Synthesis of Azapolycyclic Systems via the Intramolecular [4 + 2] Cycloaddition Chemistry of 2-(Alkylthio)-5-amidofurans

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A series of 2-(methylthio)-5-amidofurans containing tethered unsaturation were prepared via the reaction of dimethyl(methylthio)sulfonium tetrafluoroborate (DMTSF) with β-alkoxy-γ-dithiane amides **13**−**16** and **27**−**32** in 40−70% yield. Thermolysis of these furans resulted in an intramolecular Diels−Alder reaction (IMDAF). With the exception of **45** and **46**, the oxa-bridged cycloadducts could not be isolated but immediately underwent a 1,2-methylthio shift to form bicyclic lactams in 60−100% yield. It was determined that incorporation of the amido carbonyl in the tether allowed the IMDAF reaction to proceed at a lower temperature. A dramatic example of this is seen in the IMDAF reaction of furan **35**, in which the presence of an amido carbonyl as part of the dienophile tether, as opposed to the annealed ring (**66**) or the lack of a carbonyl (**67**), was necessary for the cycloaddition to occur. Furan **37**, annealed to an azepine ring, underwent the IMDAF reaction at or below room temperature. To identify structural features that promote the IMDAF reaction, a computational study was undertaken. Ground-state and transition-state energies were calculated for furans **17**, **33**, **37**, and **64** using the Becke 3LYP/6-31G* model. The theoretical results were in good agreement with those observed. The results indicate that the incorporation of an amide carbonyl as part of the tether system works to place the dienophile in closer proximity to the furan ring, thereby lowering the activation energy needed to reach the transition state.

It is well-known that aromatic heterocycles, such as furans, thiophenes, and pyrroles, can undergo Diels−Alder reactions as 4π diene components despite their aromaticity and hence expected decreased reactivity.[1−3] In fact, the proclivity of furans to undergo [4 + 2] cycloaddition with various π-bonds has attracted the attention of many research groups, as it allows for the rapid construction of valuable synthetic intermediates.[4−6] The initial cycloaddition gives rise to a substituted 7-oxabicyclo[2.2.1]hept-5-ene (7-oxanorbornene) that can be manipulated with impressive selectivity, leading to a variety of interesting target molecules.[7−16] A crucial synthetic transformation employing these intermediates involves cleavage of the oxygen bridge to produce functionalized cyclohexene derivatives.[17−22]

While the intramolecular Diels−Alder reaction of furans (IMDAF) has been the subject of many reports,[6] much less is known regarding the intramolecular cycloaddition behavior of furan Diels−Alder systems that contain heteroatoms attached directly to the furan ring.[23−25] Recent work in our laboratory has shown that

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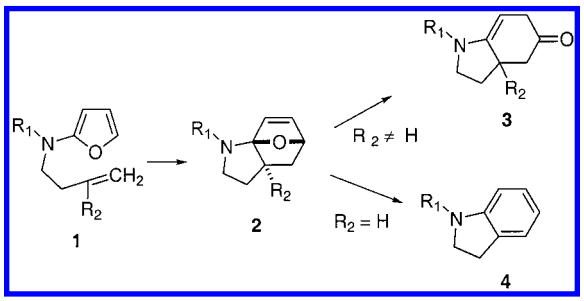
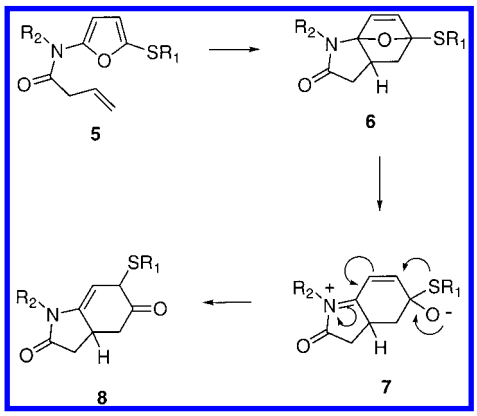
Scheme 1



the IMDAF reaction of 2-amido-substituted furans represents an effective route to indolines and tetrahydroquinolines.[26] This methodology has also been utilized for the synthesis of the hexahydroindolinone skeleton found in numerous natural products.[27] The interesting biological activity associated with alkaloids in the structurally diverse aspidosperma,[28] erythrina,[29] and stemona[30] families has also made the perhydroindole core of these alkaloids an important preparative target for which many synthetic strategies have been devised.[31] Because cycloaddition reactions such as the Diels−Alder reaction can achieve high levels of both regio- and stereoselectivity,[32] especially the intramolecular Diels−Alder reaction,[33] a synthetic approach based upon this methodology could allow for a concise construction of the perhydroindole skeleton. As part of our program designed to explore the synthetic utility of the intramolecular cycloaddition chemistry of amido-substituted furans, we have used this methodology for the preparation of hippadine,[34] (±)-dendrobine,[35] and (±)-lycorane.[36] This approach, demonstrated by the cyclization of **1** to the intermediate oxabicycle **2** (Scheme 1), was limited to systems containing an angular substituent in the resultant azabicycle **3** ($R_2 \neq H$), or else aromatic products (i.e., **4**) were formed.[26] In an effort to circumvent this aromatization, we sought to incorporate an alternate reaction pathway, such as a rearrangement, through which to alleviate the charge in the reactive intermediate (e.g. **7**). For example, a 2-(methylthio)-5-amidofuran with an appropriately tethered olefin (e.g. **5**) should undergo the cycloaddition−nitrogen-assisted ring-opening cascade (Scheme 2). Rather than lose a proton to quench the iminium ion, the ring-opened intermediate **7** could undergo a 1,2-alkylthio shift to provide **8**. Because initial studies into the cycloaddition chemistry of these furans were promising,[37] a more detailed investigation has been conducted. The results of these inquiries are reported herein.

Scheme 2



Results and Discussion

The required 2-(methylthio)-5-amidofurans necessary for the intramolecular [4 + 2] cycloaddition studies were prepared by a dimethyl(methylthio)sulfonium tetrafluoroborate (DMTSF) induced cyclization of various amido dithioacetals.[38] This approach was devised by the assumption that it should be possible to induce cyclization of the amide carbonyl group onto the resulting thionium ion formed from the DMTSF reaction of the dithioacetal. It is known that treatment of thioketals with DMTSF[39] causes the carbon−sulfur bond to become labile upon methylthiolation.[40] The resulting (alkylthio)sulfonium ion easily dissociates to produce a thionium ion and methyl disulfide.[41] Once the dihydrofuran ring has been forged, elimination of acetic acid (or its equivalent) should proceed readily to furnish the 2-(alkylthio)amidofuran. Indeed, this protocol worked well and led to the formation of various (alkylthio)amidofurans in good yield.[42] Thus, we found that treating *N*-pivaloyl-*N*-methylacetamide (**9**) with LDA followed by reaction with bis(methylsulfanyl)-acetaldehyde (**10**)[43] furnished the crossed-aldol interme-

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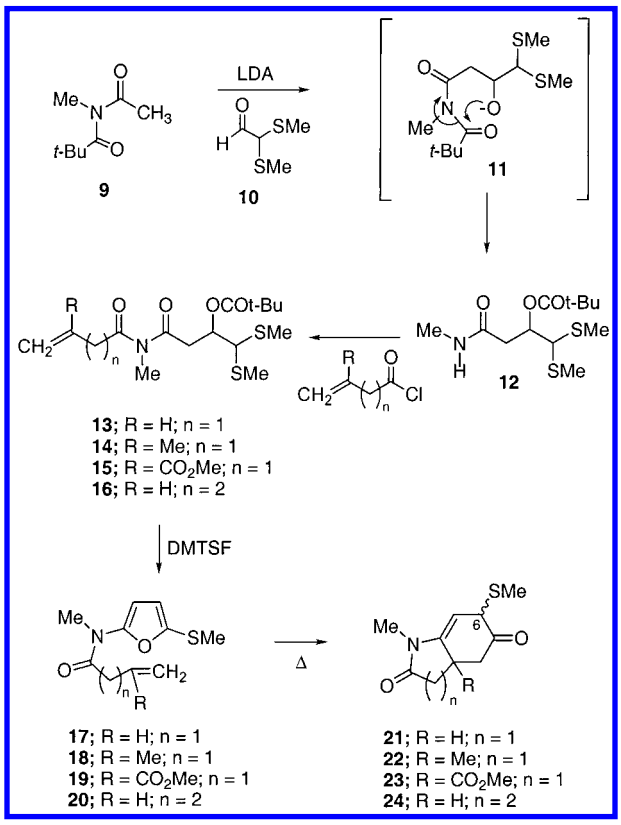
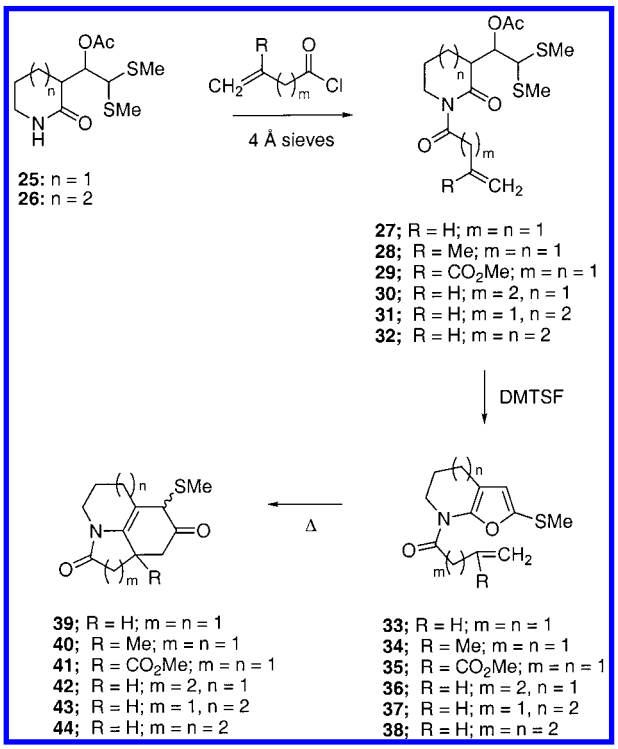
Scheme 3



