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-endo*-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 possess 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] and fullerene (C_{60}).[8] On the other hand, the synthesis and chemistry of heterocyclic cage compounds have received less attention. However, there are some reports regarding the chemistry[9] and synthesis[10–15] of oxa-cage compounds in the literature. This class of heterocyclic cages is synthesized by intramolecular alkene–oxirane ($2\sigma-2\pi$) 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** monooxa-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

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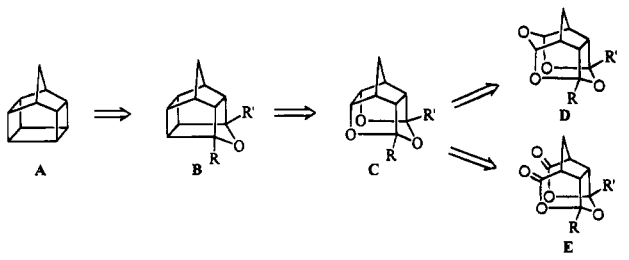
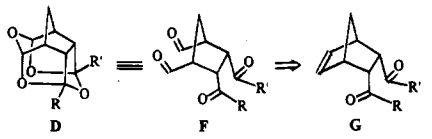
Scheme 1



Scheme 2



of cage-backboned coronands (crown ethers) containing a 2*n*-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 3*n*-crown-*n* moiety. All three types of oxa-cages, **C**, **D**, and **E**, might exhibit interesting cation-binding properties.

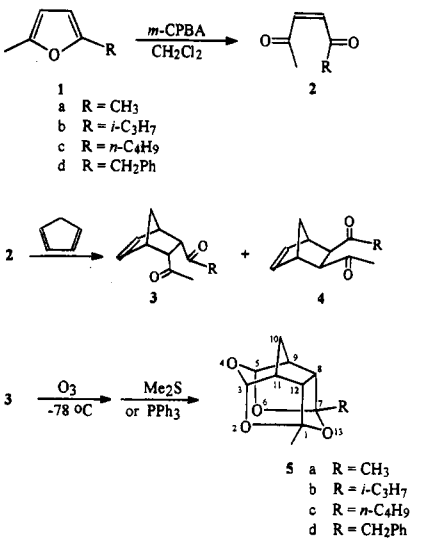
From the standpoint of retrosynthetic analysis, type **D** tetraoxa-cage compounds are equivalent to type **F**, the tetracarbonyl compounds (Scheme 2). Accordingly, the norbornene derivatives **G** might be chosen as the starting material for synthesizing type **D** or **F** compounds.

The utility of ozonolysis in organic synthesis usually centers on the transformation of an alkene bond to carbonyl groups or to an α-alkoxy hydroperoxide if an alcohol is present.[16] Recently we reported the formation of new oxa-cage compounds by ozonolysis of thioesters.[17] In addition to presenting a theoretical creation of oxa-cages, as mentioned in the Introduction, we report fully on synthesis and structures of novel tetraquinane oxa-cage compounds and tetraacetal oxa-cage compounds by ozonolysis of bis-*endo*-1,4-dione derivatives of norbornene in this paper. Also we propose two reaction mechanisms to account for the formation of these novel oxa-cages, 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 oxa-cages 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. Metalation of 2-methylfuran

Scheme 3



with *n*-BuLi in dry tetrahydrofuran (THF) followed by addition of isopropyl iodide, *n*-butyl bromide, and benzyl bromide at 25 °C for 4 h gave the alkylfurans **1b**, **1c**, and **1d** in 85–90% yields, respectively. Compounds **3b**, **3c**, **3d**, **4b**, **4c**, and **4d** were prepared from **1b**, **1c**, and **1d** in a similar sequence, Scheme 3. Ozonolysis of **3a**, **3b**, **3c**, and **3d**, all of which possess *cis-endo* stereochemistry, in dichloromethane at −78 °C followed by reduction with dimethyl sulfide or triphenylphosphine gave the tetraoxa-cage compounds **5a**, **5b**, **5c**, and **5d** in 80–85% yields, respectively.

The IR spectra of **5a–d** lacked carbonyl absorptions and showed strong absorptions near 1050 cm^{-1} for the ether C–O bonds. The ^1H 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 ^1H and ^{13}C NMR spectra showed that compound **5a** possesses a symmetry plane. The IR spectra and ^1H 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 C(9)–C(10)–C(11) are 117.5° and 99.5°, respectively, somewhat different from the ordinary bond angles with sp^3-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

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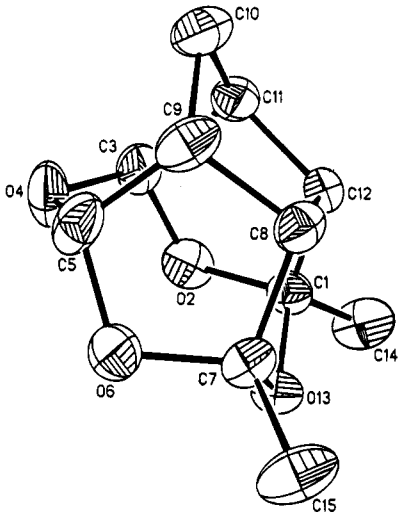
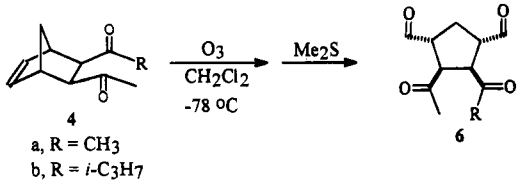


Figure 1. X-ray structure of **5a**.

