Ring-Expansion of Thioacetal Ring via Bicyclosulfonium Ylide. Effect of Protic Nucleophile on Ylide Intermediate

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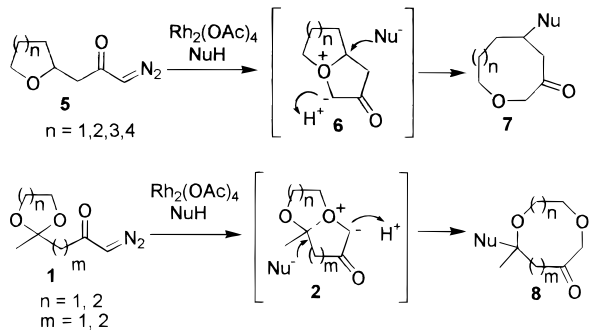
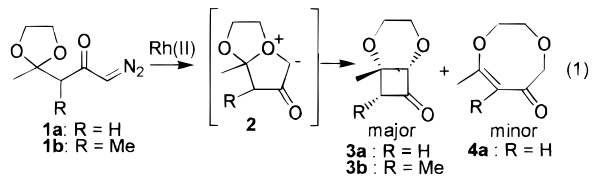
The reaction of 2-(3-diazo-2-oxopropane-1-yl)-2-methyldithiolane **9a**, 2-(4-diazo-3-oxobutane-2-yl)-2-methyldithiolane **9c**, and 2-(3-diazo-2-oxopropane-1-yl)-2-methyl-1,3-dithiane **9b** with $Rh_2(OAc)_4$ gave three-carbon ring-expansion products dithiocan-2-en-1-ones **13a**, **13c** and dithionan-2-en-1-one **13b**, respectively. 2-(5-Diazo-4-oxopentyl)-2-methyldithiolane **9e** also gave the five-carbon ring-expansion products dithionan-3-en-1-one **13e** and 5-methylenedithionane-1-one **13′e**. On the other hand, reaction of 2-(4-diazo-3-oxobutyl)-2-methyldithiolane **9d** in the presence of AcOH gave the four-carbon ring-expansion product **16d** substituted by an acetoxyl group. In addition, the reaction of 2-(3-diazo-2-oxopropyl)-2-methyl-3-oxathiolane **9f** in the absence of AcOH gave 4-oxa-7-thiocan-2-en-1-one **19** via a sulfonium ylide intermediate, whereas, in the presence of AcOH, an alternative regioisomer **20** was also formed competitively with **19** via an oxonium ylide intermediate.

Introduction

Carbenes and carbene complexes (or carbenoids) react with heteroatoms, e.g., oxygen, nitrogen, sulfur, phosphorus, and halogen, to form onium ylides, and their application to synthesis has been actively studied. The [1,2]- and [2,3]-sigmatropic rearrangements of ylides are particularly known to be useful in synthetic chemistry.[1−3] For example, sulfonium ylides are known to be stable intermediates[4] that have been widely studied and applied, e.g., in β-lactam synthesis.[5] Oxonium ylides are known to be extremely short-lived intermediates whose spectra have not yet been observed,[6] and their value in synthesis is still not well-studied. A characteristic of these onium ylides is their [1,*n*]-ambiphilicity, which is inherited from the [1,1]-ambiphilicity of carbenes or carbenoids and modified to make a useful synthetic tool for three-component-coupling reactions.[7] However, the ylides are known to be in equilibrium with carbenes, particularly oxonium and ammonium ylides, and it is therefore difficult to control the reactions.[6,8] Nevertheless, it may be easy to control the reaction of intramolecularly generated onium ylides because the equilibrium is shifted more toward the ylide side. Using this strategy, Johnson et al. first reported the [1,2]-rearrangement of oxonium ylide generated intramolecularly from a diazo ketone bearing a cyclic acetal.[9] Their report encouraged some researchers[10,11b] to study similar systems more carefully as a clue for unveiling the nature of onium ylides.

Scheme 1





Oku et al. recently reported a new method for the ring-expansion of cyclic ethers via oxonium ylides (Scheme 1).[11,12] The key to controlling the reaction was the

(1) (a) Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263. (b) Ye, T.; Mckervey, M. A. *Chem. Rev.* **1994**, *94*, 1091. (c) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223.

(2) (a) West, F. G.; Naidu, B. N.; Tester, R. W. *J. Org. Chem.* **1994**, *59*, 6892. (b) Doyle, M. P.; Ene, D. G.; Forbes, D. C.; Tedrow, J. S. *Tetrahedron Lett.* **1997**, *38*, 4367.

(3) (a) Clark, J. S.; Dosetter, A. G.; Whittingham, W. G. *Tetrahedron Lett.* **1996**, *37*, 5605. (b) Doyle, M. P.; Bagheri, V.; Claxton, E. *J. Chem. Soc., Chem. Commun.* **1990**, 46. (c) Doyle, M. P.; Griffin, J. H.; Chinn, M. S.; Leusen, D. *J. Org. Chem.* **1984**, *49*, 1917.

(4) For sulfonium ylides, see: (a) Davies, H. K. L.; Crisco, V. T. *Tetrahedron Lett.* **1987**, *28*, 371. (b) Moyer, M. P.; Feldman, P. L.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 5223. (c) Ando, W. *Acc. Chem. Res.* **1977**. *10*, 179. (d) Vedej, E. *Acc. Chem. Res.* **1984**, *17*, 358.

(5) See ref 1a and references therein.

(6) (a) Naito, I.; Oku, A.; Ohtani, N.; Fujiwara Y.; Tanimoto, Y. *J. Chem. Soc., Perkin Trans. 2* **1996**, 725. (b) Tomioka, H.; Kobayashi, N.; Murata, S.; Ohtawa, T. *J. Am. Chem. Soc.* **1991**, *113*, 8771. (c) Naito, I.; Oku, A.; Fujiwara, Y.; Tanimoto, Y.; Kobayashi, S. *J. Chem. Soc. Perkin Trans. 2* **1999**, 1051.

(7) Oku, A.; Kimura, K.; Ohwaki, S. *Acta Chem. Scand.* **1993**, *47*, 391.

(8) The equilibrium between oxonium ylide and carbene is described in ref 6a and (a) Sueda, T.; Nagaoka, T.; Goto, S.; Ochiai, M. *J. Am. Chem. Soc.* **1996**, *118*, 10141. (b) West, F. G.; Eberlein, T. H.; Tester, R. W. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2857. (c) Pirrung, M. C.; Brown, W. L.; Rege, S.; Laughton, P. *J. Am. Chem. Soc.* **1991**, *113*, 8561.

