Cyclopentene Synthesis from 1,3-Dienes via Base-Induced Ring Contraction of 3,6-Dihydro-2*H*-thiopyrans: Studies on Diastereoselection and Mechanism

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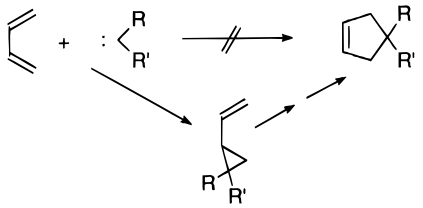
An investigation of the scope and mechanism of a new synthesis of cyclopentenes from 3,6-dihydro-2*H*-thiopyrans is described. Alkyl halides substituted with an electron-withdrawing group in the α-position were reacted with sodium thiosulfate, yielding the corresponding Bunte salts, which could be transformed to reactive thiocarbonyl compounds by elimination of the elements of bisulfite with mild base treatment. *In situ* trapping by 1,3-dienes afforded in good yields a variety of 3,6-dihydro-2*H*-thiopyrans substituted with electron-withdrawing groups at the 2-position. Exposure of these cycloadducts to strong base at low temperature effected a novel ring contraction, affording 2-(methylthio)-3-cyclopentenes after quenching with methyl iodide. The level of diastereoselectivity exhibited during the generation of these cyclopentenes was found to be dependent on the nature of the electron-withdrawing group at the 2-position of the dihydrothiopyran as well as the substitution pattern originally present in the diene component. In some cases, reducing the temperature during the ring contraction resulted in the isolation of good yields of vinyl cyclopropanes of high isomeric purity. With one substrate, highly diastereoselective rearrangement of a vinyl cyclopropane to a cyclopentene was unambiguously demonstrated, suggesting that this might be a key feature of the overall ring contraction mechanism.

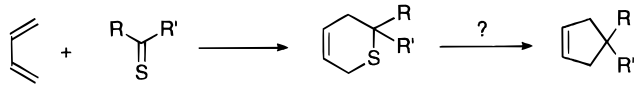
Introduction

The ubiquity with which cyclopentanoid rings are encountered in natural products continues to foster interest in stereoselective methods for their generation.[2] One strategy which has received relatively little attention is the transformation of 1,3-dienes to cyclopentenes.[2e,3] This approach is particularly appealing, considering the ready availability of conjugated dienes and the potential for translating diene geometry into product stereochemistry in a manner analogous to the enormously successful Diels−Alder reaction. In principle, this construction could be achieved directly by a [4 + 1] cycloaddition of a carbene to a 1,3-diene, ideally in a completely stereospecific fashion (Scheme 1). In practice, however, the desired outcome is typically foiled by the well-known propensity for carbenes to add exclusively to only one of the olefins, yielding vinyl cyclopropanes.[3f] Conversion to the target cyclopentenes then requires a rearrangement step by one of several possible means: direct thermolysis, chemical catalysis, or anionic acceleration (Scheme 1).[3,4]

Scheme 1



Scheme 2



A number of years ago, we were intrigued by the possibility of converting 3,6-dihydro-2*H*-thiopyrans, readily available by the hetero-Diels−Alder cycloaddition of thiocarbonyl compounds with 1,3-dienes,[5] into cyclopentenes (Scheme 2). The potential lability of the two carbon−sulfur bonds within the six-membered ring suggested that a net extrusion of sulfur might be feasible, resulting in an overall ring contraction to cyclopentenes.

The inspiration to employ base to effect this transformation was provided by ample literature precedent for

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(2) (a) Ramaiah, M. *Synthesis* **1984**, 529. (b) Paquette, L. A. *Top. Curr. Chem.* **1984**, *119*, 1. (c) Hudlicky, T.; Price, J. D. *Chem. Rev.* **1989**, *89*, 1467. (d) Ejiri, S.; Yamago, S.; Nakamura, E. *J. Am. Chem. Soc.* **1992**, *114*, 8707 and references cited therein. (e) Padwa, A.; Filipkowski, M. A.; Meske, M.; Murphree, S. S.; Watterson, S. H.; Ni, Z. *J. Org. Chem.* **1994**, *59*, 588 and references cited therein.

(3) (a) Corey, E. J.; Walinsky, S. W. *J. Am. Chem. Soc.* **1972**, *94*, 8932. (b) Negishi, E.-I.; Brown, H. C. *Synthesis* **1974**, 77. (c) Hudlicky, T.; Kosyck, F. J.; Kutchan, T. M.; Sheth, J. P. *J. Org. Chem.* **1980**, *45*, 5020. (d) Danheiser, R. L.; Martinez-Davila, D.; Auchus, R. J.; Kadonaga, J. T. *J. Am. Chem. Soc.* **1981**, *103*, 2443. (e) Danheiser, R. L.; Bronson, J. J.; Okano, K. *J. Am. Chem. Soc.* **1985**, *107*, 4579. (f) Jenneskens, L. W.; de Wolf, W. H.; Bickelhaupt, F. *Angew. Chem., Int. Ed.* **1985**, *24*, 585. (g) Xiong, H.; Rieke, R. D. *J. Am. Chem. Soc.* **1992**, *114*, 4415. (h) Shono, T.; Ishifune, M.; Kinugasa, H.; Kashimura, S. *J. Org. Chem.* **1992**, *57*, 5561.

(4) (a) Hudlicky, T.; Kutchan, T. M.; Naqvi, S. M. *Org. React.* **1985**, *33*, 247. (b) Kulinkovich, O. G. *Russ. Chem. Rev.* **1993**, *62*, 839.

(5) (a) Weinreb, S. M.; Staib, R. R. *Tetrahedron* **1982**, *38*, 3087. (b) Metzner, P. *Synthesis* **1992**, 1185. (c) Bryce, M. R.; Becher, J.; Falt-Hansen, B. In *Advances in Heterocyclic Chemistry*; Academic Press: New York, 1992; Vol. 55, p 1.

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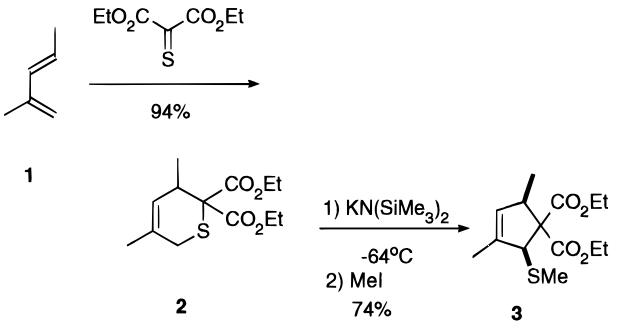
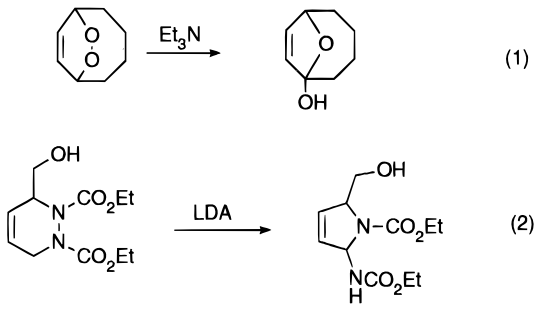
Scheme 3



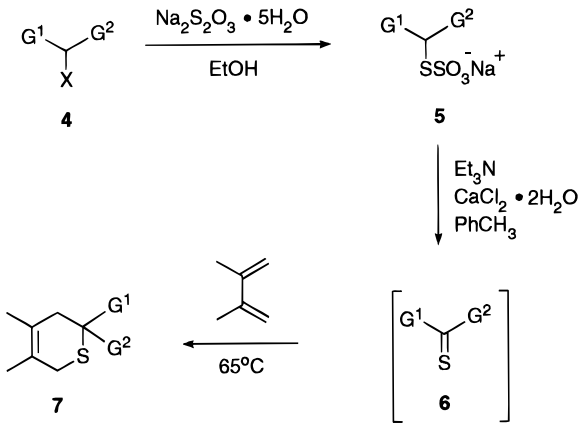
the contraction of six-membered heterocycles to five-membered heterocycles under various basic conditions.[6] Two examples are illustrated in eqs 1[6b] and 2.[6d] Presumably these reactions entail initial allylic proton abstraction from the carbon adjacent to one of the heteroatoms with concomitant E2 elimination of the other heteroatom, thereby cleaving the heteroatom−heteroatom bond. The resulting carbon−heteroatom double bond is then attacked intramolecularly by the eliminated heteroatom, giving rise to the observed products.



It seemed plausible that a similar outcome might be expected upon exposure of 3,6-dihydro-2*H*-thiopyrans to strong base, provided that the 2-position was fully substituted to block deprotonation at that site, and at least one of the 2-substituents was a suitable carbanion-stabilizing group. In fact, as reported by us in an earlier communication,[7] this approach was successfully applied to a series of diethyl 3,6-dihydro-2*H*-thiopyran-2,2-dicarboxylates, affording diethyl 2-(methylthio)-3-cyclopentene-1,1-dicarboxylates in excellent yields and with good diastereoselectivity following quenching with methyl iodide. A representative example is presented in Scheme 3, wherein 2-methyl-1,3-pentadiene (**1**) is converted in a stereoselective fashion to the *cis*-cyclopentene **3** (16:1 *cis*:*trans*) via the dihydrothiopyran **2**.[7] This was, to the best of our knowledge, the first reported example of this type of ring contraction to involve the apparent intermediacy of a carbanion.

The following report details studies aimed at expanding the scope of this methodology by the utilization of alternate potential carbanion-stabilizing groups at C-2 of the 3,6-dihydro-2*H*-thiopyran cycloadducts. In those cases where C-2 was unsymmetrically substituted, a

Scheme 4



systematic investigation of the diastereoselectivity of the rearrangement was undertaken, in particular its dependence on the steric and electronic nature of the C-2 substitution. In addition, we describe experiments designed to provide insight into the mechanism of this interesting ring contraction.

Results and Discussion

Synthesis of 3,6-Dihydro-2*H*-thiopyrans. The preparation of dihydrothiopyrans with varying substitution at C-2 was primarily achieved via hetero-Diels−Alder reaction of various thiocarbonyls with 2,3-dimethylbutadiene. This particular diene was chosen for its relatively high level of reactivity and the fact that the corresponding cycloadducts would lack chirality at C-3, greatly facilitating the determination of diastereomer ratios of the final cyclopentenes.

Thiocarbonyl generation and hetero-Diels−Alder reaction were effected by a modification of the Kirby protocol[8] which we had employed in our earlier work.[7] Various halides **4** were reacted with sodium thiosulfate in aqueous ethanol until conversion to the corresponding Bunte salts **5** was complete, as indicated by TLC analysis (Scheme 4). No attempt was made to isolate the individual Bunte salts. Rather, the crude reaction mixtures were simply diluted with diene and then subjected to slow addition of triethylamine, resulting in smooth thioketone **6** production and subsequent cycloaddition to afford 3,6-dihydro-2*H*-thiopyrans **7**.[9,10] Results are summarized in Table 1. The unoptimized yields varied quite dramatically depending on the halide substrate employed, but any dearth in efficiency was compensated for by the ease with which each reaction could be performed on multigram scale.

In some cases this procedure failed to give useful amounts of the desired cycloadducts (entries 2, 13), so alternative preparations had to be devised. Carboxamide **7m** was prepared from ester **7a** by sequential saponification, acid chloride formation, and addition of dimethyl-

(6) (a) Firl, J.; Kresze, G. *Chem. Ber.* **1966**, *99*, 3695. (b) Kayama, Y.; Oda, M.; Kitahara, Y. *Chem. Lett.* **1974**, 345. (c) Consonni, P.; Favara, D.; Omodei-Sale, A.; Bartolini, G.; Ricci, A. *J. Chem. Soc., Perkin Trans. 2* **1983**, 967. (d) Forrest, A. K.; Schmidt, R. R. *Tetrahedron Lett.* **1984**, *25*, 1769. (e) Jager, U.; Sundermeyer, W. *Chem. Ber.* **1986**, *119*, 3405. (f) Bell, S. I.; Parvez, M.; Weinreb, S. M. *J. Org. Chem.* **1991**, *56*, 373. (g) Desai, M. C.; Doty, J. L.; Stephens, L. M.; Brighty, K. E. *Tetrahedron Lett.* **1993**, *34*, 961.

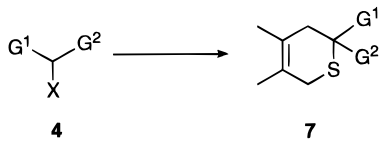
(7) Larsen, S. D. *J. Am. Chem. Soc.* **1988**, *110*, 5932.

(8) (a) Kirby, G. W.; Lochead, A. W. *J. Chem. Soc., Chem. Commun.* **1983**, 1325. (b) Kirby, G. W.; Lochead, A. W.; Sheldrake, G. N. *J. Chem. Soc., Chem. Commun.* **1984**, 922, 1469. (c) Kirby, G. W.; McGregor, W. M. *J. Chem. Soc., Perkin Trans. 1* **1990**, 3175.

(9) For closely related thioketone generations and [4 + 2] cycloadditions see: (a) Abelman, M. M. *Tetrahedron Lett.* **1991**, *32*, 7389. (b) Pinto, I. L.; Buckle, D. R.; Rami, H. K.; Smith, D. G. *Tetrahedron Lett.* **1992**, *33*, 7597. (c) Capozzi, G.; Menichetti, S.; Nativi, C.; Rosi, A. *Tetrahedron* **1992**, *48*, 9023.

(10) There are now numerous methods to generate thiocarbonyl compounds. For a recent review see: McGregor, W. M.; Sherrington, D. C. *Chem. Soc. Rev.* **1993**, *22*, 199.

Table 1. Synthesis of Dihydrothiopyrans 7 (Scheme 4)

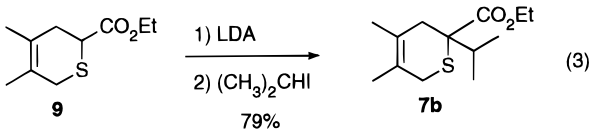


4 7

	reactant			product	
entry	G^1	G^2	X	no.	yield (%)
1	CO_2Et	CH_3	Br	**7a**	75
2	CO_2Et	i-Pr	Br	**7b**	15
3	CO_2t-Bu	CH_3	Br	**7c**	48
4	CO_2Et	Ph	Br	**7d**	86
5	-$CO_2CH_2CH_2$-		Br	**7e**	63
6	PhCO	CH_3	Br	**7f**	30
7	*p*-F-PhCO	CH_3	Cl	**7g**	35
8[a]	*p*-CF_3-PhCO	CH_3	Br	**7h**	68
9[a]	*p*-MeO-PhCO	CH_3	Br	**7i**	12
10	PhCO	Ph	Cl	**7j**	77
11	CN	CH_3	Br	**7k**	50
12	9-fluorenylidene		Br	**7l**	66
13	$CONMe_2$	CH_3	Br	**7m**	0

[a] Bromide prepared as in ref 21.

amine (Scheme 5). The hindered ester **7b** was most efficiently obtained by direct alkylation[11] of the known cycloadduct **9** with isopropyl iodide (eq 3).

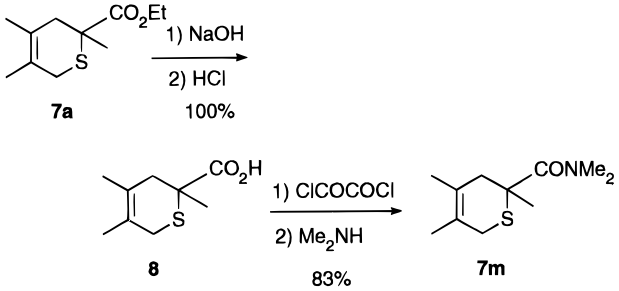


9 7b (3)

A small set of dihydrothiopyrans derived from other dienes was also created in order to evaluate the effect of diene substitution on the diastereoselectivity of the final ring contraction (Table 2). In each of these cases, ethyl 2-bromopropionate was employed as the thiocarbonyl precursor, yielding the corresponding ethyl 2-methyl-3,6-dihydro-2*H*-thiopyran-2-carboxylates **10**. Disappointingly, the level of regioselectivity in these hetero-Diels–Alder reactions was less than what we had observed with diethyl thioxomalonate.[7] Furthermore, cycloaddition of 2-methyl-1,3-pentadiene (entry 4) proceeded without significant endo selectivity, giving the major product **10f** as a 1:1 mixture of diastereomers. This was not of immediate concern, however, since it was anticipated that stereochemical integrity at C-2 would be lost in the ensuing rearrangement anyway.

