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Synthesis of 4-Oxo- and 4-*anti*-Formyl-8,10,12,13-tetraoxapentacyclo-[5.5.1.$0^{2,6}$.$0^{3,11}$.$0^{5,9}$]tridecanes

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Abstract: The synthesis of 4-oxo- and 4-*anti*-formyl-8,10,12,13-tetraoxapentacyclo[5.5.1.$0^{2,6}$.$0^{3,11}$.$0^{5,9}$]tridecanes has been accomplished. Ozonolysis of compounds **10a,b** and **12a-c** in dichloromethane at -78 ℃ followed by reduction with dimethyl sulfide gave the title compounds, 4-oxo-tetraoxa-cages **11a,b** and **14a-c**, in moderate yields. Ozonolysis of the *endo-syn* isomers **15a,b** and **18a,b** under the same reaction conditions gave 4-*anti*-formyl-tetraoxa-cages **17a,b** and **20a,b**, respectively.

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] heptacyclotetradecane (HCTD),[8] pogodane,[9] and fullerenes.[10] On the other hand, the synthesis and chemistry of heterocyclic cage compounds have received less attention. However, there are some reports regarding the chemistry[11] and synthesis[12-17] of oxa-cage compounds in the literature. This class of heterocyclic cage compounds is synthesized by intramolecular alkene-oxirane (2σ-2π) photocycloaddition,[12] by transannular cyclization of suitable compounds,[13] by tandem cyclization,[14] by dehydration of diols having the proper stereochemistry,[15] by base-promoted rearrangement,[16] and by intramolecular etherification of an alkene bond with organoselenium reagents.[17]

Recently, we developed new methods for the synthesis of a series of oxa-cage compounds, such as diacetal trioxa-cages,[18] triacetal trioxa-cages,[19] tetraacetal tetraoxa-cages,[20] tetraacetal pentaoxa-cages,[21] and pentaacetal pentaoxa-cages (the pentaoxa[5]peristylanes).[22] We also

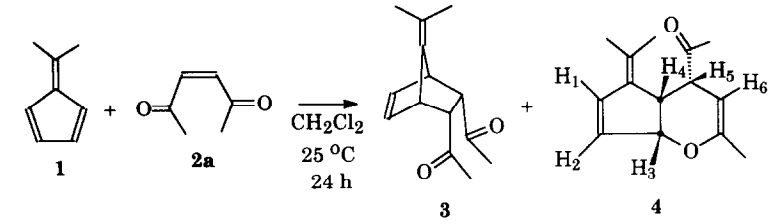
investigated the chemical nature of the acetal groups of tetraoxa-cages and discovered a novel hydride rearrangement and one-pot conversion from oxa-cages to aza-cages.[23] As part of a program that involves the synthesis, chemistry, and applications of new heterocyclic cages, we report here the synthesis of 4-oxo- and 4-*anti*-formyl-8,10,12,13-tetraoxapentacyclo-[5.5.1.$0^{2,6}$.$0^{3,11}$.$0^{5,9}$]tridecanes. 4-Oxo-8,10,12,13-tetraoxapentacyclo[5.5.1.$0^{2,6}$.$0^{3,11}$.$0^{5,9}$]tridecane is a new system for the facial selectivity study on carbonyl group. We have investigated the facial selectivity of a series of oxa-cages, and the results will be reported soon.

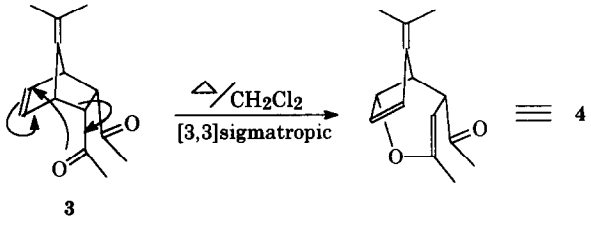
Results and Discussion

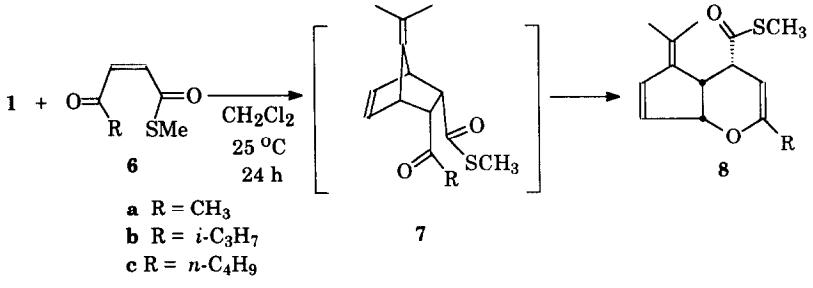
Reaction of 6,6-dimethylfulvene **1** (commercially available) with (Z)-3-hexene-2,5-dione **2a**[20a] in dichloromethane at 25 ℃ for 24 h gave the *endo* adduct **3** (10%) and compound **4** (50%) (Scheme 1). When the reaction time was prolonged at 25 ℃ for 72 h, compound **4** was obtained in 70% yield. Refluxing the adduct **3** in dichloromethane for 24 h gave **4** in 80% yield. No detectable amount of the other regioisomer **5** was obtained. The regiochemistry of **4** was determined by ^1H-^1H correlated two-dimensional NMR spectral analysis. Proton H_1 (δ 6.53) showed strong coupling to proton H_2 (δ 5.74), which, in turn, displayed coupling to proton H_3 (δ 5.30). Proton H_3 exhibited strong coupling to proton H_4 (δ 3.69), which, in turn, showed coupling to H_5 (δ 3.03), and H_5 displayed coupling to H_6 (δ 4.87). The stereochemistry of **4** was determined on the basis of NOE experiments. Irradiating the H_4 proton gives 4.8% enhancement for the H_3 proton absorptions and 4.2% enhancement for the H_5 proton absorptions. Reaction of **1** with (Z)-γ-oxo-α,β-unsaturated thioesters **6a-c**[20g] in CH_2Cl_2 at 25 ℃ for 24 h gave compounds **8a-c** in 60-65% yields. The amount of the *endo* adducts **7a-c** was too small to be isolated. We proposed that compounds **4** and **8** were obtained by a [3,3] sigmatropic rearrangement from **3** and **7**, respectively.

To improve the yields of the *endo* adducts, 6-acetoxyfulvene **9** was prepared for the Diels-Alder reaction as a diene. Reaction of **9** with the ene-diones **2a,b** in dichloromethane at 25 ℃ for 48 h gave the *endo* adducts **10a,b** in 50-55% yields, with unreacted starting compounds. Ozonolysis of **10a,b** in dichloromethane at -78 ℃ followed by reduction with dimethyl sulfide gave 4-oxo-tetraoxa-cage compounds **11a,b** in 60-66% yields (Scheme 2). Ozonolysis of **3** under the same reaction conditions gave **11a** in 65% yield. Thus, we have accomplished the synthesis of new tetraoxa-cages with a carbonyl group on the apex carbon, 4-oxo-8,10,12,13-tetraoxapentacyclo[5.5.1.$0^{2,6}$.$0^{3,11}$.$0^{5,9}$]tridecanes, in a short sequence.

