (CH), 136.79 (CH), 131.75 (CH), 131.25 (CH), 124.99 (C), 124.90 (C), 51.74 (CH), 50.89 (CH), 45.27 (CH), 44.45 (CH), 42.56 (CH), 41.80 (CH), 29.10 (CH₂), 29.04 (CH₂), 28.58 (CH₂), 27.82 (CH₂), 20.80 (CH₃), 15.93 (CH₃); LRMS m/z (rel inten) 220 (M⁺, 8), 85 (75), 71 (100); HRMS (EI) calcd for C₁₃H₁₆O₃ 220.1109, found 220.1102.

Hydrolysis of 7a and 7b. To a solution of 7a (1.6 g, 13 mmol) in methanol (10 mL) and H₂O (10 mL) was added a catalytic amount of Na₂CO₃ (80 mg, 0.78 mmol) at 25 °C. The reaction mixture was stirred at 25 °C for 1 h. After addition of saturated NH₄Cl (20 mL) and extraction
with ether (5 x 30 mL), the organic layer was washed with brine, dried over MgSO₄, and evaporated, and the residue was purified by column chromatography to give compounds 8a (64%) and 9a (16%). The same reaction conditions and procedure were applied to the preparation of 8b (65%) and 9b (15%).

2-endo-Formyl-7-syn-acetylnorbornene 8a: pale yellow oil; IR (neat) 2970, 1720, 1708, 1600, 1370 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 9.53 (d, J = 1.5 Hz, 1H), 6.23 (dd, J = 6.0 Hz, J = 3.0 Hz, 1H), 6.06 (dd, J = 6.0 Hz, J = 3.0 Hz, 1H), 3.48 (brs, 1H), 3.18 (brs, 1H), 3.06-3.03 (m, 1H), 2.54 (s, 1H), 2.11 (s, 3H), 1.91-1.83 (m, 1H), 1.58-1.52 (m, 1H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ 206.89 (C=O), 203.31 (CHO), 137.95 (CH), 132.74 (CH), 70.68 (CH), 50.08 (CH), 44.75 (CH), 43.81 (CH), 27.50 (CH₃), 25.20 (CH₂); LRMS m/z (rel inten) 164 (M⁺, 16), 136 (17), 108 (100); HRMS (EI) calcd for C₁₀H₁₂O₂ 164.0837, found 164.0838. Anal. Calcd for C₁₀H₁₂O₂: C, 73.15; H, 7.37. Found: C, 73.10; H, 7.31.

2-endo-Formyl-7-anti-acetylnorbornene 9a: pale yellow oil; IR (neat) 2970, 1720, 1708, 1600, 1370 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 9.48 (d, J = 1.5 Hz, 1H), 6.18 (dd, J = 6.0 Hz, J = 3.0 Hz, 1H), 6.00 (dd, J = 6.0 Hz, J = 3.0 Hz, 1H), 3.64 (brs, 1H), 3.34 (brs, 1H), 3.07-3.03 (m, 1H), 2.55 (brs, 1H), 2.11 (s, 3H), 1.98-1.92 (m, 1H), 1.59-1.54 (m, 1H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ 207.18 (C=O), 202.96 (CHO), 135.68 (CHO), 133.05 (CH), 71.06 (CH), 51.71 (CH), 46.06 (CH), 44.73 (CH), 29.80 (CH₃), 27.30 (CH₂); LRMS m/z (rel inten) 164 (M⁺, 21), 149 (18), 108 (100); HRMS (EI) calcd for C₁₀H₁₂O₂ 164.0837, found 164.0832. Anal. Calcd for C₁₀H₁₂O₂: C, 73.15; H, 7.37. Found: C, 73.04; H, 7.27.

2-endo-7-syn-diacetylnorbornene 8b: pale yellow oil; IR (neat) 2970, 1720, 1708, 1370 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.19 (dd, J = 5.7 Hz, J = 3.0 Hz, 1H), 5.95 (dd, J = 6.0 Hz, J = 3.0 Hz, 1H), 3.44-3.42 (m, 1H), 3.15-3.10 (m, 2H), 2.53 (brs, 1H), 2.11 (s, 3H), 1.60-1.65 (m, 1H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ 203.12 (C=O), 202.74 (C=O), 137.60 (CH), 132.33 (CH), 70.94 (CH), 49.87 (CH), 45.65 (CH), 43.81 (CH), 29.07 (CH₂), 27.47 (CH₃), 25.22 (CH₂); LRMS m/z (rel inten) 178 (M⁺, 24), 149 (51), 85 (100); HRMS (EI) calcd for C₁₁H₁₄O₂ 178.0994, found 178.1003. Anal. Calcd for C₁₁H₁₄O₂: C, 74.13; H, 7.92. Found: C, 74.01; H, 7.90.

