Rhodium-Catalyzed Rearrangement of α-Diazo Thiol Esters to Thio-Substituted Ketenes. Application in the Synthesis of Cyclobutanones, Cyclobutenones, and β-Lactams

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Exposure of α-diazo thiol esters (**1**) to the action of catalytic rhodium(II) acetate leads to a remarkably facile "thia-Wolff rearrangement", producing thio-substituted ketenes which combine with a variety of ketenophiles to provide access to α-thiocyclobutanones, cyclobutenones, and β-lactams. Reductive desulfurization of these cycloadducts takes place under mild conditions and in excellent yield, and this sequence thus represents a useful new alternative to the existing dichloroketene-based methodology for the synthesis of four-membered carbocycles and heterocycles.

Introduction

Once regarded merely as theoretical curiosities, four-membered ring compounds are recognized today as a class of molecules of great practical significance.[1] The β-lactam ring system constitutes the key structural unit in several clinically important classes of antibiotics, and four-membered carbocycles play a prominent role as intermediates for the synthesis of both cyclic and acyclic organic compounds. Cyclobutanones and cyclobutenones, in particular, have found wide application in organic synthesis, participating in ring expansion and ring cleavage processes that give rise to diverse classes of complex organic molecules.[2] For example, research in our laboratory has demonstrated that the thermal electrocyclic cleavage of cyclobutenones provides convenient access to vinylketenes, which function as valuable synthetic building blocks for the efficient construction of six- and eight-membered carbocyclic rings.[3]

The [2 + 2] cycloaddition of ketenes with alkenes and alkynes constitutes the most popular method for the synthesis of cyclobutanones and cyclobutenones.[4] Unfortunately, however, this process is truly general only for highly nucleophilic ketenophiles such as conjugated dienes and enol ethers. In general, unactivated alkenes and alkynes fail to react in good yield with either alkyl- or aryl-substituted ketenes, or with ketene itself. To circumvent this limitation, dichloroketene is usually employed as a ketene equivalent, since this electrophilic ketene reacts well with many types of unactivated multiple bonds, and the resultant cycloadducts undergo facile dechlorination under mild conditions.[4−6]

Herein we report a new method for the generation of *thio-substituted* ketenes as well as their surprisingly facile cycloaddition with both activated and unactivated alkenes and alkynes. As outlined in Scheme 1, we have found that exposure of α-diazo thiol esters (**1**) to the action of catalytic rhodium(II) acetate leads to a remarkably facile "thia-Wolff rearrangement", producing thio-substituted ketenes which combine with a variety of ketenophiles to provide access to α-thiocyclobutanones, cyclobutenones, and β-lactams. Reductive desulfurization of these cycloadducts takes place under mild conditions and in excellent yield, and this sequence thus represents a useful new alternative to the existing dichloroketene-based methodology for the synthesis of four-membered carbocycles and heterocycles.

Results and Discussion

Preparation of α-Diazo Thiol Esters. Four α-diazo thiol esters (**6a**−**d**) incorporating different thiol groups were prepared in order to examine the effect of electronic and steric factors on the thia-Wolff rearrangement and [2 + 2] cycloaddition of the resultant thio-substituted ketenes. For the synthesis of the requisite α-diazo thiol esters,[7] we chose to employ the "detrifluoroacetylative" diazo transfer strategy previously developed in our laboratory.[8] Thus, treatment of thiol esters **5a**−**d**[9] with 1.05 equiv of lithium hexamethyldisilazide in THF at −78 °C furnishes the corresponding lithium enolates, which are acylated by exposure to 1.2 equiv of trifluoroethyl

(1) For a comprehensive review of the chemistry of four-membered carbocycles, see *Methods of Organic Chemistry (Houben-Weyl)*; de Meijere, A., Ed.; Thieme: Stuttgart, Germany, 1997; Vol. E17e and f.

(2) For reviews, see: (a) Bellus, D.; Ernst, B. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 797. (b) Wong, H. N. C.; Lau, K.-L.; Tam, K.-F. *Top. Curr. Chem.* **1986**, *133*, 83. (c) Trost, B. M. *Top. Curr. Chem.* **1986**, *133*, 3. (c) Lee-Ruff, E. In *Advances in Strain in Organic Chemistry*; Halton, B., Ed.; Jai Press: London, 1991; Vol. 1, pp 167−213. (d) Moore, H. W.; Yerxa, B. R. In *Advances in Strain in Organic Chemistry*; Halton, B. Ed.; Jai Press: London, 1995; Vol. 4, pp 81−162.

(3) (a) Danheiser, R. L.; Martinez-Davila, C.; Sard, H. *Tetrahedron* **1981**, *37*, 3943. (b) Danheiser, R. L.; Gee, S. K.; Sard, H. *J. Am. Chem. Soc.* **1982**, *104*, 7670. (c) Danheiser, R. L.; Gee, S. K. *J. Org. Chem.* **1984**, *49*, 1672. (d) Loebach, J. L.; Bennett, D. M.; Danheiser, R. L. *J. Org. Chem.* **1998**, *63*, 8680. (e) Bennett, D. M.; Okamoto, I.; Danheiser, R. L. *Organic Lett.* **1999**, *1*, 641 and references therein.

(4) For recent reviews, see: (a) Hyatt, J. A.; Raynolds, P. W. *Org. Reactions* **1994**, *45*, 159. (b) Tidwell, T. T. *Ketenes*; Wiley: New York, 1995. (c) Schaumann, E.; Scheiblich, S. In *Methoden der Organischen Chemie (Houben-Weyl)*; Kropf, E., Schaumann, E., Eds.; Thieme: Stuttgart, Germany, 1993; Vol. E15, Parts 2 and 3. (d) Lee-Ruff, E. In *Methods of Organic Chemistry (Houben-Weyl)*; de Meijere, A., Ed.; Thieme: Stuttgart, Germany, 1997; Vol. E17e, pp 190−219.

(5) Reviewed in: Brady, W. T. *Tetrahedron* **1981**, *37*, 2949.

(6) Keteniminium salts are more electrophilic than ketenes and sometimes engage in satisfactory [2 + 2] cycloadditions with unactivated olefins. See: ref 4d and Schmit, C.; Falmagne, J. B.; Escudero, J.; Vanlierde, H.; Ghosez, L. *Organic Syntheses*; Wiley: New York, 1993; Collect. Vol. VIII, pp 306−309 and references therein.

(7) For reviews of the chemistry of α-diazo carbonyl compounds, see: (a) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; Wiley: New York, 1998. (b) Ye, T.; McKervey, M. A. *Chem. Rev.* **1994**, *94*, 1091. (c) Regitz, M.; Maas, G. *Diazo Compounds: Properties and Synthesis*; Academic Press: Orlando, FL, 1986.

(8) (a) Danheiser, R. L.; Miller, R. F.; Brisbois, R. G.; Park, S. Z. *J. Org. Chem.* **1990**, *55*, 1959. (b) Danheiser, R. L.; Miller, R. F.; Brisbois, R. G. *Org. Synth.* **1995**, *73*, 134.

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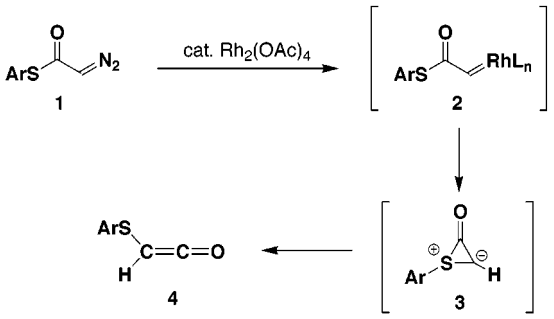
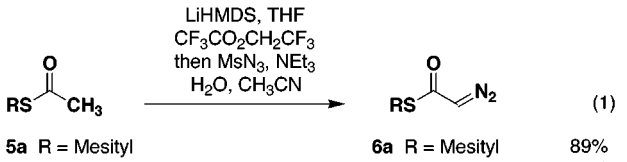
Scheme 1



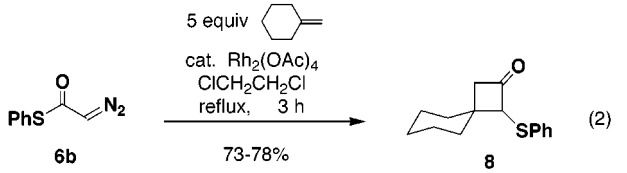
trifluoroacetate at −78 °C for 10 min. Treatment of the resulting α-trifluoroacetyl thiol esters with 1.5 equiv of MsN_3 in the presence of 1.0 equiv of water and 1.5 equiv of Et_3N in acetonitrile (25 °C, 2.5 h) then affords the desired diazo compounds **6a**−**d** in good to excellent yield after chromatographic purification (eq 1).



(1)

5a	R = Mesityl	**6a**	R = Mesityl 89%
5b	R = Ph	**6b**	R = Ph 75%
5c	R = 4-(OMe)C_6H_4	**6c**	R = 4-(OMe)C_6H_4 77%
5d	R = *t*-Bu	**6d**	R = *t*-Bu 45%

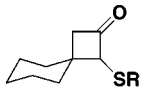
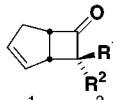
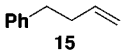
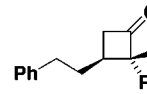
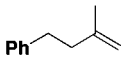
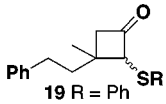
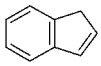
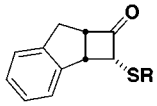
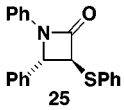
[2 + 2] Cycloaddition Reactions. Optimal conditions for the thia-Wolff rearrangement and [2 + 2] cycloaddition were developed by examining the generation of (phenylthio)ketene from **6b** and its subsequent addition to methylenecyclohexane, with the latter serving as a representative "unactivated" ketenophile. As formulated in eq 2, best results were obtained by using rhodium(II)



(2)

acetate[7,10] (0.02 equiv) to promote the novel thia-Wolff rearrangement. Copper(I) and copper(II) trifluoromethanesulfonate were found to be less effective catalysts for this transformation, and in the absence of catalyst (under otherwise identical conditions) the purely thermal Wolff rearrangement proceeded inefficiently to afford cycloadduct **8** in only 31% yield. Not surprisingly, the optimal temperature for these reactions was found to depend on the reactivity of the ketenophile. Cycloadditions involving the more nucleophilic ketenophiles proceed smoothly in refluxing dichloromethane (40 °C), while reactions with less reactive cycloaddition partners are best accomplished in 1,2-dichloroethane (83 °C). As is standard for ketene cycloadditions, an excess (3.5−10 equiv) of the ketenophile component is best employed, and the optimal protocol involves slowly adding a solution of the diazo thiol ester to a solution of the ketenophile and catalyst in order to minimize competition from ketene dimerization.