Scheme 1

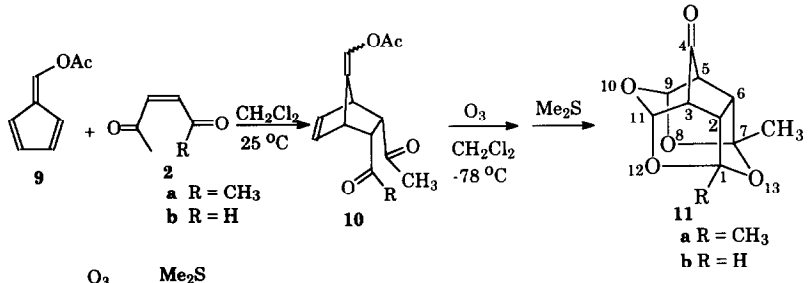


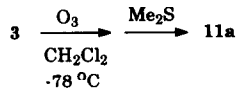




a R = CH_3
b R = i-C_3H_7
c R = n-C_4H_9

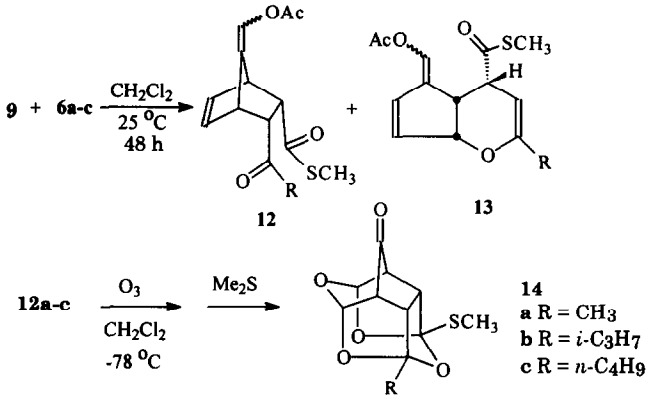
Scheme 2





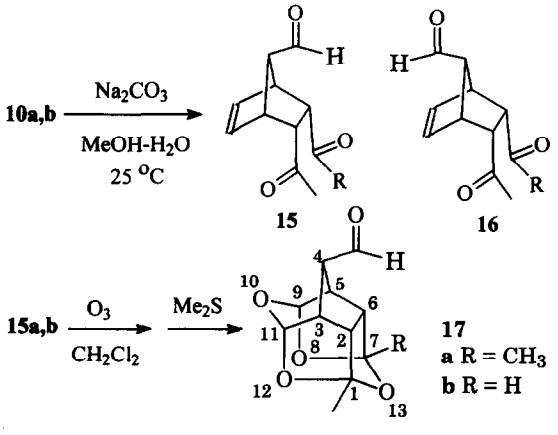
Reaction of **9** with **6a-c** in dichloromethane at 25 ℃ for 48 h gave the *endo* adducts **12a-c** (30%) and compounds **13a-c** (35%) (Scheme 3). Both compounds **12** and **13** contained two regioisomers in each case from their ^1H and ^{13}C NMR spectra. Ozonolysis of **12a-c** in dichloromethane at -78 ℃ followed by reduction with dimethyl sulfide gave 4-oxo-tetraoxa-cage compounds **14a-c** in 60-65% yields.

Scheme 3



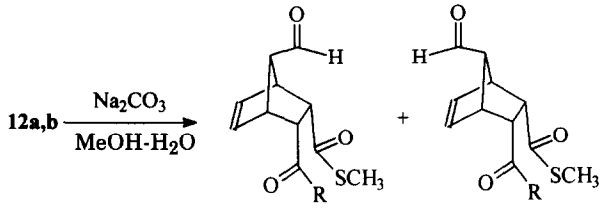
Hydrolysis of the *endo* adducts **10a,b** with a catalytic amount of sodium carbonate in aqueous methanol (1:1) at 25 ℃ gave the *endo-syn* isomers **15a,b** in 80-90% yields (Scheme 4). The amount of the *endo-anti* isomers **16a,b** was too small to be isolated. The stereochemistry of the formyl group on the apical carbon of **15** was determined by the following chemical transformation. Ozonolysis of **15a,b** in dichloromethane at -78 ℃ followed by reduction with dimethyl sulfide gave the tetraaectal tetraoxa-cages **17a,b** in 75-85% yields.

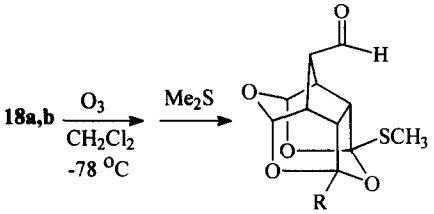
Scheme 4



Hydrolysis of the mixtures of the two regioisomers of **12a,b** with a catalytic amount of sodium carbonate in aqueous methanol (1:1) at 25 ℃ gave the *endo-syn* isomers **18a,b** and the *endo-anti* isomers **19a,b** in ratios of 7-8:1 in 80-85% yields (Scheme 5). The stereochemistry of the formyl group on the apical carbon of **18** and **19** was determined by the following chemical transformation. Ozonolysis of the *endo-syn* isomers **18a,b** in dichloromethane at -78 ℃ followed by reduction with dimethyl sulfide gave the methylthio group substituted tetraacetal tetraoxa-cages **20a,b** in 80-85% yields. As expected, the thioester group of **18a,b** participated the cyclization process.[20d]

Scheme 5





a R = CH_3
b R = *i*-C_3H_7

Conclusion

We have accomplished the synthesis of 4-oxo- and 4-*anti*-formyl-8,10,12,13-tetraoxapentacyclo[5.5.1.$0^{2,6}$.$0^{3,11}$.$0^{5,9}$]tridecanes in a short sequence. Ozonolysis of compounds **10a,b** and **12a-c** in dichloromethane at -78 ℃ followed by reduction with dimethyl sulfide gave the title compounds, 4-oxo-tetraoxa-cages **11a,b** and **14a-c**, in moderate yields. Ozonolysis of the *endo-syn* isomers **15a,b** and **18a,b** under the same reaction conditions gave 4-*anti*-formyl-tetraoxa-cages **17a,b** and **20a,b**, respectively. The formation of tetraoxa-cages can aslo be used as a probe for determining the stereochemistry of the formyl group on the apical carbon.