2-endo-7-anti-diacetylnorbornene 9b: pale yellow oil; IR (neat) 2970, 1720, 1708, 1370 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.12 (dd, J = 5.7 Hz, J = 2.7 Hz, 1H), 5.88 (dd, J = 5.7 Hz, J = 2.7 Hz, 1H), 3.41 (m, 2H), 3.15-3.06 (m, 1H), 2.95-2.89 (m, 1H), 2.85-2.78 (m, 1H), 1.97-1.89 (m, 1H), 1.63-1.58 (m, 1H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ 203.12 (C=O), 202.74 (C=O), 135.30 (CH), 130.03 (CH), 71.44 (CH), 51.80 (CH), 47.19 (CH), 44.78 (CH), 29.77 (CH₃), 28.95 (CH₃), 27.96 (CH₂); LRMS m/z (rel inten) 178 (M⁺, 27), 149 (56), 85 (100); HRMS (EI) calcd for C₁₁H₁₄O₂ 178.0994, found 178.0998. Anal. Calcd for C₁₁H₁₄O₂: C, 74.13; H, 7.92. Found: C, 74.02; H, 7.88.

Ozonolysis of the endo-anti-Norbornenes 9a and 9b. The same reaction conditions and procedure for the ozonolysis of 3a and 3b were applied for the ozonolysis of 9a and 9b in 80% yields.

1-Methyl-2,4,6,13-tetraoxapentacyclo[5.5.1.0³₁₁.0⁶₈]tridecanec 10a: white waxy solid; mp 92-93 °C; IR (CHCl₃) 2980, 2880, 1060 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.83 (d, J = 6.0 Hz, 1H), 5.51 (d, J = 5.7 Hz, 2H), 3.52-3.45 (m, 1H), 3.12-3.06 (m, 1H), 2.95-2.89 (m, 1H), 2.85-2.78...
Ozonolysis of 2-endo-7-anti-diacylnorbornenes

(m, 1H), 2.08-1.82 (m, 2H), 1.55 (s, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\), DEPT) \(\delta\) 117.65 (C), 109.52 (CH), 103.28 (CH), 102.84 (CH), 56.58 (CH), 54.24 (CH), 45.85 (CH), 45.33 (CH), 29.42 (CH\(_2\)), 24.73 (CH\(_3\)); LRMS \(m/z\) (rel inten) 196 (M\(^+\), 12), 79 (100); HRMS (EI) calcd for C\(_{10}\)H\(_{12}\)O\(_4\) 196.0736, found 196.0734. Anal. Calcd for C\(_{10}\)H\(_{12}\)O\(_4\): C, 61.22; H, 6.16. Found: C, 61.30; H, 6.08.

1,5-Dimethyl-2,4,6,13-tetraoxapentacyclo[5.5.1.0\(^3\)\'^7.0\(^5\)\'^\(8\)\']tridecane 10b: white waxy solid; mp 104-105 °C; IR (CHCl\(_3\)) 2980, 2880, 1060 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 5.77 (d, \(J=6.0\) Hz, 1H), 5.50 (d, \(J=6.6\) Hz, 1H), 3.55-3.47 (m, 1H), 3.08-3.03 (m, 1H), 2.92-2.86 (m, 1H), 2.63-2.57 (m, 1H), 1.94-1.84 (m, 2H), 1.56 (s, 3H), 1.47 (s, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\), DEPT) \(\delta\) 117.30 (C), 109.23 (C), 108.44 (CH), 103.08 (CH), 56.78 (CH), 55.61 (CH), 49.64 (CH), 45.45 (CH), 29.94 (CH\(_2\)), 25.95 (CH\(_3\)), 24.67 (CH\(_3\)); LRMS \(m/z\) (rel inten) 210 (M\(^+\), 14), 139 (65), 79 (100); HRMS (EI) calcd for C\(_{11}\)H\(_{14}\)O\(_4\) 210.0892, found 210.0889. Anal. Calcd for C\(_{11}\)H\(_{14}\)O\(_4\): C, 62.85; H, 6.71. Found: C, 62.63; H, 6.60.