Base-induced Ring Contractions of 3,6-Dihydro-2*H*-thiopyrans to Cyclopentenes. In our previous communication we described the ring contraction of dihydrothiopyran **7a**.[7] Exposure of **7a** to lithium diisopropylamide (LDA)/hexamethylphosphoramide (HMPA)[12] in THF at −78 °C followed by warming to 0 °C and quenching with methyl iodide afforded cyclopentenes **11a** and **12a** in 87% yield as an 8:1 mixture of diastereomers, respectively (Table 3, entry 1). The above protocol was used effectively in most of the examples illustrated in Table 3. In some cases, the alternate base, potassium bis(trimethylsilyl)amide (KBA), proved to be more efficient. Diastereomer assignments were made based on one of the following criteria: (1) single crystal x-ray analysis; (2) NOE analysis; or (3) analogy of the proton spectrum with one or more of the compounds assigned by X-ray or NOE.[13] A key distinguishing feature of the proton NMR spectra of these cyclopentenes is the chemical shift of the C-2 methine proton adjacent to the methylthio group. In the major diastereomer **11** this proton consistently appears 0.5−0.8 ppm downfield from the corresponding methine proton within the minor isomer **12**. This is likely a manifestation of the "syn-upfield rule" whereby protons syn to a vicinal substituent are shielded relative to the corresponding anti protons.[14] This effect has been noted to be particularly large when the vicinal substituent is methyl, and an *opposite* effect has been noted with vicinal carboxyl groups. It is thus entirely consistent that diastereomer **12**, in which the methine proton is syn to the methyl group and anti to the carboxyl group, should be characterized by the substantially upfield signal of its methine proton.

Scheme 5



7a 100% 8 83% 7m

The influence (or lack thereof) of the steric and electronic attributes of groups G^1 and G^2 on the stereochemical outcome of the rearrangement is evident from the results summarized in the Table. Entries 1−3 illustrate that the steric nature alone of either the alkyl group or the ester group at C-2 of the dihydrothiopyran had little effect on the product diastereomer ratio. However, replacing the C-2 alkyl group with either a phenyl group or a methylthio group drastically reduced the diastereoselectivity of the rearrangement, although the major isomers in each case retained the same relative stereochemistry (entries 4 and 5). Surprisingly, replacement of the methyl group of **7f** with a phenyl group (**7j**, entry 12) effected a large *increase* in diastereoselectivity and in the *opposite direction*. In this case, **12j** was the only product detected in the crude reaction mixture.[13] A significant amplification of the diastereoselectivity was also observed with the rigid spirolactone **7e** (entry 6), which rearranged almost exclusively to *trans*-spirolactone **11e**. Entries 8−11 summarize experiments designed to examine what impact the electron-withdrawing ability of G^1 might have independent of steric factors. In these cases, it was necessary to employ KBA as base to achieve uniformly good yields. Although this resulted in significant erosion of the diastereoselectivity in the rearrangement of dihydrothiopyran **7f** (entry 7 vs 8), it was nevertheless sufficient to illustrate the complete lack of

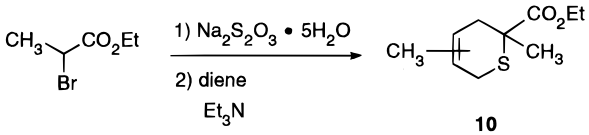
(11) Kirby, G. W.; Mahajan, M. P.; Rahman, M. S. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2033.

(12) *HMPA is now considered to be a highly dangerous carcinogen!* We have recently observed that *N*,*N*′-dimethyl-*N*,*N*′-propyleneurea (DMPU) may be substituted for HMPA in several of the reactions described herein with little or no loss of stereoselectivity. Mukhopadhyay, T.; Seebach, D. *Helv. Chim. Acta* **1982**, *65*, 385.

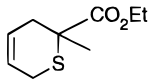
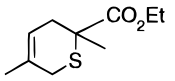
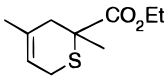
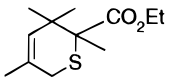
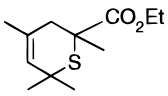
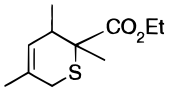
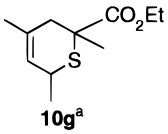
(13) ORTEP diagrams for structures **12j**, **12m**, and **21** and NOE analyses of structures **11a**, **11d**, **12d**, **12f**, **13b**, **13c**, **14b**, **14c**, **18m**, **19**, and **20** are provided in the supporting information. The full X-ray data will also be included in a separate manuscript: Watt, W.; Fisher, P. V.; Larsen, S. D. *Acta Cryst. Sect. B* **1996**, submitted for publication. The author has deposited atomic coordinates for these structures with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

(14) Anteunis, M.; Danneels, D. *Org. Magn. Reson.* **1975**, *7*, 345.

Table 2. Synthesis of Dihydrothiopyrans 10

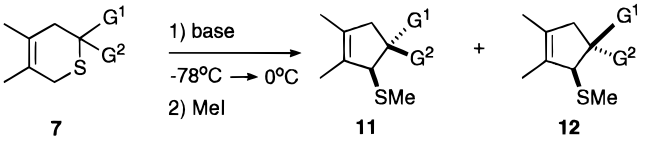


10

entry	diene	product(s)	(ratio)	yield (%)
1		 **10a**		33
2		 **10b**  **10c**	(3:2)	68
3		 **10d**  **10e**	(4:1)	15
4		 **10f**[a]  **10g**[a]	(9:1)	65

[a]Isolated as a 1:1 mixture of diastereomers

Table 3. Ring Contraction of Dihydrothiopyrans 7



7 **11** **12**

	reactant				product(s)		
entry	no.	G^1	G^2	conditions[a]	no.	ratio[b]	yield (%)
1	**7a**	CO_2Et	CH_3	A	**11a/12a**	8:1	87
2	**7b**	CO_2Et	i-Pr	A	**11b/12b**	8.5:1	84
3	**7c**	CO_2t-Bu	CH_3	A	**11c/12c**	8:1	95
4	**7d**	CO_2Et	Ph	A	**11d/12d**	2:1	93
5	**7w**[c]	CO_2Et	SMe	A	**11w/12w**	2:1	61
6	**7e**	$-CO_2CH_2CH_2-$		A	**11e**	>15:1	71
7	**7f**	PhCO	CH_3	A	**11f/12f**	10:1	63
8	**7f**	PhCO	CH_3	B	**11f/12f**	2.5:1	75
9	**7g**	*p*-F-PhCO	CH_3	B	**11g/12g**	2.5:1	69
10	**7h**	*p*-CF_3-PhCO	CH_3	B	**11h/12h**	2.5:1	72
11	**7i**	*p*-MeO-PhCO	CH_3	B	**11i/12i**	2.5:1	83
12	**7j**	PhCO	Ph	A	**12j**	<1:20	93
13	**7k**	CN	CH_3	A			0

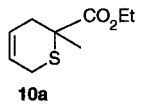
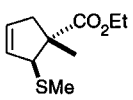
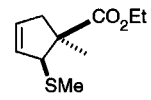
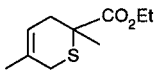
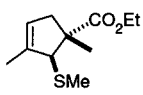
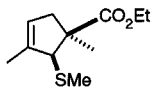
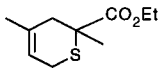
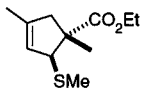
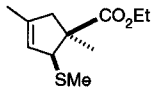
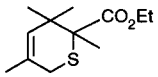
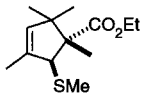
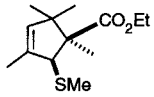
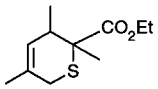
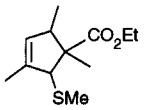
[a] Condition A: LDA/HMPA, −78 °C → 0 °C; B: KBA/18-crown-6, −78 °C → 0 °C. [b] Ratio of **11**:**12** determined by ^{1}H NMR integration of signals in crude product mixtures. [c] Prepared as in reference 20.

effect which the para substituent on the aromatic ring had on the outcome of the rearrangement. The final entry in Table 3 indicates that the scope of this methodology could not be expanded to include the use of nitriles as the carbanion-stabilizing group.

Table 4 summarizes the disappointing results obtained upon rearrangement of the variously substituted ethyl 2-methyl-3,6-dihydro-2*H*-thiopyran-2-carboxylates **10** from Table 2. The totally unsubstituted dihydrothiopyran **10a** (entry 1) underwent ring contraction in a less diastereoselective fashion than did the corresponding 4,5-dimethyl analog **7a** (Table 3). Also, introduction of two methyl groups at C-3 of the dihydrothiopyran (**10d**, entry 3) completely abolished the diastereoselectivity of the ring contraction. The results within entry 2 are intriguing and may provide insight into the mechanism of the rearrangement. When the inseparable mixture of isoprene cycloadducts **10b** and **10c** was subjected to base, the individual regioisomers underwent ring contraction with differing levels of diastereoselectivity. The 4-methyl isomer **10c** was clearly more selective in its transformation to the *trans* cyclopentene diastereomer than was the 5-methyl isomer **10b**.[15] The 3,5-dimethyl isomer **10f** was completely nonselective during the ring contraction, affording a nearly statistical mixture of all four possible diastereomeric cyclopentenes **13f** (entry 4). This last

(15) Regioisomer assignments for the mixture of isomers were made based on NOE analysis (see supporting information). Diastereomer assignments were made based on the relative chemical shifts of the C-2 methine protons (vide supra).

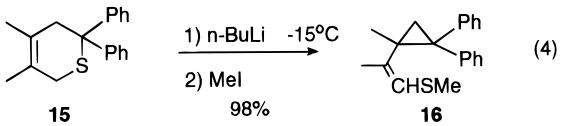
Table 4. Ring Contraction[a] of Dihydrothiopyrans 10

entry	substrate	product(s)	(ratio)	yield (%)
1	 **10a**	 **13a**  **14a**	(3:1)	43[f]
2[b]	 **10b**	 **13b**  **14b**	(2:1)	82[c]
	 **10c**	 **13c**  **14c**	(7:1)	
3	 **10d**	 **13d**  **14d**	(1:1)	78
4[d]	 **10f**	 **13f**	(2:2:2:1)[e]	55

[a]All reactions were effected under conditions A in Table 3; entries 1 and 2 were warmed to 25°C before MeI quench. [b]The inseparable regioisomers **10b** and **10c** were reacted as a mixture. [c]Combined yield of all isomers. [d]**10f** was reacted as a 1:1 mixture of diastereomers. [e]The minor isomer was assigned as 1,2-*trans*-1,5-*cis*. [f]Also isolated was 5% of an 8:1 mixture of vinyl cyclopropanes **19** and **20** (eq 7).

result was particularly disappointing in light of the high degree of diastereoselectivity observed previously during the rearrangement of the related dihydrothiopyran malonate **2** (Scheme 3).

Base-induced Ring Contractions of 3,6-Dihydro-2*H*-thiopyrans to Vinyl Cyclopropanes. In 1970, Biellmann first reported the rearrangement of 4,5-dimethyl-2,2-diphenyl-3,6-dihydro-2*H*-thiopyran (**15**) to vinyl cyclopropane **16** following deprotonation with *n*-butyllithium at low temperature and subsequent quenching with methyl iodide (eq 4).[16]



15 **16** (4)

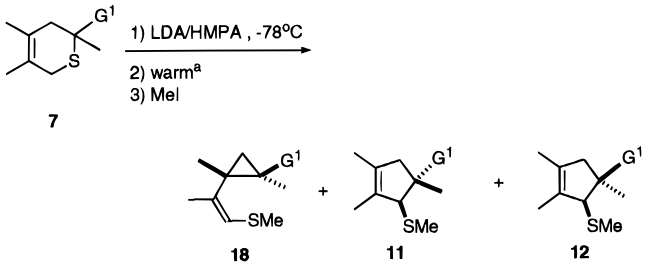
When we subjected Biellmann's substrate **15** to our LDA/HMPA protocol, we obtained a mixture of three- and five-membered rings, **16** and **17** (eq 5). Rather surprisingly, allowing our reaction to stir for prolonged periods at room temperature did *not* increase the proportion of cyclopentene **17**, suggesting that no equilibration of vinyl cyclopropane to five-membered ring was occurring. A dramatically different result was seen with the closely-related fluorenyl dihydrothiopyran **7l**[17] (eq 6), which rearranged entirely to cyclopentene **11l** under our conditions at or below 0 °C. It is tempting to speculate that the greater carbanion-stabilizing ability of the fluorenyl substitution at C-2 of **7l** relative to the simple diphenyl substitution of **15** was responsible for the complete conversion to five-membered ring product.

Three-membered ring product was also observed when the base-induced rearrangement of ester **7a** was carried out without warming above −45 °C, whereupon vinyl cyclopropane **18a** was the major product along with a 3:1 mixture of cyclopentenes **11a** and **12a** (Table 5, entry 1).[7] Under otherwise identical conditions, warming to 0 °C prior to the methyl iodide quench gave exclusively an 8:1 mixture of cyclopentenes **11a** and **12a** (entry 2), suggesting that here a vinyl cyclopropane might be an intermediate in the formation of the cyclopentenes. *Of particular interest was the observation that the mixture of diastereomeric cyclopentenes became enriched in the proportion of **11a** (from 3:1 to 8:1) when the reaction was warmed until no more cyclopropane was obtained.* A shift to cyclopentene products with enhanced diastereoselectivity upon warming was also noted with the dihydrothiopyran

(16) (a) Biellmann, J. F.; Ducep, J. B. *Tetrahedron Lett.* **1970**, 2899. (b) Biellmann, J. F.; Ducep, J. B.; Vicens, J. J. *Tetrahedron* **1976**, *32*, 1801. For related work see: (c) Reglier, M.; Julia, S. A. *Tetrahedron Lett.* **1983**, *24*, 2387. (d) Reglier, M.; Julia, S. A. *Tetrahedron Lett.* **1985**, *26*, 2319.

(17) Middleton, W. J. *J. Org. Chem.* **1965**, *30*, 1390.

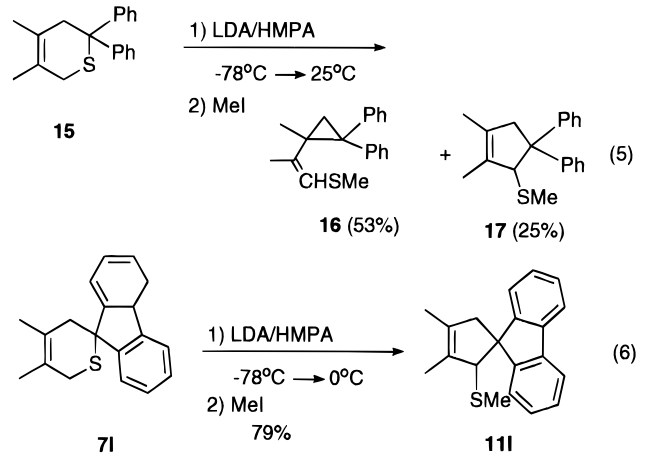
Table 5. Conversion of Dihydrothiopyrans 7 to Cyclopropanes 18 or Cyclopentenes 11 and 12



	reactant			product(s)		
entry	G^1	no.	conditions[a]	nos.	ratio	yield (%)
1	CO_2Et	**7a**	−45 °C, 10 min	**18a/11a/12a**	7/3/1	64
2	CO_2Et	**7a**	0 °C, 30 min	**18a/11a/12a**	0/8/1	87
3	$CONMe_2$	**7m**	0 °C, 30 min	**18m/11m/12m**	12/1/3	81
4	$CONMe_2$	**7m**	25 °C, 24 h	**18m/11m/12m**	1/14/3	88

[a] Reaction conditions prior to MeI quench.

