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Synthesis of New Type Diacetal Trioxa-Cage Compounds via an Intramolecular Nucleophilic Addition of the Hydroxy Group to the Carbonyl Oxide Group

Hsien-Jen Wu,* Ching-Shiun Chao, and Chu-Chung Lin

Department of Applied Chemistry, National Chiao Tung University, Hsinchu, Taiwan, China

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The synthesis of diacetal trioxa-cage compounds with a new type of skeleton is reported. Ozonolysis of the diols **2a**−**f**, **21**, **24**, and **33** in CH_2Cl_2 at −78 °C followed by reduction with Me_2S gave the diacetal trioxa-cages **3a**−**f**, **22**, **25**, and **34** in 70−80% yields, respectively. A mechanism via an intramolecular nucleophilic addition of the hydroxy group of the diols to the carbonyl oxide group is proposed for the formation of the diacetal trioxa-cages. The effect of the number of carbon atoms at the bridge of the diols on the formation of the diacetal trioxa-cage skeleton was examined. Ozonolysis of the diols **13** and **15** under the same reaction conditions gave compounds **16** and **18,** respectively. No detectable amount of the trioxa-cages **17** and **19** was obtained. For the synthesis of the diacetal trioxa-cages **28a**−**c** and **31**, which possess an alkene bond intact, ozonolysis of the diols **27a**−**c** and **30** was performed by controlling the amount of ozone.

Introduction

The synthesis and chemistry of polycyclic cage compounds have attracted considerable attention in recent years.[1] The vast majority of the work reported in this area has dealt with carbocyclic cage compounds. These cage compounds have played a key role in theoretical organic chemistry by providing rigid and often symmetric frameworks for evaluating theories put forth on the physicochemical properties of organic molecules. In addition, some precursors of these cage compounds are important building blocks for the synthesis of polycyclic unnatural and natural products. Heterocyclic cage compounds have also received attention in recent years from synthetic as well as mechanistic consideration. The main purpose for the studies was the desire to compare the reactivity pattern of carbon cage compounds with their heterologues. We envision that studies on the synthesis and chemistry of heterocyclic cage compounds can greatly expand the scopes and utilities of cage compounds.

There are some reports regarding the chemistry[2] and synthesis[3−8] of oxa-cage compounds in the literature. This class of heterocyclic cage compounds is synthesized by intramolecular alkene−oxirane ($2\sigma-2\pi$) photocycloaddition,[3] by transannular cyclization of suitable compounds,[4] by tandem cyclization,[5] by dehydration of diols having the proper stereochemistry,[6] by base-promoted rearrangement,[7] and by intamolecular etherification of an alkene bond with organoselenium reagents.[8] Recently, we utilized ozonolysis reaction for the synthesis of a series of oxa-cage compounds, such as triacetal trioxa-cages,[9] tetraacetal tetraoxa-cages,[10] tetraacetal pentaoxa-cages,[11] and pentaacetal pentaoxa-cages (the pentaoxa-[5]peristylanes).[12] Later on, we investigated the chemical nature of the acetal group of tetraoxa-cages and discovered a hydride rearrangement and an one-pot conversion from oxa-cages to aza-cages.[13] We also developed a method for the synthesis of diacetal trioxa-cages **C** via the iodo-cages **B** by iodine-induced sequential cyclization of norbornene derivatives **A** (Scheme 1).[14]

An intermolecular nucleophilic addition of a hydroxy group to a carbonyl oxide, for instance, ozonolysis of an olefin in an alcohol, affords an α-alkoxy hydroperoxide and a carbonyl compound.[15] This reaction is usually used

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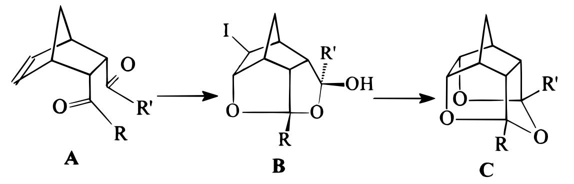
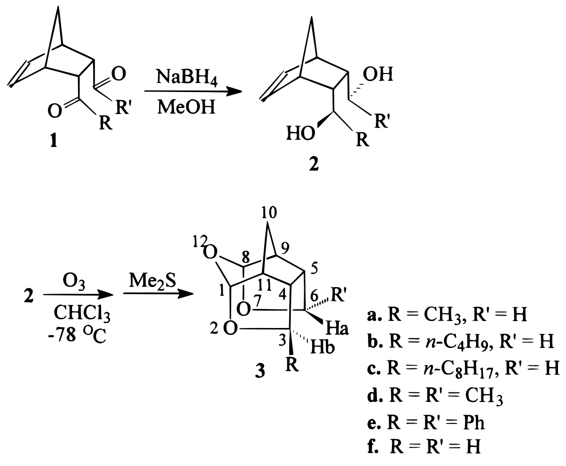
Scheme 1



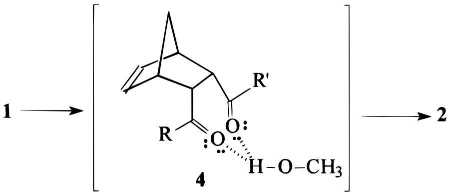
for the determination of the regiochemistry of carbonyl oxide formation from primary ozonide fragmentation because the product composition reflects the regioselectivity in the primary ozonide cleavage.[16] This reaction has also been utilized for the synthesis of terminally differentiated compounds.[17] As part of a program that involves the synthesis, chemistry, and applications of new heterocyclic cages, we report here the synthesis of diacetal trioxa-cage compounds with a new type of skeleton via an intramolecular nucleophilic addition of the hydroxy group to the carbonyl oxide which is generated by ozonolysis of the alkene bond.