General Procedure for the Ozonolysis of 3a, 3b, and 9a in CDCl\(_3\) for Taking the \(^1\)H and \(^{13}\)C NMR Spectral Data of the Final Ozonides 11a, 11b, and 14. A solution of 3a (20 mg, 0.13 mmol) in CDCl\(_3\) (1.5 mL) was cooled to -78 °C, and ozone was bubbled through it at -78 °C until the solution turned light blue. After bubbling with N\(_2\) to get rid of excess ozone, the solution was transferred to an NMR tube, and the \(^1\)H and \(^{13}\)C NMR spectra were taken at -30 °C. The NMR spectral data of the crude ozonolysis product indicated that ozonolysis of 3a in CDCl\(_3\) at -78 °C gave the final ozonide 11a (> 90%). The same reaction conditions and procedure were applied to the preparation of 11b (> 90%) and 14 (80%).

3,4-bis-endo-Diformyl-8,9,10-trioxatricyclo[5.2.1.O\(^2\)\'^7.0\(^8\)\']decane 11a: \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 9.84 (s, 1H), 9.50 (s, 1H), 6.25 (s, 1H), 5.77 (s, 1H), 3.17-3.11 (m, 1H), 3.00-2.86 (m, 2H), 2.79-2.71 (m, 1H), 2.21-2.12 (m, 2H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\), DEPT) \(\delta\) 201.27 (CHO), 198.09 (CHO), 103.51 (CH), 101.04 (CH), 55.35 (CH), 52.32 (CH), 46.84 (CH), 45.10 (CH), 27.53 (CH\(_2\)).

3-endo-Formyl-4-endo-acetyl-8,9,10-trioxatricyclo[5.2.1.O\(^6\)\'^7.0\(^8\)\']decane 11b: \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 9.69 (s, 1H), 6.16 (s, 1H), 5.72 (s, 1H), 3.18-3.14 (m, 1H), 2.96-2.70 (m, 3H), 2.17 (s, 3H), 2.26-2.04 (m, 2H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\), DEPT) \(\delta\) 207.24 (C=O), 198.15 (CHO), 103.19 (CH), 101.42 (CH), 54.62 (CH), 54.42 (CH), 47.14 (CH), 45.42 (CH), 29.86 (CH\(_2\)), 27.56 (CH\(_3\)).

3-endo-Formyl-4-endo-acetyl-8,9,10-trioxatricyclo[5.2.1.O\(^6\)\'^7.0\(^8\)\']decane 14: \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 9.97 (s, 1H), 9.71 (s, 1H), 5.76 (s, 1H), 3.23-2.79 (m, 4H), 2.31-2.01 (m, 2H), 1.68 (s, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\), DEPT) \(\delta\) 200.89 (CHO), 198.76 (CHO), 110.22 (C), 104.62 (CH), 56.08 (CH), 52.53 (CH), 51.16 (CH), 46.90 (CH), 27.61 (CH\(_2\)), 14.33 (CH\(_3\)).

Formation of the Tetraquinane Oxa-Cage Compound 15. A solution of 3a (0.42 g, 2.9 mmol) in dichloromethane (20 mL) was cooled to -78 °C, and ozone was bubbled through it at -78 °C until the solution turned light blue. To this solution was added triethylamine (0.29 g, 2.9 mmol) at -78 °C. Then, the reaction mixture was stirred at room temperature for 3 h. The solvent was evaporated, and the crude product was purified by column chromatography to give 15 (0.48 g, 85%).
Oxidation of 15 with PCC. To a solution of 15 (0.20 g, 1.0 mmol) in dichloromethane (30 mL) was added PCC (0.44 g, 2.0 mmol) at 0 °C. The reaction mixture was stirred at 25 °C for 12 h. The solution was filtered through silica gel and Celite. The solvent was evaporated, and the crude product was purified by column chromatography to give the symmetrical bislactone 16 in 80% yield.

2,8-Dioxo-3,5,7-trioxatetracyclo[7.2.1.0^4.11.0^6.1°]dodecane 16: white waxy solid; mp 255-256 °C; IR (CHCl₃) 2960, 1770, 1107 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.19 (d, J = 3.6 Hz, 2H), 4.04 (brs, 2H), 3.34 (brs, 2H), 2.67 (brs, 2H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ 177.26 (2CO), 108.03 (2CH), 52.70 (2CH), 46.70 (2CH), 37.93 (CH₂); LRMS m/z (rel inten) 196 (M⁺, 5), 97 (78), 152 (100); HRMS (EI) calcd for C₉H₈O₅ 196.0372, found 196.0374. Anal. Calcd for C₉H₈O₅: C, 55.11; H, 4.11. Found: C, 55.20; H, 4.07.

