Synthesis of Novel Acetal Thia-Cage Compounds

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The synthesis of novel acetal thia-cage compounds has been accomplished by the direct substitution for the oxygen atom by the sulfur atom in the reaction of the acetal groups of oxa-cages with Lawesson reagent (LR). Reaction of the tetraoxa-cage compound **2** with LR in dichloromethane at 25 °C sequentially gave the monothia-, dithia-, trithia-, and tetrathia-cage compounds **3**, **6**, **7**, and **9**. The reaction mechanism for the conversion from oxa-cages into thia-cages was proposed. The diacetal trioxa-cages **18**−**20** and **24**−**26** were also transformed into the thia-cages **21**−**23** and **27**−**29**, respectively. Reaction of the trioxa-cages **34** and **35** with LR under the same reaction conditions gave the thia-cages **36** and **37** with the carbonyl group intact. Treatment of the pentaoxa[5]-peristylane **40** with LR in chloroform under supersonic shaking at refluxing temperature gave the monothia[5]peristylane **41** and the dithia[5]peristylane **42**. Attempts to synthesize the thia[5]-peristylanes from the tetraoxa-cage **51** and the transformation from the parent (unsubstituted) pentaoxa[5]peristylane **46** to the thia-cages have been made. Reaction of the pentaoxa[5]-peristylane **40** with P_2S_5 in refluxing toluene gave **41**, **42**, and a rearrangement product **47**. The synthesis of new heterocyclic cage compounds **59** and **60**, which contain oxygen, nitrogen, and sulfur atoms in the same molecule, was also 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. The cage compounds have played a key role in theoretical organic chemistry by providing rigid and often symmetric frameworks for evaluating theories put forth on the physicochemical properties of organic molecules. In addition, some precursors of these cage compounds are important building blocks for the synthesis of polycyclic synthetic and natural products. Heterocyclic cage compounds have also received attention in recent years from synthetic as well as mechanistic consideration. The main purpose for the studies was the desire to compare the reactivity pattern of carbon cage compounds with their heterologues. We envision that studies on the synthesis and chemistry of heterocyclic cage compounds can greatly expand the scope and utilities of cage compounds.

There are some reports regarding the chemistry[2] and synthesis[3−8] of oxa-cage compounds in the literature. Prinzbach et al. recently reported skeletal expansions of (homo)dodecahedranes to give novel heteropolycyclic cage compounds by ozonolysis reaction.[8] Recently, we utilized ozonolysis reaction for the synthesis of a series of oxa-cage compounds, such as diacetal trioxa-cages,[9] triacetal trioxa-cages,[10] tetraacetal tetraoxa-cages,[11] tetraacetal pentaoxa-cages,[12] and pentaacetal pentaoxa-cages (the pentaoxa[5]peristylanes).[13] Later on, we investigated the chemical nature of acetal group of tetraoxa-cages and discovered a $TiCl_4$-mediated hydride rearrangement reaction[14] and a one-pot conversion from oxa-cages to aza-cages mediated by iodotrimethylsilane in nitriles.[15] We also developed a method for the synthesis of dioxa-cages[16] and trioxa-cages[17] via the iodine-induced cyclization reaction of norbornene derivatives.

2,4-Bis(4-methoxyphenyl)-1,3-dithiaphosphetane-2,4-

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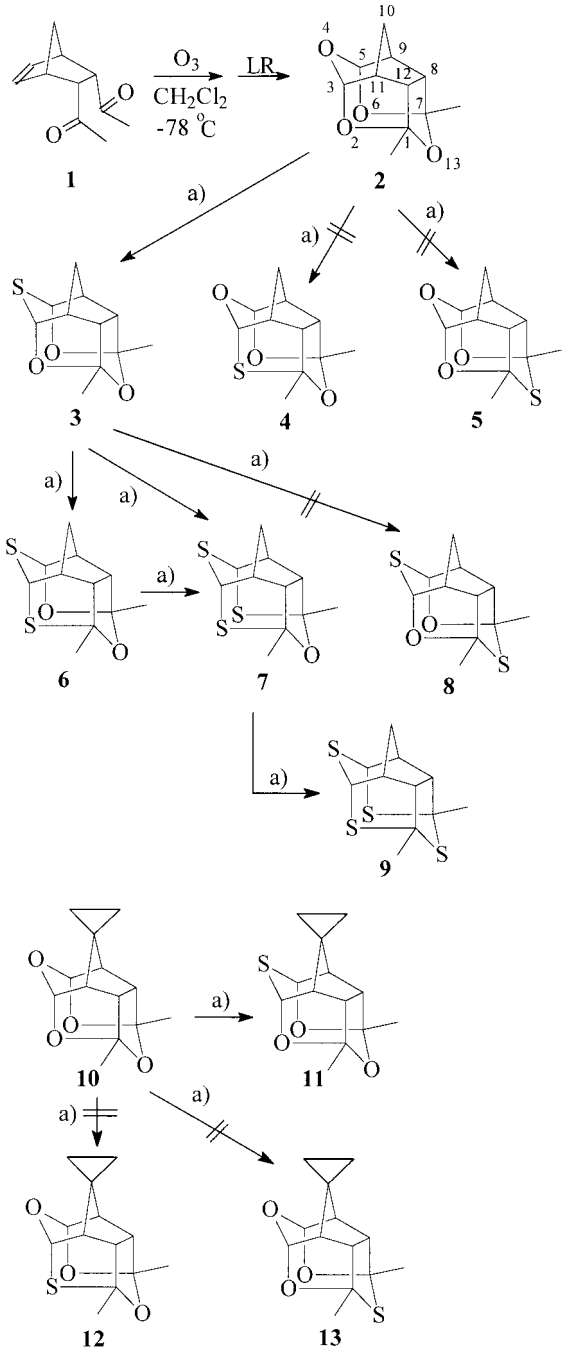
disulfide, commonly known as Lawesson's reagent (LR), has been used as a powerful, mild, and versatile reagent for the conversion of a wide variety of carbonyls into thiocarbonyl compounds.[18,19] In the reaction of LR with acetal group, synthetically equivalent to carbonyl group, products with incorporation of a dithiophosphine ylide moiety were obtained in leading to the dithiaphosphorates.[20] As part of a program that involves the synthesis, chemistry, and applications of new heterocyclic cage compounds, we report here the first direct substitution for the oxygen atom by the sulfur atom in the reaction of acetal groups of oxa-cages with LR to give the novel thia-cage compounds. There are only few examples for the synthesis of thia-cage compounds in the literature.[21]

Results and Discussion

Ozonolysis of compound **1**[11a] in dichloromethane at −78 °C followed by treatment with 1.2 equiv of LR gave the tetraoxa-cage compound **2** in 94% yield. In this reaction LR acts as a reducing agent, the same as dimethyl sulfide. Treatment of the tetraoxa-cage **2** with 1 equiv of LR in dichloromethane at room temperature gave the monothia-cage compound **3** in 89% yield (Scheme 1). No detectable amount of the other monothia-cage compounds **4** or **5** was obtained. The substitution for the oxygen atom by the sulfur atom took place regioselectively on the oxygen atom O-4 of **2**. We attribute the highly regioselective substitution to the angle strain of the unusually large bond angle of C(3)−O(4)-C(5) (117.5°). Recently, we reported a remarkable effect of C−O−C bond angle strain on the regioselective double nucleophilic substitution of the acetal group of tetraoxa-cages.[14a] Reaction of the monothia-cage **3** with 1 equiv of LR under the same reaction conditions gave the dithia-cage compound **6** in 78% yield and the trithia-cage compound **7** in 11% yield. No detectable amount of the other dithia-cage **8** was obtained. The trithia-cage **7** was also obtained in 85% yield by reaction of the dithia-cage **6** with 1 equiv of LR under the same reaction conditions. Treatment of the trithia-cage **7** with excess of LR at room temperature for a longer reaction time gave the tetrathia-cage compound **9** in 82% yield. Thus, we have discovered for the first time the direct substitution for the oxygen atom by the sulfur atom in the reaction of the acetal groups with LR to give novel thia-cage compounds. In this case, the oxygen atoms O-4, O-2, O-6, and O-13 of the tetraoxa-cage **2** were sequentially replaced by sulfur atoms starting from the oxygen atom O-4. Reaction of the tetraoxa-cage compound **10**[11i] with 1 equiv of LR in dichloromethane at room temperature gave the monothia-cage **11** in 85% yield. Also, no detectable amount of the other monothia-cage compounds **12** and **13** was obtained. The cyclopropane ring on the apex carbon did not interfere with the regioselective substitution for the oxygen atom O-4 of **10** by the sulfur atom. Diphosphorus pentasulfide P_2S_5 also affected the transformation from the tetraoxa-cage **2** to the thia-cage compounds **3**, **6**, **7**, and **9**, but the

Scheme 1



a) LR, CH_2Cl_2, 25 °C

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substitution reaction took place more slowly. Higher temperature and longer reaction time were required for the transformation when P_2S_5 was used.