diate **11**, which underwent a rapid N-/O-acyl transfer reaction to provide the secondary amide **12** upon aqueous workup. Attempts to acylate this amide under basic conditions (i.e., Et_3N, DMAP, etc.) resulted only in elimination of the pivalate. Using 4 Å molecular sieves as a neutral acid scavenger,[44] however, resulted in the formation of imides **13**−**16** in good yield (60−90%) (Scheme 3). These imides were then treated with DMTSF to produce the 2-(alkylthio)-5-amidofurans **17**−**20** in 40−70% yield.

With a satisfactory method for the synthesis of the cycloaddition precursors in place, we became interested in evaluating the facility with which these (thioalkyl)-amidofuranyl systems would undergo cycloaddition. We noted that in the case of imide **15** (R = CO_2Me; n = 1), the furan (i.e., **19**) could not be isolated from the DMTSF reaction. Rather, lactam **23** was obtained in 68% isolated yield. Several of the other amidofuran substrates also spontaneously underwent [4 + 2] cycloaddition at room temperature (ca. 15 h) to produce bicyclic lactams, although heating accelerated the cascade. For convenience, therefore, furans **17**, **18**, and **20** were not purified; the crude products were immediately thermolyzed to provide the bicyclic lactams. In a typical example, heating a toluene solution of crude furan **17** (R = H; n = 1) at reflux for 2 h produced **21** in 72% yield. In stark contrast, furan **20** (R = H, n = 2)[45] failed to produce **24** even when heated at 200 °C in a sealed tube. In all cases, the bicyclic

Scheme 4



lactam products **21**−**23** were isolated (after silica gel chromatography) as mixtures (1:1) that were diastereomeric about the C(6) stereocenter. However, examination of the ^1H NMR spectra of the crude reaction mixtures indicated that only one diastereomer was initially produced in each reaction. Thus, it appears that the diastereomeric ratios obtained upon isolation are the result of a facile epimerization of the C(6) center on silica gel separation and are not kinetically derived (vide infra).

Encouraged by both the success of the cycloaddition−rearrangement cascade and the apparent generality of the amido(thioalkyl)furan synthesis, more complex cyclization systems, wherein the furan was fused to a nitrogen heterocycle, were examined. Accordingly, cyclization precursors **33**−**38** were prepared by the sequential acylation of lactams **25** or **26** with an appropriate acid chloride and reaction of the resulting diimides **27**−**32** with DMTSF (Scheme 4). Formation of tricyclic lactams **39** (92%) and **40** (61%) required heating the requisite furan at reflux in toluene, whereas the reaction of **36** to give **42** (76% yield) needed to be carried out at 150 °C in a sealed tube. Furan **38** (R = H, $m = n$ = 2) also required 150 °C to effect the Diels−Alder reaction, but tricyclic lactam **44** was not formed. Rather, the remarkably robust oxabicycle **45** was isolated in 75% yield (Scheme 5). Amido(thioalkyl)furans **35** (R = CO_2-Me; $m = n$ = 1) and **37** (R = H; m = 1, n = 2) could not be isolated because the Diels−Alder cycloaddition occurs under the conditions of their formation. While **37** proceeds directly to the tricyclic lactam **43** in 64% yield, furan **35** provided oxabicycle **46** in 77% yield. Heating a benzene solution of this cycloadduct at reflux provided the tricyclic lactam **41** in 77% yield. The relative stereochemistry of **46** was secured by a single-crystal X-ray analysis.

To further illustrate the viability of the cycloaddition/rearrangement cascade as a practical strategy for the synthesis of complex polyazacyclic systems, we studied

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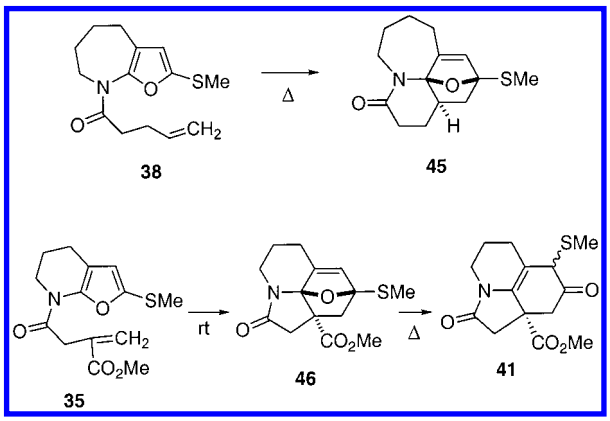
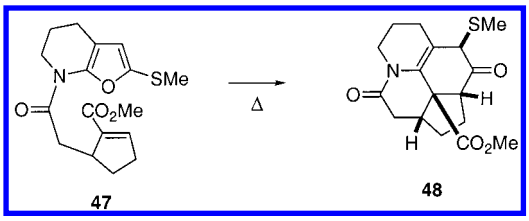
(45) Experimental details for the preparation of **20** and **66** and their spectroscopic properties are given in the Supporting Information.

Scheme 5

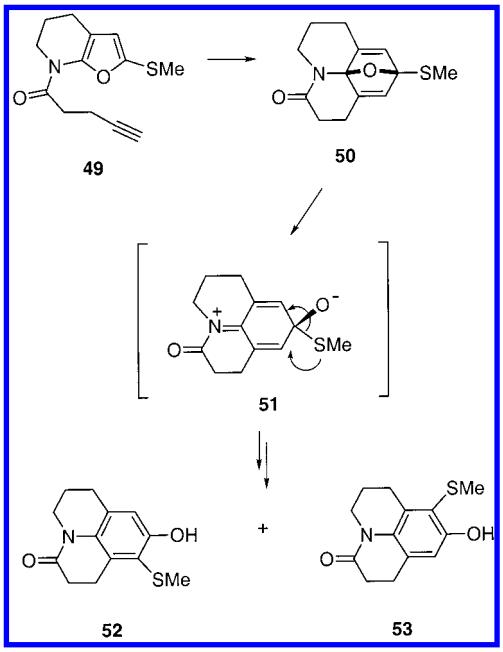


the IMDAF behavior of the related amidofuran **47**. We were gratified to find that heating **47** at 110 °C for 2 h gave the rearranged amide **48** as a single diastereomer in 80% yield. The relative stereochemistry of **48** was unequivocally established by X-ray crystallographic analysis.

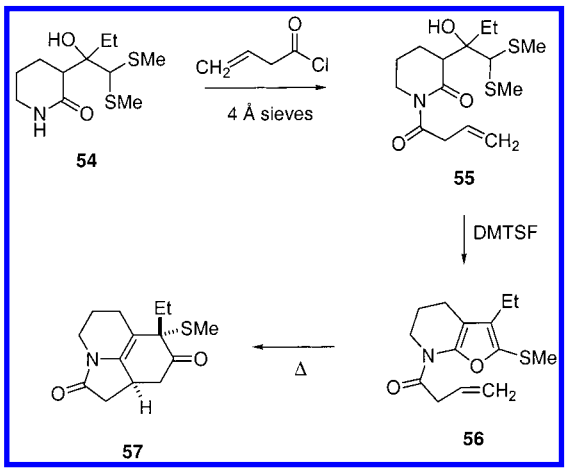


In addition to the simple substituted alkenes shown in Scheme 4, tethered alkynes also participate in the cycloaddition cascade, although at a much slower rate. For example, when furan **49** was heated to 160 °C for 2 days, a 1:1 mixture of **52** and **53** was isolated in nearly quantitative yield (Scheme 6). From the oxa-bridged cycloadduct **50**, two possible 1,2-alkylthio shifts can occur to alleviate the charge on the transient N-acyl iminium ion **51**. Indeed, both rearrangement pathways occurred to an equal extent, providing a 1:1 mixture of the isomeric phenols.