Table 1. Preparation of Cyclobutanones and β-Lactams from α-Diazo Thiol Esters

entry	alkene or imine	diazo thiol ester	reaction conditions[a]	product[b]	% yield (ratio)[c]
1	 **7**	**6b**	A	 **8** R = Ph	73-78
2	**7**	**6a**	A	**9** R = Ar	78-81
3	**7**	**6c**	A	**10** R = 4-MeOC_6H_4	69
4	**7**	**6d**	A	**11** R = *t*-Bu	37
5	 **12**	**6b**	B	 **13a** R^1 = H, R^2 = SPh **13b** R^1 = SPh, R^2 = H	90-96 (5-11:1)
6	**12**	**6a**	B	**14a** R^1 = H, R^2 = SAr **14b** R^1 = SAr, R^2 = H	92 (98:2)
7	 **15**	**6b**	A	 **16a** R^1 = H, R^2 = SPh **16b** R^1 = SPh, R^2 = H	20 (75:25)
8	**15**	**6a**	A	**17a** R^1 = H, R^2 = SAr **17b** R^1 = SAr, R^2 = H	62 (83:17)
9	 **18**	**6b**	A	 **19** R = Ph	32 (75:25)
10	**18**	**6a**	A	**20** R = Ar	59 (57:43)
11	 **21**	**6b**	A	 **22** R = Ph	48-51
12	**21**	**6a**	A	**23** R = Ar	58
13	**PhCH=NPh** **24**	**6b**	B	 **25**	85

[a] The diazo thiol ester is treated with 0.02 equiv of $Rh_2(OAc)_4$ and 5 equiv of alkene (10 equiv in entries 6, 7, and 8) or 3.5 equiv of imine (entry 13). Procedure A: reaction in 1,2-dichloroethane at 83 °C for 3 h. Procedure B: reaction in dichloromethane at 40 °C for 3 h. [b] Ar = 2,4,6-trimethylphenyl (mesityl). [c] Isolated yield and ratio of diastereoisomers.

Table 1 delineates the scope of this approach to the synthesis of α-thiocyclobutanones and β-lactams. As illustrated in entries 1−4, aryl thiol esters are superior substrates for the reaction as compared to the *tert*-butylthio derivative **6d**, and the mesityl thiol ester **6a** has proven to be particularly effective in reactions with less ketenophilic alkenes (see entries 7 and 8, and 9 and 10). With the more reactive ketenophiles, however, nearly identical results are obtained using either the mesityl α-diazo thiol ester **6a** or the more readily available

(9) Thiol esters **5a**, **5c**, and **5d** were prepared by acylation of the appropriate thiol with acetyl chloride in CH_2Cl_2−pyridine according to the general procedure described in Danheiser, R. L.; Nowick, J. S. *J. Org. Chem.* **1991**, *56*, 1176. *S*-Phenyl thioacetate (**5b**) is commercially available. The thiols required for the preparation of **5a** and **5c** were synthesized by reduction of the corresponding commercially available arylsulfonyl chlorides using the general procedure of Caesar, P. D. In *Organic Syntheses*; Wiley: New York, 1963; Collect. Vol. IV, pp 695−697.

(10) Review: Adams, J.; Spero, D. M. *Tetrahedron* **1991**, *47*, 1765.

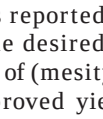
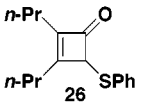
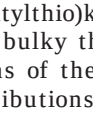
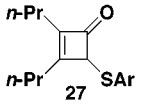
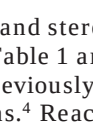
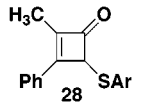
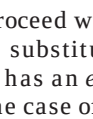
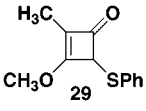
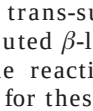
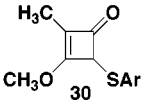
thiophenyl ester **6b** (see entries 1 and 2, and 5 and 6). The efficiency of the reaction of **6a** with unactivated alkenes is especially notable and compares favorably with results obtained previously employing dichloroketene. For example, addition of dichloroketene to methylenecyclohexane is reported to proceed in 55% yield,[11] while up to 81% of the desired [2 + 2] cycloadduct is produced in the reaction of (mesitylthio)ketene with this olefin (entry 2). The improved yields observed in cycloadditions involving (mesitylthio)ketene are likely due to the shielding effect of the bulky thioaryl group which may suppress side reactions of the ketene such as dimerization, although contributions by subtle electronic effects cannot be excluded.

The regio- and stereochemical outcome of the reactions recorded in Table 1 are consistent with predictions based on trends previously observed in other ketene [2 + 2] cycloadditions.[4] Reactions involving cyclic alkenes (e.g., **12** and **21**) proceed with a strong preference for products in which the substituent derived from the monosubstituted ketene has an *endo* orientation on the new bicyclic system. In the case of acyclic olefins (e.g., **15**), the major products are trans-substituted cyclobutanones, and the trans-substituted β-lactam is the exclusive product obtained in the reaction of imine **24**.[12] Stereochemical assignments for these cycloadducts are based primarily on ^{1}H NMR studies; it is well documented that the vicinal coupling constant for protons attached at C_2 and C_3 in cyclobutanones is larger in the case of cis-substituted isomers.[13−15] Additional support for the stereochemical assignment in entry 8 was obtained through an equilibration study. Thus, exposure of a 3.5:1 mixture of **17a** and **17b** to 1.1 equiv of LiOMe in MeOH (25 °C, 11 h) resulted in the formation of a 9.4:1 mixture enriched in the thermodynamically favored trans-substituted isomer **17a**.

Table 2 summarizes the results of our studies on the cycloaddition of (arylthio)ketenes with acetylenic ketenophiles. Once again, (mesitylthio)ketene displays superior reactivity to (phenylthio)ketene, especially in reactions with unactivated ketenophiles such as 4-octyne (entries 1 and 2). Although addition to methoxypropyne was found to be an efficient process, cycloadditions of (arylthio)ketenes with less-activated acetylenes do not proceed as efficiently as the corresponding reactions of dichloroketene,[16] and attempted addition to phenylacetylene resulted in a complex mixture of products.

Discussion of Mechanism. As outlined in Scheme 1, we propose that the conversion of α-diazo thiol esters to thio-substituted ketenes proceeds via the initial formation of a rhodium carbenoid **2**, followed by subsequent

Table 2. Preparation of Cyclobutenones from α-Diazo Thiol Esters

entry	alkyne	diazo thiol ester	reaction conditions[a]	product[b]	% yield[c]
1		**6b**	A	 **26**	14
2		**6a**	A	 **27**	38
3		**6a**	A	 **28**	50
4		**6b**	B	 **29**	72
5		**6a**	B	 **30**	71-92

[a] The diazo thiol ester is treated with 0.02 equiv of $Rh_2(OAc)_4$ and 3.5−5 equiv of alkyne. Procedure A: reaction in 1,2-dichloroethane at 83 °C for 3 h. Procedure B: reaction in dichloromethane at 40 °C for 3 h. [b] Ar = 2,4,6-trimethylphenyl (mesityl). [c] Isolated yield.

"thia-Wolff rearrangement" to generate ketene **4**. Originally discovered in 1912, the Wolff rearrangement[17] is widely employed today as a method for the homologation of carboxylic acids (the Arndt−Eistert reaction), the ring contraction of cyclic ketones, and the in situ generation of ketenes for trapping in [2 + 2] cycloadditions.[18] The Wolff rearrangement is commonly effected by thermolysis or irradiation of α-diazo carbonyl compounds, or by reaction with silver salts. It is well established that *rhodium* carbenes derived from α-diazo carbonyl compounds generally do *not* rearrange to ketenes, and in fact these species play an important role as synthetic intermediates that undergo efficient C−H, O−H, and N−H insertion reactions, react with heteroatom nucleophiles to form ylides, and combine with alkenes and alkynes in cycloadditions leading to cyclopropanes and cyclopropenes.[7a,b,10,19] Few reports have appeared previously describing Wolff rearrangements of α-diazo carbonyl compounds promoted by rhodium carboxylates.[20,21] We suggest that the unusual facility of the Wolff rearrangement of **2** is due to the ability of the thiol ester sulfur to capture the rhodium carbenoid in a process leading to the cyclic sulfonium ylide **3**. The formation of cyclic sulfonium ylides by intramolecular attack of sulfides on rhodium carbenes

(11) Dunkelblum, E. *Tetrahedron* **1976**, *32*, 975.

(12) For a discussion of the stereochemical course of imine−ketene cycloadditions, see: Georg, G. I.; Ravikumar, V. T. In *The Organic Chemistry of β-Lactams*; Georg, G. I., Ed.; VCH: New York, 1993; pp 295−368.

(13) For examples, see: (a) Rey, M.; Roberts, S.; Dieffenbacher, A.; Dreiding, A. S. *Helv. Chim. Acta* **1970**, *53*, 417. (b) DoMinh, T.; Strausz, O. P. *J. Am. Chem. Soc.* **1970**, *92*, 1766. (c) Rey, M.; Roberts, S. M.; Dreiding, A. S.; Roussel, A.; Vanlierde, H.; Toppet, S.; Ghosez, L. *Helv. Chim. Acta.* **1982**, *65*, 703.

(14) The stereochemistry of **13a** was established by comparison of ^{1}H NMR data with that previously reported for this compound: see Michel, P.; O'Donnell, M.; Biname, R.; Hesbain-Frisque, A. M.; Ghosez, L.; Declercq, J. P.; Germain, G.; Arte, E.; Van Meerssche, M. *Tetrahedron Lett.* **1980**, *21*, 2577.

(15) A similar trend has been observed for 3,4-disubstituted β-lactams. See Bachi, M. D.; Goldberg, O. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2332.

(16) For example, see: Danheiser, R. L.; Savariar, S. *Tetrahedron Lett.* **1987**, *28*, 3299.

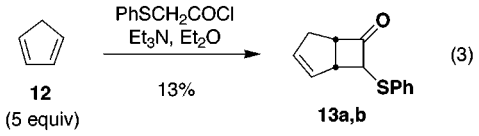
(17) For reviews, see: ref 7 and (a) Zollinger, H. *Diazo Chemistry II: Aliphatic, Inorganic, and Organometallic Compounds*; VCH: New York, 1995. (b) Gill, G. B. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Pattenden, G., Eds.; Pergamon Press: New York, 1991; Vol. 3, pp 887−912. (c) Ando, W. In *The Chemistry of the Diazonium and Diazo Groups*; Patai, S., Ed.; Wiley: New York, 1978; Part 1, Chapter 9, pp 458−475. (d) Meier, H.; Zeller, K.-P. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 32.