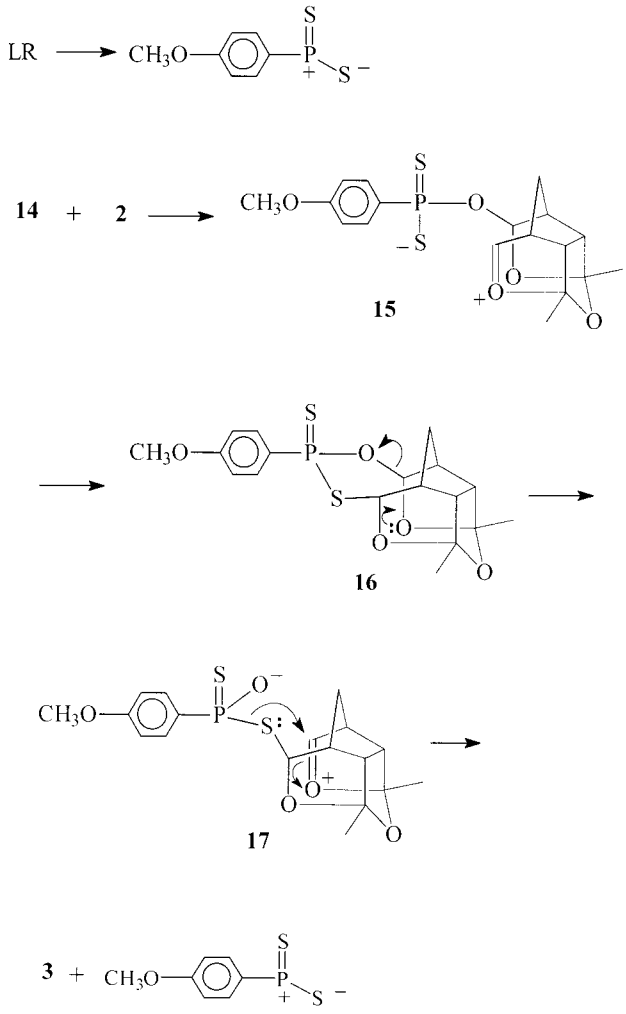
The ^{1}H NMR spectrum of the monothia-cage **3** revealed one doublet at δ 5.67 for the two acetal protons on C-3 and C-5, one broad singlet at δ 3.22 for the four protons on C-8, C-9, C-11, and C-12, one multiplet at δ 2.02−1.74 for the protons on C-10, and one singlet at δ 1.49 for the angular methyl protons. In our previous report, the ^{1}H NMR spectrum of the tetraoxa-cage **2** displayed one doublet at δ 5.43 for the two acetal protons on C-3 and C-5.[11a] The monothia-acetal protons of **3** showed more downfield absorptions than the acetal protons of **2** in their ^{1}H NMR spectra. In most cases, monothia-acetal protons usually displayed more upfield absorptions than their corresponding acetal protons. On the other hand, the ^{13}C NMR spectrum of **3** exhibited one peak at δ 87.3 for the monothia-acetal carbons C-3 and C-5, which was normally more upfield than the absorptions for the acetal carbons of the tetraoxa-cage **2** (at δ 102.8). The ^{1}H NMR spectra of the trithia-cage **7** and tetrathia-cage **9** revealed doublets at δ 5.08 and 5.23 for the two dithia-acetal protons, respectively. These values are also exceptionally downfield from ordinary dithia-acetal protons. The X-ray ORTEP structure of **3**, reported as Supporting Information, showed the bond angle of C(3)−S(4)−C(5) to be 102°. In the case of the tetraoxa-cage **2**, the bond angle of C(3)−O(4)−C(5) was found to be 117.5°.

A mechanism is proposed for the conversion of the tetraoxa-cage compound **2** into the thia-cage compounds. The reactive species of LR for the conversion of various carbonyls into thiocarbonyls was proposed to be the ylide **14**,[18,19] but not firmly established. In our cases, we also support that the reactive species of LR is the ylide **14**. Electrophilic attack of the phosphorus atom of the ylide **14** on the oxygen atom O-4 of **2** followed by cleavage of the C(3)−O(4) bond gave the zwitterion **15** (Scheme 2). Nucleophilic addition of the negatively charged sulfur anion into the positively charged carbon of the oxonium ion gave the intermediate **16**. Cleavage of the C(5)−O bond leading to the zwitterion **17**, followed by nucleophilic addition of the sulfur atom and cleavage of the P−S bond, gave the monothia-cage **3**. The same mechanism can be used to account for the formation of the dithia-, trithia-, and tetrathia-cage compounds from their corresponding precursors.

The synthesis of thia-cage compounds was also performed with trioxa-cages. Reactions of the trioxa-cage compounds **18a**−**c**, **19**, and **20** with excess of LR in dichloromethane at 25 °C gave the monothia-cage compounds **21a**−**c**, **22** and **23** in 80−85% yields, respectively (Scheme 3). Treatment of the trioxa-cages **24**−**26** with excess of LR under the same reaction conditions gave the thia-cages **27**−**29** in 80−82% yields. In this case, only the central oxygen atom of the trioxa-cages was replaced by the sulfur atom. The cyclopropane ring on the apex carbon of the oxa-cages **24**−**26** did not interfere the transformation from oxa-cages into thia-cages. Diphosphorus pentasulfide was also affective for the transformation from the trioxa-cages **18a**−**c**, **19**, and **20** to the thia-cages **21a**−**c**, **22**, and **23**.

To test the chemoselectivity for the substitution reaction of LR with an acetal group and a carbonyl group, the following experiments were performed. Ozonolysis of the diols **30** and **31** with controlled amount of ozone in dichloromethane at −78 °C followed by reduction with

Scheme 2



dimethyl sulfide in the presence of Amberlyst-15 gave the trioxa-cage compounds **32** and **33** in 80−82% yields. Ozonolysis of **32** and **33** in dichloromethane at −78 °C followed by reduction with dimethyl sulfide gave compounds **34** and **35** in 78−80% yields (Scheme 4). If the ozonolysis reaction of the diols **30** and **31** were carried out with excess of ozone, the trioxa-cage compounds **34** and **35** were obtained in 25−30% yields. The overall yields for the synthesis of **34** and **35** from **30** and **31** by a two step ozonolysis sequence are better than a one step conversion. Treatment of the trioxa-cage compounds **34** and **35** with 1 equiv of LR in dichloromethane at 25 °C gave the monothia-cages **36** and **37** in 80−82% yields. No detectable amount of the thione compounds **38** and **39** was obtained. Therefore, the reaction rates for the transformation from the oxa-cages to the thia-cages are faster than that for the conversion from the carbonyls to the thiocarbonyls. π-Facial stereoselectivity for the nucleophilic additions to the carbonyl group of compounds **34** and **35** was also performed.[22]