Formation of the Acetate 17. A solution of 3a (0.42 g, 2.9 mmol) in dichloromethane (20 mL) was cooled to -78 °C, and ozone was bubbled through it at -78 °C until the solution turned light blue. To this solution was added triethylamine (0.31 g, 3.1 mmol) and acetic anhydride (0.31 g, 3.1 mmol) at -78 °C. Then, the reaction mixture was stirred at 25 °C for 3 h. The solvent was evaporated, and the crude product was purified by column chromatography to give 17 (0.61 g, 85%). 8β-Acetoxy-2-oxo-3,5,7-trioxatetracyclo[7.2.1.0^4.11.0^6.1°]dodecane 17: white waxy solid; mp 185-186 °C; IR (CHCl₃) 2980, 1770, 1745, 1100 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.17 (d, J = 5.1 Hz, 1H), 6.09 (s, 1H), 6.04 (d, J = 5.1 Hz, 1H), 3.74-3.66 (m, 2H), 3.20 (dd, J = 9.6 Hz, 1H, 2.69-2.51 (m, 1H), 2.04 (s, 3H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ 176.94 (C=O), 169.42 (C=O), 112.17 (CH), 107.47 (CH), 104.10 (CH), 55.03 (CH), 52.06 (CH), 49.87 (CH), 46.47 (CH), 37.46 (CH₂), 21.09 (CH₃); LRMS m/z (rel inten) 240 (M⁺, 22), 152 (34), 117 (100); HRMS (EI) calcd for C₁₁H₁₂O₆ 240.0634, found 240.0637. Anal. Calcd for C₁₁H₁₂O₆: C, 55.00; H, 5.04. Found: C, 55.12; H, 5.06.

Formation of the Tetraquinane Oxa-Cage Compound 18. The same reaction conditions and procedure for the preparation of 15 from 3a were applied to the preparation of 18 from ozonolysis of 3b in 85% yield.

8-Hydroxy-8-methyl-2-oxo-3,5,7-trioxatetracyclo[7.2.1.0^4.11.0^6.1°]dodecane 18 which is a mixture of two stereoisomers: white waxy solid; mp 116-117 °C; IR (CHCl₃) 3450, 2980, 1770, 1745, 1100 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.08 (d, J = 6.0 Hz, 1H), 5.86 (d, J = 6.6 Hz, 1H), 5.73 (d, J = 4.2 Hz, 1H), 5.69 (d, J = 6.0 Hz, 1H), 3.68-3.59 (m, 4H), 3.23-3.07 (m, 2H), 2.63-2.56 (m, 2H), 2.45-2.08 (m, 6H), 1.33 (s, 3H), 1.30 (s, 3H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ 181.83 (CO), 180.49 (CO), 111.94 (CH), 110.77 (CH), 110.33 (CH), 109.31 (C), 108.50 (C), 108.09 (CH), 58.56 (CH), 57.65 (CH), 55.61 (CH), 54.07 (CH), 52.99 (CH), 52.41 (CH), 49.84 (CH), 48.97 (CH), 35.54 (CH₂), 34.05 (CH₂), 28.95 (CH₃), 24.53 (CH₃); LRMS m/z (rel inten) 212 (M⁺, 11), 194 (87),
Ozonolysis of 2-endo-7-anti-diacylnorbornenes

152 (100); HRMS (EI) calcd for C_{10}H_{12}O_5, 212.0685, found 212.0674. Anal. Calcd for C_{10}H_{12}O_5: C, 56.60; H, 5.70. Found: C, 56.47; H, 5.61.

**Acetylation of 18.** To a solution of 18 (0.21 g, 1.0 mmol) in dichloromethane (20 mL) was added acetic anhydride (0.11 g, 1.1 mmol) and triethylamine (0.11 g, 1.1 mmol) at room temperature. The reaction mixture was stirred at 25 °C for 4 h. After addition of saturated NH_4Cl (10 mL) and extracted with ether (3 x 20 mL), the organic layer was washed with brine, dried over MgSO_4, and evaporated, and the residue was purified by column chromatography to give compound 19 as major product (60%) and compound 20 as minor product (20%).