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. ^1H NMR spectra were determined at 300 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 values were obtained with a high resolution mass spectrometer at the Department of Chemistry, National Tsing Hua University. Elemental analyses were performed at the microanalysis laboratory of National Taiwan University. 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_2Cl_2 was distilled from CaH_2 under nitrogen.

Reaction of 6,6-Dimethylfulvene with (Z)-3-Hexene-2,5-dione 2a.

To a solution of (Z)-3-hexene-2,5-dione **2a**[20a] (1.1 g, 9.5 mmol) in dichloromethane (20 mL) was added 6,6-dimethylfulvene (1.0 g, 9.4 mmol) at 25 °C. The reaction mixture was stirred at 25 °C for 24 h. The solvent was evaporated and the crude product was purified by column chromatography to give the *endo* adduct **3** (0.21 g, 10%) and compound **4** (1.02 g, 50%). Spectral data for **3**: pale yellow oil; IR (neat) 2980, 1710, 1380 cm^{-1},^1H NMR (300 MHz, $CDCl_3$) δ 6.33 (brs, 2H), 3.62 (brs, 2H), 3.35 (brs, 2H), 2.10 (s, 6H), 1.57 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 206.43 (2CO), 144.34 (C), 137.89 (C), 134.55 (2CH), 57.08 (2CH), 46.41 (2CH), 29.97 ($2CH_3$), 19.44 ($2CH_3$); LRMS *m/z* (rel inten) 218 (M^+, 36), 203 (40), 112 (100); HRMS (EI) calcd for $C_{14}H_{18}O_2$ 218.1307, found 218.1301.

Spectral data for **4**: pale yellow oil; IR (neat) 2980, 1705, 1360 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.53 (d, J = 6.0 Hz, 1H), 5.74 (dd, J = 6.0, 1.5 Hz, 1H), 5.30 (dd, J = 8.1, 1.5 Hz, 1H), 4.87 (d, J = 4.5 Hz, 1H), 3.69 (dd, J = 6.6, 4.5 Hz, 1H), 3.03 (dd, J = 8.1, 6.6 Hz, 1H) , 2.16 (s, 3H), 1.74 (s, 3H), 1.70 (s, 3H), 1.65 (s, 3H), ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 206.57 (CO), 151.91 (C), 140.43 (C), 133.67 (CH), 132.36 (CH), 123.01 (C), 96.64 (CH) 81.55 (CH), 49.26 (CH), 40.06 (CH), 27.18 (CH_3), 20.56 (CH_3), 20.24 (CH_3), 20.13 (CH_3); LRMS *m/z* (rel inten) 218 (M^+, 21), 203 (100); HRMS (EI) calcd for $C_{14}H_{18}O_2$ 218.1307, found 218.1312.

Refluxing the *endo* Adduct 2a in Dichloromethane. To a solution of **2a** (1.0 g, 4.6 mmol)

in dichloromethane (50 mL) was refluxed at 45 ℃ for 48 h. After cooling, the solvent was evaporated and crude product was purified by column chromatography to give 3a (0.80 g, 80%).

General Procedure for Reaction of 6,6-Dimethylfulvene with (Z)-γ-Oxo-α,β-unsaturated Thioesters 6a-c. To a solution of (Z)-methyl-γ-oxo-2-pententhioate **6a** (1.36 g, 9.4 mmol) in dichloromethane (20 mL) was added 6,6-dimethylfulvene (1.0 g, 9.4 mmol) at 25 ℃. The reaction mixture was stirred at 25 ℃ for 48 h. The solvent was evaporated and the crude product was purified by column chromatography to give **8a** in 65% yield with unreacted starting compounds. Spectral data for **8a**: pale yellow oil; IR (neat) 2960, 2880, 1685, 1380 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$) δ 6.52 (d, J = 5.7 Hz, 1H), 5.78 (dd, J = 5.7, 1.5 Hz, 1H), 5.29 (dd, J = 7.2, 1.5 Hz, 1H), 4.83 (d, J = 4.5 Hz, 1H), 3.66 (dd, J = 6.9, 4.5 Hz, 1H), 3.16 (dd, J = 7.2, 6.9 Hz, 1H) , 2.28 (s, 3H), 1.76 (s, 3H), 1.75 (s, 3H), 1.70 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 202.26 (COS), 153.34 (C), 139.96 (C), 133.76 (CH), 133.06 (CH), 124.81 (C), 96.78 (CH), 81.66 (CH), 49.87 (CH), 42.36 (CH), 21.20 (CH_3), 20.88 (CH_3), 20.59 (CH_3), 12.08 (SCH_3); LRMS m/z (rel inten) 250 (M^+, 18), 203 (100); HRMS (EI) calcd for $C_{14}H_{18}O_2S$ 250.1028, found 250.1024.

Spectral data for **8b**: pale yellow oil; yield 63% IR (neat) 2960, 1685, 1380 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.53 (d, J = 5.7 Hz, 1H), 5.72 (dd, J = 5.7, 1.5 Hz, 1H), 5.32 (dd, J = 7.2, 1.5 Hz, 1H), 4.90 (d, J = 4.8 Hz, 1H), 3.77 (dd, J = 6.9, 4.8 Hz, 1H), 3.14 (dd, J = 7.2, 6.9 Hz, 1H) , 2.26 (s, 3H), 2.24-2.17 (m, 1H), 1.75 (s, 3H), 1.74 (s, 3H), 1.04 (d, J = 6.6 Hz, 3H), 1.03 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 202.64 (COS), 161.76 (C), 140.29 (C), 134.14 (CH), 132.83 (CH), 124.43 (C), 95.04 (CH), 81.84 (CH), 49.58 (CH), 43.35 (CH), 32.57 (CH), 21.03 (CH_3), 20.85 (CH_3), 19.63 (CH_3), 19.34 (CH_3), 12.11 (SCH_3); LRMS m/z (rel inten) 278 (M^+, 8), 231 (100); HRMS (EI) calcd for $C_{16}H_{22}O_2S$ 278.1341, found 278.1338.

Spectral data for **8c**: pale yellow oil; IR (neat) 2970, 1685, 1370 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.52 (d, J = 6.0 Hz, 1H), 5.75 (dd, J = 6.0, 1.5 Hz, 1H), 5.29 (dd, J = 7.2, 1.5 Hz, 1H), 4.85 (d, J = 4.5 Hz, 1H), 3.70 (dd, J = 6.9, 4.5 Hz, 1H), 3.14 (dd, J = 7.2, 6.9 Hz, 1H) , 2.27 (s, 3H), 2.05-1.98 (m, 2H), 1.75 (s, 3H), 1.72 (s, 3H), 1.48-1.25 (m, 4H), 0.89 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 202.35 (COS), 156.95 (C), 140.17 (C), 133.90 (CH), 133.06 (CH), 124.58 (C), 96.52 (CH), 81.69 (CH), 49.79 (CH), 42.79 (CH), 34.14 (CH_2), 28.25 (CH_2), 22.22 (CH_2), 21.15 (CH_3), , 20.83 (CH_3), 13.80 (CH_3), 12.08 (SCH_3); LRMS m/z (rel inten) 292 (M^+, 11), 245 (100); HRMS (EI) calcd for $C_{17}H_{24}O_2S$ 292.1497, found 292.1489.

