Novel Oxa-Cage Compounds: Synthesis, Structures, and the Formation Mechanism of Tetraacetal Oxa-Cages and Convex Tetraquinane Oxa-Cages

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Several novel tetraacetal oxa-cage compounds 5a–d and convex tetraquinane oxa-cage compounds 16a–d and 17b–d are synthesized from alkylfurans in three steps. Ozonolysis of the cis-enol-dione 1,4-diones 3a–d in dichloromethane at −78 °C followed by reduction with dimethyl sulfide gives the oxa-cages 5a–d in high yields, respectively. The structures of these new tetraacetal oxa-cages are deduced from their spectral data and proven for the first time by X-ray analysis of the crystalline compound 5a. Ozonolysis of 3a–d in dichloromethane at −78 °C followed by treatment with triethylamine gives the convex tetraquinane oxa-cages 16a–d and 17b–d in 85–90% yields, respectively. The structures of these novel convex tetraquinane oxa-cages are finally proven by X-ray analysis of the crystalline compound 16a. Two reaction mechanisms via the common final ozonides are proposed for the formation of these two different types of oxa-cage compounds. The structures of the final ozonides formed by ozonolysis of the norbornene derivatives 3 are deduced to be 9 with endo stereochemistry on the basis of their spectral data and the formation of these two types of oxa-cages from the final ozonides. In reaction with the final ozonides, triethylamine is found to act as a base instead of a reducing agent, a different function from that of dimethyl sulfide. The synthesis of oxa-cages 24 and 25, which possesses aromatic substituents directly on the skeleton, has also been accomplished.

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, such as triprismane,2 tetraprismane (cubane),3 pentaprismane,4 homopentaprismane,5 hexaprismane,6 dodecahedrane,7 fullerene (C60),8 and convex tetraquinane oxa-cage compounds.9 On the other hand, the synthesis and chemistry of heterocyclic cage compounds have received less attention. However, there are some reports regarding the chemistry9 and synthesis10–13 of oxa-cage compounds in the literature. This class of heterocyclic cages is synthesized by intramolecular alkene–oxirane (2σ–2π) photocycloaddition,10 by transannular cyclization of suitable compounds,11 by tandem cyclization,12 by dehydration of diols having the proper stereochemistry,13 by base-promoted rearrangement,14 and by intramolecular etherification of the alkene bond with organoselenium reagents.15

We visualized that the “creation” of oxa-cage compounds from carbocyclic cages might be achieved by replacing the skeletal carbon atoms with oxygen atoms at the proper positions and by extending the skeletal backbone. For instance, starting with homopentaprismane (A), one might be able to “create” the following four different types of oxa-cage compounds, types B, C, D, and E (Scheme 1). Whereas type B monoacetal oxa-cage compounds are known, the other three types of oxa-cages are novel. We viewed types C and D oxa-cages as cage-backboned diacetal and tetraacetal crown ethers, respectively, and type E oxa-cages as tetraquinane crown ether lactones. Type D oxa-cages, in particular, can be viewed as a class of suitable compounds,11 by tandem cyclization,12 by dehydration of diols having the proper stereochemistry,13 by base-promoted rearrangement,14 and by intramolecular etherification of the alkene bond with organoselenium reagents.15

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of cage-backboned coronands (crown ethers) containing a 2n-crown-n moiety in which the ligand oxygen atoms are separated by one bridging carbon atom, whereas most known coronands are composed of repeating ethyleneoxy units to give the 3n-crown-n moiety. All three types of tetracarbonyl compounds (Scheme 2). Accordingly, the binding properties of cage-backboned coronands (crown ethers) containing known coronands are composed of repeating ethyleneoxy material for synthesizing type oxacycles, norbornene derivatives are separated by one bridging carbon atom, whereas most on synthesis and structures of novel tetraquinane oxacycles, as mentioned in the Introduction, we report fully in this paper. Also we propose two reaction mechanisms to account for the formation of these novel oxacycles, as well as deducing the stereochemistry of the final ozonide center on the transformation of an alkene bond to ketal functional groups via ozonolysis.\(^{19}\) The utility of ozonolysis in organic synthesis usually centers on the transformation of an alkene bond to carbonyl groups or to an alkoxy hydroperoxide if an alcohol is present.\(^{16}\) Recently we reported the formation of new oxacycle compounds by ozonolysis of thioesters.\(^{17}\) In addition to presenting a theoretical creation of oxacycles, as mentioned in the Introduction, we report fully on synthesis and structures of novel tetraquinane oxacycle compounds and tetracetal oxacycle compounds by ozonolysis of bis-endol,4-dione derivatives of norbornene in this paper. Also we propose two reaction mechanisms to account for the formation of these novel oxacycles, as well as deducing the stereochemistry of the final ozonide and the carbonyl oxide generated by ozonolysis of norbornene derivatives by using the formation of new oxacycles as probes. We also demonstrate that the final ozonides react differently with triethylamine and dimethyl sulfide.

