A New Method for the Preparation of 2-Thio Substituted Furans by Methylsulfanylation of γ-Dithiane Carbonyl Compounds

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Several related methods for the preparation of differentially substituted 2-thiofurans are described. The general procedure involves the formation of a thionium ion from a γ-dithianyl substituted carbonyl compound followed by cyclization of this reactive intermediate onto the tethered carbonyl group. Two methods for thionium ion generation were explored. One of these involved an acid-catalyzed reaction of β-ketenedithioacetals, prepared from the condensation of 2,2-bis(methylsulfanyl)acetaldehyde with a variety of ketones. Cyclization followed by loss of methane thiol gave 2-thiofurans **17**, **18** and **23**, **24** in 70−90% yield. Attempts to prepare 5-heteroatom substituted 2-thiofurans from the corresponding β-ketenedithioacetal amides or esters were unsuccessful, leading to 1,2-thio rearranged products. A more successful route involved the reaction of β-acetoxy-γ-thianyl carbonyl compounds with dimethyl(methylthio)sulfonium tetrafluoroborate (DMTSF). Treatment of the dithiane with this reagent resulted in the smooth generation of a thionium ion. Cyclization followed by loss of acetic acid afforded thiofurans **17**, **18**, **23**, **47**−**49**, **51**, and **61**−**64** in 40−100% yield. The *N*-butenyl substituted thioamido furan furnished a rearranged hexahydropyrroloquinolin-2-one in high yield when heated at 110 °C.

The synthesis of variously substituted furans continues to be of considerable interest[1−3] due to the presence of this heteroaromatic nucleus in commercially important pharmaceuticals,[4] fragrances, and dyes.[5] Furans are also common substructures in numerous naturally occurring biologically active compounds.[6,7] These heteroaromatics also serve as useful intermediates for the synthesis of aromatic, acyclic, and cyclic molecules.[8] Accordingly, many strategies have been developed for the preparation of substituted furans.[9] 2-Alkylthio furans are particularly attractive intermediates that have found usage in organic synthesis. They undergo a variety of reactions including addition/elimination,[10] nickel-catalyzed Grignard coupling,[11] Michael addition,[12] *ortho*-metalation,[13] and acid hydrolysis to butenolides,[14] as well as [4 + 2]-cycloaddition chemistry.[15] Although a number of synthetic procedures are available for their formation,[13,16] most of the existing methods often require harsh conditions and are frequently based on the use of a preexisting furan ring. Examples include the addition/elimination of thiols,[17] sulfanylation of *ortho*-metalated anions,[18] metalation of disulfides,[13] and alkylation of furan thiolates.[19] Our own interest in this area stems from the facility with which 2-alkylthio-5-amino substituted furans undergo Diels−Alder cycloaddition chemistry and the potential use of the resulting oxabicyclic adducts for alkaloid synthesis (Scheme 1).[20] Although this methodology al-

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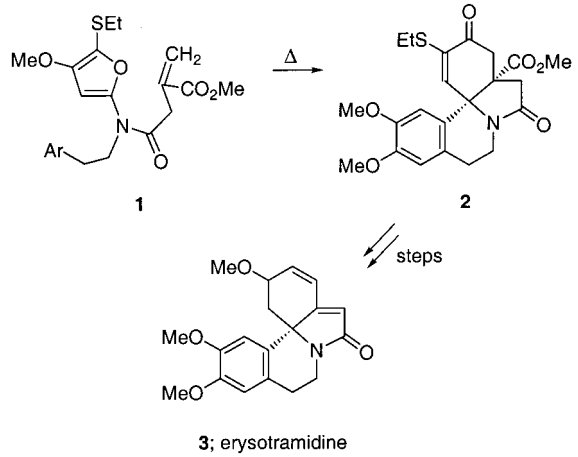
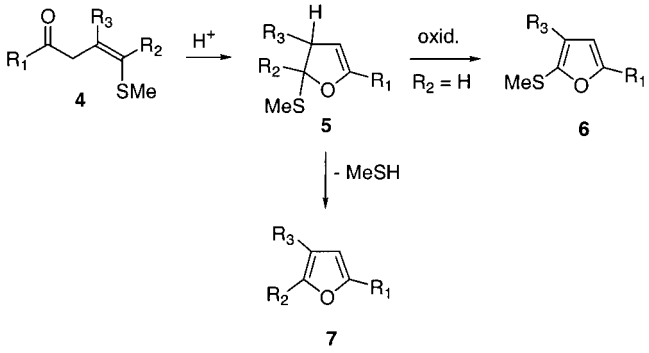
Scheme 1



Scheme 2



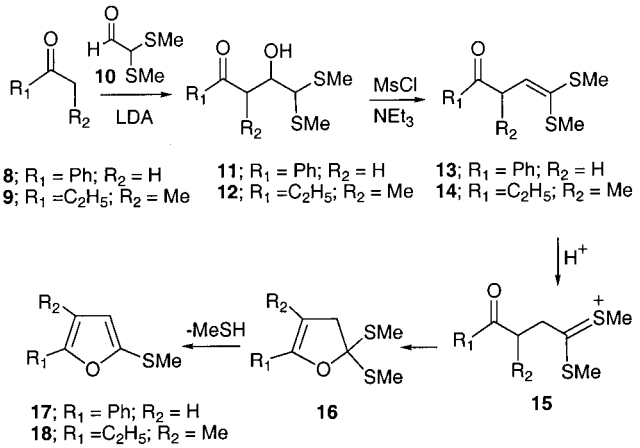
lowed for the facile and rapid access to the erythrinane skeleton,[21] there were limitations in the synthesis of the starting thio-amidofuran system that prompted us to explore alternate methods of preparing these useful heterocycles. Consequently, we decided to develop a general method for the preparation of 2-thio substituted furans with the intention of using these substrates as reactive dienes for alkaloid synthesis. In an earlier report we described some preliminary results in this area,[22] and in this paper we expand on our initial findings.

Results and Discussion

2-Alkylthio substituted furans have been prepared from the acid-catalyzed cyclization of ketones onto vinyl sulfides.[23,24] A drawback to this procedure is that after the thionium ion is trapped by the neighboring carbonyl oxygen to furnish a dihydrofuran, a subsequent oxidation step is necessary in order to produce the thiofuran ring system (i.e., **6**). In the absence of an oxidant, elimination of the thiol group would normally occur leading to the formation of a simple furan **7** (Scheme 2).

We reasoned that the use of a ketene dithioacetal would allow for both the facile formation and subsequent cyclization of a thionium ion and also permit rapid

Scheme 3



aromatization of the dihydrofuran by loss of sulfide, thereby avoiding the need for a subsequent oxidation step. Ketene dithioacetals are well-known to generate thionium ions under acidic conditions and have been trapped with tethered nucleophiles to give polycyclic products.[25−28] Indeed, our early work showed that the acid-catalyzed reaction of β-oxo ketene thioacetals **13** and **14** gave furans **17** and **18** in 70% and 83% yield, respectively.[22] This reaction presumably proceeds by a *protonation−cyclization−elimination* sequence as outlined in Scheme 3. The starting ketene dithioacetals were prepared by an aldol condensation of ketones **8** and **9** with bis(methylsulfanyl)acetaldehyde[29] (**10**) followed by dehydration with mesyl chloride and triethylamine.

Interestingly, when the related cyclic aldol condensation products **19** and **20** were subjected to identical elimination conditions, the expected ketene dithioacetals were not isolated, but rather the rearranged *trans*-dithiosubstituted dihydrofurans **21** and **22** were formed in 66% and 94% yield, respectively. Conversion to the corresponding furanyl systems was readily achieved in 87% and 89% by heating a sample of the appropriate dihydrofuran with a trace of camphorsulfonic acid at 110 °C. The formation of the rearranged dihydrofuran can be envisioned to proceed via an episulfonium ion intermediate (i.e., **25**) formed by [1,2]-SR participation followed by enolization and subsequent ring opening (Scheme 4). Episulfonium ions are well-recognized reactive intermediates that have been postulated many times in the literature to rationalize the stereoselectivity observed upon treating 1,2-thio alcohols with acid.[30] A preferred 5-*endo* cyclization (rather than 4-*exo*) by the enol oxygen atom on the three-membered cationic intermediate nicely accounts for the observed products. The observed *trans*-relationship of the methylthio groups in the final product is seemingly related to thermodynamic issues. It is not at all clear, however, why these cyclic β-hydroxy ketones (i.e., **19** and **20**) prefer to give dihydrofurans rather than eliminate water, as was encountered with the acyclic

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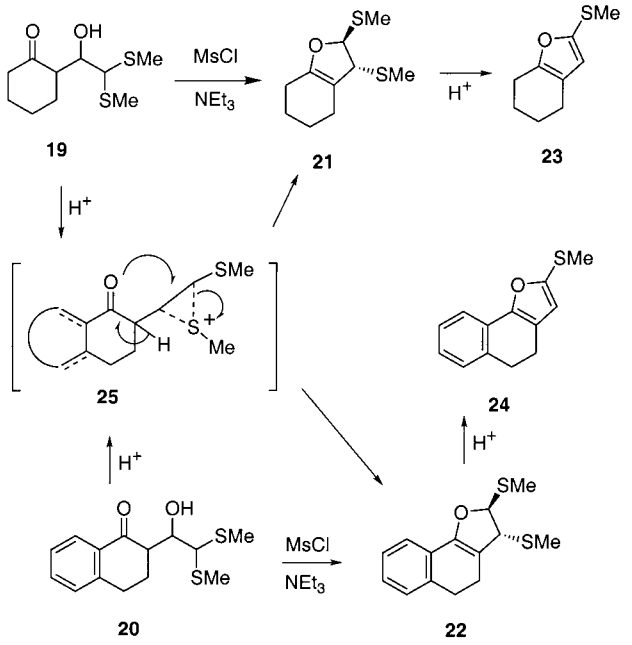
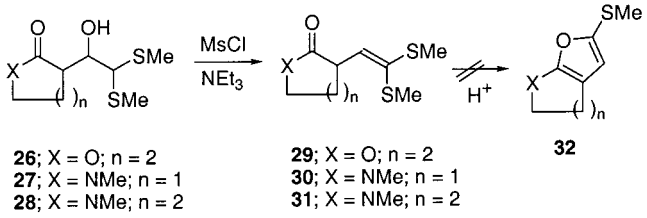
Scheme 4



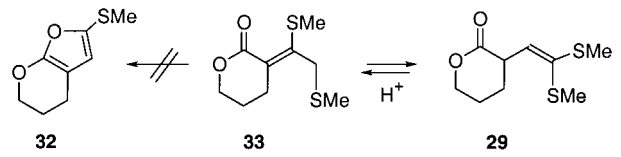
Scheme 5



26; X = O; n = 2
27; X = NMe; n = 1
28; X = NMe; n = 2

29; X = O; n = 2
30; X = NMe; n = 1
31; X = NMe; n = 2

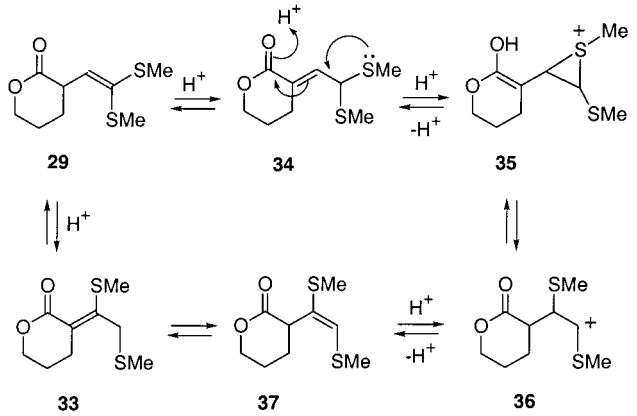
Scheme 6



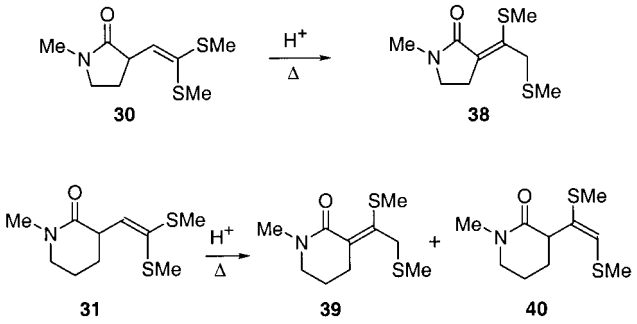
systems (i.e., **11** and **12**). The closer proximity of the enol oxygen atom to the episulfonium ion may play an important role here. Restricted rotation about the bond between the α-carbon and the carbonyl group could create an environment wherein the enol oxygen atom is properly oriented to facilitate the cyclization reaction.