General Procedure for Reaction of 6-Acetoxyfulvene with (Z)-2-Ene-1,4-diones 2a,b. To a solution of **2a** (0.82 g, 7.4 mmol) in dichloromethane (20 mL) was added 6-acetoxyfulvene (1.0 g, 7.3 mmol) at 25 ℃. The reaction mixture was stirred at 25 ℃ for 48 h. The solvent was

evaporated and the crude product was purified by column chromatography to give the *endo* adduct **10a** (0.98 g, 55%). In the case of **10b**, the product contained two regioisomers. Spectral data for **10a**: pale yellow oil; IR (neat) 2980, 2880, 1755, 1710, 1225 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.60 (s, 1H), 6.32 -6.29 (m, 2H), 3.87 (brs, 1H), 3.50-3.42 (m, 3H), 2.13 (s, 3H) 2.11 (s, 3H) 2.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 205.41 (CO), 205.35 (CO) , 168.17 (CO), 136.76 (C), 134.49 (CH), 133.50 (CH), 116.45 (CH), 57.33 (CH), 56.14 (CH), 46.70 (CH), 44.75 (CH), 29.97 (CH_3), 29.89 (CH_3), 20.59 (CH_3); LRMS *m/z* (rel inten) 248 (M^+, 26), 233 (100); HRMS (EI) calcd for $C_{14}H_{16}O_4$ 248.1049, found 248.1044.

Spectral data for **10b**: pale yellow oil; yield 55% IR (neat) 2980, 1755, 1720, 1710, 1225 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.55 and 9.54 (d, J = 3.0 Hz, 1H), 6.66 and 6.62 (s, 1H), 6.56-6.48 (m, 1H), 6.23-6.16 (m, 1H), 4.02 and 3.90 (brs, 1H), 3.77-3.71 (m, 1H), 3.64 and 3.50 (brs, 1H), 3.10-3.03 (m, 1H), 2.23 and 2.20 (s, 3H), 2.16 and 2.13 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 205.43 (CO), 205.39 (CO), 200.64 (CHO), 200.60 (CHO), 168.06 (2CO), 136.98 (CH), 136.73 (C), 136.51 (C), 135.80 (CH), 133.51 (CH), 132.41 (CH), 116.82 (CH), 116.80 (CH), 59.85 (CH), 58.76 (CH), 55.93 (CH), 54.80 (CH), 47.12 (CH), 45.41 (CH), 45.14 (CH), 43.59 (CH), 28.88 (CH_3), 28.83 (CH_3), 20.66 (CH_3) , 20.62 (CH_3); LRMS *m/z* (rel inten) 234 (M^+, 12), 219 (100); HRMS (EI) calcd for $C_{13}H_{14}O_4$ 234.0892, found 234.0896.

Synthesis of Tetraoxa-Cages 11a,b from Ozonolysis of 10a,b. A solution of **10a** (1.0 g, 4.0 mmol) in dichloromethane (30 mL) was cooled to -78 ℃, and ozone was bubbled through it at -78 ℃ until the solution turned light blue. To this solution was added dimethyl sulfide (0.56 g, 9.0 mmol) at -78 ℃. 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 **11a** (0.59 g, 66%).

1,7-Dimethyl-4-oxo-8,10,12,13-tetraoxapentacyclo[5.5.1.$0^{2,6}$.$0^{3,11}$.$0^{5,9}$]tridecanes 11a: white waxy solid; mp 122-123 ℃; IR ($CHCl_3$) 2880, 1765, 1380, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.87 (d, J = 5.7 Hz, 2H), 3.28-3.16 (m, 4H), 1.64 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 204.97 (CO), 121.00 (2C) , 107.27 (2CH), 55.09 (2CH), 50.40 (2CH), 24.90 ($2CH_3$); LRMS *m/z* (rel inten) 224 (M^+, 23), 196 (100); HRMS (EI) calcd for $C_{11}H_{12}O_5$ 224.0685, found 224.0689; Anal, calcd for $C_{11}H_{12}O_5$: C, 58.91; H,5.40, found: C, 58.82; H, 5.45.

1-Methyl-4-oxo-4,8,10,13-tetraoxapentacyclo[5.5.1.$0^{2,6}$.$0^{3,11}$.$0^{5,9}$]tridecane 11b: white waxy solid; mp 94-95 ℃; yield 60%; IR ($CHCl_3$) 2980, 2880, 1765, 1070 cm^{-1}; ^1H NMR (300 Hz, $CDCl_3$) δ 6.15 (d, J = 5.1 Hz, 1H), 5.87 (d, J = 6.6 Hz, 2H), 3.62-3.56 (m, 1H), 3.22-3.10 (m, 3H), 1.65 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 205.00 (CO), 121.35 (C), 112.52 (CH), 107.54 (CH),

107.39 (CH), 55.06 (CH), 54.59 (CH), 49.20 (CH), 47.08 (CH), 24.53 (CH_3); LRMS *m/z* (rel inten) 210 (M^+, 37), 182 (100); HRMS (EI) calcd for $C_{10}H_{10}O_5$ 210.0528, found 210.0531; Anal. calcd for $C_{10}H_{10}O_5$: C, 57.13; H, 4.80, found: C, 57.01; H, 4.88.

Synthesis of Tetraacetal Tetraoxa-Cage 11a from Ozonolysis of 3. The same reaction conditions and procedure as for the ozonolysis of **10a,b** were applied for the ozonolysis of **3** to give the tetraoxa-cage **11a** in 65% yield.