**Results and Discussion**

**Synthesis and Structure of Type D Tetraoxa- Cages.** The tetraoxa-cage compounds 5a, 5b, 5c, and 5d were synthesized from alkylfurans in three steps. Oxidation of 2,5-dimethylfuran (1a, commercial available) with m-chloroperoxybenzoic acid (m-CPBA)\(^{18}\) in dichloromethane at 0 °C gave the cis-enedione 2a. Diels–Alder reaction of 2a with cyclopentadiene at room temperature gave the *endo* adduct 3a as the major product and the *exo* adduct 4a as the minor product in a ratio of 10:1 in 90% yield. Metatation of 2-methylfuran with n-BuLi in dry tetrahydrofuran (THF) followed by addition of isopropyl iodide, n-butyli bromide, and benzyl bromide at 25 °C for 4 h gave the alkylfurans 1b, 1c, and 1d in 85–90% yields, respectively.

![Scheme 1](image1)

![Scheme 2](image2)

With ^{1}H NMR of 5a–d lacked carbonyl absorptions and showed strong absorptions near 1060 cm\(^{-1}\) for the ether C–O bonds. The ^{1}H NMR spectrum of 5a revealed one doublet at δ 5.43 for the two acetal protons on C-3 and C-5, one doublet of doublets at δ 3.09 for the two protons on C-8 and C-12, and one multiplet at δ 2.88–2.78 for the bridgehead protons. The absorption at δ 2.08 (a singlet) for the methyl ketone protons of 3a shifted to δ 1.47 for the angular methyl protons of 5a. The ^{13}C NMR spectrum of 5a lacked any carbonyl absorption and displayed one peak at δ 102.8 for the acetal carbons, one singlet at δ 117.0 for the quaternary carbons, and one peak at δ 24.8 for the angular methyl carbons. Both ^{1}H and ^{13}C NMR spectra showed that compound 5a possesses a symmetry plane. The IR spectra and ^{1}H and ^{13}C NMR spectra of 5b, 5c, and 5d revealed that these compounds possess the same skeleton as 5a.

The structure of these novel heterocyclic cage compounds with four oxygen atoms in the framework is proven for the first time by X-ray analysis of the crystalline compound 5a, Figure 1. The oxygen atom O-4 is shown to be in the boat conformation with respect to the apex carbon atom C-10. The bond angles of C(3)–O(4)–C(5) and O(9)–C(10)–O(11) are 117.5° and 99.5°, respectively, somewhat different from the ordinary bond angles with sp\(^{2}\)-hybridized atoms.

Thus, we have demonstrated a novel transformation of an alkene bond to ketal functional groups via ozonolysis of an olefin in dichloromethane at −78 °C followed by a reductive workup. Ozonolysis of an alkene bond under the same reaction conditions usually gives carbonyl compounds.\(^{16}\)

Ozonolysis of the *exo* isomers 4a and 4b in dichloromethane at −78 °C followed by reduction with dimethyl sulfide gave the tetracarbonyl compounds 6a and 6b in
Reaction Mechanism for Formation of Tetraoxa-Cages 5a–d and a Plausible Structure for the Final Ozonide. In order to understand the reaction mechanism that forms tetraoxa-cages 5a–d, we investigated the structure of the final ozonide 9 formed by ozonolysis of 3a. We chose ozonolysis of 3a to determine the structure of the final ozonide to avoid regiochemistry complication during the formation of the carbonyl oxide and hence the final ozonide. Ozonolysis of 3a 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. In order to obtain ¹H and ¹³C NMR spectra of 9, we performed ozonolysis of a small amount of 3a in CDCl₃ at −78 °C to give the final ozonide 9 as the sole product. After ¹H and ¹³C NMR spectra were obtained at low temperature, the ozonide 9 was reduced with dimethyl sulfide at −78 °C to give the tetraoxa-cage 5a in 85% yield. The ¹H NMR spectrum of 9 reveals a singlet at δ 5.60 for the methine proton on C7 and a singlet at δ 1.52 for the bridgehead methyl protons, indicating that the carbonyl oxide group of 8 reacted intramolecularly with the endo acetyl group to form the final ozonide 9 (Scheme 5).