(9) Roskamp, E. J.; Johnson, C. R. *J. Am. Chem. Soc.* **1986**, *108*, 6062.

(10) (a) Brogan, J. B.; Bauer, C. B.; Rogers, R. D.; Zercher, C. K. *Tetrahedron Lett.* **1996**, *37*, 5053. (b) Brogan, J. B.; Zercher, C. K.; Bauer, C. B.; Rogers, R. D. *J. Org. Chem.* **1997**, *62*, 3902. (c) Tester, R. W.; West, F. G. *Tetrahedron Lett.* **1998**, *39*, 4631.

(11) For the ring-expansion of bicyclic oxonium ylides, see: (a) Oku, A.; Ohki, S.; Yoshida T.; Kimura, K. *J. Chem. Soc., Chem. Commun.* **1996**, 1077. (b) Oku, A.; Murai N.; Baird, J. *J. Org. Chem.* **1997**, *62*, 2123. (c) Mori, T.; Taniguchi, M.; Suzuki, F.; Doi, H.; Oku, A. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3623. (d) Mori, T.; Oku, A. *J. Chem. Soc., Chem. Commun.* **1999**, 1339.

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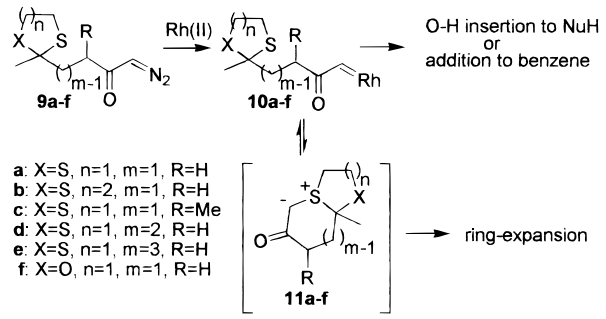
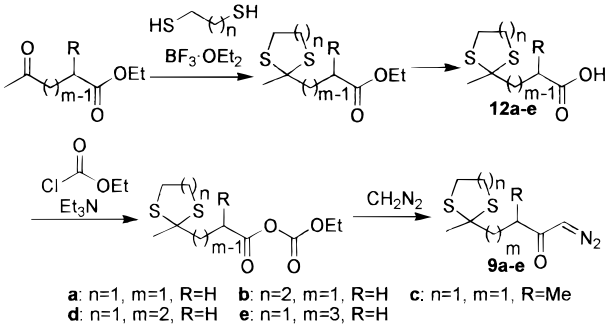
Scheme 2



Scheme 3



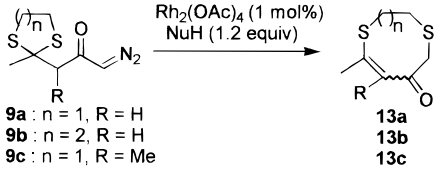
trapping of bicyclic oxonium ylides **2** or **6** by a protic nucleophile. For the synthesis of medium-sized cylic ethers, ring-closing reactions of alcohols bearing a carbenoid group are also known, but the product yields are comparably low.[13] Consequently, we expected that the intramolecular formation of bicyclic ylide may be useful as a method for synthesizing medium-sized heterocycles.

We report here the ring-expansion of sulfonium ylide **11** in comparison with the results of the above-mentioned oxonium ylide reactions (Scheme 2). We first expected that the difference between oxonium and sulfonium ylides would be reflected in their ring-expansion. The key step in the target ring-expansion must be the bond-dissociation of the thioacetal ring. In general, a thioacetal ring cannot be cleaved by hard Lewis acids (e.g., alkali metal or alkali earth metals), but is easily cleaved easily by soft Lewis acids containing transition metals (e.g., Hg, Cu).[14] Since the structural drawing of bicyclic sulfonium ylide intermediate **11** shows that a carbenoid carbon is bound intramolecularly to a sulfur atom as a soft Lewis acid, we expected that dissociation of the central bond would occur easily.

Results and Discussion

Ring-Expansion of Bicyclo[*n*.3.0]sulfonium Ylides Generated from Diazocarbonyl-Substituted Cyclic Dithioacetals. The synthetic route for diazo ketones **9** bearing a cyclic dithioacetal ring is shown in Scheme 3.[15]

Table 1. Ring-Expansion of 9a−c in the Presence of $Rh_2(OAc)_4$ and a Protic Nucleophile[a]



entry	substrate **9**	NuH	yield of **13**
1	**a**	none	91
2	**a**	MeOH	94
3	**a**	AcOH	92
4	**b**	none	84
5	**b**	MeOH	90
6	**b**	AcOH	89
7	**c**	none	91

[a] In benzene at room temperature.

For the reaction of diazo ketone **9**, it was added to a mixed benzene solution of protic nucleophile (1.2 equiv), e.g., MeOH or AcOH, and 1 mol % of $Rh_2(OAc)_4$, and the combined mixture was stirred for 5 h at room temperature. After the consumption of diazo ketone **9** was monitored by TLC, the reaction mixture was washed with water and subjected to flash column chromatography or preparative HPLC for product separation.

In general, the decomposition of diazo ketones bearing a sulfide unit requires high temperatures because the catalyst activity of $Rh_2(OAc)_4$ is doped by sulfur atoms.[16] In the present reaction, however, the decomposition proceeded slowly but steadily at ambient temperatures and was complete within an average of 5 h.

The Rh(II)-catalyzed decomposition of diazo ketone **9a** bearing a dithiolane ring in the absence of a protic nucleophile gave eight-membered dithiaenone **13a** in nearly quantitative yield (Table 1). Since we previously reported that the double-bond configuration of compound **4a** was *Z* based on an X-ray crystallographic analysis,[11d] we also expected that **13a** would have an analogous *Z* configuration. However, we could not crystallize **13a** by any means. It was also reported that the reaction of **1a** gave **3a** as the major product by [1,2]-rearrangement (eq 1).[9] Therefore, our result shows a remarkable characteristic of sulfonium ylides. In addition, while the reaction of **1** in the presence of a protic nucleophile (MeOH or AcOH) gave compound **8**, which was substituted by a nucleophile (Scheme 1),[11b] the analogous reaction of **9a** in the presence of a protic nucleophile gave enone **13a** quantitatively, which was not substituted by the nucleophile (entries 2, 3).