General Procedure for the Reactions of 6-Acetoxyfulvene with (Z)-γ-Oxo-α,β-unsaturated Thioesters 6a-c. To a solution of **6a** (1.1 g, 7.4 mmol) in dichloromethane (30 mL) was added 6-acetoxyfulvene (1.0 g, 7.3 mmol) at 25 ℃. The reaction mixture was stirred at 25 ℃ for 48 h. The solvent was evaporated, and the crude product was purified by column chromatography to give the *endo* adduct **12a** (0.60 g, 30%) and compound **13a** (0.70 g, 35%). In each case, both the *endo* adducts **12a-c** and compounds **13a-c** contained two regioisomers, and their spectral data were taken as mixtures of two regioisomers. Spectral data for **12a**: pale yellow oil; IR (neat) 2980, 1755, 1710, 1690, 1220 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.62 and 6.59 (s, 1H), 6.58-6.53 (m, 1H), 6.16-6.09 (m, 1H), 3.93 and 3.83 (brs, 1H), 3.81-3.76 (m, 1H), 3.57 and 3.42 (brs, 1H), 3.31-3.25 (m, 1H), 2.30 and 2.29 (s, 3H), 2.15 and 2.12 (s, 3H), 2.05 and 2.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 205.27 (2CO), 197.24 (2COS), 168.14 (CO), 168.16 (CO), 137.10 (CH), 136.48 (C), 136.13 (C), 135.99 (CH), 132.52 (CH), 131.47 (CH), 116.71 (CH), 116.69 (CH), 58.05 (CH), 57.11 (CH), 56.85 (CH), 56.09 (CH), 48.59 (CH), 46.56 (CH), 46.01 (CH), 44.16 (CH), 30.65 (CH_3), 30.62 (CH_3), 20.65 (CH_3), 20.60 (CH_3), 11.76 (SCH_3), 11.73 (SCH_3); LRMS *m/z* (rel inten) 280 (M^+, 21), 233 (100); HRMS (EI) calcd for $C_{14}H_{16}O_4S$ 280.0769, found 208.0761.

Spectral data for **13a**: pale yellow oil; IR (neat) 2980, 1760, 1685, 1215, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29 and 7.03 (s, 1H), 6.68 and 6.29 (d, J = 5.7 Hz, 1H), 6.08 and 5.95 (dd, J = 5.7, 2.1 Hz, 1H), 5.20 and 5.11 (dd, J = 8.1, 2.1 Hz, 1H), 4.84 and 4.72 (d, J = 5.1 Hz, 1H), 3.84-3.80 (m, 1H), 3.53-3.46 (m, 1H), 2.32 and 2.31 (s, 3H), 2.16 and 2.15 (s, 3H), 1.75 and 1.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 201.21 (COS), 201.14 (COS), 167.40 (CO), 167.27 (CO), 153.63 (2C), 135.36 (CH), 134.88 (CH), 133.17 (CH), 132.06 (C), 130.76 (CH), 130.35 (C), 129.00 (CH), 127.21 (CH), 96.30 (CH), 93.94 (CH), 80.80 (CH), 79.34 (CH), 48.43 (CH), 47.46 (CH), 40.41 (CH), 39.52 (CH), 20.58 ($2CH_3$), 20.47 ($2CH_3$), 11.85 ($2SCH_3$); LRMS *m/z* (rel inten) 280 (M^+, 8), 233 (100); HRMS (EI) calcd for $C_{14}H_{16}O_4S$ 280.0769, found 280.0756.

Spectral data for **12b**: pale yellow oil; IR (neat) 2980, 1755, 1710, 1690, 1220 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.63 and 6.59 (s, 1H), 6.60-6.54 (m, 1H), 6.15-6.09 (m, 1H), 3.93 and 3.80 (brs,

1H), 3.79-3.72 (m, 1H), 3.55 and 3.37 (brs, 1H) 3.52-3.45 (m, 1H), 2.48-2.38 (m, 1H), 2.28 and 2.27 (s, 3H), 2.15 and 2.12 (s, 3H), 1.09 and 1.07 (d, J = 6.6 Hz, 3H), 1.04 and 1.02 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 211.87 (2CO), 197.18 (2COS), 168.22 (2CO), 137.41 (CH), 136.61 (C), 136.39 (C), 136.35 (CH), 132.09 (CH), 131.03 (CH), 116.58 (CH), 116.52 (CH), 57.39 (CH), 56.45 (CH), 54.63 (CH), 53.51 (CH), 48.46 (CH), 46.38 (CH), 46.26 (CH), 44.39 (CH), 41.40 (2CH), 20.66 ($2CH_3$), 19.80 (CH_3), 19.71 (CH_3), 17.28 ($2CH_3$), 11.73 (SCH_3), 11.70 (SCH_3); LRMS m/z (rel inten) 308 (M^+, 12), 261 (100); HRMS (EI) calcd for $C_{16}H_{20}O_4S$ 308.1082, found 308.1078.

Spectral data for **13b**: pale yellow oil; yield 33 %; IR (neat) 2980, 1760, 1685, 1215, 1070 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 and 7.02 (s, 1H), 6.66 and 6.28 (d, J = 6.0 Hz, 1H), 6.02 and 5.91 (dd, J = 6.0, 2.1 Hz, 1H), 5.23 and 5.14 (dd, J = 7.2, 2.1 Hz, 1H), 4.91 and 4.81 (d, J = 4.8 Hz, 1H), 3.95-3.91 and 3.74-3.69 (m, 1H), 3.63-3.60 and 3.53-3.50 (m, 1H), 2.34 and 2.31 (s, 3H), 2.30-2.20 (m, 1H), 2.17 and 2.16 (s, 3H), 1.02 and 1.00 (d, J = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 201.60 (2COS), 167.45 (CO), 167.37 (CO), 162.32 (2C), 135.36 (CH), 134.92 (CH), 133.37 (CH), 132.31 (C), 130.89 (CH), 130.80 (C), 128.80 (CH), 127.14 (CH), 94.95 (CH), 93.23 (CH), 81.32 (CH), 80.19 (CH), 48.30 (CH), 47.26 (CH), 41.51 (CH), 40.56 (CH), 32.55 (CH), 32.48 (CH), 19.73 (CH_3), 19.69 (CH_3), 19.53 (CH_3), 19.41 (CH_3), 11.96 (CH_3), 11.94 (CH_3),11.69 (CH_3), 11.44 (CH_3); LRMS m/z (rel inten) 308 (M^+, 14), 261 (100); HRMS (EI) calcd for $C_{16}H_{20}O_4S$ 308.1082, found 308.1088.

Spectral data for **12c**: pale yellow oil; yield 31%; IR (neat) 2980, 1755, 1710, 1690, 1220 cm^{-1};^{1}H NMR (300 MHz, $CDCl_3$) δ 6.61 and 6.58 (s, 1H), 6.57-6.50 (m, 1H), 6.17-6.10 (m, 1H), 3.92 and 3.79 (brs, 1H), 3.78-3.71 (m, 1H), 3.53 and 3.40 (brs, 1H) 3.35-3.25 (m, 1H), 2.28 and 2.26 (s, 3H), 2.28-2.20 (m, 2H), 2.15 and 2.12 (s, 3H), 1.60-1.20 (m, 4H), 0.88 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 207.74 (2CO), 197.25 (2COS), 168.22 (2CO), 137.04 (CH), 136.61 (C), 136.33 (C), 135.96 (CH), 132.53 (CH), 131.49 (CH), 116.62 (CH), 116.59 (CH), 57.21 (CH), 57.07 (CH), 56.21 (CH), 55.90 (CH), 48.46 (CH), 46.40 (CH), 46.17 (CH), 44.30 (CH), 43.27 ($2CH_2$), 25.85 ($2CH_2$), 22.27 ($2CH_2$), 20.68 (CH_3), 20.64 (CH_3), 13.82 ($2CH_3$), 11.79 (SCH_3), 11.76 (SCH_3); LRMS m/z (rel inten) 322 (M^+, 16), 275 (100); HRMS (EI) calcd for $C_{17}H_{22}O_4S$ 322.1239, found 322.1235.