Scheme 4

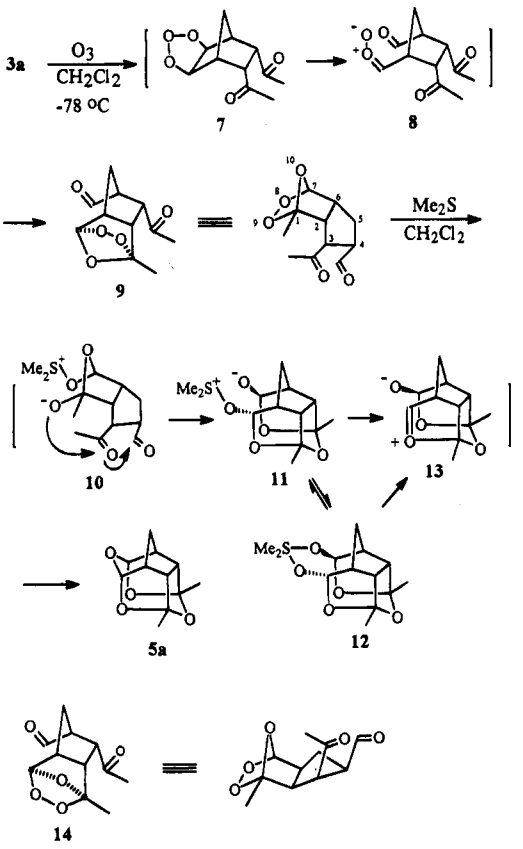


80–85% yields, respectively, Scheme 4. No detectable amounts of cage compounds **5a** and **5b** were obtained. Only the isomers **3a–d** with *cis-endo* stereochemistry gave the corresponding tetraoxa-cage compounds.[19]

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 $CDCl_3$. In order to obtain ^1H and ^{13}C NMR spectra of **9**, we performed ozonolysis of a small amount of **3a** in $CDCl_3$ at −78 °C to give the final ozonide **9** as the sole product. After ^1H and ^{13}C 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 C_7 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[20] from **7** leads to the *syn*-oriented carbonyl oxide **8**. At −78 °C, before

Scheme 5



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,[21] 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-

(19) Ozonolysis of the trans-isomers of the Diels–Alder cycloadducts gave the trioxa-cage compounds. Wu, H. J.; Wu, C. I.; Lin, C. C. Submitted for publication.

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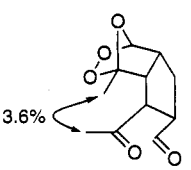
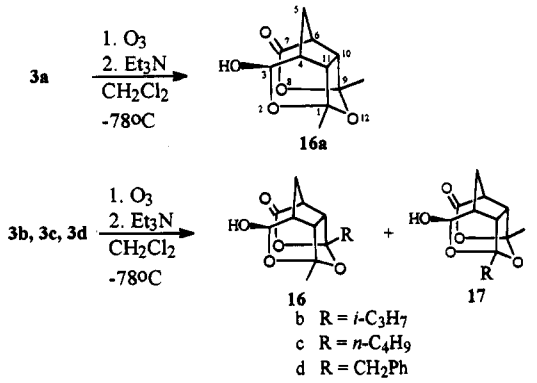
(21) Quantitative NOE experiments: irradiated δ 1.52 (the ozonide ring bridgehead methyl protons), enhanced δ 2.21 (3.6%, the methyl ketone protons).

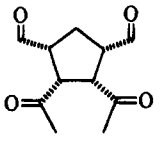


Scheme 6



formed alkoxide ions to the carbonyl groups was stereochemically 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 δ 9.60 for the aldehyde proton and a singlet at δ 5.60 for the methine proton on C_7. Ten minutes after addition of dimethyl sulfide at 20 °C, the ^{1}H NMR spectrum revealed a doublet at δ 5.35 for the two acetal protons of **5a** and a broad singlet at δ 5.28, in addition to the two singlets at δ 9.60 and 5.60. One hour after addition of dimethyl sulfide at 20 °C, the intensity of the two singlets at δ 9.60 and 5.60 decreased whereas the intensity of the doublets at δ 5.35 and the broad singlet at δ 5.28 increased. After 3 h at 20 °C, only the doublet at δ 5.35 for the two acetal protons was observed. We assigned the broad singlet at δ 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.



15

Refinements of the basic Criegee mechanism[22] by incorporating carbonyl oxide stereoisomerism[23] have been proposed to account for the overall stereochemistry of the final ozonide formation.[24] 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.[24] 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 Me_2S in CH_2Cl_2 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.[20]

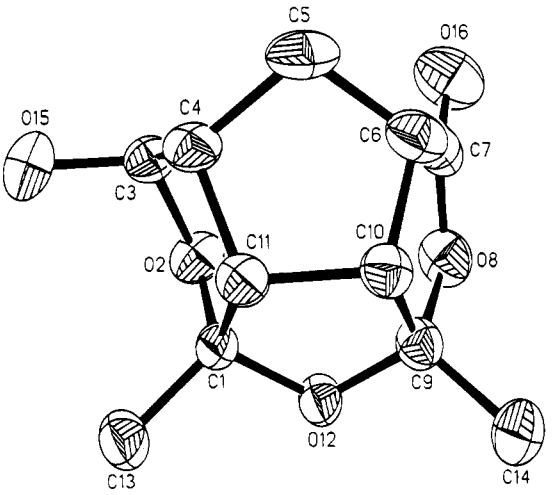


Figure 2. ORTEP diagram of **16a**.