A mechanism is proposed for formation of the tetraoxa-cage compounds 5a–d by ozonolysis of 3a–d, Scheme 5. 1,3-Dipolar cycloaddition of an ozone molecule with the alkene bond of 3a via the exo face gave the 1,2,3-trioxolane 7. A least-motion fragmentation from 7 leads to the syn-oriented carbonyl oxide 8. At −78 °C, before free rotation of the carbonyl oxide group, rapid intramolecular 1,3-dipolar cycloaddition of the syn carbonyl oxide group to the endo acetyl group gave the final ozonide 9 with endo stereochemistry. Based on the reduction of 9 with dimethyl sulfide in dichloromethane at −78 °C to give 5a and NOE experiments, we conclude that the stereochemistry of the final ozonide is consistent with the endo product 9 rather than the exo isomer 14. Electron donation from dimethyl sulfide to the sterically less hindered oxygen atom of the endo peroxide bond of the final ozonide 9 followed by heterolytic cleavage of the peroxide bond and sequential nucleophilic addition of the newly-formed alkoxide ions to the adjacent carbonyl groups gave the intermediates 11 and 12. Loss of a neutral dimethyl sulfoxide molecule from 11 or 12 followed by intramolecular nucleophilic addition of the stereochemically closed alkoxide ion to the oxonium ion gave the tetraoxa-cage compound 5a. If the final ozonide was the isomer 14, with an exo stereochemistry, reduction of 14 with dimethyl sulfide via heterolytic cleavage of the peroxide bond could not give the observed product 5a since sequential nucleophilic addition of the newly-

Figure 1. X-ray structure of 5a.

Scheme 4

\[
\begin{align*}
\text{O}_3 & \to \text{O}_2 \\
\text{CH}_2\text{CH}_2 & \text{-78 °C} \\
\text{Me}_2\text{S} & \text{CH}_2\text{Cl}_2 \\
\end{align*}
\]

80–85% yields, respectively, Scheme 4. No detectable amounts of cage compounds 5a and 5b were obtained. Only the isomers 3a–d with cis-endo stereochemistry gave the corresponding tetraoxa-cage compounds.¹⁹

formed alkoxide ions to the carbonyl groups was stereocchemically impossible. Consequently, formation of the tetraoxa-cage 5a from 14 would be impossible.

We also used $^1$H NMR to monitor the reaction of the final ozonide 9 with dimethyl sulfide. Before the addition of dimethyl sulfide, the $^1$H NMR spectrum of 9 showed a singlet at $\delta$ 9.60 for the aldehyde proton and a singlet at $\delta$ 5.60 for the methine proton on C5. Ten minutes after addition of dimethyl sulfide at 20 °C, the $^1$H NMR spectrum revealed a doublet at $\delta$ 5.35 for the two acetal protons of 5a and a broad singlet at $\delta$ 5.28, in addition to the two singlets at $\delta$ 9.60 and 5.60. One hour after addition of dimethyl sulfide at 20 °C, the intensity of the two singlets at $\delta$ 9.60 and 5.60 decreased whereas the intensity of the doublet at $\delta$ 5.35 and the broad singlet at $\delta$ 5.28 increased. After 3 h at 20 °C, only the doublet at $\delta$ 5.35 for the two acetal protons was observed. We assigned the broad singlet at $\delta$ 5.28 for the acetal protons of the intermediate 12. No detectable amount of the tetracarbonyl compound 15 was observed. Nevertheless, this time-dependent $^1$H NMR study cannot rule out the possibility of 5a formation via the tetracarbonyl compound 15 as the reaction intermediate.