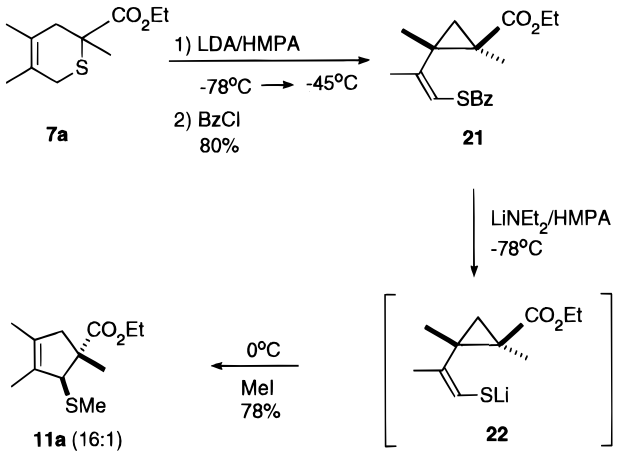
carboxamide **7m** (Table 5, entries 3 and 4). It is very interesting to note here that the vinyl cyclopropanes **18** in each case were isolated as a single diastereomer and olefin isomer.[13]



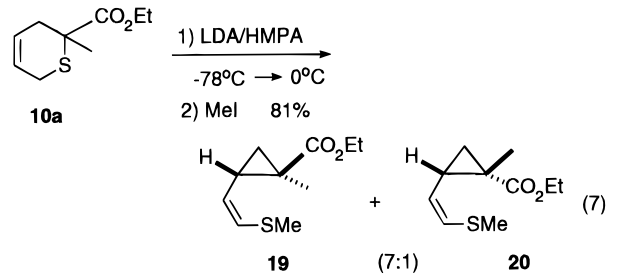
It is clear from the data presented in Table 5 that the rate at which the apparent vinyl cyclopropane to cyclopentene rearrangement occurs is dependent on the nature of the electron-withdrawing group G^1. Carboxamide **7m** afforded almost exclusively vinyl cyclopropane products under the same conditions (0 °C, 30 min) that ester **7a** was converted entirely to cyclopentenes (entries 2 and 3). Complete conversion of carboxamide **7m** to cyclopentenes required 24 h at 25 °C! We have also observed that the degree of methyl substitution on the dihydrothiopyran affects this rate. The simple dihydrothiopyran **10a**, bearing no methyl groups on the olefin, rearranged only to vinyl cyclopropanes **19** and **20** when the temperature was maintained at 0 °C (eq 7). The closely related 4,5-dimethyldihydrothiopyran **7a**, as mentioned above, gave entirely cyclopentenes under these conditions. Warming **10a** to 25 °C was required for complete conversion to cyclopentenes (Table 4, entry 1), suggesting that methyl substitution somehow facilitates this vinyl cyclopropane to cyclopentene rearrangement.

Mechanistic Studies. The results in Table 5 strongly suggested that the major diastereomeric cyclopentenes were arising largely via the stereoselective rearrangement of vinyl cyclopropanes. To support this mechanism,

Scheme 6



we designed an experiment to prove that the rearrangement in question was plausible. When the low temper-

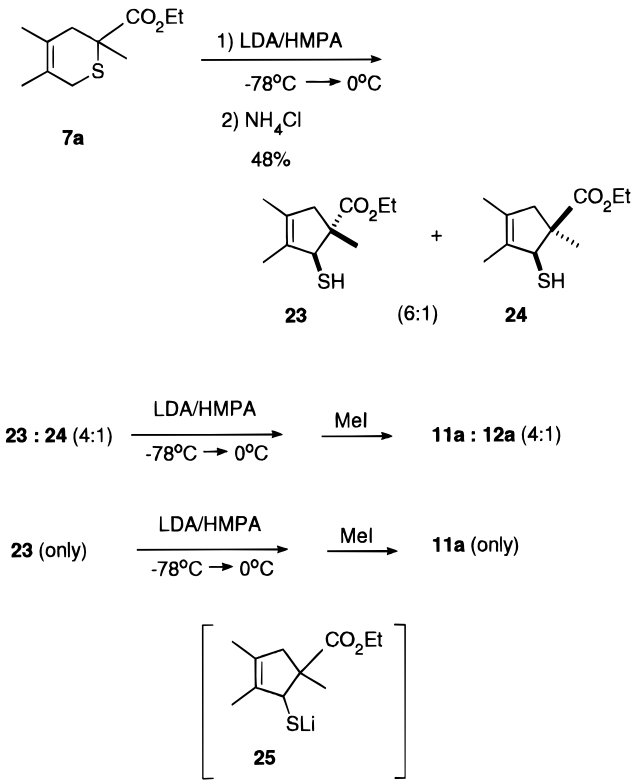


ature rearrangement protocol was carried out on dihydrothiopyran ester **7a** followed by quenching with benzoyl chloride instead of methyl iodide, benzoate **21** was isolated in 80% yield as a single isomer (Scheme 6). The relative configuration was unambiguously established by single crystal X-ray analysis.[13] It was anticipated that exposure of **21** to lithium dialkylamide base under conditions approximating that of the standard rearrangement protocol would result in cleavage of the thioester and subsequent release of lithio vinyl cyclopropane **22**. In the event, lithium diethylamide/HMPA addition at −78 °C followed by warming to 0 °C and quenching with methyl iodide provided cyclopentene **11a** in good yield and with excellent diastereoselectivity (Scheme 6). The high isomeric purity of the cyclopentene product obtained in this experiment is consistent with the isomeric enrichment seen in the previous experiments (Table 5) following the disappearance of vinyl cyclopropane.

One of the entries in Table 3 which displayed poor diastereoselectivity (entry 4) was examined further to determine if vinyl cyclopropane intermediate(s) could be identified. The temperature at which methyl iodide quenching was performed was steadily reduced until starting material began to be recovered (at −78 °C). At no point was vinyl cyclopropane ever detected, and the product cyclopentene was isolated as an unchanging 2:1 mixture of diastereomers, suggesting that this particular example might not proceed via a vinyl cyclopropane, perhaps accounting for the poor diastereoselectivity.

The evidence that vinyl cyclopropanes were equilibrating to cyclopentenes raised the question of whether the product cyclopentenes themselves might be capable of equilibrating, resulting in thermodynamic diastereomeric mixtures rather than kinetic ones. To address this question, mercaptans **23** and **24** were prepared by

Scheme 7

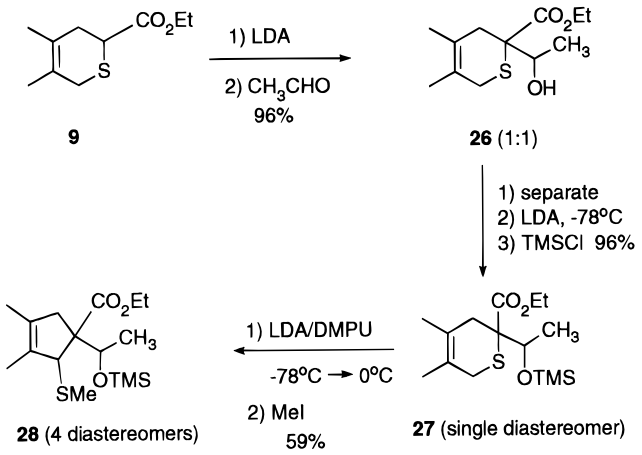


quenching the rearrangement of **7a** with ammonium chloride (Scheme 7). Resubmitting either a 4:1 mixture of **23**:**24** or pure **23** to the rearrangement conditions followed by quenching with methyl iodide gave, respectively, a 4:1 mixture of methylthio cyclopentenes **11a**:**12a** or only **11a**, establishing that equilibration of the intermediate lithio mercaptides **25** by a retro aldol-like process was not occurring.

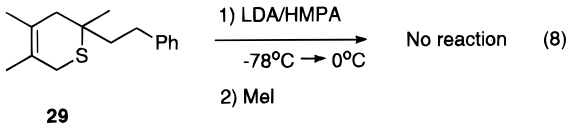
One other key mechanistic question was addressed in this study. It had been assumed that the initial event following deprotonation of the dihydrothiopyrans α to the sulfur was an E2-like elimination of a stabilized carbanion, evidence for which would be the loss of stereochemical integrity at the C-2 carbon. To establish that this was occurring, dihydrothiopyran **9** was condensed with acetaldehyde under standard aldol conditions to afford a 1:1 mixture of alcohols **26** (Scheme 8). Separation of the alcohols by flash chromatography followed by protection of the hydroxyl with TMSCl provided a single diastereomeric silyl ether **27**. If the relative stereochemistry between the two chiral centers of **27** were preserved during the ensuing base-induced rearrangement, only two possible diastereomeric cyclopentenes could be formed. In the event, subjecting **27** to the standard rearrangement conditions afforded cyclopentene **28** as a mixture of all four possible diastereomers, indicating that the ring contraction proceeded at least in part with stereochemical scrambling at C-2 of the dihydrothiopyran, thereby providing evidence for intermediate carbanion formation at that carbon.

One final piece of evidence supporting the necessity for generating a carbanion at C-2 of the dihydrothiopyran was provided by an attempted rearrangement of dihydrothiopyran **29**,[18] which lacks any carbanion-stabilizing

Scheme 8



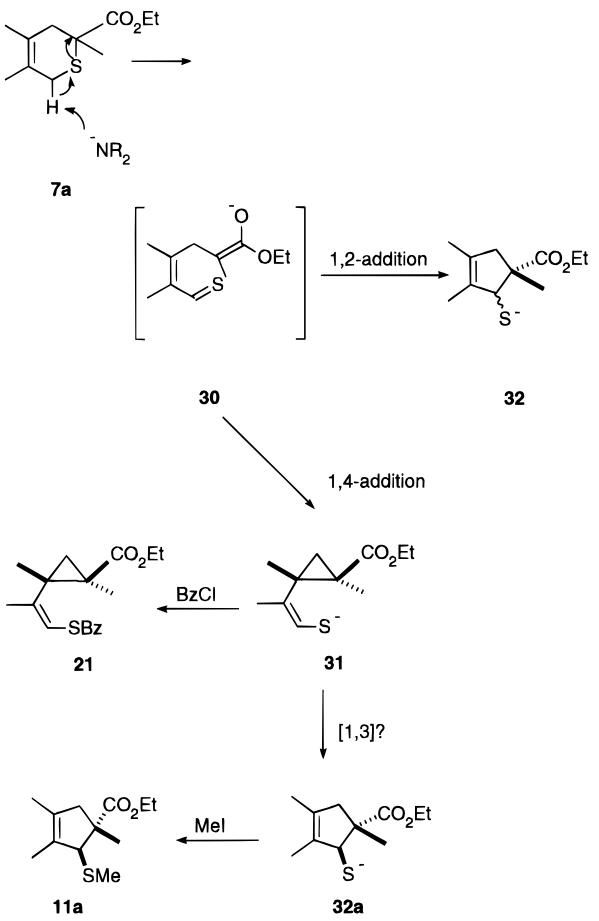
groups at C-2 (eq 8). Subjecting **29** to our standard conditions resulted only in recovery of unchanged starting material, suggesting that a concerted E2-like elimination of a carbanionic C-2 center might be a required first step in the rearrangement process.



Unfortunately, it is simply not possible to propose a mechanism for this novel base-induced rearrangement of 3,6-dihydro-2*H*-thiopyrans to vinyl cyclopropanes and cyclopentenes which accounts for all of the observations of this study. The data accumulated to this point, however, support a process which entails the following: (1) generation of an intermediate carbanion at C-2 of the dihydrothiopyran; (2) formation of a vinyl cyclopropane intermediate with at least some of the substrates; and (3) the rearrangement of a vinyl cyclopropane to a cyclopentene at low temperature. One plausible sequence is presented in Scheme 9 for the rearrangement of dihydrothiopyran **7a** since most of our data was gathered for this particular substrate. Proton abstraction at C-6 could be accompanied by rapid E2-elimination of a stabilized carbanion, cleaving the C-2−sulfur bond and forming a reactive thioaldehyde. This unstable intermediate would be expected to undergo a rapid intramolecular thioaldol condensation via either 1,2 or 1,4-addition of the incipient enolate to the thioaldehyde. To account for the formation of benzoate **21** (Scheme 6), the enolate would have to attack the thioaldehyde by a 1,4-addition via the conformer **30**, in which the unsaturated thioaldehyde remains in conjugation with the olefin in the cisoid conformation. Direct 1,2-addition to give cyclopentenes **32** would also be possible, particularly after rotation of the thiocarbonyl out of planarity with the olefin. The high degree of diastereoselectivity observed in the conversion of **21** to **11a** (Scheme 6) suggests a concerted anionic-accelerated [1,3]sigmatropic rearrangement of vinyl cyclopropane **31** to cyclopentene **32a**. Although the stereochemical outcome is *opposite* to what one would expect from a thermally allowed rearrangement,[19] anion-accelerated vinylcyclopropane rearrange-

(18) Degl'Innocenti, A.; Capperucci, A.; Mordini, A.; Reginato, G.; Ricci, A.; Cerreta, F. *Tetrahedron Lett.* **1993**, *34*, 873.
(19) Baldwin, J. E.; Bonacorsi, S., Jr. *J. Org. Chem.* **1994**, *59*, 7401.
(20) Vedejs, E.; Arnost, M. J.; Dolphin, J. M.; Eustache, J. *J. Org. Chem.* **1980**, *45*, 2601.
(21) Prepared by the method of Kajigaeshi, S.; Kakinami, T.; Okamoto, T.; Fujiisaki, S. *Bull. Chem. Soc.* **1987**, *60*, 1159. We found chloroform to be superior to the reported solvent, dichloromethane, for these preparations.

Scheme 9



ments have previously been reported that occur by "non-allowed" pathways.[3d]

The results presented in Table 5 imply that following the formation of **30** there is competitive 1,4 and 1,2-addition to the thioaldehyde, the former being highly diastereoselective and the latter much less so. The initially formed mixture of cyclopentenes **32**, formed by relatively nonselective 1,2-addition, is then enriched in the major diastereomer as the reaction is warmed and **31** rearranges diastereoselectively to **32a**. An obvious question is: why should the 1,4-addition to form vinyl cyclopropane be so much more diastereoselective than the direct 1,2-addition? At this point, we can only speculate that 1,4-addition is more sterically demanding due to the requirement that the thioaldehyde be planar (conjugated) with the olefin. 1,2-Addition, on the other hand, can occur to the thioaldehyde even after it has rotated out of plane with the olefin.

Conclusions

With this work, we have established a general synthesis of usefully functionalized cyclopentenes from 1,3-dienes and alkyl halides bearing at least one carbanion-stabilizing group bound to the same carbon as the halogen. The two-step protocol proceeds in most cases in overall good to excellent yields and is readily executed on a multigram scale. We have delineated two limitations to the scope. First, the regioselectivity of the initial hetero Diels−Alder reaction is not impressive; however, this does not present a liability when the minor regioisomeric cycloadduct possesses substitution at C-6 (e.g. **10g** in Table 2), since this prevents reaction with strong base in the ensuing step.[7] Secondly, the degree of diastereoselectivity in the ring contraction with dihydrothiopyrans bearing unsymmetrical substitution at C-2 is substrate-dependent, particularly with regard to the alkyl substitution pattern present in the original diene component. This is in contrast to the malonate substrates bearing symmetrical substitution at C-2 (e.g. **2**), which rearrange with a high degree of diastereoselectivity.[7]

With some dihydrothiopyran substrates, reducing the temperature of the base-induced ring contraction resulted in the isolation of vinyl cyclopropanes of high isomeric purity and in good yields, suggesting that vinyl cyclopropanes might be intermediates in the formation of cyclopentenes. With one substrate (**7a**), we demonstrated unambiguously that such a rearrangement is possible and proceeds with high diastereoselectivity.

The synthetic utility of the cyclopentenes generated during the course of this work remains to be explored, as does the obvious potential for this methodology to be developed into a diastereoselective synthesis of cyclopropanes from 1,3-dienes. Research toward these ends is ongoing and will be reported in due course.