Spectral data for **13c**: pale yellow oil; yield 31%; IR (neat) 2980, 1760, 1685, 1215, 1070 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 and 7.03 (s, 1H), 6.68 and 6.29 (d, J = 5.7 Hz, 1H), 6.05 and 5.93 (dd, J = 5.7, 2.1 Hz, 1H), 5.22 and 5.12 (dd, J = 7.2, 2.1 Hz, 1H), 4.87 and 4.76 (d, J = 3.6 Hz, 1H), 3.90-3.86 and 3.70-3.65 (m, 1H), 3.55-3.45 (m, 1H), 2.33 and 2.31 (s, 3H), 2.18 and 2.16 (s, 3H), 2.05 -1.98 (m, 2H), 1.46-1.23 (m, 4H), 0.90 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$,

DEPT) δ 201.46 (COS), 201.40 (COS), 167.53 (CO), 167.43 (CO), 157.47 (2C), 135.47 (CH), 135.01 (CH), 133.32 (CH), 132.30 (C), 130.83 (CH), 130.70 (C), 128.96 (CH), 127.25 (CH), 96.34 (CH), 94.21 (CH), 81.07 (CH), 79.92 (CH), 48.80 (CH), 47.46 (CH), 41.03 (CH), 40.10 (CH), 34.09 (CH_2), 34.05 (CH_2), 28.45 (CH_2), 28.30 (CH_2), 22.19 ($2CH_2$), 20.68 ($2CH_3$), 13.84 ($2CH_3$), 11.96 ($2SCH_3$); LRMS *m/z* (rel inten) 322 (M^+, 13), 275 (100); HRMS (EI) calcd for $C_{17}H_{22}O_4S$ 322.1239, found 322.1230.

Synthesis of Tetraoxa-Cages 14a-c from Ozonolysis of 12a-c. The same reaction conditions and procedure as for the synthesis of tetraoxa-cages **11a,b** from ozonolysis of **10a,b** were applied for the synthesis of tetraoxa-cages **14a-c** from ozonolysis of **12a-c**.

1-Methylthio-7-methyl-4-oxo-8,10,12,13-tetraoxapentacyclo[5.5.1.$0^{2,6}$.$0^{3,11}$.$0^{5,9}$]tridecane 14a: white waxy solid; mp 88-89 °C; yield 62%; IR ($CHCl_3$) 2880, 1765, 1380, 1070 cm^{-1}; ^1H NMR (300 Hz, $CDCl_3$) δ 5.94 (d, J = 6.0 Hz, 1H), 5.89 (d, J = 6.0 Hz, 1H), 3.62 (dd, J = 9.9, 6.0 Hz, 1H), 3.32 (dd, J = 9.9, 6.0 Hz, 1H), 3.28-3.16 (m, 2H), 2.26 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 203.74 (CO), 125.63 (C), 122.06 (C), 107.98 (CH), 107.42 (CH), 55.01 (CH), 54.61 (CH), 52.79 (CH), 50.02 (CH), 24.58 (CH_3), 12.94 (SCH_3); LRMS *m/z* (rel inten) 256 (M^+, 32), 209 (100); HRMS (EI) calcd for $C_{11}H_{12}O_5S$ 256.0405, Found 256.0411; Anal. calcd for $C_{11}H_{12}O_5S$: C, 51.55; H 4.72, found: C,51.47; H, 4.77.

1-Methylthio-7-isopropyl-4-oxo-8,10,12,13-tetraoxapentacyclo[5.5.1.$0^{2,6}$.$0^{3,11}$.$0^{5,9}$]-tridecane 14b: white waxy solid; mp 65-66 °C; yield 60%; IR ($CHCl_3$) 2880, 1765, 1380, 1070 cm^{-1}; ^1H NMR (300 Hz, $CDCl_3$) δ 5.94 (d, J = 6.6 Hz, 1H), 5.91 (d, J = 6.6 Hz, 1H), 3.56 (dd, J = 10.2, 6.6Hz, 1H), 3.32 (dd, J = 10.2, 6.6 Hz, 1H), 3.26 (dd, J = 7.2, 6.6 Hz, 1H), 3.08 (dd, J = 7.2, 6.6 Hz, 1H), 2.26 (s, 3H), 2.22-2.14 (m, 1H), 1.03 (d, J = 6.6 Hz, 3H), 1.01 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$, DEPT) δ 203.96 (CO), 126.64 (C), 125.75 (C), 107.95 (CH), 107.44 (CH), 55.29 (CH), 54.66 (CH), 52.30 (CH), 46.49 (CH), 34.77 (CH), 17.14 (CH_3), 17.07 (CH_3), 13.01 (SCH_3); LRMS *m/z* (rel inten) 284 (M^+, 19), 237 (100); HRMS (EI) calcd for $C_{13}H_{16}O_5S$ 284.0718, found 284.0723; Anal. calcd for $C_{13}H_{16}O_5S$: C, 54.92; H, 5.68, found:C, 54.84; H, 5.74.

1-Methylthio-7-butyl-4-oxo-8,10,12,13-Tetraoxapentacyclo[5.5.1.$0^{2,6}$.$0^{3,11}$.$0^{5,9}$]tridecane 14c: white waxy solid; mp 60-61 °C; yield 64%; IR ($CHCl_3$) 2980, 2880, 1765, 1070 cm^{-1}; ^1H NMR (300 Hz, $CDCl_3$) δ 5.94 (d, J = 6.0 Hz, 1H), 5.90 (d, J = 6.0 Hz, 1H), 3.58 (dd, J = 10.2, 6.0 Hz, 1H), 3.34-3.25 (m, 2H), 3.17 (dd, J = 7.2, 6.0 Hz, 1H), 2.26 (s, 3H), 1.93-1.86 (m, 2H), 1.70-1.62 (m, 2H), 1.40-1.32 (m, 2H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 203.89 (CO), 125.60 (C), 124.24 (C), 107.97 (CH), 107.38 (CH), 55.16 (CH), 54.61 (CH), 52.45 (CH), 48.33 (CH), 37.09 (CH_2), 26.07 (CH_2), 22.53 (CH_2),13.90 (CH_3), 12.99 (SCH_3); LRMS *m/z* (rel inten) 298 (M^+, 14), 251 (100); HRMS (EI) calcd for $C_{14}H_{18}O_5S$ 298.0875, found 298.0870;

Anal. calcd for $C_{14}H_{18}O_6S$: C, 56.36; H, 6.09, found: C,56.29; H, 6.14.