Results and Discussion

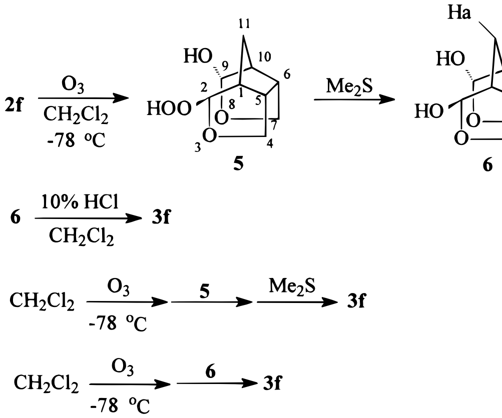
Scheme 2



Scheme 3



Scheme 4



Reduction of 2,3-bis-*endo*-diacylnorbornenes **1a**−**e**[14a] with $NaBH_4$ in MeOH gave the diols **2a**−**e** in 75−80% yields.[18] Compound **2f** was prepared by reduction of maleic anhydride-cyclopentadiene adduct with $LiAlH_4$ in dry THF. The stereochemistry of the hydroxy groups of **2a**−**e** was difficult to assign at this stage and was determined by the following chemical transformation. Ozonolysis of **2a**−**f** in CH_2Cl_2 at −78 °C followed by reduction with Me_2S gave the diacetal trioxa-cages **3a**−**f** in 60−70% yields (Scheme 2). Trioxa-cages **3a**−**f** possess a new type of skeleton which is different from the previously synthesized diacetal trioxa-cages **C**.[14] The ^1H NMR spectrum of **3d** revealed a quartet at δ 4.49 for the protons on C_3 and C_6 whereas the ^1H NMR spectrum of **3e** displayed a singlet at δ 5.14 for the same protons. The coupling constants ($J = 0$ Hz) suggest that there are zero H−H coupling between H_4 and H_b (or H_5 and H_a). This is consistent with our assignment that H_a and H_b are *endo* (rather than *exo*) in compounds **3a**−**f**. The stereochemistry of the alkyl group of **3** was also determined on the basis of NOE experiments of **3a**. Irradiating the C_3 proton H_b (δ4.44) gives 9.9% enhancement for the H_a proton absorptions on C_6 and 4.3% enhancement for the methyl proton peak. Irradiating the methyl protons (δ1.19) gives 4.5% enhancement for the H_b proton absorptions, 3.2% enhancement for the C_4 proton peak, and no enhancement for the H_a proton absorptions on C_6. Irradiating the H_a proton on C_6 (δ4.23) gives 10.2% enhancement for the H_b proton peak, 3.1% enhancement for the C_5 proton peak, and no enhancement for the methyl proton absorptions. Thus, we have accomplished the synthesis of trioxa-cages with a new type of skeleton in a short sequence.

To account for the high stereoselectivity of the reduction reaction of **1a**−**e** with $NaBH_4$ in MeOH, we propose that compounds **1a**−**e** may adopt conformation **4** in the protic solvent by virtue of double hydrogen bonding (Scheme 3). Nucleophilic attack of $NaBH_4$ on the carbonyl groups of **4** from the sterically less hindered outside face gives the major products **2a**−**e**.

Ozonolysis of **2f** in CH_2Cl_2 at −78 °C without reduction gave the hydroperoxide **5** in 80% yield (Scheme 4). The ^1H NMR spectrum of **5** displayed two singlets at δ5.34 and 5.30 for the two hemiacetal protons on C_2 and C_9. The coupling constants ($J = 0$ Hz) may imply that the proton on C_2 is trans to the C_1 proton, and the proton on C_9 is trans to the C_{10} proton. Reduction of the purified **5** with Me_2S gave the dihemiacetal **6** in 90% yield. Both ^1H and ^{13}C NMR spectra showed that compound **6**

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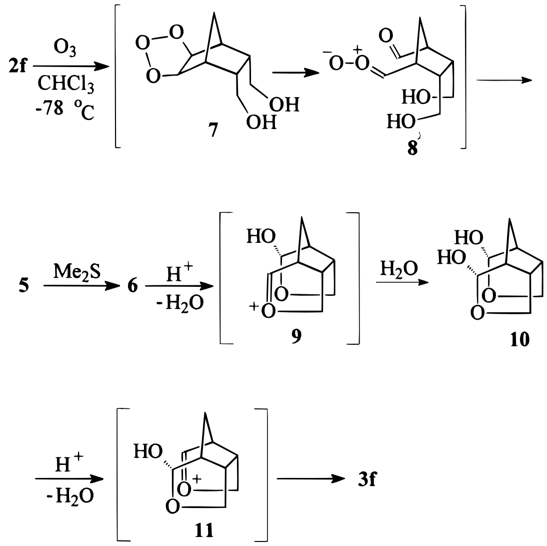
Scheme 5

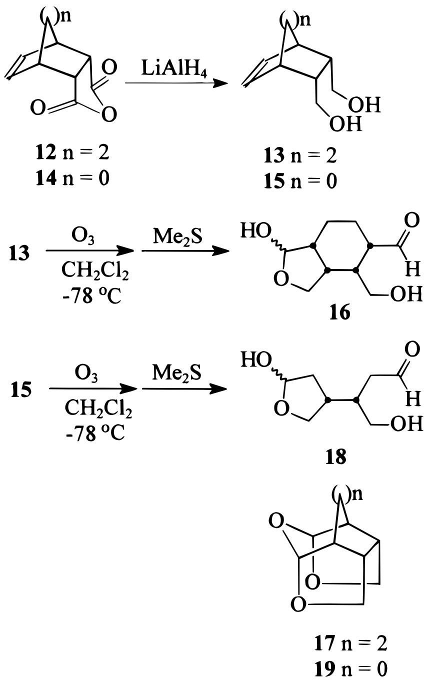


possesses a symmetry plane. The stereochemistry of the hydroxy groups of **6** was determined on the basis of NOE experiments. Irradiating the hemiacetal protons (δ5.30) gives 3.9% enhancement for the syn proton H_a absorptions on C_{11} and 2.0% enhancement for the C_1 and C_{10} proton peak. Also, the coupling constant ($J = 0$ Hz) is consistent with the assignment that the hemiacetal protons on C_2 and C_9 are trans to the protons on C_1 and C_{10}. Treatment of **6** with 10% HCl in CH_2Cl_2 gave the trioxa-cages **3f** in 70% yield. When the hydroperoxide **5** was dissolved in an ozonated CH_2Cl_2 solution and then Me_2S was added, the trioxa-cage **3f** was obtained as the major product. Also, addition of **6** in an ozonated CH_2Cl_2 solution gave **3f** as the major product. These results imply that the ozonated CH_2Cl_2 blank solution is acidic.

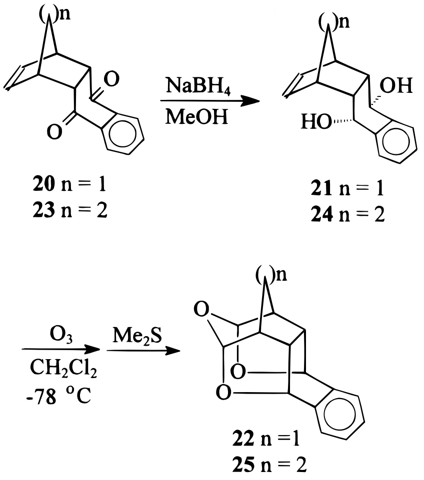
A mechanism is proposed for the ozonolysis of **2** to give the trioxa-cages **3**. 1,3-Dipolar cycloaddition of an ozone molecule with the alkene bond of **2f** via the *exo* face gave the 1,2,3-trioxolane (primary ozonide) **7**. Fragmentation of **7** leading to the carbonyl oxide **8**, which was followed by intramolecular nucleophilic addition of the hydroxy groups to the carbonyl oxide group and the aldehyde group, gave the hydroperoxide **5**. Reduction of **5** with dimethyl sulfide gave **6**. Acid-catalyzed anomerization of **6,** followed by dehydration, gave the trioxa-cages **3f** (Scheme 5).