Experimental Section

Melting points were determined on a capillary apparatus and are uncorrected. ^{1}H NMR spectra were recorded at 300 MHz in $CDCl_3$ with TMS as internal standard unless otherwise noted and are reported as ppm. ^{13}C NMR spectra were recorded at 75 MHz in the same solvent. IR spectra were recorded either as neat liquids (film) or as mineral oil mulls (mull). Electron impact (EI) mass spectra were obtained with an ionization voltage of 70 eV. Data are reported in the form *m*/*z* (relative intensity). In some cases, high resolution mass spectral (HRMS) data are reported for the *m*/*z* of the parent ion, using EI or fast atom bombardment (FAB). All moisture-sensitive reactions were conducted under a nitrogen atmosphere in oven- or flame-dried glassware. Unless specified, all commercially available solvents and reagents were used without further purification. THF was Aldrich "anhydrous", packaged in Sure-Seal bottles. Solvent removal was by rotary evaporator operating at house vacuum (20−40 Torr). Flash chromatography was accomplished with EM Science silica (230−400 mesh ASTM).

2*H*-Thiopyran-2,2-dicarboxylic Acid, 3,6-Dihydro-3,5-dimethyl-, Diethyl Ester (2). A mixture of diethyl chloromalonate (11.3 mL, 70 mmol) and sodium thiosulfate pentahydrate (21.7 g, 87.5 mmol) in absolute ethanol (70 mL) was stirred at 48 °C for 19 h. The yellow mixture was diluted with toluene (140 mL) before the addition of calcium chloride dihydrate (15.4 g, 105 mmol) and *trans*-2-methyl-1,3-pentadiene (4.93 g, 60.0 mmol). While stirring at room temp, a solution of triethylamine (9.8 mL, 70 mmol) in toluene (35 mL) was added via syringe pump at a rate of 8.4 mL/h. The thick mixture was stirred an additional 1.5 h following addition. The mixture was diluted with ether (200 mL) and washed with saturated aqueous $NaHCO_3$. The organic phase was dried over magnesium sulfate and concentrated in vacuo, leaving a pale yellow oil (19.7 g). NMR analysis indicated a 12:1 mixture of regioisomers had been formed with **2** as the major isomer. Flash chromatography (20% ether/hexane) provided pure **2** along with its minor regioisomer (15.47 g, 94%) as a colorless oil which solidified on standing. Regioisomerically pure **2** could be obtained by recrystallization from hexane (colorless prisms, mp 46−48 °C). ^{1}H NMR 5.50 (m, 1 H), 4.25 (m, 4 H), 3.07, 2.78 (ABq, J = 17 Hz, 2 H), 3.00 (m, 1 H), 1.72 (bs, 3 H), 1.28 (t, J = 7 Hz, 3 H), 1.26 (t, J = 7 Hz, 3 H), 1.06 (d, J = 7 Hz, 3 H); IR (film) 1733, 1247, 1207, 1044 cm^{-1}; EI MS 272 (M^+, 60), 183 (91), 125 (100). Anal. Calcd for $C_{13}H_{20}O_4S$: C, 57.33; H, 7.40; S, 11.77. Found: C, 57.04; H, 7.27; S, 11.73.

3-Cyclopentene-1,1-dicarboxylic Acid, 3,5-Dimethyl-2-(methylthio)-, Diethyl Ester (3). A solution of **2** (5.00 g,

18.4 mmol) in THF (95 mL) was cooled to −64 °C before the addition via syringe drive (2.5 mL/min) of a solution of KBA (0.5 M in toluene, 62 mL, 31 mmol). The pale yellow solution was stirred at −64 °C for 7 h before the addition of methyl iodide (5.7 mL, 92 mmol). Stirring was continued for 1 h before the solution was allowed to warm to room temp. The reaction was then diluted with ether (250 mL) and washed successively with saturated aqueous $NaHCO_3$ and water. The organic layer was dried over magnesium sulfate and concentrated in vacuo, leaving a yellow oil (6.3 g). NMR analysis indicated that a 16:1 mixture of diastereomers had been formed. Flash chromatography (17% ether/hexane) provided pure **3**, still as a mixture of diastereomers, as a colorless oil (3.91 g, 74%). ^{1}H NMR Major diastereomer: 5.24 (bs, 1 H), 4.22 (m, 4 H), 4.09 (bs, 1 H), 3.16 (m, 1 H), 2.22 (s, 3 H), 1.82 (bs, 3 H), 1.29 (t, J = 7 Hz, 3 H), 1.27 (t, J = 7 Hz, 3 H), 1.26 (d, J = 6 Hz, 3 H); minor diastereomer: 5.22 (bs, 1 H), 4.1−4.4 (m, 4 H), 4.05 (bs, 1 H), 3.57 (m, 1 H), 1.90 (s, 3 H), 1.80 (bs, 3 H), 1.29 (t, J = 7 Hz, 3 H), 1.25 (t, J = 7 Hz, 3 H), 1.02 (d, J = 7 Hz, 3 H); remaining data is for the mixture: IR (film) 1732, 1253, 1214, 1205 cm^{-1}; EI MS 286 (M^+, 100), 225 (90), 165 (86). Anal. Calcd for $C_{14}H_{22}O_4S$: C, 58.72; H, 7.74. Found: C, 59.08; H, 7.94.

2*H*-Thiopyran-2-carboxylic Acid, 3,6-Dihydro-2,4,5-trimethyl-, Ethyl Ester (7a). General Procedure. A mixture of ethyl 2-bromopropionate (13.0 mL, 100 mmol) and sodium thiosulfate pentahydrate (37.2 g, 150 mmol) in absolute ethanol (100 mL) was stirred at 60−65 °C for 17 h (or until starting halide was consumed, as determined by TLC analysis). The mixture was diluted with toluene (230 mL) before the addition of calcium chloride dihydrate (24 g, 160 mmol) and 2,3-dimethylbutadiene (30 mL, 260 mmol). While stirring at 60−65 °C, a solution of triethylamine (18 mL, 130 mmol) in toluene (17 mL) was added via syringe pump at a rate of 5.1 mL/h. After addition was complete, the mixture was stirred an additional 1 h at the same temperature before cooling. The mixture was diluted with ether (300 mL) and washed with saturated aqueous $NaHCO_3$. Drying of the organic phase with $MgSO_4$ and concentration in vacuo afforded a yellow oil. Flash chromatography (7% ether/hexane) gave pure product (16 g, 75%) as a pale yellow oil. ^{1}H NMR 4.17 (m, 2 H), 3.24, 2.93 (ABq, J = 16 Hz, 2 H), 2.63, 2.23 (ABq, J = 16 Hz, 2 H), 1.71 (s, 3 H), 1.69 (s, 3 H), 1.51 (s, 3 H), 1.26 (t, J = 7 Hz, 3 H); IR (film)1727 (s), 1233 (s), 1217 (s), 1161 (s) cm^{-1}; EI MS 214 (M^+, 59), 141 (91), 139 (99). Anal. Calcd for $C_{11}H_{18}O_2S$: C, 61.65; H, 8.46. Found: C, 62.04; H, 8.46. HRMS: Calcd: 214.1027. Found: 214.1017.

2*H*-Thiopyran-2-carboxylic Acid, 3,6-Dihydro-4,5-dimethyl-2-(1′-methylethyl)-, Ethyl Ester (7b) by Method of Equation 3. To a cooled solution (−10 °C) of **9** (2 0 g, 10 mmol) and HMPA (2.6 mL, 15 mmol) in THF (100 mL) was added LDA (22 mL, 20 mmol, 0.9 M in cyclohexane). The solution was stirred at −10 °C over a period of 0.5 h followed by addition of 2-iodopropane (5.0 mL, 50 mmol) and allowed to gradually warm to room temperature over a period of 2 h. The reaction mixture was diluted with diethyl ether (100 mL) and saturated sodium bicarbonate (80 mL) with stirring over a period of 5 min. The organic portion was washed with water (2 × 25 mL), dried ($MgSO_4$), and concentrated to give a red oil. Purification via column chromatography (10% Et_2O/hexanes) afforded 1.9 g (79%) of **7b** as a colorless oil. IR (film) 2973, 1725 cm^{-1}; ^{1}H NMR 4.27−4.09 (m, 2H), 3.22−2.85 (ABq, J = 17 Hz, 2H), 2.52, 2.33 (ABq, J = 17 Hz, 2H), 2.19 (heptet, J = 7 Hz, 1H), 1.70 (s, 6H), 1.25 (t, J = 6 Hz, 3H), 1.04 (d, J = 7 Hz, 3H), 1.01 (d, J = 7 Hz, 3H); ^{13}C NMR 172.9, 126.5, 121.9, 60.8, 36.9, 34.8, 30.4, 20.2, 18.9, 18.0, 17.8, 17.4, 14.0; HRMS calcd for $C_{13}H_{22}O_2S$ 242.1340; found 242.1355.

2*H*-Thiopyran-2-carboxylic Acid, 3,6-Dihydro-2,4,5-trimethyl-, 1′,1-Dimethyl Ester (7c). By the method described for **7a**: Purification via flash chromatography (10% ether/hexanes) afforded **7c** (48%) as a pale yellow oil: IR (film) 2978, 1723 cm^{-1}; ^{1}H NMR 3.24, 2.91 (ABq, J = 17 Hz, 2H), 2.56, 2.20 (ABq, J = 17 Hz, 2H), 1.71 (s, 3H), 1.69 (s, 3H), 1.48 (s, 3H), 1.44 (s, 9H); ^{13}C NMR 172.8, 125.9, 121.5, 80.7, 46.6, 42.2, 30.9, 27.6, 25.2, 20.2, 18.9; HRMS calcd for $C_{13}H_{22}O_2S$ 242.1340; found 242.1328.

2*H*-Thiopyran-2-carboxylic Acid, 3,6-Dihydro-4,5-dimethyl-2-phenyl-, Ethyl Ester (7d). By the method described for **7a**: Purification via flash chromatography (10% Et_2O/hexanes) afforded **7d** (86%) as a white solid: mp = 44−45 °C; IR (mull) 3028, 2927, 1728 cm^{-1}; ^{1}H NMR 7.52−7.45 (m, 2H), 7.34−7.22 (m, 3H), 4.24−4.07 (m, 2H), 3.13, 2.81 (ABq, J = 16 Hz, 2H), 2.98, 2.83 (ABq, J = 17 Hz, 2H), 1.75 (s, 3H), 1.68 (s, 3H), 1.18 (t, J = 7 Hz, 3H); ^{13}C NMR 172.0, 139.8, 128.0, 127.2, 126.3, 125.8, 122.9, 61.5, 55.0, 40.8, 31.2, 20.1, 18.8, 13.7. Anal. Calcd for $C_{16}H_{20}O_2S$: C, 69.53; H, 7.29. Found: C, 69.34; H, 7.36.

2-Oxa-6-thiaspiro[4.5]dec-8-en-1-one, 8,9-Dimethyl- (7e). By the method described for **7a**: Flash chromatography (20% ethyl acetate/hexane) gave the product as a yellow oil (63%) which solidified on standing. Recrystallization from aqueous ethanol afforded white needles (5.83 g, mp 55−56 °C). ^{1}H NMR 4.3−4.5 (m, 2 H), 3.40 (d, AB, J = 15 Hz, 1 H), 2.90 (d, AB, J = 15 Hz, 1 H), 2.2−2.45 (m, 4 H), 1.78 (s, 3 H), 1.72 (s, 3 H); IR (mull) 3003, 1754 (s), 1184 (s) cm^{-1}; MS (EI) 198 (M^+, 99), 165 (38), 151 (56). Anal. Calcd for $C_{10}H_{14}O_2S$: C, 60.58; H, 7.12. Found: C, 60.39; H, 7.26.

Methanone, 3,6-Dihydro-2,4,5-trimethyl-2*H*-thiopyran-2-yl-, Phenyl- (7f). By the method described for **7a**: Flash chromatography (8% ether/hexane) yielded **7f** as a yellow oil (30% yield). ^{1}H NMR 1.67 (s, 3H), 1.71 (s, 3H), 1.76 (s, 3H), 2.19, 2.74 (ABq, 2H, J = 17 Hz), 2.85, 3.05 (ABq, 2H, J = 17 Hz); IR (mull) 1665, 1455, 1446, 1244, 1162 cm^{-1}; MS (EI) 246 (M^+, 9) 141 (100). Anal. Calcd for $C_{15}H_{18}OS$: C, 73.13; H, 7.36; S, 13.01. Found: C, 71.86; H, 7.37; S, 14.89.

Methanone, 3,6-Dihydro-2,4,5-trimethyl-2*H*-thiopyran-2-yl-, 4-Fluorophenyl- (7g). By the method described for **7a**: Purification via flash chromatography (8% Et_2O/hexanes) afforded **7g** (35%) as an oil. IR (mull) 3076, 2914, 1672, 1598 cm^{-1}; ^{1}H NMR 8.3−8.2 (m, 2H), 7.06 (t, J = 8 Hz, 2H), 3.02, 2.84 (ABq, J = 17 Hz, 2H), 2.72, 2.17 (ABq, J = 17 Hz, 2H), 1.75 (s, 3H), 1.69 (s, 3H), 1.64 (s, 3H); ^{13}C NMR 198.2, 164.7 (d, J_F = 252 Hz), 132.2 (d, J_F = 9 Hz), 131.8, 127.1, 120.8, 114.70 (d, J_F = 21 Hz), 50.1, 42.8, 30.8, 26.4, 20.0, 18.9. Anal. Calcd for $C_{15}H_{17}OSF$: C, 68.15; H, 6.48. Found: C, 67.85; H, 6.51.

Methanone, (3,6-Dihydro-2,4,5-trimethyl-2*H*-thiopyran-2-yl)-, 4-(Trifluoromethyl)phenyl- (7h). By the method described for **7a**: Purification via flash chromatography (10% Et_2O/hexanes) afforded **7h** (68%) as a white solid: mp = 40−41 °C; IR (mull) 3005, 2925, 1676 cm^{-1}; ^{1}H NMR 8.23 (d, J = 8 Hz, 2H), 7.65 (d, J = 8 Hz, 2H), 3.02, 2.84 (ABq, J = 17 Hz, 2H), 2.70, 2.19 (ABq, J = 17 Hz, 2H), 1.75 (s, 3H), 1.71 (s, 3H), 1.62 (s, 3H); ^{13}C NMR 199.2, 139.3, 132.9 (q, J_F = 32 Hz), 129.5, 126.9, 124.8, 123.5 (q, J_F = 270 Hz), 120.9, 50.2, 42.3, 30.7, 26.1, 20.0, 18.9. Anal. Calcd for $C_{16}H_{17}OSF_3$: C, 61.13; H, 5.45. Found: C, 61.17; H, 5.59.

Methanone, 3,6-Dihydro-2,4,5-trimethyl-2*H*-thiopyran-2-yl-, (4-Methoxyphenyl)- (7i). By the method described for **7a**: Purification via flash chromatography (10% Et_2O/hexanes) afforded **7i** (12%) as a white solid: mp = 64−65 °C; IR (mull) 3007, 2927, 1658, 1601 cm^{-1}; ^{1}H NMR 8.29−8.24 (m, 2H), 6.91−6.85 (m, 2H), 3.86 (s, 3H), 3.03, 2.84 (ABq, J = 17 Hz, 2H), 2.76, 2.15 (ABq, J = 17 Hz, 2H), 1.76 (s, 3H), 1.69 (s, 3H), 1.67 (s, 3H); ^{13}C NMR 198.2, 162.6, 132.2, 128.0, 127.4, 121.0, 113.0, 55.3, 50.4, 43.2, 31.1, 26.8, 20.2, 19.0. Anal. Calcd for $C_{16}H_{20}O_2S$: C, 69.53; H, 7.29. Found: C, 69.19; H, 7.29.