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 group and at 3500−3200 cm^{-1} for the hydroxyl group. Its ^{1}H NMR spectrum revealed one doublet at δ 5.16 (J = 2.7 Hz) for the hemiacetal proton on C_3. The small coupling constant implies that the proton on C_3 is *trans* to the proton C_4. The absorption at δ 2.08 (singlet) for the methyl ketone protons of **3a** shifted to δ 1.59 and 1.62 for the angular methyl protons of **16a**. The ^{13}C NMR spectrum of **16a** displayed one singlet at δ 178.1 for the lactone carbonyl carbon, two singlets at δ 119.2 and 115.8 for the quaternary carbons, and one peak at δ 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 oxa-cages 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.[25]

Ozonolysis of **3a** in dichloromethane at −78 °C, followed by treatment with triethylamine and acetic anhydride,[26] 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 dichlo-

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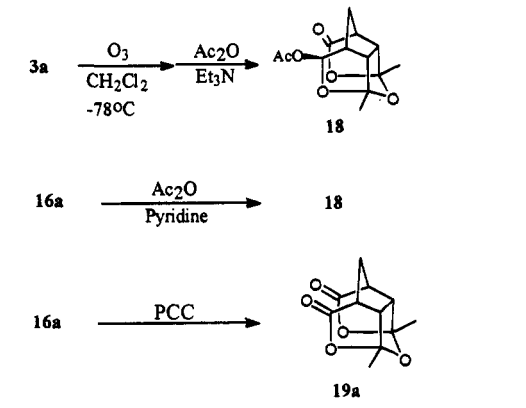
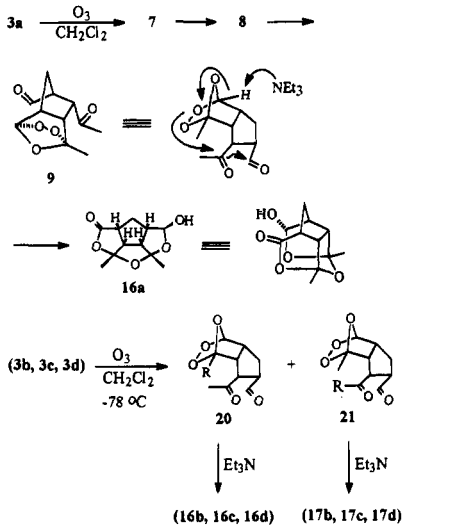
(26) Schreiber, S. L.; Claus, R. E.; Reagan, J. *Tetrahedron Lett.* **1982**, *23*, 3867.

Scheme 7



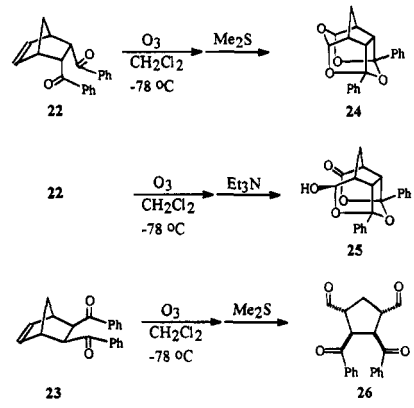
Scheme 8



romethane at room temperature gave **19a** in 75% yield. Bislactones **19b**, **19c**, and **19d** were also obtained from the oxidation of the mixtures of **16b** and **17b**, **16c** and **17c**, and **16d** and **17d**, respectively. The ^1H and ^{13}C spectra of **19a** showed that it possesses a symmetry plane.

Reaction Mechanism for Formation of the Convex Tetraquinane Oxa-Cages 16a–d and 17b–d. A mechanism is proposed for formation of the convex tetraquinane cages **16** and **17** by ozonolysis of **3** followed by treatment with triethylamine, Scheme 8. A least-motion fragmentation of the primary ozonide **7** leading to the *syn*-oriented carbonyl oxide **8** followed by 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. Proton abstraction of the ozonide ring proton of **9** by triethylamine 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 observed product **16a**. If the final ozonide was the isomer **14** (Scheme 5), with an *exo* stereochemistry, proton abstraction of the ozonide ring proton of **14** by triethylamine

Scheme 9



followed by heterolytic cleavage of the peroxide bond could not give the observed product **16a** since the sequential nucleophilic addition of the newly-formed alkoxide ions to the carbonyl groups was stereochemically impossible. Thus, we deduced again that the structure of the final ozonide formed by ozonolysis of **3** in dichloromethane at −78 °C was the *endo* isomer **9** instead of the *exo* isomer **14**. Ozonolysis of **3b**, **3c**, and **3d** formed the ozonides **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 °C followed by reduction with dimethyl sulfide gave the tetraoxa-cage compound **24** in 85% yield. Ozonolysis of **22** in dichloromethane at −78 °C followed by treatment with triethylamine gave compound **25** in 87% yield. Ozonolysis of the *exo* isomer **23** in dichloromethane at −78 °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 tetraacetal tetraoxa-cage compounds **5a–d**

(27) (a) Razumovskii, S. D.; Zaikov, G. E. *Ozone and its Reactions with Organic Compounds*; Elsevier: The Netherlands, 1984; Chapter 9, pp 370. (b) Pobedimskii, D. G.; Razumovskii, S. D. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1970**, *3*, 602; *Chem. Abstr.* **1970**, *73*, 13853n.

(28) (a) Pasto, D. J.; Duncan, J. A.; Silversmith, E. F. *J. Chem. Educ.* **1974**, *51*, 277. (b) Silversmith, E. F.; Dunson, F. C. *J. Chem. Educ.* **1973**, *50*, 568.

and convex tetraquinane oxa-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-cages. We deduced that the structure of the final ozonide formed by ozonolysis of **3a** is **9** with *endo* stereochemistry. The stereochemistry of the final ozonides and the carbonyl oxides 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 demonstrated. An acid–base proton-transfer process instead of an oxidation–reduction electron-transfer process occurs between the amine and the final ozonide. We also synthesize 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 $CHCl_3$ solutions or on neat thin films between NaCl disks. ^1H NMR spectra were determined at 300 or 400 MHz, and ^{13}C NMR 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 spectra 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 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 F_{254}) 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 benzophenone ketyl under nitrogen. CH_2Cl_2 was distilled from CaH_2 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 g, 24.4 mmol) at 0 °C, and the reaction mixture was stirred at room temperature for 4 h. After addition of saturated NH_4Cl (20 mL) and extraction with ether (3 × 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 **1b** (2.6 g, 87%): IR (neat) 2980, 2940, 2880, 2870, 1610 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.83–5.79 (m, 2H), 2.87–2.80 (m, 1H), 2.25 (s, 3H), 1.22 (d, J = 7.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.67 (C), 149.93 (C), 105.50 (CH), 102.99 (CH), 27.73 (CH), 21.17 ($2CH_3$), 13.42 (CH_3); LRMS *m/z* (rel inten) 124 (M^+, 100), 83 (23).