6a-Acetoxy-8a-acetyl-2-oxo-3,5-dioxatricyclo[5.2.1.0^4,9]decane 19: white waxy solid; mp 112-113 °C; IR (CHCl_3) 2980, 1775, 1740, 1704, 1370 cm⁻¹; ¹H NMR (300 MHz, CDCl_3) δ 6.12 (s, 1H), 6.11 (d, J = 6.0 Hz, 1H), 3.75-3.70 (m, 1H), 3.35-3.12 (m, 3H), 2.48-2.36 (m, 1H), 2.25 (s, 3H), 2.22-2.12 (m, 1H), 2.08 (s, 3H); ¹³C NMR (75 MHz, CDCl_3, DEPT) δ 205.70 (C=O), 176.36 (C=O), 169.28 (C=O), 106.05 (CH), 99.38 (CH), 57.28 (CH), 50.95 (CH), 49.29 (CH), 42.56 (CH), 30.94 (CH₂), 29.92 (CH₃), 20.91 (CH₃); LRMS m/z (rel inten) 254 (M⁺, 11), 231 (14), 117 (100); HRMS (EI) calcd for C_{12}H_{14}O_6: M⁺, 254.0790, found 254.0786. Anal. Calcd for C_{12}H_{14}O_6: C, 56.69; H, 5.55. Found: C, 56.52; H, 5.46.

6a-Acetoxy-8-α-acetyl-2-oxo-3,5-dioxatricyclo[5.2.1.0^4,9]decane 20: white waxy solid; mp 120-121 °C; IR (CHCl_3) 2980, 1775, 1740, 1704, 1370 cm⁻¹; ¹H NMR (300 MHz, CDCl_3) δ 6.23 (s, 1H), 6.10 (d, J = 6.6 Hz, 1H), 3.75-3.67 (m, 1H), 3.26-3.15 (m, 2H), 2.84-2.75 (m, 1H), 2.62-2.55 (m, 1H), 2.26 (s, 3H), 2.23-2.09 (m, 1H), 2.05 (s, 3H); ¹³C NMR (75 MHz, CDCl_3, DEPT) δ 205.90 (C=O), 177.06 (C=O), 169.39 (C=O), 106.20 (CH), 100.57 (CH), 54.07 (CH), 51.62 (CH), 47.57 (CH), 44.92 (CH), 36.09 (CH₂), 29.89 (CH₃), 21.03 (CH₃); LRMS m/z (rel inten) 254 (M⁺, 9), 195 (31), 152 (100); HRMS (EI) calcd for C_{12}H_{14}O_6: M⁺, 254.0798, found 254.0798. Anal. Calcd for C_{12}H_{14}O_6: C, 56.69; H, 5.55. Found: C, 56.54; H, 5.42.

**Conversion of 19 to 20.** To a solution of 19 (0.15 g, 0.60 mmol) in dichloromethane (20 mL) was added triethylamine (0.12 g, 1.2 mmol) at 25 °C. The reaction mixture was stirred at 25 °C for 24 h. After addition of saturated NH_4Cl (10 mL) and extracted with ether (3 x 20 mL), the organic layer was washed with brine, dried over MgSO_4, and evaporated, and the residue was purified by column chromatography to give 20 in 95% yield.

**Formation of the Tetraquinane Oxa-Cage Compound 21.** The same reaction conditions and procedure for the preparation of 15 from 3a were applied to the preparation of 21 from ozonolysis of 9a in 70% yield.

8β-Hydroxy-4-methyl-2-oxo-3,5,7-trioxatetracyclo[7.2.1.0^4,8.0^6,10]dodecane 21: white waxy solid; mp 158-159 °C; IR (CHCl_3) 2980, 1770, 1107 cm⁻¹; ¹H NMR (300 MHz, CDCl_3) δ 6.01 (d, J = 5.1 Hz, 1H), 5.39 (d, J = 2.1 Hz, 1H), 3.75-3.67 (m, 1H), 3.38-3.23 (m, 2H), 2.97 (d, J = 3.0 Hz, 1H), 2.75 (m, 1H), 2.62 (d, J = 14.7 Hz, 1H), 2.48-2.37 (m, 1H), 1.70 (s, 3H); ¹³C NMR (75 MHz, CDCl_3, DEPT) δ 177.55 (CO), 116.71 (C), 110.57 (CH), 104.36 (CH), 56.17 (CH), 56.02 (CH), 50.72 (CH), 48.07 (CH), 36.91 (CH₂), 24.85 (CH₃); LRMS m/z (rel inten) 212 (M⁺, 59), 197 (100); HRMS (EI) calcd for C_{10}H_{14}O_5: M⁺, 212.0685, found 212.0682. Anal. Calcd for C_{10}H_{14}O_5: C, 56.60; H, 5.70. Found: C, 56.52; H, 5.66.
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References and Notes:
12. The author has deposited atomic coordinates for 4a with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

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