Refrains of the basic Criegee mechanism by incorporating carbonyl oxide stereochemistry have been proposed to account for the overall stereochemistry of the final ozonide formation. The deduction of carbonyl oxide stereochemistry was resolved experimentally by accomplishing intramolecular cycloaddition of a carbonyl oxide to two carbonyl groups tethered by an equal number of carbon atoms. Our results indicate that formation of tetraoxa-cage compounds can serve to probe the stereochemistry of the final ozonide, which, in turn, can serve to probe the stereochemistry of the carbonyl oxide. The reduction of 9 with Me2S in CH2Cl2 at −78 °C to give 5a indicates that the final ozonide 9 possesses endo stereochemistry (Scheme 5). The formation of 9 with endo stereochemistry indicates that the carbonyl oxide 8 possesses syn geometry formed from 7, which is consistent with the least-motion fragmentation principle.

Synthesis and Structure of Type E Convex Tetraquinane Oxa-Cages. Ozonolysis of compound 3a, which possesses cis-endo stereochemistry, in dichloromethane at −78 °C, followed by treatment with triethylamine instead of dimethyl sulfide, gave the convex tetraquinane oxa-cage compound 16a in 90% yield. Ozonolysis of 3b, 3c, and 3d under the same reaction conditions in each case gave two isomers 16b–d and 17b−d in ratios of 1:1 in 85–90% yields, respectively, Scheme 6.

The IR spectrum of 16a showed absorptions at 1765 cm$^{-1}$ for the five-membered lactone carbonyl and at 3500–3200 cm$^{-1}$ for the hydroxyl group. Its $^1$H NMR spectrum revealed one doublet at $\delta$ 5.16 ($J = 2.7$ Hz) for the hemiacetal proton on C3. The small coupling constant implies that the proton on C3 is trans to the proton C4. The absorption at $\delta$ 2.08 (singlet) for the methyl ketone protons of 3a shifted to $\delta$ 1.59 and 1.62 for the angular methyl protons of 16a. The $^{13}$C NMR spectrum of 16a displayed one singlet at $\delta$ 178.1 for the lactone carbonyl carbon, two singlets at $\delta$ 119.2 and 115.8 for the quaternary carbons, and one peak at $\delta$ 104.9 for the hemiacetal carbon. The structure of 16a was finally proven by X-ray analysis to possess a convex trioxa-tetraquinane skeleton. An ORTEP diagram of the crystalline compound 16a is shown in Figure 2. The IR spectra and $^1$H and $^{13}$C NMR spectra of 16b−d and 17b−d revealed that these compounds possess the same skeleton as 16a.

Thus, we have accomplished the synthesis of novel convex tetraquinane oxacages via ozonolysis of norbornene derivatives in dichloromethane at −78 °C followed by treatment with triethylamine. Under the same reaction conditions, ozonolysis of an olefin has been reported to give an acid.

Ozonolysis of 3a in dichloromethane at −78 °C, followed by treatment with triethylamine and acetic anhydride, directly gave 18 in 80% yield, which was also obtained by reaction of 16a with acetic anhydride in pyridine at room temperature, Scheme 7. Oxidation of 16a with pyridinium chlorochromate (PCC) in dichloromethane gave 18 in 75% yield.
Scheme 7

\[ \begin{align*}
3a & \xrightarrow{\text{O}_3, \text{CH}_2\text{Cl}_2, -78{}^\circ\text{C}} \text{AcO} \xrightarrow{\text{EtN}} 18 \\
16a & \xrightarrow{\text{AcO}, \text{Pyridine}} 18 \\
16a & \xrightarrow{\text{PCC}} 19a
\end{align*} \]

(16b + 17b) \xrightarrow{\text{PCC}} 19b
(16c + 17c) \xrightarrow{\text{PCC}} 19c
(16d + 17d) \xrightarrow{\text{PCC}} 19d, 19b-19d

Scheme 8

\[ \begin{align*}
3a & \xrightarrow{\text{O}_3, \text{CH}_2\text{Cl}_2, -78{}^\circ\text{C}} \xrightarrow{\text{AcO}} \xrightarrow{\text{Pyridine}} \xrightarrow{\text{EtN}} 18 \\
7 & \rightarrow 8 \\
9 & \xrightarrow{\text{NB₃}} 16a
\end{align*} \]

\[ \begin{align*}
(3b, 3c, 3d) & \xrightarrow{\text{O}_3, \text{CH}_2\text{Cl}_2, -78{}^\circ\text{C}} 20 \\
20 & \xrightarrow{\text{EtN}} 21 \\
(16b, 16c, 16d) & \rightarrow (17b, 17c, 17d)
\end{align*} \]