The same reaction conditions and procedure were applied to the preparation of **1c** and **1d**.

2-Methyl-5-*n*-butylfuran (1c): pale yellow oil; yield 90%; IR (neat) 2980, 2940, 2880, 2870, 1610 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.83 (s, 2H), 2.56 (t, J = 7.4 Hz, 1H), 2.25 (s, 3H), 1.63–1.56 (m, 2H), 1.44–1.36 (m, 2H), 0.92 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.77 (C), 149.99 (C), 105.67 (CH), 105.03 (CH), 30.29 (CH_2), 27.73 (CH_2), 22.28 (CH_2), 13.83 (CH_3), 13.48 (CH_3); LRMS *m/z* (rel inten) 138 (M^+, 100).

2-Methyl-5-benzylfuran (1d): pale yellow oil; yield 85%; IR (neat) 3010, 2980, 2885, 1620 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.21 (m, 5H), 5.84 (s, 2H), 3.90 (s, 2H), 2.23 (s, 3H); ^{13}C NMR (75 Mhz, $CDCl_3$) δ 152.61 (C), 150.86 (C), 138.30 (C), 128.69 (2CH), 128.60 (2CH), 128.34 (CH), 106.81 (CH), 105.93 (CH), 34.46 (CH_2), 13.45 (CH_3); LRMS *m/z* (rel inten) 172 (M^+, 100), 83 (32).

General Procedure for the Oxidation of 2-Methyl-5-alkylfurans 1a–d with *m*-Chloroperoxybenzoic Acid (*m*-CPBA). To a solution of 2,5-dimethylfuran (2 g, 20.8 mmol) in dichloromethane (180 mL) was added *m*-CPBA (3.59 g, 20.8 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. To this solution was added saturated Na_2CO_3 (50 mL). After separation, the water layer was extracted with dichloromethane (3 × 40 mL). The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated to give **2a** (1.98 g, 85%). Compounds **2a–d** were used for the next step, Diels–Alder reaction without purification, since **2a–d** were sensitive *cis–trans* isomerization by heat or silica gel treatment. Spectral data for **2a**: pale yellow oil; IR (neat) 2980, 2880, 1697, 1620 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.32 (s, 2H), 2.30 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.87 (2C), 135.56 (2C), 29.57 (2C); LRMS *m/z* (rel inten) 112 (M^+, 85), 95 (32), 83 (100).

The same reaction conditions and procedure were applied to the preparation of **2b–d**.

(*Z*)-6-Methyl-3-heptene-2,5-dione (2b): pale yellow oil; yield 82%; IR (neat) 2980, 2880, 1697, 1620 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.42 (ABq, J = 12 Hz, δ_A 6.47, δ_B 6.38, 2H), 2.80–2.71 (m, 1H), 2.29 (s, 3H), 1.15 (d, J = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.56, 200.69, 136.61, 134.19, 40.20, 29.36, 17.45 (2C); LRMS *m/z* (rel inten) 140 (M^+, 24), 98 (72), 71 (100).

(*Z*)-3-Nonene-2,5-dione (2c): pale yellow oil; yield 83%; IR (neat) 2980, 2880, 1700, 1620 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.32 (ABq, J = 13 Hz, δ_A 6.37, δ_B 6.27, 2H), 2.55 (t, J = 7.8 Hz, 2H), 2.30 (s, 3H), 1.57–1.65 (m, 2H), 1.32–1.39 (m, 2H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.87, 200.77, 136.03, 135.30, 42.27, 29.74, 25.52, 22.19, 13.83; LRMS *m/z* (rel inten) 154 (M^+, 8), 111 (24), 97 (100).

(*Z*)-1-Phenyl-3-hexene-2,5-dione (2d): pale yellow oil; yield 82%; IR (neat) 3020, 1740, 1610 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.22 (m, 5H), 6.28 (ABq, J = 11.7 Hz, δ_A 6.29, δ_B 6.27, 2H), 3.82 (s, 2H), 2.240 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.36, 199.90, 135.91, 134.92, 132.97, 129.39, 128.46, 126.94, 49.09, 29.42; LRMS *m/z* (rel inten) 188 (M^+, 40), 145 (33), 68 (100).

General Procedure for the Diels–Alder Reaction of 2a–d with Cyclopentadiene. To a solution of **2a** (2.0 g, 17.9 mmol) in dichloromethane (3 mL) was added 1,3-cyclopentadiene (2.4 g, 35.7 mmol) at 25 °C. The reaction mixture was stirred at 25 °C for 2 h. The solvent was evaporated, and the crude product was purified by column chromatography to give the *endo* adduct **3a** (2.6 g, 14.6 mmol, 82%) and the *exo* adduct **4a** (0.25 g, 1.4 mmol, 8.0%).

Spectral data for 3a: white waxy solid; mp 50–50.5 °C; IR ($CHCl_3$) 2970, 1710, 1595, 1370 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.19 (s, 2H), 3.39 (s, 2H), 3.18 (s, 2H), 2.08 (s, 6H), 1.38–1.53 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.75 (2C), 134.34 (2C), 57.07 (2C), 48.24 (2C), 46.55 (2C), 29.94 (2C); LRMS *m/z* (rel inten) 178 (M^+, 29), 135 (59), 66 (100); HRMS (EI) calcd for $C_{11}H_{14}O_2$ 178.0994, found 178.0986.