Scheme 6



Scheme 7



As described above, a majority of the bicyclic lactams were isolated as mixtures of diastereomers. However, monitoring the thermolysis by ^{1}H NMR spectroscopy showed that only one diastereomer was present in the crude reaction mixture prior to silica gel chromatography. Because the stereogenic center adjacent to the ketone moiety is readily epimerized, the relative stereochemistry of the kinetically formed products could not be easily assigned. A mechanistic probe wherein the final product lacks the easily epimerizable center would allow for the isolation of the kinetic product. To this end, furan **56** was synthesized from amide **54** via acylation with vinyl acetic acid chloride followed by exposure of the resulting imide **55** to DMTSF and *p*-TsOH[42] (Scheme 7). Thermolysis of **56** in toluene at 110 °C for 1 h produced the tricyclic lactam **57** in 70% yield as a single diastereomer whose relative stereochemistry was established by X-ray analysis.

The X-ray crystal structure of oxabicycle **46** reveals a preferred exo orientation of the tether in the Diels−Alder adduct. This stereochemical result is consistent with that reported by others for related furanyl systems possessing short tethers.[46,47] The ring-opened lactams (i.e., **39**−**43**) are derived from an IMDAF cycloaddition where the sidearm of the tethered alkenyl group is oriented syn (exo) with respect to the oxygen bridge. Products resulting from an endo sidearm transition state were neither detected nor isolated. This result is not so surprising since, in these mobile cycloaddition equilibria, the exo adducts are expected to be thermodynamically more favored. It should also be noted that bicyclic lactam **57** possesses a configuration in which the methylthio group and the angular hydrogen are on the same face. This feature, combined with the exclusive formation of one diastereomer in the thermolysis of **56**, suggest a concerted 1,2-shift of the methylthio group. While a stepwise elimination−stereoselective addition of the methylthio substituent is possible, the lack of stereodirecting features within these systems is inconsistent with the observed degree of stereoselectivity. It should be noted that a somewhat related methylthio group migration was

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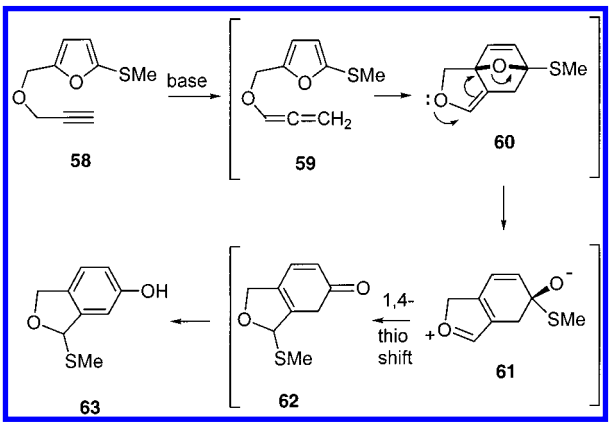
Scheme 8



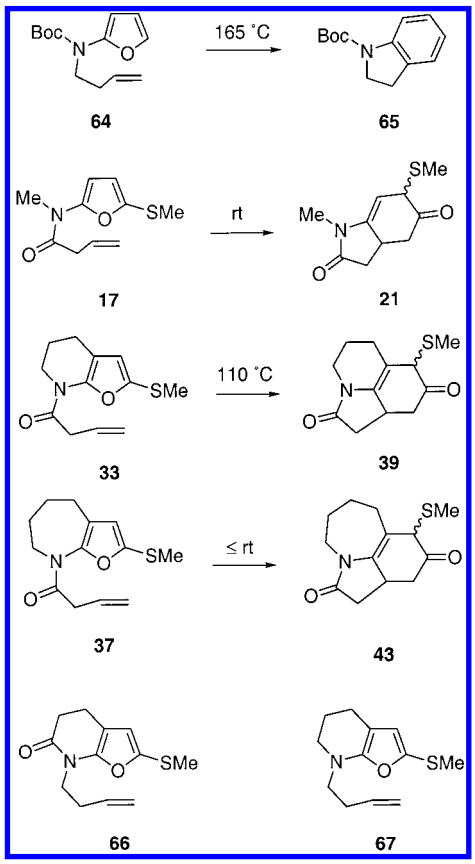
reported by Wu and co-workers[48] in their studies of the intramolecular Diels−Alder reaction of a furan containing a tethered allenyl ether dienophile (Scheme 8). The initially formed cycloadduct **60** was proposed to undergo ring opening of the bridged oxygen atom to produce zwitterion **61**, which underwent a subsequent 1,4-methylthio shift to eventually give phenol **63**. In contrast to our studies, the alkylthio shift encountered with **60** was proposed to proceed via a tight ion pair.

One of the more striking features of the intramolecular Diels−Alder cascade reactions outlined in the above schemes is the variable reactivity of structurally similar substrates. Previous work from this laboratory, for example, demonstrated that amidofuran **64** required heating to 165 °C to undergo a cascade that furnished **65** (Scheme 9). In stark contrast, 2-(alkylthio)-5-amidofuran **17** produced **21** when left at room temperature for 12 h (vide supra). Likewise, the amidofuran **33**, in which the furan is fused to a six-membered ring, required heating to 110 °C to afford **39**. However, furan **37**, in which the heteroaromatic ring is fused to a seven-membered ring, could not be isolated, as **43** was produced under the reaction conditions used to form the furan. Interestingly, systems that differed from furan **33** only in the placement or deletion of the amide carbonyl group would not undergo the initial Diels−Alder reaction. For example, furans **66** and **67** resisted cyclization even at temperatures up to 200 °C.

The primary structural differences between **64** and **17** are the presence of a methylthio group on the furan and the location of the amide carbonyl in **17**. That alkylthio substituents are known to have little effect on the facility of Diels−Alder reactions combined with the lack of reactivity in **66** and **67** implicates the placement of the carbonyl center within the dienophilic tether as the more important structural change.

Dramatic effects originating from the placement of a carbonyl group on the tether have previously been noted. In one example involving an intramolecular dipolar cycloaddition, a severe steric interaction was found in the transition state, while no such interaction was identifiable in either the starting material or product ground states.[49] Introduction of a carbonyl group on the tethered dipolarophile relieved the source of the strain. Similarly,

Scheme 9



the effects of amide- and ester-linked tethers on the diastereoselectivity of intramolecular Diels−Alder reactions have been attributed to relative transition state stabilities.[50] Jung and Gervay, however, reported data for intramolecular Diels−Alder reactions which suggest that substitution on the tether results in an increase in the population of reactive rotamers.[51] Thus, the rate enhancement was suggested to originate from a restricted rotation, producing a lowest energy ground state conformer that is more energetically similar to the reactive conformer.

Because there was no clear precedent regarding whether the origin of the rate differences resided either in ground-state conformational effects or in relative strain within the transition states, we investigated the ground-state conformations of **64**, **17**, **33**, and **37** as well as the transition states through which these reactants must pass to obtain the corresponding oxabicycles. Initial attempts to explore the conformational space of these molecules using MM2* and MMFF force fields were inconclusive because of the inadequate parametrization of the force fields for these amidofuran systems.[52] Density functional methods were therefore employed for the

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(52) For MMFF parameters see: Halgren, T. A. *J. Comput. Chem.* **1999**, *20*, 730. For a comparison of parameters see: Gundertofte, K.; Liljefors, T.; Norrby, P. O.; Petersson, I. *J. Comput. Chem.* **1996**, *17*, 429.

conformational search. Using the B3LYP/3-21G* model[53,54] as implemented by Gaussian 98,[55] ground-state conformations were explored by optimizing structures with, for example, various gauche and anti comformations about rotatable bonds. Transition states for each of the Diels–Alder reactions were also located (Figure 1).[56]

Initial results from B3LYP/3-21G* optimizations showed relative activation energies that were consistent with experimental observations. Single-point calculations using the 6-31G* basis set, however, predicted a relative energy of activation for the conversion of **64a** to **A** that was much lower than expected. Reoptimization of the structures in Figure 1 using the 6-31G* basis set confirmed the single-point energy calculations without significantly altering the optimized geometry. Because density functional theory is known to overemphasize the resonance stabilization of aromatic compounds,[57,58] single-point MP2/6-311+G*//B3LYP/6-31G* calculations were performed. These results also predict a lower energy of activation for the conversion of **64a** to **A** than was experimentally observed (vide infra).

Examination of the optimized transition states **A**–**D** revealed no obvious strain or large steric interactions. The ground-state conformations, however, contained two features that may explain the observed differences in reactivity. The first feature involves the conformation that the carbonyl enforces within the tether. In compound **64a**, for example, the substituents on the adjacent methylene carbons C(3′) and C(4′) prefer an anti conformation that projects the olefin away from the furan. A gauche conformation is required for the reaction to proceed. In compound **17a**, however, the C(3′)–C(4′) bond has a nearly synclinal orientation with respect to the amide carbonyl (O–C(4′)–C(3′)–C(2′) = −100.8°),[59] and this conformation places the olefin in much closer proximity to the furan than the conformation of **64a**.