The reaction of diazo ketone **9b** substituted by a dithiane ring also gave the enone **13b**, quantitatively, regardless of the absence or presence of a protic nucleophile (entries 4−6). Similarly, the reaction of **9c** in the absence of a protic nucleophile gave enone **13c** in high yield, in marked contrast to the reaction of acetal **1b** (eq 1), where [1,2]-rearrangement product **3b** was the sole product.[8]

(12) For the ring-expansion of bicyclic oxonium ions, see: (a) Kamada, T.; Ge-Quing; Abe, M.; Oku, A. *J. Chem. Soc., Perkin Trans. 1* **1996**, 413. (b) Nakata, T.; Nomura, S.; Matukura, H. *Tetrahedron Lett.* **1996**, *37*, 213. (c) Nakata, T.; Nomura, S.; Matukura, H.; Morimoto, M. *Tetrahedron Lett.* **1996**, *37*, 217. (d) Morimoto, M.; Matukura, H.; Nakata, T. *Tetrahedron* Lett. **1996**, *37*, 6365.

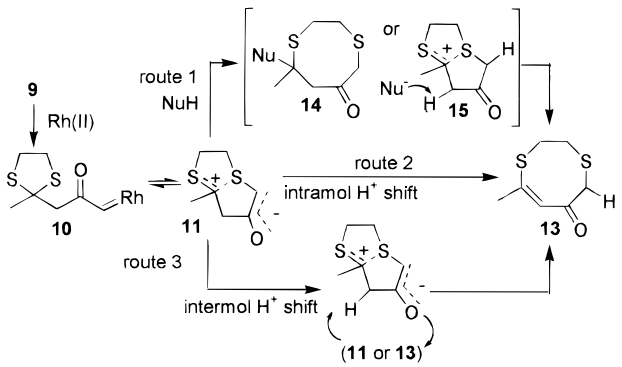
(13) (a) Heslin, J. C.; Moody, C. J.; Slawin, A. M. Z.; Williams, D. J. *Tetrahedron Lett.* **1986**, *27*, 1403. (b) Noels, A. F.; Demonceau, A.; Petiniot, N.; Hubert, A. J.; Teyssie, P. *Tetrahedron* **1982**, *38*, 2733. (c) Davies, H. G.; Roberts, S. M.; Wakefield, B. J.; Winders, J. A. *J. Chem. Soc., Chem. Commun.* **1985**, 1166. (d) Harada, T.; Akiba, E.; Tujimoto, K.; Oku, A. *Tetrahedron Lett.* **1985**, *26*, 4483.

(14) Grobel, B.; T., Seebach, D. *Synthesis* **1977**, 357.

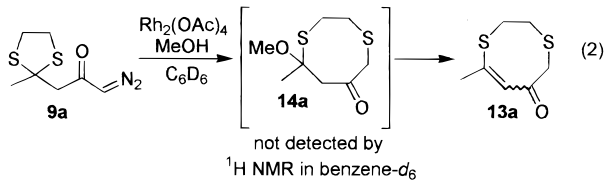
(15) For the synthesis of diazo ketones **9a**−**f**, see: (a) Hatch, R. P.; Shringarpure, J.; Weinreb, S. M. *J. Org. Chem.* **1978**, *43*, 4172. (b) Daignault, R. A.; Eliel, E. L. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. V, p 303. (c) Johnson, J. R.; Hanger, F. D. *Organic Syntheses*; Wiley: New York, 1941; Collect. Vol. I, p 351. (d) Warren, C. K.; Weedon, B. C. L. *J. Chem. Soc.* **1958**, 3972. (e) Padwa, A.; Fryxell, G. E.; Zhi, L. *J. Am. Chem. Soc.* **1990**, *112*, 3100. (f) Boer, T. J.; Backer, H. *Organic Syntheses*; Wiley: New York, 1963; Collect. Vol. IV, p 250.

(16) Doyle, M. P.; Tamblyn, W. H.; Bagheri, V. *J. Org. Chem.* **1981**, *46*, 5094.

Scheme 4

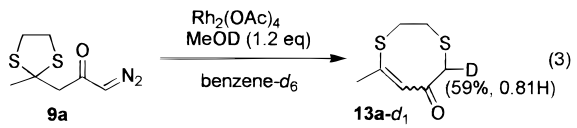


When MeOH or AcOH was used as a nucleophile, ring-expansion product **13** seemed to be formed from intermediate **14** during the workup procedure (eq 2).[11b] To confirm this, the reaction with **9a** was performed in C_6D_6 in the presence of a protic nucleophile for the detection of **14** by ^{1}H NMR. However, the detection was unsuccessful. Nevertheless, we cannot rule out the intermediacy of **14**.



In all cases, cyclic dithiaenone **13** was obtained quantitatively and no other byproducts were obtained. On the basis of the above observation, we propose the reaction mechanisms in Scheme 4 for the formation of enones **13**. (1) In the presence of a protic nucleophile, protonation of sulfonium ylide **11** occurs promptly forming sulfonium ion **15**, followed by the attack of conjugate base to give ring-expanded **14**, or/and the deprotonation of **15** by the conjugate base to give **13**. The intermediate **14** may undergo an E1-type elimination of AcOH to give **13**. (2) In the absence of protic nucleophiles, **13** is formed directly from the ylide **11** by either an intramolecular (route 2) or intermolecular (route 3) proton shift.

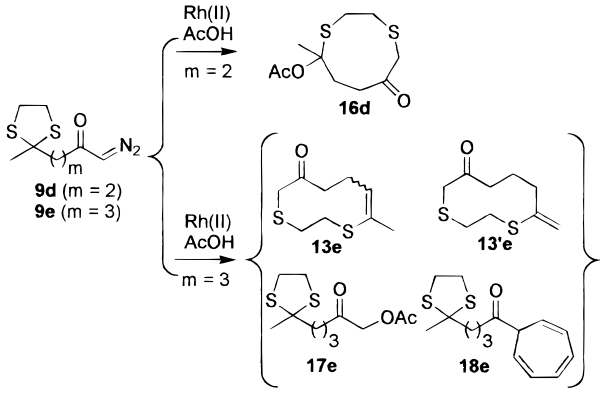
To verify mechanism 1, the reaction of **9a** was performed in the presence of methanol-OD (>99%-*d*) (eq 3), and it was found that the anionic center of ylide **11** was deuterated effectively. This result indicates that the reaction proceeds via mechanism (1) in the presence of nucleophiles.



To verify mechanism (2), the reaction of a mixture of deuterated **9a** (**9a**-d_3) and nondeuterated **9b** (**9b**-d_0) (ratio = 1:1) was monitored by ^{1}H NMR analysis.