Spectral data for 4a: white waxy solid; mp 41–42 °C; IR ($CHCl_3$) 2970, 1710, 1595, 1370 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.23 (s, 2H), 3.07 (s, 2H), 2.71 (s, 2H), 2.16 (s, 6H), 1.74 (d, J = 8.4 Hz, 2H), 1.40 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.12 (2C), 137.81 (2C), 55.38 (2C), 45.21 (2C), 44.02 (2C), 30.29 (2C); LRMS *m/z* (rel inten) 178 (M^+, 26), 135 (61), 66 (100); HRMS (EI) calcd for $C_{11}H_{14}O_2$ 178.0994, found 178.0990.

The same reaction conditions and procedure were applied to the preparation of **3b–d** and **4b,c**.

Spectral data for 3b: pale yellow oil; IR (neat) 2980, 1710, 1600, 1370 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.19–6.13 (m, 2H), 3.60 (dd, J = 9.5, 2.7 Hz, 1H), 3.37 (dd, J = 9.3, 3.6 Hz, 1H), 3.19 (brs, 1H), 3.13 (brs, 1H), 2.61–2.57 (m, 1H), 2.03 (s, 3H), 1.47–1.37 (m, 2H), 1.12 (d, J = 6.6 Hz, 3H), 1.05 (d, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.10, 206.57, 134.57, 133.85, 57.42, 53.72, 48.16, 46.73, 46.35, 40.23, 29.48, 18.70, 18.14; LRMS *m/z* (rel inten) 206 (M^+, 26), 135 (32), 97 (100); HRMS (EI) calcd for $C_{13}H_{18}O_2$ 206.1307, found 206.1302.

Spectral data for 4b: pale yellow oil; IR (neat) 2980, 1710, 1600, 1370 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.24 (s, 2H), 3.12 (brs, 1H), 2.97–2.94 (m, 2H), 2.71–2.56 (m, 2H), 2.04 (s, 3H), 1.78 (d, J = 9.6 Hz, 1H), 1.38 (d, J = 9.2 Hz, 1H), 1.13 (d, J = 6.6 Hz, 3H), 1.10 (d, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.97, 208.03, 138.13, 137.60, 55.56, 52.53, 45.88, 44.63, 43.99, 40.96, 29.94, 18.55, 18.12; LRMS *m/z* (rel inten) 206 (M^+, 26), 135 (32), 97 (100); HRMS (EI) calcd for $C_{13}H_{18}O_2$ 206.1307, found 206.1304.

Spectral data for 3c: pale yellow oil; yield 83%; IR (neat) 2980, 1710, 1600, 1370 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.23 (dd, J = 3.6, 6 Hz, 1H), 6.14 (dd, J = 3.6, 6.0 Hz, 1H), 3.45–3.31 (m, 2H), 3.17 (m, 2H), 2.33–2.39 (m, 2H), 2.06 (s, 3H), 1.26–1.57 (m, 6H), 0.98 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.16, 206.92, 134.60, 134.31, 57.30, 56.28, 48.39, 46.90, 46.52, 42.50, 30.09, 25.95, 22.37, 13.89; LRMS *m/z* (rel inten) 220 (M^+, 62), 135 (84), 85 (100); HRMS (EI) calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1462.

Spectral data for 4c: pale yellow oil; yield 9%; IR (neat) 2980, 1710, 1600, 1370 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.23 (brs, 2H), 3.10 (brs, 1H), 3.01 (brs, 1H), 2.79 (dd, J = 2.1, 9 Hz, 1H), 2.58 (dd, J = 1.5, 9 Hz, 1H), 2.42–2.49 (m, 2H), 2.13 (s, 3H), 1.26–1.80 (m, 8H), 0.91 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.53, 208.38, 138.13, 137.75, 55.44, 54.71, 45.68, 44.86, 44.16, 42.97, 30.32, 25.92, 22.31, 13.83; LRMS *m/z* (rel inten) 220 (M^+, 58), 135 (80), 85 (100); HRMS (EI) calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1465.

Spectral data for 3d: white waxy solid; yield 80%; mp 49–50 °C; IR ($CHCl_3$) 2975, 1710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33–7.21 (m, 5H), 6.21 (dd, J = 6.0, 3.3 Hz, 1H), 6.10 (dd, J = 6.0, 2.9 Hz, 1H), 3.63 (ABq, J = 15 Hz, δ_A 3.69, δ_B 6.57, 2H), 3.42–3.32 (m, 2H), 3.17 (brs, 1H), 3.07 (brs, 1H), 2.03 (s, 3H), 1.42–1.24 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.43 (2C), 135.22, 134.43, 133.38, 129.39, 128.31, 126.56, 57.57, 54.91, 49.90, 48.07, 46.64, 46.52, 29.33; LRMS *m/z* (rel inten) 254 (M^+, 21), 163 (31), 97 (100), 91 (68); HRMS (EI) calcd for $C_{17}H_{18}O_2$ 254.1307, found 254.1300.

General Procedure for the Ozonolysis of 3a–d. Formation of the Tetraacetal Oxa-Cage Compounds 5a–d. The solution of **3a** (0.5 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 was added dimethyl sulfide (0.52 g, 8.4 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 chromatography to give the tetraacetal oxa-cage compound **5a** (0.5 g, 85%). Spectral data for **5a**: white waxy solid; mp 102–103 °C; IR ($CHCl_3$) 2980, 2880, 1060 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.43 (d, J = 6.0 Hz, 2H), 3.09 (dd, J = 2.7, 5.0 Hz, 2H), 2.88–2.78 (m, 2H), 1.90–1.85 (m, 1H), 1.76–1.70 (m, 1H), 1.47 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 117.01 (2C), 102.76 (2CH), 57.36 (2CH), 45.56 (2CH), 29.01 (CH_2), 24.82 (2CH_3); LRMS *m/z* (rel inten) 210 (M^+, 17), 167 (100), 139 (48); HRMS (EI) calcd for $C_{11}H_{14}O_4$ 210.0892, found 210.0870.[29]