Scheme 9

\[ \begin{align*}
\text{O}_3 & \xrightarrow{\text{CH}_2\text{Cl}_2, -78{}^\circ\text{C}} \text{Me}_2\text{S} \rightarrow 22 \\
16b & \rightarrow 16a-d \\
17b & \rightarrow 17b-d
\end{align*} \]

The oxidation of the mixtures of tetraoxa-cage 19a, 19b, 19c, and 19d respectively, with dimethyl sulfide gave the tetraoxa-cage 20 and 21 in each case, which, after treatment with triethylamine, gave 16 and 17, respectively, Scheme 8.

Razumovskii et al.,\(^{27}\) reported the occurrence of an oxidation-reduction electron-transfer process when the final ozonides were reacted with triethylamine. In our experiments, reaction of the final ozonides 9, 20, and 21 with dimethyl sulfide gave the tetraoxa-cages 5a–d (Schemes 3 and 5) whereas reaction of 9, 20, and 21 with triethylamine gave the convex tetraquinane oxa-cages 16a–d and 17b–d (Schemes 6 and 8). Thus, our experimental results indicated that the reaction between the final ozonides and triethylamine proceeded via an acid-base proton-transfer process.\(^{25}\) In other words, triethylamine acts as a base rather than as a reducing agent in reacting with final ozonides if there is at least one proton present at the bridgehead of the final ozonide ring.

**Synthesis of Other Oxa-Cages.** To understand how aromatic carbonyls affected formation of the previously synthesized oxa-cage skeletons, compound 22 was prepared\(^{28}\) for ozonolysis study. Ozonolysis of the endo isomer 22 in dichloromethane at \(-78{}^\circ\text{C}\) followed by reduction with dimethyl sulfide gave the tetraoxa-cage compound 24 in 85% yield. Ozonolysis of 22 in dichloromethane at \(-78{}^\circ\text{C}\) followed by treatment with triethylamine gave compound 25 in 87% yield. Ozonolysis of the exo isomer 23 in dichloromethane at \(-78{}^\circ\text{C}\) followed by reduction with dimethyl sulfide gave the tetracarbonyl compound 26 as the sole product; no detectable amount of tetraoxa-cage 24 was obtained, Scheme 9.

**Conclusions**

In summary, we have accomplished the synthesis of several novel tetracetal tetraoxa-cage compounds 5a–d

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and convex tetraoxa-cage compounds 16a-d, 17c,d, and 19a-d from alkylfurans in a short sequence. The structures of these novel oxa-cage compounds were proven by X-ray analysis of the crystalline compounds 5a and 16a. Two reaction mechanisms via the common final ozonides were proposed for formation of the tetraacetal tetraoxa-cages and the convex tetraquinane oxa-cage. We deduced that the structure of the final ozonide formed by ozonolysis of 3a is Z with endo stereochemistry. The stereochemistry of the final ozonides and the carbonoxy radicals generated by ozonolysis of the norbornene derivatives 3a-d was deduced by using formation of these two types of oxa-cage compounds as a probe. The difference in function between triethylamine and dimethyl sulfide in reaction with the final ozonide was measured. We also synthesized oxa-cages 24 and 25, which possess aromatic substituents directly on the skeleton. Besides, in the introduction, we have demonstrated the "creation" of oxa-cage compounds from suitable carbocyclic cages. A study on the synthetic applications for these new oxa-cages is underway.

Experimental Section

General. Melting points were determined in capillary tubes with a Laboratory Devices melting point apparatus and are uncorrected. Infrared spectra were recorded in CHCl₃ solutions or on neat thin films between NaCl disks. ¹H NMR spectra were determined at 300 or 400 MHz, and ¹³C 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 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. X-ray analyses were determined by the microanalysis laboratory of National Taiwan University. X-ray analyses 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 carried out using Kieselgel 60 (70-230 mesh) as the stationary phase. THF was distilled immediately prior to use from sodium benzenephene ketyl under nitrogen. CH₂Cl₂ was distilled from CaH₂ under nitrogen.

General Procedure for the Preparation of 2-Methyl-5-alkylfurans 1b-d. To a solution of 2-methylfuran (2.0 g, 24.4 mmol) in dry THF (40 mL) was added n-BuLi (10.2 mL, 25.6 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 4 h. To this solution was added isopropyl iodide (4.1 mL, 24.4 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 4 h. After addition of saturated NH₄Cl (20 mL) and extraction with ether (3 × 30 mL), the organic layer was washed with brine, dried over MgSO₄, and evaporated to give 1b-d.