(18) For examples in the context of an aromatic annulation strategy, see: Danheiser, R. L.; Brisbois, R. G.; Kowalczyk, J. J.; Miller, R. F. *J. Am. Chem. Soc.* **1990**, *112*, 3093.

is well documented in the literature,[22] although we are not aware of any prior examples that involve thiol esters or that lead to the formation of three-membered rings.[23]

Several prior reports have described the generation of thio-substituted ketenes via the *photochemical* Wolff rearrangement,[24] and we therefore investigated the feasibility of preparing α-thiocyclobutanones and cyclobutenones by irradiation of α-diazo thiol esters in the presence of alkene and alkyne ketenophiles. Unfortunately, this photochemical reaction has not proven to be an efficient process. For example, irradiation (300 nm) of a solution of diazo thiol ester **6b** and methylenecyclohexane in benzene led to polymeric products with no cyclobutanone detectable by ^{1}H NMR analysis of the crude product mixture.

Few examples of [2 + 2] cycloadditions involving thio-substituted ketenes have been described previously. To our knowledge, Ghosez has reported the only prior example of a [2 + 2] cycloaddition involving (phenylthio)-ketene, namely the addition of this ketene to cyclopentadiene to afford the expected bicyclo[3.2.0]butanone in undesignated yield.[14] Several cycloadditions involving *alkyl*(phenylthio)ketenes with *activated* alkenes and imines have been reported.[25] In these prior studies, the thio-substituted ketenes were generated via the triethylamine-promoted dehydrohalogenation of acyl chlorides,[25a−c] or by photochemical rearrangement of Fischer chromium−carbene complexes.[25d−e] In the latter process, cycloaddition is believed to involve a chromium−ketene complex rather than a free ketene.[26] Interestingly, our results suggest that cycloadditions involving thio-substituted ketenes generated by the rhodium-catalyzed decomposition of α-diazo thiol esters proceed more efficiently than reactions involving the same ketenes produced via the standard dehydrohalogenation protocol. For example, we found that treatment of an ether solution of 1 equiv of phenylthioacetyl chloride with 1 equiv of Et_3N in the presence of excess cyclopentadiene (25 °C, 29 h) afforded **13a**,**b** in only 13% yield (eq 3). Note that this cycloadduct



is obtained in nearly quantitative yield when (phenylthio)ketene is generated via the thia-Wolff rearrangement strategy (Table 1, entry 5). Similarly, less than 5% of the desired cycloadduct was obtained from the reaction of phenylthioacetyl chloride with triethylamine (1,2-dichloroethane, reflux) in the presence of 10 equiv of the unactivated olefin 4-phenyl-1-butene (**15**).

Several factors may contribute to the exceptional efficiency of the [2 + 2] cycloadditions of ketenes generated via the thia-Wolff rearrangement. In our procedure, the thio-substituted ketenes are likely generated in low effective concentration, which should work to minimize dimerization and polymerization of these reactive intermediates. Also significant may be the fact that in this method the ketenes are generated in the absence of substances that might promote decomposition, such as the amine hydrochlorides and Lewis acidic metal salts (e.g., $ZnCl_2$) that are present when ketenes are generated via the classical dehydrohalogenation and reductive dechlorination procedures. Finally, we cannot exclude the possibility that rhodium may play a role by remaining complexed to the thio-substituted ketene, thereby facilitating subsequent [2 + 2] cycloaddition reactions.

Synthetic Transformations of α-Thiocyclobutanones. The limited utility of ketene itself in [2 + 2] cycloaddition reactions has stimulated the search for electrophilic ketene equivalents that engage in efficient cycloadditions with alkenes and alkynes and furnish products that can easily be transformed to simple cyclobutanones and cyclobutenones. Due largely to pioneering work by Brady and Ghosez, dichloroketene stands uncontested today as the most efficacious ketene equivalent for [2 + 2] cycloadditions.[4,5] Our discovery that (arylthio)ketenes generated via the rhodium-catalyzed thia-Wolff rearrangement engage in cycloadditions with efficiency rivaling and even surpassing that of dichloroketene suggested to us that this class of ketenes might also play an important role in the synthesis of four-membered carbocycles and heterocycles. Key to this expectation was the assumption that excision of thioaryl substituents from the resulting [2 + 2] cycloadducts could be achieved under mild conditions and in high yield.

A wide variety of reagents are available for the reductive cleavage of carbon−sulfur bonds, including Raney nickel, zinc metal, tributyltin hydride, nickel boride, various metal complex reducing agents, and several alkali metals.[27] Table 3 summarizes the results of our study of the desulfurization of α-thiocyclobutanone cycloadducts **22** and **23**. As expected, both substrates undergo smooth desulfurization upon exposure to either tributyltin hydride or activated zinc dust. For the latter

(19) Reviews: (a) Doyle, M. P. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Hegedus, L. S., Eds.; Pergamon Press: New York, 1995; Vol. 12, Chapter 5.2, pp 387−468. (b) Davies, H. M. L. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Semmelhack, M. F., Eds.; Pergamon Press: New York, 1991; Vol. 4, pp 1031−1067. (c) Taber, D. F. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Pattenden, G., Eds.; Pergamon Press: New York, 1991; Vol. 3, pp 1045−1062.

(20) (a) Taylor, E. C.; Davies, H. M. L. *Tetrahedron Lett.* **1983**, *24*, 5453. (b) Pirrung, M. C.; Morehead, A. T., Jr. *J. Am. Chem. Soc.* **1994**, *116*, 8991. (c) Yong, K.; Salim, M.; Capretta, A. *J. Org. Chem.* **1998**, *63*, 9828. (d) Lee, Y. R.; Suk, J. Y.; Kim, B. S. *Tetrahedron Lett.* **1999**, *40*, 8219.

(21) Marsden has recently observed that α-silyl-α-diazo ketones (but not esters) undergo Wolff rearrangement when heated in the presence of catalytic rhodium(II) octanoate. In this case the anomalous rearrangement pathway (here involving alkyl or aryl group migration) is most likely facilitated by the ability of the silyl group to stabilize the resulting *β*-acylium cation intermediate. See Marsden, S. P.; Pang, W.-K. *J. Chem. Soc., Chem. Commun.* **1999**, 1199.

(22) Reviewed in chapter 7 of ref 7a and Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263.

(23) For examples of cyclizations leading to *four*-membered cyclic sulfonium ylides, see: Davies H. M. L.; Crisco, L. V. T. *Tetrahedron Lett.* **1987**, *28*, 371.

(24) (a) Hixson, S. S.; Hixson, S. H. *J. Org. Chem.* **1971**, *37*, 1279. (b) Georgian, V.; Boyer, S. K.; Edwards, B. *J. Org. Chem.* **1980**, *45*, 1686. (c) Jones, J.; Kresge, A. J. *J. Org. Chem.* **1992**, *57*, 6467.

(25) (a) Ishida, M.; Minami, T.; Agawa, T. *J. Org. Chem.* **1979**, *44*, 2067. (b) Palomo, C.; Cossio, F. P.; Odriozola, J. M.; Oiarbide, M.; Ontoria, J. M. *Tetrahedron Lett.* **1989**, *30*, 4577. (c) Palomo, C.; Cossio, F. P.; Odriozola, J. M.; Oiarbide, M.; Ontoria, J. M. *J. Org. Chem.* **1991**, *56*, 4418. (d) Köbbing, S.; Mattay, J. *Tetrahedron Lett.* **1992**, *33*, 927. (e) Köbbing, S.; Mattay, J.; Raabe, G. *Chem. Ber.* **1993**, *126*, 1849.

(26) Hegedus and co-workers discovered this method for the generation of metal−ketene complexes from Fischer carbenes and have systematically investigated the chemistry of these species. For a review, see Hegedus, L. *Tetrahedron* **1997**, *53*, 4105.

(27) For reviews, see: (a) Caubère, P.; Coutrot, P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1990; Vol. 8, pp 835−847. (b) Block, E. In *Chemistry of Ethers, Hydroxyl Groups and Their Sulphur Analogues*; Patai, S., Ed.; Wiley: New York, 1980; pp 585−608.

Table 3. Reduction of α-Thiocyclobutanones

22 R = Ph
23 R = Mesityl

31

entry	substrate	conditions[a]	yield (%)
1	**22**	A	89
2	**23**	A	98
3	**22**	B	84
4	**23**	B	93

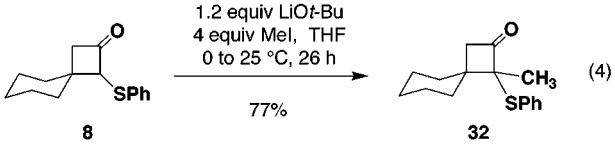
[a] Procedure A: reduction with 1.2−1.7 equiv of Bu_3SnH and cat. AIBN in toluene at reflux for 1 h. Procedure B: reduction with 20−25 equiv of Zn dust in aqueous THF in the presence of NH_4Cl at reflux for 25−42 h.

reduction, the method of Holton[28] proved optimal. Thus, treatment of either **22** or **23** with excess activated zinc dust in a 1:1 mixture of THF and aq saturated NH_4Cl solution (reflux, 25−42 h) led to the smooth formation of cyclobutanone **31** in excellent yield after purification by column chromatography.

We next turned our attention to the analogous reduction of α-(thioaryl)cyclobutenones. Dechlorination of 4,4-dichlorocyclobutenones cannot be achieved under conventional conditions using either tin hydride reagents or zinc metal,[29] but can be accomplished in good yield by employing the protocol developed independently in our laboratory[30] and that of Dreiding.[31] Unfortunately, to date our attempts to effect reduction of α-thiocyclobutenone **28** under a variety of conditions have led to a complex mixture of products together with unreacted starting material.

Regioselective Alkylation of α-Thiocyclobutanones. Like ketene itself, alkyl-substituted ketenes are known to be very poor partners for cycloaddition with unactivated olefins. We reasoned that (arylthio)ketenes might have the capacity to function as useful *alkylketene equivalents*, provided that the α-thiocyclobutanone cycloadducts could be alkylated regioselectively[32] and that the resulting substituted sulfides would undergo efficient desulfurization.

Optimal conditions for the alkylation of α-thiocyclobutanones were developed employing the cycloadduct **8** derived from methylenecyclohexane, a particularly challenging substrate for alkylation due to the adjacent quaternary center. In the event, attempted alkylation of **8** with methyl iodide using potassium *tert*-butoxide as base in DMF led to the desired substituted cyclobutanone accompanied by a significant amount of a byproduct resulting from *O*-alkylation of the intermediate enolate. Better results were obtained by using the lithium enolate and a less polar solvent. Thus, treatment of **8** with lithium *tert*-butoxide in THF followed by excess methyl iodide afforded the desired alkylation product **32** in good yield after chromatographic purification (eq 4).