Recently, we accomplished the synthesis of pentaoxa[5]peristylanes.[13] Consequently, the synthesis of thia[5]peristylanes is an important task to us. Reaction of the pentaoxa[5]peristylane **40** with 3 equiv of LR in chloroform under supersonic shaking at refluxing temperature gave the monothia[5]peristylane **41** in 46% yield and the

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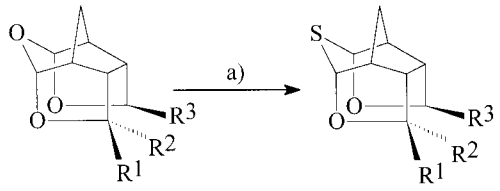
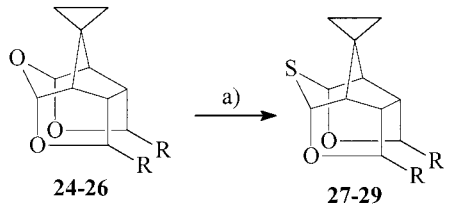
Scheme 3



18a-c, 19, 20 21a-c, 22, 23

	18a 21a	18b 21b	18c 21c	19 22	20 23
R^1	H	CH_3	*n*-C_4H_9	H	H
R^2	H	H	H	$-CH_2$	
R^3	H	H	H	$-CH_2$	

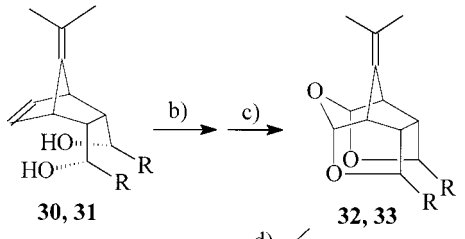


24-26 27-29

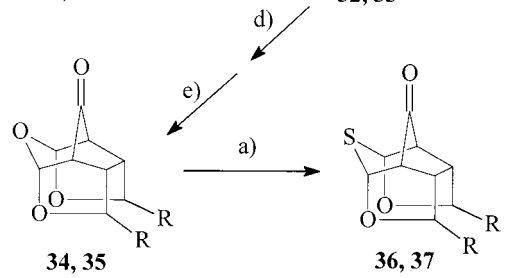
	24, 27	25, 28	26, 29
R	H	$-CH_2$	
R	H	$-CH_2$	

a) LR, CH_2Cl_2, 25 °C

Scheme 4

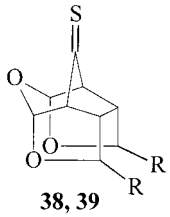


30, 31 32, 33



34, 35 36, 37

	30, 32, 34, 36, 38	31, 33, 35, 37, 39
R	H	$-CH_2$
R	H	$-CH_2$



38, 39

a) LR, CH_2Cl_2, 25 °C
b) O_3 (controlled amount), CH_2Cl_2, -78 °C
c) Me_2S, Amberlyst-15
d) O_3, CH_2Cl_2, -78 °C
e) Me_2S

dithia[5]peristylane **42** in 26% yield (Scheme 5). When a large excess of LR was used and long reaction time was employed, no detectable amount of the trithia[5]peristylane **43**, the tetrathia[5]peristylane **44**, and the pentathia[5]-peristylane **45** was obtained. If the reaction was performed in dichloromethane at 25 °C without supersonic shaking, the starting compound **40** remained unchanged and no formation of **41** or **42** was observed. Treatment of the pentaoxa[5]peristylane **46** with excess of LR in chloroform or *o*-dichlorobenzene under supersonic shaking at refluxing temperature remained unchanged starting compound **46**. No detectable amount of the monothia-, dithia-, trithia-, tetrathia- or pentathia[5]peristylanes was observed. Recently, Mehta et al. reported[23] that the "oxa-bowl" **46** possesses a fascinating columnar architecture built around numerous C−H···O interactions in the crystal, in which all the ten CH units and five oxygen atoms are involved. Whether the strong force of these numerous columnar C−H···O interaction prevents the conversion from **46** to its thia[5]peristylanes or not needs to be further studied. Treatment of **40** with large excess of P_2S_5 in toluene at refluxing temperature gave the monothia[5]peristylane **41** in 35%, the dithia[5]peristylane **42** in 20% yield, and a rearrangement product **47** in 12% yield. The structure of **47** was proven by X-ray analysis and reported as Supporting Information. The reaction mechanism for the formation of **47** may proceed via the trithia[5]peristylane **43** and the intermediates **48** and **49**.

We also attempted to synthesize the trithia[5]peristylane **43**, the tetrathia[5]peristylane **44**, and the pentathia[5]-peristylane **45** by another route. Ozonolysis of compound **50**[11d] with a controlled amount of ozone in dichloromethane at −78 °C followed by reduction with dimethyl sulfide gave the tetraoxa-cage compound **51** in 55% yield (Scheme 6). Hydrolysis of **51** with potassium carbonate in methanol gave compound **52** in 95% yield. Treatment of **52** with Amberlyst-15 in dichloromethane at 25 °C gave the pentaoxa[5]peristylane **40** in 62% yield. Reaction of **51** with 1 equiv of LR in dichloromethane at room temperature gave the monothia-cage **53** in 75% yield. Hydrolysis of **53** with potassium carbonate in methanol gave compound **54** in 90% yield. Treatment of **54** with Amberlyst-15 in dichloromethane at 25 °C remained unchanged. No detectable amount of the monothia[5]-peristylane **41** was obtained. Since the transformation from **54** to **41** failed, no attempt for the transformation from **51** to the thia[5]peristylanes **43**−**45** via the intermediates **55**−**57** was made.

Finally, we turned our attention for the synthesis of new heterocyclic cage compounds which contain oxygen, nitrogen, and sulfur atoms in the same molecule. Treatment of the aza-cages **58a,b**[24] with 2 equiv of LR in chloroform under supersonic shaking at refluxing temperature gave the thia-aza-oxa-cage compounds **59a,b**