To understand the effect of the number of carbon atoms at the bridge on the formation of the diacetal trioxa-cage skeleton, we prepared compounds **13** and **15**. Diels–Alder reaction of maleic anhydride with 1,3-cyclohexadiene followed by reduction of the cycloadduct **12** with $LiAlH_4$ gave the diol **13**. Reduction of compound **14** (commerically available) with $LiAlH_4$ gave the diol **15**. Ozonolysis of **13** in CH_2Cl_2 at −78 °C followed by reduction with Me_2S gave compound **16** in 70% yield (Scheme 6). No detectable amount of the diacetal trioxa-cage **17** was obtained. Ozonolysis of **15** under the same reaction conditions gave compound **18** in 75% yield. No detectable amount of the trioxa-cage **19** was obtained. Thus, the number of carbon atoms at the bridge could affect the formation of the diacetal trioxa-cage skeleton.

Scheme 6



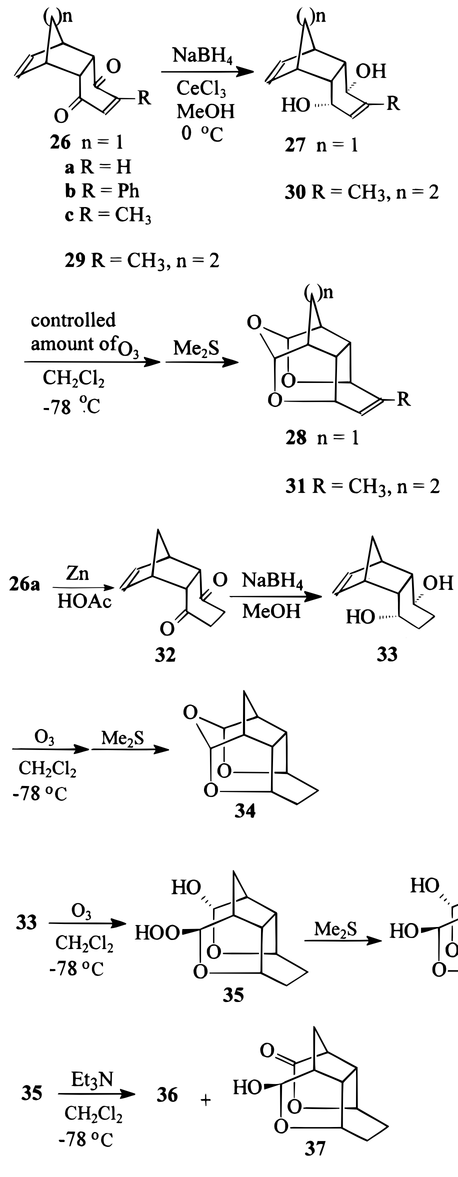
Scheme 7



To extend the synthesis of diacetal trioxa-cages, the cycloadducts of quinone derivatives were prepared. Reduction of the cyclopentadiene–naphthoquinone and cyclohexadiene–naphthoquinone cycloadducts **20** and **23** with sodium borohydride in methanol gave the diols **21** and **24** in 87–90% yields, respectively. Nucleophilic addition of $NaBH_4$ on the carbonyl groups from the sterically less hindered *exo* face gave the observed products **21** and **24**. Ozonolysis of the diols **21** and **24** in CH_2Cl_2 at −78 °C followed by reduction with Me_2S gave the diacetal trioxa-cages **22** and **25** in 70–80% yields, respectively (Scheme 7). Thus, we have demonstrated that the formation of the trioxa-cages **22** and **25** can be used as a probe for the determination of the stereochemistry of the hydroxy groups of the diols **21** and **24**. In the case of ozonolysis of **24**, which possessess two carbon atoms at the bridge and a benzo-group bound ring, the formation of trioxa-cages **25** takes place, different from the case of ozonolysis of **13**.

Reduction of the cyclopentadiene–benzoquinone cycloadducts **26a**–**c** and the cyclohexadiene–benzoquinone cycloadduct **29** with $NaBH_4$ in the presence of $CeCl_3$[19] in MeOH at 0 °C gave diols **27a**–**c** and **30** in 80–85% yields, respectively. Ozonolysis of **27a**–**c** and **30** in CH_2Cl_2 at −78 °C with controlled amount of ozone, followed by

Scheme 8



reduction with Me$_2$S, gave the diacetal trioxa-cages **28a**–**c** and **31** in 30–40% yields, respectively (Scheme 8). Thus, the synthesis of diacetal trioxa-cages with an alkene bond intact could be accomplished by controlling the amount of ozone. Treatment of **26a** with Zn powder in glacial HOAc[20] at 25 °C gave compound **32** in 90% yield. Reduction of **32** with NaBH$_4$ in MeOH gave the diol **33**. Ozonolysis of **33** in CH$_2$Cl$_2$ at −78 °C followed by reduction with Me$_2$S gave the trioxa-cage **34** in 80% yield. Ozonolysis of **33** in CH$_2$Cl$_2$ at −78 °C without reduction gave the hydroperoxide **35** in 85% yield. Reduction of purified **35** with Me$_2$S gave the dihemiacetal **36** in 90% yield. Treatment of **35** with Et$_3$N in CH$_2$Cl$_2$ at 25 °C gave **36** (60%) and the lactone **37** (33%). Thus, in reaction with the hydroperoxide **35**, Et$_3$N acts as a reducing agent to give **36** and acts as a base to give **37**.

Conclusion

The synthesis of new type diacetal trioxa-cage compounds **3a**–**f**, **22**, **25**, and **34** via ozonolysis of the diols **2a**–**f**, **21**, **24**, and **33** has been accomplished in a short sequence in good yields. A mechanism via an intramolecular nucleophilic addition of the hydroxy group of the diols to the carbonyl oxide group generated by ozonolysis reaction is proposed for the formation of the diacetal trioxa-cages. The number of carbon atoms at the bridge of the diols was found to affect the formation of the trioxa-cage skeleton. Ozonolysis of the diols **13** and **15** under the same reaction conditions did not give the corresponding trioxa-cage compounds **17** and **19**. The synthesis of the diacetal trioxa-cage compounds **28a**–**c** and **31**, which possess an alkene bond intact, has been accomplished by ozonolysis of the diols **27a**–**c** and **30**, controlling the amount of ozone.