8 **32** (4)

Similar conditions also proved effective for the regioselective *C*-alkylation of the bicyclic adduct obtained from [2 + 2] cycloaddition of (phenylthio)ketene with cyclopentadiene. As outlined in Scheme 2, methylation and benzylation of the lithium enolate derived from **13a** proceed in excellent yield to furnish products in which alkylation has occurred mainly from the less sterically encumbered convex (exo) face of the bicyclic system. Reduction with tributyltin hydride then affords the expected cyclobutanones in which the predominant product has the α-alkyl substituent in the endo orientation due to the preference for delivery of hydrogen to the convex face of the bicyclic intermediate radical.[33] Note that this sequence provides an alternative route to **35** which is only produced in 33% yield via the cycloaddition of methylketene with cyclopentadiene.[34]

Experiments aimed at extending the scope of this strategy to include less reactive alkylating agents thus far have not been fruitful. Attempted alkylation of both **8** and **13a** with 1-iodo-3-phenylpropane under the conditions described above gave complex mixtures including the desired cyclobutanones as well as products of *O*-alkylation.

Oxidation of α-Thiocyclobutanones. We anticipate that a variety of functionalized four-membered carbocycles should be available via further synthetic elaboration of the products of (arylthio)ketene cycloadditions. For example, oxidation at the α position of the cyclobutanone ring can be readily achieved by Pummerer rearrangement of the sulfoxide derived from α-thiocyclobutanone **8** (Scheme 3). Either sodium periodate or *m*-CPBA chemoselectively transforms **8** to the corresponding sulfoxide (**37**),[35] and exposure of **37** to the action of catalytic *p*-toluenesulfonic acid in Ac_2O−toluene then provides the desired Pummerer rearrangement[36] product **38** in excellent yield.

Ring Expansion of α-Thiocyclobutanones. Ring strain renders cyclobutanones exceptionally reactive as substrates in many ring expansion reactions,[37] and in fact the products of dichloroketene cycloadditions have found extensive use in the synthesis of cyclopentanones.[38] Our

(28) Holton, R. A.; Crouse, D. J.; Williams, A. D.; Kennedy, R. M. *J. Org. Chem.* **1987**, *52*, 2317.

(29) Hassner, A.; Dillon, J. L., Jr. *J. Org. Chem.* **1983**, *48*, 3382.

(30) (a) Reference 16. (b) Danheiser, R. L.; Savariar, S.; Cha, D. D. *Organic Syntheses*; Wiley: New York, 1993; Collect. Vol. VIII, pp 82−86.

(31) Ammann, A. A.; Rey, M.; Dreiding, A. S. *Helv. Chim. Acta* **1987**, *70*, 321.

(32) For examples of the regioselective alkylation of α-thiocyclobutanones, see: (a) Coates, R. M.; Pigott, H. D.; Ollinger, J. *Tetrahedron Lett.* **1974**, 3955. (b) Cohen, T.; Ouellette, D.; Pushpananda, K.; Senaratne, A.; Yu, L.-C. *Tetrahedron Lett.* **1981**, *22*, 3377.

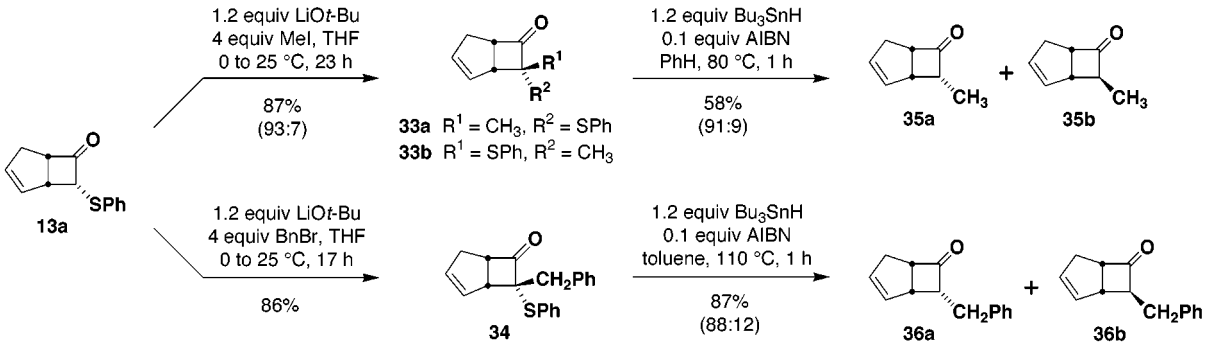
(33) The stereochemistry of **35a** and **35b** was assigned by ^1H NMR analysis as previously described by: (a) Rey, M.; Roberts, S.; Dieffenbacher, A.; Dreiding, A. S. *Helv. Chim. Acta* **1970**, *53*, 417. (b) Brady, W. T.; Hoff, E. F., Jr.; Roe, J., R.; Parry, J., F. H. *J. Am. Chem. Soc.* **1969**, *91*, 5679.

(34) Brady, W. T.; Hoff, E. F., Jr. *J. Org. Chem.* **1970**, *35*, 3733.

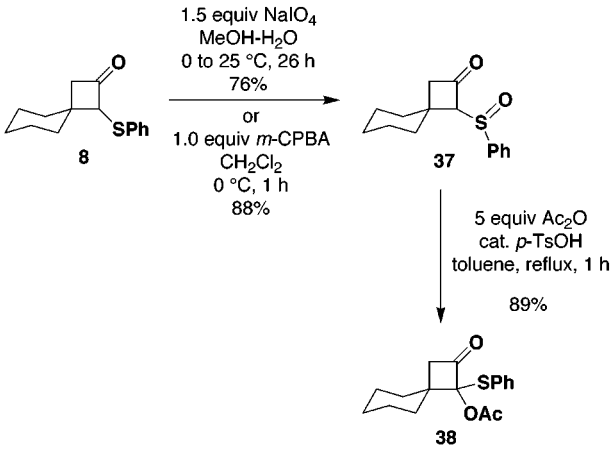
(35) For a review of methods for the oxidation of sulfides to sulfoxides, see Madesclaire, M. *Tetrahedron* **1986**, *42*, 5459.

(36) For reviews, see: (a) Grierson, D. S.; Husson, H. P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 6; pp 924−946. (b) Kennedy, M.; McKervey, M. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 7, pp 193−206. (c) De Lucchi, O.; Miotti, U.; Modena, G. *Org. React.* **1991**, *40*, 157.

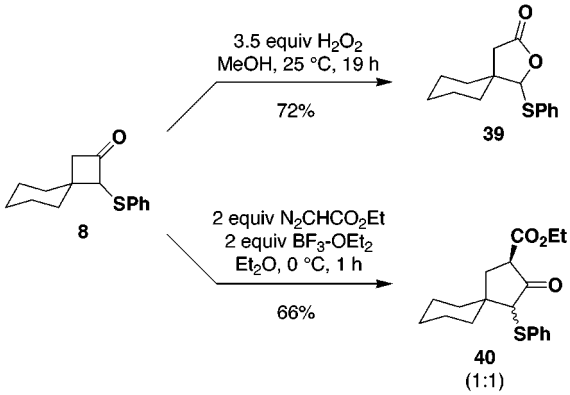
Scheme 2



Scheme 3



Scheme 4



exploratory studies suggest that α-thiocyclobutanones may prove to be equally valuable as intermediates for the synthesis of five-membered rings. As outlined in Scheme 4, Baeyer−Villiger rearrangement of **8** to the five-membered lactone **39** occurs smoothly on exposure to hydrogen peroxide in methanol at room temperature. Interestingly, the exclusive product in this reaction is the lactone produced by migration of the phenylthio-substituted carbon atom.

Attempted ring expansion[37] of α-thiocyclobutanones such as **8** employing diazomethane either alone or in the presence of boron trifluoride etherate led only to the recovery of the cyclobutanone in near-quantitative yield. On the other hand, similar reaction with ethyl diazoacetate rapidly produced the desired cyclopentanone **40** in good yield as a 1:1 mixture of diastereomers (Scheme 4). NMR studies confirmed the identity of the product as the expected cyclopentanone resulting from predominant migration of the less-substituted carbon atom[37] in the four-membered ring.

Conclusion

α-Diazo thiol esters undergo a remarkably facile "thia-Wolff rearrangement" in the presence of catalytic rhodium(II) acetate to produce (arylthio)ketenes which combine with a variety of ketenophiles to provide access to α-thiocyclobutanones, cyclobutenones, and *β*-lactams. Reductive desulfurization of these cycloadducts takes place under mild conditions and in excellent yield, and this sequence thus represents a useful new alternative to the existing dichloroketene-based methodology for the synthesis of four-membered carbocycles and heterocycles.

Experimental Section

Materials. Commercial grade reagents and solvents were used without further purification except as indicated below. Acetonitrile, boron trifluoride etherate, dichloromethane, 1,2-dichloroethane, diisopropylamine, 1,1,1,3,3,3-hexamethyldisilazane, pyridine, toluene, and triethylamine were distilled from calcium hydride. THF was distilled from sodium benzophenone ketyl or dianion. Acetyl chloride was distilled from quinoline. *N*,*N*-Dimethylformamide was sequentially dried in three stages over activated 3 Å molecular sieves. Tributyltin hydride was distilled under reduced pressure. Methyl iodide was passed through a short column of neutral alumina or distilled immediately prior to use. Molecular sieves were heated at 90 °C under vacuum for 12 h and stored in a desiccator jar until use. 4-Phenyl-1-butene and 2-methyl-4-phenyl-1-butene were prepared by Wittig methylenation of the corresponding carbonyl compounds. Zinc metal was activated by the procedure of Nozoe et al.[39]

General Procedures. All reactions were performed in flame-dried glassware under a positive pressure of argon and stirred magnetically unless otherwise indicated. Air- and moisture-sensitive liquids and solutions were transferred via syringe or cannula and were introduced into reaction vessels through rubber septa. Reaction product solutions and chromatography fractions were concentrated using a Büchi rotary evaporator at approximately 20 mmHg and then at ca. 0.1 mmHg (vacuum pump) unless otherwise indicated. Column chromatography was performed using 230−400 mesh Merck or Baker silica gel. Melting points and boiling points are uncorrected.

(37) For reviews of ring expansion methods, see: (a) Wovkulich, P. M. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 1, pp 843−899. (b) Hesse, M. *Ring Enlargement in Organic Chemistry*; VCH: Weinheim, 1991. (c) Gutsche, C. D.; Redmore, D. *Carbocyclic Ring Expansions Reactions*; Academic Press: New York, 1968. (d) Haufe, G.; Mann, G. *The Chemistry of Alicyclic Compounds*; Elsevier: Berlin, 1989; pp 240−372.

(38) (a) Greene, A. E.; Deprés, J.-P. *J. Am. Chem. Soc.* **1979**, *101*, 4003. (b) Au−Yeung, B.-W.; Fleming, I. *J. Chem. Soc., Chem. Commun.* **1977**, 81.

(39) Tsuda, K.; Ohki, E.; Nozoe, S. *J. Org. Chem.* **1963**, *28*, 783.