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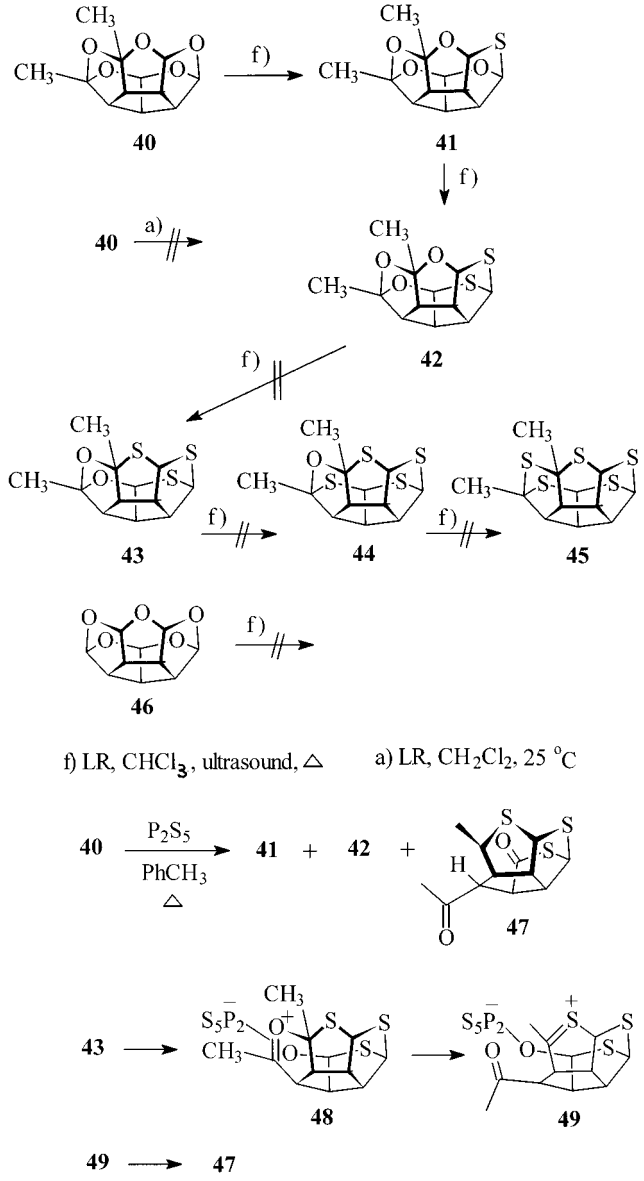
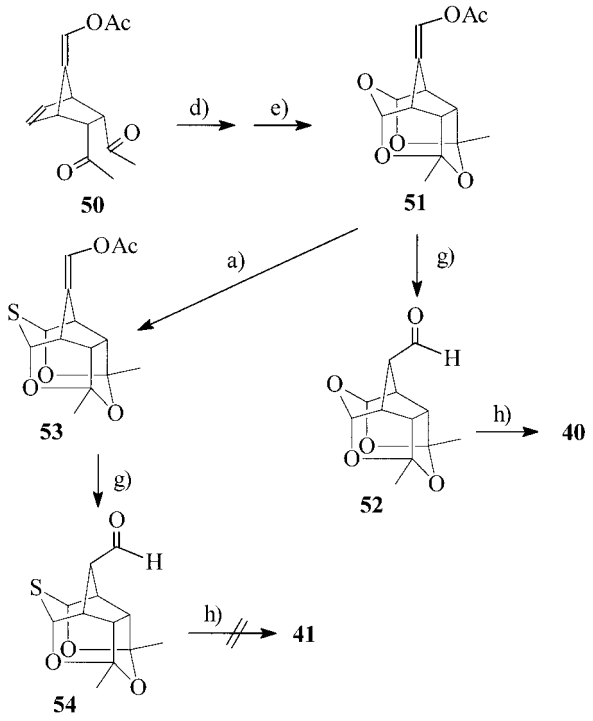
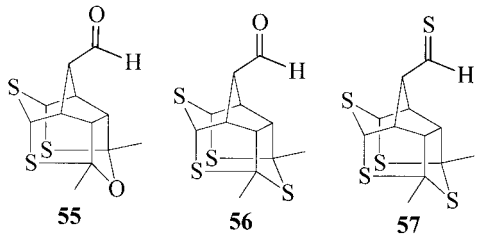
(24) Wu, C. Y.; Lin, H. C.; Wang, Z. Y,; Wu, T. L.; Liu, Y. C.; Wu, H. J. submitted for publication.

Scheme 5

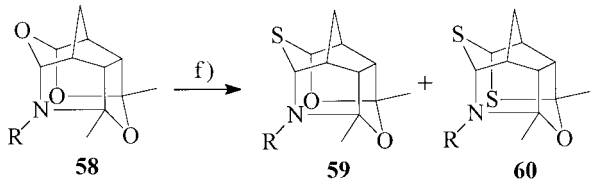


Scheme 6





Scheme 7



(48%) and **60a,b** (21%). (Scheme 7). Reaction of the aza-cage compound **58b** with 2 equiv of LR in dichloromethane at 25 °C gave the thia-aza-oxa-cage **59b** in 55% yield.

Conclusion

We have accomplished the synthesis of novel thia-cage compounds by reaction of acetal oxa-cages with LR. These transformations involve the direct substitution for the oxygen atom by the sulfur atom by reaction of the acetal groups of the oxa-cages with LR. The reaction mechanism for the transformations from the oxa-cages into the thia-cages was proposed via the ylide **14** as the reactive species of LR. The order for the sequential replacement of the oxygen atoms of the tetraoxa-cage **2** by the sulfur atom may attribute to the ring strain and steric effects. In the cases of the trioxa-cage compounds **21**−**23** and **27**−**29**, only the central acetal oxygen atom was replaced by the sulfur atom since the other two oxygen atoms are like ethers in chemical nature. In the reaction of **34** and **35** with LR, the substitution of the acetal group by the sulfur atom is faster than the conversion of the carbonyl group to the thiocarbonyl group. Diphosphorus pentasulfide P_2S_5 also affected the conversion from the oxa-cages to the thia-cages. The synthesis of the monothia[5]peristylane **41** and the dithia[5]peristylane **42** was achieved, but attempts for the other thia[5]peristylanes failed. In the reaction of **40** with P_2S_5 at higher temperature, an unexpected rearrangement product **47** was obtained in addition to **41** and **42**. New heterocyclic cage compounds **59a,b** and **60a,b** with oxygen, nitrogen, and sulfur atoms in the same molecule were also synthesized.

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 as 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 this department. X-ray analyses were carried out on a diffractometer at the Department of Chemistry, National Tsing Hua 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.

Synthesis of Monothia-Cage Compound 3. To a solution of the tetraoxa-cage compound **2** (0.51 g, 2.4 mmol) in dichloromethane (100 mL) was added Lawesson's reagent (0.98 g, 2.4 mmol) at room temperature. The reaction mixture was stirred at room temperature for 3 h. After filtration, the solvent was evaporated and the crude product was purified by column chromatography to give the monothia-cage compound **3** (0.47 g, 87%).

1,7-Dimethyl-2,6,13-trioxa-4-thiapentacyclo[5.5.-1.0^{3,11}.0^{5,9}.0^{8,12}]tridecane 3. White solid; mp 103−104 °C; IR ($CHCl_3$) 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.68 (d, J = 7.8 Hz, 2H), 3.22 (brs, 4H), 2.02−1.98 (m, 1H), 1.86−1.73 (m, 1H), 1.49 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 117.16 (2C), 87.32 (2CH), 59.20 (2CH), 47.74 (2CH), 33.05 (CH_2), 26.24 ($2CH_3$); LRMS *m*/*z* (rel int) 226 (M^+, 100), HRMS (EI) calcd for $C_{11}H_{14}O_3S$ 226.0663, found 226.0669. Anal. Calcd for $C_{11}H_{14}O_3S$: C, 58.39; H, 6.24; S, 14.14. Found: C, 58.52; H, 6.32; S, 14.09.

Reaction of the Monothia-Cage 3 with LR. Synthesis of the Dithia-Cage 6. To a solution of the monothia-cage compound **3** (0.45 g, 2.0 mmol) in dichloromethane (80 mL) was added LR (0.90 g, 2.2 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. After filtration, the solvent was evaporated and the crude product was purified by column chromatography to give the dithia-cage **6** (0.38 g, 78%) and the trithia-cage **7** (0.057 g, 11%). No detectable amount of the other dithia-cage **8** was obtained.

1,7-Dimethyl-6,13-dioxa-2,4-dithiapentacyclo[5.5.-1.0^{3,11}.0^{5,9}.0^{8,12}]tridecane 6. White solid; mp 114−115 °C; IR ($CHCl_3$) 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.74 (d, J = 7.8 Hz, 1H), 4.95 (d, J = 8.4 Hz, 1H), 3.45−3.40 (m, 2H), 3.28−3.20 (m, 2H), 2.15−2.09 (m, 1H), 1.88−1.81 (m, 1H), 1.72 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 117.26 (C), 105.09 (C), 88.31 (CH), 66.40 (CH), 59.55 (CH), 58.15 (CH), 53.93 (CH), 47.07 (CH), 33.90 (CH_2), 30.28 (CH_3), 26.53 (CH_3); LRMS *m*/*z* (rel int) 242 (M^+, 100), HRMS (EI) calcd for $C_{11}H_{14}O_2S_2$ 242.0435, found 242.0441. Anal. Calcd for $C_{11}H_{14}O_2S_2$: C, 54.54; H, 5.83; S, 26.42. Found: C, 54.65; H, 5.91; S, 26.33.