Methanone, 3,6-Dihydro-4,5-dimethyl-2-phenyl-2*H*-thiopyran-2-yl-, Phenyl- (7j). By the method described for **7a**: Purification via flash chromatography (10% Et_2O/hexanes) afforded **7j** (77%) as a white solid: mp = 92−93 °C; IR (mull) 2912, 1673, 1597 cm^{-1}; ^{1}H NMR 7.70−7.66 (m, 2H), 7.49−7.19 (m, 8H), 3.03, 2.86 (ABq, J = 16 Hz, 2H), 2.94, 2.51 (ABq, J = 16 Hz, 2H), 1.75 (s, 3H), 1.70 (s, 3H); ^{13}C NMR 196.4, 141.8, 134.8, 132.0, 130.1, 128.9, 127.6, 127.5, 126.2, 122.1, 60.2, 44.4, 30.9, 19.9, 19.0, one carbon not seen. Anal. Calcd for $C_{20}H_{20}OS$: C, 77.92; H, 6.49. Found: C, 77.98; H, 6.43.

2*H*-Thiopyran-2-carbonitrile, 3,6-Dihydro-2,4,5-trimethyl- (7k). By the method described for **7a**: Flash chromatography (10% ether/hexane) provided **7k** (50%) as a light yellow mobile liquid. ^{1}H NMR 3.69 and 2.96 (ABq, 2H, J = 17 Hz), 2.46 and 2.36 (ABq, 2H, J = 17 Hz), 1.78 (s, 3H), 1.70

(s, 3H), 1.67 (s, 3H); IR (film) 2230, 1449, 1416, 1381 cm^{-1}; EI MS 167 (M^+, 100), 82 (72), 67 (39); HRMS calcd for $C_9H_{13}NS$ 167.0769; found 167.0774.

2-(9-Fluorenylidene)-3,6-dihydro-2*H*-4,5-dimethylthiopyran (7l). By the method described for **7a**: Recrystallization from 95% ethanol yielded 66% yield of product. An analytical sample was obtained by recrystallization from hexane (mp 122−124 °C, lit.[17] 125 °C). ^1H NMR 1.81 (s, 3H), 2.00 (bs, 3H), 2.68 (bs, 2H), 3.47 (bs, 2H), 7.30−7.52 (m, 6H), 7.76−7.81 (dm, J = 5.0 Hz, 2H); IR (mull) 1446, 732 cm^{-1}; MS (EI) 278, (M^+, 24), 196 (100). Anal. Calcd for $C_{19}H_{18}S$: C, 81.97; H, 6.52; S, 11.52. Found: C, 82.20; H, 6.59; S, 11.73.

2*H*-Thiopyran-2-carboxamide, 3,6-Dihydro-*N*,*N*,2,4,5-pentamethyl- (7m). To an ice cold solution of **8** (1.0 g, 5.4 mmol) in methylene dichloride (30 mL) and dimethylformamide (42 mL, 0.5 mmol) was added oxalyl chloride (1.4 mL, 16.0 mmol) via syringe. The resulting solution was stirred at 0 °C over a period of 0.75 h before the addition of excess dimethylamine (3.0 mL, 29 mmol) via cannula and continued stirring over a period of 1 h. The reaction mixture was diluted with diethyl ether (50 mL) and washed with water, and the organic portion was dried ($MgSO_4$) and concentrated to give 1.13 g of an oily solid. Purification via flash chromatography (1:1 Et_2O/hexanes) afforded 960 mg (83%) of **7m** as a white solid: mp = 41 °C; IR (mull) 2909, 1627 cm^{-1}; ^1H NMR 3.18 (br s, 3H), 3.12 (br s, 3H), 2.90, 2.10 (ABq, J = 16 Hz, 2H), 2.85 (1/2 of an ABq, J = 18 Hz, 1H, second half obscured), 1.73 (s, 3H), 1.71 (s, 3H), 1.53 (s, 3H); ^{13}C NMR 172.5, 128.2, 121.0, 46.2, 45.0, 38.9 (br), 31.5, 25.0, 20.2, 19.0. Anal. Calcd for $C_{11}H_{19}ONS$: C, 61.93; H, 8.98; N, 6.56. Found: C, 61.83; H, 9.00; N, 6.53.

2*H*-Thiopyran-2-carboxylic Acid, 3,6-Dihydro-2,4,5-trimethyl- (8). To **7a** (5 g, 23 mmol) in ethanol (95%, 200 mL) was added 8 M potassium hydroxide (12 mL, 92 mmol), and the reaction mixture was stirred at ambient temperature over a period of 17 h. The milky white solution was concentrated by rotary evaporation, diluted with water (30 mL), and neutralized with concentrated hydrochloric acid. The aqueous solution was saturated with solid sodium chloride and extracted with hot ethyl acetate (4 × 150 mL). The organic portion was dried ($MgSO_4$) and concentrated to give 4.4 g (100%) of **8** as a white solid. An analytical sample could be obtained by recrystallizing from hexanes/diethyl ether: mp = 90−92 °C; IR (mull) 2924, 1700, 1414 cm^{-1}; ^1H NMR 6.17 (br s, 1H), 3.29, 2.92 (ABq, J = 17 Hz, 2H), 2.63, 2.23 (ABq, J = 17 Hz, 2H), 1.72 (s, 3H), 1.69 (s, 3H), 1.54 (s, 3H); ^{13}C NMR 179.5, 125.9, 121.9, 46.2, 41.7, 30.9, 25.6, 20.1, 19.0; HRMS calcd for $C_9H_{14}O_2S$ 186.0714; found 186.0724.

2*H*-Thiopyran-2-carboxylic acid, 3,6-Dihydro-, Ethyl Ester (10a). Ethyl bromoproprionate (9.1 mL, 70 mmol) and sodium thiosulfate pentahydrate (22 g, 88 mmol) were stirred in ethanol (95%, 70 mL) at 60 °C for 24 h. The solution was cooled to −78 °C followed by addition of toluene (140 mL), calcium chloride dihydrate (15 g, 102 mmol), 1,3-butadiene (42 mL, 924 mmol), and triethylamine (10 mL, 72 mmol). The resulting reaction mixture was placed in a Parr bomb and heated to 100 °C over a period of 2 h and then cooled to 40 °C over a period of 18 h. The reaction mixture was cooled to room temperature followed by dilution with diethyl ether (300 mL) and saturated sodium bicarbonate (200 mL). The organic portion was washed with saturated sodium bicarbonate, dried ($MgSO_4$) and concentrated to give 13 g of a pale yellow oil. Purification via flash chromatography (10% Et_2O/hexanes) afforded 4.3 g (33%) of **10a** as a colorless oil: IR (film) 3025, 2979, 1725 cm^{-1}; ^1H NMR 5.90−5.78 (m, 2H), 4.19 (q, J = 7 Hz, 2H), 3.35, 3.07 (ABq of multiplets, J = 16 Hz, 2H), 2.78, 2.28 (ABq of multiplets J = 16 Hz, 2H), 1.53 (s, 3H), 1.27 (t, J = 7 Hz, 3H); ^{13}C NMR 173.7, 126.7, 122.4, 61.4, 45.2, 35.7, 25.8, 25.5, 14.1; HRMS calcd for $C_9H_{14}O_2S$ 186.0714; found 186.0723.

2*H*-Thiopyran-2-carboxylic Acid, 3,6-Dihydro-2,5-dimethyl-, Ethyl Ester (10b) and 2*H*-Thiopyran-2-carboxylic Acid, 3,6-Dihydro-2,4-dimethyl-, Ethyl Ester (10c). Ethyl bromoproprionate (18 mL, 140 mmol) and sodium thiosulfate pentahydrate (43 g, 175 mmol) were stirred in ethanol (95%, 140 mL) at 60 °C for 17 h. The reaction mixture was diluted with toluene (280 mL) followed by addition of calcium chloride dihydrate (31 g, 210 mmol) and 2-methyl-1,3-butadiene (56 mL, 560 mmol). To the resulting mixture was added triethylamine (24 mL, 175 mmol) dissolved in toluene (26 mL) at a rate of 5.4 mL/h via syringe pump. After addition was complete the reaction mixture was allowed to stir at 60 °C over a period of 6 h, cooled to room temperature, and then diluted with diethyl ether (300 mL) and saturated sodium bicarbonate (200 mL). The organic portion was washed with saturated sodium bicarbonate, dried ($MgSO_4$), and concentrated to give a pale yellow oil. Purification via flash chromatography (10% Et_2O/hexanes) afforded 19 g (68%) of **10b**:**10c** as a 3:2 mixture of regioisomers (colorless oil). Analytical data was obtained on the inseparable mixture. IR (neat) 3043, 2979, 1725 cm^{-1}; ^1H NMR (**10b**) 5.52−5.50 (m, 1H), 4.18 (q, J = 7 Hz, 2H), 3.25, 2.91 (ABq, J = 16 Hz, 2H), 2.73, 2.26 (ABq of multiplets, J = 17 Hz, 2H), 1.74 (s, 3H), 1.52 (s, 3H), 1.26 (t, J = 7 Hz, 3H); (**10c**) 5.58−5.56 (m, 1H), 4.18 (q, J = 7 Hz, 2H), 3.31, 3.06 (ABq of multiplets, J = 16 Hz, 2H), 2.60, 2.18 (ABq, J = 17 Hz, 2H), 1.74 (s, 3H), 1.54 (s, 3H), 1.26 (t, J = 7 Hz, 3H); ^{13}C NMR 173.8, 173.0, 134.1, 129.5, 120.9, 116.2, 61.2, 46.0, 45.0, 40.5, 36.4, 29.5, 26.1, 25.5, 25.2, 24.6, 23.9, 14.0; HRMS calcd for $C_{10}H_{16}O_2S$ 200.0871; found 200.0874.

2*H*-Thiopyran-2-carboxylic Acid, 3,6-Dihydro-2,3,3,5-tetramethyl-, Ethyl Ester (10d). Ethyl bromoproprionate (3.3 mL, 26 mmol) and sodium thiosulfate pentahydrate (8 g, 32 mmol) were stirred in ethanol (95%, 30 mL) at 60 °C for 18 h. The reaction mixture was diluted with toluene (45 mL) followed by addition of calcium chloride dihydrate (6 g, 39 mmol) and 2,4-dimethyl-1,3-pentadiene (5.0 g, 52 mmol). To the resulting mixture was added triethylamine (4.5 mL, 32 mmol) dissolved in toluene (35 mL) at a rate of 1.67 mL/h via syringe. After addition was complete the reaction mixture was allowed to stir at 60 °C over a period of 1 h, cooled to room temperature, and diluted with diethyl ether (100 mL) and saturated sodium bicarbonate (75 mL). The organic portion was washed with saturated sodium bicarbonate, dried ($MgSO_4$), and concentrated to give an orange oil. Purification via repeated flash chromatography (10% Et_2O/hexanes) afforded 0.87 g (15%) of **10d** and **10e** as a 4:1 mixture of regioisomers. Analytical data was obtained with the mixture. IR (neat) 2973, 1724 cm^{-1}; ^1H NMR (**10d**) 5.13 (q, J = 1 Hz, 1H), 4.22−4.08 (m, 2H), 3.12, 2.92 (ABq, J = 17 Hz, 2H), 1.74 (d, J = 1 Hz, 3H), 1.49 (s, 3H), 1.27 (t, J = 7 Hz, 3H), 1.13 (s, 3H), 1.07 (s, 3H); (**10e**) 5.30 (m, 1H), 4.22−4.08 (m, 2H), 2.63, 2.08 (ABq, J = 17 Hz, 2H), 1.77 (bs, 3H), 1.51 (s, 3H), 1.31 (s, 3H), 1.28 (s, 3H), 1.27 (t, J = 7 Hz); HRMS calcd for $C_{12}H_{20}O_2S$ 228.1184; found 228.1189.

2*H*-Thiopyran-2-carboxylic Acid, 3,6-Dihydro-2,3,5-trimethyl-, Ethyl Ester (10f). Ethyl bromoproprionate (9.0 mL, 70 mmol) and sodium thiosulfate pentahydrate (22 g, 88 mmol) were stirred in ethanol (95%, 70 mL) at 60 °C for 18 h. The reaction mixture was diluted with toluene (140 mL) followed by addition of calcium chloride dihydrate (15 g, 105 mmol) and 2-methyl-1,3-pentadiene (5.0 g, 61 mmol). To the resulting mixture was added triethylamine (10 mL, 70 mmol) dissolved in toluene (35 mL) at a rate of 8.4 mL/h via syringe pump. After addition was complete the reaction mixture was allowed to stir at 60 °C over a period of 1 h and cooled to room temperature followed by dilution with diethyl ether (200 mL) and saturated sodium bicarbonate (150 mL). The organic portion was washed with saturated sodium bicarbonate, dried ($MgSO_4$), and concentrated to give 13 g of an orange oil. NMR analysis indicated that a 9:1 mixture of **10f**:**10g** had been formed, each as a 1:1 mixture of diastereomers. Purification via flash chromatography (10% Et_2O/hexanes) afforded 8.4 g (65%) of **10f**:**10g**, as a colorless oil, unchanged in isomer ratios. Analytical data was obtained on the mixture (data reported only for **10f** diastereomers). IR (neat) 3037, 2976, 1727 cm^{-1}; ^1H NMR 5.40−5.37 (m, 1H), 5.35−5.32 (m, 1H), 4.25−4.11 (m, 4H, both isomers), 3.17, 2.91 (ABq, J = 17 Hz, 2H), 3.07, 3.00 (ABq of multiplets, J = 17 Hz, 2H), 2.90 (bm, 1H), 2.46−2.39 (m, 1H), 1.75 (s, 3H), 1.68 (s, 3H), 1.56 (s, 3H), 1.39 (s, 3H), 1.33−1.20 (m, 6H, both isomers), 1.04 (d, J = 7 Hz, 3H), 1.03 (d, J = 7 Hz, 3H); ^{13}C NMR 174.2, 173.1, 128.9, 128.4, 127.9, 126.6, 61.4, 61.0, 50.2, 49.4, 39.1, 36.5, 29.5, 29.4, 24.4, 23.9,

20.7, 17.7, 16.9, 14.1; HRMS calcd for $C_{11}H_{18}O_2S$ 214.1027; found 214.1030.

3-Cyclopentene-1-carboxylic Acid, 1,3,4-Trimethyl-2-(methylthio)-, Ethyl Ester (11a/12a). LDA (bis THF complex, 1.05 M in hexane, 11.6 mL, 12.1 mmol) was added over 10 min to a −78 °C solution of sulfide **7a** (2.00 g, 9.33 mmol) and HMPA (2.1 mL, 12 mmol) in THF (50 mL) under nitrogen. The bright yellow solution was then stirred at that temp for 1 h and then allowed to warm to 0 °C for 30 min. Neat methyl iodide (2.9 mL, 47 mmol) was added, and the reaction was stirred for another 30 min at 0 °C. The reaction was diluted with ether (50 mL) and washed successively with saturated aqueous $NaHCO_3$ and water. The organic phase was dried over magnesium sulfate and concentrated in vacuo, affording an amber oil (2.26 g). NMR analysis indicated an 8:1 mixture of **11a**:**12a** had formed. Flash chromatography (10% ether/hexane) provided the product as a mixture of diastereomers (1.85 g, 87%). A pure sample of **11a** could be obtained by HPLC (Whatman M9 silica, 1% ether/hexane, 3.5 mL/min). ^{1}H NMR (**11a**) 4.13 (q, J = 7 Hz, 2 H), 4.00 (bs, 1 H), 2.81, 2.11 (ABq, J = 16 Hz, 2 H), 1.94 (s, 3 H), 1.68 (s, 3 H), 1.64 (s, 3 H), 1.42 (s, 3 H), 1.24 (t, J = 7 Hz, 3 H); (**12a**) 4.20 (q, J = 7 Hz, 2 H), 3.21 (bs, 1 H), 3.12, 1.90 (ABq, J = 16 Hz, 2 H), 1.81 (s, 3 H), 1.69 (s, 3 H), 1.66 (s, 3 H), 1.57 (s, 3 H), 1.30 (t, J = 7 Hz, 3 H); remaining data is for the mixture: IR (film) 1728 (s), 1446, 1177 (s), 1097 (s); MS (EI) 228 (M^+, 25), 107 (99). Anal. Calcd for $C_{12}H_{20}O_2S$: C, 63.12; H, 8.83; S, 14.04. Found: C, 62.66; H, 8.79; S, 13.54; HRMS calcd 228.1184; found 228.1184.