Encouraged by the facility with which the above ketene dithioacetals cyclized to give 2-alkylthio substituted furans, we next investigated the related reaction using substrates derived from the aldol condensation of lactones and lactams with aldehyde **10** (Scheme 5). With these systems, dehydration proceeded smoothly to give ketene dithioacetals **29**−**31**. However, when **29**−**31** were subjected to the acid-catalyzed conditions employed earlier, none of the desired furan (i.e., **32**) could be detected. Instead, products arising from a 1,2-methylthio shift were isolated. For example, subjection of **29** to the aforementioned acidic conditions gave the rearranged thio-conjugated lactone **33** in 80% yield together with unreacted starting material (Scheme 6). Interestingly, when **33** was subjected to the same acidic conditions, thioketene acetal **29** was formed in 20% yield in addition to recovered **33**. We believe that the interconversion of **29** and **33** occurs via the transient episulfonium ion **35** (Scheme 7). The critical step leading to the formation of

Scheme 7



Scheme 8

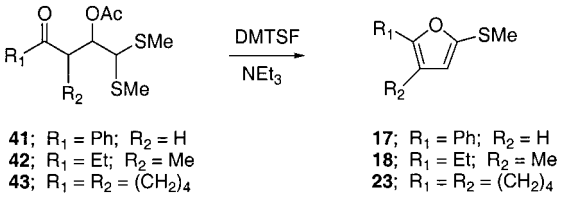


35 involves an acid-induced 1,3-hydrogen shift of **29** to give **34**, which is followed by conjugate addition of the neighboring methylthio group onto the activated π-bond. Once formed, episulfonium ion **35** can undergo a subsequent ring opening in the opposite direction to produce thionium ion **36**, which undergoes deprotonation and double bond isomerization to give **33**. A related set of reactions also takes place when **33** is subjected to the acidic conditions, eventually giving thioketene acetal **29** as the minor product (20%) from the equilibrating mixture.

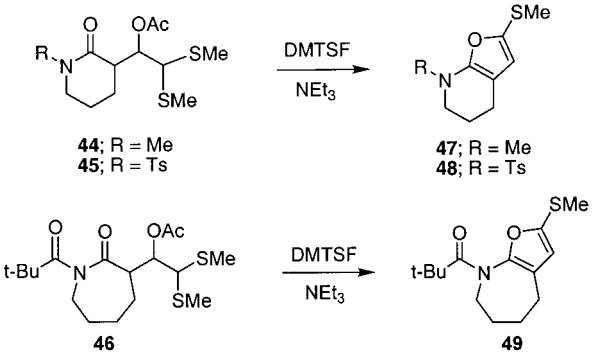
Related rearrangements occurred with the amido substituted ketene thioacetals **30** and **31** (Scheme 8). Thus, heating a sample of pyrrolidinone **30** with camphorsulfonic acid in toluene at 120 °C afforded the rearranged thio-conjugated lactam **38** in 83% yield. Similarly, the acid-catalyzed reaction of the homologous piperidinone **31** furnished **39** as the major reaction product (40%), together with lesser quantities (22%) of **40** derived by a 1,3-hydrogen shift from **39**. Presumably these products are formed in a fashion analogous to that described above with the lactone system (see Scheme 7). The difference in the acid-catalyzed behavior of **29**−**31** from that encountered with ketene thioacetals **13** and **14** may be related to the lower concentration of the enol tautomer of the lactone and/or lactam, thereby permitting methylthio group migration to compete with cyclization.

The series of steps shown in Scheme **7**, although credible in retrospect, was totally unexpected. Our inability to prepare the furanyl systems **32** from the acid-catalyzed reaction of the thioketene acetals **29**−**31** led us to consider some alternate ways to synthesize these compounds. It was known that treatment of thioketals with dimethyl(methylthio)sulfonium tetrafluoroborate (DMTSF)[31] causes the carbon−sulfur bond to become labile upon methylthiolation.[32,33] The initially formed

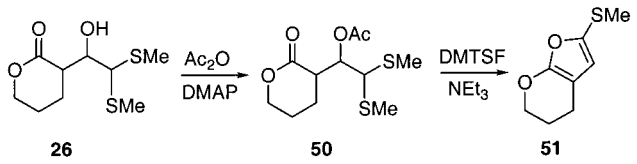
Scheme 9



Scheme 10



Scheme 11

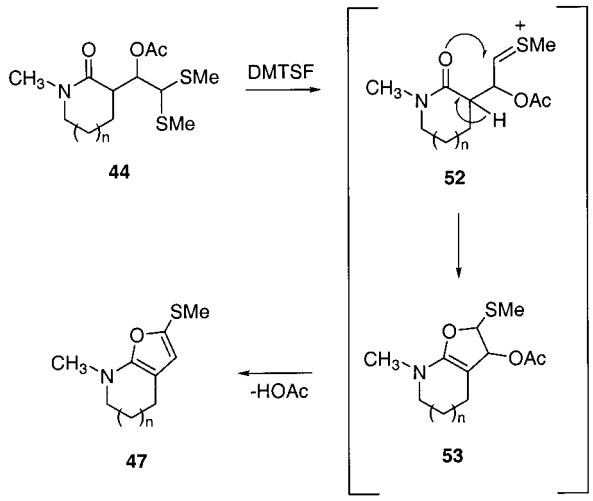


alkylthiosulfonium ion easily dissociates to produce a thionium ion and methyl disulfide.[34,35] We reasoned that by converting the hydroxyl group present in the lactone and lactam derived aldol products to the corresponding acetates, it should be possible to promote cyclization of the lactone/lactam carbonyl group onto the resulting thionium ion formed from the DMTSF-induced reaction. Once the dihydrofuran ring has been forged, elimination of acetic acid should proceed readily to furnish the desired cyclic alkoxy and/or amido substituted furans. Indeed, this two step protocol worked extremely well for acetates **41**−**43**, resulting in the formation of thiofurans **17**, **18**, and **23** in high yield (Scheme 9). Moreover, we found that this protocol could also be successfully executed with *N*-substituted lactams **44**−**46**, giving rise to the corresponding cyclic aminofurans **47**−**49** in 98%, 87%, and 78% yield, respectively (Scheme 10).

A representative example of a 2-oxo-5-thiofuran that was prepared using this method is outlined in Scheme 11. Thus, the aldol product **26** derived from *δ*-valerolactone and aldehyde **10** was acetylated in high yield using acetic anhydride. When the resulting acetate **50** was treated with DMSTF and NEt_3, the cyclic 2-oxo-5-thiofuran **51** was obtained in 40% yield. Although unstable to silica gel chromatography, furan **51** could be purified by filtration through basic alumina and was stable for prolonged periods when stored at −10 °C.

The ease with which the S−S bond of (dimethylthio)-sulfonium salts are cleaved by nucleophilic reagents was

Scheme 12



first documented by Helmkamp and co-workers in their work on the preparation of DMTSF and its addition to alkenes and alkynes.[36] These reactions, and related studies by Meerwein,[37] indicate that reagents such as DMTSF may be regarded as sulfanyl derivatives and can function as a potential source of alkylsulfanyl ions.[31,38] It was known from earlier work in the literature that carbon−sulfur bonds of sulfides become labile on alkylsulfanylation and that the sulfonium ions so formed are highly reactive intermediates that seldom can be isolated.[32] It follows, therefore, that the conversion of **44**−**46** (or **50**) to **47**−**49** (or **51**) upon treatment with DMTSF proceeds by the pathway outlined in Scheme 12. Methylthiolation of one of the methylthio groups with DMTSF first produces an alkylthiosulfonium salt that easily dissociates to generate thionium ion **52** and methyl disulfide. Attack of the amido carbonyl oxygen onto the cationic center produces dihydrofuran **53** as a transient intermediate that readily loses acetic acid to furnish the observed thio substituted furan **47**.

Simple 2-alkylamino substituted furans such as **47** are extremely susceptible toward hydrolysis and are difficult to work with. However, the presence of an electron-withdrawing group on the nitrogen atom (i.e., tosyl, acetyl) stabilizes the furan ring and allows for the ready isolation of substrates suitable for cycloaddition studies (vide infra). Since we were particularly interested in using *N*-acylamido furans containing olefinic tethers as substrates for alkaloid synthesis, we required an easy method for their preparation. The facility with which the DMTSF-induced reaction of the acetoxy substituted thioacetal **44** gave furan **47** prompted us to investigate a related approach toward various *N*-acylamido substituted furans. After some experimentation, we found that these systems can be prepared by the mixed aldol reaction of the *N*-trimethylsilyl protected *δ*-valerolactam[42] (or *ϵ*-caprolactam) with bis(methylsulfanyl)acetaldehyde **10**.

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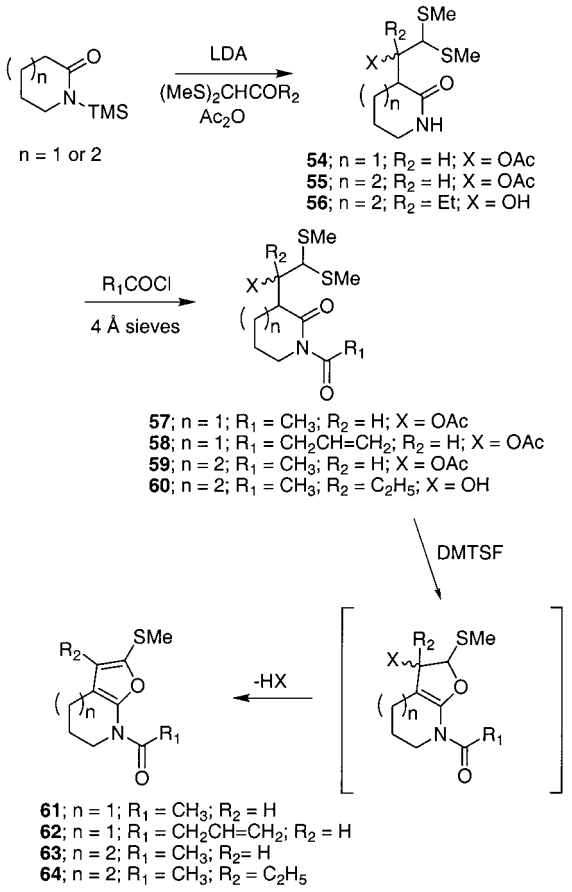
Scheme 13

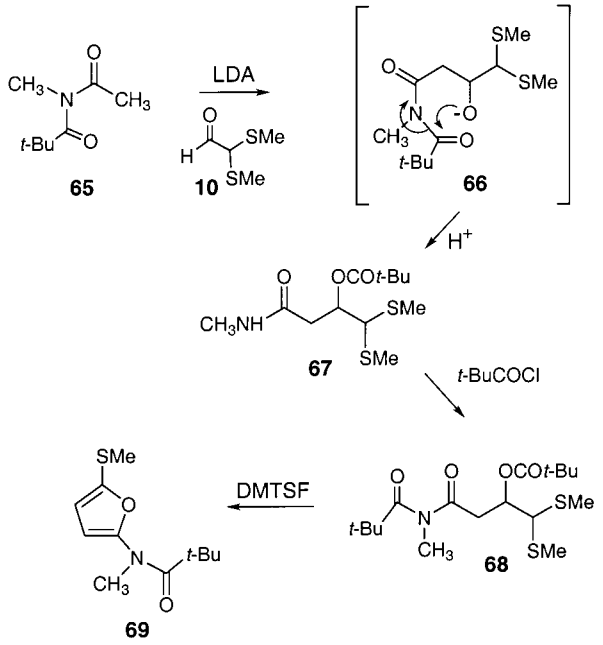


Quenching the reaction with acetic anhydride followed by aqueous workup provided the expected aldol product (i.e., **54** or **55**) in high yield as a mixture of diastereomers (Scheme 13). The cyclic lactams were acylated with acetic anhydride or an acid chloride using powdered 4Å molecular sieves as a neutral acid scavenger to provide the corresponding imides **57**−**60** in high yield. Subsequent treatment with DMTSF afforded the desired *N*-acylamido furans **61**−**63** in yields ranging from 55% to 70%. Compounds **56** and **60** are prepared from 1,1-bis(methylsulfanyl)butan-2-one instead of bis(methylsulfanyl)-acetaldehyde (**10**). With this system the tertiary alcohol does not need to be acylated for the subsequent transformation to furan **64**.