Experimental Section

General. Melting points were determined in capillary tubes with a Laboratory Devices melting point apparatus and uncorrected. Infrared spectra were recorded in CHCl$_3$ solutions or on neat thin films between NaCl disks. ^{1}H NMR spectra were determined at 300 MHz, and ^{13}C NMR spectra were determined at 75 MHz on Fourier transform spectrometers. Chemical shifts are reported in ppm relative to TMS in the solvents specified. The multiplicities of ^{13}C 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 this department. For thin-layer chromatography (TLC) analysis, precoated TLC plates (Kieselgel 60 F$_{254}$) 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. CH$_2$Cl$_2$ was distilled from CaH$_2$ under nitrogen.

Reduction of Compound 1e with Sodium Borohydride in Methanol. To a solution of compound **1e**[10a] (0.83 g, 3.0 mmol) in MeOH (20 mL) was added NaBH$_4$ (0.13 g, 3.3 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h. The solvent was evaporated, and saturated NH$_4$Cl (20 mL) was added. After extraction with ether (5 × 30 mL), the organic layer was washed with brine, dried over MgSO$_4$, and evaporated, and the residue was purified by column chromatography to give the diol **2e** (0.68 g, 80%). The diols **2a**–**d** were prepared from **1a**–**d** by the same reaction conditions.[18] Spectral data for **2e:** white solid; mp 146–147 °C; IR (CHCl$_3$) 3500–3300, 1600, 750, 700 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.39–7.26 (m, 10H), 6.10 (brs, 2H), 4.54–4.51 (m, 2H), 2.83–2.80 (m, 2H), 2.12 (brs, 2H) 1.22–1.10 (m, 2H); ^{13}C NMR (75 MHz, CDCl$_3$, DEPT) δ 143.62 (2C), 134.99 (2CH), 128.53 (4CH), 127.86 (2CH), 126.84 (4CH), 75.44 (2CH), 51.66 (2CH), 48.93 (CH$_2$), 47.53 (2CH); LRMS *m/z* (rel int) 282 (M$^+$, 10), 77 (100); HRMS (EI) calcd for $C_{19}H_{22}O_2$ 282.1619, found 282.1610.

General Procedure for the Ozonolysis of 2a–f. Formation of the Diacetal Trioxa-Cage Compounds 3a–f. A solution of **2a** (0.50 g, 3.0 mmol) in CH$_2$Cl$_2$ (30 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 Me$_2$S (0.52 g, 8.4 mmol) at −78 °C, and the reaction mixture was stirred at room temperature for 5 h. The solvent was evaporated, and the crude product was purified by column chromatography to give the diacetal trioxa-cage compound **3a** (0.38 g, 70%).

3b-Methyl-2,7,12-trioxatetracyclo[6.3.1.0^{4,11}.0^{5,9}]dodecane 3a: White waxy solid; mp 58–59 °C; IR (CHCl$_3$) 2960, 1050 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ5.40 (d, J = 6.6 Hz, 2H), 4.44 (q, J = 6.6 Hz, 1H), 4.23 (d, J = 9.6 Hz, 1H), 3.86 (dd, J = 9.6, 5.2 Hz, 1H), 2.91–2.86 (m, 1H), 2.76–2.70 (m, 1H), 2.64–2.57 (m, 1H), 2.35–2.29 (m, 1H), 1.82–1.65 (m, 2H), 1.19 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, CDCl$_3$, DEPT) δ 103.89 (CH), 103.86 (CH), 76.43 (CH), 69.40 (CH$_2$), 47.88 (CH), 46.19 (CH), 45.17 (CH), 42.45 (CH), 23.81 (CH$_2$), 23.49

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(CH_3); LRMS *m/z* (rel int) 182 (M^+, 5), 81 (100); HRMS (EI) calcd for $C_{10}H_{14}O_3$ 182.0943, found 182.0949. Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.90; H, 7.75. Found: C, 65.78; H, 7.69..

3β-*n*-Butyl-2,7,12-trioxatetracyclo[6.3.1.0^{4,11}.0^{5,9}]dodecane 3b: white waxy solid; mp 50−51 °C; IR ($CHCl_3$) 2960, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ5.43 (d, J = 6.6 Hz, 1H), 5.41 (d, J = 6.6 Hz, 1H), 4.23−4.19 (m, 2H), 3.85 (dd, J = 9.6, 5.1 Hz, 1H), 2.82−2.75 (m, 1H), 2.74−2.70 (m, 1H), 2.62−2.58 (m, 1H), 2.40−2.30 (m, 1H), 1.77−1.69 (m, 2H), 1.50−1.25 (m, 6H), 0.89 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 103.77 (CH), 103.68 (CH), 80.47 (CH), 69.37 (CH_2), 46.20 (CH), 46.08 (CH), 45.40 (CH), 42.48 (CH), 37.04 (CH_2), 28.02 (CH_2) 23.81 (CH_2), 22.42 (CH_2), 13.89 (CH_3); LRMS *m/z* (rel int) 224 (M^+, 14), 109 (100); HRMS (EI) calcd for $C_{13}H_{20}O_3$ 224.1413, found 224.1402. Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.72; H, 8.91..

3β-*n*-Octyl-2,7,12-trioxatetracyclo[6.3.1.0^{4,11}.0^{5,9}]dodecane 3c: white waxy solid; mp 45−47 °C; IR ($CHCl_3$) 2950, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ5.44 (d, J = 6.6 Hz, 1H), 5.41 (d, J = 6.6 Hz, 1H), 4.23−4.20 (m, 2H), 3.85 (dd, J = 9.6, 5.1 Hz, 1H), 2.81−2.75 (m, 1H), 2.73−2.68 (m, 1H), 2.61−2.54 (m, 1H), 2.37−2.32 (m, 1H), 1.81−1.66 (m, 2H), 1.38−1.26 (m, 14H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 103.89 (CH), 103.79 (CH), 80.61 (CH), 69.49 (CH_2), 46.34 (CH), 46.21 (CH), 45.52 (CH), 42.63 (CH), 37.48 (CH_2), 31.80 (CH_2) 29.49 (2CH_2), 29.19 (CH_2), 26.00 (CH_2), 23.94 (CH_2) 22.59 (CH_2), 14.04 (CH_3); LRMS *m/z* (rel int) 280 (M^+, 10), 109 (100); HRMS (EI) calcd for $C_{17}H_{28}O_3$ 280.2038, found 280.2047. Anal. Calcd for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C, 72.74; H, 10.16.