The energy differences associated with a single bond rotation cannot account for the larger differences in activation barrier, but a second conformational feature appears to place **17a** closer to a reactive conformation than **64a**. The C(3)–C(2)–N–C(4′) dihedral angle in **64a** was calculated to be 172.5°, while the same angle in **17a** was 131.7°. The C(3)–C(2)–N–C(4′) dihedral angle in **A** was calculated to be 123.4°, while the same torsional angles in **B**–**D** were calculated to be approximately 130°. Thus, the rotation about the C(2)–N bond appears to be biased toward a reactive conformer in **17a**. Conformer **17b**, which is similar to the low-energy conformation **64a**, was calculated to be less than 0.1 kcal/mol higher in energy than **17a** due to an $A^{1,3}$ interaction between the methyl substituent on the nitrogen and the protons on C(3′) (Figure 2). The oxygen in the carbamate moiety of **64** does not produce this destabilizing interaction.

Preferred ring conformations dictate the C(3)–C(2)–N–C(4) dihedral angle in **33a** and **37a**. The six-membered ring annealed to the furan in **33a** adopts a half-chair conformation in which the C(3)–C(2)–N–C(4) dihedral angle is 156.0°. The seven-membered ring annealed to the furan in **37a** adopts a low-energy

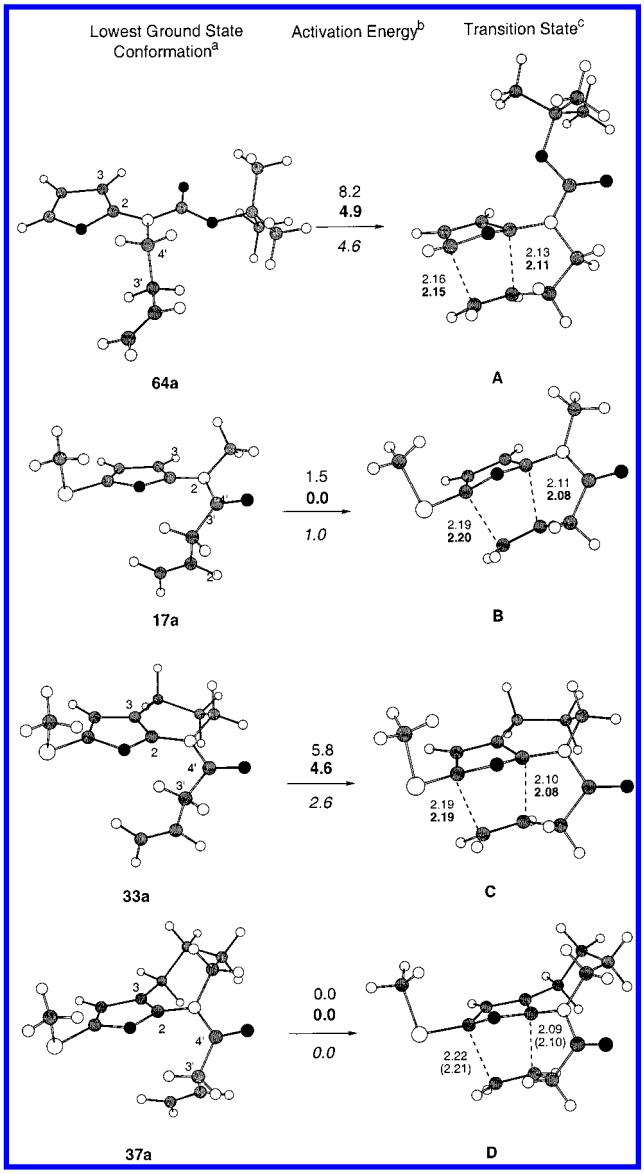

Figure 1. (a) B3LYP/6-31G* optimized ground-state conformations. (b) Calculated relative energies of activation in kcal/mol at B3LYP/3-21G*, B3LYP/6-31G* (in bodlface), and MP2/6-311+G*//B3LYP/6-31G (in italics). (c) Corresponding transition states with transitional bond lengths in angstroms as optimized at B3LYP/3-21G* and B3LYP/6-31G* (in boldface) levels of theory.

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(56) Transition state structures were characterized by one imaginary vibrational frequency (Nimag = 1) corresponding to the bonding event. No zero-point energy corrections were applied to any of the calculated structures.

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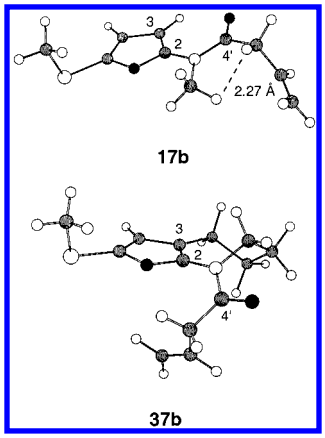
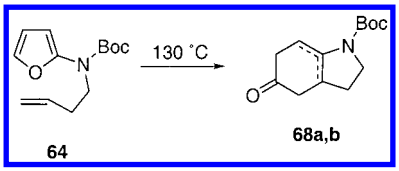


Figure 2. Second low-energy conformations of **17** and **37**.

conformation that imparts a 119.7° angle, but a simple ring flip provides a conformation (**37b**) in which the angle increases to 132.7° (Figure 2). The rapid interconversion of **37a** and **37b** (a calculated 2.2 kcal/mol energy difference) allows **37** to adopt a reactive conformation more easily than **64** or **33**. The differences in reactivity among furans **64**, **17**, **33**, and **37**, therefore, appear to correlate with a bias in the rotation about the C(2)−N bond.

While the effects attributed to the placement of the carbonyl and the effects that stem from the rotational bias about the C(2)−N bond appear to be localized to the ground state, some of the structural features may destabilize the transition states. For example, the geometry of furan **33** that is required to reach a transition state is difficult for a cyclohexene-like ring to achieve. Significant ring strain may, therefore, account for the higher calculated activation energy. The correlation between ground-state conformational preferences and reactivity is, however, significant.

The small difference in calculated activation energies between the conversion of **64** to **65** and **33** to **39** caused us to reexamine the conditions under which these cycloadditions occur. It was discovered that the intramolecular Diels−Alder reaction of **64** proceeded at 130 °C (35 °C lower than previously observed) to produce a mixture (3:2) of enamino ketones **68a**,**b** in 64% yield. At lower temperatures (e.g. 110 °C), however, decomposition pathways were faster than cycloaddition, and a lower limit could not be determined.



In summary, a highly convergent synthesis of hexahydropyrroloquinolinone derivatives has been devised using an IMDAF cycloaddition reaction of 2-(methylthio)-5-amidofurans. Conformational effects that have a dramatic impact on the relative reaction rates were identified in the low-energy ground-state conformations of furans **64**, **17**, **33**, and **37**. Specifically, the placement of a carbonyl in the tether caused the molecules to adopt conformations that were much closer to the reactive conformations than molecules that lacked this tether carbonyl. A bias in the rotation about the C(2)−N bond was also found to correlate with the rates at which these molecules undergo intramolecular Diels−Alder cycloadditions. Application of this methodology toward the construction of more complex alkaloids containing these skeletons is currently in progress in our laboratory and will be reported at a later date.

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.

2,2-Dimethylpropionic Acid 1-(Bis((methylsulfanyl)-methyl)-3-(but-3-enoylmethylamino)-3-oxopropyl Ester (13). To a solution containing 0.4 g (1.4 mmol) of amide **12**[42] in 8 mL of CH_2Cl_2 was added 0.3 g (2.7 mmol) of 3-butenoyl chloride[60] followed by 1.5 g of powdered molecular sieves. After it was stirred at room temperature overnight, the suspension was filtered through a pad of silica and washed several times with diethyl 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 0.5 g (87%) of **13** as a yellow oil: IR (neat) 1731, 1700, 1639, 1152, and 1075 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.16 (s, 9H), 2.16 (s, 3H), 2.17 (s, 3H), 3.09 (dd, 1H, J = 17.2 and 7.6 Hz), 3.19 (s, 3H), 3.41−3.47 (m, 3H), 3.94 (d, 1H, J = 4.4 Hz), 5.11−5.20 (m, 2H), 5.52−5.57 (m, 1H), and 5.89−5.99 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 15.0, 27.2, 31.4, 38.9, 40.9, 42.8, 57.7, 71.4, 118.9, 130.5, 172.8, 174.1, and 177.6; HRMS calcd for $C_{16}H_{27}NO_4S_2$ 361.1381, found 361.1380.