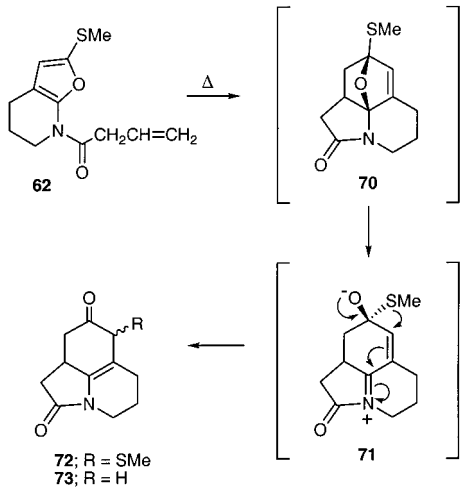
An unexpected acyl rearrangement was encountered when *N*-pivaloyl-*N*-methylacetamide (**65**) was employed as the starting amide. With this system, the initially formed crossed-aldol intermediate **66** underwent a rapid N−O acyl transfer reaction to provide the secondary amide **67** upon aqueous workup. Further reaction of **67** with pivaloyl chloride afforded imide **68** in 80% yield, which on treatment with DMTSF furnished the acyclic amido thiofuran **69** in 61% yield (Scheme 14).

With a satisfactory method for the synthesis of the cycloaddition precursors in place, we became interested in evaluating the facility with which these thiofuranyl systems would react. At the outset, our principal concern

Scheme 14



Scheme 15



was whether the cyclic amido thiofuran system would undergo an intramolecular Diels−Alder reaction, since this step was critical for our planned alkaloid syntheses. We therefore initiated a simple model study and discovered that the thermolysis of the *N*-butenyl substituted thioamido furan **62** furnished the rearranged hexahydropyrroloquinolin-2-one **72** as the only isolable product in 92% yield as a 3:2 mixture of diastereomers after silica gel chromatography (Scheme 15). Demethylthioation occurred smoothly when a sample of **72** was subjected to Raney-nickel reduction in 95% ethanol, producing **73** in 85% yield. The initially formed oxo-bridged cycloadduct **70** could not be isolated as it readily underwent ring opening to produce the transient *N*-acyl iminium ion **71**. A subsequent 1,2-methylthio shift afforded the observed product. The stage is now set for us to explore the synthetic use of these thiofurans in [4 + 2]-cycloaddition chemistry, and we will report our findings at a later date.

In summary, we have described a mild method for the preparation of differentially substituted 2-alkylthio sub-

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stituted furans from readily available starting materials. This method should be useful for the preparation of a wide assortment of thio substituted furans containing acid-sensitive functional groups. Application of this methodology toward the construction of more complex alkaloids is currently in progress in our laboratory.

Experimental Section

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70 eV. Unless otherwise noted, all reactions were performed in flame-dried glassware under an atmosphere of dry argon. Solutions were evaporated under reduced pressure with a rotary evaporator, and the residue was chromatographed on a silica gel column using a 5% ethyl acetate/hexane mixture as the eluent unless specified otherwise. All solids were recrystallized from 3% ethyl acetate/hexane for analytical data.

General Procedure for the Preparation of 2-Substituted Thiofurans Using DMTSF. To a sample of the appropriate thioacetal using either CH_2Cl_2 or CH_3CN (0.2 M) as the solvent at −40 °C was added 1 equiv of DMTSF. The mixture was stirred at −40 °C for 30 min and then warmed to 0 °C. After 4 h of stirring at 0 °C, 5 equiv of Et_3N was added. The mixture was diluted with diethyl ether and poured into a saturated aqueous $NaHCO_3$ solution. The organic phase was separated, and the aqueous phase was washed with ether. The organic layer was dried over anhydrous K_2CO_3, the solvent was removed under reduced pressure, and the residue was subjected to silica gel chromatography.

3-Hydroxy-4,4-bis(methylsulfanyl)-1-phenylbutan-1-one (11). To a cooled solution of 1.3 mL (9.1 mmol) of diisopropylamine at −40 °C in THF (18 mL) was added *n*-butyllithium (4.0 mL of a 2.5 M solution in hexane). The reaction mixture was stirred at this temperature for 40 min and then cooled to −78 °C. To this solution was added dropwise 1.0 mL (8 mmol) of acetophenone (**8**). The reaction mixture was stirred at −78 °C for 40 min, and to this solution was added 1.0 g (7.5 mmol) of 2,2-bis(methylsulfanyl)acetaldehyde (**10**)[39] dissolved in THF (8 mL). The reaction mixture was stirred for 1 h at −78 °C and was quenched with a saturated NH_4Cl solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The organic phase was combined and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 1.6 g (84%) of **11** as a colorless oil: IR (neat) 3467, 1674, 1211, and 1040 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.14 (s, 3H), 2.18 (s, 3H), 3.32 (dd, 1H, J = 17.4 and 8.0 Hz), 3.47 (d, 1H, J = 3.2 Hz), 3.48 (dd, 1H, J = 17.4 and 3.6 Hz), 3.80 (d, 1H, J = 6.0 Hz), 4.44 (m, 1H), 7.42 (dd, 2H, J = 8.2 and 7.8 Hz), 7.53 (t, 1H, J = 8.2 Hz), and 7.93 (d, 2H, J = 7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 14.4, 42.3, 60.5, 69.2, 128.0, 128.4, 133.3, 136.5, and 199.1; HRMS calcd for $C_{12}H_{16}O_2S_2$ 256.0592, found 256.0587.

4,4-Bis(methylsulfanyl)-1-phenylbut-3-en-1-one (13). To a solution containing 0.9 g (3.6 mmol) of alcohol **11** in toluene (18 mL) at 0 °C was added 0.8 mL (5.4 mmol) of Et_3N and 0.3 mL (4 mmol) of mesyl chloride. The reaction mixture was stirred at 0 °C for 1 h, and to this solution was added 2.5 mL (9 mmol) of additional Et_3N. The mixture was warmed to room temperature for 30 min and was then heated at reflux for 6 h. The reaction mixture was cooled to room temperature, poured into ether, and washed with a saturated aqueous sodium bicarbonate solution. The organic layer was dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure. The crude oil was purified by flash silica gel chromatography to give 0.65 g (76%) of **13** as a colorless oil: IR (neat) 1681, 1595, 1332, and 1204 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.33 (s, 3H), 2.34 (s, 3H), 4.10 (d, 2H, J = 6.6 Hz), 6.13 (t, 1H, J = 6.6 Hz), 7.48 (dd, 2H, J = 8.2 and 7.6 Hz), 7.58 (t, 1H, J = 7.6 Hz), and 8.00 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 16.8, 17.0, 40.2, 124.2, 128.1, 128.5, 133.1, 136.0, 136.3, and 196.9. Anal. Calcd for $C_{12}H_{14}OS_2$: C, 60.49; H, 5.93. Found: C, 60.24; H, 5.87.

2-Methylsulfanyl-5-phenylfuran (17). To a sample of 0.3 g (1.1 mmol) of **13** in toluene (11 mL) was added a catalytic amount of camphorsulfonic acid. The reaction mixture was heated to reflux for 6 h and was then cooled to room temperature. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.15 g (72%) of **17** as a colorless oil: IR (neat) 1496, 1474, 1019, and 756 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.50 (s, 3H), 6.54 (d, 1H, J = 3.4 Hz), 6.65 (d, 1H, J = 3.4 Hz), 7.29 (m, 1H), 7.41 (m, 2H), and 7.71 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.2, 106.5, 116.4, 123.6, 127.5, 128.6, 130.3, 146.7, and 155.9. Anal. Calcd for $C_{11}H_{10}OS$: C, 69.46; H, 5.30. Found: C, 69.28; H, 5.24.

4-Methyl-6,6-bis(methylsulfanyl)hex-5-en-3-one (14). To a solution of 1.8 mL (13 mmol) of diisopropylamine in THF (26 mL) at −40 °C was added *n*-butyllithium (5.6 mL of a 2.5 M solution in hexane). The reaction mixture was stirred at this temperature for 40 min and was then cooled to −78 °C. To this solution was added dropwise 1.2 mL (12 mmol) of 3-pentanone (**9**). The solution was stirred at −78 °C for 40 min, and to this solution was added 1.4 g (10 mmol) of 2,2-bis(methylsulfanyl)acetaldehyde (**10**) dissolved in THF (10 mL). The reaction mixture was stirred for 1 h and was quenched with a saturated aqueous NH_4Cl solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic phase was dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 1.9 g (81%) of 5-hydroxy-4-methyl-6,6-bis(methylsulfanyl)-hexan-3-one (**12**), which consisted of a 1:1 inseparable mixture of diastereomers. The mixture was used in the next step without further purification.

To a solution of 0.8 g (3.5 mmol) of the above alcohol in toluene (18 mL) was added 0.7 mL (5 mmol) of Et_3N followed by 0.3 mL (4 mmol) of mesyl chloride. The reaction mixture was stirred at 0 °C for 1 h, and to this solution was added 2.5 mL (9 mmol) of additional Et_3N. The mixture was warmed to room temperature for 30 min and was then heated at reflux for 6 h. The reaction mixture was cooled to room temperature, poured into ether, and washed with a saturated aqueous $NaHCO_3$ solution. The organic layer was dried over anhydrous $MgSO_4$, the solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.5 g (70%) of **14** as a colorless oil: IR (neat) 2968, 1709, 1446, and 848 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.98 (t, 3H, J = 7.1 Hz), 1.19 (d, 3H, J = 7.0 Hz), 2.20 (s, 3H), 2.28 (s, 3H), 2.33−2.60 (m, 2H), 3.39 (q, 1H, J = 7.0 Hz), and 6.16 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 7.96, 15.7, 15.9, 17.1, 33.6, 53.1, 129.5, 133.4, and 210.1; HRMS calcd for $C_9H_{16}OS_2$ 204.0643, found 204.0651.

2-Ethyl-3-methyl-5-(methylsulfanyl)furan (18). To a 0.6 g (3 mmol) sample of **14** in toluene (30 mL) was added a catalytic amount of camphorsulfonic acid. The reaction mixture was heated to reflux for 36 h then cooled to room temperature. The solvent was removed under reduced pressure, and the crude residue was purified by flash silica gel chromatography to give 0.3 g (56%) of **18** as a colorless oil: IR (neat) 2919, 1432, 1190, and 1069 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.20 (t, 3H, J = 7.6 Hz), 1.93 (s, 3H), 2.36 (s, 3H), 2.58 (q, 2H, J = 7.6 Hz), and 6.23 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.55, 12.8, 19.3, 19.6, 114.8, 118.0, 143.0, and 155.1. Anal. Calcd for $C_8H_{12}OS$: C, 61.51; H, 7.75. Found: C, 61.42; H, 7.59.

2-(1-Hydroxy-2,2-bis(methylsulfanyl)ethyl)cyclohexanone (19). To a solution of 1.6 mL (11 mmol) of diisopropylamine in THF (20 mL) at −40 °C was added *n*-butyllithium (5 mL of a 2.5 M solution in hexane). The reaction mixture was stirred at this temperature for 40 min and was then cooled to −78 °C. To this mixture was added dropwise 1.1 mL (10 mmol) of cyclohexanone. The solution was stirred at −78 °C for 40 min, and 1.3 g (9 mmol) of 2,2-bis(methylsulfanyl)acetaldehyde (**10**) dissolved in THF (10 mL) was added. The solution was stirred for 1 h and was then quenched with a saturated aqueous NH_4Cl solution. The

organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic phase was dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 1.6 g (74%) of **19** as a white solid: mp 75−76.5 °C; IR (neat) 3504, 1697, and 1125 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.59−1.78 (m, 3H), 1.91 (m, 1H), 2.08 (m, 2H), 2.16 (s, 3H), 2.17 (s, 3H), 2.19−2.44 (m, 2H), 2.95 (m, 1H), 3.56 (d, 1H, J = 4.8 Hz), 3.86 (d, 1H, J = 5.6 Hz), and 3.90 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.2, 14.0, 24.8, 27.5, 30.9, 42.8, 53.3, 57.9, 75.0, and 214.6. Anal. Calcd for $C_{10}H_{18}O_2S_2$: C, 51.27; H, 7.75. Found: C, 51.04; H, 7.52.