1-Isopropyl-7-methyl-2,4,6,13-tetraoxapentacyclo-[5.5.1.0.^{3,11}0.^{5,9}0^{8,12}]tridecane (5b): white waxy solid; yield 84%; mp 70–71 °C; IR ($CHCl_3$) 2980, 2880, 1060 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.41 (d, J = 6.3 Hz, 1H), 5.40 (d, J = 6.3 Hz, 1H), 3.11–2.95 (m, 2H), 2.84–2.63 (m, 2H), 1.94–1.67 (m, 3H), 1.42 (s, 3H), 0.87 (d, J = 6.9 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 121.55 (C), 117.03 (C), 102.79 (CH), 102.70 (CH), 56.90 (CH), 53.37 (CH), 45.91 (CH), 45.74 (CH), 34.17 (CH), 29.01 (CH_2), 24.58 (CH_3), 16.95 (CH_3), 16.86 (CH_3); LRMS *m/z* (rel inten) 238 (M^+, 47), 195 (100), 149 (73); HRMS (EI) calcd for $C_{13}H_{18}O_4$ 238.1205, found 238.1223. Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.51; H, 7.62. Found: C, 65.42, H, 7.71.

1-*n*-Butyl-7-methyl-2,4,6,13-tetraoxapentacyclo-[5.5.1.0.^{3,11}0.^{5,9}0^{8,12}]tridecane (5c): white waxy solid; yield 85%; mp 69–70 °C; IR ($CHCl_3$) 2980, 2880, 1060 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.44 (d, J = 6.3 Hz, 2H), 3.16–3.01 (m, 2H), 2.85–2.72 (m, 2H), 1.90–1.86 (m, 1H), 1.77–1.68 (m, 3H), 1.47 (s, 3H), 1.36–1.20 (m, 4H), 0.84 (t, J = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 119.45 (C), 117.21 (C), 103.05 (CH), 102.90 (CH), 57.39 (CH), 55.73 (CH), 46.00 (CH), 45.88 (CH), 37.43 (CH_2), 29.30 (CH_2), 26.33 (CH_2), 24.99 (CH_3), 22.66 (CH_2), 13.95 (CH_3); LRMS *m/z* (rel inten) 252 (M^+, 18), 210 (100), 139 (98); HRMS (EI) calcd for $C_{14}H_{20}O_4$ 252.1361, found 252.1362. Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.63; H, 7.99. Found: C, 66.70; H, 7.97.

1-Benzyl-7-methyl-2,4,6,13-tetraoxapentacyclo-[5.5.1.0.^{3,11}0.^{5,9}0^{8,12}]tridecane (5d): white waxy solid; yield 84%; mp 80–81 °C; IR ($CHCl_3$) 3030, 2970, 1384, 1060 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29–7.22 (m, 5H), 5.48 (d, J = 6.0 Hz, 1H), 5.41 (d, J = 6.6 Hz, 1H), 3.15–2.93 (m, 4H), 2.78–2.86 (m, 1H), 2.30–2.38 (m, 1H), 1.84–1.63 (m, 2H), 1.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 136.24 (C), 130.32 (2CH), 127.84 (2CH), 126.47 (CH), 118.84 (C), 117.33 (C), 102.99 (2CH), 57.13 (CH), 55.00 (CH), 45.77 (2CH), 43.26 (CH_2), 29.10 (CH_2), 24.73 (CH_3); LRMS *m/z* (rel inten) 286 (M^+, 18), 195 (100), 91 (59); HRMS (EI) calcd for $C_{17}H_{18}O_4$ 286.1205, found 286.1226.

General Procedure for the Oznolysis of 4a and 4b. Formation of the Tetracarbonyl 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 (1 mL) 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 flash column chromatography to give the tetracarbonyl compound **6a** (0.042 g, 72%): pale yellow oil; IR (neat) 2970, 1725, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.72 (s, 2H), 3.52–3.50 (m, 2H), 3.34–3.28 (m, 2H), 2.19 (s, 6H), 2.19–2.10 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.28, 199.87, 53.95, 51.71, 28.63, 24.23; LRMS *m/z* (rel inten) 210 (M^+, 51), 181 (36), 153 (40), 139 (100); HRMS (EI) calcd for $C_{11}H_{14}O_4$ 210.0892, found 210.0895.

Spectral data for 6b: pale yellow oil; yield 70%; IR (neat) 2970, 1720, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.74 (s, 1H), 9.69 (s, 1H), 3.83 (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 Hz, 3H), 1.09 (d, J = 6.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.07, 205.67, 200.34, 199.61, 54.42, 52.50, 51.83, 51.42, 39.65, 28.72, 24.53, 18.58, 18.29; LRMS *m/z* (rel inten) 238 (M^+, 7), 195 (100), 149 (47); HRMS (EI) calcd for $C_{13}H_{18}O_4$ 238.1205, found 238.1211.

^1H and ^{13}C NMR Spectral Data of the Final Ozonide 9. The solution of **3a** (0.050 g, 0.28 mmol) in $CDCl_3$ (1.0 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 ^{13}C NMR spectra were taken at 20 °C. Spectral data for **9**: ^1H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 205.49 (C=O), 201.99 (CH), 110.54 (C), 104.71 (CH), 57.80 (CH), 51.56 (CH), 50.08 (CH), 46.67 (CH), 29.62 (CH_3), 28.40 (CH_2), 13.98 (CH_3). Quantitative NOE experiment: irr δ 1.52 (the bridgehead methyl protons), enhanced δ 2.21 (3.6%, the methyl ketone protons).

Time-Dependent ^1H NMR Spectra of the Reaction of the Final Ozonide 9 with Dimethyl Sulfide. A solution of **3a** (0.050 g, 0.28 mmol) in $CDCl_3$ (1.0 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 ^{13}C NMR spectra were taken

(29) The author has deposited atomic coordinates for compounds **5a** and **16a** 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.

at 20 °C. The NMR tube was then cooled to −78 °C, and excess dimethyl sulfide was added to the solution. After 10 min, a second ^{1}H NMR spectrum was taken at 20 °C. A third, fourth, and fifth ^{1}H NMR spectra were taken at 20 °C after another 20 min, 1 h, and 3 h, respectively.