1,7-Dimethyl-2,4,6-trithia-13-oxapentacyclo[5.5.-1.0^{3,11}.0^{5,9}.0^{8,12}]tridecane 7. White solid; mp 129−130 °C; IR ($CHCl_3$) 1050, 655 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.08 (d, J = 8.4 Hz, 2H), 3.43 (brs, 4H), 2.24−2.20 (m, 1H), 1.95−1.84 (m, 1H), 1.76 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 104.95 (2C), 67.70 (2CH), 59.09 (2CH), 52.60 (2CH), 35.13 (CH_2), 31.40 ($2CH_3$); LRMS *m*/*z* (rel int) 258 (M^+, 100); HRMS (EI) calcd for $C_{11}H_{14}OS_3$ 258.0206, found 258.0213. Anal. Calcd for $C_{11}H_{14}OS_3$: C, 51.16; H, 5.47; S, 37.17. Found: C, 51.30; H, 5.56; S, 37.06.

Synthesis of the Trithia-Cage 7 from the Dithia-Cage 6. The same reaction conditions and procedure as that of the formation of the dithia-cage **6** from the monothia-cage **3** were applied for the conversion of the dithia-cage **6** into the trithia-cage **7**.

Reaction of the Trithia-Cage 7 with LR. Synthesis of the Tetrathia-Cage 9. To a solution of the trithia-cage compound **7** (0.52 g, 2.0 mmol) in dichloromethane (100 mL) was added LR (2.0 g, 4.8 mmol) at room temperature. The reaction mixture was stirred at room temperature for 48 h. After filtration, the solvent was evaporated and the crude product was purified by column chromatography to give the tetrathia-cage **9** (0.45 g, 82%).

1,7-Dimethyl-2,4,6,13-tetrathiapentacyclo[5.5.-1.0^{3,11}.0^{5,9}.0^{8,12}]tridecane 9. White solid; mp 137−138 °C; IR ($CHCl_3$) 655 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.23 (d, J = 9.6 Hz, 2H), 3.66−3.63 (m, 2H), 3.34−3.28 (m, 2H), 2.37−2.35 (m, 1H), 2.00−1.94 (m, 1H), 1.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 75.92 (2C), 75.49 (2CH), 60.51 (2CH), 50.41 (2CH), 36.04 (CH_2), 34.62 ($2CH_3$); LRMS *m*/*z* (rel int) 274 (M^+, 100), HRMS (EI) calcd for $C_{11}H_{14}S_4$ 273.9978, found 273.9985. Anal. Calcd for $C_{11}H_{14}S_4$: C, 48.18; H, 5.15; S, 46.67. Found: C, 48.26; H, 5.19; S, 46.55.

Reaction of the Tetraoxa-Cage 10 with LR. Synthesis of the Monothia-Cage 11. The same reaction conditions and procedure as that of the reaction of the tetraoxa-cage **2** with LR were applied for the conversion of **10** into **11**.

Spectral Data for 11. White solid; mp 130−132 °C; IR ($CHCl_3$) 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.69 (d, J = 10.2 Hz, 2H), 3.39 (dd, J = 5.4, 3.0 Hz, 2H), 2.65−2.60 (m, 2H), 1.52 (s, 6H), 0.81 (dd, J = 8.7, 6.6 Hz, 2H), 0.49 (dd, J = 8.7, 6.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 117.47 (2C), 86.79 (2CH), 58.85 (2CH), 55.84 (2CH), 27.66 (C), 26.23 ($2CH_3$) 11.70 (CH_2), 6.65 (CH_2); LRMS *m*/*z* (rel int) 252 (M^+, 78), 149 (100); HRMS (EI) calcd for $C_{13}H_{16}O_3S$ 252.0820, found 252.0826. Anal. Calcd for $C_{13}H_{16}O_3S$: C, 61.88; H, 6.40; S, 12.68. Found: C, 61.95; H, 6.48; S, 12.62.

General Procedure for the Synthesis of Thia-Cages 21a−c. The same reaction conditions and procedure as that of the reaction of **2** with LR were applied for the conversion of **18a−c** into **21a−c**.

2,7-Dioxa-12-thiatetracyclo[6.3.1.0^{4,11}.0^{5,9}]dodecane 21a. White solid; mp 118−120 °C; IR ($CHCl_3$) 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.62 (d, J = 8.1 Hz, 2H), 4.01−3.93 (m, 4H), 3.02−2.97 (m, 2H), 2.75−2.73 (m, 2H), 1.88−1.84 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 88.52 (2CH), 68.71 ($2CH_2$), 47.17 (2CH), 43.39 (2CH), 29.52 (CH_2); LRMS *m*/*z* (rel int) 184 (M^+, 42), 69 (100); HRMS (EI) calcd for $C_9H_{12}O_2S$ 184.0558, found 184.0562. Anal. Calcd for $C_9H_{12}O_2S$: C, 58.68; H, 6.57; S, 17.37. Found: C, 58.72; H, 6.65; S, 17.30.

General Procedure for the Synthesis of Thia-Cages 22 and 23. The same reaction conditions and procedure as that of the reaction of **2** with LR were applied for the conversion of **19** and **20** into **22** and **23**.

2,7-Dioxa-13-thiapentacyclo[6.4.1.1^{9,12}.0^{3,11}.0^{6,10}]tetradecane 22. White solid; mp 143−144 °C; IR ($CHCl_3$) 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.57 (d, J = 8.1 Hz, 2H), 4.43−4.35 (m, 2H), 3.08−2.95 (m, 2H), 2.60−2.50 (m, 2H), 2.06−1.92 (m, 2H), 1.82−1.56 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 88.73 (2CH), 75.81 (2CH), 48.35 (2CH), 41.98 (2CH), 29.54 (CH_2), 22.73 ($2CH_2$); LRMS *m*/*z* (rel int) 210 (M^+, 85), 131 (100); HRMS (EI) calcd for $C_{11}H_{14}O_2S$ 210.0741, found 210.0745. Anal. Calcd for $C_{11}H_{14}O_2S$: C, 62.84; H, 6.72; S, 15.22. Found: C, 62.78; H, 6.77; S, 15.16.

2,7-Dioxa-13-thia-4,5-benzopentacyclo[6.4.1.1^{9,12}.0^{3,11}.0^{6,10}]-tetradecane 23. White solid; mp 175−176 °C; IR ($CHCl_3$) 1610, 1050, 760 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36−7.28 (m, 4H), 5.65 (d, J = 8.1 Hz, 2H), 5.06 (brs, 2H), 3.40−3.32 (m, 2H), 3.04−2.96 (m, 2H), 2.04−2.01 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 134.96 (2C), 130.77 (2CH), 129.03 (2CH), 88.16 (2CH), 78.88 (2CH), 47.53 (2CH), 45.44 (2CH), 32.41 (CH_2); LRMS *m*/*z* (rel int) 258 (M^+, 50), 134 (100); HRMS (EI) calcd for $C_{15}H_{14}O_2S$ 258.0714, found 258.0710. Anal. Calcd for $C_{15}H_{14}O_2S$: C, 69.75; H, 5.47; S, 12.39. Found: C, 69.83; H, 5.52; S, 12.31.

General Procedure for the Synthesis of Thia-Cages 27−29. The same reaction conditions and procedure as that

of the reaction of **2** with LR were applied for the conversion of **24**−**26** into **27**−**29**.

Spectral Data for 27. White solid; mp 70−72 °C; IR ($CHCl_3$) 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.61 (d, J = 8.1 Hz, 2H), 4.09−3.94 (m, 4H), 2.95−2.91 (m, 2H), 2.42−2.36 (m, 2H), 0.85 (dd, J = 8.1, 5.7 Hz, 2H), 0.52 (dd, J = 8.1, 5.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 88.01 (2CH), 69.13 ($2CH_2$), 55.31 (2CH), 43.60 (2CH), 24.39 (C), 11.98 (CH_2), 6.08 (CH_2); LRMS *m*/*z* (rel int) 210 (M^+, 29), 95 (100); HRMS (EI) calcd for $C_{11}H_{14}O_2S$ 210.0714, found 210.0718. Anal. Calcd for $C_{11}H_{14}O_2S$: C, 62.84; H, 6.72; S, 15.22. Found: C, 62.89; H, 6.78; S, 15.14.