2,2-Dimethylpropionic Acid 1-([Methyl(3-methylbut-3-enoyl)carbamoyl]methyl)-2,2-Bis(methylsulfanyl) Ethyl Ester (14). To a solution containing 1.0 g (3.5 mmol) of amide **12** in 18 mL of CH_2Cl_2 was added 0.7 g (5.9 mmol) of 3-methylbut-3-enoyl chloride[61] followed by 3.5 g of powdered molecular sieves. After it was stirred at room temperature overnight, the suspension was filtered through a pad of silica and washed several times with diethyl 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 0.5 g (41%) of **14** as a yellow oil: IR (neat) 1731, 1480, 1275, and 1153 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.19 (s, 9H), 1.81 (s, 3H), 2.19 (s, 3H), 2.20 (s, 3H), 3.13 (dd, 1H, J = 17.0 and 7.2 Hz), 3.20 (s, 3H), 3.37 (s, 2H), 3.50 (dd, 1H, J = 17.0 and 5.0 Hz), 3.96 (d, 1H, J = 5.0 Hz), 4.79 (s, 1H), 4.96−4.97 (m, 1H), and 5.56−5.60 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 15.1, 22.9, 27.3, 31.7, 39.0, 41.3, 46.9, 57.8, 71.5, 114.9, 138.9, 172.9, 173.8, and 177.8; HRMS calcd for $C_{17}H_{29}NO_4S_2$ 375.1538, found 373.1537.

***N*-[3-((2,2-Dimethylpropionyl)oxy)-4,4-bis(methylsulfanyl)butyryl]-*N*-methyl-2-methylene Succinamic Acid Methyl Ester (15).** To a solution containing 0.3 g (1.0 mmol) of amide **12** in 5 mL of CH_2Cl_2 was added 0.2 g (1.4 mmol) of 3-(methoxycarbonyl)but-3-enoyl chloride[62] followed by 1.0 g of powdered molecular sieves. After it was stirred at room temperature overnight, the suspension was filtered through a pad of silica and washed several times with diethyl 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 0.3 g (66%) of **15** as a yellow oil: IR (neat) 1726, 1695, 1209, 1152, and 1086 cm^{-1}; ^1H NMR

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(400 MHz, $CDCl_3$) δ 1.09 (s, 9H), 2.08 (s, 3H), 2.09 (s, 3H), 2.99 (dd, 1H, J = 17.0 and 7.4 Hz), 3.14 (s, 3H), 3.34 (dd, 1H, J = 17.0 and 4.8 Hz), 3.61 (s, 2H), 3.65 (s, 3H), 3.85 (d, 1H, J = 4.8 Hz), 5.44−5.49 (m, 1H), 5.56 (s, 1H), and 6.22 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 14.8, 27.0, 31.2, 38.7, 40.5, 41.6, 52.0, 57.5, 71.1, 128.2, 134.2, 166.6, 172.5, 173.2, and 177.3. Anal. Calcd for $C_{18}H_{29}NO_6S_2$: C, 51.53; H, 6.97; N, 3.34. Found: C, 51.42; H, 6.85; N, 3.22.

But-3-enoic Acid Methyl(5-(methylsulfanyl)furan-2-yl)amide (17). To a solution containing 0.9 g (2.4 mmol) of amide **13** in 12 mL of CH_3CN was added 0.5 g (2.4 mmol) of DMTSF in one portion at −40 °C. The mixture was stirred for 1 h at −40 °C, and 1.7 mL (12 mmol) of triethylamine was added. The reaction mixture was diluted with diethyl ether, poured over a saturated aqueous $NaHCO_3$ solution, extracted with diethyl ether, and dried over K_2CO_3. The solvent was removed under reduced pressure, and the crude mixture was subjected to flash silica gel chromatography to give 0.2 g (39%) of **17** as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 2.99−3.01 (m, 2H), 3.19 (s, 3H), 4.99−5.11 (m, 2H), 5.83−5.91 (m, 1H), 6.06 (d, 1H, J = 3.2 Hz), and 6.42 (d, 1H, J = 3.2 Hz). As a consequence of its lability, the furan was used in the next step without further purification.

3-Methylbut-3-enoic Acid Methyl(5-(methylsulfanyl)-furan-2-yl)amide (18). To a solution containing 0.5 g (1.4 mmol) of amide **14** in 7 mL of CH_3CN was added 0.3 g (1.4 mmol) of DMTSF in one portion at −40 °C. The mixture was stirred for 1 h at −40 °C, and 1.0 mL (7.0 mmol) of triethylamine was added. The mixture was diluted with diethyl ether, poured over a saturated aqueous $NaHCO_3$ solution, extracted with diethyl ether, and dried over K_2CO_3. The solvent was removed under reduced pressure, and the crude mixture was subjected to flash silica gel chromatography to give 0.2 g (62%) of **18** as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.72 (s, 3H), 2.41 (s, 3H), 2.99 (s, 3H), 3.20 (s, 2H), 4.63 (s, 1H), 4.83 (s, 1H), 6.05 (d, 1H, J = 3.2 Hz), and 6.40 (d, 1H, J = 3.2 Hz). As a consequence of its lability, the furan was used in the next step without further purification.

1-Methyl-6-(methylsulfanyl)-1,3*a*,4,6-tetrahydro-3*H*-indole-2,5-dione (21). A solution of 0.08 g (0.4 mmol) of furan **17** in 6 mL of toluene was heated at reflux for 2 h. After it was cooled to room temperature, the reaction mixture was concentrated under reduced pressure and subjected to silica gel chromatography to give 0.06 g (72%) of **21** as a yellow oil: IR (film) 1731, 1669, 1429, 1316, and 1260 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) major diastereomer δ 2.07 (s, 3H), 2.16−2.33 (m, 2H), 2.76 (dd, 1H, J = 17.4 and 9.8 Hz), 2.93 (s, 3H), 3.02 (dd, 1H, J = 18.4 and 6.4 Hz), 3.55−3.59 (m, 1H), 3.62 (d, 1H, J = 6.8 Hz), and 5.00 (dd, 1H, J = 6.6 and 2.6 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) (minor diastereomer) δ 2.10 (s, 3H), 2.24−2.33 (m, 1H), 2.55 (dd, 1H, J = 12.2 and 4.2 Hz), 2.68 (dd, 1H, J = 16.8 and 8.4 Hz), 2.93 (s, 3H), 3.02−3.12 (m, 1H), 3.53−3.61 (m, 2H), and 4.84 (t, 1H, J = 2.8 Hz);^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0, 16.3, 26.3, 26.4, 29.8, 35.0, 36.2, 36.4, 39.0, 41.5, 49.0, 49.9, 91.3, 94.1, 145.6, 149.3, 173.9, 174.4, 200.8, and 202.1. Anal. Calcd for $C_{10}H_{13}NO_2S$: C, 56.85; H, 6.21; N, 6.63. Found: C, 56.72; H, 6.11; N, 6.45.

1,3*a*-Dimethyl-6-(methylsulfanyl)-1,3*a*,4,6-tetrahydro-3*H*-indole-2,5-dione (22). A solution of 0.2 g (0.9 mmol) of furan **18** in 5 mL of toluene was heated at reflux for 3 h. After it was cooled, the reaction mixture was concentrated under reduced pressure and subjected to silica gel chromatography to give 0.1 g (42%) of **22** as a pale yellow oil: IR (neat) 1731, 1670, 1327, and 1111 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) (major diastereomer) δ 1.12 (s, 3H), 2.12 (s, 3H), 2.31−2.51 (m, 3H), 2.94 (s, 3H), 3.14 (d, 1H, J = 12.4 Hz), 3.57 (d, 1H, J = 3.2 Hz), and 4.78 (d, 1H, J = 3.2 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) (minor diastereomer) δ 1.40 (s, 3H), 2.27 (s, 3H), 2.31−2.41 (m, 2H), 2.58 (d, 1H, J = 17.0 Hz), 2.82 (d, 1H, J = 17.0 Hz), 2.96 (s, 3H), 3.73 (d, 1H, J = 5.6 Hz), and 4.98 (d, 1H, J = 5.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3, 17.1, 26.5, 26.6, 27.6, 29.2, 37.4, 40.2, 44.5, 45.6, 45.7, 48.2, 49.4, 50.8, 150.3, 151.4, 173.4, 202.4, and 205.1. Anal. Calcd for $C_{11}H_{15}NO_2S$: C, 58.65; H, 6.72; N, 6.22. Found: C, 58.59; H, 6.81; N, 6.14.

1-Methyl-6-(methylsufanyl)-2,5-dioxo-1,2,3,4,5,6-hexahydroindole-3*a*-carboxylic Acid Methyl Ester (23). To a solution containing 0.6 g (1.4 mmol) of imide **15** in 7 mL of CH_3CN was added 0.3 g (1.4 mmol) of DMTSF in one portion at −40 °C. The mixture was stirred for 1 h at −40 °C, and 1 mL (7 mmol) of triethylamine was added. The reaction mixture was diluted with diethyl ether, poured over a saturated aqueous $NaHCO_3$ solution, extracted with diethyl ether, and dried over K_2CO_3. The solvent was removed under reduced pressure, and the crude mixture was subjected to flash silica gel chromatography to give 0.3 g (68%) of **23** as a yellow oil: IR (neat) 1731, 1675, 1388, and 1224 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) (major diastereomer) δ 2.16 (s, 3H), 2.44 (d, 1H, J = 17.6 Hz), 2.74−2.77 (m, 1H), 2.78 (d, 1H, J = 14.4 Hz), 2.93 (s, 1H), 3.06 (d, 1H, J = 16.4 Hz), 3.63 (s, 3H), 3.66−3.70 (m, 1H), and 4.98 (d, 1H, J = 3.2 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) (minor diastereomer) δ 2.11 (s, 3H), 2.49 (d, 1H, J = 17.6 Hz), 2.74−2.79 (m, 1H), 2.97 (d, 1H, J = 14.4 Hz), 2.98 (s, 3H), 3.50 (d, 1H, J = 17.6 Hz), 3.64−3.69 (m, 1H), 3.65 (s, 3H), and 5.11 (d, 1H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.4, 16.5, 26.6, 26.8, 39.8, 42.0, 42.4, 45.0, 45.9, 46.2, 47.9, 48.2, 49.9, 53.5, 94.7, 97.6, 142.7, 145.9, 171.7, 172.2, 172.5, 172.6, 200.2, and 200.9. Anal. Calcd for $C_{12}H_{15}NO_4S$: C, 53.51; H, 5.62; N, 5.20. Found: C, 53.42; H, 5.51; N, 5.15.