General Procedure for Formation of Tetraquinane Oxa-Cage Compounds 16a−c 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 −78 °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 ($CHCl_3$) 3450, 2960, 1767, 1107 cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD) δ 5.16 (d, J = 2.7 hz, 1H), 3.59−3.41 (m, 2H), 3.32−3.29 (m, 2H), 2.78−2.64 (m, 1H), 2.48−2.33 (m, 2H), 1.62 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (75 MHz, CD_3COCD_3, DEPT) δ 178.09 (C=O), 119.17 (C), 115.76 (C), 104.95 (CH), 60.38 (CH), 57.52 (CH), 52.98 (CH), 48.49 (CH), 36.92 (CH_2), 26.43 (CH_3), 25.09 (CH_3); LRMS *m/z* (rel inten) 226 (M^+, 2), 180(39), 137(82), 43 (100); HRMS (EI) calcd for $C_{11}H_{14}O_5$ 226.0841, found 226.0838.[29]

Spectral data for 16b + 17b: white waxy solid; yield 87%; mp 140−141 °C; IR ($CHCl_3$) 3450, 2960, 1767, 1107 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.36 (d, J = 3.9 Hz, 2H), 3.49−3.13 (m, 7H), 2.64−2.57 (m, 4H), 2.40−2.25 (m, 2H), 2.16−2.06 (m, 3H), 1.66 (s, 3H), 1.65 (s, 3H), 1.03−0.95 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 178.05 (C=O), 123.39 (C), 120.41 (C), 119.60 (C), 115.69 (C), 104.39 (CH), 104.01 (CH), 59.58 (CH), 56.46 (CH), 53.20 (CH), 52.47 (CH), 51.80 (CH), 48.24 (CH), 48.16 (CH), 36.99 (CH_2), 36.56 (CH_2), 35.13 (CH), 34.58 (CH), 26.01 (CH_3), 25.05 (CH_3), 17.33 (CH_3), 16.95 (CH_3), 16.45 (CH_3), 16.34 (CH_3); LRMS *m/z* (rel inten) 254 (M^+, 6), 210 (24), 165 (100), 139 (91); HRMS (EI) calcd for $C_{13}H_{18}O_5$ 254.1154, found 254.1142.

Spectral data for 16c + 17c: white waxy solid; yield 88%; mp 145−145.5 °C; IR ($CHCl_3$) 3450, 2960, 1767, 1107 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.35 (brs, 2H), 3.71 (brs, 2H), 3.43−3.18 (m, 6H), 2.82−2.36 (m, 6H), 1.91−1.88 (m, 4H), 1.66 (s, 6H), 1.42−1.36 (m, 8H), 0.94−0.89 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 177.93 (C=O), 121.53 (C), 119.60 (C), 117.99 (C), 115.81 (C), 104.39 (CH), 104.16 (CH), 59.66 (CH), 58.18 (CH), 56.90 (CH), 55.47 (CH), 51.77 (CH), 51.68 (CH), 48.10 (CH), 38.51 (CH_2), 37.35 (CH_2), 37.05 (CH_2), 36.91 (CH_2), 26.22 (CH_2), 26.16 (CH_3), 25.43 (CH_2), 25.08 (CH_3), 22.63 (CH_2), 22.43 (CH_2), 13.98 (CH_3), 13.86 (CH_3); LRMS *m/z* (rel inten) 268 (M^+, 17), 211(54), 137 (95), 85 (100); HRMS (EI) calcd for $C_{14}H_{20}O_5$ 268.1311, found 268.1325.

Spectral data for 16d + 17d: white waxy solid; yield 86%; mp 129−130 °C; IR ($CHCl_3$) 3430, 2950, 1765, 1640 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 177.67 (C=O), 134.14 (C), 130.64 (CH), 130.44 (CH), 128.43 (CH), 128.16 (CH), 127.29 (CH), 126.79 (CH), 120.85 (C), 119.80 (C), 117.06 (C), 115.84 (C), 104.51 (CH), 104.42 (CH), 59.58 (CH), 57.22 (CH), 56.78 (CH), 54.62 (CH), 51.88 (CH), 51.68 (CH), 48.01 (CH), 47.95 (CH), 44.51 (CH_2), 43.26 (CH_2), 36.91 (CH_2), 36.85 (CH_2), 26.01 (CH_3), 24.64 (CH_3); LRMS *m/z* (rel inten) 302 (M^+, 8), 258 (60), 181 (100); HRMS (EI) calcd for $C_{17}H_{18}O_5$ 302.1154, found 302.1158.

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 6 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 ($CHCl_3$) 2890, 1770, 1765, 1100 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 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), 1.65 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 176.74 (C=O), 169.45 (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_2), 25.31 (CH_3), 24.93 (CH_3), 21.20 (CH_3); LRMS *m/z* (rel inten) 224 (15), 180 (31), 137 (67), 43 (100); HRMS (EI) calcd for $C_{13}H_{16}O_6$ 268.0947, found 268.0962. Anal. Calcd for $C_{13}H_{16}O_6$: C, 58.19; H, 6.01. Found: C, 58.23; H, 6.03.

General Procedure for the Synthesis of the Tetraquinane Oxa-Cage Bislactones 19a−c. To a solution of **16a** (0.30 g, 1.3 mmol) in dichloromethane (20 mL) were added pyridinium chlorochromate (0.57 g, 2.6 mmol) and Celite (2 g). The reaction mixture was stirred at room temperature for 4 h. Then, the reaction mixture was filtered through Celite. The solvent was evaporated, and the crude product was purified by column chromatography to give **19a** (0.22 g, 75%).