Spectral Data for 28. Highly viscous oil; IR ($CHCl_3$) 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.16 (d, J = 6.9 Hz, 2H), 4.55−4.50 (m, 2H), 3.05−3.00 (m, 2H), 2.73−2.70 (m, 2H), 1.84−1.62 (m, 4H), 0.75−0.56 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 80.64 (2CH), 74.61 (2CH), 62.70 (2CH), 42.37 (2CH), 26.63 (C), 22.87 ($2CH_2$), 11.35 (CH_2), 7.15 (CH_2); LRMS *m*/*z* (rel int) 236 (M^+, 9), 91 (100); HRMS (EI) calcd for $C_{13}H_{16}O_2S$ 236.0871, found 236.0876. Anal. Calcd for $C_{13}H_{16}O_2S$: C, 66.08; H, 6.83; S, 13.54. Found: C, 66.17; H, 6.91; S, 13.48.

Spectral Data for 29. White solid; mp 282−284 °C; IR ($CHCl_3$) 1610, 1060, 760 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36 (brs, 4H), 5.66 (d, J = 9.6 Hz, 2H), 5.10 (d, J = 5.7 Hz, 2H), 3.21 (dd, J = 5.7, 2.4 Hz, 2H), 2.81 (dd, J = 9.6, 2.4 Hz, 2H), 0.92 (dd, J = 8.4, 6.0 Hz, 2H), 0.60 (dd, J = 8.4, 6.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 134.91 (2C), 130.77 (2CH), 129.06 (2CH), 87.79 (2CH), 79.40 (2CH), 56.09 (2CH), 45.44 (2CH), 27.35 (C), 11.37 (CH_2), 7.05 (CH_2),; LRMS *m*/*z* (rel int) 284 (M^+, 96), 165 (100); HRMS (EI) calcd for $C_{17}H_{16}O_2S$ 284.0871, found 284.0877. Anal. Calcd for $C_{17}H_{16}O_2S$: C, 71.81; H, 5.68; S, 11.25. Found: C, 71.90; H, 5.75; S, 11.19.

General Procedure for the Ozonolysis of the Diols 30 and 31 with a Controlled Amount of Ozone. Synthesis of the Trioxa-Cages 32 and 33. A solution of **30** (0.39 g, 2.0 mmol) in dichloromethane (80 mL) was cooled to −78 °C and ozone was bubbled through it at −78 °C until compound **30** was consumed by thin-layer chromatography tracing. To this solution was added dimethyl sulfide (0.36 g, 5.8 mmol) and Amberlyst-15 (0.40 g) at −78 °C, and the reaction mixture was stirred at room temperature for 12 h, After filtration, the solvent was evaporated, and the crude product was purified by column chromatography to give the diacetal trioxa-cage **32** (0.33 g, 80%).

10-Isopropylidene-2,7,12-trioxatetracyclo[6.3.1.$0^{4,11}$.$0^{5,9}$]dodecane 32. White solid; mp 117−119 °C; IR ($CHCl_3$) 1060 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.47 (d, J = 6.3 Hz, 2H), 4.27 (d, J = 9.3 Hz, 2H), 3.96−3.92 (m, 2H), 3.40−3.36 (m, 2H), 2.67 (brs, 2H), 1.78 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 126.47 (C), 124.41 (C), 105.32 (2CH), 69.86 ($2CH_2$), 49.58 (2CH), 41.69 (2CH), 20.62 ($2CH_3$); LRMS *m*/*z* (rel int) 208 (M^+, 21), 165 (100); HRMS (EI) calcd for $C_{12}H_{16}O_3$ 208.1099, found 208.1091. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.19; H, 7.75. Found: C, 69.24; H, 7.82.

14-Isopropylidene-2,7,13-trioxapentacyclo[6.4.1.1^{9,12}.$0^{3,11}$.$0^{6,10}$]tetradecane 33. White solid; mp 122−124 °C; IR ($CHCl_3$) 1060 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.49 (d, J = 6.3 Hz, 2H), 4.43−4.40 (m, 2H), 3.54−3.46 (m, 2H), 2.43−2.40 (m, 2H), 2.20−2.08 (m, 2H), 1.80−1.76 (m, 2H), 1.76 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 126.91 (C), 123.62 (C), 105.14 (2CH), 76.57 (2CH), 50.60 (2CH), 39.24 (2CH), 21.21 ($2CH_2$), 20.46 ($2CH_3$); LRMS *m*/*z* (rel int) 234 (M^+, 28), 159 (100), 145 (98); HRMS (EI) calcd for $C_{14}H_{18}O_3$ 234.1255, found 234.1249. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.76; H, 7.75. Found: C, 71.82; C, 7.72.

General Procedure for the Synthesis of the Trioxa-Cages 34 and 35 from Ozonolysis of 32 and 33. A solution of **32** (0.42 g, 2.0 mmol) in dichloromethane (80 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 (0.36 g, 5.8 mmol) at −78 °C, and the reaction mixture was stirred at room temperature for 8 h. The solvent was evaporated, and the crude product was purified by column chromatography to give the diacetal trioxa-cage **34** (0.28 g, 78%).

10-Oxo-2,7,12-trioxatetracyclo[6.3.1.$0^{4,11}$.$0^{5,9}$]dodecane 34. White solid; mp 101−102 °C; IR ($CHCl_3$) 1768, 1055 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.88 (d, J = 6.3 Hz, 2H), 4.57 (d, J = 9.9 Hz, 2H), 4.07−4.02 (m, 2H), 3.05−2.94 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ_206.51 (CO), 109.66 (2CH), 71.45 ($2CH_2$), 55.48 (2CH), 38.63 (2CH); LRMS *m*/*z* (rel int) 182 (M^+, 20), 68 (100); HRMS (EI) calcd for $C_9H_{10}O_4$ 182.0579, found 182.0586. Anal. Calcd for $C_9H_{10}O_4$: C, 59.32; H, 5.54. Found: C, 59.38; H, 5.59.

14-Oxo-2,7,13-trioxapentacyclo[6.4.1.1^{9,12}.$0^{3,11}$.$0^{6,10}$]tetradecane 35. White solid; mp 126−128 °C; IR ($CHCl_3$) 1768, 1060 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.88 (d, J = 6.3 Hz, 2H), 4.56−4.54 (m, 2H), 3.07−3.03 (m, 2H), 2.82−2.77 (m, 2H), 2.33−2.27 (m, 2H), 1.92−1.83 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 206.49 (CO), 109.29 (2CH), 78.68 (2CH), 56.66 (2CH), 36.21 (2CH), 20.67 ($2CH_2$); LRMS *m*/*z* (rel int) 208 (M^+, 80), 162 (90), 81 (100); HRMS (EI) calcd for $C_{11}H_{12}O_4$ 208.0735, found 208.0729. Anal. Calcd for $C_{11}H_{12}O_4$: C, 63.44; H, 5.81. Found: C, 63.52; H, 5.86.

General Procedure for the Reaction of 34 and 35 with LR. Formation of Thia-Cages 36 and 37. The same reaction conditions and procedure as that of the reaction of **2** with LR were applied for the reaction of **34** and **35** with LR chemoselectively to give the thia-cages **36** and **37**.

10-Oxo-2,7-dioxa-12-thiatetracyclo[6.3.1.$0^{4,11}$.$0^{5,9}$]dodecane 36. White solid; mp 125 °C (decomposed); IR ($CHCl_3$) 1765, 1060 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.94 (d, J = 8.1 Hz, 2H), 4.39 (d, J = 8.4 Hz, 2H), 4.17−4.10 (m, 2H), 3.18−3.06 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 207.96 (CO), 92.13 (2CH), 71.30 ($2CH_2$), 55.17 (2CH), 39.24 (2CH); LRMS *m*/*z* (rel int) 198 (M^+, 4), 69 (100); HRMS (EI) calcd for $C_9H_{10}O_3S$ 198.0350, found 198.0358. Anal. Calcd for $C_9H_{10}O_3S$: C, 54.54; H, 5.09; S, 16.14. Found: C, 54.60; H, 5.13; S, 16.08.