Spectral data for 2a: pale yellow oil; yield 82%; IR (neat) 2980, 2980, 1697, 1620 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.40-7.21 (m, 5H), 5.84 (s, 2H), 2.87-2.80 (m, 1H), 2.25 (s, 3H), 1.63-1.56 (m, 2H), 0.92 (t, J = 7.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 154.77 (C), 149.99 (C), 105.67 (CH), 105.03 (CH), 27.73 (CH), 22.28 (CH₃), 13.83 (CH₃), 13.48 (CH₃); LRMS m/z (rel inten) 158 (M⁺, 100), 140 (M⁺, 83). Spectral data for 2b-d: white waxy solid; mp 50-50.5 °C; IR (CHCl₃) 2970, 1710, 1595, 1370 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.32 (s, 2H), 2.60-2.57 (m, 1H), 2.30 (s, 3H), 1.23-1.32 (m, 2H), 0.92 (t, J = 7.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 160.67 (C), 152.61 (C), 138.30 (CH), 129.03 (CH), 26.34 (CH₃), 22.15 (CH₃); LRMS m/z (rel inten) 140 (M⁺, 8), 111 (24), 97 (100).
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The NMR spectra were taken at 20 °C. Spectral data for 4a: H NMR (CDCl₃) δ 9.72 (s, 1H), 9.69 (s, 1H), 9.63 (dd, J = 7.4, 4.2 Hz, 1H), 3.46–3.32 (m, 2H), 3.18–3.14 (m, 1H), 2.77–2.68 (m, 1H), 2.20–2.40 (m, 2H), 2.13 (s, 3H), 1.13 (d, J = 6.0 Hz, 3H), 1.09 (d, J = 6.0 Hz, 3H); 13C NMR (CDCl₃) δ 205.14 (C-O), 201.89 (CH), 150.34, 159.67, 151.73, 154.62, 52.50, 51.83, 51.42, 39.65, 29.72, 24.56, 18.58, 18.28; LRMS m/z (rel inten) 238 (M⁺, 7), 195 (100), 149 (47); HRMS (EI) ecalcd for C₁₃H₁₈O₆ 286.1205, found 286.1226.

General Procedure for the Determination of the Tetraacetal Compounds 6a and 6b. A solution of 4a (0.05 g, 0.24 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 (0.52 g, 8.4 mmol) at −78 °C until the solution turned light blue. The solution was then transferred to an NMR tube, and the NMR spectra were taken at 20 °C. Spectral data for 9: 1H NMR (300 MHz, CDCl₃) δ 9.64 (s, 1H), 5.60 (s, 1H), 3.07 (dd, J = 7.2, 7.2 Hz, 1H), 2.97–2.77 (m, 3H), 2.21 (s, 3H), 2.14–2.01 (m, 2H), 1.52 (s, 3H); 13C NMR (75 MHz, CDCl₃) δ 206.49 (C-O), 201.51 (CH), 150.34, 154.73, 157.05, 137.65, 130.32 (2C), 127.84 (2CH), 126.47 (CH), 118.34 (C), 117.33 (C), 102.99 (2CH), 57.13 (CH), 55.00 (CH), 45.77 (2CH), 43.28 (2CH), 24.99 (2CH), 22.66 (2CH), 19.35 (CH); LRMS m/z (rel inten) 296 (M⁺, 18), 195 (100), 91 (98); HRMS (EI) ecalcd for C₁₃H₁₈O₆ 286.1205, found 286.1226.

**1135**NMR Spectra of the Reaction of the Final Ozonide 9 with Dimethyl Sulfide. A solution of 3a (0.059 g, 0.28 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. The solution was then transferred to an NMR tube, and the 1H and 13C NMR spectra were taken...
at 20°C. The NMR tube was then cooled to −78°C, and excess dimethyl sulfoxide was added to the solution. After 10 min, a second 1H NMR spectrum was taken at 20°C. A third, fourth, and fifth 1H NMR spectra were taken at 20°C after another 20 min, 1 h, and 3 h, respectively.