3-Cyclopentene-1-carboxylic Acid, 1,3,4-Trimethyl-2-(methylthio)-, Ethyl Ester (11a, by Rearrangement of Cyclopropane 19). Cyclopropane **19** (350 mg, 1.1 mmol) was dissolved in THF (5 mL). HMPA (250 μL, 1.4 mmol) was added via syringe, and the solution was cooled to −78 °C. To the stirring solution was added lithium diethylamide (2.3 mL, 1.4 mmol, 0.6 M in THF, generated from diethylamine (1.05 mL, 10 mmol) and n-BuLi (6.25 mL, 10 mmol, 1.6 M in hexanes) at −78 °C) via syringe, and the reaction mixture was stirred at −78 °C over a period of 0.5 h. The solution was warmed to 0 °C and stirred over a period of 0.25 h followed by addition of iodomethane (340 mL, 5.5 mmol) via syringe. The solution was stirred for an additional 10 min followed by partitioning between diethyl ether (100 mL) and saturated sodium bicarbonate (10 mL). The organic portion was dried ($MgSO_4$) and filtered over a plug of silica gel (7 g), rinsing with diethyl ether. NMR analysis indicated that **11a**:**12a** were present in a 16:1 ratio. Flash chromatography (10% Et_2O/hexanes) afforded 198 mg (79%) of **11a**:**12a** as a 16:1 mixture of diastereomers.

3-Cyclopentene-1-carboxylic Acid, 3,4-Dimethyl-1-(1′-methylethyl)-2-(methylthio)-, Ethyl Ester (11b/12b). General Procedure for Ring Contraction to Cyclopentenes. 7b (970 mg, 4.0 mmol) was dissolved in THF (40 mL). HMPA (0.90 mL, 5.2 mmol) was added via syringe, and the solution was cooled to −78 °C. To the stirring solution was added LDA·THF (6.0 mL, 5.2 mmol, 0.9 M in cyclohexane) via syringe, and the reaction mixture was stirred at −78 °C over a period of 0.5 h. The solution was warmed to 0 °C and stirred over a period of 0.5 h before the addition of iodomethane (1.24 mL, 20.0 mmol) via syringe. The solution was stirred for an additional 10 min before partitioning between diethyl ether (80 mL) and saturated sodium bicarbonate (20 mL). The organic portion was washed with water, dried ($MgSO_4$), and filtered. Purification via flash chromatography (10% Et_2O/hexanes) afforded 864 mg (84%) of **11b**:**12b** as a 17:2 mixture of diastereomers. Analytical data was obtained on the mixture. IR (neat) 2973, 1721, 1445 cm^{-1}; ^{1}H NMR (**11b**) 4.3−4.0 (m, 3H), 2.81, 2.04 (ABq, J = 15 Hz, 2H), 2.31 (heptet, J = 7 Hz, 1H) 1.83 (s, 3H), 1.68−1.62 (m, 6H), 1.24 (t, J = 7 Hz, 3H), 0.98 (d, J = 7 Hz, 3H), 0.92 (d, J = 7 Hz, 3H); (**12b**) 4.3−4.0 (m, 2H), 3.27 (br s, 1H), 2.96, 1.99 (ABq, J = 17 Hz, 2H), 2.22 (heptet, J = 7 Hz, 1H), 1.80 (s, 3H), 1.59 (br s, 6H), 1.26 (t, J = 7 Hz, 3H), 0.84 (d, J = 7 Hz, 3H), 0.68 (d, J = 7 Hz, 3H); ^{13}C NMR (**11b**) 175.1, 133.6, 130.4, 63.8, 61.3, 61.2, 45.0, 32.3, 19.7, 18.6, 14.2 13.7, 12.4, 12.2; (**12b**) 174.4, 134.0, 126.9, 61.6, 61.3, 60.2, 38.8, 35.3, 18.6, 17.7, 17.0, 14.0, 13.3, 11.5; HRMS calcd for $C_{14}H_{24}O_2S$ 256.1497; found 256.1501.

3-Cyclopentene-1-carboxylic Acid, 1,3,4-Trimethyl-2-(methylthio)-, 1,1-Dimethylethyl Ester (11c/12c). By the method outlined for the preparation of **11b/12b**: Purification via flash chromatography (5% Et_2O/hexanes) afforded 95% of **11c**:**12c** as an 8:1 diastereomeric mixture. Analytical data was obtained on the mixture. IR (film) 2976, 1724 cm^{-1}; ^{1}H NMR (**11c**) 3.95 (s, 1H), 2.75, 2.07 (ABq, J = 16 Hz, 2H), 1.94 (s, 3H) 1.68 (s, 3H), 1.64 (s, 3H), 1.43 (s, 9H), 1.38 (s, 3H); (**12c**) 3.15 (s, 1H), 3.03, 1.87 (ABq, J = 16 Hz, 2H), 1.83 (s, 3H), 1.50 (s, 9H), 1.29 (s, 3H), vinyl methyls obscured; ^{13}C NMR (**11c**) 176.9, 132.8, 129.5, 80.1, 64.1, 52.6, 48.2, 27.9, 21.6, 13.9, 13.8, 12.5. Anal. Calcd for $C_{14}H_{24}O_2S$: C, 65.58; H, 9.43. Found: C, 65.97; H, 9.31.

3-Cyclopentene-1-carboxylic Acid, 3,4-Dimethyl-2-(methylthio)-1-phenyl-, Ethyl Ester (11d/12d). By the method outlined for the preparation of **11b/12b**: Purification via flash chromatography (8% Et_2O/hexanes) afforded **11d**:**12d** (93%) as a colorless oil and a 2:1 mixture of diastereomers. Analytical data was obtained on the mixture. IR (film) 3024, 1728, 1601 cm^{-1}; ^{1}H NMR (400 MHz) (**11d**) 7.39−7.37 (m, 2H), 7.32−7.28 (m, 2H), 7.24−7.20 (m, 1H), 4.42 (s, 1H), 4.12−3.94 (m, 2H), 3.06, 2.95 (ABq, J = 16 Hz, 2H), 1.76 (s, 3H), 1.74 (s, 3H), 1.49 (s, 3H), 1.10 (t, J = 7 Hz, 3H); (**12d**) 7.26−7.15 (m, 5H), 4.21−4.10 (m, 2H), 3.94 (s, 1H), 3.45, 2.24 (ABq, J = 16 Hz, 2H), 1.94 (s, 3H), 1.78 (s, 3H), 1.59 (s, 3H), 1.19 (t, J = 7 Hz, 3H); HRMS calcd for $C_{17}H_{22}O_2S$ 290.1340; found 290.1341.

2-Oxaspiro[4.4]non-7-en-1-one, 7,8-Dimethyl-6-(methylthio)- (11e). By the method outlined for the preparation of **11b/12b**: Purification via flash chromatography (10% Et_2O/hexanes) afforded **11e** (71%) as a 15:1 diastereomeric mixture (the minor isomer was tentatively assigned and was not resolved). The major isomer **11e** was recrystallized from pentanes (−20 °C) to afford 170 mg (67%) of white needles (mp = 55−56 °C). IR (mull) 2918, 1754, cm^{-1}; ^{1}H NMR 4.35−4.22 (m, 2H), 3.81 (s, 1H), 2.88 (ddd, J = 13, 7, 6 Hz, 1H), 2.65, 2.28 (ABq, J = 17 Hz, 2H), 2.17 (ddd, J = 13, 7, 6 Hz, 1H), 1.82 (s, 3H), 1.72 (s, 6H); ^{13}C NMR 181.3, 131.9, 128.9, 65.9, 61.9, 49.6, 47.5, 33.5, 13.7, 12.4, 11.7. Anal. Calcd for $C_{11}H_{16}O_2S$: C, 62.23; H, 7.59. Found: C, 62.05; H, 7.58.

Methanone, Phenyl-, 1,3,4-Trimethyl-2-(methylthio)-3-cyclopenten-1-yl- (11f/12f). By the method outlined for the preparation of **11b/12b**: Flash chromatography (8% ether/hexane) yielded **11f**:**12f** as a very pale yellow oil (63% yield), which was a 10:1 mixture of diastereomers. ^{1}H NMR (**11f**) 1.62 (s, 3H), 1.68 (s, 6H), 1.95 (s, 3H), 2.22, 3.18 (ABq, 2H, J = 16 Hz), 4.25 (s, 1H), 7.39−7,53 (m, 3H), 7.83−7.86 (m, 2H); (**12f**) 1.42 (s, 3H), 1.70 (s, 3H), 1.65−1.72 (m, 6H), 1.90, 3.41 (ABq, J = 16 Hz, 2H), 3.69 (s, 1H), 7.4−7.55 (m, 3H), 7.85 (m, 2H); IR (film) 1674, 1447, 973, 713, 697; MS(EI) 260 (M^+, 2), 105 (100); HRMS calcd for $C_{16}H_{20}OS$ 260.1235; found 260.1228.

Methanone, 4-Fluorophenyl-, 1,3,4-Trimethyl-2-(methylthio)-3-cyclopenten-1-yl- (11g/12g). 7g (290 mg, 1.1 mmol) was dissolved in THF (10 mL). 18-Crown-6 (580 mg, 2.2 mmol) was added, and the solution was cooled to −78 °C. To the stirring solution was added KBA (4.4 mL, 2.2 mmol, 0.5 M in toluene) via syringe, and the reaction mixture was stirred at −78 °C over a period of 0.5 h. The solution was warmed to 0 °C and stirred over a period of 0.5 h followed by addition of iodomethane (340 mL, 5.5 mmol) via syringe. The solution was stirred for an additional 10 min followed by partitioning between ether and saturated aqueous sodium bicarbonate. The organic portion was washed with water, dried ($MgSO_4$), and filtered. Purification via preparative layer chromatography (silica gel, 1 mm thickness, 33% Et_2O/hexanes) afforded 212 mg (69%) of **11g**:**12g** as a 5:2 diastereomeric mixture. Analytical data was obtained on the mixture. IR (film) 3073, 2917, 1673, 1599 cm^{-1}; ^{1}H NMR (**11g**) 7.95−787 (m, 2H), 7.12−7.03 (m, 2H), 4.21 (s, 1H), 3.19, 2.22 (ABq, J = 16 Hz, 2H), 1.94 (s, 3H), 1.68 (s, 6H), 1.60 (s, 3H); (**12g**) 7.95−7.87 (m, 2H), 7.12−7.03 (m, 2H), 3.66 (s, 1H), 3.42, 1.89 (ABq, J = 17 Hz, 2H), 1.76 (s, 3H), 1.71 (s, 3H), 1.66 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (mixture) 202.1, 200.6, 164.7 (d, J_F = 252 Hz), 164.4 (d, J_F = 251 Hz), 133.6, 133.2, 132.9, 132.0 (d, J_F = 9 Hz), 131.8 (d, J_F = 9 Hz), 131.3, 130.0, 128.5, 125.5, 115.2 (d,

J_F = 21 Hz), 114.9 (d, J_F = 21 Hz), 63.6, 62.8, 58.8, 56.2, 49.4, 48.3, 28.7, 23.7, 13.8, 13.2, 12.6, 11.7, 10.7. Anal. Calcd for $C_{16}H_{19}OSF$: C, 69.03; H, 6.88. Found: C, 68.99; H, 6.92.

Methanone, 4-(Trifluoromethyl)phenyl-, 1,3,4-Trimethyl-2-(methylthio)-3-cyclopenten-1-yl- (11h/12h). By the method described for the preparation of **11g/12g**: Purification via flash chromatography (10% Et_2O/hexanes) afforded **11h**:**12h** (72%) as a 5:2 diastereomeric mixture. Analytical data was obtained on the mixture. IR (film) 3068, 2976, 1682 cm^{-1}; ^1H NMR (**11h**) 7.91 (d, J = 8 Hz, 2H), 7.69 (d, J = 8 Hz, 2H), 4.17 (s, 1H), 3.11, 2.24 (ABq, J = 17 Hz, 2H), 1.95 (s, 3H), 1.69 (s, 6H), 1.60 (s, 3H); (**12h**) 7.95 (d, J = 8 Hz, 2H), 7.69 (d, J = 8 Hz, 2H), 3.67 (s, 1H), 3.42, 1.83 (ABq, J = 16 Hz, 2H), 1.77 (s, 3H), 1.72 (s, 3H), 1.70 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (**11h**) 203.8, 138.9, 132.9, 129.6, 129.4, 129.1, 125.3, 125.2, 63.5, 56.6, 49.2, 23.3, 13.9, 13.5, 12.6; (**12h**) 201.3, 140.3, 133.1, 129.6, 125.5, 125.0, 124.9, 62.6, 56.4, 47.9, 28.2, 13.6, 11.5, 10.5 (one carbon resonance not seen). Anal. Calcd for $C_{17}H_{19}OSF_3$: C, 62.18; H, 5.83. Found: C, 62.01; H, 5.97.

Methanone, 4-Methoxyphenyl-, 1,3,4-Trimethyl-2-(methylthio)-3-cyclopenten-1-yl- (11i/12i). By the method described for the preparation of **11g/12g**: Flash chromatography (10% ether/hexane) afforded a pure mixture of the two diastereomers (5:2 **11i**:**12i**) (83%) as a pale yellow oil. ^1H NMR (**11i**) 7.91 (d, 2H, J = 9 Hz), 6.90 (d, 2H, J = 9 Hz), 4.26 (bs, 1H), 3.84 (s, 3H), 3.24 and 2.19 (ABq, 2H, J = 15 Hz), 1.94 (s, 3H), 1.69 (s, 3H), 1.65 (s, 3H), 1.61 (s, 3H); (**12i**) 7.78 (d, 2H, J = 9 Hz), 6.91 (d, 2H, J = 9 Hz), 3.84 (s, 3H), 3.67 (bs, 1H), 3.42 and 1.89 (ABq, 2H, J = 16 Hz), 1.75 (s, 3H), 1.72 (s, 3H), 1.69 (s, 3H), 1.43 (s, 3H); Remaining data is for the mixture: IR (film) 1666 (s), 1602 (s), 1258 (s), 1169 (s); MS (EI) 290 (M^+, 3), 135 (99). HRMS (EI) calcd for $C_{17}H_{22}O_2S$ 290.1340; found 290.1349.

Spiro[3-cyclopentene-1,9′-[9*H*]fluorene], 3,4-Dimethyl-2-(methylthio)- (11l). By the method outlined for the preparation of **11b/12b**: Flash chromatography (2% ether/hexane) yielded **11l** (79%) as a pale yellow oil. ^1H NMR 1.45 (s, 3H), 1.82 (s, 3H), 1.89 (s, 3H), 2.57, 2.98 (ABq, J = 16 Hz, 2H), 3.70 (s, 1H), 7.21−7.45 (m, 5H), 7.67−7.71 (m, 2H), 7.83 (d, J = 7 Hz, 1H); IR (film) 2914, 1448, 738 cm^{-1}; MS (EI) 292 (M^+, 14), 245 (100); HRMS calcd for $C_{20}H_{20}S$ 292.1276; found 292.1286.