2,4,6-Trimethylbenzenethiol.[40] Zinc−mercury amalgam was prepared by the following procedure. A 500-mL, one-necked, round-bottomed flask equipped with an argon inlet adapter was charged with mercury(II) chloride (7.48 g, 27.6 mmol), 112 mL of water, and concentrated hydrochloric acid (3.8 mL, 45.9 mmol). The resulting clear solution was stirred rapidly as zinc dust (37.4 g, 572 mmol) was added. The reaction mixture was stirred at 25 °C for 15 min and then filtered through a Büchner funnel. The resulting gray amalgam was washed sequentially with 100 mL of water containing five drops of concentrated hydrochloric acid, 100 mL of ethanol, and 150 mL of diethyl ether. The amalgam was not allowed to dry completely. A 500-mL, three-necked, round-bottomed flask equipped with a reflux condenser fitted with an argon inlet adapter, a glass stopper, and a mechanical stirrer was charged with a 33% solution of sulfuric acid that was prepared from concentrated sulfuric acid (63 mL, 610 mmol) and 119 mL of water. 2,4,6-Trimethylbenzenesulfonyl chloride (10 g, 45.7 mmol) was added, and the freshly prepared Zn−Hg amalgam was added in portions over ca. 1 min (exothermic reaction). The reaction mixture was heated at reflux for 4 h (during which time a white precipitate formed) and then was allowed to stand at 25 °C for 12 h. The resulting mixture was filtered through a Büchner funnel with the aid of four 100-mL portions of warm diethyl ether. The aqueous phase was separated and extracted with two 100-mL portions of diethyl ether, and the combined organic phases were washed with two 100-mL portions of water and 100 mL of brine, dried over $MgSO_4$, filtered, and concentrated to give 4.52 g of a cloudy, pale yellow oil. Distillation through a Vigreux column at reduced pressure afforded 3.78 g (54%) of the thiol as a colorless liquid with properties consistent with those previously reported for this compound.

***S*-2,4,6-Trimethylphenyl Ethanethioate**[41] **(5a).** A 100-mL, three-necked, round-bottomed flask equipped with an argon inlet adapter, glass stopper, and a rubber septum was charged with 2,4,6-trimethylbenzenethiol (1.81 g, 11.9 mmol), 35 mL of dichloromethane, and pyridine (1.15 mL, 1.12 g, 14.2 mmol) and cooled to 0 °C. Acetyl chloride (1.0 mL, 1.10 g, 14.1 mmol) was added slowly via syringe over ca. 8 min. The resulting mixture was stirred at 0 °C for 10 min and then at 25 °C for 2 h. The resulting cloudy white mixture was poured into 20 mL of water, and the aqueous phase was separated and extracted with two 10-mL portions of dichloromethane. The combined organic phases were washed with 20 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 2.38 g of a pale yellow oil. Column chromatograpy on 48 g of silica gel (gradient elution with 0−2.5% ethyl acetate−hexane) provided 2.21 g (96%) of thiol ester **5a** as a white solid: mp 54.5−55.5 °C; IR (CCl_4) 3020, 2960, 2940, 2910, 2840, 1700, and 1600 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.98 (s, 2 H), 2.41 (s, 3 H), 2.31 (s, 6 H), and 2.29 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.8, 142.4, 139.9, 129.2, 123.9, 30.1, 21.5, and 21.1.

General Procedure for Diazo Transfer. *S*-Phenyl 2-Diazoethanethioate (6b). A 100-mL, three-necked, round-bottomed flask equipped with an argon inlet adapter, rubber septum, and a pressure-equalizing addition funnel fitted with a rubber septum was charged with 1,1,1,3,3,3-hexamethyldisilazane (1.50 mL, 1.15 g, 7.11 mmol) and 18 mL of THF and then cooled at 0 °C while *n*-BuLi (2.40 M in hexane, 2.90 mL, 6.96 mmol) was added rapidly dropwise. The resulting solution was stirred at 0 °C for 15 min, and then cooled at −78 °C while a solution of phenyl thioacetate (0.89 mL, 1.0 g, 6.57 mmol) in 14 mL of THF was added dropwise over 15 min. The reaction mixture was stirred at −78 °C for 30 min, and then 2,2,2-trifluoroethyl trifluoroacetate (1.10 mL, 1.61 g, 8.21 mmol) was added rapidly in one portion. The reaction mixture was stirred at −78 °C for 10 min and then partitioned between 40 mL of 5% HCl solution and 50 mL of diethyl ether. The aqueous phase was separated and extracted with two 40-mL portions of ether, and the combined organic phases were washed with 45 mL of brine and concentrated to afford 2.25 g of a yellow oil which was immediately dissolved in 25 mL of acetonitrile and transferred via cannula to a 100-mL, three-necked, round-bottomed flask equipped as described above. Water (0.118 mL, 0.118 g, 6.55 mmol) and triethylamine (1.40 mL, 1.02 g, 10.0 mmol) were added rapidly, and then a solution of methanesulfonyl azide (1.15 mL, 1.20 g, 9.89 mmol) in 28 mL of acetonitrile was added over 20 min. The resulting yellow solution was stirred at 25 °C for 2.5 h and then concentrated to a volume of ca. 10 mL. The residue was diluted with 50 mL of diethyl ether and washed with three 40-mL portions of 10% NaOH solution and 40 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 1.18 g of an orange oil. Column chromatography on 70 g of silica gel (gradient elution with 5−10% ethyl acetate−hexane) provided 0.885 g (76%) of α-diazo thiol ester **6b** as a yellow oil: IR (film) 3090, 3060, 2260, 2100, and 1625 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38−7.52 (m, 5 H), and 5.25 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.1, 135.3, 129.8, 129.3, 127.3, and 54.2.

***S*-2,4,6-Trimethylphenyl 2-Diazoethanethioate (6a).** Reaction of thiol ester **5a** (1.0 g, 5.15 mmol) with LiHMDS (5.46 mmol) and 2,2,2-trifluoroethyl trifluoroacetate (0.83 mL, 1.22 g, 6.20 mmol) in 26 mL of THF according to the general procedure provided 1.88 g of a yellow oil which was diluted with 24 mL of acetonitrile and treated with water (0.093 mL, 0.093 g, 5.16 mmol), triethylamine (1.10 mL, 0.799 g, 7.89 mmol), and a solution of MsN_3 (0.90 mL, 0.938 g, 7.74 mmol) in 20 mL of acetonitrile at 25 °C for 2.5 h to afford 1.2 g of a yellow solid. Column chromatography on 60 g of silica gel (gradient elution with 2.5−5% ethyl acetate−hexane) provided 1.01 g (89%) of α-diazo thiol ester **6a** as a pale yellow solid: mp 91.5−93 °C; IR (CCl_4) 3100, 3010, 2960, 2940, 2910, 2840, 2100, 1630, and 1600, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.00 (s, 2 H), 5.18 (s, 1 H), 2.39 (s, 6 H), and 2.30 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.4, 143.2, 140.5, 129.4, 123.6, 53.3, 21.8, and 21.1.

General Procedure for Generation of Thioketenes and Cycloaddition. 2-(Phenylthio)spiro[3.5]nonan-1-one (8). A 25-mL, two-necked, round-bottomed flask equipped with a rubber septum and a reflux condenser fitted with a rubber septum and inlet needle was charged with rhodium(II) acetate (0.010 g, 0.023 mmol), 3.5 mL of dichloroethane, and methylenecyclohexane (0.680 mL, 0.544 g, 5.66 mmol). The rubber septum was replaced with a glass stopper, and the green reaction mixture was heated at reflux while a solution of α-diazo thiol ester **6b** (0.202 g, 1.13 mmol) in 2.5 mL of dichloroethane was added dropwise via syringe pump (through the reflux condenser) over 2.25 h. An additional 1.5 mL of dichloroethane was used to rinse the syringe and was added to the reaction mixture over ca. 5 min. The reaction mixture was cooled to 25 °C and then concentrated to afford 0.279 g of a brown oil. Column chromatography on 28 g of silica gel (gradient elution with 2.5−5% ethyl acetate−hexane) gave 0.219 g of cyclobutanone **8** (78%) as a yellow oil: IR (film) 3040, 2920, 2840, 1770, and 1580 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.43−7.47 (m, 2 H), 7.19−7.31 (m, 3 H), 4.19 (app s, 1 H), 2.89 (d, J = 18.2 Hz, 1 H), 2.75−2.85 (d of m, J = 17.8 Hz, 1 H), 1.54−1.83 (m, 7 H), and 1.24−1.43 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 135.4, 130.5, 129.0, 126.8, 69.2, 54.6, 38.3, 37.2, 32.2, 25.4, 24.2, and 23.1.

2-(2,4,6-Trimethylphenylthio)spiro[3.5]nonan-1-one (9). Reaction of α-diazo thiol ester **6a** (0.100 g, 0.454 mmol) with methylenecyclohexane (ca. 87% purity, 0.310 mL, 0.216 g, 2.24 mmol) and rhodium(II) acetate (0.004 g, 0.009 mmol) in 5 mL of dichloroethane for 3 h according to the general procedure provided 0.150 g of a green oil. Column chromatography on 15 g of silica gel (gradient elution with 0−1% ethyl acetate−hexane) yielded 0.106 g (81%) of **9** as a pale yellow solid: mp 89−90 °C; IR (CCl_4) 3020, 2920, 2850, 1780, and 1600 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.92 (s, 2 H), 3.62 (s, 1 H), 2.83

(40) For recent alternative procedures for the preparation of this thiol, see: (a) Blower, P. J.; Dilworth, J. R.; Hutchinson, J. P.; Zubieta, J. A. *J. Chem. Soc., Dalton Trans.* **1985**, 1533. (b) Garratt, D. G.; Beaulieu, P. L. *Can. J. Chem.* **1980**, *58*, 2737.

(41) For previous reports of the preparation of **5a**, see: (a) Kuliev, A. M. *J. Org. Chem. USSR* **1978**, *14*, 2437. (b) Petrillo, G. Novi; M.; Garbarino, G.; Filiberti, M. *Tetrahedron Lett.* **1988**, *29*, 4185.

(d, J = 17.3 Hz, 1 H), 2.66 (d, J = 17.0 Hz, 1 H), 2.53 (s, 6 H), 2.25 (s, 3 H), 1.54−1.89 (m, 7 H), and 1.31−1.44 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 142.9, 138.5, 129.4, 129.1, 70.8, 53.9, 37.9, 36.9, 32.0, 25.4, 24.3, 23.1, 22.1, and 20.9. Anal. Calcd for $C_{18}H_{24}OS$: C, 74.95; H, 8.39. Found: C, 74.67; H, 8.44.