In this reaction (eq 4), product **13b** was found to have deuterium scrambled at the anionic center of ylide **11b**, and no H−D exchange was observed at the diazo carbon of unreacted **9b**. In addition, H−D exchange between deuterated **13a**-d_m and nondeuterated **13b**-d_0, both of them were prepared independently, was not observed after stirring their mixture for 5 h in the presence of $Rh_2(OAc)_4$ (eq 5). These observations indicate that enone **13** is predominantly formed by the proton exchange between two molecules of ylides **11** and between the ylide and product **13**, as depicted in Scheme 4.

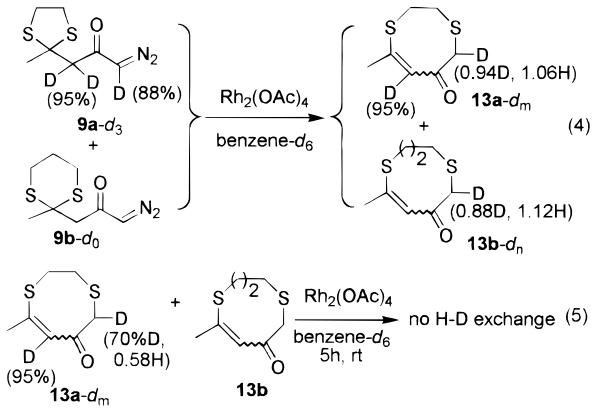
Table 2. Ring-Expansion of 9d,e in the Presence of $Rh_2(OAc)_4$ and a Protic Nucleophile[a]



entry	substrate **9**	AcOH (equiv)	products (yield,[b] %)				
			16d	**13e**	**13′e**	**17e**	**18e**
1	**d**	1.2	92				
2	**e**	none		26	9		4
3	**e**	1.2		trace	17	12	4
4	**e**	2.4		3	22	17	4
5	**e**	10				25	

[a] In benzene at room temperature. [b] Determined by ^{1}H NMR.

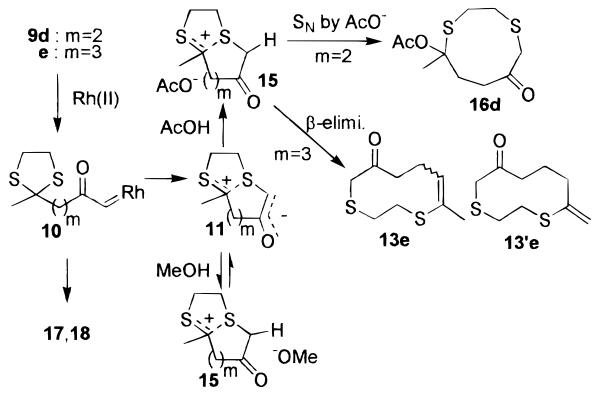
All of the experimental results, i.e., excellent yields of ring-expansion products, suppression of [1,2]-rearrangement and intermolecular proton exchange, can be attributed to the stability of sulfonium ylides.[1]



Effect of the Length of the Chain Tethering Diazo Ketone to the Dithioacetal Ring. For the ring expansion, we previously reported that the side chain tethering the diazocarbonyl moiety to an ethereal ring should be one carbon long for cyclic ethers[11a] and two carbons long for cyclic acetals (Scheme 1).[11b] To not only clarify the limitations of the tethering chain with bicyclic sulfonium ylides that is required for ring-expansion but also to apply this reaction to the synthesis of medium-sized cyclic dithiaenones, analogous Rh(II)-catalyzed reactions of dithiolanes with side chains of different lengths were examined (Table 2).

Rh(II)-catalyzed reactions of **9d** (m = 2) in both the absence and presence of MeOH (pK_a = 15.0)[17] gave a complex product mixture, the analysis of which was impossible. On the other hand, when AcOH (pK_a = 4.8)[17] was used in place of MeOH, the reaction gave acetoxy-

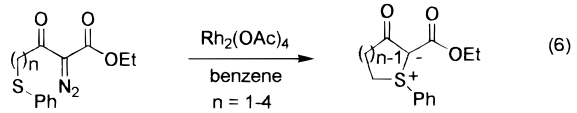
Scheme 5



substituted ring-expansion product **16d** in good yield (entry 1).

We suppose that the efficiency of the ring-expansion of sulfonium ylides in the presence of protic nucleophiles depends on the acidity of the nucleophiles, as we previously found in the case of oxonium ylides.[11a,b] As shown in Scheme 5, ylide **11d** can be protonated by AcOH faster than MeOH to give sulfonium ion **15d**, and consequently, its side reactions are suppressed (Scheme 5).

With a longer side-chain ($m = 3$), **9e** behaved similarly though less efficiently (Table 2, entries 2−5). Davies et al. reported that a seven-membered monocyclic sulfonium ylide can be formed from a linear substrate (eq 6).[4a] Our result with **9e** shows that a seven-membered ylide **11e** can also be formed.



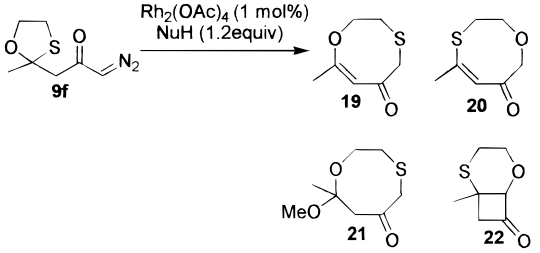
(6)

Thus, the reaction of **9e** in the absence of a protic nucleophile gave 10-membered ring-expansion product **13e** (one isomer), which has an endo double bond, though in low yield (entry 2). Interestingly, the yield of **13′e**, which has an exo methylene bond, increased versus that of **13e** as the amount of acetic acid increased (entries 3 and 4). For the selective formation **13′e** from **9e**, the use of an appropriate amount of AcOH seems essential. Other products **17** and **18** were evidently formed by O−H insertion and addition to benzene, respectively. This result indicates that bicyclo[5.3.0]sulfonium ylide can be formed, though not as effectively as in smaller systems. With **9d** and **9e**, which have a longer side-chain than **9a**−**c**, the mechanism shown in Scheme 4 does not seem to be applicable, since the products are not conjugated enones and, therefore, the intermolecular pathway depicted in Scheme 4 may not be the case. At present, this difference between **9d** and **9e** cannot be explained and ring-expansion is still not the major outcome.

Ring-Expansion of an Oxathiolane Ring Tethered to a Carbenoid. Sulfonium ylides (*S*-ylide) are more stable than oxonium ylides (*O*-ylide), and the formation of *O*-ylide from the carbenoid is thought to be reversible. On this basis, if the reactions of both ylides are slow relative to the equilibrium of *O*-ylide, products from

(17) The pK_a values are those measured in aqueous systems. We refer to these values based on the assumption that the order of acidity in nonaqueous systems may be proportional to those in aqueous systems.