3-Cyclopentene-1-carboxamide, *N*,*N*,1,3,4-Pentamethyl-2-(methylthio)- (11m/12m) and Cyclopropanecarboxamide, *N*,*N*,1,2-Tetramethyl-2-[1-methyl-2-(methylthio)-ethenyl]- (18m) (by Conditions of Table 5, Entry 4). 7m (435 mg, 2.0 mmol) was dissolved in THF (15 mL). HMPA (0.460 mL, 2.6 mmol) was added via syringe, and the solution was cooled to −78 °C. To the stirring solution was added LDA·THF (1.2 mL, 1.4 mmol, 1.2 M in cyclohexane) via syringe, and the reaction mixture was stirred at −78 °C over a period of 0.5 h. The solution was warmed to ambient temperature and stirred over a period of 24 h followed by addition of iodomethane (0.620 mL, 10.0 mmol) via syringe. The solution was stirred for an additional 10 min followed by partitioning between diethyl ether (100 mL) and saturated sodium bicarbonate (30 mL). The organic portion was washed with water, dried ($MgSO_4$), and filtered to give a brown oil. Analysis of the crude reaction mixture by ^1H NMR (300 MHz) showed a 14:3:1 ratio of **11m**:**12m**:**18m**, respectively. Purification via flash chromatography (1:1 ether/hexanes then 100% ether) afforded 375 mg (82%) of **11m**:**12m** as a 5:1 mixture of diastereomers (colorless oil) and 27 mg (6%) of **18m** (white solid). Analytical data was obtained on the mixture of **11m**:**12m**. IR (neat) 2917, 1632 cm^{-1}; ^1H NMR (**11m**) 3.95 (s, 1H), 3.20, 2.06 (ABq, J = 17 Hz, 2H), 2.94 (s, 6H), 1.90 (s, 3H), 1.67 (s, 6H), 1.46 (s, 3H); (**12m**) 3.36, 1.94 (ABq, J = 17 Hz, 2H), 3.27 (s, 1H), 3.01 (brs, 6H), 1.74 (s, 3H), 1.72 (s, 3H), 1.66 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (**11m**) 176.3, 133.2, 128.5, 63.8, 54.6, 50.5, 38.0 (br, 2C), 22.6, 13.9, 12.9, 12.6; (**12m**) 174.8, 133.4, 125.3, 63.0, 54.7, 51.0, 38.7, 37.2, 27.0, 13.8, 12.0, 9.9. Anal. Calcd for $C_{12}H_{21}ONS$: C, 63.39; H, 9.31; N, 6.16. Found: C, 63.47; H, 9.31; N, 5.98. (**18m**) mp = 58−60 °C; IR (mull) 3003, 2921, 1625, 1592 cm^{-1}; ^1H NMR 5.70 (s, 1H), 3.18 (s, 3H), 2.94 (s, 3H), 2.24, (s, 3H), 1.87 (s, 3H), 1.28 (s, 3H), 1.15, 1.05 (ABq, J = 5 Hz, 2H), 1.06 (s, 3H); ^{13}C NMR 173.1, 133.6, 126.1, 37.3, 35.4, 31.3, 30.5, 26.1, 22.2, 19.5, 19.1, 17.6. Anal. Calcd for $C_{12}H_{21}ONS$: C, 63.39; H, 9.31; N, 6.16. Found: C, 63.66; H, 9.34; N, 6.33.

11m/12m and 18m (by Conditions of Table 5, Entry 3). 7m (680 mg, 3.2 mmol) was dissolved in THF (30 mL). HMPA (0.730 mL, 4.2 mmol) was added via syringe, and the solution was cooled to −78 °C. To the stirring solution was added LDA·THF (4.6 mL, 4.2 mmol, 0.9 M in cyclohexane) via syringe, and the reaction mixture was stirred at −78 °C over a period of 0.5 h. The solution was warmed to 0 °C temperature and stirred over a period of 0.5 h followed by addition of iodomethane (1.0 mL, 16.0 mmol) via syringe. The solution was stirred for an additional 10 min followed by partitioning with diethyl ether (200 mL) and saturated sodium bicarbonate (20 mL). The organic portion was washed with water, and the aqueous layer was extracted with ethyl acetate. The combined organic portions were dried ($MgSO_4$) and filtered to give a brown oil. Purification via flash chromatography (1:1 Et_2O/hexanes) afforded 154 mg (21%) of **11m**:**12m** as a 1:3 mixture of diastereomers and 437 mg (60%) of **18m** as a crystalline solid. Recrystallization of **11m**:**12m** from ether/hexanes afforded analytically pure **12m**, mp = 101−102 °C, suitable for single crystal X-ray diffraction analysis.

3-Cyclopentene-1-carboxylic Acid, 1,2-Bis(methylthio)-3,4-dimethyl- (11w/12w). By the method outlined for the preparation of **11b/12b**: Purification via flash chromatography (10% Et_2O/hexanes) afforded **11w**:**12w** (61%) as a 2:1 mixture of diastereomers (oil). Analytical data was obtained on the mixture. IR (film) 2919, 1722 cm^{-1}; ^1H NMR (**11w**) 4.20 (s, 1H), 4.20 (q, J = 7 Hz, 2H), 3.17, 2.38 (ABq, J = 15 Hz, 2H), 2.10 (s, 3H), 1.95 (s, 3H), 1.69 (s, 6H), 1.28 (t, J = 7 Hz, 3H); (**12w**) 4.30−4.16 (m, 2H), 3.49 (s, 1H), 3.23, 2.21 (ABq, J = 20 Hz, 2H), 2.18 (s, 3H), 1.92 (s, 3H), 1.71 (s, 6H), 1.35 (t, J = 7 Hz, 3H); HRMS calcd for $C_{12}H_{20}O_2S_2$ 260.0905; found 260.0902.

Methanone, Phenyl-, 1,3,4-Trimethyl-1-phenyl-2-(methylthio)-3-cyclopenten-1-yl- (12j). By the method outlined for the preparation of **11b/12b**: Purification via flash chromatography (10% Et_2O/hexanes) afforded **12j** (93%) as a >20:1 mixture of diastereomers. Recrystallization from pentanes afforded analytically pure **12j** (mp = 112 °C). IR (mull) 3052, 3023, 1670, 1595 cm^{-1}; ^1H NMR 7.65−7.60 (m, 2H), 7.36−7.08 (m, 8H), 4.24 (s, 1H), 3.78, 2.11 (ABq, J = 17 Hz, 2H), 1.86 (s, 3H), 1.66 (s, 3H), 1.65 (s, 3H); ^{13}C NMR 197.6, 146.6, 137.1, 132.7, 131.6, 129.8, 128.8, 128.0, 127.2, 126.5, 125.5, 66.3, 60.3, 50.5, 13.9, 11.7, 11.6. Anal. Calcd for $C_{21}H_{22}OS$: C, 78.22; H, 6.88. Found: C, 78.37; H, 7.07.

3-Cyclopentene-1-carboxylic Acid, 1-Methyl-2-(methylthio)-, Ethyl Ester (13a/14a). 10a (625 mg, 3.4 mmol) was dissolved in THF (15 mL). HMPA (0.760 mL, 4.4 mmol) was added via syringe and the solution was cooled to −78 °C. To the stirring solution was added LDA·THF (3.8 mL, 4.4 mmol, 1.1 M in cyclohexane) via syringe, and the reaction mixture was stirred at −78 °C over a period of 0.5 h. The solution was warmed to ambient temperature and stirred over a period of 2 h followed by addition of iodomethane (1.0 mL, 17.0 mmol) via syringe. The solution was stirred for an additional 10 min and then partitioned between diethyl ether (100 mL) and saturated sodium bicarbonate (10 mL). The organic portion was dried ($MgSO_4$) and concentrated. Purification via flash chromatography (10% Et_2O/hexanes) afforded 290 mg (43%) of **13a**:**14a** as a 3:1 mixture of diastereomers and 32 mg (5%) of **19**:**20** as an 8:1 mixture of isomers. Analytical data was obtained on the mixture. IR (film) 3063, 2980, 1727, 1611 cm^{-1}; ^1H NMR (**13a**) 5.80−5.74 (m, 1H), 5.70−5.62 (m, 1H), 4.24 (d, J = 3 Hz, 1H), 4.15 (q, J = 7 Hz, 2H), 2.97, 2.22 (ABq of multiplets, J = 17 Hz, 2H), 2.06 (s, 3H), 1.42 (s, 3H), 1.24 (t, J = 7 Hz, 1H); (**14a**) 5.85−5.80 (m, 1H), 5.55−5.51 (m, 1H), 4.26−4.14 (m, 2H, obscured), 3.48 (br s, 1H), 3.15, 2.09 (ABq of multiplets, J = 17 Hz, 2H), 1.95 (s, 3H), 1.37 (s, 3H), 1.31 (t, J = 7 Hz, 3H); ^{13}C NMR (**13a**) 177.2, 130.7, 130.2, 60.8, 58.5, 52.7, 43.8, 21.3, 14.6, 14.0; (**14a**) 174.6, 130.4, 127.8, 60.6, 59.7, 54.4, 41.8, 26.4, 14.1, 12.8; FAB HRMS calcd for $C_{10}H_{16}O_2S$ (M − 1) 199.0792; found 199.0796.

3-Cyclopentene-1-carboxylic Acid, 1,3-Dimethyl-2-(methylthio)- (13b/14b) and 3-Cyclopentene-1-carboxylic Acid, 1,4-Dimethyl-2-(methylthio)- (13c/14c). To a −78 °C

solution of **10b** and **10c** (3:2, 2.11 g, 9.8 mmol) and DMPU (12 mL) in THF (100 mL) was added dropwise LDA·THF (12 mL, 1.1 M, 12.7 mmol). The solution was stirred at −78 °C for 30 min and then allowed to come to room temperature for 2 h. Methyl iodide (3.1 mL, 50 mmol) was added. After 30 min, the reaction was partitioned between ether and saturated aqueous sodium bicarbonate, and the organic phase was washed with water, dried over sodium sulfate, and concentrated. NMR analysis of the crude mixture indicated that the four possible isomers **13b**:**14b**:**13c**:**14c** were present in a ratio of 14:7:13:2, respectively. Flash chromatography (10% ether/hexane) provided the same mixture of isomers free of other impurities (1.74 g, 82%) as a colorless oil. Isomer assignments were based on NOE analysis (see supporting information) and on the relative chemical shifts of the methine protons adjacent to the methylthio group (vide supra). Analytical data was obtained on the mixture. IR (film) 3048, 2979, 2930, 1728, 1655 cm^{-1}; ^1H NMR (**13b**) 5.41 (bs, 1H), 4.14 (q, J = 7 Hz, 2H), 3.99 (s, 1H), 2.87, 2.09 (ABq of multiplets, J = 17 Hz, 2H), 1.96 (s, 3H), 1.78 (s, 3H), 1.42 (s, 3H), 1.24 (t, J = 7 Hz, 1H); (**14c**) 5.17 (bs, 1H), 4.25−4.10 (2H, obscured), 3.44 (s, 1H), 3.10 (half of ABq, 1H, other half obscured), 1.96 (s, 3H), 1.75 (bs, 3H), 1.38 (s, 3H), 1.25 (t, 3H, obscured); (**13c**) 5.26 (bm, 1H), 4.20 (bs, 1H), 4.15 (q, 2H, obscured), 2.86, 2.16 (ABq, J = 17 Hz, 2H), 2.06 (s, 3H), 1.72 (bs, 3H), 1.41 (s, 3H), 1.25 (t, J = 7 Hz, 3H); (**14b**) 5.46 (s, 1H), 4.25−4.17 (m, 2H, obscured), 3.17 (s, 1H), 3.05, 2.00, (ABq of multiplets, J = 17 Hz, 2H), 1.85 (s, 3H), 1.76 (bs, 3H), 1.36 (s, 3H), 1.31 (t, J = 7 Hz, 3H); HRMS calcd for $C_{11}H_{18}O_2S$ 214.1027; found 214.1039.

3-Cyclopentene-1-carboxylic Acid, 1,3,5,5-Tetramethyl-2-(methylthio)-, Ethyl Ester (13d/14d). A mixture of **10d** and **10e** (4:1, 353 mg, 1.5 mmol) was dissolved in THF (10 mL). HMPA (0.350 mL, 2.0 mmol) was added via syringe, and the solution was cooled to −78 °C. To the stirring solution was added LDA·THF (1.75 mL, 2.0 mmol, 1.1 M in cyclohexane) via syringe, and the reaction mixture was stirred at −78 °C over a period of 0.5 h. The solution was warmed to 0 °C and stirred over a period of 0.5 h followed by addition of iodomethane (470 mL, 7.5 mmol) via syringe. The solution was stirred for an additional 10 min followed by partitioning between diethyl ether (50 mL) and saturated sodium bicarbonate (10 mL). The organic portion was dried ($MgSO_4$), filtered over a plug of silica gel (7 g, rinsing with diethyl ether), and concentrated. Purification via flash chromatography (10% Et_2O/hexanes) afforded 284 mg (78%) of **13d:14d** as a 1:1 mixture of diastereomers (colorless oil). Analytical data was obtained on the mixture. IR (film) 2975, 1725 cm^{-1}; ^1H NMR (both isomers) 5.87 (s, 1H), 5.77 (s, 1H), 5.09 (bs, 1H), 4.31 (bs, 1H), 4.21−4.10 (m, 4H, both isomers), 2.16 (s, 3H), 1.90 (bs, 3H), 1.82−1.77 (bs, 6H, both isomers), 1.67 (bs, 3H), 1.52 (s, 6H, both isomers), 1.31−1.24 (m, 9H, both isomers), 1.08 (s, 3H), 0.89 (s, 3H). Anal. Calcd for $C_{13}H_{22}O_2S$: C, 64.42; H, 9.15. Found: C, 64.06; H, 9.11.

3-Cyclopentene-1-carboxylic Acid, 1,3,5-Trimethyl-2-(methylthio)-, Ethyl Ester (13f/13f′/13f″/13f‴). To a −78 °C solution of ester **10f** (1:1 mixture of diastereomers, 1.00 g, 4.66 mmol) in dry THF (25 mL) and HMPA (1.0 mL, 6.1 mmol) was added LDA (mono THF, 1.3 M in cyclohexane, 4.6 mL, 6.1 mmol) dropwise. The solution was stirred at −78 °C for 30 min and then at 0 °C for 30 min. The reaction was quenched by the addition of methyl iodide (1.45 mL, 23 mmol) and then stirred another 30 min at 0 °C. The reaction was partitioned between saturated $NaHCO_3$ and ether, and the organic layer was washed with water and then dried over $MgSO_4$. Concentration in vacuo provided an orange oil (1.18 g) which was an approximately 2:2:2:1 mixture of cyclopentene diastereomers (minor isomer: **13f‴**) in combination with a mixture of vinyl cyclopropanes (about 2:1 five-membered ring: three-membered ring). Flash chromatography (5% ether/hexane) provided a mixture of three of the cyclopentene diastereomers (**13f′**−**13f‴**) (0.52 g, 49%) along with the fourth diastereomer **13f** as a mixture with vinyl cyclopropanes (63 mg, 6%), all as colorless oils. Analyses were performed on the mixture. ^1H NMR ($CDCl_3$) (significant peaks only): **13f**: 3.25 (bs, 1H), 2.58 (m, 1H), 2.20 (s, 3H), 1.03 (d, 3H, J = 7 Hz); **13f′**: 3.37 (m, 1H), 3.17 (bs), 1.90 (s, 3H), 0.96 (d, 3H, J = 7 Hz); **13f″**: 4.10 (bs, 1H), 2.98 (m, 1H), 2.09 (s, 3H), 0.98 (d, 3H, J = 7 Hz); **13f‴**: 4.18 (bs, 1H), 2.50 (m, 1H), 2.04 (s, 3H), 0.90 (d, 3H, J = 7 Hz); remaining data is for the mixture of **13f′**−**13f‴**. IR (film) 2975 (s), 1727 (s), 1240 (s), 1218 (s), 1114 (s); MS (EI) 228 (M^+, 20), 107 (99); HRMS (EI) calcd for $C_{12}H_{20}O_2S$ 228.1184; found 228.1181. The minor isomer (**13f‴**) was tentatively assigned as 1,2-*trans*-1,5-*cis* based on the chemical shifts of the two methine protons relative to the other isomers (vide supra).