3β,6β-Dimethyl-2,7,12-trioxatetracyclo[6.3.1.0^{4,11}.0^{5,9}]dodecane 3d: white waxy solid; mp 66−67 °C; IR ($CHCl_3$) 2970, 1055 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ5.43 (d, J = 6.3 Hz, 2H), 4.49 (q, J = 6.3 Hz 2H), 2.89−2.84 (m, 2H), 2.33−2.31 (m, 2H), 1.80−1.63 (m, 2H), 1.18 (d, J = 6.3 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 103.80 (2CH), 76.46 (2CH), 48.23 (2CH), 44.77 (2CH), 23.61 (CH_2), 23.31 (2CH_3); LRMS *m/z* (rel int) 196 (M^+, 10), 83 (100); HRMS (EI) calcd for $C_{11}H_{16}O_3$ 196.1099, found 196.1090. Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.31; H, 8.22. Found: C, 67.41; H, 8.30.

3β,6β-Diphenyl-2,7,12-trioxatetracyclo[6.3.1.0^{4,11}.0^{5,9}]dodecane 3e: white waxy solid; mp 148−149 °C; IR ($CHCl_3$) 3060, 1050, 750, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ6.91−6.74 (m, 10H) 5.71 (d, J = 6.6 Hz, 2H), 5.14 (s, 2H), 3.11−3.08 (m, 2H), 3.04−3.01 (m, 2H), 1.92−1.90 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 138.74 (2C), 128.54 (2CH), 127.66 (4CH), 126.07 (4CH), 103.13 (2CH), 82.59 (2CH), 50.85 (2CH), 45.79 (2CH), 23.97 (CH_2); LRMS *m/z* (rel int) 320 (M^+, 10), 77 (100); HRMS (EI) calcd for $C_{21}H_{20}O_3$ 320.1421, found 320.1430. Anal. Calcd for $C_{21}H_{20}O_3$: C, 78.72; H, 6.30. Found: C, 78.80; H, 6.42.

2,7,12-Trioxatetracyclo[6.3.1.0^{4,11}.0^{5,9}]dodecane 3f: white waxy solid; mp 89−90 °C; IR ($CHCl_3$) 2960, 1050 cm^{-1}; ^1H NMR(300 MHz, $CDCl_3$) δ 5.44 (d, J = 6.3 Hz, 2H), 4.18 (d, J = 9.6 Hz, 2H), 3.90 (dd, J = 9.6, 5.1 Hz, 2H), 2.78−2.73 (m, 2H), 2.67−2.61 (m, 2H), 1.85−1.70 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 103.97 (2CH), 69.34 (2CH_2), 46.51 (2CH), 42.10 (2CH), 23.97 (CH_2); LRMS *m/z* (rel int) 168 (M^+, 10), 109 (100); HRMS (EI) calcd for $C_9H_{12}O_3$ 168.0786, found 168.0780. Anal. Calcd for $C_9H_{12}O_3$: C, 64.26; H, 7.20. Found: C, 64.38; H, 7.31.

Ozonolysis of 2f Without Reduction. A solution of **2e** (0.46 g, 3.0 mmol) in CH_2Cl_2 (30 mL) was cooled to −78 °C, and ozone was bubbled through it at −78 °C until the solution turned light blue. After 10 min stirring, the solvent was evaporated, and the crude product was purified by column chromatography to give the hydroperoxide **5** (0.53 g, 80%): pale yellow oil; IR ($CHCl_3$) 3500−3300, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.47 (s, 1H), 5.34 (s, 1H), 5.30 (s, 1H), 4.14−4.00 (m, 2H), 3.90−3.78 (m, 2H), 3.58 (brs, 1H); 3.12−2.94 (m, 2H), 2.76−2.62 (m, 2H), 2.30−2.20 (m, 1H), 1.40−1.30 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 112.15 (CH), 102.30 (CH), 69.15 (CH_2), 68.15 (CH_2), 53.94 (CH), 49.84 (CH), 45.03 (CH), 44.73 (CH), 32.10 (CH_2); LRMS *m/z* (rel int) 202 (M^+, 20), 91 (100); HRMS (EI) calcd for $C_9H_{14}O_5$ 202.0841, found 202.0847. Anal. Calcd for $C_9H_{14}O_5$: C, 53.44; H, 6.98. Found: C, 53.60; H, 7.10.

Reduction of 5 with Dimethyl Sulfide. To a solution of purified **5** (0.41 g, 2.0 mmol) in CH_2Cl_2 (20 mL) was added excess Me_2S (0.62 g, 10 mmol) at 25 °C. 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 the dihemiacetal **6** (0.34 g, 90%): pale yellow oil; IR ($CHCl_3$) 3500−3300, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.31 (s, 2H), 4.15−4.05 (m, 2H), 3.82−3.75 (m, 2H), 3.13 (brs, 2H), 3.06−3.00 (m, 2H), 2.76−2.65 (m, 2H), 2.22−2.12 (m, 1H), 1.32−1.17 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 102.45 (2CH), 68.41 (2CH_2), 54.10 (2CH), 44.68 (2CH), 31.99 (CH_2); LRMS *m/z* (rel int) 186 (M^+, 10), 79 (38), 109 (100); HRMS (EI) calcd for $C_9H_{14}O_4$ 186.0892, found 186.0899. Anal. Calcd for $C_9H_{14}O_4$: C, 58.04; H, 7.58. Found: C, 58.17; H, 7.69.

Treatment of 6 with 10% HCl. To a solution of **6** (0.37 g, 2.0 mmol) in CH_2Cl_2 (30 mL) was added 10% HCl (0.5 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 1 h. Saturated $NaHCO_3$ (5 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated, and the residue was purified by column chromatography to give the diacetal trioxa-cage **3e** in 70% yield.

Reduction of 5 with Dimethyl Sulfide in an Ozonated Dichloromethane Solution. Dichloromethane (30 mL) was cooled to −78 °C, and ozone was bubbled through it at −78 °C. Compound **5** (0.2 g, 1.0 mmol) was added to the solvent at −78 °C. To this solution was then added Me_2S (0.31 g, 5.0 mmol) at −78 °C, and the reaction mixture was stirred at room temperature for 2 h. The solvent was evaporated, and the crude product was purified by column chromatography to give **3e** in 80% yield.

Treatment of 6 with an Ozonated Dichloromethane Solution. Dichloromethane (30 mL) was cooled to −78 °C, and ozone was bubbled through it at −78 °C. Compound **6** (1.86 g, 1.0 mmol) was added to the ozonated solvent at −78 °C, and the reaction mixture was stirred at −78 °C for 1 h. The solvent was evaporated, and the crude product was purified by column chromatography to give **3e** in 85% yield.