General Procedure for The Hydrolysis of 10a,b with Na_2CO_3 in Aqueous Methanol. To a solution of **10a** (1.0 g, 4.0 mmol) in methanol (10 mL) and water (10 mL) was added Na_2CO_3 (0.040 g, 0.40 mmol) at 25 °C. The reaction mixture was stirred at 25 °C for 2 h. The solvent evaporated, and saturated NH_4Cl solution (10 mL) was added. The reaction mixture was extracted with ether (5 x 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 *endo-syn* isomer **15a** (0.74 g, 90%). The amount of the *endo-anti* isomer **16a** was too small to be isolated.

2,3-Bis-*endo*-diacetyl-7-*syn*-formylbicyclo[2.2.1]-5-heptene 15a: pale yellow oil; IR (neat) 2980, 2880, 1720, 1710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.60 (s, 1H), 6.26 (brs, 2H), 3.46 (brs, 2H), 3.32 (bres, 2H), 2.53 (brs, 1H), 2.10 (s,6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 205.61 (2CO), 200.10 (CHO), 134.66 (2CH), 68.00 (CH), 54.68 (2CH), 45.74 (2CH), 30.00 ($2CH_3$); LRMS *m/z* (rel inten) 206 (M^+, 17), 128 (100); HRMS (EI) calcd for $C_{12}H_{14}O_3$ 206.0943, found 206.0948.

2-*endo*-Acetyl-3-*endo*-7-*syn*-diformylbicyclo[2.2.1]-5-heptene 15b: pale yellow oil; IR (neat) 2980, 2880, 1720, 1710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.60 (s, 1H), 9.54 (d, J = 2.1 Hz, 1H), 6.47 (dd, J = 6.0, 3.0 Hz, 1H), 6.13 (dd, J = 6.0, 3.0 Hz, 1H), 3.71 (dd, J = 9.3, 3.6 Hz, 1H) 3.58 (brs, 1H), 3.51 (brs, 1H), 2.96-2.91 (m, 1H), 2.60 (s, 1H), 2.19 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 205.83 (CO), 200.35 (CHO), 199.61 (CHO), 136.87 (CH), 133.55 (CH), 68.60 (CH), 56.78 (CH), 53.51 (CH), 46.07 (CH), 44.55 (CH), 28.88 (CH_3); LRMS *m/z* (rel inten) 192 (M^+, 12), 114 (100); HRMS (EI) calcd for $C_{11}H_{12}O_3$ 192.0786, found 192.0789.

Ozonolysis of 15a,b. Formation of Tetraoxa-Cages 17a,b. The same reaction conditions and procedure as for the ozonolysis of **10a,b** were applied for the ozonolysis of **15a,b** to give the tetraoxa-cages **17a,b**.

1,7-Dimethyl-4-*anti*-formyl-8,10,12,13-tetraoxapentacyclo[5.5.1.$0^{2,6}$.$0^{3,11}$.$0^{5,9}$]tridecane 17a: white waxy solid; mp 55-56 °C; yield 85%; IR ($CHCl_3$) 2970, 1720, 1070 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.73 (s, 1H), 5.63 (d, J = 5.7 Hz, 2H), 3.22-3.18 (m, 5H), 1.54 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 199.52 (CHO), 117.65 (2C) , 102.79 (2CH), 56.20 (2CH), 55.44 (CH), 45.85 (2CH), 24.96 ($2CH_3$); LRMS *m/z* (rel inten) 238 (M^+, 41), 223 (100); HRMS (EI) calcd for $C_{12}H_{14}O_5$ 238.0841, found 238.0835; Anal. calcd for $C_{12}H_{14}O_5$; C, 60.48; H, 5.93, found ; C, 60.40; H, 5.97.

1-Methyl-4-*anti*-formyl-8,10,12,13-tetraoxapentacyclo[5.5.1.$0^{2,6}$.$0^{3,11}$.$0^{5,9}$]tridecane 17b: highly viscous oil; yield 75%; IR ($CHCl_3$) 2980, 1720, 1070 cm^{-1}; ^1H NMR (300 Hz, $CDCl_3$) δ

9.75 (s, 1H), 5.85 (d, J = 5.4 Hz, 1H), 5.63 (d, J = 6.0 Hz, 1H), 5.62 (d, J = 6.0 Hz, 1H), 3.51-3.46 (m, 1H), 3.28-3.04 (m, 4H), 1.55 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$, DEPT) δ 199.43 (CHO), 118.02 (C), 109.60 (CH), 103.06 (CH), 102.63 (CH), 55.47 (CH), 55.08 (CH), 52.76 (CH), 45.82 (CH), 45.38 (CH), 24.59 (CH_3); LRMS m/z (rel inten) 224 (M^+, 27), 209 (100); HRMS (EI) calcd for $C_{11}H_{12}O_5$ 224.0685, found 224.0689; Anal. calcd for $C_{11}H_{12}O_5$: C, 58.91; H, 5.40, found: C, 58.80; H, 5.47.

General Procedure for The Hydrolysis of 12a,b with Na_2CO_3 in Aqueous Methanol. The same reaction conditions and procedure as for the hydrolysis of **10a,b** were applied for the hydrolysis of **12a,b** to give the *endo-syn* isomers **18a,b** as the major products and the *endo-anti* isomers **19a,b** as the minor products.

Spectral data for **18a**: pale yellow oil; yield 75%; IR (neat) 2980, 2880, 1720, 1710 , 1690 cm^{-1};^{1}H NMR (300 MHz, $CDCl_3$) δ 9.60 (s, 1H), 6.54 (dd, J = 6.0, 3.0 Hz, 1H), 6.06 (dd, J = 6.0, 3.0 Hz, 1H), 3.75 (dd, J = 9.0, 3.6 Hz, 1H), 3.51 (brs, 1H), 3.41 (brs, 1H), 3.14 (dd, J = 9.0, 3.6 Hz, 1H), 2.52 (brs, 1H), 2.28 (s, 3H) 2.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 205.34 (CO), 199.94 (CHO) , 197.59 (COS), 137.30 (CH), 132.64 (CH), 68.14 (CH), 55.56 (CH), 54.60 (CH), 47.61 (CH), 45.22 (CH), 30.78 (CH_3), 11.81 (SCH_3); LRMS m/z (rel inten) 238 (M^+, 24), 191 (100); HRMS (EI) calcd for $C_{12}H_{14}O_3S$ 238.0664, found 238.0667.