8. General Procedure for the Preparation of Tetraquaternary Oxa-Cage Compounds 16a–e and 17b,c.

A solution of 3a (0.50 g, 2.8 mmol) in dichloromethane (20 mL) was cooled to −78°C, and ozone was bubbled through it at 1°C until the solution turned light blue. To this solution was added triethylamine (0.28 g, 2.8 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 16a (0.57 g, 90%). Spectral data for 16a: white waxy solid; mp 164-164.5°C; IR (CHCl3) 3450, 2960, 1767, 1107 cm−1; 1H NMR (300 MHz, CDCl3) δ 5.16 (d, J = 2.7 Hz, 1H), 3.05–3.30 (m, 2H), 1.86–2.02 (m, 2H), 1.31–1.63 (m, 7H), and 0.80–1.01 (m, 18H); LRMS m/z (rel. int.) 226 (M+), 210 (24), 165 (100), 139 (91); HRMS (EI) calced for C12H20O3: 226.1311, found 226.1309.

Spectral data for 16b + 17b: white waxy solid; yield 87%; mp 140–141°C; IR (CHCl3) 3450, 2960, 1767, 1107 cm−1; 1H NMR (300 MHz, CDC13) δ 5.36 (d, J = 3.9 Hz, 2H), 3.49–3.13 (m, 7H), 2.64–2.57 (m, 4H), 2.30–2.25 (m, 2H), 2.16–2.06 (m, 3H), 1.66 (s, 3H), 1.65 (s, 3H), 1.03–0.95 (m, 12H); 13C NMR (75 MHz, CDCl3, DEPT) δ 186.75 (C=O), 129.10 (C), 115.01 (C), 114.50 (C), 105.36 (CH3), 104.05 (CH3), 76.48 (CH), 53.20 (CH2), 46.88 (CH2), 37.53 (CH2), 37.33 (CH2), 36.58 (CH2), 25.98 (CH3), LRMS m/z (rel int.) 226 (M+), 210 (24), 165 (100), 139 (91); HRMS (EI) calced for C12H20O3: 226.1311, found 226.1309.

Spectral data for 16c + 17c: white waxy solid; yield 88%; mp 129–130°C; IR (CHCl3) 3450, 2960, 1767, 1107 cm−1; 1H NMR (300 MHz, CDCl3) δ 5.11 (d, J = 2.8 Hz, 1H), 2.60 (s, 3H), 1.88–2.36 (m, 6H), 1.91–1.88 (m, 4H), 1.66 (s, 6H), 1.42–1.36 (m, 8H), 0.94–0.89 (m, 6H); 13C NMR (75 MHz, CDCl3, DEPT) δ 186.49 (C=O), 134.49 (C), 119.60 (C), 118.99 (C), 111.35 (C), 106.49 (C), 102.09 (CH3), 76.39 (CH), 54.97 (CH2), 49.43 (CH2), 43.79 (CH2), 43.51 (CH2), 37.35 (CH2), 36.90 (CH2), 25.43 (CH3), 24.43 (CH3), 19.22 (CH3), 18.86 (CH3); LRMS m/z (rel int.) 268 (M+), 210 (24), 165 (100), 139 (91); HRMS (EI) calced for C12H20O3: 226.1311, found 226.1309.

Spectral data for 16d + 17d: white waxy solid; yield 86%; mp 129–130°C; IR (CHCl3) 3450, 2960, 1767, 1600 cm−1; 1H NMR (300 MHz, CDCl3) δ 7.33–7.25 (m, 10H), 5.38 (d, J = 2.4 Hz, 1H), 5.33 (d, J = 1.8 Hz, 1H), 3.45–3.10 (m, 10H), 2.74–2.19 (m, 8H), 1.63 (s, 3H), 1.52 (s, 3H); 13C NMR (75 MHz, CDCl3, DEPT) δ 177.67 (C=O), 134.14 (C), 130.64 (CH3), 130.44 (CH3), 128.43 (CH3), 128.16 (CH3), 127.29 (CH3), 126.79 (CH3), 126.80 (CH3), 118.90 (C), 117.06 (C), 111.74 (C), 104.52 (CH3), 104.60 (CH3), 95.89 (CH3), 57.22 (CH), 56.78 (CH), 54.62 (CH), 51.88 (CH), 51.68 (CH), 48.01 (CH), 47.95 (CH), 45.41 (CH2), 43.24 (CH2), 36.91 (CH2), 36.85 (CH2), 26.01 (CH3), 24.64 (CH3); LRMS m/z (rel int.) 302 (M+), 258 (60), 181 (100); HRMS (EI) calced for C12H20O3: 226.1311, found 226.1309.