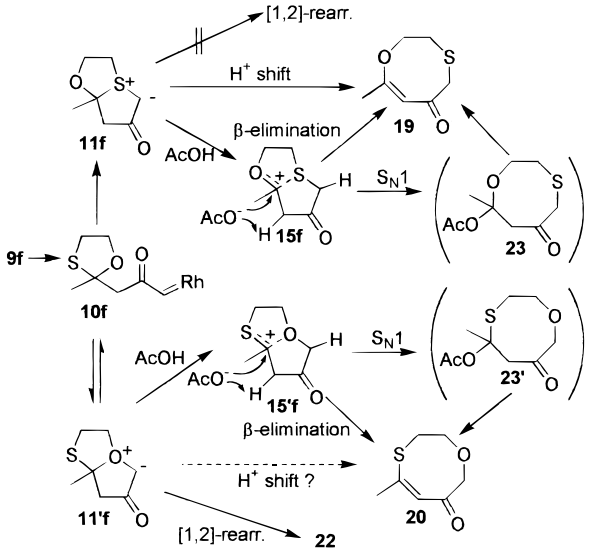
Table 3. Ring-Expansion of 1f in the Presence of $Rh_2(OAc)_4$ and a Protic Nucleophile[a]



		products(%)			
entry	NuH[b]	**19**	**20**	**21**	**22**
1	none	41			3
2	MeOH	40		7	6
3	AcOH	53	27		10

[a] In benzene at room temperature. [b] pK_a value of NuH: MeOH 15.0, AcOH 4.8; see ref 17.

Scheme 6



S-ylide will be obtained selectively. But, if the rate of formation of *O*-ylide is comparable with that of *S*-ylide and following reactions of both ylides can be made fast enough to prevent the equilibrium between *O*-ylide and carbenoid, the product distribution will depend on the rates of formation of the two ylides. To clarify this argument, oxathiolane **9f**, which has a structure that is appropriate for comparing both ylides on the basis of ring-expansion, was prepared by the same method shown in Scheme 2. The results of its reaction are shown in Table 3.

In the absence of a protic nucleophile, the major product was *S*-ylide-derived ring-expansion product **19** and a minor product was **22**, which was formed from the *O*-ylide by [1,2]-rearrangement. In the presence of MeOH, **19** was still formed as the major product together with *S*-ylide-derived ring-expansion product **21**. On the other hand, in the presence of AcOH, formation of *O*-ylide-derived ring-expansion product **20** competed with the formation of **19**. This result can be explained as follows (Scheme 6). (1) The formation of *O*-ylide **11′f** can compete kinetically with the formation of *S*-ylide **11f**, but in the absence of a protic nucleophile and even in the presence of MeOH, which has a low acidity (entries 1 and 2), **11′f** isomerizes to thermodynamically more stable **11f** via

carbenoid **10f**. Thus, **19** from *S*-ylide **11f** can dominate the product mixture. (2) In the presence of AcOH, which has a high acidity (entry 3), the rapid protonation of both **11f** and **11′f** takes place to form both sulfonium ion **15f** and oxonium ion **15′f** by preventing the formation of an equilibrium between **11′f** and **11f**, thus resulting in the production of **19** and **20**, respectively.

Summary

The $Rh_2(OAc)_4$-catalyzed reaction of diazo ketones bearing a dithioacetal ring **9a**−**c** gave three-carbon ring-expansion products **13a**−**c** in good yield, and similarly, **9e**, which has a longer chain than **9a**−**c** by two carbons, gave five-carbon ring-expansion product **13e**. Analogously, the reaction of **9d** in the presence of AcOH gave AcO-substituted four-carbon ring-expansion product **16d**. These results clearly indicate that the formation of bicyclo[(3−4).(3−5)0.0]sulfonium ylides **11a**−**e** is the key step of the reaction. The reaction of oxathiolane **9f** also demonstrated that both *S*- and *O*-ylides are formed under kinetic control, followed by the establishment of an equilibrium biased toward the *S*-ylide to give predominantly **19**. However, the presence of a protic nucleophile suppresses the equilibrium by protonating the initially formed ylides to give both **19** and **20** derived from *S*- and *O*-ylide, respectively. These results help shed light on the differences and similarities between *S*- and *O*-ylides.

Experimental Section

General Methods. Chemical shifts of ^{1}H NMR spectra (500 MHz) and ^{13}C NMR spectra (126 MHz) in $CDCl_3$ were expressed in ppm (δ). Flash column chromatography was performed using silica gel (Wakogel C-300) and a mixed eluent of AcOEt in hexane (normally 50:50). To separate and purify some products that were unstable on silica gel, chromatography by LC-908 (JAI) equipped with a GPC column (JAIGEL 1H, carrier: $CHCl_3$) was performed. Reaction solvents were dried and distilled before use.

Preparation of Carboxylic Acids Bearing a Dithioacetal Ring, 12a−e.[15a,c,d] To a CH_2Cl_2 solution of keto ester (20 mmol) and dithiol (30 mmol) was added BF_3−ether complex (1 mL) under a N_2 atmosphere, and the mixture was stirred at room temperature for 24 h. The reaction mixture was washed with 25 mL of aqueous NaOH (5%) and 50 mL of water, successively, and the solvent was removed under reduced pressure. To the residue was added 1 g (25 mmol) of NaOH dissolved in 20 mL of water, and the mixture was refluxed for 7 h. After cooling, the mixture was washed with ether to extract impurities. To the aqueous layer was added 2.5 mL of 37% HCl. The mixture was extracted three times with 30 mL of ether, and the combined organic layer was dried over anhydrous $MgSO_4$. After filtration, solvent was removed under reduced pressure, and the residue was used as the crude carboxylic acid without further purification.

(2-Methyldithiolan-2-yl)acetic acid (12a): ^{1}H NMR 1.94 (3H, s), 3.09 (2H, s), 3.32−3.41 (4H, m), 9.0−11.0 (1H, broad); ^{13}C NMR 31.5, 40.0 (−S*C*H$_2$*C*H$_2$S−), 50.0, 61.8, 175.1; IR (KBr) 1705 (s, C=O) cm^{-1}; mp 66−68 °C; yield 84%.