Cyclopropane, 1,1-Diphenyl-2-methyl-2-[2-(methylthio)-1-(methyl)ethenyl]- (16) and Cyclopentene, 1,2-Dimethyl-3-(methylthio)-4,4-diphenyl- (17). To a −78 °C solution of **15**[16b] (690 mg, 2.46 mmol) and HMPA (0.549 mL, 3.16 mmol) in dry THF (14 mL) was added LDA (1.03 M in hexane, 3.02 mL, 3.16 mmol) dropwise. The deep wine-red reaction was stirred at −78 °C for 1 h and then warmed to 25 °C for 30 min. Methyl iodide (0.23 mL, 3.7 mmol) was added, and the solution was stirred for 10 min before partitioning between ether and saturated aqueous sodium bicarbonate. The organic phase was washed with water, dried over magnesium sulfate, and concentrated to a viscous yellow oil (0.69 g). Flash chromatography (2% ether/hexane) provided pure **16** (149 mg), a mixture of **16** and **17** (356 mg), and pure **17** (63 mg). The total yield was 78%. The proton NMR spectrum of **16** agreed with that reported in the literature.[16b] Analysis of cyclopentene **17**: ^1H NMR 7.1−7.3 (m, 10H), 4.19 (bs, 1H), 3.37, 2.55 (ABq, J = 15 Hz, 2H), 1.87 (bs, 3H), 1.68 (bs, 3H), 1.59 (s, 3H); ^{13}C NMR (multiplicity) 150.6 (s), 145.9 (s), 132.1 (s), 131.1 (s), 128.9, 127.7, 127.4, 127.2, 125.9, 125.5 (all d), 65.4 (d), 58.4 (s), 50.0 (t), 14.0, 13.6, 12.3 (all q); IR (film) 2919, 1493, 1443, 696 cm^{-1}; HRMS calcd for $C_{20}H_{22}S$ 294.1442; found 294.1455.

Cyclopropanecarboxylic Acid, 2-[2-(methylthio)-1-methylethenyl]-, 1,2-Dimethyl-, Ethyl Ester (18a). To a −78 °C solution of **7a** (4.50 g, 21.0 mmol) and HMPA (4.7 mL, 27 mmol) in THF (125 mL) was added LDA bis(THF) (1.06 M in hexane, 26 mL, 27 mmol) via syringe drive over about 10 min. The brown solution was stirred at that temperature for 1 h and then at −45 °C for 10 min before quenching with methyl iodide (6.5 mL, 105 mmol). The reaction was stirred at −45 °C for 15 min and then warmed to room temperature. After dilution with ether (250 mL), the solution was washed with saturated aqueous $NaHCO_3$ and then water. Drying of the organic phase over $MgSO_4$ and concentration in vacuo left an amber oil (5 g). NMR analysis indicated a 7:3:1 mixture of **18a**:**11a**:**12a**. Flash chromatography (3:1 chloroform:hexane) provided the mixture free from other impurities (3.07 g, 64%) but could not separate the components. An analytical sample of **18a** was obtained by HPLC (Waters Prep 500A, 60% methylene chloride/hexane). ^1H NMR 5.71 (bs, 1H), 4.16 (q, 2H, J = 7 Hz), 2.23 (s, 3H), 1.76 (s, 3H), 1.39 (half of ABq, 1H, J = 5 Hz), 1.2−1.3 (half of ABq, 1H, obscured), 1.274 (s, 3H), 1.269 (t, 3H, J = 7 Hz), 1.25 (s, 3H); ^{13}C NMR (multiplicity) 173.8 (s), 134.1 (s), 125.1 (d), 60.3 (t), 33.1 (s), 30.0 (s), 25.6 (t), 22.2 (q), 17.8 (q), 17.5 (q), 17.2 (q), 14.3 (q); IR (film) 1720, 1440, 1290, 1220, 1170, 1140^{-1}; EI MS 228 (M^+, 7), 107 (100); HRMS calcd for $C_{12}H_{20}O_2S$ 228.1184; found 228.1174.

Cyclopropanecarboxylic Acid, 2-[2-(Methylthio)-ethenyl]-1-methyl-, Ethyl Ester (19/20). 10a (308 mg, 1.66 mmol) was dissolved in THF (10 mL). HMPA (0.375 mL, 2.2 mmol) was added via syringe, and the solution was cooled to −78 °C. To the stirring solution was added (LDA·THF, 1.7 mL, 2.2 mmol, 1.3 M in cyclohexane) via syringe, and the reaction mixture was stirred at −78 °C over a period of 0.5 h. The solution was warmed to 0 °C and stirred over a period of 0.5 h followed by addition of iodomethane (0.52 mL, 8.3 mmol) via syringe. The solution was stirred for an additional 10 min before partitioning between diethyl ether (100 mL) and saturated sodium bicarbonate (10 mL). The organic portion was dried ($MgSO_4$), filtered over a plug of Celite with diethyl ether, and concentrated. Purification via preparative layer chromatography (silica gel, 1 mm, 10% Et_2O/hexanes) afforded 269 mg (81%) of **19**:**20** as an 7:1 mixture of diastereomers along with ca. 5% of **13a**:**14a** (1:2) (colorless oil). Analytical data was obtained on the mixture. IR (film) 3082, 2981, 1718, 1604 cm^{-1}; ^1H NMR (**19**) 6.08 (d, J = 9 Hz, 1H), 5.21 (t, J = 9 Hz, 1H), 4.15 (q, J = 6 Hz, 2H), 2.30 (s, 3H), 2.25 (br t, J = 9 Hz,

1H), 1.65 (dd, J = 9, 4 Hz, 1H), 1.27 (s, 3H), 1.25 (t, J = 7 Hz, 3H), 0.71 (dd, J = 6.5, 4 Hz, 1H); (**20**) (apparent peaks only) 5.94 (d, J = 9 Hz, 1H), 5.50 (t, J = 9 Hz, 1H), 2.29 (s, 3H), 1.90 (br m, 1H), 1.47 (m, 1H), 1.07 (dd, J = 9, 4 Hz, 1H). Anal. Calcd for $C_{10}H_{16}O_2S$: C, 59.96; H, 8.05. Found: C, 59.64; H, 8.07.

Cyclopropanecarboxylic Acid, 2-[2-(Benzoylthio)-1-methylethenyl]-, 1,2-Dimethyl-, Ethyl Ester (21). To a −78 °C solution of **7a** (1.25 g, 5.8 mmol) in THF (45 mL) and HMPA (1.3 mL, 7.6 mmol) was added LDA·THF (5.1 mL, 7.6 mmol, 1.5 M in cyclohexane) via syringe. The reaction mixture was stirred over a period of 0.5 h at −78 °C and then warmed to −45 °C and stirred over a period of 40 min. This was followed by addition of benzoyl chloride (3.5 mL, 30.0 mmol) via syringe. The solution was stirred for an additional 0.5 h and then poured into diethyl ether (50 mL) and saturated sodium bicarbonate (20 mL). The organic portion was washed with water, dried ($MgSO_4$), and filtered. Purification via flash chromatography (10% Et_2O/hexanes) afforded 1.61 g (86%) of **21** contaminated with a small amount (approximately 10%) of cyclopentenes as a 1:1 mixture of diastereomers. Analytically pure **21** suitable for single crystal X-ray diffraction analysis could be obtained via fractional recrystallization from pentanes (−30 °C) then ethanol/water (3:1, −20 °C). mp = 42−43 °C; IR (mull) 3035, 2929, 1720, 1672, 1595 cm^{-1}; ^1H NMR 8.00−7.97 (m, 2H), 7.62−7.56 (m, 1H), 7.50−7.44 (m, 2H), 6.72 (s, 1H), 4.22−4.13 (m, 2H), 2.04 (s, 3H), 1.48 (br s, 1H), 1.33−1.25 m, 9H), 0.99 (br s, 1H). Anal. Calcd for $C_{18}H_{22}O_3S$: C, 67.89; H, 6.96; S, 10.07. Found: C, 67.91; H, 6.95; S, 10.10.

Cyclopentene-1-carboxylic Acid, 2-Mercapto-1,3,4-trimethyl-, Ethyl Ester (23/24). To a −78 °C solution of **7a** (1.0 g, 4.7 mmol) dissolved in THF (50 mL) and HMPA (1.0 mL, 6.1 mmol) was added LDA·THF (5.5 mL, 6.1 mmol). The reaction mixture was allowed to stir at −78 °C over a period of 0.5 h and then warmed to 0 °C and stirred over for 0.5 h before partitioning between diethyl ether (100 mL) and saturated ammonium chloride (50 mL). The organic portion was washed with water, dried ($MgSO_4$), filtered over a plug of silica gel with ether, and concentrated to give an orange oil. Purification via flash chromatography (10% Et_2O/hexanes) afforded 0.48 g (48%) of **23**:**24** as a 6:1 mixture of diastereomers and ca. 5% of unreacted **7a** (colorless oil). A pure sample of **23** could be obtained by repeat chromatography. IR (film) 2933, 2914, 2564, 1728 cm^{-1}; ^1H NMR (**23**) 4.19 (br d, J = 9 Hz, 1H), 4.13 (q, J = 7 Hz, 2H), 2.80, 2.22 (ABq, J = 16 Hz, 2H), 1.69 (s, 3H), 1.62 (s, 3H), 1.38 (s, 3H), 1.24 (t, J = 7 Hz, 3H), 1.22 (d, J = 9 Hz, 1H); (**24**) (apparent peaks only) 4.19 (q, J = 7 Hz, 2H), 3.42 (br d, J = 8 Hz, 1H), 3.18, 1.92 (ABq, J = 16 Hz, 2H), 1.63 (s, 3H), 1.62 (s, 3H), 1.48 (d, J = 8 Hz, 1H); HRMS calcd for $C_{11}H_{18}O_2S$ 214.1027; found 214.1039.

2*H*-Thiopyran-2-carboxylic Acid, 3,6-Dihydro-4,5-dimethyl-2-(1-hydroxyethyl)-, Ethyl Ester (26). To a −78 °C solution of **9**[11] (1.27 g, 6.3 mmol) in THF (40 mL) was added LDA·THF (6.3 mL, 8.2 mmol, 1.3 M in cyclohexane). The reaction mixture was allowed to stir at −78 °C over a period of 0.5 h followed by addition of excess acetaldehyde (3.5 mL, 63 mmol) via cannula. The reaction mixture was allowed to stir at −78 °C over a period of 10 min before directly partitioning between diethyl ether (100 mL) and saturated sodium bicarbonate (50 mL). The organic portion was dried ($MgSO_4$) and concentrated to give 2.5 g of a yellow oil. Purification via flash chromatography (1:1 Et_2O/hexanes) afforded 1.48 g (96%) of **26** as a 1:1 mixture of diastereomers. Analytical data obtained on the mixture: IR (film) 3486, 2932, 2910, 1727 cm^{-1}. Anal. Calcd for $C_{12}H_{20}O_3S$: C, 58.98; H, 8.25. Found: C, 58.72; H, 8.33. The individual diastereomers could be separated via iterative column chromatography using silica gel and eluting with 1:1 Et_2O/hexanes. ^1H NMR (**26**, *high* R_f) 4.28−4.12 (m, 2H), 4.04 (quintet, J = 6 Hz, 1H), 3.14, 2.98 (ABq, J = 16 Hz, 2H), 2.77 (d, J = 6 Hz, 1H), 2.56, 2.48 (ABq, J = 16Hz, 2H), 1.76 (s, 3H), 1.73 (s, 3H), 1.32−1.23 (m, 6H); (**26**, *low* R_f) 4.28−4.16 (m, 2H), 3.94 (quintet, J = 7 Hz, 1H), 3.13, 2.97 (ABq, J = 17 Hz, 2H), 2.78 (d, J = 7 Hz, 1H), 2.56, 2.32 (ABq, J = 17 Hz, 2H), 1.72 (s, 6H), 1.30−1.23 (m, 6H); ^{13}C NMR (**26**, *high* R_f) 173.0, 127.3, 123.6, 71.0, 61.5, 58.4, 34.6, 30.8, 20.4, 19.0, 17.9, 14.1; (**26**, *low* R_f) 172.4, 126.1, 122.9, 71.4, 61.4, 57.4, 36.8, 30.3, 20.2, 19.0, 18.4, 14.1.

2*H*-Thiopyran-2-carboxylic Acid, 3,6-Dihydro-4,5-dimethyl-2-[1-[(trimethylsilyl)oxy]ethyl]-, Ethyl Ester (27). To a −78 °C solution of **26** (*high* R_f) (717 mg, 2.9 mmol) in THF (15 mL) was added LDA·THF (2.9 mL, 3.2 mmol, 1.1 M in cyclohexane). The reaction mixture was allowed to stir at −78 °C over a period of 0.5 h followed by addition of trimethylsilyl chloride (1.1 mL, 6.3 mmol) via syringe. The reaction mixture was warmed to 0 °C and stirred over a period of 10 min before being partitioned between diethyl ether (100 mL) and saturated sodium bicarbonate (20 mL). The organic portion was dried ($MgSO_4$) and concentrated to give 2.0 g of a yellow oil. Purification via flash chromatography (10% Et_2O/hexanes) afforded 900 mg (96%) of **27** as a single diastereomer (colorless oil). IR (film) 2980, 1728 cm^{-1}; ^1H NMR 4.12−3.94 (m, 3H), 3.03, 2.74 (ABq, J = 16 Hz, 2H), 2.37, 2.32 (ABq, J = 16 Hz, 2H), 1.59 (s, 3H), 1.56 (s, 3H), 1.12 (t, J = 7 Hz, 3H), 1.07 (d, J = 6 Hz, 3H), 0.00 (s, 9H); ^{13}C NMR 172.0, 126.7, 122.2, 71.6, 60.8, 57.5, 34.6, 30.7, 20.1, 19.2, 16.8, 13.9, 0.0; FAB HRMS calcd for $C_{15}H_{28}O_3SSi$ (M + 1) 317.1607; found 317.1602.

3-Cyclopentene-1-carboxylic Acid, 3,4-Dimethyl-2-(methylthio)-1-[1-[(trimethylsilyl)oxy]ethyl]-, Ethyl Ester (28). **27** (single high R_f diastereomer, 70 mg, 0.2 mmol) was dissolved in THF (2 mL), and DMPU (0.240 mL) was added. The solution was cooled to −78 °C before the addition of LDA·THF (0.220 mL, 0.3 mmol, 1.3 M in cyclohexane) via syringe, and the reaction mixture was stirred at −78 °C over a period of 0.5 h. The solution was warmed to 0 °C and stirred over a period of 0.5 h before the addition of iodomethane (68 mL, 1.1 mmol) via syringe. The solution was stirred for an additional 10 min and then poured into diethyl ether (25 mL) and saturated sodium bicarbonate (10 mL). The organic portion was dried ($MgSO_4$) and concentrated to give a yellow oil. Purification via preparative layer chromatography (silica gel, 1 mm thickness, 75 g, 10% Et_2O/hexanes) gave 43 mg (59%) of **28** as a 20:10:7:1 mixture of diastereomers (**28**:**28′**:**28″**:**28‴**), determined by NMR integration of the methine protons α to the sulfur. Analytical data was obtained on the mixture. IR (film) 2974, 1733, 1722 cm^{-1}; ^1H NMR (diagnostic signals only) (**28**) 4.47 (q, J = 6 Hz, 1H), 3.95 (bs, 1H), 2.58, 2.03 (ABq, J = 16 Hz), 1.83 (s, 3H), 1.58 (bs, 3H), 1.53 (bs, 3H); (**28′**) 4.19 (q, J = 6 Hz, 1H), 3.80 (bs, 1H), 2.75, 2.05 (ABq, J = 16 Hz), 1.74 (s, 3H); (**28″**) 3.34 (bs, 1H), 2.81, 2.20 (ABq, J = 16 Hz, 2H), 1.73 (s, 3H), 1.00 (d, J = 6 Hz); (**28‴**) 4.25 (q, 1H, J = 6 Hz), 3.00 (bs, 1H), 0.78 (d, J = 6 Hz, 3H). Anal. Calcd for $C_{16}H_{30}O_3SSi$: C, 58.14; H, 9.15. Found: C, 58.34; H, 9.05.

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Supporting Information Available: ^1H NMR spectra for compounds **7a**, **7b**, **7c**, **7k**, **8**, **10a**, **10b/10c**, **10d/10e**, **10f**, **11a**, **11b/12b**, **11d/12d**, **11f**, **11i/12i**, **11l**, **11w/12w**, **13a/14a**, **13b/13c**, **14b/14c**, **13f**, **17**, **18a**, **23**, **27**; NOE analyses of compounds **11a**, **11d/12d**, **12f**, **18m**, **13b/14b**, **13c/14c**, **19/20**; ORTEP diagrams[13] of compounds **12j**, **12m**, **21** (31 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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