7-(Phenylthio)bicyclo[3.2.0]hept-2-en-6-one (13a, 13b).[14] A 100-mL, three-necked, round-bottomed flask equipped with a reflux condenser fitted with a pressure-equalizing addition funnel (fitted with a rubber septum and an inlet needle), glass stopper, and a rubber septum was charged with rhodium(II) acetate (0.086 g, 0.19 mmol), 35 mL of dichloromethane, and freshly prepared cyclopentadiene (3.90 mL, 3.20 g, 48.4 mmol). The green reaction mixture was heated at reflux while a solution of α-diazo thiol ester **6b** (1.74 g, 9.76 mmol) in 25 mL of dichloromethane was added dropwise via the addition funnel over ca. 2.5 h. The reaction mixture was cooled to 25 °C and then concentrated to give a brown oil. Column chromatograpy on 50 g of silica gel (gradient elution with 5−10% ethyl acetate−hexane) followed by similar purification of mixed fractions on 5 g of silica gel provided 2.02 g (96%) of cyclobutanones **13a** and **13b** (92:8 by ^{1}H NMR analysis) as a yellow solid: mp 77−85 °C; IR (film) 3050, 3040, 3010, 2840, 1775, and 1580 cm^{-1}. For **13a:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39−7.43 (m, 2 H), 7.20−7.31 (m, 3 H), 5.93−5.97 (m, 1 H), 5.83−5.89 (m, 1 H), 4.77−4.81 (m, 1 H), 3.87−3.97 (m, 2 H), 2.73−2.82 (d of m, 1 H), and 2.44−2.56 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.1, 135.5, 135.5, 129.9, 129.3, 129.0, 126.6, 65.6, 59.9, 44.5, and 35.2. Anal. Calcd for $C_{13}H_{12}OS$: C, 72.19; H, 5.59. Found: C, 71.95; H, 5.59.

7-*endo*-(2,4,6-Trimethylphenylthio)bicyclo[3.2.0]hept-2-en-6-one (14a, 14b). Reaction of α-diazo thiol ester **6a** (0.123 mg, 0.558 mmol) with freshly prepared cyclopentadiene (0.46 mL, 0.377 g, 5.71 mmol) and rhodium(II) acetate (0.005 g, 0.011 mmol) in 4 mL of dichloromethane for 3 h according to the general procedure provided 0.180 g of a green oil. Column chromatography on 18 g of silica gel (gradient elution with 0−0.5% ethyl acetate−hexane) afforded 0.133 g (92%) of **14a** and **14b** (98:2 by ^{1}H NMR analysis) as a white solid: mp 77−88 °C; IR (CCl_4) 3040, 3010, 2940, 2910, 2840, 1775, and 1595 cm^{-1}. For **14a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.92 (s, 2 H), 5.96−5.98 (m, 2 H), 4.23 (dd, J = 8.8, 2.3 Hz, 1 H), 3.84 (app t, J = 7.3 Hz, 1 H), 3.75 (app t, J = 7.9 Hz, 1 H), 2.75 (d, J = 17.6 Hz, 1 H), 2.53 (s, 6 H), 2.42−2.51 (m, 1 H), and 2.25 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.7, 142.7, 138.5, 135.4, 130.1, 129.8, 129.0, 67.9, 59.4, 45.2, 35.1, 22.2, and 21.0.

3-(2-Phenylethyl)-2-(2,4,6-trimethylphenylthio)cyclobutanone (17a, 17b). Reaction of α-diazo thiol ester **6a** (0.200 g, 0.908 mmol) with 4-phenyl-1-butene (1.20 g, 9.08 mmol) and rhodium(II) acetate (0.008 g, 0.018 mmol) in 7 mL of dichloroethane for 3 h according to the general procedure provided 1.4 g of a brown-green oil. Excess alkene was removed by column chromatography on 10 g of silica gel (gradient elution with 0−2% ethyl acetate−hexane) which provided 0.250 g of a brown oil. Column chromatography on 50 g of silica gel (gradient elution with 1−5% ethyl acetate−hexane) yielded 0.183 g (62%) of cyclobutanones **17a** and **17b** (83:17 by ^{1}H NMR analysis): IR (film) 3080, 3060, 3020, 2920, 2840, 1775, and 1595 cm^{-1}. For **17a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19−7.30 (m, 3 H), 7.11 (d, J = 7.2 Hz, 2 H), 6.91 (s, 2 H), 4.09 (dt, J = 9.4, 2.7 Hz, 1 H, **17b**), 3.77 (dt, J = 6.7, 2.9 Hz, 1 H), 3.12 (ddd, J = 17.5, 9.1, 2.7 Hz, 1 H), 2.51−2.66 (m, 3 H), 2.48 (s, 6 H), 2.25 (s, 3 H), 2.14−2.25 (m, 1 H), 1.91−2.07 (m, 1 H), and 1.73−1.88 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.0, 143.2, 141.1, 138.9, 129.1, 128.5, 128.3, 127.9, 126.1, 64.9, 49.6, 37.1, 34.3, 33.1, 22.1, and 21.0.

3-Methyl-3-(2-phenylethyl)-2-(2,4,6-trimethylphenylthio)cyclobutanone (20a, 20b). Reaction of α-diazo thiol ester **6a** (0.075 g, 0.340 mmol) with 2-methyl-4-phenyl-1-butene (0.254 g, 1.74 mmol) and rhodium(II) acetate (0.003 g, 0.007 mmol) in 2.5 mL of dichloroethane for 3 h according to the general procedure gave 0.389 g of a green oil. Column chromatography on 30 g of silica gel (gradient elution with 0−5% ethyl acetate−hexane) yielded 0.068 g (59%) of cyclobutanones **20a** and **20b** (57:43 by ^{1}H NMR analysis) as a yellow oil: IR (film) 3050, 3020, 2940, 2920, 2840, 1780, and 1600 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17−7.33 (m, 8 H, **20a**, **20b**), 7.14 (d, J = 6.6 Hz, 2 H, **20a**), 6.92 (s, 4 H, **20a**, **20b**), 3.80 (app t, J = 2.4 Hz, 1 H, **20a**), 3.73 (app t, J = 2.1 Hz, 1 H, **20b**), 2.93 (dd, J = 16.8, 2 Hz, 1 H, **20b**), 2.57−2.86 (m, 6 H, **20a**, **20b**), 2.53 (s, 12 H, **20a**, **20b**), 2.25 (s, 6 H, **20a**, **20b**), 2.15 (d of t, J = 12.4, 5.1 Hz, 1 H, **20b**), 1.80−2.02 (m, 2 H, **20a**; m, 1 H, **20b**), 1.48 (s, 3 H, **20b**), and 1.39 (s, 3 H, **20a**); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.3, 204.1, 142.9, 142.7, 141.8, 141.5, 138.7, 129.5, 129.2, 129.1, 128.5, 128.3, 128.2, 126.0, 71.9, 70.9, 55.5, 54.5, 43.7, 38.5, 36.0, 35.7, 32.1, 31.6, 26.0, 22.1, and 21.0.

2-(Phenylthio)-1,2,2a,7a-tetrahydro-7*H*-cyclobut[*a*]inden-1-one (22). Reaction of α-diazo thiol ester **6b** (0.298 g, 1.67 mmol) with indene (1.0 mL, 0.996 g, 8.57 mmol) and rhodium(II) acetate (0.015 g, 0.034 mmol) in 11 mL of dichloroethane for 2.5 h according to the general procedure provided a brown oil. Column chromatograpy on 45 g of silica gel (gradient elution with 5−10% ethyl acetate−hexane) provided 0.316 g of a pale yellow solid which was recrystallized from ethyl acetate−hexane to afford 0.214 g (48%) of **22** as pale yellow crystals: mp 94−96 °C; IR (CCl_4) 3060, 3020, 2950, 2910, 2840, 1770, and 1670 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20−7.42 (m, 9 H), 4.98 (dd, J = 9.0, 3.8 Hz, 1 H), 4.41 (app t, J = 8.3 Hz, 1 H), 4.08−4.15 (m, 1 H), 3.36 (d, J = 16.5 Hz, 1 H), and 3.12 (dd, J = 16.6, 9.8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.7, 143.8, 139.0, 135.7, 130.0, 129.0, 128.3, 127.6, 126.7, 126.6, 125.5, 65.6, 60.3, 43.5, and 34.4.

2-(2,4,6-Trimethylphenylthio)-1,2,2a,7a-tetrahydro-7*H*-cyclobut[*a*]inden-1-one (23). Reaction of α-diazo thiol ester **6a** (0.302 g, 1.37 mmol) with indene (0.80 mL, 0.797 g, 6.86 mmol) and rhodium(II) acetate (0.012 g, 0.027 mmol) in 10 mL of dichloroethane for 2.75 h according to the general procedure provided 1.1 g of an oil. Column chromatography on 22 g of silica gel (gradient elution with 5−20% ethyl acetate−hexane) gave 0.335 g of a pale yellow solid which was recrystallized from ethyl acetate−hexane to afford 0.244 g (58%) of **23** as fluffy white crystals: mp 165.5−167.5 °C; IR (CCl_4) 3050, 3010, 2940, 2900, 2840, and 1750 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58−7.61 (m, 1 H), 7.24−7.30 (m, 3 H), 6.93 (s, 2 H), 4.34 (dd, 9.4, 3.0 Hz, 1 H), 4.29 (app t, J = 9.4 Hz, 1 H), 3.90−3.96 (br t, 1 H), 3.34 (d, J = 16.5 Hz, 1 H), 3.08 (dd, J = 16.7, 9.7 Hz, 1 H), 2.55 (s, 6 H), and 2.25 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.2, 143.8, 142.6, 139.4, 138.5, 130.6, 129.0, 128.1, 127.8, 126.6, 125.4, 67.9, 59.6, 43.8, 34.4, 22.3, and 21.0.

***trans*-1,4-Diphenyl-3-(phenylthio)-azetidin-2-one (25).** Reaction of α-diazo thiol ester **6b** (0.045 g, 0.253 mmol) with *N*-benzylideneaniline (0.160 g, 0.883 mmol) and rhodium(II) acetate (0.003 g, 0.007 mmol) in 2.25 mL of dichloromethane for 3 h according to the general procedure provided a light brown oil. Column chromatography on 10 g of silica gel (gradient elution with 0−5% ethyl acetate−hexane) yielded 0.071 g (85%) of β-lactam **25** as an off-white solid: mp 116−117 °C; IR (CCl_4) 3060, 3030, 2920, 1760, and 1590 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, J = 7.2 Hz, 2 H), 7.17−7.35 (m, 12 H), 7.00−7.04 (m, 1 H), 4.81 (d, J = 2.5 Hz, 1 H), and 4.26 (d, J = 2.5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.3, 137.1, 136.2, 132.2, 132.1, 129.2, 129.0, 128.9, 128.0, 125.9, 124.3, 117.2, 62.9, and 61.4.