Acetic Acid 1-(1-But-3-enoyl-2-oxopiperidin-3-yl)-2,2-bis(methylsulfanyl) Ethyl Ester (27). To a 2.1 g (7.6 mmol) sample of **25** 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.[60] The reaction mixture was stirred at 25 °C for 15 h and 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 title compound as a yellow oil which 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}; ^{1}H NMR (400 MHz, $CDCl_3$) (diastereomer A) δ 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 = 6.8 and 0.8 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 = 8.0 and 4.2 Hz), and 5.94−6.04 (m, 1H); ^{1}H NMR (400 MHz, $CDCl_3$) (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; ^{13}C NMR (100 MHz, $CDCl_3$)(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 $C_{15}H_{23}NO_4S_2$: 345.1068, found 345.1071.

Acetic Acid 1-[1-(3-Methyl-but-3-enoyl)-2-oxopiperidin-3-yl]-2,2-bis(methylsulfanyl) Ethyl Ester (28). To a 1.6 g (5.6 mmol) sample of lactam **25**[142] in CH_2Cl_2 (50 mL) was added 6 g of oven-dried 4 Å powdered molecular sieves and 1.0 g (8.4 mmol) of 3-methylbut-3-enoyl chloride.[61] The mixture was stirred at room temperature for 15 h, followed by filtration through a plug of silica with diethyl ether. The filtrate was washed with a saturated aqueous $NaHCO_3$ solution and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 1.3 g (64%) of **28** as a colorless oil consisting of a 1:1 mixture of diastereomers. For analytical purposes the diastereomers were separated by HPLC: IR (neat) 1748, 1652, 1476, and 1424 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) (diastereomer A) δ 1.75 (m, 3H), 1.79 (s, 3H), 1.95 (m, 1H), 2.08 (s, 3H), 2.15 (s, 3H), 2.20 (s, 3H), 3.25 (m, 1H), 3.61 (s, 2H), 3.76 (m, 2H), 3.90 (d, 1H, J = 8.0 Hz), 4.72 (m, 1H), 4.89 (m, 1H), and 5.69 (dd, 1H, J = 7.6 and 4.4 Hz); ^{1}H NMR (400 MHz, $CDCl_3$) (diastereomer B) δ 1.69 (m, 2H), 1.79 (s, 3H), 2.01 (m, 2H), 2.11 (s, 3H), 2.12 (s, 3H), 2.14 (s, 3H), 3.17 (m, 1H), 3.60 (s, 1H), 3.61 (m, 1H), 3.63 (s, 1H), 3.85 (m, 1H), 4.22 (d, 1H, J =

9.2 Hz), 4.74 (s, 1H), 4.90 (s, 1H), and 5.39 (dd, 1H, J = 9.4 and 3.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) (diastereomer A) δ 13.3, 14.1, 21.0, 21.1, 21.7, 23.1, 43.6, 46.0, 47.8, 56.9, 72.2, 114.2, 140.1, 140.1, 169.8, 173.6, and 174.5; ^{13}C NMR (100 MHz, $CDCl_3$) (diastereomer B) δ 13.0, 13.7, 21.2, 22.0, 23.1, 23.9, 43.9, 46.3, 47.9, 56.5, 73.7, 114.3, 140.1, 170.3, 172.4, and 174.7; HRMS calcd for $C_{16}H_{25}NO_4S_2$ 359.1225, found 359.1236.

2-(2-[3-(1-Acetoxy-2,2-bis(methylsulfanyl)ethyl)-2-oxopiperidin-1-yl]-2-oxoethyl) Acrylic Acid Methyl Ester (29). To a 0.5 g (1.8 mmol) sample of lactam **25** in CH_2Cl_2 (10 mL) was added 1.8 g of oven-dried powdered 4 Å molecular sieves and 0.44 g (2.7 mmol) of 3-(methoxycarbonyl)but-3-enoyl chloride.[62] The mixture was stirred at room temperature for 15 h, followed by filtration through a plug of silica with diethyl ether. The filtrate was washed with a saturated aqueous $NaHCO_3$ solution and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.6 g (90%) of **29** as a pale wax which consisted of a 1:1 mixture of diastereomers: IR (neat) 1744, 1699, 1371, and 1149 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.63−1.83 (m, 4H), 1.92−2.00 (m, 2H), 2.08 (s, 3H), 2.11 (s, 3H), 2.11 (s, 3H), 2.14 (s, 3H), 2.14 (s, 3H), 2.19 (s, 3H), 2.16−2.22 (m, 1H), 2.33−2.89 (m, 1H), 2.55−3.62 (m, 1H), 3.62−3.78 (m, 4H), 3.73 (s, 6H), 3.85−3.88 (m, 6H), 4.22 (d, 1H, J = 9.6 Hz), 5.39 (dd, 1H, J = 9.6 and 3.2 Hz), 5.69 (m, 2H), 5.70 (dd, 1H, J = 8.4 and 4.0 Hz), and 5.26 (dd, 2H, J = 3.2 and 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.9, 13.1, 13.5, 13.9, 20.9, 21.0, 21.1, 21.6, 21.8, 23.7, 43.4, 43.5, 43.7, 44.1, 46.0, 46.3, 52.2, 56.5, 56.7, 72.0, 73.6, 127.9, 128.0, 135.1, 135.2, 167.1, 169.8, 170.3, 172.5, 173.7, 174.0, and 174.2. Anal. Calcd for $C_{17}H_{25}NO_6S_2$: C, 50.60; H, 6.24; N, 3.47. Found: C, 50.33; H, 6.19; N, 3.56.

Acetic Acid 2,2-Bis(methylsulfanyl)-1-(2-oxo-1-pent-4-enoylpiperidin-3-yl) Ethyl Ester (30). To a 2.1 g (7.5 mmol) sample of lactam **25** in CH_2Cl_2 (40 mL) was added 7.5 g of oven-dried 4 Å powdered molecular sieves and 1.3 g (11 mmol) of pent-4-enoyl chloride.[63] The mixture was stirred at room temperature for 15 h, followed by filtration through a plug of silica with diethyl ether. The filtrate was washed with a saturated aqueous $NaHCO_3$ solution and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 2.5 g (92%) of **30** as a yellow oil consisting of a 1:1 mixture of diastereomers. For analytical purposes the diastereomers were separated by HPLC: IR (neat) 1745, 1688, 1368, and 1289 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) (diastereomer A) δ 1.67−1.84 (m, 2H), 1.94−1.97 (m, 1H), 2.02−2.10 (m, 1H), 2.07 (s, 3H), 2.14 (s, 3H), 2.19 (s, 3H), 2.34−2.40 (m, 2H), 2.95−3.00 (m, 2H), 3.22−3.27 (m, 1H), 3.72−3.75 (m, 2H), 3.90 (d, 1H, J = 8.0 Hz), 4.95−5.07 (m, 2H), 5.69 (dd, 1H, J = 8.0 and 4.0 Hz), and 5.78−5.88 (m, 1H); ^{1}H NMR (400 MHz, $CDCl_3$) (diastereomer B) δ 1.59−1.79 (m, 2H), 1.93−2.06 (m, 2H), 2.10 (s, 3H), 2.11 (s, 3H), 2.14 (s, 3H), 2.37−2.42 (m, 2H), 2.97−3.01 (m, 2H), 3.17 (ddd, 1H, J = 11.4, 6.6, and 3.2 Hz), 3.60 (ddd, 1H, J = 13.6, 9.6, and 4.2 Hz), 3.81−3.87 (m, 1H), 4.33 (d, 1H, J = 9.6 Hz), 4.96−5.08 (m, 2H), 5.39 (dd, 1H, J = 9.6 and 3.2 Hz), and 5.79−5.90 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (diastereomer A) δ 13.2, 14.0, 21.0, 21.0, 21.7, 29.1, 39.0, 43.4, 46.0, 56.8, 72.1, 115.5, 137.5, 169.8, 173.6, and 176.2; ^{13}C NMR (100 MHz, $CDCl_3$) (diastereomer B) δ 12.9, 13.6, 21.2, 21.9, 23.8, 29.1, 39.0, 43.8, 46.3, 56.5, 73.6, 115.4, 137.6, 170.3, 172.3, and 176.4. Anal. Calcd for $C_{16}H_{25}NO_4S_2$: C, 53.46; H, 7.02; N, 3.90. Found: C, 53.17; H, 7.05; N, 3.88.