Spectral data for **19a**: pale yellow oil; yield 10%; IR (neat) 2980, 2880, 1720, 1710, 1690 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.59 (d, J = 2.1 Hz, 1H), 6.50 (dd, J = 6.0, 3.0 Hz, 1H), 6.05 (dd, J = 6.0, 3.0 Hz, 1H), 3.83 (dd, J = 9.0, 3.6 Hz, 1H), 3.60 (brs, 1H), 3.49 (brs, 1H), 3.31 (dd, J = 9.0, 3.6 Hz, 1H), 2.38 (brs, 1H), 2.28 (s, 3H) 2.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 204.96 (CO), 203.01 (CHO) , 197.06 (COS), 135.48 (CH), 130.80 (CH), 69.10 (CH), 57.60 (CH), 56.57 (CH), 49.85 (CH), 47.41 (CH), 30.66 (CH_3), 11.81 (SCH_3); LRMS m/z (rel inten) 238 (M^+, 32), 191 (100); HRMS (EI) calcd for $C_{12}H_{14}O_3S$ 238.0664, found 238.0670.

Spectral data for **18b**: pale yellow oil; yield 70%; IR (neat) 2980, 2880, 1720, 1710 , 1690, 1380 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.62 (s, 1H), 6.54 (dd, J = 5.7, 3.0 Hz, 1H), 6.06 (dd, J = 5.7, 3.0 Hz, 1H), 3.72 (dd, J = 9.6, 3.6 Hz, 1H), 3.51 (brs, 1H), 3.36-3.32 (m, 2H), 2.53 (brs, 1H), 2.43-2.36 (m, 1H), 2.26 (s, 3H), 1.06 (d, J = 6.0 Hz, 3H), 1.03 (d, J = 6.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 211.95 (CO), 200.04 (CHO) , 197.53 (COS), 137.53 (CH), 132.34 (CH), 68.28 (CH), 54.93 (CH), 52.13 (CH), 47.38 (CH), 45.44 (CH), 41.48 (CH), 19.86 (CH_3), 17.32 (CH_3), 11.75 (SCH_3); LRMS m/z (rel inten) 266 (M^+, 27), 219 (100); HRMS (EI) calcd for $C_{14}H_{18}O_3S$ 266.0977, found 266.0974.

Spectral data for **19b**: pale yellow oil; yield 10%; IR (neat) 2980, 2880, 1720, 1710, 1690 cm^{-1}; ^{1}H

NMR (300 MHz, $CDCl_3$) δ 9.60 (d, J = 2.1 Hz, 1H), 6.50 (dd, J = 6.0, 3.0 Hz, 1H), 6.06 (dd, J = 6.0, 3.0 Hz, 1H), 3.80 (dd, J=10.2, 3.6 Hz, 1H), 3.61 (brs, 1H), 3.54 (dd, J = 10.2, 3.6 Hz, 1H), 3.44 (brs, 1H), 2.46-2.38 (m, 2H), 2.27 (s, 3H) 1.09 (d, J = 6.6 Hz, 3H), 1.06 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 211.49 (CO), 203.12 (CHO) , 196.99 (COS), 135.66 (CH), 130.46 (CH), 69.18 (CH), 56.91 (CH), 54.11 (CH), 49.61 (CH), 47.65 (CH), 41.39 (CH), 19.75 (CH_3), 17.27 (CH_3), 11.72 (SCH_3); LRMS m/z (rel inten) 266 (M^+, 21), 219 (100); HRMS (EI) calcd for $C_{14}H_{18}O_3S$ 266.0977, found 266.0985.

General Procedure for the Ozonolysis of 18a,b. Formation of Tetraoxa-Cages 20a,b. The same reaction conditions and procedure as for the ozonolysis of **10a,b** were applied for the ozonolysis of **18a,b** to give the tetraoxa-cages **20a,b**..

1-Methylthio-7-Methyl-4-*anti*-formyl-8,10,12,13-tetraoxapentacyclo[5.5.1.$0^{2,6}$.$0^{3,11}$.$0^{5,9}$]-tridecane 20a: highly viscous oil; yield 85%; IR ($CHCl_3$) 2970, 1720, 1070 cm^{-1}; ^1H NMR (300 Hz, $CDCl_3$) δ 9.74 (s, 1H), 5.71 (d, J = 6.0 Hz, 1H), 5.65 (d, J = 6.0 Hz, 1H), 3.58 (dd, J = 10.8, 5.4 Hz, 1H), 3.34-3.18 (m, 4H), 2.20 (s, 3H), 1.57 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$, DEPT) δ 199.22 (CHO), 122.74 (C), 118.71 (C), 103.68 (CH), 102.95 (CH), 58.49 (CH), 55.63 (CH), 55.06 (CH), 45.82 (CH), 45.47 (CH), 24.53 (CH_3), 12.87 (SCH_3); LRMS m/z (rel inten) 270 (M^+, 48), 223 (100); HRMS (EI) calcd for $C_{12}H_{14}O_5S$ 270.0562, found 270.0567; Anal. calcd for $C_{12}H_{14}O_5S$: C, 53.32; H, 5.22, found: C,53.24; H, 5.28.

1-Methylthio-7-isopropyl-4-*anti*-formyl-8,10,12,13-tetraoxapentacyclo-[5.5.1.$0^{2,6}$.$0^{3,11}$.$0^{5,9}$]tridecane 20b: highly viscous oil; yield 80%; IR ($CHCl_3$) 2980, 1720, 1380, 1070 cm^{-1}; ^1H NMR (300 Hz, $CDCl_3$) δ 9.75 (s, 1H), 5.70 (d, J = 5.7 Hz, 1H), 5.66 (d, J = 5.7 Hz, 1H), 3.50 (dd, J = 10.5, 5.4 Hz, 1H), 3.30-3.20 (m, 3H), 3.13-3.08 (m, 1H), 2.21 (s, 3H), 2.08-2.01 (m, 1H), 0.99 (d, J = 6.0 Hz, 3H), 0.96 (d, J = 6.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 199.33 (CHO), 123.24 (C), 122.82 (C), 103.62 (CH), 102.87 (CH), 57.99 (CH), 55.13 (CH), 51.89 (CH), 46.01 (CH), 45.55 (CH), 34.52 (CH), 17.10 (CH_3), 17.00 (CH_3), 12.94 (SCH_3); LRMS m/z (rel inten) 298 (M^+, 24), 251 (100); HRMS (EI) calcd for $C_{14}H_{18}O_5S$ 298.0875, found 298.0869; Anal. calcd for $C_{14}H_{18}O_5S$: C, 56.36; H, 6.09, found: C, 56.24; H, 6.16.

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