(2-Methyl-1,3-dithian-2-yl)acetic acid (12b): ^{1}H NMR 1.80 (3H, s), 1.84−1.93 (1H, m including J = 14.0 Hz), 2.10−2.16 (1H, m including J = 14.0 Hz), 2.76−2.80 (2H, m including J = 14.5 Hz), 3.03−3.11 (2H, m including J = 14.8 Hz), 3.11 (2H, s), 9.0−11.0 (1H, broad); ^{13}C NMR 24.4, 26.9 (−S*C*H$_2$CH$_2$*C*H$_2$S−), 28.2, 45.2, 45.5, 174.3; IR (KBr) 1700 (s) cm^{-1}; mp 120−121 °C; yield 87%.

2-(2-Methyldithiolan-2-yl)propionic acid (12c): ^{1}H NMR 1.45 (3H, d, J = 7.1 Hz), 1.89 (s, 3H), 3.03 (1H, q, J = 7.1 Hz), 3.25−3.39 (m, 4H), 9.0−11.0 (1H, broad); ^{13}C NMR 15.9, 28.9, 39.7, 39.9, 52.3, 67.2, 180.3; IR (KBr) 1700 (s) cm^{-1}; mp 66−68 °C; yield 43%.

3-(2-Methyldithiolan-2-yl)propionic acid (12d): ^{1}H NMR 1.79 (3H, s), 2.22−2.26 (2H, m including triplet, J = 8.0 Hz), 2.65−2.68 (2H, m including triplet, J = 8.0 Hz), 3.28−3.38 (4H, m), 9.0−11.0 (1H, broad); ^{13}C NMR 31.7, 32.9, 39.2, 40.3 (−S*C*H$_2$*C*H$_2$S−), 65.8, 179.5; IR (KBr) 1720 (s) cm^{-1}; mp 48−49 °C; yield 91%.

4-(2-Methyldithiolan-2-yl)butanoic acid (12e): ^{1}H NMR 1.76 (3H, s), 1.84−1.97 (4H, m, J = 7.5 Hz), 2.39 (2H, t, J = 7.5 Hz), 3.27−3.36 (4H, m), 9.0−11.0 (1H, broad); ^{13}C NMR 22.3, 32.3, 33.9, 39.9 (−S*C*H$_2$*C*H$_2$S−), 44.8, 66.2, 179.7; IR (liquid film) 1710 (s) cm^{-1}; mp 39−41 °C; yield 82%.

Preparation of Carboxylic Acid Bearing an Oxathiolane (12f).[15b,c,d] Acid **3f** was prepared by acid-catalyzed azeotropic acetalization followed by alkaline hydrolysis.

(2-Methyloxathiolan-2-yl)acetic acid (12f): ^{1}H NMR 1.74 (3H, s), 2.89 (1H, d, J = 15.5 Hz), 2.96 (1H, d, J = 15.5 Hz), 3.04−3.14 (2H, m), 4.13−4.22 (2H, m), 11.0−9.0 (1H, broad); ^{13}C NMR 29.0, 33.8, 47.7, 70.5, 91.0, 175.4; IR 1705 (s) cm^{-1}; yield 81%.

Preparation of Diazo Ketones Bearing a Thioacetal Ring, 9a−f.[15e] To a THF solution (30 mL) of carboxylic acid **12** (8 mmol) under a N_2 atmosphere were added successively 1.34 mL of triethylamine (9.6 mmol) and 0.92 mL of ethyl chloroformate (9.6 mmol). After being stirred for 1 h, the mixture was filtered through a glass filter to remove solids of NH_4Cl and the filtrate was condensed under reduced pressure. The residue was added to an ether solution of diazomethane, which was prepared from 100 mmol of *p*-toluenesulfonyl-*N*-methyl-*N*-nitrosoamide according to the general procedure.[15f] After being stirred for 1 day or longer, the mixture was condensed under reduced pressure and the residue was purified by silica gel flash chromatography to isolate diazo ketones. These compounds were not stable enough to be treated under conditions for elemental analysis and HRMS measurement. Although they did not detonate during our handling in glassware at room temperature, storage in a refrigerator below 5 °C is recommended. Cutaneous contact must be avoided because diazo compounds are normally suspected to be carcinogens!

2-(3-Diazo-2-oxopropyl)-2-methyldithiolane (9a): ^{1}H NMR 1.88 (3H, s), 3.00 (2H, s), 3.30−3.39 (4H, m), 5.43 (1H, s); ^{13}C NMR 32.2, 39.8 (−S*C*H$_2$*C*H$_2$S−), 55.6, 55.8, 62.8, 191.0; IR (liquid film) 2100 (s, =N$_2$), 1640 (s, C=O) cm^{-1}; yield 74%.

2-(3-Diazo-2-oxopropyl)-2-methyl-1,3-dithiane (9b): ^{1}H NMR 1.80 (3H, s), 1.92−2.00 (m, 1H), 2.02−2.08 (m, 1H), 2.86−2.93 (m, 4H), 2.94 (s, 2H), 5.48 (s, 1H); ^{13}C NMR 24.6 26.9 (−S*C*H$_2$CH$_2$*C*H$_2$S−), 28.1, 46.5, 51.3, 56.7, 190.0; IR (liquid film) 2100 (s), 1635 (s) cm^{-1}; yield 55%.

2-(4-Diazo-3-oxobutane-2-yl)-2-methyldithiolane (9c): ^{1}H NMR 1.35 (3H, d, J = 7.0 Hz), 1.83 (3H, s), 2.87−2.89 (1H, q, J = 7.0 Hz), 3.23−3.35 (4H, m), 5.43 (1H, s); ^{13}C NMR 16.0, 30.4, 39.8, 39.9, 55.4, 56.4, 68.2, 195.7; IR (liquid film) 2100 (s), 1640 (s); yield 16%.

2-(4-Diazo-3-oxobutyl)-2-methyldithiolane (9d): ^{1}H NMR 1.75 (3H, s), 2.20−2.23 (2H, m), 2.58 (2H, broad), 3.25−3.35 (m, 4H), 5.28 (1H, s); ^{13}C NMR 32.8, 38.5, 39.4, 40.1 (−S*C*H$_2$*C*H$_2$S−), 54.4, 66.1, 194.1; IR (liquid film) 2100 (s), 1640 (s) cm^{-1}; yield 84%.

2-(5-Diazo-4-oxopentyl)-2-methyldithiolane (9e): ^{1}H NMR 1.74 (3H, s), 1.81−1.88 (2H, m including J = 5.7 Hz), 1.90−1.94 (2H, m), 2.33 (2H, m including t, J = 5.7 Hz), 3.26−3.35 (4H, m), 5.28 (1H, s); ^{13}C NMR 22.8, 32.3, 39.9 (−S*C*H$_2$*C*H$_2$S−), 40.7, 44.9, 54.3, 66.3, 194.4; IR (liquid film) 2100 (s), 1640 (s) cm^{-1}; yield 54%.