Acetic Acid 1-(1-But-3-enoyl-2-oxoazepan-3-yl)-2,2-bis-(methylsulfanyl) Ethyl Ester (31). To a 1.9 g (6.4 mmol) sample of lactam **25** in CH_2Cl_2 (35 mL) was added 6.4 g of oven-dried 4 Å powdered molecular sieves and 1.0 g (9.5 mmol) of but-3-enoyl chloride.[60] The mixture was stirred at room temperature for 15 h, followed by filtration through a plug of silica with diethyl ether. The filtrate was washed with a saturated aqueous $NaHCO_3$ solution and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 2.0 g (85%) of **31** as a yellow oil consisting of a 4:1 mixture of diastereomers. For analytical purposes the diastereomers were separated by HPLC: IR (neat) 1748, 1694, 1179, and 1143 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) (major diastereomer) δ 1.24−1.55 (m, 2H), 1.58−1.65 (m, 1H), 1.82−1.95 (m, 3H), 2.14 (s, 3H), 2.17 (s, 3H), 2.20 (s, 3H), 3.20−3.26 (m, 1H), 3.48−3.53 (m, 1H), 3.65 (m, 2H), 4.04 (d, 1H, J = 4.4 Hz), 4.70−4.75 (m, 1H), 5.11−5.17 (m, 2H), 5.65 (dd, 1H, J = 8.0 and 4.4 Hz), and 5.93−6.03 (m, 1H); ^{1}H NMR (400 MHz, $CDCl_3$) (minor diastereomer) δ 1.37−1.55 (m, 2H), 1.60−1.69 (m, 1H), 1.83−1.97 (m, 3H), 2.11 (s, 3H), 2.12 (s, 3H), 2.14 (s, 3H), 3.15−3.21 (m, 1H), 3.44−3.48 (m, 1H), 3.58−3.73 (m, 2H), 4.19 (d, 1H, J = 7.2 Hz), 4.69−4.74 (m, 1H), 5.35−5.38 (m, 1H), 5.09−5.14 (m, 2H), 5.36 (t, 1H, J = 6.6 Hz), and 5.94−6.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (major diastereomer) δ 14.3, 15.1, 21.1, 26.5, 27.7, 27.8, 42.6, 44.4, 48.5, 57.0, 73.6, 118.4, 131.5, 170.4, 174.5, and 177.0; ^{13}C NMR (100 MHz, $CDCl_3$) (minor diastereomer) δ 12.7, 14.6, 21.2, 27.2, 27.6, 27.6, 42.4, 44.3, 48.2, 56.5, 73.7, 118.2, 131.6, 170.7, 174.5, and 176.0. Anal. Calcd for $C_{16}H_{25}NO_4S_2$: C, 53.45; H, 7.01; N, 3.90. Found: C, 53.60; H, 7.12; N, 3.93.

Acetic Acid 2,2-Bis(methylsulfanyl)-1-(2-oxo-1-pent-4-enoylazepan-3-yl) Ethyl Ester (32). To a 1.0 g (3.6 mmol) sample of **26** in CH_2Cl_2 (20 mL) was added 3.6 g of oven-dried 4 Å powdered molecular sieves and 0.6 g (5.2 mmol) of pent-4-enoyl chloride.[63] The mixture was stirred at room temperature for 15 h, followed by filtration through a plug of silica with diethyl ether. The filtrate was washed with a saturated aqueous $NaHCO_3$ solution and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.9 g (69%) of **32** as a yellow oil consisting of a 4:1 mixture of diastereomers. For analytical purposes a sample of the diastereomers was separated by HPLC: IR (neat) 1747, 1696, 1369, and 1143 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) (major diastereomer) δ 1.35−1.55 (m, 2H), 1.58−1.69 (m, 1H), 1.82−1.96 (m, 3H), 2.11 (s, 3H), 2.12 (s, 3H), 2.14 (s, 3H), 2.35−2.41 (m, 2H), 2.88−3.06 (m, 2H), 3.16 (dd, 1H, J = 14.8 and 11.6 Hz), 3.43−3.47 (m, 1H), 4.19 (d, 1H, J = 7.6 Hz), 4.69−4.75 (m, 1H), 4.95−5.06 (m, 2H), 5.36 (dd, 1H, J = 7.6 and 6.0 Hz), and 5.78−5.88 (m, 1H); ^{1}H NMR (400 MHz, $CDCl_3$) (minor diastereomer) δ 1.40−1.52 (m, 2H), 1.58−1.64 (m, 1H), 1.81−1.94 (m, 3H), 2.13 (s, 3H), 2.16 (s, 3H), 2.19 (s, 3H), 2.39 (dd, 2H, J = 13.6 and 7.2 Hz), 2.87−3.03 (m, 2H), 3.21 (dd, 1H, J 14.8 and 11.6 Hz), 3.47−3.51 (m, 1H), 4.05 (d, 1H, J = 4.4 Hz), 4.69−4.74 (m, 1H), 4.97−5.07 (m, 2H), 5.64 (dd, 1H, J = 8.0 and 4.4 Hz), and 5.79−5.89 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (major diastereomer) δ 12.7, 14.6, 21.2, 27.3, 27.7, 27.7, 29.4, 39.0, 42.4, 48.3, 56.5, 73.8, 115.4, 137.6, 170.8, 175.9, and 176.0; ^{13}C NMR (100 MHz, $CDCl_3$) (minor diastereomer) δ 14.3, 15.2, 21.0, 26.5, 27.7, 27.8, 29.3, 39.1, 42.5, 48.5, 57.1, 73.7, 115.5, 137.5, 170.4, 175.8, and 177.0; HRMS calcd for $C_{16}H_{25}NO_4S_2$ 373.1381, found 373.1379.

***N*-(2-(Methylsulfanyl)-5,6-dihydro-4*H*-furo[2,3-*b*]pyridine)but-3-enamide (33).** To a 0.6 g (1.9 mmol) sample of **27** 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 furan **33** 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. Anal. Calcd for $C_{12}H_{15}NO_2S$: C, 60.74; H, 6.38; N, 5.91. Found: C, 60.69; H, 6.07; N, 6.08.

3-Methyl-*N*-(2-(methylsulfanyl)-5,6-dihydro-4*H*-furo-[2,3-*b*]pyridin-7-yl)but-3-enamide (34). To a 1.0 g (2.8 mmol) sample of **28** in CH_3CN (15 mL) at −40 °C was added 0.6 g (3.0 mmol) of DMTSF. The reaction mixture was stirred at −40 °C for 3 h, and then 2.1 mL (15 mmol) of triethylamine was added. The mixture was diluted with diethyl ether, and poured into a saturated aqueous $NaHCO_3$ solution. The organic

(63) Rosenblum, S. B.; Huynh, T.; Afonso, A.; Davis, H. R., Jr. *Tetrahedron* **2000**, *56*, 5735.

phase was separated, and the aqueous phase was washed with diethyl ether. The combined organic layer was dried over anhydrous K_2CO_3, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.5 g (66%) of furan **34** as a clear oil: IR (neat) 1766, 1672, 1512, 1425, and 1145 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.83 (s, 3H), 1.86−1.92 (m, 2H), 2.37 (s, 3H), 2.45 (t, 2H, J = 6.4 Hz), 3.83−3.86 (m, 2H), 4.78 (s, 1H), 4.88 (s, 1H), and 6.37 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.2, 20.7, 23.1, 23.2, 43.2, 44.9, 105.2, 113.7, 118.0, 139.8, 140.9, 146.4, and 168.8. Anal. Calcd for $C_{13}H_{17}NO_2S$: C, 62.13; H, 6.82; N, 5.58. Found: C, 62.08; H, 6.63; N, 5.44.

***N*-(2-(Methylsulfanyl)-5,6-dihydro-4*H*-furo[2,3-*b*]pyridin-7-yl)pent-4-enamide (36).** To a 0.9 g (2.4 mmol) sample of **30** in CH_3CN (12 mL) at −40 °C was added 0.5 g (2.4 mmol) of DMTSF. The reaction mixture was stirred at −40 °C for 3 h, and then 1.7 mL (12 mmol) of triethylamine 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 diethyl ether. The combined organic layer was dried over anhydrous K_2CO_3, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.4 g (61%) of furan **36** as a clear oil: IR (neat) 1621, 1508, and 1381 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.86−1.92 (m, 2H), 2.37 (s, 3H), 2.42−2.47 (m, 2H), 2.45 (t, 2H, J = 6.4 Hz), 2.86 (t, 2H, J = 7.8 Hz), 3.81−3.84 (m, 2H), 4.98−5.11 (m, 2H), 5.85−5.95 (m, 1H), and 6.37 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 20.7, 23.3, 29.4, 35.4, 43.1, 105.2, 115.3, 117.8, 137.7, 140.9, 146.5, and 170.5. Anal. Calcd for $C_{13}H_{17}NO_2S$: C, 62.13; H, 6.82; N, 5.58. Found: C, 62.09; H, 6.72; N, 5.49.