***trans*-2,3-Bis(methylsulfanyl)-2,3,4,5,6,7-hexahydrobenzofuran (21).** To a sample of **19** in toluene (14 mL) at 0 °C was added 0.6 mL (4 mmol) of Et_3N followed by 0.2 mL (3 mmol) of mesyl chloride. The mixture was stirred at 0 °C for 1 h, and 1.0 mL (7 mmol) of additional Et_3N was added. The solution was warmed to room temperature for 30 min and was then heated to reflux for 6 h. The mixture was cooled to room temperature, poured into ether, and washed with a saturated aqueous $NaHCO_3$ solution. The organic layer was dried over anhydrous $MgSO_4$, the solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.4 g (66%) of **21** as a colorless oil: IR (neat) 2925, 1704, 1195, and 916 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.59−1.76 (m, 4H), 1.95 (s, 3H), 1.97−2.20 (m, 4H), 2.23 (s, 3H), 3.63 (bs, 1H), 5.46 (d, 1H, J = 3.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.0, 13.6, 21.2, 22.5, 22.6, 23.1, 57.0, 92.5, 105.4, 152.9. Anal. Calcd for $C_{10}H_{16}OS_2$: C, 55.54; H, 7.46. Found: C, 55.36; H, 7.25.

2-Methylsulfanyl-4,5,6,7-tetrahydrobenzofuran (23). To a sample of 0.8 g (2.7 mmol) of **21** in toluene (90 mL) was added a catalytic amount of camphorsulfonic acid. The mixture was heated at reflux for 6 h and was then cooled to room temperature. The solvent was removed under reduced pressure, and the crude residue was purified by silica gel chromatography to give 0.4 g (87%) of **23** as a colorless oil: IR (neat) 2932, 1495, and 1118 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.70 (m, 2H), 1.81 (m, 2H), 2.36 (s, 3H), 2.35−2.39 (m, 2H), 2.55−2.59 (m, 2H), and 6.26 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.7, 21.9, 22.9 (2), 23.3, 116.3, 118.7, 144.1, and 153.7. Anal. Calcd for $C_9H_{12}OS$: C, 64.26; H, 7.20. Found: C, 64.13; H, 7.09.

2-(1-Hydroxy-2,2-bis(methylsulfanyl)ethyl)-3,4-dihydro-2*H*-naphthalen-1-one (20). To a solution of 1.1 mL (7.5 mmol) of diisopropylamine in THF (14 mL) at −40 °C was added *n*-butyllithium (3.3 mL of a 2.5 M solution in hexane). The reaction mixture was stirred at this temperature for 40 min and was then cooled to −78 °C. To this solution was added 0.9 mL (6.8 mmol) of α-tetralone. The solution was stirred at −78 °C for 40 min, and 0.8 g (6.2 mmol) of 2,2-bis(methylsulfanyl)acetaldehyde (**10**) dissolved in THF (7 mL) was added. The mixture was stirred for 1 h and was quenched with a saturated aqueous NH_4Cl solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic phase was dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 1.0 g (58%) of **20** as a colorless oil: IR (neat) 3495, 2919, 1674, 1595, 1453, and 1289 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.17 (s, 3H), 2.19 (s, 3H), 2.14−2.56 (m, 2H), 2.91 (d, 1H, J = 2.8 Hz), 3.02−3.13 (m, 3H), 3.89 (d, 1H, J = 9.0 Hz), 4.49 (ddd, 1H, J = 9.0, 3.2, and 2.8 Hz), 7.23 (m, 2H), 7.47 (dt, 1H, J = 7.3 and 1.5 Hz), and 8.03 (dd, 1H, J = 7.8 and 1.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.1, 13.8, 22.3, 28.8, 49.9, 59.1, 69.5, 126.5, 127.3, 128.5, 132.6, 133.4, 143.9, and 198.4; HRMS calcd for $C_{14}H_{18}O_2S_2$ 282.0748, found 282.0746.

***trans*-2,3-Bis(methylsulfanyl)-2,3,4,5-tetrahydronaphtho[1,2-*b*]furan (22).** To a solution of 0.5 g (1.7 mmol) of **20** in toluene (9 mL) at 0 °C was added 0.4 mL (2.6 mmol) of Et_3N followed by 0.15 mL (1.9 mmol) of mesyl chloride. The reaction mixture was stirred at 0 °C for 1 h, and 0.6 mL (4.3 mmol) of additional Et_3N was added. The mixture was warmed to room temperature for 30 min and then heated to reflux for 6 h. The solution was cooled to room temperature, poured into ether, and washed with a saturated solution of $NaHCO_3$. The organic layer was dried over anhydrous $MgSO_4$, the solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.4 g (94%) of **22** as a white solid: mp 86−87 °C; IR (neat) 2919, 1674, 1417, and 905 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.02 (s, 3H), 2.32 (s, 3H), 2.47 (m, 2H), 2.99 (t, 2H, J = 7.9 Hz), 3.87 (dt, 1H, J = 3.5 and 1.3 Hz), 5.74 (d, 1H, J = 3.5 Hz), 7.20 (m, 3H), and 7.33 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.1, 13.5, 20.0, 28.4, 56.8, 93.6, 107.7, 120.9, 126.3, 127.2, 127.4, 128.1, 136.4, 150.7. Anal. Calcd for $C_{14}H_{16}OS_2$: C, 63.62; H, 6.11. Found: C, 63.55; H, 5.89.

2-Methylsulfanyl-4,5-tetrahydronaphtho[1,2-*b*]furan (24). To a 0.3 g (1.2 mmol) sample of **22** in toluene (25 mL) was added a catalytic amount of camphorsulfonic acid. The mixture was heated at reflux for 6 h and was then cooled to room temperature. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.23 g (89%) of **24** as a colorless oil: IR (neat) 2919, 1773, 1674, and 1040 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.46 (s, 3H), 2.70 (t, 2H, J = 7.6 Hz), 2.95 (t, 2H, J = 7.6 Hz), 6.40 (s, 1H), 7.12−7.26 (m, 3H), and 7.49 (d, 1H, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.5, 20.9, 29.0, 115.6, 119.3, 120.6, 126.5, 126.6, 127.5, 127.8, 134.4, 146.5, and 152.0. Anal. Calcd for $C_{13}H_{12}OS$: C, 72.20; H, 5.60. Found: C, 72.14; H, 5.51.

3-(1-Hydroxy-2,2-bis(methylsulfanyl)ethyl)tetrahydropyran-2-one (26). To a 1.5 mL (11 mmol) solution of diisopropylamine in THF (22 mL) at −40 °C was added *n*-butyllithium (5 mL of a 2.5 M solution in hexane). The reaction mixture was stirred at this temperature for 40 min and was then cooled to −78 °C. To this solution was added 1.0 g (10 mmol) of δ-valerolactone. The solution was stirred at −78 °C for 40 min, and 1.2 g (9.0 mmol) of 2,2-bis(methylsulfanyl)acetaldehyde (**10**) dissolved in THF (9 mL) was added. The reaction mixture was stirred for 1 h and was quenched with a saturated aqueous NH_4Cl solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic phase was dried over anhydrous $MgSO_4$, the solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 1.5 g (71%) of **26** as a colorless oil: IR (neat) 3483, 1718, 1390, and 1084 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.77 (m, 1H), 1.90 (m, 2H), 2.02 (m, 1H), 2.11 (s, 3H), 2.14 (s, 3H), 3.10 (ddd, 1H, J = 12.4, 8.0 and 4.8 Hz), 3.70 (d, 1H, J = 3.2 Hz), 3.83 (m, 1H), 4.02 (d, 1H, J = 7.2 Hz), and 4.31 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.2, 13.9, 21.9, 22.3, 42.8, 58.0, 68.6, 74.3, and 173.0; HRMS calcd for $C_9H_{16}O_3S_2$ 236.0541, found 236.0540.

3-(2,2-Bis(methylsulfanyl)vinyl)tetrahydropyran-2-one (29). To a 0.7 g (3 mmol) sample of **26** in toluene (14 mL) at 0 °C was added 0.6 mL (4.3 mmol) of Et_3N followed by 0.25 mL (3 mmol) of mesyl chloride. The reaction mixture was stirred at 0 °C for 1 h, and 1.0 mL (7.2 mmol) of additional Et_3N was added. The mixture was warmed to room temperature for 30 min and then heated at reflux for 6 h. The reaction mixture was cooled to room temperature, poured into ether, and washed with a saturated aqueous $NaHCO_3$ solution. The organic layer was dried over anhydrous $MgSO_4$, the solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.4 g (62%) of **29** as a colorless oil: IR (neat) 2925, 1725, 1628, and 1139 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.85−2.14 (m, 4H), 2.28 (s, 3H), 2.32 (s, 3H), 3.44 (dd, 1H, J = 10.4 and 7.2 Hz), 4.36 (dd, 1H, J = 7.2 and 5.2 Hz), and 6.43 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.2, 16.8, 21.9, 26.0, 50.5, 69.6, 127.8, 138.7, and 170.9; HRMS calcd for $C_9H_{14}O_2S_2$ 218.0435, found 218.0428.

3-(1,2-Bis(methylsulfanyl)ethylidene)tetrahydropyran-2-one (33). To a 0.3 g (1.4 mmol) sample of **29** in toluene (20 mL) was added a catalytic amount of camphorsulfonic acid. The reaction mixture was heated at reflux for 3 h, cooled to room temperature, poured into ether, and washed with a saturated aqueous $NaHCO_3$ solution. The organic layer was separated and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.25 g (80%) of **33** as a

colorless oil: IR (neat) 2918, 1683, 1544, and 1111 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.93 (m, 2H), 2.11 (s, 3H), 2.48 (S, 3H), 2.52 (t, 2H, J = 7.2 Hz), 4.11 (s, 2H), and 4.18 (t, 2H, J = 5.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.9, 14.5, 22.7, 26.8, 31.3, 67.6, 119.2, 154.3, and 164.6; HRMS calcd for $C_9H_{14}O_2S_2$ 218.0435, found 218.0431.

3-(2,2-Bis(methylsulfanyl)vinyl)-1-methyl-pyrrolidin-2-one (30). To a solution of 1.6 mL (11 mmol) of diisopropylamine in THF (22 mL) at −40 °C was added *n*-butyllithium (5 mL of a 2.5 M solution in hexane). The reaction mixture was stirred at this temperature for 40 min and was then cooled to −78 °C. To this solution was added 1.0 g (10 mmol) of *N*-methylpyrrolidinone. The solution was stirred at −78 °C for 40 min, and 1.2 g (9.1 mmol) of 2,2-bis(methylsulfanyl)-acetaldehyde (**10**) dissolved in THF (9 mL) was added. The reaction mixture was stirred for 1 h and was quenched with a saturated aqueous NH_4Cl solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic phase was dried over anhydrous $MgSO_4$, the solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 1.3 g (61%) of 3-[(1-hydroxy-2,2-bis(methylsulfanyl)ethyl)]-1-methylpyrrolidin-2-one (**27**) as a 1:1 inseparable mixture of diastereomers, which was used directly in the next step without further purification.

To a 1.3 g (5.6 mmol) sample of the above alcohol in toluene (28 mL) at 0 °C was added 1.2 mL (8 mmol) of Et_3N followed by 0.5 mL (6 mmol) of mesyl chloride. The mixture was stirred at 0 °C for 1 h, and 1.9 mL (14 mmol) of additional Et_3N was added. The mixture was warmed to room temperature for 30 min and then heated at reflux for 6 h. The solution was cooled to room temperature, poured into ether, and washed with a saturated solution of $NaHCO_3$. The organic layer was dried over anhydrous $MgSO_4$, the solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.8 g (65%) of **30** as a colorless oil: IR (neat) 2919, 1688, 1282, and 1097 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.02−2.22 (m, 2H), 2.25 (s, 3H), 2.32 (s, 3H), 2.86 (s, 3H), 3.25−3.45 (m, 3H), and 6.45 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 16.1, 16.9, 24.9, 30.1, 47.6, 50.9, 128.3, 137.5, and 173.2; HRMS calcd for $C_9H_{15}NOS_2$ 217.0595, found 217.0595.

3-(1,2-Bis(methylsulfanyl)ethylidene)-1-methylpyrrolidin-2-one (38). To a solution of 0.6 g (2.7 mmol) of **30** in toluene (30 mL) was added a catalytic amount of camphorsulfonic acid. The reaction mixture was heated at reflux for 16 h and cooled to room temperature. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.5 g (83%) of **38** as a white solid: mp 78−79 °C; IR (neat) 2919, 1666, 1425, and 1076 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.97 (s, 3H), 2.31 (s, 3H), 2.57 (t, 2H, J = 6.6 Hz), 2.76 (s, 3H), 3.26 (t, 2H, J = 6.6 Hz), and 4.18 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.0, 14.0, 25.0, 27.9, 29.8, 45.4, 124.7, 140.9, and 166.2. Anal. Calcd for $C_9H_{15}NOS_2$: C, 49.74; H, 6.96; N, 6.44. Found: C, 49.89; H, 7.08; N, 6.49.