2-(3-Diazo-2-oxopropyl)-2-methyl-3-oxathiolane (9f): ^{1}H NMR (500 MHz) 1.69 (3H, s), 2.84 (1H, d, J = 14.7 Hz), 2.90 (1H, d, J = 14.7 Hz), 3.03−3.13 (2H, m), 4.10−4.15 (1H, m), 4.18−4.22 (1H, m), 5.45 (1H, s); ^{13}C NMR 29.3, 34.0, 53.9, 55.9, 70.3, 91.8, 191.0; IR 2100 (s), 1630 cm^{-1}; yield 46%.

Deuteration of 9a. To a solution of diazo ketone **9a** (606 mg, 3 mmol) in methanol-OD (>99% D) was added *t*-BuOK (11.2 mg, 0.1 mmol) dissolved in 1 mL of methanol-OD under an N_2 atmosphere, and the mixture was stirred for 27 h.

Without condensation, the reaction mixture was purified by silica gel flash chromatography to give deuterated diazo ketone **9a**-d_3 (510 mg) in 84% yield. Deuteration at the C-3 methine and C-1 methylene positions of **9a**-d_3 was monitored and calculated on the basis of ^{1}H NMR integration: ^{1}H NMR 1.88 (1H, s), 3.00 (0.08H, 95% D, s), 3.30−3.39 (4H, m), 5.43 (0.12H, 88% D, s).

General Procedure for the $Rh_2(OAc)_4$-Catalyzed Reaction of Diazo Ketones, 9a−f. To a benzene solution (9 mL) of $Rh_2(OAc)_4$ (4.4 mg, 1 mol %) and a protic nucleophile (1.2 mmol, when used) was added a benzene solution (1 mL) of diazo ketone **9** (1.0 mmol) under an N_2 atmosphere. The reaction mixture was usually stirred for 5 h at room temperature until the diazo ketone was not detectable by TLC monitoring. After workup with 10 mL of water (when AcOH was used as a protic nucleophile, saturated aqueous $NaHCO_3$ was used instead of water), the organic layer was dried over anhydrous $MgSO_4$. After filtration, solvent was removed under reduced pressure and the residue was chromatographed on a silica gel flash column or HPLC.

3-Methyl-4,7-dithiocan-2-ene-1-one (13a): ^{1}H NMR 2.17 (3H, d, J = 1.0 Hz), 2.95−2.97 (2H, m), 3.13−3.15 (2H, m), 3.71 (2H, s), 6.15 (1H, q, J = 1.0 Hz); ^{13}C NMR 27.8, 33.3, 35.4, 39.0, 126.9, 150.2, 200.2; IR (liquid film) 1650 (s, C═O) cm^{-1}; HRMS (EI) calcd for $C_7H_{10}OS_2$ (M^+): 174.0173, found 174.0152. Anal. Calcd for $C_7H_{10}OS_2$: C, 48.23; H, 5.78. Found: C, 48.15; H, 5.78.

3-Methyl-4,8-dithionan-2-ene-1-one (13b): ^{1}H NMR 2.04 (2H, tt, J = 5.5, 6.2 Hz), 2.17 (3H, d, J = 0.9 Hz), 2.94 (2H, t, J = 5.5, Hz), 3.01 (2H, t, J = 6.2 Hz), 3.86 (2H, s), 6.24 (1H, q, J = 0.9 Hz); ^{13}C NMR 27.1, 31.4, 32.8, 35.6, 41.8, 131.1, 148.6, 200.9; IR (liquid film) 1660 (s) cm^{-1}; HRMS (EI) calcd for $C_8H_{12}OS_2$ (M^+) 188.0330, found 188.0308. Anal. Calcd for $C_8H_{12}OS_2$: C, 51.02; H, 6.42. Found: C, 50.79; H, 6.29.

2,3-Dimethyl-4,7-dithiocan-2-ene-1-one (13c): ^{1}H NMR 1.83 (3H, q, J = 1.0 Hz), 2.12 (3H, q, J = 1.0 Hz), 2.91−2.93 (2H, m), 3.05−3.07 (2H, s), 3.71 (2H, m); ^{13}C NMR 17.0, 21.2, 34.4, 37.6, 44.1, 130.4, 140.2, 204.1; IR (KBr) 1680 (s) cm^{-1}; HRMS (EI) calcd for $C_8H_{12}OS_2$ (M^+) 188.0330, found 188.0308. Anal. Calcd for $C_8H_{12}OS_2$: C, 51.02; H, 6.42. Found: C, 50.81; H, 6.26.

4-Acetoxy-4-methyl-5,8-dithionan-1-one (16d). This product was purified by GPC method: ^{1}H NMR 1.89 (3H, s), 2.02 (3H, s), 2.47−2.57 (2H, m including J = 3.5, 4.0 Hz), 2.76−2.81 (1H, m including J = 3.5 Hz), 2.86−3.00 (3H, m including J = 15.5, 4.0, 3.5, 3.0 Hz), 3.04−3.09 (1H, m including J = 15.5 Hz), 3.14−3.20 (1H, m, J = 3.5, 3.0 Hz), 3.39 (2H, s); ^{13}C NMR 22.3, 24.6, 31.6, 35.9, 36.6, 38.5, 46.1, 90.9, 169.2, 207.6; IR (liquid film) 1740 (s, Ac), 1700 (s, C═O) cm^{-1}; HRMS (EI) calcd for $C_{10}H_{16}O_3S_2$ (M^+) 248.0539, found 248.0518.

5-Methyl-6,9-dithiecan-4-ene-1-one (13e) and 5-Methylene-6,9-dithiecan-1-one (13′e). The mixture of isomers **13e** and **13′e** was not separable by either flash column chromatography or HPLC. Therefore, the ^{1}H NMR and ^{13}C NMR spectra of the two mixtures with different isomer ratios (**13e**:**13e′** = 0.21:0.89 and 0.91:0.09) were analyzed. IR spectroscopy and elemental analysis were also performed on the latter mixture.

13e: ^{1}H NMR 1.97 (3H, d, J = 1.0 Hz), 2.53 (2H, td, J = 8.1, 6.0 Hz), 2.67−2.72 (4H, m), 2.86 (2H, t, J = 6.0 Hz), 3.23 (2H, s), 6.07 (1H, tq, J = 8.1, 1.0 Hz); ^{13}C NMR 20.2, 25.7, 29.7, 30.6, 38.4, 43.4, 127.9, 136.6, 205.9.