Formation of Compound 18. A solution of 3a (0.50 g, 2.8 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 were added triethylamine (0.34 g, 3.4 mmol) and acetic anhydride (0.29 g, 2.8 mmol) at −78°C, and the reaction mixture was then stirred at room temperature for 3 h. The solvent was evaporated, and the crude product was purified by flash column chromatography to give compound 18 (0.56 g, 75%); white waxy solid; yield 80%; mp 143–143.5°C; IR (CHCl3) 2980, 1770, 1765, 1105 cm−1; 1H NMR (300 MHz, CDCl3) δ 6.08 (s, 1H), 3.47–3.39 (m, 2H), 3.25 (dd, J = 8.7, 9.3 Hz, 1H), 2.87 (dd, J = 9, 7.8 Hz, 1H), 2.74–2.69 (m, 1H), 2.47–2.41 (m, 1H), 2.04 (s, 3H), 1.69 (s, 3H), 1.85 (s, 3H); 13C NMR (75 MHz, CDCl3, DEPT) δ 176.74 (C=O), 168.45 (C=O), 121.32 (C), 115.90 (C), 104.10 (CH), 59.34 (CH), 57.54 (CH), 50.98 (CH), 47.81 (CH), 37.52 (CH), 25.31 (CH), 24.93 (CH3), 21.20 (CH2); LRMS m/z (rel int.) 224 (15), 180 (31), 137 (67), 43 (100); HRMS (EI) calced for C21H28O4: 326.0947, found 326.0962. Anal. Calcd for C21H28O4: C, 58.19; H, 6.01. Found: C, 58.29; H, 5.92.

Formation of Compound 19. The same reaction conditions and procedure as for the synthesis of 5a–d from ozonolysis of 3a–d were applied to the ozonolysis of 22. Spectral data for 24: white waxy solid; yield 78%; mp 223–224°C; IR (CHCl3) 3450, 3020, 1765, 1620; 1H NMR (300 MHz, CDCl3, CD3SOCD2) δ 7.62–7.35 (m, 10H), 6.86 (d, J = 5.1 Hz, 1H), 5.34 (dd, J = 5.1 Hz, J = 2.8 Hz, 1H), 3.97–3.40 (m, 4H), 2.72–
2.67 (m, 1H), 2.45–2.33 (m, 1H); 13C NMR (75 MHz, CD3SOCD3, DEPT) δ 178.81 (C=O), 141.36 (C), 139.47 (C), 129.04 (CH), 128.60 (2CH), 128.25 (CH), 127.99 (2CH), 126.01 (2CH), 125.13 (2CH), 119.01 (C), 115.17 (C), 105.15 (CH), 62.29 (CH), 58.73 (CH), 52.23 (CH), 47.43 (CH), 36.21 (CH2); LRMS m/z (rel inten) 350 (M+, 2), 105 (72), 85 (100); HRMS (EI) calcd for C21H18O5 350.1154, found 350.1160.

Ozonolysis of Compound 23. The same reaction conditions and procedure as for the ozonolysis of 4a and 4b were applied to the ozonolysis of 23. Spectral data for 26: pale yellow oil; yield 71%; IR (neat) 3030, 2890, 1722, 1674, 1580 cm⁻¹; 1H NMR (300 MHz, CDCl3) δ 9.81 (s, 2H), 7.76–7.24 (m, 10H), 4.53 (dd, J = 3, 1.5 Hz, 2H), 3.70–3.66 (m, 2H), 2.44–2.35 (m, 2H); 13C NMR (75 MHz, CDCl3) δ 200.34, 198.30, 135.99, 133.18, 128.54, 128.25, 53.23, 50.11, 24.67; LRMS m/z (rel inten) 334 (M+, 43), 305 (72), 229 (61), 201 (100); HRMS (EI) calcd for C20H16O4, 334.1205, found 334.1227.

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Supporting Information Available: 1H and 13C NMR spectra of 5a–d, 9, 16a–d, 18, 19a–d, 24, and 25 and the time-dependent 1H NMR spectra of the reaction of the final ozonide 9 with Me₂S (19 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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