2-Methyl-3-phenyl-4-(2,4,6-trimethylphenylthio)cyclobuten-1-one (28). Reaction of α-diazo thiol ester **6a** (0.155 g, 0.704 mmol) with 3-phenyl-2-propyne (0.425 mL, 0.394 g, 3.40 mmol) and rhodium(II) acetate (0.007 g, 0.016 mmol) in 5 mL of dichloroethane for 3 h according to the general procedure provided 0.535 g of a dark green oil. Column chromatography on 53 g of silica gel (gradient elution with 5−10% ethyl acetate−hexane) afforded 0.109 g (50%) of **28** as an orange oil: IR (film) 3040, 3020, 2940, 2920, 2840, 1760, and 1610 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65−7.68 (m, 2 H), 7.47−7.50 (m, 3 H), 6.92 (s, 2 H), 4.84 (q, J = 2.0 Hz, 1 H), 2.46 (s, 6 H), 2.26 (s, 3 H), and 1.97 (d, J = 1.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.7, 165.9, 143.7, 143.0, 138.7, 131.3, 131.2, 129.4, 129.1, 129.0, 127.8, 64.7, 22.3, 21.0, and 9.5.

3-Methoxy-2-methyl-4-(phenylthio)cyclobuten-1-one (29). Reaction of α-diazo thiol ester **6b** (0.101 g, 0.567 mmol)

with 1-methoxypropyne (0.166 mL, 0.139 g, 1.98 mmol) and rhodium(II) acetate (0.005 g, 0.011 mmol) in 5 mL of dichloromethane for 3 h according to the general procedure gave 0.137 g of a brown oil. Column chromatography on 15 g of silica gel (gradient elution with 20−30% ethyl acetate−hexane) yielded 0.090 g (72%) of cyclobutenone **29** as a yellow oil: IR (film) 3020, 2990, 2940, 2910, 2850, 1760, and 1620 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47−7.50 (m, 2 H), 7.29−7.31 (m, 3 H), 4.59 (q, J = 1.8 Hz, 1 H), 4.14 (s, 3 H), and 1.54 (d, J = 1.7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.2, 176.1, 134.1, 130.8, 128.7, 128.2, 120.8, 62.7, 59.7, and 6.6. Anal. Calcd for $C_{12}H_{12}O_2S$: C, 65.43; H, 5.49. Found: C, 65.22; H, 5.58.

3-Methoxy-2-methyl-4-(2,4,6-trimethylphenylthio)cyclobuten-1-one (30). Reaction of α-diazo thiol ester **6a** (0.050 g, 0.227 mmol) with 1-methoxypropyne (0.066 mL, 0.055 g, 0.787 mmol) and rhodium(II) acetate (0.002 g, 0.005 mmol) in 1.9 mL of dichloromethane for 3 h according to the general procedure provided a light brown oil. Column chromatography on 6 g of silica gel (elution with 15% ethyl acetate−hexane) gave 0.042 g (71%) of cyclobutenone **30** as a yellow oil: IR (film) 3025, 2980, 2955, 2880, 1780, and 1640 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.92 (s, 2 H), 4.30 (q, J = 2.1 Hz, 1 H), 4.12 (s, 3 H), 2.52 (s, 6 H), 2.24 (s, 3 H), and 1.63 (d, J = 1.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.5, 177.0, 143.9, 138.8, 129.0, 127.0, 119.6, 63.5, 59.6, 22.1, 21.0, and 6.9.

1,2,2a,7a-Tetrahydro-7*H*-cyclobut[*a*]inden-1-one (31).[42] **Procedure A: Tributyltin Hydride Reduction.** A 10-mL, one-necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with sulfide **22** (0.094 g, 0.353 mmol) and 2.5 mL of toluene. The flask was fitted with a reflux condenser, and the reaction mixture was heated at reflux while a solution of tributyltin hydride (0.114 mL, 0.123 g, 0.424 mmol) and AIBN (0.006 g, 0.037 mmol) in 2.5 mL of toluene was added dropwise (through the condenser) over 35 min. After 1 h, the reaction mixture was cooled to 25 °C and concentrated by rotary evaporation at 0 °C to afford 0.250 g of a yellow oil. Column chromatography on 20 g of silica gel (gradient elution with 5−10% ethyl acetate−hexane) provided 0.050 g (89%) of **31** as a colorless oil which solidified upon storage at 0 °C: mp 33.5−36 °C; IR (film) 3060, 3010, 2940, 2900, 2840, and 1775 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.21−7.31 (m, 4 H), 4.03−4.06 (m, 2 H), 3.55−3.65 (m, 1 H), 3.30 (d, J = 16.8 Hz, 1 H), 3.04−3.13 (m, 1 H), and 2.88 (d, J = 17.7 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.2, 144.5, 143.0, 127.4, 125.3, 125.0, 62.7, 55.6, 36.5, and 33.9. **Procedure B: Zinc Reduction.** A 25-mL, one-necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with sulfide **22** (0.095 g, 0.357 mmol) and 4 mL of THF. Activated zinc dust (0.466 g, 7.13 mmol) was added in one portion, followed by 4 mL of saturated aq NH_4Cl solution. The flask was fitted with a reflux condenser, and the reaction mixture was heated at reflux with vigorous stirring for 25 h. The resulting mixture was cooled to 25 °C and filtered with the aid of diethyl ether. The combined filtrates were washed with two 10-mL portions of saturated aqueous $NaHCO_3$, and the combined aqueous phases were extracted with 10 mL of diethyl ether. The combined organic layers were washed with 10 mL of brine, dried over $MgSO_4$, filtered, and concentrated by rotary evaporation at 0 °C to afford 0.088 g of crude product. Column chromatography on 9 g of silica gel (gradient elution with 5−10% ethyl acetate−hexane) furnished 0.047 g (84%) of **31** as an oil which solidified upon storage at 0 °C (this material was contaminated with <5% starting material as determined by ^1H NMR analysis).

2-Methyl-2-(phenylthio)spiro[3.5]nonan-1-one (32). A 10-mL, two-necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with lithium *tert*-butoxide (0.043 g, 0.537 mmol) and 2 mL of THF and cooled at 0 °C while a solution of α-thiocyclobutanone **8** (0.110 g, 0.446 mmol) in 1.5 mL of THF was added dropwise via cannula over ca. 3 min. The resulting yellow solution was stirred at 0 °C for 30 min, and then methyl iodide (0.110 mL, 0.251 g, 1.77 mmol) was added rapidly dropwise. The ice bath was removed, the flask was wrapped with aluminum foil, and the reaction mixture was stirred at 25 °C for 26 h. The resulting yellow mixture was partitioned between 10 mL of diethyl ether and 10 mL of saturated aqueous NH_4Cl, and the organic phase was separated and washed with 5 mL of water. The combined aqueous layers were extracted with 5 mL of diethyl ether, and the combined organic layers were washed with 8 mL of brine, dried over $MgSO_4$, filtered, and concentrated to provide 0.104 g of an oil. Column chromatography on 13 g of silica gel (gradient elution with 0−2.5% ethyl acetate−hexane) afforded 0.089 g (77%) of cyclobutanone **32** (contaminated with ca. 8% of *O*-alkylation product): IR (film) 3050, 2920, 2840, 1770, and 1580 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.49 (dd, J = 7.7, 2.1 Hz, 2 H), 7.28−7.33 (m, 3 H), 3.43 (d, J = 16.2 Hz, 1 H), 2.75 (d, J = 16.4 Hz, 1 H), 2.03−2.06 (m, 1 H), 1.23−1.76 (m, 9 H), and 1.23 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.4, 136.1, 134.1, 128.8, 128.7, 128.6, 128.5, 71.2, 53.2, 38.8, 34.5, 33.6, 32.5, 25.6, 23.8, 23.3, and 15.5.

7-Methyl-7-(phenylthio)bicyclo[3.2.0]hept-2-en-6-one (33a, 33b). A 10-mL, two-necked, round-bottomed flask equipped with an argon inlet adapter and rubber septum was charged with lithium *t*-butoxide (0.068 g, 0.849 mmol) and 2.5 mL of THF and cooled at 0 °C while a solution of α-thiocyclobutanone **13a** (0.153 g, 0.707 mmol) in 2.5 mL of THF was added dropwise via cannula over ca. 10 min. The resulting solution was stirred at 0 °C for 30 min, and methyl iodide (0.175 mL, 0.399 g, 2.81 mmol) was then added rapidly dropwise. The ice bath was removed, the flask was wrapped in aluminum foil, and the orange reaction mixture was stirred at 25 °C for 23 h and then partitioned between 10 mL of diethyl ether and 10 mL of saturated aqueous NH_4Cl. The organic layer was separated and washed with 5 mL of water, and the combined aqueous phases were extracted with 5 mL of diethyl ether. The combined organic phases were washed with 10 mL of brine, dried over $MgSO_4$, filtered, and concentrated to give 0.163 g of an orange oil. Column chromatography on 16 g of silica gel (gradient elution with 2.5−5% ethyl acetate−hexane) afforded 0.142 g (87%) of cyclobutanones **33a** and **33b** (93:7 by ^1H NMR analysis): IR (film) 3050, 2950, 2910, 2850, 1770, and 1580 cm^{-1}. For **33a**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.57−7.60 (m, 2 H), 7.28−7.32 (m, 3 H), 5.90−5.96 (m, 2 H), 3.96−4.03 (app t, 1 H), 3.46−3.51 (m, 1 H), 2.74−2.82 (m, 1 H), 2.46−2.56 (app dd, 1 H), and 1.48 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.6, 135.0, 134.9, 131.6, 129.8, 128.7, 128.0, 70.7, 57.7, 51.9, 34.6, and 22.9.

7-*exo*-(Phenylmethyl)-7-(phenylthio)bicyclo[3.2.0]hept-2-en-6-one (34). A 10-mL, two-necked, round-bottomed flask equipped with an argon inlet adapter and a rubber septum was charged with lithium *tert*-butoxide (0.070 mg, 0.874 mmol) and 2.5 mL of THF and cooled at 0 °C while a solution of α-thiocyclobutanone **13a** (0.157 g, 0.726 mmol) in 2.5 mL of THF was added dropwise via cannula over ca. 8 min. The resulting orange solution was stirred at 0 °C for 30 min, and benzyl bromide (0.345 mL, 0.496 g, 2.90 mmol) was then added rapidly dropwise. The ice bath was removed, the flask was wrapped in aluminum foil, and the reaction mixture was stirred at 25 °C for 17 h and then partitioned between 10 mL of saturated aq NH_4Cl and 10 mL of diethyl ether. The organic layer was separated and washed with 10 mL of water, and the combined aqueous phases were extracted with 10 mL of diethyl ether. The combined organic phases were washed with 8 mL of brine, dried over $MgSO_4$, filtered, and concentrated to give 0.402 g of an orange oil. Column chromatography on 25 g of silica gel (gradient elution with 2.5−5% ethyl acetate−hexane) afforded 0.192 g (86%) of cyclobutanone **34** (contaminated with ca. 8% of *O*-alkylation product): IR (film) 3060, 3030, 2960, 2920, 2860, 1775, 1600, and 1580 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.66 (dd, J = 8.2, 2.0 Hz, 2 H), 7.22−7.34 (m, 6 H), 7.10 (dd, J = 8.1, 2.0 Hz, 2 H), 5.88 (s, 2 H), 3.63 (dd, J = 8.2, 1.3 Hz, 1 H), 3.10 (d, J = 13.8 Hz, 1 H), 2.97 (d, J = 13.8 Hz, 1 H), 2.93 (ddd, J = 9.7, 8.0, 1.6 Hz, 1 H), 2.66 (ddd, J = 18.1, 3.1, 1.7 Hz, 1 H), and 2.29 (ddd, J = 18.1, 10.2, 2.1

(42) Jeffs, P. W.; Molina, G.; Cass, M. W.; Cortese, N. A. *J. Org. Chem.* **1982**, *47*, 3871.

Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.8, 136.2, 135.1, 134.6, 131.8, 130.1, 129.4, 128.9, 128.5, 128.0, 127.0, 74.9, 59.3, 48.3, 41.5, and 34.6.

7-(Phenylmethyl)bicyclo[3.2.0]hept-2-en-6-one (36a, 36b). A 10-mL, one-necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with sulfide **33** (0.159 g, 0.519 mmol) and 4.5 mL of toluene. The flask was fitted with a reflux condenser and heated at reflux while a solution of tributyltin hydride (0.167 mL, 0.181 g, 0.621 mmol) and AIBN (0.009 g, 0.055 mmol) in 2.5 mL of toluene was added dropwise (through the reflux condenser) over 35 min. After 20 min, the reaction mixture was cooled to 25 °C and concentrated to afford 0.344 g of a colorless oil. Column chromatography on 35 g of silica gel and then again on 10 g of silica gel (gradient elution with 2.5−5% ethyl acetate−hexane) provided 0.089 g (87%) of cyclobutanones **36a** and **36b** (88:12 by ^{1}H NMR analysis): For **36a**: IR (film) 3080, 3060, 3020, 2940, 2910, 2840, 1770, and 1600 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27−7.32 (m, 2 H), 7.17−7.24 (m, 3 H), 5.91−5.92 (m, 1 H), 5.74−5.79 (m, 1 H), 3.75−3.85 (m, 2 H), 3.59−3.66 (m, 1 H), 2.94 (dd, J = 14.7, 5.0 Hz, 1 H), 2.63−2.72 (m, 1 H), 2.67 (dd, J = ∼15, 5 Hz, 1 H), and 2.41 (dddd, J = 17.1, 6.8, 3.9, 2.0 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.3, 139.5, 135.1, 129.5, 128.5, 128.3, 126.1, 65.5, 59.4, 42.5, 34.1, and 30.6.

2-(Phenylsulfinyl)spiro[3.5]nonan-1-one (37). Procedure A: *m*-CPBA Oxidation. A 25-mL, two-necked, round-bottomed flask equipped with an argon inlet adapter and a rubber septum was charged with sulfide **8** (0.101 g, 0.410 mmol) and 5 mL of dichloromethane and cooled at 0 °C while a solution of *m*-CPBA (85%, 0.083 g, 0.409 mmol) in 3 mL of dichloromethane was added dropwise by syringe over 8 min. The reaction mixture was stirred at 0 °C for 70 min and was then partitioned between 40 mL of diethyl ether and 10 mL of 10% aqueous Na_2SO_3. The organic phase was separated and washed with two 10-mL portions of saturated aqueous $NaHCO_3$ and 10 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 0.110 g of a light brown oil. Column chromatography on 10 g of silica gel (gradient elution with 20−30% ethyl acetate−hexane) gave 0.095 g (88%) of sulfoxide **37** as a colorless oil (60:40 mixture of diastereomers by ^{1}H NMR analysis): IR (film) 3040, 2920, 2840, 2220, and 1770 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72−7.75 (m, 2 H), 7.63−7.67 (m, 2 H), 7.50−7.57 (m, 6 H), 4.03 (app t, J = 2.4 Hz, 1 H), 3.66 (dd, J = 4.5, 2.3 Hz, 1 H), 3.08 (dd, J = 17.1, 2.0 Hz, 1H), 2.97 (dd, J = 17.5, 1.1 Hz, 1H), 2.82 (ddd, J = 17.5, 3.0, 1.4 Hz, 1 H), 2.76 (dd, J = 17.2, 4.6 Hz, 1 H), 2.22−2.29 (m, 2 H), 2.05−2.12 (m, 1 H), and 1.26−2.01 (m, 17 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.6, 197.3, 142.7, 141.6, 131.6, 131.3, 129.2, 129.1, 125.0, 124.7, 87.0, 84.5, 58.9, 55.9, 39.1, 38.1, 38.0, 37.1, 32.2, 25.3, 25.1, 23.8, 23.5, and 22.9. Anal. Calcd for $C_{15}H_{18}O_2S$: C, 68.67; H, 6.92. Found: C, 68.71; H, 7.01. **Procedure B: $NaIO_4$ Oxidation.** A 10-mL, one-necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with sodium periodate (0.125 g, 0.584 mmol) and 1.25 mL of water and cooled at 0 °C while a solution of sulfide **8** (0.096 g, 0.390 mmol) in 1.25 mL of methanol was added dropwise via cannula. The resulting cloudy white reaction mixture was stirred at 0 °C for 30 min and then at 25 °C for 26 h. The resulting mixture was partitioned between 10 mL of dichloromethane and 10 mL of water, and the aqueous phase was separated and extracted with three 10-mL portions of dichloromethane. The combined organic phases were dried over $MgSO_4$, filtered, and concentrated to afford 0.109 g of a yellow oil. Column chromatography on 10 g of silica gel (gradient elution with 20−30% ethyl acetate−hexane) yielded 0.078 g (76%) of sulfoxide **37** as an off-white solid, mp 78−83 °C (60:40 mixture of diastereomers by ^{1}H NMR analysis).

2-Acetoxy-2-(phenylthio)spiro[3.5]nonan-1-one (38). A 10-mL, one-necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with a solution of sulfoxide **37** (0.091 g, 0.35 mmol) in 3 mL of toluene. Acetic anhydride (0.164 mL, 0.177 g, 1.74 mmol) and *p*-toluenesulfonic acid (0.002 g, 0.001 mmol) were added, and the flask was fitted with a reflux condenser and heated at reflux for 1 h. The resulting mixture was cooled to 25 °C and concentrated to afford 0.113 g of an oil. Column chromatography on 6 g of silica gel (gradient elution with 5−10% ethyl acetate−hexane) provided 0.094 g (89%) of α-acetoxy sulfide **38** as a colorless oil: IR (film) 3040, 3000, 2920, 2840, 1780, and 1745 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29−7.44 (m, 5 H), 3.27 (d, J = 16.5 Hz, 1 H), 2.71 (d, J = 16.5 Hz, 1 H), 2.13−2.21 (m, 2 H), 2.11 (s, 3 H), 1.67−1.84 (m, 3 H), 1.43−1.45 (m, 2 H), and 1.18−1.33 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.9, 168.6, 135.1, 129.3, 129.2, 128.9, 98.4, 49.8, 44.2, 32.6, 30.5, 25.3, 24.0, 22.5, and 21.2.

Lactone 39. A 10-mL, one-necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with α-thiocyclobutanone **8** (0.060 g, 0.244 mmol), 3 mL of methanol, and then 30% aq hydrogen peroxide (0.110 mL, 0.033 g, 0.970 mmol). The reaction mixture was stirred at 25 °C for 23 h and then partitioned between 8 mL of dichloromethane and 8 mL of water. The aqueous phase was saturated with sodium chloride and extracted with three 8-mL portions of dichloromethane. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated to provide 0.068 g of an oil. Column chromatography on 30 g of silica gel (gradient elution with 5−10% ethyl acetate−hexane) afforded 0.046 g (72%) of **39** as a colorless oil: IR (film) 3020, 2900, 2820, and 1760 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53−7.56 (m, 2 H), 7.29−7.36 (m, 3 H), 5.49 (s, 1 H), 2.62 (d, J = 17.1 Hz, 1 H), 2.38 (d, J = 17.6 Hz, 1 H), and 1.34−1.70 (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.2, 132.9, 132.5, 129.2, 128.1, 96.6, 44.9, 40.0, 34.9, 31.6, 25.4, 22.7, and 22.7.

2-(Phenylthio)-2′-carbethoxyspiro[4.5]decan-1-one (40a, 40b). A 10-mL, two-necked, round-bottomed flask equipped with an argon inlet adapter and rubber septum was charged with cyclobutanone **8** (0.048 g, 0.195 mmol) and 0.750 mL of diethyl ether and was cooled at 0 °C while boron trifluoride etherate (0.048 mL, 0.055 g, 0.390 mmol) was added in one portion. To the resulting mixture was then added dropwise over 10 min a solution of ethyl diazoacetate (0.041 mL, 0.044 g, 0.390 mmol) in 1.25 mL of diethyl ether by syringe down the side of the flask (so that it would be cooled before contact with the reaction mixture). The reaction mixture was stirred at 0 °C for 1.5 h and then diluted with 5 mL of diethyl ether and washed with 3-mL portions of saturated aqueous $NaHCO_3$, water, and then brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated to provide 0.062 g of a yellow oil. Column chromatography on 6 g of silica gel (gradient elution with 5−10% ethyl acetate−hexane) afforded 0.043 g (66%) of cyclopentanones **40a** and **40b** (1:1 by ^{1}H NMR analysis): IR (film) 3040, 2960, 2910, 2840, 1750, 1720, and 1660 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44−7.49 (m, 4 H), 7.24−7.33 (m, 6 H), 4.16−4.27 (m, 4 H), 3.53 (dd, J = 9.6, 7.8 Hz, 1 H), 3.49 (s, 1 H), 3.48 (s, 1 H), 3.33 (app t, J = 9.5 Hz, 1 H), 2.47 (two dd, J = 13.5, 10.0 Hz, 2 H), 2.11 (dd, J = 13.6, 8.0 Hz, 1 H), 2.06 (dd, J = 14.4, 9.5 Hz, 1 H), 1.20−1.85 (m, 20 H), 1.29 (app t, J = 7.7 Hz, 3 H), and 1.28 (app t, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.0, 202.5, 169.6, 168.8, 134.3, 133.4, 132.3, 131.9, 129.0, 128.8, 128.1, 127.5, 66.2, 62.2, 61.6, 61.5, 50.4, 50.3, 42.0, 41.3, 36.6, 36.4, 34.0, 33.0, 31.1, 25.6, 25.4, 22.2, 22.1, 14.2, and 14.1.

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Supporting Information Available: ^{1}H NMR spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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