13′e: ^{1}H NMR 2.06−2.11 (2H, m including J = 6.5 Hz), 2.28 (2H, t, J = 6.5 Hz), 2.73−2.76 (2H, m), 2.87−2.90 (2H, m), 3.00−3.02 (2H, m), 3.57 (2H, s), 4.92 (1H, s), 5.24 (1H, s); ^{13}C NMR 23.5, 28.8, 33.4, 35.1, 39.6, 42.2, 111.1, 125.9, 141.8, 205.5.

Mixture of 13e and 13′e (0.91:0.09): IR (KBr) 1700 (s, C═O) cm^{-1}; HRMS (EI) calcd for $C_9H_{14}OS_2$ (M^+) 202.0486, found 202.0484. Anal. Calcd for $C_9H_{14}OS_2$: C, 53.42; H, 6.98. Found: C, 53.09; H, 6.82.

2-(5-Acetoxy-4-oxopentyl)-2-methyldithiolane (17e): ^{1}H NMR 1.76 (3H, s), 1.84−1.94 (4H, m including J = 7.0 Hz), 2.17 (3H, s), 2.47 (2H, t, J = 7.0 Hz), 3.28−3.37 (4H, m), 4.65 (2H, s); ^{13}C NMR 20.4, 20.9, 32.2, 38.5, 39.9, 44.8, 66.3, 67.9, 170.2, 203.3; IR (liquid film) 1750 (s, Ac), 1730 (s, C═O) cm^{-1}; HRMS (EI) calcd for $C_{11}H_{18}O_3S_2$ (M^+) 262.0697, found 262.0710. Anal. Calcd for $C_{11}H_{18}O_3S_2$: C, 50.35; H, 6.92. Found: C, 50.60, H, 6.74.

2-[4-(Cycloheptatrienyl)-4-oxobutyl]-2-methyldithiolane (18e): ^{1}H NMR 1.77 (3H, s), 1.84−1.94 (4H, m, including J = 7.0 Hz), 2.39 (1H, t, J = 6.0 Hz), 2.60 (2H, t, J = 7.0 Hz), 3.28−3.37 (4H, m), 5.03 (2H, dd, J = 6.0, 7.5 Hz), 6.30 (2H, ddd, J = 3.0, 3.5, 7.5 Hz), 6.57 (2H, dd, J = 3.0, 3.5); ^{13}C NMR 21.5, 32.2, 39.9, 41.4, 45.1, 47.5, 66.4,105.6, 126.2, 129.7, 208.9; IR (liquid film) 1720 (s, C═O) cm^{-1}; HRMS (EI) calcd for $C_{15}H_{20}OS_2$ (M^+) 280.0955, found 280.0950.

3-Methyl-4-oxa-7-thiocan-2-ene-1-one (19): ^{1}H NMR 1.97 (3H, d, J = 0.3 Hz), 2.92 (2H, t, J = 5.0 Hz), 3.64 (2H, s), 4.20 (2H, t, J = 5.0 Hz), 5.48 (1H, q, J = 0.3 Hz); ^{13}C NMR 20.9, 32.2, 40.6, 70.5, 114.9, 168.1, 196.5; IR (liquid film) 1650 (s, C═O) cm^{-1}; HRMS (EI) calcd for $C_7H_{10}O_2S$ (M^+) 158.0401, found 158.0379. Anal. Calcd for $C_7H_{10}O_2S$: C, 53.14; H, 6.37. Found: C, 53.10; H, 6.23.

3-Methyl-7-oxa-4-thiocan-2-en-1-one (20): ^{1}H NMR 2.13 (3H, d, J = 1.2 Hz), 3.03 (2H, t, J = 5.2 Hz), 3.99 (2H, t, J = 5.2 Hz), 4.15 (2H,s), 5.94 (1H, q, J = 1.2 Hz); ^{13}C NMR 26.6, 32.4, 74.1, 121.0, 125.9, 152.8, 202.8; IR (liquid film) 1640 cm^{-1}; HRMS (EI) calcd for $C_7H_{10}O_2S$ (M^+) 158.0401, found 158.0379; mp 79−80 °C. Anal. Calcd for $C_7H_{10}O_2S$: C, 53.14; H, 6.37. Found: C, 52.87; H, 6.23.

3-Methoxy-3-methyl-4-oxa-7-thiocan-1-one (21): ^{1}H NMR 1.30 (3H, d, J = 1.2 Hz), 2.40 (1H, d, J = 13.0 Hz), 2.60 (1H, m including J = 15.0 Hz), 2.95 (1H, m including couplings of J = 15.0, 12.0 Hz), 3.22 (3H, s), 3.27 (1H, d, J = 16.8 Hz), 3.47 (1H, d, J = 16.8 Hz), 3.98 (1H, m including J = 13.0 Hz), 4.04 (1H, dq, J = 13.0, 1.2 Hz), 4.23 (1H, m including J = 13.0, 12.0 Hz); ^{13}C NMR 22.1, 34.0, 42.7, 47.3, 48.6, 64.3, 99.6, 208.3; IR (liquid film) 1700 (s, C═O) cm^{-1}; HRMS (EI) calcd for $C_8H_{14}O_3S$ (M^+) 190.0664, found 190.0664. Anal. Calcd for $C_8H_{14}O_3S$: C, 50.50; H, 7.42. Found: C, 50.21; H, 7.31.

6-Methyl-2-oxa-5-thiabicyclo[4.2.0]octan-8-one (22): ^{1}H NMR 1.84 (3H, s), 2.20 (1H, m including couplings of J = 14.0, 1.8 Hz), 2.65 (1H, dd, J = 16.0, 1.7 Hz), 2.74 (1H, dd, J = 16.0, 1.5 Hz), 2.85 (1H, m including couplings of J = 14.0, 2.8 Hz), 3.82 (1H, m including J = 11.6, 1.8 Hz), 4.05 (1H, m including, J = 11.6, 2.8 Hz), 4.61 (1H, dd, J = 1.7, 1.5 Hz); ^{13}C NMR 22.4, 27.1, 33.4, 52.9, 63.6, 88.0, 201.4; IR (liquid film) 1790 (s, C═O) cm^{-1}; HRMS (EI) calcd for $C_7H_{10}O_2S$ (M^+) 158.0401, found 158.0385.

Supporting Information Available: Spectra for compounds **9a−f**, **13a−c**, **13e**, **13′e**, **16d**, **19**, and **20−22**. This material is available free of charge via the Internet at http://pubs.acs.org.

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