3-(1-Hydroxy-2,2-bis(methylsulfanyl)ethyl)-1-methylpiperidin-2-one (28). To a 11 mL (77 mmol) solution of diisopropylamine in THF (150 mL) at −40 °C was added *n*-butyllithium (34 mL of a 2.5 M solution in hexane). The reaction mixture was stirred at this temperature for 40 min and was then cooled to −78 °C. To this solution was added 8 mL (70 mmol) of *N*-methylpiperidone. The solution was stirred at −78 °C for 40 min, and 8.6 g (63 mmol) of 2,2-bis-(methylsulfanyl)acetaldehyde (**10**) in THF (130 mL) was added. The reaction mixture was stirred for 1 h and was quenched with a saturated aqueous NH_4Cl solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic phase was dried over anhydrous $MgSO_4$, the solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 11.4 g (73%) of **28** as a 1.7:1 mixture of diastereomers. The major diastereomer was crystallized from ethyl acetate: mp 90−91 °C; IR (neat) 3388, 1617, 1197, and 1083 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.75−1.91 (m, 4H), 2.07 (s, 3H), 2.10 (s, 3H), 2.75 (m, 1H), 2.90 (s, 3H), 3.28 (m, 1H), 3.31 (m, 1H), 3.63 (d, 1H, J = 9.6 Hz), and 4.32 (dd, 1H, J = 9.6 and 2.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.3, 13.3, 19.8, 22.0, 35.0, 44.0, 49.7, 58.7, 70.5, and 170.7. Anal. Calcd for $C_{10}H_{19}NO_2S_2$: C, 48.18; H, 7.69; N, 5.62. Found: C, 48.13; H, 7.48; N, 5.47.

3-(2,2-Bis(methylsulfanyl)vinyl)-1-methyl-piperidin-2-one (31). To a 3.8 g (15 mmol) sample of **28** in toluene (70 mL) at 0 °C was added 3 mL (23 mmol) of Et_3N followed by 1.3 mL (17 mmol) of mesyl chloride. The reaction mixture was stirred at 0 °C for 2 h, and 5.3 mL (38 mmol) of additional Et_3N was added. The mixture was warmed to room temperature for 2 h and was then heated at reflux for 6 h. The solution was cooled to room temperature and was poured into ether. The organic phase was washed with 10% NaOH, followed by brine, and then dried over anhydrous $MgSO_4$. Silica gel chromatography provided 2.7 g (78%) of **31** as a colorless oil: IR (neat) 2919, 1638, 1496, and 1047 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.70−1.78 (m, 1H), 1.80−1.90 (m, 2H), 1.99−2.07 (m, 1H), 2.23 (s, 3H), 2.29 (s, 3H), 2.93 (s, 3H), 3.19−3.27 (m, 2H), 3.32−3.38 (m, 1H), and 6.24 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.9, 16.8, 20.9, 27.4, 35.0, 50.0, 51.0, 130.2, 136.1, and 169.2; HRMS calcd for $C_{10}H_{17}NOS_2$ 231.0752, found 231.0751.

3-(1,2-Bis(methylsulfanyl)ethylidene)-1-methyl-piperidin-2-one (39). To a 0.7 g (3.2 mmol) sample of **31** in toluene (30 mL) was added a catalytic amount of camphorsulfonic acid. The reaction mixture was heated at reflux for 24 h and then cooled to room temperature. The solvent was removed under reduced pressure, and the crude residue was purified by flash silica gel chromatography to give 0.07 g (10%) of recovered starting material and 0.3 g (41%) of a clear oil whose structure was assigned as **39** on the basis of its spectral properties: IR (neat) 3395, 1617, 1553, and 1190 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.87 (m, 2H), 2.14 (s, 3H), 2.42 (s, 3H), 2.61 (t, 2H, J = 6.4 Hz), 2.98 (s, 3H), 3.30 (t, 2H, J = 5.6 Hz), and 4.27 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.3, 14.7, 23.0, 28.5, 31.8, 35.4, 49.6, 125.5, 145.1, and 164.4; HRMS calcd for $C_{10}H_{17}NOS_2$ 231.0752, found 231.0748.

3-(1,2-Bis(methylsulfanyl)vinyl)-1-methyl-piperidin-2-one (40). The minor fraction that was isolated from the chromatography column contained 0.16 g (22%) of a colorless oil whose structure was assigned as **40** on the basis of its spectral properties: IR (neat) 2919, 1638, 1432, and 1197 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.83 (m, 1H), 1.98 (m, 3H), 2.28 (s, 3H), 2.29 (s, 3H), 2.95 (s, 3H), 3.26 (m, 1H), 3.41 (dt, 1H, J = 11.6 and 4.0 Hz), 3.73 (dd, 1H, J = 10.0 and 6.8 Hz), and 5.85 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.8, 17.9, 22.5, 27.2, 35.1, 47.2, 50.1, 122.4, 136.5, and 168.4; HRMS calcd for $C_{10}H_{17}NOS_2$ 231.0752, found 231.0756.

Acetic Acid 1-(Bis(methylsulfanyl)methyl)-3-oxo-3-phenyl-propyl Ester (41). To a 0.7 g (2.5 mmol) sample of alcohol **11** in CH_2Cl_2 (5 mL) at 0 °C were added 0.6 mL (7.6 mmol) of pyridine, 0.03 g (0.25 mmol) of DMAP, and 0.5 mL (5 mmol) of acetic anhydride. The mixture was stirred at 0 °C for 2 h, warmed to room temperature for 10 min, and poured into a saturated aqueous $NaHCO_3$ solution. The organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the crude residue was purified by flash silica gel chromatography to give 0.7 g (96%) of **41** as a colorless oil: IR (neat) 2904, 1736, 1225, and 1026 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.05 (s, 3H), 2.21 (s, 3H), 2.23 (s, 3H), 3.46 (dd, 1H, J = 17.5 and 7.3 Hz), 3.61 (dd, 1H, J = 17.5 and 5.1 Hz), 4.02 (d, 1H, J = 4.4 Hz), 5.75 (ddd, 1H, J = 7.3, 5.1 and 4.4 Hz), 7.47 (t, 2H, J = 8.3 Hz), 7.58 (t, 1H, J = 7.9 Hz), and 7.96 (d, 2H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7, 15.0, 21.0, 39.9, 57.4, 71.3, 128.1, 128.7, 133.4, 136.6, 170.1, and 196.5; HRMS calcd for $C_{14}H_{18}O_3S_2$ 298.0697, found 298.0695. Treatment of this acetate with DMTSF and NEt_3 gave furan **17** in 93% yield.

Acetic Acid 1-(Bis(methylsulfanyl)methyl)-2-methyl-3-oxo-pentyl Ester (42). To a 0.9 g (4.0 mmol) sample of alcohol **12** in CH_2Cl_2 (8 mL) at 0 °C were added 1 mL (12 mmol) of pyridine, 0.05 g (0.4 mmol) of DMAP, and 0.8 mL (8 mmol)

of acetic anhydride. The reaction mixture was stirred at 0 °C for 2 h, warmed to room temperature for 10 min, and poured into a saturated aqueous $NaHCO_3$ solution. The organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 1.0 g (93%) of the *syn* diastereomer of **42**: IR (neat) 2969, 1709, and 1218 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.03 (t, 3H, J = 7.3 Hz), 1.14 (d, 3H, J = 7.0 Hz), 2.05 (s, 3H), 2.14 (s, 3H), 2.17 (s, 3H), 2.42−2.61 (m, 2H), 3.23 (dq, J = 7.3 and 7.0 Hz), 3.83 (d, 1H, J = 5.2 Hz), and 5.37 (dd, 1H, J = 7.3 and 5.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 7.60, 13.6, 13.8, 14.6, 20.7, 35.2, 47.7, 56.2, 74.6, 169.8, and 211.4; HRMS calcd for $C_9H_{16}OS_2$ 264.0854, found 264.0852. Treatment of this acetate with DMTSF and NEt_3 gave furan **18** in 91% yield.

Acetic Acid 2,2-Bis(methylsulfanyl)-1-(2-oxo-cyclohexyl) Ethyl Ester (43). To a 0.8 g (3.4 mmol) sample of **19** in CH_2Cl_2 (7 mL) at 0 °C were added 0.8 mL (10 mmol) of pyridine, 0.04 g (0.3 mmol) of DMAP, and 0.6 mL (6.8 mmol) of acetic anhydride. The reaction mixture was stirred at 0 °C for 2 h, warmed to room temperature for 10 min, and poured into a saturated aqueous $NaHCO_3$ solution. The organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.9 g (90%) of **43** as a colorless oil: IR (neat) 2933, 1752, 1425, and 1012 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.55 (m, 1H), 1.67 (m, 2H), 1.87 (m, 1H), 2.01 (m, 2H), 2.05 (s, 3H), 2.10 (s, 3H), 2.11 (s, 3H), 2.21−2.41 (m, 2H), 3.00 (m, 1H), 4.15 (d, 1H, J = 7.3 Hz), 5.23 (dd, 1H, J = 7.3 and 5.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.9, 14.1, 20.9, 24.6, 27.2, 30.5, 42.4, 51.7, 56.1, 72.3, 170.3, 209.4; HRMS calcd for $C_{10}H_{16}OS_2$ 276.0854, found 276.0854. Treatment of this acetate with DMTSF and NEt_3 gave furan **23** in 96% yield.

Acetic Acid 1-(1-Methyl-2-oxopiperidin-3-yl)-2,2-bis-(methylsulfanyl) Ethyl Ester (44). To a solution containing 2.7 mL (19 mmol) of diisopropylamine in THF (60 mL) cooled to −40 °C was added *n*-butyllithium (12 mL of a 1.5 M solution in hexane). After 1 h of stirring, the reaction was cooled to −75 °C, and 2 g (18 mmol) of 1-methyl-2-piperidone was added as a THF solution (10 mL). The temperature was raised to −40 °C, and the reaction was stirred for 30 min. The temperature was lowered to −75 °C, and 2.5 g (18 mmol) of 2,2-bis-(methylsulfanyl)acetaldehyde (**10**) in 20 mL of THF was added dropwise. The mixture was stirred for an additional 30 min, and 2.5 mL (26 mmol) of acetic anhydride was added. The solution was slowly warmed to room temperature overnight, poured into a saturated aqueous $NaHCO_3$ solution, and extracted with CH_2Cl_2. The solvent was removed under reduced pressure, and flash silica gel chromatography of the residue afforded 3.5 g (69%) of **44** as a yellow oil that consisted of a 1:1 mixture of diastereomers: IR (neat) 2920, 1743, 1498, and 1035 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (major diastereomer) δ 1.60−2.00 (m, 4H), 2.06 (s, 3H), 2.16 (s, 3H), 2.17 (s, 3H), 2.91 (s, 3H), 3.01−3.08 (m, 1H), 3.21−3.47 (m, 2H), 4.16 (d, 1H, J = 6.8 Hz), and 5.68 (t, 1H, J = 6.2 Hz); (minor diastereomer) δ 1.60−2.00 (m, 4H), 2.08 (s, 3H), 2.10 (s, 3H), 2.16 (s, 3H), 2.90 (s, 3H), 3.01−3.08 (m, 1H), 3.21−3.47 (m, 2H), 4.61 (d, 1H, J = 10.0 Hz), and 5.19 (dd, 1H, J = 10.0 and 2.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (major diastereomer) δ 13.8, 14.4, 21.0, 22.2, 22.4, 35.2, 43.4, 50.0, 57.7, 72.9, 169.7, and 170.0; (minor diastereomer) δ 12.7, 13.7, 21.3, 22.5, 25.7, 35.0, 43.0, 49.9, 57.2, 74.6, 168.8, and 170.6; HRMS calcd for $C_{12}H_{21}NO_3S_2$ 244.1007, found 244.1019.

***N*-Methyl-2-methylsulfanyl-4,5,6,7-tetrahydrofuro[2,3-*b*]pyridine (47).** To a solution containing 0.1 g (0.3 mmol) of **44** in CH_2Cl_2 (2.5 mL) was added 0.07 g (0.4 mmol) of DMTSF in one portion at −40 °C. Following the general procedure, silica gel chromatography of the crude reaction mixture gave 0.05 g (87%) of **47** as a yellow oil: IR (neat) 2919, 1623, 1408, and 1045 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.85−1.93 (m, 2H), 2.30 (s, 3H), 2.37 (t, 2H, J = 8.4 Hz), 2.82 (s, 3H), 2.99−3.03 (m, 2H), and 6.31 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 21.3, 22.8, 38.3, 51.9, 96.5, 119.8, 135.6, and 157.6; HRMS calcd for $C_9H_{13}NOS$ 183.0718, found 183.0718.