Spectral data for 19a: white waxy solid; mp 165−167 °C; IR ($CHCl_3$) 2960, 1767, 1107 cm^{-1}; ^{1}H NMR (300 MHz, CD_3COCD_3) δ 3.82 (dd, J = 6.3, 3.2 Hz, 2H), 3.43−3.38 (m, 2H), 2.75−2.51 (m, 2H), 1.67 (s, 6H); ^{13}C NMR (75 MHz, CD_3COCD_3, DEPT) δ 176.46 (2 C=O), 116.29 (2C), 57.46 (2CH), 47.76 (2CH), 37.65 (CH_2), 24.74 ($2CH_3$); LRMS *m/z* (rel inten) 224 (M^+, 3), 180 (100); HRMS (EI) calcd for $C_{11}H_{12}O_5$ 224.0685, found 224.0690.

Spectral data for 19b: white waxy solid; yield 73%; mp 177−178 °C; IR ($CHCl_3$) 2970, 1767, 1107 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.71−3.54 (m, 2H), 3.33 (dd, J = 9, 8.9 Hz, 1H), 3.21 (dd, J = 9, 8.9 Hz, 1H), 2.94−2.89 (m, 1H), 2.60−2.49 (m, 1H), 2.20−2.13 (m, 1H), 1.71 (s, 3H), 1.03 (d, J = 6.6 Hz, 3H), 1.01 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 175.92 (C=O), 175.66 (C=O), 120.15 (C), 115.72 (C), 56.37 (CH), 53.08 (CH), 47.34 (CH), 47.16 (CH), 37.43 (CH_2), 34.69 (CH), 24.67 (CH_3), 16.37 (CH_3), 16.19 (CH_3); LRMS *m/z* (rel inten) 252 (M^+, 3), 208 (51), 165 (35), 71 (100); HRMS (EI) calcd for $C_{13}H_{16}O_5$ 252.0998, found 252.0987. Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.88; H, 6.40. Found: C, 61.95; H, 6.36.

Spectral data for 19c: white waxy solid; yield 74%; mp 160.5−161.5 °C; IR ($CHCl_3$) 2970, 1767, 1107 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.73−3.61 (m, 2H), 3.37−3.24 (m, 2H), 2.90−2.84 (m, 1H), 2.63−2.52 (m, 1H), 1.97−1.89 (m, 2H), 1.71 (s, 3H), 1.43−1.38 (m, 4H), 0.93 (t, J = 6.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 176.09 (C=O), 175.95 (C=O), 117.85 (C), 115.78 (C), 56.31 (CH), 55.00 (CH), 47.14 (CH), 47.08 (CH), 37.40 (CH_2), 37.08 (CH_2), 25.20 (CH_2), 24.64 (CH_3), 22.34 (CH_2), 13.77 (CH_3); LRMS *m/z* (rel inten) 266 (M^+, 2), 222 (56), 85 (100); HRMS (EI) calcd for $C_{14}H_{18}O_5$ 266.1154, found 266.1163.

Spectral data for 19d: white waxy solid; yield 74%; mp 218−219 °C; IR ($CHCl_3$) 3050, 2970, 1767, 1107 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36−7.27 (m, 10H), 3.61 (dd, J = 11, 9.0 Hz, 1H), 3.42 (dd, J = 11, 9.3 Hz, 1H), 3.33−3.15 (m, 3H), 2.88−2.83 (m, 1H), 2.69 (dd, J = 9.3, 9.0 Hz, 1H), 2.41−2.30 (m, 1H), 1.63 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 175.16 (C=O), 175.09 (C=O), 133.41 (C), 130.47 (2CH), 128.72 (2CH), 127.64 (CH), 56.40 (CH), 54.36 (CH), 46.97 (CH), 46.95 (CH), 43.01 (CH_2), 37.40 (CH_2), 24.70 (CH_3); LRMS *m/z* (rel inten) 300 (M^+, 35), 256 (22), 209 (100); HRMS (EI) calcd for $C_{17}H_{16}O_5$ 300.0998, found 300.0996.

Formation of the Tetraoxa-Cage Compound 24. 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 85%; mp 190−191 °C; IR ($CHCl_3$) 3070, 2980, 1580, 1100; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60−7.55 (m, 4H), 7.44−7.29 (m, 6H), 5.83 (d, J = 6.3 Hz, 2H), 3.52 (dd, J = 3.0, 3.0 Hz, 2H), 3.09−3.03 (m, 2H), 2.09−2.05 (m, 1H), 1.90−1.84 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 140.98 (2C), 128.31 (2CH), 128.19 (4CH), 125.51 (4CH), 118.20 (2C), 103.84 (2CH), 60.77 (2CH), 46.20 (2CH), 29.39 (CH_2); LRMS *m/z* (rel inten) 334 (M^+, 18), 305 (13), 212 (12), 145 (10), 105 (100); HRMS (EI) calcd for $C_{21}H_{18}O_4$ 334.1205, found 334.1205. Anal. Calcd for $C_{21}H_{18}O_4$: C, 75.42; H, 5.43. Found: C, 75.37; H, 5.44.

Formation of Compound 25. The same reaction conditions and procedure as for the synthesis of **16a−d** and **17b−d** from ozonolysis of **3a−d** were applied to the ozonolysis of **22**. Spectral data for **25**: white waxy solid; yield 87%; mp 223−224 °C; IR ($CHCl_3$) 3450, 3020, 1765, 1620; ^{1}H NMR (300 MHz, CD_3SOCD_3) δ 7.62−7.35 (m, 10H), 6.98 (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); ^{13}C NMR (75 MHz, CD_3SOCD_3, DEPT) δ 178.31 (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 (CH_2); LRMS *m/z* (rel inten) 350 (M^+, 2), 105 (72), 85 (100); HRMS (EI) calcd for $C_{21}H_{18}O_5$ 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, $CDCl_3$) 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); ^{13}C NMR (75 MHz, $CDCl_3$) 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 $C_{21}H_{18}O_4$ 334.1205, found 334.1227.

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Supporting Information Available: ^1H and ^{13}C 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 Me_2S (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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