14-Oxo-2,7-dioxa-13-thiapentacyclo[6.4.1.1^{9,12}.$0^{3,11}$.$0^{6,10}$]tetradecane 37. White solid; mp 180−182 °C (decomposed); IR ($CHCl_3$) 1765, 1060 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.94 (d, J = 8.7 Hz, 2H), 4.68−4.62 (m, 2H), 3.34−3.25 (m, 2H), 3.00−2.92 (m, 2H), 2.32−2.20 (m, 2H), 1.92−1.80 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 207.64 (CO), 91.96 (2CH), 78.58 (2CH), 56.50 (2CH), 37.84 (2CH), 22.05 ($2CH_2$); LRMS *m*/*z* (rel int) 224 (M^+, 30), 81 (100); HRMS (EI) calcd for $C_{11}H_{12}O_3S$ 224.0507, found 224.0512. Anal. Calcd for $C_{11}H_{12}O_3S$: C, 58.92; H, 5.40; S, 14.27. Found: C, 58.97; H, 5.44; S, 14.20.

Reaction of the Pentaoxa[5]peristylane 40 with LR. The same reaction conditions and procedure as that of the reaction of **2** with LR were applied for the reaction of the pentaoxa[5]peristylane **40** with LR to remain the unchanged starting compound **40**.

Synthesis of the Thia[5]peristylanes 41 and 42. To a solution of the pentaoxa[5]peristylane **40** (0.50 g, 2.1 mmol) in chloroform (100 mL) was added excess of LR (3.0 g, 7.2 mmol) at room temperature. The reaction mixture was stirred with supersonic shaking at refluxing temperature for 12 h. After cooling and filtration, the solvent was evaporated and the crude product was purified by column chromatography to give the monothia[5]peristylane **41** (0.25 g, 46%) and the dithia[5]peristylane **42** (0.18 g, 26%).

Monothiatetraoxa[5]peristylane 41. White solid; mp 221−223 °C; IR ($CHCl_3$) 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.88 (d, J = 6.9 Hz, 1H), δ 5.71 (d, J = 5.7 Hz, 1H), 5.70 (d, J = 6.6 Hz, 1H), 4.04−3.88 (m, 2H), 3.54−3.50 (m, 1H), 3.34−3.28 (m, 2H), 1.49 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 121.32 (C), 120.59 (C), 111.59 (CH), 96.41 (CH), 93.93 (CH), 65.90 (CH), 65.37 (CH), 63.98 (CH), 62.55 (CH), 57.60 (CH), 26.62 (CH_3), 25.63 (CH_3); LRMS *m*/*z* (rel int) 254 (M^+, 100); HRMS (EI) calcd for $C_{12}H_{14}O_4S$ 254.0612, found 254.0601. Anal. Calcd for $C_{12}H_{14}O_4S$: C, 56.68; H, 5.55; S, 12.58. Found: C, 56.62; H, 5.61; S, 12.50.

Dithiatrioxa[5]peristylane 42. White solid; mp 234−236 °C; IR ($CHCl_3$) 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.59

(d, J = 6.3 Hz, 2H), 5.45 (d, J = 9.3 Hz, 1H), 4.46−4.34 (m, 1H), 3.72−3.62 (m, 2H), 3.24−3.20 (m, 2H), 1.48 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 121.70 (2C), 93.00 (2CH), 72.31 (CH), 64.97 (CH), 64.36 (2CH), 63.95 (2CH), 24.47 ($2CH_3$); LRMS m/z (rel int) 270 (M^+, 100); HRMS (EI) calcd for $C_{12}H_{14}O_3S_2$ 270.0384, found 270.0397. Anal. Calcd for $C_{12}H_{14}O_3S_2$: C, 53.33; H, 5.23; S, 23.68. Found: C, 53.40; H, 5.28; S, 23.59.

Reaction of the Pentaoxa[5]peristylane 46 with LR. The same reaction conditions and procedure as that of the synthesis of the thia[5]peristylanes **41** and **42** were applied for the reaction of the unsubstituted pentaoxa[5]peristylane **46** with LR to give the unchanged starting compound **46**. When the reaction was performed in toluene at refluxing temperature, the starting compound **46** still remained unchanged.

Reaction of the Pentaoxa[5]peristylane 40 with P_4S_{10}. To a solution of the pentaoxa[5]peristylane **40** (0.50 g, 2.1 mmol) in toluene (80 mL) was added P_4S_{10} (2.4 g, 5.4 mmol) at room temperature. The reaction mixture was stirred at refluxing temperature for 24 h. After cooling and filtration, the solvent was evaporated and the crude product was purified by column chromatography to give the monothia[5]peristylane **41** (0.19 g, 35%) the dithia[5]peristylane **42** (0.14 g, 20%), and a rearrangement product **47** (0.072 g, 12%). Then the reaction mixture was stirred at refluxing temperature for 120 h. The rearrangement product **47** was obtained in 72% yield.

Spectral Data for 47. White solid; mp 208−209 °C; IR ($CHCl_3$) 1730, 1720, 1100 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.51 (d, J = 8.4 Hz, 1H), 5.28 (d, J = 8.4 Hz, 1H), 4.11−4.00 (m, 2H), 3.71−3.64 (m, 2H), 3.50−3.46 (m, 1H), 2.58−2.52 (m, 1H), 2.26 (s, 3H), 1.38 (d, J = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 208.89 (CO), 206.37 (CO), 66.86 (CH), 62.82 (CH), 61.10 (CH), 60.94 (CH), 60.52 (CH), 58.71 (CH), 58.21 (CH), 48.55 (CH), 28.42 (CH_3), 18.96 (CH_3); LRMS m/z (rel int) 286 (M^+, 30), 226 (100); HRMS (EI) calcd for $C_{12}H_{14}O_2S_3$ 286.0155, found 286.0151. Anal. Calcd for $C_{12}H_{14}O_2S_3$: C, 50.35; H, 4.93; S, 33.54. Found: C, 50.41; H, 4.97; S, 33.44.

Preparation of the Tetraoxa-Cage Compound 51. A solution of **50** (0.50 g, 2.0 mmol) in dichloromethane (80 mL) was cooled to −78 °C, and ozone was bubbled through it at −78 °C for 6 min. To this solution was added dimethyl sulfide (0.60 g, 9.9 mmol), and the reaction mixture was stirred at room temperature for 24 h. The solvent was evaporated, and the crude product was purified by column chromatography to give the tetraoxa-cage **51** (0.31 g, 55%).

Spectral Data for 51. White solid; mp 98−100 °C; IR ($CHCl_3$) 1755, 1250, 1050 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10 (s, 1H), 5.62 (d, J = 6.3 Hz, 1H), 5.56 (d, J = 6.3 Hz, 1H), 3.80−3.76 (m, 1H), 3.36−3.31 (m, 1H), 3.21−3.15 (m, 2H), 2.17 (s, 3H), 1.56 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 167.59 (CO), 127.02 (CH), 122.73 (C), 117.74 (2C), 104.18 (CH), 103.85 (CH), 56.20 (2CH), 48.88 (CH), 46.61 (CH), 24.87 ($2CH_3$), 20.47 (CH_3); LRMS m/z (rel int) 280 (M^+, 14), 221 (100); HRMS (EI) calcd for $C_{14}H_{16}O_6$ 280.0946, found 280.0941.

Hydrolysis of Tetraoxa-Cage 51. To a solution of **51** (0.50 g, 1.8 mmol) in methanol (80 mL) was added solid potassium carbonate (1.7 g, 10 mmol) at 25 °C. The reaction mixture was stirred at 25 °C for 1 h. After filtration, the solvent was evaporated, and the crude product was purified by column chromatography to give compound **52** (0.40 g, 93%).