3-(1-Hydroxy-2,2-bis(methylsulfanyl)ethyl-1-(toluene-4-sulfonyl)-piperidin-2-one. To a 1.2 mL (8.7 mmol) solution of diisopropylamine in THF (40 mL) at −40 °C was added *n*-butyllithium (3.6 mL of a 2.5 M solution in hexane). The mixture was stirred at this temperature for 40 min and then cooled to −78 °C. To this solution was added a 2.0 g (8 mmol) sample of *N*-(*p*-toluenesulfonyl)-*δ*-valerolactam[40] in hot toluene (20 mL). The solution was stirred at −78 °C for 40 min, and 1.0 g (7.5 mmol) of 2,2-bis(methylsulfanyl)acetaldehyde (**10**) dissolved in THF (8 mL) was added. The mixture was stirred for 1 h and quenched with a saturated aqueous NH_4Cl solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic phase was dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 2.2 g (76%) of the above titled compound as a colorless oil: IR (neat) 3509, 1688, 1168, and 1083 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.65 (m, 1H), 1.76−1.90 (m, 2H), 1.91−2.10 (m, 1H), 2.00 (s, 3H), 2.08 (s, 3H), 2.43 (s, 3H), 2.96 (m, 1H), 3.42 (s, 1H), 3.76−3.92 (m, 3H), 4.10 (m, 1H), 7.29 (d, 2H, J = 7.9 Hz), and 7.86 (d, 2H, J = 7.9 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.2, 13.6, 21.6, 22.6, 23.4, 46.4, 46.5, 58.4, 74.0, 128.6, 128.7, 129.3, 144.7, and 171.5; HRMS calcd for $C_{16}H_{23}NO_4S_3$ 389.0789, found 389.0788.

Acetic Acid 2,2-Bis(methylsulfanyl)-1-[2-oxo-1-(toluene-4-sulfonyl)-piperidin-3-yl] Ethyl Ester (45). To a 3.9 g (10 mmol) sample of the above compound in CH_2Cl_2 (20 mL) at 0 °C were added 2.4 mL (30 mmol) of pyridine, 0.12 g (1.0 mmol) of DMAP, and 1.9 mL (20 mmol) of acetic anhydride. The reaction mixture was stirred at 0 °C for 2 h, warmed to room temperature for 10 min, and poured into a saturated aqueous $NaHCO_3$ solution. The organic phase was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was crystallized to give 3.6 g (84%) of **45** as a white solid: mp 140−141.5 °C; IR (neat) 2919, 1745, 1225, and 1161 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.57−1.73 (m, 1H), 1.74−1.82 (m, 1H), 1.79 (s, 3H), 1.94−1.97 (m, 1H), 1.99 (s, 3H), 2.00 (s, 3H), 2.04−2.10 (m, 1H), 2.42 (s, 3H), 2.96 (ddd, 1H, J = 11.7, 6.7 and 2.5 Hz), 3.63 (dt, 1H, J = 12.1 and 3.8 Hz), 3.97 (d, 1H, J = 10.2 Hz), 4.21 (m, 1H), 5.31 (dd, 1H, J = 10.2 and 2.5 Hz), 7.28 (d, 2H, J = 8.3 Hz), and 7.87 (d, 2H, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.0, 13.1, 20.8, 21.6, 22.8, 23.0, 46.0, 46.7, 55.5, 73.2, 128.8, 129.1, 136.1, 144.5, 168.1, and 169.7. Anal. Calcd for $C_{18}H_{25}NO_5S_3$: C, 50.09; H, 5.84; N, 3.25. Found: C, 50.05; H, 5.89; N, 3.25.

***N*-(Toluene-4-sulfonyl)-2-methylsulfanyl-4,5,6,7-tetrahydrofuro[2,3-*b*]-pyridine (48).** To a 0.05 g (0.1 mmol) sample of **45** in CH_2Cl_2 (5 mL) at −40 °C was added 0.03 g (0.1 mmol) of DMTSF. Following the general procedure, flash silica gel chromatography of the reaction mixture gave 0.04 g (98%) of **48** as a colorless oil: IR (neat) 2926, 1624, and 1190 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.42 (m, 2H), 2.20 (t, 2H, J = 6.4 Hz), 2.37 (s, 3H), 2.38 (s, 3H), 3.68 (m, 2H), 6.23 (s, 1H), 7.23 (d, 2H, J = 8.4 Hz), and 7.61 (d, 2H, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.6, 19.8, 20.6, 21.6, 47.9, 107.4, 116.5, 127.5, 129.7, 135.2, 142.4, 144.2, and 144.8; HRMS calcd for $C_{15}H_{17}NO_3S_2$ 323.0650, found 323.0655.

Acetic Acid 1-[1-(2,2-Dimethyl-propionyl)-2-oxo-azepan-3-yl]-2,2-bis(methylsulfanyl) Ethyl Ester (46). To a cooled solution of 1.5 mL (11 mmol) of diisopropylamine at −40 °C in THF (20 mL) was added *n*-butyllithium (7.2 mL of a 1.5 M solution in hexane). The mixture was stirred at −40 °C for 30 min and was then cooled to −78 °C. To this solution was added dropwise a solution of 2.0 g (10 mmol) of acetic acid 1-(2,2-dimethyl-propionyl)-azepan-2-one[41] in THF (10 mL). The mixture was warmed to −40 °C and was stirred at this temperature for 30 min before cooling to −78 °C. To this solution was added 1.5 g (11 mmol) of 2,2-bis(methylsulfanyl)-acetaldehyde (**10**) in 30 mL of THF. The solution was stirred for 30 min before the addition of 1.4 mL (15 mmol) of acetic

anhydride. The mixture was warmed to room temperature, stirred for 12 h, poured into a saturated aqueous Na_2CO_3 solution, and extracted with ethyl acetate. The organic phase was washed with water and brine. After drying over anhydrous $MgSO_4$, the solvent was removed under reduced pressure, and the residue was purified by recrystallization from hexane/ether to give 2.7 g (72%) of **46** as a white solid: mp 115−116 °C; IR (film) 2923, 1748, 1705, and 1219 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.28 (s, 9H), 1.60−1.65 (m, 3H), 1.79−1.82 (m, 1H), 1.87−1.93 (m, 2H), 2.09 (s, 3H), 2.14 (s, 3H), 2.14 (s, 3H), 3.33−3.42 (m, 2H), 3.74−3.79 (m, 1H), 4.21 (d, 1H, J = 6.8 Hz), and 5.38 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.9, 14.6, 21.2, 27.1, 28.1, 28.6, 44.4, 47.1, 47.2, 56.5, 73.6, 170.7, 175.7, and 191.4. Anal. Calcd for $C_{17}H_{29}NO_4S_2$: C, 54.37; H, 7.78; N, 3.37. Found: C, 54.43; H, 7.73; N, 3.83.

***N*-(2-Methylsulfanyl-4,5,6,7-tetrahydrofuro[2,3-*b*]azepin-2,2-dimethyl Propionamide (49).** To a sample of 1.0 g (2.7 mmol) of **46** in CH_2Cl_2 (10 mL) at −40 °C was added 0.7 g (3.5 mmol) of DMTSF. Following the general procedure, flash silica gel chromatography of the reaction mixture gave 0.6 g (78%) of **49** as a white solid: mp 60−62 °C; IR (neat) 2986, 1661, 1628, and 1162 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.12 (s, 9H), 1.58−1.61 (m, 2H), 1.76−1.84 (m, 2H), 2.35−2.39 (m, 2H), 2.39 (s, 3H), 3.61 (bs, 2H), and 6.31 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.8, 24.8, 25.8, 28.1, 29.9, 30.7, 40.9, 48.1, 117.9, 118.7, 141.2, and 178.3. Anal. Calcd for $C_{14}H_{21}NO_2S$: C, 62.89; H, 7.92; N, 5.24. Found: C, 62.77; H, 7.75; N, 5.19.

Acetic Acid 2,2-Bis(methylsulfanyl)-1-(2-oxo-tetrahydropyran-3-yl) Ethyl Ester (50). To a cooled solution of 1.2 g (5.2 mmol) of **26** in CH_2Cl_2 (10 mL) at 0 °C was added 0.06 g (0.5 mmol) of DMAP, 0.5 mL (5.6 mmol) of pyridine, and 0.5 mL (5.3 mmol) of acetic anhydride. The reaction was slowly warmed to room temperature and was stirred for 4 h before the reaction mixture was poured into a saturated aqueous $NaHCO_3$ solution. The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic layer was washed with water and then brine. After drying over anhydrous $MgSO_4$, the solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to provide 1.3 g (87%) of **50** as a colorless oil: IR (neat) 2958, 1748, 1437, and 1229 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.66−1.76 (m, 1H), 1.87−1.95 (m, 2H), 2.05−2.11 (m, 1H), 2.11 (s, 3H), 2.13 (s, 3H), 2.16 (s, 3H), 3.27 (ddd, 1H, J = 11.6, 7.2, and 2.8 Hz), 4.25−4.31 (m, 1H), 4.36 (d, 1H, J = 9.2 Hz), 4.34−4.38 (m, 1H), and 5.26 (dd, 1H, J = 9.6 and 3.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.1, 13.5, 21.2, 22.6, 23.2, 42.4, 56.4, 69.1, 73.5, 169.8, and 170.5; HRMS calcd for $C_{11}H_{18}O_4S_2$ 278.0646, found 278.0645.

2-Methylsulfanyl-5,6-dihydro-4*H*-furo[2,3-*b*]pyran (51). To a solution of 0.2 g (0.7 mmol) of **50** in CH_2Cl_2 (1.5 mL) cooled to −40 °C was added 0.16 g (0.8 mmol) of DMTSF. Following the general procedure, chromatography of the crude reaction through a plug of basic alumina gave 0.05 g (40%) of **51** as a colorless oil: IR (neat) 2991, 1638, 1517, and 978 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.90−1.98 (m, 2H), 2.31 (s, 3H), 2.39 (t, 2H, J = 6.2 Hz), 4.25−4.28 (m, 2H), and 6.33 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.9, 21.0, 23.2, 69.8, 92.1, 119.1, 135.0, and 158.3. Anal. Calcd for $C_8H_{10}O_2S$: C, 56.46; H, 5.93. Found: C, 56.31, H, 5.87.

Acetic Acid 2,2-Bis(methylsulfanyl)-1-(2-oxo-piperidin-3-yl) Ethyl Ester (54). To 5.0 mL (36 mmol) diisopropylamine in THF (100 mL) cooled to 0 °C was added *n*-butyllithium (24 mL of a 1.5 M solution in hexane). The mixture was stirred at 0 °C for 30 min, and then 6.1 g (36 mmol) of *N*-trimethylsilyl δ-valerolactam[42] dissolved in THF (50 mL) was added. The reaction mixture was stirred at 0 °C for 30 min and then cooled to −78 °C. A solution of 5.0 g (37 mmol) of 2,2-bis(methylsulfanyl)acetaldehyde (**10**) dissolved in THF (50 mL) was added over a 3 h period. After the addition was complete, 5.0 mL (53 mmol) of acetic anhydride was added, and the mixture was slowly warmed to room temperature and stirred for 12 h. The solution was poured into a saturated aqueous $NaHCO_3$ solution, and the organic phase was separated. The aqueous phase was washed with ethyl acetate, and the organic layer was dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to provide 6.9 g (70%) of **54** as a 1:1 mixture of diastereomers: IR (neat) 3299, 1742, 1661, and 1231 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (diastereomer A) δ 1.62 (m, 1H), 1.73 (m, 1H), 1.92 (m, 2H), 2.08 (s, 3H), 2.10 (s, 3H), 2.18 (s, 3H), 3.09 (ddd, 1H, J = 10.8, 6.0, and 2.4 Hz), 3.25 (m, 2H), 4.58 (d, 1H, J = 10 Hz), 5.19 (dd, 1H, J = 10 and 2.4 Hz), and 6.13 (s, 1H); (diastereomer B) δ 1.71 (m, 2H), 1.96 (m, 2H), 2.08 (s, 3H), 2.16 (s, 3H), 2.18 (s, 3H), 3.05 (m, 1H), 3.29 (m, 2H), 4.06 (d, 1H, J = 7.6 Hz), and 5.69 (dd, 1H, J = 7.6 and 4.8 Hz), and 5.83 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (diastereomer A) δ 12.9, 13.6, 21.3, 22.3, 25.2, 42.3, 42.8, 56.9, 74.3, 170.7, and 171.0; (diastereomer B) δ 13.4, 14.2, 21.0, 21.7, 22.0, 31.2, 43.2, 57.2, 72.3, 169.9, and 171.7; HRMS calcd for $C_{11}H_{19}NO_3S_2$ 277.0806, found 277.0804.