Ozonolysis of Compound 13 and 15. The same reaction conditions and procedure as for the ozonolysis of **2a−f** were applied for the ozonolysis of **13** and **15** to give compounds **16** and **18** in 70−75% yields, respectively. No detectable amount of the diacetal trioxa-cage compounds **17** and **19** was obtained. Spectral data for **16**: pale yellow oil; IR ($CHCl_3$) 3500−3300, 2930, 1720, 1060 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.71 (s, 1H), 5.15 (d, J = 3.0 Hz, 1H), 4.12−4.08 (m, 1H), 4.00−3.88 (m, 2H), 3.54−3.50 (m, 1H), 2.48−2.42 (m, 1H), 2.26−2.22 (m, 1H), 2.20−2.13 (m, 4H), 1.97−1.80 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 203.70 (CHO), 101.14 (CH), 72.10 (CH_2), 61.14 (CH_2), 52.23 (CH), 39.48 (CH), 38.72 (CH), 32.16 (CH), 21.44 (CH_2), 19.47 (CH_2); LRMS *m/z* (rel int) 200 (M^+, 20), 46 (100); HRMS (EI) calcd for $C_{10}H_{16}O_4$ 200.1049, found 200.1062.

Spectral data for **18**: pale yellow oil; IR ($CHCl_3$) 3600−3300, 2970, 1720, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.82 (s, 1H), 5.34 (d, J = 3.0 Hz, 1H), 4.11−4.02 (m, 2H), 3.94 (dd, J = 8.1, 4.2 Hz, 1H), 3.38 (d, J = 12 Hz, 1H), 2.90−2.60 (m, 2H), 2.47 (brs, 1H), 2.28−2.20 (m, 1H), 2.06 (d, J = 12 Hz, 1H), 1.70 (brs, 2H), 1.51−1.40 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 200.87 (CHO), 99.18 (CH), 73.30 (CH_2), 63.12 (CH_2), 46.18 (CH_2), 36.86 (CH), 32.95 (CH_2), 32.05 (CH); LRMS *m/z* (rel int) 174 (M^+, 24), 46 (100); HRMS (EI) calcd for $C_8H_{14}O_4$ 174.0892, found 174.0881.

Reduction of Compound 20 with Sodium Borohydride in Methanol. The same reaction conditions and procedure as for the reduction of **1e** were applied for the reduction of **20** to give compound **21** in 87% yield. white solid; mp 148−150 °C; IR ($CHCl_3$) 3500−3300, 3030, 2980 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.25−7.13 (m, 4H), 5.07 (brs, 2H), 4.90 (brs, 2H), 4.87−4.83 (m, 2H), 3.04−2.90 (m, 4H), 1.32−1.17 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 139.99 (2C), 134.20 (2CH), 127.26 (2CH), 122.77 (2CH), 69.34 (2CH), 49.58 (CH_2), 46.03 (2CH), 45.59 (2CH); LRMS *m/z* (rel int) 228 (M^+, 7), 19 (100);

HRMS (EI) calcd for $C_{15}H_{16}O_2$ 228.1151, found 228.1163. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.91; H, 7.07. Found: C, 78.80; H, 7.15.

Ozonolysis of Compound 21. Formation of Trioxa-Cage 22. The same reaction conditions and procedure as for the ozonolysis of **2a**–**f** were applied for the ozonolysis of **21** to give the trioxa-cage **22** in 75% yield. Spectral data for **22**: white solid; mp 163–163.5 °C; IR ($CHCl_3$) 3020, 2980, 1035 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.30 (m, 4H), 5.48 (d, $J = 6.6$ Hz, 2H), 5.12–5.08 (m, 2H), 3.01 (brs, 2H), 2.86–2.81 (m, 2H), 1.89 (brs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 135.10 (2C), 129.94 (2CH), 128.57 (2CH), 103.40 (2CH), 79.74 (2CH), 47.31 (2CH), 43.55 (2CH), 26.16 (CH_2); LRMS *m/z* (rel int) 242 (M^+, 100); HRMS (EI) calcd for $C_{15}H_{14}O_3$ 242.0943, found 242.0939; Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.35; H, 5.83. Found: C, 74.47; H, 5.92.

Reduction of Compound 23 with Sodium Borohydride in Methanol. The same reaction conditions and procedure as for the reduction of **1e** were applied for the reduction of **23** to give compound **24** in 90% yield: white solid; mp 181–182 °C; IR ($CHCl_3$) 3500–3300, 3050, 1600, 1080 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30–7.20 (m, 4H), 6.35 (brs, 2H), 4.68 (brs, 2H), 3.00 (brs, 2H), 2.76 (brs, 2H), 2.20 (brs, 2H), 1.61–1.54 (m, 2H), 1.37–1.33 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 140.53 (2C), 132.52 (2CH), 128.34 (2CH), 128.06 (2CH), 72.22 (2CH), 46.00 (2CH), 33.63 (2CH), 26.32 ($2CH_2$); LRMS *m/z* (rel int) 242 (M^+, 42), 166 (51), 76 (100); HRMS (EI) calcd for $C_{16}H_{18}O_2$ 242.1307, found 242.1315. Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.30; H, 7.49. Found: C, 79.45; H, 7.60.

Ozonolysis of Compound 24. Formation of Trioxa-Cage 25. The same reaction conditions and procedure as for the ozonolysis of **2a**–**f** were applied for the ozonolysis of **24** to give the trioxa-cage **25** in 70% yield: white solid; mp 132–133 °C; IR ($CHCl_3$ 3020, 2925, 1030 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.43–7.36 (m, 4H), 5.39 (d, $J = 5.4$ Hz, 2H), 4.97 (d, $J = 2.4$ Hz, 2H), 2.70–2.67 (m, 2H), 2.48–2.45 (m, 2H), 2.14–1.90 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 135.10 (2C), 129.24 (2CH), 128.57 (2CH), 104.86 (2CH), 80.85 (2CH), 44.60 (2CH), 35.80 (2CH), 16.08 ($2CH_2$); LRMS *m/z* (rel int) 256 (M^+, 100); HRMS (EI) calcd for $C_{16}H_{16}O_3$ 256.1099, found 256.1091. Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.97; H, 6.30. Found: C, 74.86; H, 6.38.

General Procedure for the Reduction of 26a–c with Sodium Borohydride in the Presence of $CeCl_3$. To a solution of compound **26b** (2.5 g, 10 mmol) in MeOH (50 mL) were added $NaBH_4$ (0.57 g, 15 mmol) and $CeCl_3 \cdot 7H_2O$ (8.6 g, 23 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 3 h. The solvent was evaporated, and saturated NH_4Cl (30 mL) was added. After extraction with ether (5 × 30 mL), the organic layer was washed with brine, dried over $MgSO_4$, and evaporated, and the residue was purified by column chromatography to give the diol **27b** (2.04 g, 80%). The diol **27a** is a known compound.[6c]

Spectral data for **27b**: white solid; mp 190–191 °C; IR ($CHCl_3$) 3500–3300, 1640, 1600, 750, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37–7.17 (m, 5H), 6.03–5.95 (m, 2H), 5.78–5.76 (m, 1H), 4.84 (s, 1H), 4.74–4.71 (m, 1H) 4.49–4.44 (m, 1H), 3.34 (s, 1H), 3.00–2.93 (m, 2H), 2.80–2.68 (m, 2H), 1.38 (brs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 144.57 (C), 141.01 (C), 136.15 (CH), 134.84 (CH), 131.28 (CH), 128.95 (2CH), 128.31 (2CH), 127.87 (CH), 68.87 (CH), 67.27 (CH), 51.59 (CH_2), 46.64 (CH), 46.49 (CH), 45.82 (CH), 45.21 (CH); LRMS *m/z* (rel int) 254 (M^+, 11), 222 (100); HRMS (EI) calcd for $C_{17}H_{18}O_2$ 254.1367, found 254.1379. Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.27; H, 7.14. Found: C, 80.40; H, 7.25.