1,7-Dimethyl-10-*anti*-formyl-2,4,6,13-tetraoxapentacyclo[5.5.1.0^{3,11}.0^{5,9}.0^{8,12}]tridecane 52. White waxy solid; mp 55−56 °C; IR ($CHCl_3$) 1720, 1050 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.74 (s, 1H), 5.64 (d, J = 5.7 Hz, 2H), 3.24−3.16 (m, 5H), 1.55 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 199.54 (CHO), 117.67 (2C), 102.79 (2CH), 56.22 (2CH), 55.46 (CH), 45.86 (2CH), 24.97 ($2CH_3$); LRMS m/z (rel int) 238 (M^+, 42), 223 (100); HRMS (EI) calcd for $C_{12}H_{14}O_5$ 238.0841, found 238.0848.

Reaction of the Tetraoxa-Cage 52 with Amberlyst-15. To a solution of the tetraoxa-cage **52** (0.48 g, 2.0 mmol) in dichloromethane (100 mL) was added Amberlyst-15 resin (2.5 g) at 25 °C. The reaction mixture was stirred at 25 °C for 48 h. After filtration, the solvent was evaporated, and the crude product was purified by column chromatography to give the pentaoxa[5]peristylane **40** (0.30 g, 62%), which has been synthesized by a different route.

Reaction of the Tetraoxa-Cage 51 with LR. To a solution of the tetraoxa-cage **51** (0.56 g, 2.0 mmol) in dichloromethane (80 mL) was added LR (1.8 g, 4.4 mmol) at room temperature. The reaction mixture was stirred at room temperature for 6 h. After filtration, the solvent was evaporated, and the crude product was purified by column chromatography to give the monothia-cage **53** (0.44 g, 75%).

Spectral Data for 53. White solid; mp 113−115 °C; IR ($CHCl_3$) 1755, 1250, 1050 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01 (s, 1H), 5.86 (d, J = 8.7 Hz, 1H), 5.79 (d, J = 8.7 Hz, 1H), 4.17−4.10 (m, 1H), 3.69−3.63 (m, 1H), 3.31−3.25 (m, 2H), 2.15 (s, 3H), 1.55 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 167.68 (CO), 128.11 (CH), 125.51 (C), 117.99 (2C), 88.89 (CH), 88.16 (CH), 57.95 (CH), 57.72 (CH), 51.12 (CH), 48.42 (CH), 26.16 ($2CH_3$), 20.64 (CH_3); LRMS m/z (rel int) 296 (M^+, 14), 237 (100); HRMS (EI) calcd for $C_{14}H_{16}O_5S$ 296.0718, found 296.0722. Anal. Calcd for $C_{14}H_{16}O_5S$: C, 56.74; H, 5.45; S, 10.80. Found: C, 56.70; H, 5.52; S, 10.87.

Hydrolysis of the Monothia-Cage 53. The same reaction conditions and procedure for the hydrolysis of the tetraoxa-cage **51** were applied for the hydrolysis of the monothia-cage **53** to give compound **54** in 92% yield.

1,7-Dimethyl-10-*anti*-formyl-2,6,13-trioxa-4-thiapentacyclo[5.5.1.0^{3,11}.0^{5,9}.0^{8,12}]tridecane 54. White solid; mp 102−104 °C; IR ($CHCl_3$) 1720, 1050 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.70 (s, 1H), 5.83 (d, J = 8.4 Hz, 2H), 3.61−3.54 (m, 2H), 3.30−3.22 (m, 3H), 1.52 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 199.44 (CHO), 117.47 (2C), 87.19 (2CH), 59.74 (CH), 57.77 (2CH), 47.72 (2CH), 26.09 ($2CH_3$); LRMS m/z (rel int) 254 (M^+, 3), 226 (100); HRMS (EI) calcd for $C_{12}H_{14}O_4S$ 254.0612, found 254.0617. Anal. Calcd for $C_{12}H_{14}O_4S$: C, 56.68; H, 5.55; S, 12.58. Found: C, 56.76; H, 5.60; S, 12.52.

Reaction of the Monothia-Cage 54 with Amberlyst-15. The same reaction conditions and procedure as that of the reaction of the tetraoxa-cage **52** with Amberlyst-15 to give the pentaoxa[5]peristylane **40** were applied for the reaction of the monothia-cage **54** with Amberlyst-15 to remain the unchanged starting compound **54**. No conversion from **54** to the monothia-[5]peristylane **41** was obtained.

General Procedure for the Synthesis of New Thia-aza-oxa-Cage Compounds 59a,b and 60a,b. The same reaction conditions and procedure as that of the synthesis of the thia-[5]peristylanes **41** and **42** from the pentaoxa[5]peristylane **40** were applied for the reaction of the aza-cages **58a,b** with LR to give the new thia-aza-oxa-cages **59a,b** and **60a,b**.

1,7,N-Trimethyl-2-aza-4-thia-6,13-dioxapentacyclo-[5.5.1.0^{3,11}.0^{5,9}.0^{8,12}]tridecane 59a. White solid; mp 86−88 °C; IR ($CHCl_3$) 1060 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.57 (d, J = 6.9 Hz, 1H), 4.75 (d, J = 6.9 Hz, 1H), 3.20−2.85 (m, 4H), 2.45 (s, 3H), 2.07 (d, J = 12.9 Hz, 1H), 1.76−1.66 (m, 1H), 1.44 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 116.50 (C), 103.71 (C), 87.49 (CH), 75.05 (CH), 59.97 (2CH), 48.60 (CH), 43.94 (CH), 32.09 (CH_2), 30.47 (CH_3), 26.65 (CH_3), 26.13 (CH_3); LRMS m/z (rel int) 239 (M^+, 27), 168 (100); HRMS (EI) calcd for $C_{12}H_{17}O_2NS$ 239.0980, found 239.0986. Anal. Cacd for $C_{12}H_{17}O_2NS$: C, 60.23; H, 7.17; N, 5.86; S, 13.37. Famd: C, 60.35; H, 7.24; N, 5.81; S, 13.31.

1,7,N-Trimethyl-2-aza-4,6-dithia-13-oxapentacyclo-[5.5.1.0^{3,11}.0^{5,9}.0^{8,12}]tridecane 60a. White solid; mp 97−99 °C; IR ($CHCl_3$) 1060, 660 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.83 (d, J = 7.8 Hz, 1H),_4.82 (d, J = 6.9 Hz, 1H),_3.40−3.28 (m, 2H), 3.18−3.08 (m, 1H), 3.01−2.93 (m, 1H), 2.49 (s, 3H), 2.19 (d, J = 12.6 Hz, 1H), 1.78−1.68 (m, 1H), 1.65 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 104.64 (C), 103.77 (C), 75.96 (CH), 67.38 (CH), 60.17 (CH), 58.55 (CH), 55.13 (CH), 43.70 (CH), 33.39 (CH_2), 30.71 (CH_3), 30.37 (CH_3), 26.71 (CH_3); LRMS m/z (rel int) 255 (M^+, 100); HRMS (EI) calcd for $C_{12}H_{17}ONS_2$ 255.0751, found 255.0758. Anal. Cacd for $C_{12}H_{17}ONS_2$: C, 56.45; H, 6.72; N, 5.49; S, 25.07. Found: C, 56.56; H, 6.78; N, 5.43; S, 25.02.

Reaction of 58b with LR in Dichloromethane at 25 °C. The same reaction conditions and procedure as that of the

reaction of **2** with LR were applied for the reaction of **58b** with 2 equiv of LR in CH_2Cl_2 at 25 °C to give **59b** in 55% yield.

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Supporting Information Available: ^1H and ^{13}C NMR spectral data for compounds **21b**, **21c**, **59b**, and **60b**, and the X-ray data for compounds **3** and **47**. This material is available free of charge via the Internet at http://pubs.acs.org

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