Acetic Acid 1-(1-Acetyl-2-oxo-piperidin-3-yl)-2,2-bis-(methylsulfanyl) Ethyl Ester (57). To a 1.0 g (3.8 mmol) sample of **54** dissolved in CH_2Cl_2 (20 mL) were added 4 g of oven-dried 4 Å powdered molecular sieves and 0.4 mL (5.6 mmol) of acetyl chloride. The mixture was stirred at room temperature for 15 h and was filtered through a plug of silica with ether. The organic layer was washed with a saturated aqueous $NaHCO_3$ solution and dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to provide 1.0 g (80%) of **57** as a 1:1 mixture of diastereomers: IR (neat) 2919, 1751, 1695, and 1160 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) (diastereomer A) δ 1.68−1.84 (m, 2H), 1.88−2.02 (m, 1H), 2.02−2.10 (m, 1H), 2.07 (s, 3H), 2.14 (s, 3H), 2.19 (s, 3H), 2.48 (s, 3H), 3.25 (ddd, 1H, J = 11.2, 7.0, and 4.2 Hz), 3.66−3.79 (m, 2H), 3.89 (d, 1H, J = 8 Hz), and 5.69 (dd, 1H, J = 8.0 and 4.4 Hz); (diastereomer B) δ 1.60−1.78 (m, 2H), 1.93−2.09 (m, 2H), 2.10 (s, 3H), 2.11 (s, 3H), 2.14 (s, 3H), 2.50 (s, 3H), 3.16 (ddd, J = 11.2, 6.4, and 3.2 Hz), 3.58 (ddd, 1H, J = 13.6, and 9.6, and 4.4 Hz), 3.82−3.88 (m, 1H), 4.21 (d, 1H, J = 9.6 Hz), and 5.40 (dd, 1H, J = 9.6 and 3.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (diastereomer A) δ 13.2, 13.9, 21.0, 21.1, 21.7, 27.8, 43.4, 46.0, 56.8, 72.2, 169.8, 173.7, and 173.7; (diastereomer B) 12.9, 13.6, 21.2, 21.9, 23.8, 27.9, 43.8, 46.63, 56.4, 73.6, 170.3, 172.4, and 174.0; HRMS calcd for $C_{13}H_{21}NO_4S_2$ 319.0912, found 319.0913.

***N*-(2-Methylsulfanyl-5,6-dihydro-4*H*-furo[2,3-*b*]pyridine)acetamide (61).** To a sample of 0.2 g (0.6 mmol) of **57** in CH_2Cl_2 (3 mL) cooled to −40 °C was added 0.12 g (0.6 mmol) of DMTSF. Following the general procedure, flash silica gel chromatography of the crude reaction mixture gave 0.08 g (64%) of **61** as a yellow oil: IR (neat) 2995, 1676, 1431, and 1379 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.87 (m, 2H), 2.35 (s, 3H), 2.42 (s, 3H), 2.43 (t, 2H, J = 6.4 Hz), 3.80 (m, 2H), and 6.35 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 20.6, 23.1, 24.5, 42.9, 104.9, 117.8, 140.8, 146.5, and 168.2; HRMS calcd for $C_{10}H_{13}NO_2S$ 211.0667, found 211.0662.

Acetic Acid 1-(1-But-3-enoyl-2-oxo-piperidin-3-yl)-2,2-bis(methylsulfanyl) Ethyl Ester (58). To a 2.1 g (7.6 mmol) sample of **54** dissolved in CH_2Cl_2 (40 mL) was added 7.6 g of oven-dried 4 Å powdered molecular sieves followed by 1.3 g (13 mmol) of but-3-enoyl chloride.[43] The reaction was stirred at 25 °C for 15 h then filtered through a silica gel column and washed with ether. The organic phase was washed with a saturated aqueous $NaHCO_3$ solution and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the crude mixture was subjected to flash silica gel chromatography to give 2.5 g (94%) of the titled compound as a yellow oil that contained a 1:1 mixture of diastereomers. For analytical purposes, the diastereomers were separated by HPLC: IR (neat) 1751, 1689, 1425, and 1238 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ (diastereomer A) 1.68−1.85 (m, 2H), 1.92−1.98 (m, 1H), 2.03−2.10 (m, 1H), 2.08 (s, 3H), 2.15 (s, 3H), 2.20 (s, 3H), 3.23−3.30 (m, 1H), 3.66 (dd, 2H, J = 0.8 and 6.8 Hz), 3.72−3.77 (m, 2H), 3.90 (d, 1H, J = 8.0 Hz), 5.10−5.16 (m, 2H), 5.70 (dd, 1H, J = 4.2 and 8.0 Hz), and 5.94−6.04 (m, 1H));

(43) Knapp, S.; Levorse, A. *J. Org. Chem.* **1988**, *53*, 4006.

(diastereomer B) δ 1.60−1.80 (m, 2H), 1.94−2.07 (m, 2H), 2.11 (s, 3H), 2.21 (s, 3H), 2.14 (s, 3H), 3.15 (m, 1H), 3.57−3.64 (m, 1H), 3.66−3.69 (m, 2H), 3.82−3.89 (m, 1H), 4.22 (d, 1H, J = 9.6 Hz), 5.11−5.17 (m, 2H), 5.40 (dd, 1H, J = 9.6 and 3.2 Hz), and 5.97−6.07 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (diastereomer A) δ 13.2, 14.0, 21.0, 21.7, 43.6, 44.2, 46.0, 56.8, 72.1, 118.4, 131.4, 169.8, 173.7, and 174.8; (diastereomer B) δ 12.9, 13.6, 21.2, 21.9, 23.7, 43.9, 44.3, 46.3, 56.4, 73.6, 118.3, 131.6, 170.3, 172.4, and 175.1; HRMS calcd for $C_{15}H_{23}NO_4S_2Li$ [M + Li]$^+$ 352.1229, found 352.1232.

***N*-(2-Methylsulfanyl-5,6-dihydro-4*H*-furo[2,3-*b*]pyridine)-but-3-enamide (62).** To a 0.6 g (1.9 mmol) sample of **58** in CH_2Cl_2 (10 mL) was added 0.5 g (2.4 mmol) of DMTSF in one portion at −40 °C. Following the general procedure, flash silica gel chromatography of the crude reaction mixture gave 0.3 g (68%) of **62** as a clear oil: IR (neat) 1673, 1624, 1510, and 1368 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.85−1.91 (m, 2H), 2.44 (t, 2H, J = 6.4 Hz), 3.55 (d, 2H, J = 7.2 Hz), 3.80−3.83 (m, 2H), 5.14−5.20 (m, 2H), 6.94−6.05 (m, 1H), and 6.36 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.2, 20.6, 23.1, 41.0, 43.1, 105.3, 117.8, 118.3, 131.5, 141.0, 146.2, and 169.0; HRMS calcd for $C_{12}H_{15}NO_2S$ 237.0823, found 237.0815.

Acetic Acid 2,2-Bis(methylsulfanyl)-1-(2-oxo-azepan-3-yl) Ethyl Ester (55). To 5.3 mL (38 mmol) of diisopropylamine in THF (100 mL) cooled to 0 °C was added *n*-butyllithium (38 mmol, 30 mL of a 1.25 M solution in hexane). The mixture was stirred at 0 °C for 30 min. To this solution was added 8.0 g (38 mmol) of 1-trimethylsilanyl-azepan-2-one[42] dissolved in THF (50 mL). The reaction mixture was stirred at 0 °C for 30 min and then cooled to −78 °C. A solution of 5.2 g (38 mmol) of 2,2-bis(methylsulfanyl)acetaldehyde (**10**) dissolved in THF (50 mL) was added dropwise. After addition of the aldehyde, 5.2 mL (55 mmol) of acetic anhydride was added, and the mixture was slowly warmed to room temperature and stirred for 12 h. The reaction mixture was poured into a saturated aqueous solution of $NaHCO_3$, and the organic phase was separated. The aqueous phase was washed with EtOAc, and the combined organic layers were dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to provide 8.8 g (80%) of **55** as a yellow oil consisting of a 4:1 mixture of diastereomers: IR (neat) 1743, 1666, 1434, and 1236 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) (major diastereomer) δ 1.42−1.83 (m, 5H), 1.96−2.08 (m, 1H), 2.21 (s, 6H), 2.15 (s, 3H), 3.10−3.35 (m, 3H), 4.39 (d, 1H, J = 10.4 Hz), 5.32 (dd, 1H, J = 10.0 and 7.2 Hz), and 5.84 (t, 1H, J = 8.0 Hz); (minor diastereomer) δ 1.36−1.48 (m, 2H), 1.53−1.64 (m, 1H), 1.67−1.71 (m, 1H), 1.79−1.84 (m, 1H), 1.98−2.03 (m, 1H), 2.12 (s, 3H), 2.17 (s, 3H), 2.18 (s, 3H), 3.15−3.21 (m, 2H), 3.32−3.40 (m, 1H), 4.20 (d, 1H, J = 3.2 Hz), 5.65 (dd, 1H, J = 9.2 and 2.8 Hz), and 6.04 (t, 1H, J = 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (major diastereomer) δ 12.8, 14.5, 21.3, 27.0, 29.2, 29.3, 42.4, 45.5, 56.5, 73.7, 171.1, and 176.4; (minor diastereomer) δ 14.8, 15.4, 21.0, 25.9, 29.3, 29.4, 42.2, 45.5, 57.2, 73.6, 170.6, and 177.4. Anal. Calcd for $C_{12}H_{21}NO_3S_2$: C, 49.46; H, 7.26; N, 4.81. Found: C, 49.31; H, 7.22; N, 4.73.

Acetic Acid 1-(1-Acetyl-2-oxo-azepan-3-yl)-2,2-bis-(methylsulfanyl) Ethyl Ester (59). To a 1.0 g (3.5 mmol) sample of **55** in CH_2Cl_2 (20 mL) were added 3.5 g of oven dried 4 Å powdered molecular sieves and 0.4 mL (5.2 mmol) of acetyl chloride. The mixture was stirred at room temperature for 15 h, followed by filtration through a plug of silica with ether. The organic layer was washed with a saturated aqueous $NaHCO_3$ solution and dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.9 g (75%) of **59** as a yellow oil that contained a 4:1 mixture of diastereomers: IR (neat) 1747, 1699, 1395, and 1115 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36−1.56 (m, 2H), 1.60−1.69 (m, 1H), 1.84−1.95 (m, 3H) 2.12 (s, 3H, major diastereomer), 2.13 (s, 3H), 2.15 (s, 3H, major diastereomer), 2.17 (s, 3H, minor diastereomer), 2.19 (s, 3H, minor diastereomer), 2.48 (s, 3H, minor diastereomer), 2.49 (s, 3H, major diastereomer), 3.13−3.23 (m, 1H), 3.44−3.52 (m, 1H), 4.04 (d, 1H, J = 4.4 Hz, minor diasteromer), 4.19 (d, 1H, J = 7.0 Hz, major diastereomer), 4.71−4.77 (m, 1H), 5.37 (dd, 1H, J = 7.0 and 6.0 Hz, major diastereomer), and 5.64 (dd, 1H, J = 7.6 and 4.4 Hz, minor diastereomer); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.7, 14.3, 14.6, 15.1, 21.0, 21.2, 26.6, 27.3, 27.7, 27.7, 27.9, 27.9, 42.2, 42.2, 48.2, 48.4, 56.5, 57.1, 73.7, 73.7, 170.4, 170.8, 173.3, 173.4, 176.2, and 177.1; HRMS calcd for $C_{14}H_{23}NO_4S_2Li$ [M + Li] 340.1229. Found: 340.1221.

***N*-(2-Methylsulfanyl-4,5,6,7-tetrahydrofuro[2,3-*b*]-azepine)acetamide (63).** To a 0.5 g (1.5 mmol) sample of **59** in CH_3CN (15 mL) was added 0.3 g (1.5 mmol) of DMTSF in one portion at −40 °C. Following the general procedure, flash silica gel chromatography of the reaction mixture gave 0.2 g (55%) of **63** as a yellow oil: IR (neat) 1686, 1442, 1378, and 1203 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.59−1.64 (m, 2H), 1.77−1.82 (m, 2H), 2.38 (s, 3H), 2.39−2.42 (m, 2H), 3.62−3.65 (m, 2H), and 6.29 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 22.8, 24.7, 25.9, 30.5, 45.6, 117.3, 118.3, 142.2, 148.9, and 171.0; HRMS calcd for $C_{11}H_{15}NO_2S$ 225.0823, found 225.0823.