Spectral data for **27c**: white solid; mp 199–200 °C; IR ($CHCl_3$) 3500–3300, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.82 (dd, $J = 5.7$, 2.7 Hz, 1H), 5.77 (dd, $J = 5.7$, 3.0 Hz, 1H), 5.01 (brs, 1H), 4.89 (brs, 2H), 4.38–4.35 (m, 1H), 4.28 (brs, 1H), 2.98–2.96 (m, 2H), 2.78–2.74 (m, 2H), 1.61 (d, $J = 1.5$ Hz, 3H), 1.29–1.28 (m, 2H); ^{13}C NMR (75 MHz, CD_3COCD_3, DEPT) δ 137.43 (C), 137.37 (CH), 133.76 (CH), 126.44 (CH), 70.18 (CH), 67.94 (CH), 50.31 (CH_2), 46.52 (CH), 46.41 (CH), 44.80 (CH), 44.08 (CH), 18.23 (CH_3); LRMS *m/z* (rel int) 192 (M^+, 5), 175 (100); HRMS (EI) calcd for $C_{12}H_{16}O_2$192.1151, found 192.1165. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.96; H, 8.39. Found: C, 75.10; H, 8.51.

Ozonolysis of 27a–c with Controlled Amount of Ozone. Synthesis of the Trioxa-Cages 28a–c. A solution of **27b** (0.50 g, 2.0 mmol) in CH_2Cl_2 (40 mL) was cooled to −78 °C, and ozone was bubbled through it at −78 °C until compound **27b** was consumed by thin-layer chromatography tracing. To this solution was added Me_2S (0.36 g, 5.8 mmol) at −78 °C, and the reaction mixture was stirred at room temperature for 5 h. The solvent was evaporated, and the crude product was purified by column chromatography to give the diacetal trioxa-cage **28b** (0.21 g, 40%).

8,10,12-Trioxapentacyclo[5.5.2.0^{2,6}.0^{3,11}.0^{5,9}]-13-tetradecene 28a: white solid; mp 155–156 °C; IR ($CHCl_3$) 2980, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.41 (dd, $J = 4.2$, 2.4 Hz, 2H), 5.45 (d, $J = 6.3$ Hz, 2H), 4.66–4.64 (m, 2H), 2.92–2.88 (m, 2H), 2.78–2.72 (m, 2H), 1.98–1.84 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 132.19 (2CH), 103.40 (2CH), 73.74 (2CH), 47.66 (2CH), 43.11 (2CH), 26.62 (CH_2), LRMS *m/z* (rel int) 192 (M^+, 8), 117 (100); HRMS (EI) calcd for $C_{11}H_{12}O_3$ 192.0786, found 192.0798. Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.72; H, 6.30. Found: C, 68.82; H, 6.39.

13-Phenyl-8,10,12-trioxapentacyclo[5.5.2.0^{2,6}.0^{3,11}.0^{5,9}]-13-tetradecene 28b: white solid; mp 141–142 °C; IR ($CHCl_3$) 2860, 1640, 1040, 750, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.52–7.26 (m, 5H), 6.56 (d, $J = 6.6$ Hz, 1H), 5.54 (d, $J = 6.6$ Hz, 1H), 5.47 (d, $J = 6.6$ Hz, 1H), 4.96 (d, $J = 6.0$ Hz, 1H), 4.84 (dd, $J = 6.6$, 6.0 Hz, 1H), 3.02–2.70 (m, 4H), 2.00–1.89 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 143.49 (C), 140.14 (C), 128.25 (2CH), 127.79 (CH), 126.36 (2CH), 125.92 (CH), 103.72 (CH), 103.22 (CH), 77.20 (CH), 74.90 (CH), 47.63 (CH), 47.57 (CH), 44.40 (CH), 42.12 (CH), 26.74 (CH_2); LRMS *m/z* (rel int) 268 (M^+, 100); HRMS (EI) calcd for $C_{17}H_{16}O_3$ 268.1099, found 268.1095. Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.09; H, 6.01. Found: C, 76.21; H, 6.10.

13-Methyl-8,10,12-trioxapentacyclo[5.5.2.0^{2,6}.0^{3,11}.0^{5,9}]-13-tetradecene 28c: white solid; mp 152–153 °C; IR ($CHCl_3$) 2950, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.06–6.03 (m, 1H), 5.46 (d, $J = 6.6$ Hz, 1H), 5.42 (d, $J = 6.3$ Hz, 1H), 4.64 (dd, $J = 6.3$, 6.3 Hz, 1H), 4.42 (d, $J = 6.0$ Hz, 1H), 2.91–2.88 (m, 2H), 2.82–2.62 (m, 2H), 1.97 (s, 3H), 1.95–1.87 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 140.98 (C), 124.85 (CH), 103.55 (CH), 103.19 (CH), 78.84 (CH), 74.95 (CH), 47.67 (CH), 47.59 (CH), 43.72 (CH), 42.25 (CH), 26.71 (CH_2), 23.33 (CH_3); LRMS *m/z* (rel int) 206 (M^+, 11), 117 (100); HRMS (EI) calcd for $C_{12}H_{14}O_3$ 206.0943, found 206.0937. Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.87; H, 6.85. Found: C, 69.95; H, 6.92.

Reduction of Compound 29 with $NaBH_4$ in the Presence of $CeCl_3$. The same reaction conditions and procedure as for the reduction of **26a**–**c** were applied for the reduction of **29** to give the diol **30** in 90% yield. Spectral data for **30**: white solid; mp 174–175 °C; IR ($CHCl_3$) 3500–3300, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.31–6.25 (m, 2H), 6.01–5.98 (m, 1H), 4.15 (d, $J = 6.3$, 4.2 Hz, 1H), 3.90 (d, $J = 4.2$ Hz, 1H), 2.70 (brs, 2H), 2.59 (brs, 2H), 2.12–1.98 (m, 2H), 1.86 (d, $J = 1.5$ Hz, 3H), 1.57–1.54 (m, 2H), 1.33–1.30 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 146.16 (C), 132.44 (CH), 131.82 (CH), 128.44 (CH), 70.80 (CH), 66.35 (CH), 45.47 (CH), 45.22 (CH), 33.63 (CH), 33.48 (CH), 26.33 (CH), 26.15 (CH_2), 22.05 (CH_3); LRMS *m/z* (rel int) 206 (M^+, 29), (100), 191 (58); HRMS (EI) calcd for $C_{13}H_{18}O_2$ 206.1307, found 206.1316. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.68; H, 8.80. Found: C, 75.82; H, 8.92.