3-[1-(Bis(methylsulfanyl)methyl)-1-hydroxy-propyl]-azepan-2-one (56). To 9.8 mL (70 mmol) of diisopropylamine in THF (150 mL) cooled to 0 °C was added *n*-butyllithium (46 mL of a 1.5 M solution in hexane). The reaction mixture was stirred at 0 °C for 30 min and then 13 g (70 mmol) of 1-trimethylsilanyl-azepan-2-one[42] dissolved in THF (100 mL) was added dropwise over 30 min. The solution was stirred at 0 °C for an additional 30 min and then cooled to −78 °C. To this mixture was added 11.4 g (70 mmol) of 1,1-bis(methylsulfanyl)-butan-2-one[44] in 100 mL of THF. After the addition was complete, the mixture was stirred for an additional 30 min before being poured into saturated aqueous NH_4Cl solution. The organic phase was separated, and the aqueous phase was washed with ethyl acetate. The combined organic layer was dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 13 g (65%) of **56** as a light yellow oil that contained a 1.5:1 inseparable mixture of diastereomers: IR (neat) 1708, 1644, 1476, and 1434 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, 3H, J = 7.6 Hz, major diastereomer), 0.87 (t, 3H, J = 7.8 Hz, minor diastereomer), 1.34−2.10 (m, 8H), 2.14 (s, 3H), 2.18 (s, 3H, minor diastereomer), 2.19 (s, 3H, minor diastereomer), 2.20 (s, 3H, major diastereomer), 2.93−2.96 (m, 1H, minor diastereomer), 3.09−3.15 (m, 1H), 3.23−3.26 (m, 1H, major diastereomer), 3.27−3.38 (m, 1H), 3.91 (s, 1H, minor diastereomer), 4.10 (d, 1H, J = 1.6 Hz, major diastereomer), 5.01 (s, 1H, major diastereomer), 5.10 (s, 1H, minor diastereomer), and 6.75 (t, 1H, J = 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.8, 9.6, 17.0, 17.5, 17.7, 18.2, 24.1, 24.8, 27.8, 28.3, 28.4, 28.5, 28.8, 30.2, 41.6, 41.7, 45.8, 46.9, 64.8, 65.9, 79.4, 80.5, 180.7, and 181.2. Anal. Calcd for $C_{12}H_{23}NO_2S_2$: C, 47.63; H, 6.90; N, 5.02. Found: C, 47.56; H, 6.94; N, 5.13.

1-Acetyl-3-[1-(bis(methylsulfanyl)methyl)-1-hydroxy-propyl]-azepan-2-one (60). To a 2.0 g (7.3 mmol) sample of the above alcohol in CH_2Cl_2 (40 mL) was added 7 g of oven-dried 4 Å powdered molecular sieves and 0.8 mL (11 mmol) of acetyl chloride. The mixture was stirred at room temperature for 15 h, followed by filtration through a plug of silica with ether. The organic layer was washed with a saturated aqueous $NaHCO_3$ solution and dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 1.5 g (64%) of **60** as a colorless oil that contained a 1.5:1 inseparable mixture of diastereomers: IR (neat) 1702, 1462, 1396, and 1189 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, 3H, J = 7.6 Hz, major diastereomer), 0.96 (t, 3H, J = 7.6 Hz, minor diastereomer), 1.48−2.17 (m, 8H), 2.18 (s, 3H, major diastereomer), 2.23 (s, 3H, minor diastereomer), 2.25 (s, 3H, minor diastereomer), 2.27 (s, 3H, major diastereomer), 2.46 (s, 3H, minor diastereomer), 2.50 (s, 3H, major diastereomer), 3.18−3.31 (m, 1H), 3.37−3.41 (m, 1H, minor diastereomer), 3.42 (dd, 1H, J = 9.4 and 3.4 Hz, major diastereomer), 3.78 (s, 1H, minor

(44) Solladie, G.; Boeffel, D.; Maignan, J. *Tetrahedron* **1996**, *52*, 2065.

diastereomer), 4.01 (s, 1H, minor diastereomer), 4.06 (d, 1H, J = 1.2 Hz, major diastereomer), 4.30 (s, 1H, major diastereomer), and 4.71 (dt, 1H, J = 15.2 and 4.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.9, 9.9, 16.9, 17.1, 17.8, 18.0, 25.1, 25.5, 26.6, 27.0, 27.2, 27.3, 27.8, 28.0, 28.2, 30.2, 41.9, 42.1, 48.7, 51.0, 65.1, 65.8, 80.0, 81.4, 173.4, 179.8, and 180.8; HRMS calcd for $C_{14}H_{23}NO_2S_2$ [M − H_2O] 301.1170, found 301.1176.

***N*-(3-Ethyl-2-methylsulfanyl-4,5,6,7-tetrahydrofuro-[2,3-*b*]azepine)-acetamide (64).** To a solution of 0.3 g (1.0 mmol) of **60** in CH_2Cl_2 (5 mL) cooled to −40 °C was added 0.2 g (1.0 mmol) of DMTSF. Following the general procedure, flash silica gel chromatography of the reaction mixture provided 0.15 g (56%) of **64** as a yellow oil: IR (neat) 1687, 1634, and 1377 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09 (t, 3H, J = 7.6 Hz), 1.60−1.66 (m, 2H), 1.78−1.84 (m, 2H), 2.07 (s, 3H), 2.31 (s, 3H), 2.37−2.40 (m, 2H), 2.46 (q, 2H, J = 7.6 Hz), and 3.63−3.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6, 18.1, 20.1, 22.8, 23.0, 25.8, 30.5, 45.5, 116.6, 133.4, 137.9, 148.6, and 171.0; HRMS calcd for $C_{13}H_{19}NO_2S$ 253.1136, found 253.1143.

2,2-Dimethylpropionic Acid 1-Methylcarbamoylmethyl-2,2-bis(methylsulfanyl) Ethyl Ester (67). To a solution containing 0.5 mL (3.5 mmol) of diisopropylamine in THF (11 mL) cooled to 0 °C was added *n*-butyllithium (2.3 mL of a 1.5 M solution in hexane). After stirring for 1 h, the mixture was cooled to −40 °C, 0.5 g (3.2 mmol) of *N*-methyl-pivalylacetamide (**65**)[45] in 2 mL of THF was added, and the mixture was stirred for 1 h. The temperature was lowered to −75 °C, and 0.4 g (3.3 mmol) of 2,2-bis(methylsulfanyl)acetaldehyde (**10**) was added dropwise as a THF solution (4 mL). The reaction mixture was stirred for an additional 30 min and was quenched by the addition of a saturated aqueous NH_4Cl solution. The solution was slowly warmed to room temperature and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure. Silica gel column chromatography of the crude residue afforded 0.5 g (49%) of **67** as a yellow oil: IR (neat) 1731, 1649, 1562, and 1152 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 9H), 2.20 (d, 6H, J = 8.8 Hz), 2.59 (dd, 1H, J = 14.6 and 7.4 Hz), 2.79 (d, 3H, J = 4.8 Hz), 2.86 (dd, 1H, J = 14.6 and 5.4 Hz), 4.00 (d, 1H, J = 4.8 Hz), 5.42−5.46 (m, 1H), and 5.62 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 15.1, 26.5, 27.2, 38.6, 39.1, 57.7, 72.1, 169.9, and 177.8; HRMS calcd for $C_{12}H_{23}NO_3S_2$ 293.1119, found 293.1118.

2,2-Dimethylpropionic Acid 1-(Bis(methylsulfanyl-methyl)-3-[(2,2-dimethylpropionyl)-methylamino]-3-oxo-propyl Ester (68). To a solution containing 1.0 g (3.4 mmol) of **67** in CH_2Cl_2 (17 mL) was added 0.8 mL (6.5 mmol) of trimethylacetyl chloride followed by 3.4 g of powdered molecular sieves. After stirring at room temperature for 12 h, the suspension was filtered through a pad of silica gel and washed several times with ether. The filtrate was washed with a saturated aqueous $NaHCO_3$ solution, dried over $MgSO_4$, and concentrated under reduced pressure. The crude reaction mixture was subjected to flash silica gel chromatography to give 1.0 g (80%) of **68** as a yellow oil: IR (neat) 1808, 1690, 1475, and 1060 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (s, 9H), 1.27 (s, 9H), 2.11 (s, 3H), 2.12 (s, 3H), 2.83 (dd, 1H, J = 21.6 and 9.6 Hz), 3.08 (s, 3H), 3.19 (dd, 1H, J = 22.4 and 7.2 Hz), 3.89 (d, 1H, J = 5.6 Hz), and 5.46−5.52 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 14.9, 27.1, 28.2, 32.6, 38.8, 39.2, 42.5, 57.6, 71.7, 172.7, 177.4, and 185.2; HRMS calcd for $C_{17}H_{31}NO_4S_2$ 377.1694, found 377.1693.

2,2-(*N*-Trimethyl-*N*-(5-methylsulfanylfuran-2-yl)-propionamide (69). To a solution containing 1.0 g (2.7 mmol) of **68** in CH_3CN (14 mL) was added 0.6 g (2.9 mmol) of DMTSF in one portion at −40 °C. Following the general procedure, flash silica gel chromatography of the reaction mixture gave 0.4 g (59%) of **69** as a pale yellow oil: IR (neat) 1665, 1608, 1332, and 1101 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 (s, 9H), 2.39 (s, 3H), 3.15 (s, 3H), 6.07 (d, 1H, J = 3.2 Hz), and 6.41 (d, 1H, J = 3.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.3, 28.6, 39.6, 40.8, 107.0, 115.9, 144.6, 151.6, and 179.2; HRMS calcd for $C_{11}H_{17}NO_2S$ 227.0980, found 227.0978.

7-Methylsulfanyl-5,6,9,9a-tetrahydro-1*H*,4*H*,7*H*-pyrrolo-[3,2,1-*ij*]quinoline-2,8-dione (72). A 0.7 g (3.0 mmol) sample of **62** dissolved in toluene (15 mL) was heated at reflux for 1 h at 110 °C. The reaction mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The crude residue was purified by flash silica gel chromatography to provide 0.6 g (92%) of **72** as a yellow oil that consisted of a 1.4:1 mixture of diatereomers: IR (neat) 1716, 1682, 1420, and 1197 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.84−1.94 (m, 4H), 1.99−2.07 (m, 2H), 2.10 (s, 3H), 2.12 (s, 3H), 2.16−2.32 (m, 4H), 2.32−2.47 (m, 1H), 2.58−2.60 (m, 1H), 2.67 (dd, 1H, J = 16.4 and 8.4 Hz), 2.76 (dd, 1H, J = 17.2 and 10 Hz), 3.02−3.08 (m, 3H), 3.35−3.46 (m, 5H), and 3.59−3.69 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9, 16.1, 21.1, 21.2, 22.8, 23.6, 29.3, 34.0, 37.1, 37.2, 38.8, 39.1, 39.5, 42.1, 52.9, 54.0, 102.4, 103.7, 138.3, 140.7, 173.2, 173.3, 201.2, and 201.4; HRMS calcd for $C_{12}H_{15}NO_2S$ 237.0823, found 237.0819.

5,6,9,9a-Tetrahydro-1*H*,4*H*,7*H*-pyrrolo[3,2,1-*ij*]quinoline-2,8-dione (73). To a 0.1 g (0.4 mmol) sample of **72** dissolved in EtOH (2 mL) was added an excess of Raney nickel. The reaction mixture was stirred at room temperature for 15 h and then filtered through a pad of Celite, which was subsequently washed with EtOAc. The solvent was removed under reduced pressure, and the crude residue was purified by flash silica gel chromatography to provide 0.04 g (42%) of **73** as a clear oil: IR (film) 1687, 1602, 1411, and 1362 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.80−2.10 (m, 4H), 2.26 (dd, 1H, J = 16.8 and 8.8 Hz), 2.38 (dd, 1H, J = 14.6 and 12.6 Hz), 2.71−2.86 (m, 3H), 2.93−3.00 (m, 1H), 3.07−3.16 (m, 1H), 3.31−3.37 (m, 1H), and 3.75−3.80 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 24.8, 31.5, 37.3, 38.8, 42.1, 45.1, 103.4, 135.7, 173.1, and 208.3; HRMS calcd for $C_{11}H_{13}NO_2$ 191.0946, found 191.0947.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for new compounds lacking elemental analyses. This material is available free of charge via the Internet at http://pubs.acs.org.

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