Ozonolysis of 30 with Controlled Amount of Ozone. Formation of the Trioxa-Cage 31. The same reaction conditions and procedure as for the ozonolysis of **27a**–**c** were applied for the ozonolysis of **30** to give the trioxa-cage **31** in 30% yield. Spectral data for **31**: white solid; mp 132–133 °C; IR ($CHCl_3$) 2950, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.13 (d, $J = 6.3$ Hz, 1H), 5.31 (d, $J = 5.4$ Hz, 1H), 5.28 (d, $J = 5.4$ Hz, 1H), 4.47 (dd, $J = 6.3$, 4.8 Hz, 1H), 4.27 (d, $J = 4.8$ Hz, 1H), 2.58–2.51 (m, 2H), 2.40–2.17 (m, 2H), 2.05–1.86 (m, 4H), 1.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 142.13 (C), 125.62 (CH), 104.93 (CH), 104.71 (CH), 80.14 (CH), 76.31 (CH), 44.89 (CH), 44.80 (CH), 36.03 (CH), 34.94 (CH), 23.07 (CH), 16.41 (CH_2), 16.34 (CH_2); LRMS *m*/*z* (rel int) 220 (M^+, 26), 66 (100); HRMS (EI) calcd for $C_{13}H_{16}O_3$ 220.1099, found 220.1091. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.87; H, 7.33. Found: C, 70.75; H, 7.41.

Ozonolysis of Compound 33. Synthesis of Trioxa-Cage 34. The same reaction conditions and procedure as for the ozonolysis of **2a**−**f** were applied for the ozonolysis of **33** to give the trioxa-cage **34** in 80% yield: white solid; mp 161−162 °C; IR ($CHCl_3$) 2900, 1060 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.45 (d, $J = 6.3$ Hz, 2H), 4.43−4.40 (m, 2H), 2.94−2.84 (m, 2H), 2.42−2.36 (m, 2H), 2.17−2.09 (m, 2H), 1.76−1.60 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 103.40 (2CH), 75.78 (2CH), 47.25 (2CH), 39.39 (2CH), 23.74 (CH_2), 20.94 ($2CH_2$); LRMS *m*/*z* (rel int) 194 (M^+, 100); HRMS (EI) calcd for $C_{11}H_{14}O_3$ 194.0943, found 194.0949. Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.01; H, 7.27. Found: C, 68.12; H, 7.35.

Ozonolysis of 33 without Reduction. A solution of **33** (0.36 g, 2.0 mmol) in CH_2Cl_2 (30 mL) was cooled to −78 °C, and ozone was bubbled through it at −78 °C until the solution turned light blue. After 10 min stirring, the solvent was evaporated, and the crude product was purified by column chromatography to give the hydroperoxide **35** (0.38 g, 85%): white solid; mp 108−109 °C; IR ($CHCl_3$) 3500−3200, 1100 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.94 (s, 1H), 5.33 (s, 1H), 5.28 (s, 1H), 4.44−4.41 (m, 2H), 4.17 (brs, 1H), 2.97−2.86 (m, 2H), 2.76−2.67 (m, 2H), 2.14−2.05 (m, 1H), 1.68−1.60 (m, 4H), 1.12−1.00 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 109.37 (CH), 99.61 (CH), 76.02 (CH), 74.48 (CH), 54.99 (CH), 51.26 (CH), 41.91 (CH), 41.67 (CH), 33.59 (CH_2), 24.29 (CH_2), 24.03 (CH_2); LRMS *m*/*z* (rel int) 228 (M^+, 4), 119 (74), 91 (100); HRMS (EI) calcd for $C_{11}H_{16}O_5$ 228.0997, found 228.0985. Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.87; H, 7.07. Found: C, 57.98; H, 7.16.

Reduction of 35 with Dimethyl Sulfide. To a solution of pure compound **35** (0.23 g, 1.0 mmol) in CH_2Cl_2 (20 mL) was added excess Me_2S (0.62 g, 10 mmol) at 25 °C. 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 the dihemiacetal **36** (0.20 g, 90%): white solid; mp 149−150 °C; IR ($CHCl_3$) 3500−3200, 1100 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.29 (s, 1H), 4.75−4.72 (m, 2H), 4.50 (brs, 2H), 3.00−2.88 (m, 2H), 2.78−2.68 (m, 2H), 2.10−1.63 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 99.90 (2CH), 74.71 (2CH), 55.29 (2CH), 41.63 (2CH), 33.34 (CH_2), 24.31 ($2CH_2$); LRMS *m*/*z* (rel int) 212 (M^+, 4), 148 (100), 117 (76); HRMS (EI) calcd for $C_{11}H_{16}O_4$ 212.1049, found 212.1040. Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.23; H, 7.60. Found: C, 62.36; H, 7.71.

Reaction of 35 with Triethylamine. To a solution of pure compound **35** (0.46 g, 2.0 mmol) in CH_2Cl_2 (40 mL) was added Et_3N (1.5 g, 15 mmol) at 25 °C. The reaction mixture was stirred at 25 °C for 4 h. The solvent was evaporated, and the crude product was purified by column chromatography to give the dihemiacetal **36** (0.25 g, 60%) and the lactone **37** (0.138 g, 33%). Spectral data for **37**: white solid; 158−159 °C; IR ($CHCl_3$) 3500−3300, 1770, 1250 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.30 (s, 1H), 4.74−4.72 (m, 1H), 4.52−4.46 (m, 1H), 3.21−2.88 (m, 4H), 2.38−2.33 (m, 1H), 1.85−1.63 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 178.24 (CO), 100.63 (CH), 76.91 (CH), 73.37 (CH), 56.14 (CH), 47.95 (CH), 42.65 (CH), 40.87 (CH), 33.69 (CH_2), 24.05 (CH_2), 23.16 (CH_2); LRMS *m*/*z* (rel int) 210 (M^+, 6), 119 (100), 92 (94); HRMS (EI) calcd for $C_{11}H_{14}O_4$ 210.0892, found 210.0899. Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.83; H, 6.72. Found: C, 62.97; H, 6.84.

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Supporting Information Available: ^1H and ^{13}C NMR spectra data of compounds **3a, 3d, 5, 6, 16, 18, 25,** and **31** (9 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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