***N*-(2-(Methylsulfanyl)-4,5,6,7-tetrahydrofuro[2,3-*b*]azepin-8-yl)pent-4-enamide (38).** To a 0.7 g (1.9 mmol) sample of **32** in CH_3CN (10 mL) at −40 °C was added 0.4 g (1.9 mmol) of DMTSF. The reaction mixture was stirred at −40 °C for 3 h, and then 1.3 mL (9 mmol) of triethylamine 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 diethyl ether. The combined organic layer was dried over anhydrous K_2CO_3, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.25 g (49%) of furan **38** as a colorless oil: IR (neat) 1685, 1441, 1295, and 1163 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.58−1.64 (m, 2H), 1.76−1.81 (m, 2H), 2.33−2.42 (m, 6H), 2.38 (s, 3H), 3.63−3.65 (m, 2H), 4.94−5.02 (m, 2H), and 5.74−5.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 24.8, 25.9, 29.4, 30.7, 33.9, 45.7, 99.5, 115.3, 117.6, 118.3, 137.5, 1423, and 172.9. Anal. Calcd for $C_{14}H_{19}NO_2S$: C, 63.37; H, 7.22; N, 5.28. Found: C, 63.19; H, 7.11; N, 5.06.

7-(Methylsulfanyl)-5,6,9,9*a*-tetrahydro-1*H*,4*H*,7*H*-pyrrolo[3,2,1-*ij*]quinoline-2,8-dione (39). A 0.7 g (3.0 mmol) sample of furan **33** 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 **39** as a yellow oil which consisted of a 1.4:1 mixture of diastereomers: IR (neat) 1716, 1682, 1420, and 1197 cm^{-1}; ^1H 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. Anal. Calcd for $C_{12}H_{15}NO_2S$: C, 60.74; H, 6.38; N, 5.91. Found: C, 60.51; H, 6.27; N, 5.74.

9*a*-Methyl-7-(methylsulfanyl)-5,6,9,9*a*-tetrahydro-1*H*,4*H*,7*H*-pyrrolo[3,2,1-*ij*]quinoline-2,8-dione (40). A solution of 0.1 g (0.4 mmol) of furan **34** in toluene (2 mL) was heated at reflux for 7 h. The reaction mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to provide 0.06 g (61%) of **40** as a orange oil which consisted of a 1:1 mixture of inseparable diastereomers: IR (neat) 1732, 1689, 1601, 1275, and 1204 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.13 (s, 3H), 1.38 (s, 3H), 1.62−2.03 (m, 6H), 2.10 (s, 3H), 2.24 (s, 3H), 2.29−2.57 (m, 6H), 2.83 (d, 1H, J = 16.8 Hz), 3.17 (d, 1H, J = 12.4 Hz), 3.26−3.30 (m, 1H), 3.31−3.41 (m, 1H), 3.42 (s, 1H), 3.48 (s, 1H), 3.59−3.65 (m, 1H), and 3.74−3.80 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0, 16.9, 21.1, 22.7, 24.0, 27.5, 28.6, 36.5, 38.8, 39.0, 39.1, 45.2, 46.2, 46.3, 50.8, 52.7, 53.5, 102.7, 103.4, 142.6, 143.5, 172.4, 172.6, 201.6, and 204.9. Anal. Calcd for $C_{13}H_{17}NO_2S$: C, 62.13; H, 6.82; N, 5.58. Found: C, 62.01; H, 6.59; N, 5.53.

7-(Methylsulfanyl)-2,8-dioxo-1,2,5,6,8,9-hexahydro-4*H*,7*H*-pyrrolo[3,2,1-*ij*]quinoline-9*a*-carboxylic Acid Methyl Ester (41). A solution of 0.5 g (1.3 mmol) of cycloadduct **46** (vide infra) dissolved in benzene (7 mL) was heated at reflux for 1 h. The reaction mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to provide 0.3 g (77%) of **41** as a pale yellow oil consisting of a 1:1 mixture of diastereomers: IR (neat) 1732, 1435, 1201, and 1172 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.75−2.10 (m, 4H), 2.11 (s, 3H), 2.13 (s, 3H), 2.35−2.52 (m, 4H), 2.77−2.81 (m, 2H), 3.05 (s, 1H), 3.09 (d, 1H, J = 2.0 Hz), 3.35−3.48 (m, 2H), 3.43 (s, 1H), 3.52−3.60 (m, 2H), 3.53 (s, 1H), 3.65 (s, 3H), 3.68 (s, 3H), and 3.71−3.78 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.1, 16.4, 20.7, 20.7, 23.4, 24.1, 39.0, 39.3, 40.6, 42.4, 42.7, 45.3, 45.6, 49.2, 52.3, 52.4, 53.5, 105.6, 107.0, 135.6, 137.8, 171.2, 171.7, 172.0, 172.6, 199.0, and 201.2. Anal. Calcd for $C_{14}H_{17}NO_4S$: C, 56.93; H, 5.81; N, 4.75. Found: C, 56.77; H, 5.69; N, 4.72.

8-(Methylsulfanyl)-1,2,6,7,10,10*a*-hexahydro-5*H*,8*H*-pyrido[3,2,1-*ij*]quinoline-3,9-dione (42). To an oven-dried, heavy-walled, high-pressure tube equipped with a magnetic stirring bar and rubber septum was added a solution of 0.1 g (0.4 mmol) of furan **36** in toluene (4 mL). Argon was bubbled through the solution for 15 min, and the septum was replaced with a threaded Teflon cap containing a rubber O-ring seal. The vessel was heated at 150 °C behind a protective shield for 15 h. The mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.08 g (76%) of **42** as a clear oil consisting of a 3:2 mixture of diastereomers: IR (neat) 1716, 1669, 1297, and 1197 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.51 (qd, 1H, J = 13.2 and 4.0 Hz, minor diastereomer), 1.68 (qd, 1H, J = 13.2 and 5.0 Hz, major diastereomer), 1.75−2.03 (m, 4H), 2.08 (s, 3H, minor diastereomer), 2.11 (s, 3H, major diastereomer), 2.17−2.67 (m, 4H), 2.89 (dd, 1H, J = 18.4 and 5.6 Hz, minor diastereomer), 3.16 (t, 1H, J = 12.6 Hz, major diastereomer), 3.26 (s, 1H, minor diastereomer), 3.35−3.48 (m, 2H), and 3.97−4.08 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.0, 16.4, 21.1, 21.3, 26.2, 26.3, 27.5, 31.8, 32.4, 32.5, 36.5, 40.1, 40.5, 40.8, 42.5, 54.4, 55.1, 108.9, 109.5, 134.3, 136.0, 168.2, 168.5, 201.9, and 202.4. Anal. Calcd for $C_{13}H_{17}NO_2S$: C, 62.13; H, 6.82; N, 5.58. Found: C, 62.06; H, 6.67; N, 5.33.

Further heating of **42** at 200 °C gave 0.13 g (82%) of 9-hydroxy-1,2,6,7-tetrahydro-5*H*-pyrido[3,2,1-*ij*]quinolin-3-one as a white solid: mp 220−221 °C; IR (film) 1727, 1632, 1180, and 1154 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.82−1.85 (m, 2H), 2.50−2.54 (m, 2H), 2.67−2.70 (m, 2H), 2.73−2.77 (m, 2H), 3.75−3.77 (m, 2H), and 6.42−6.44 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 22.9, 26.2, 28.3, 32.5, 42.2, 114.1, 114.9, 128.4, 128.6, 129.2, 154.4, and 171.5. Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.90; H, 6.45; N, 6.89. Found: C, 70.78; H, 6.32; N, 6.66.

8-(Methylsulfanyl)-4,5,6,7,10,10*a*-hexahydro-1*H*,8*H*-azepino[3,2,1-*hi*]indole-2,9-dione (43). To a 0.5 g (1.4 mmol) sample of **31** dissolved in CH_3CN (10 mL) at −40 °C was added 0.3 g (1.4 mmol) of DMTSF. The reaction mixture was stirred at −40 °C for 3 h, and then 1.0 mL (7.1 mmol) of triethylamine 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 diethyl ether. The combined organic layer was dried over

anhydrous K_2CO_3, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.2 g (64%) of **43** as a yellow oil consisting of a 3:2 mixture of diastereomers: IR (neat) 1716, 1669, 1284, and 1197 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.64−2.00 (m, 10H), 2.06 (s, 3H, minor diastereomer), 2.09 (s, 3H, major diastereomer), 2.14−2.66 (m, 10H), 3.05−3.08 (m, 1H, minor diastereomer), 3.10−3.19 (m, 1H, major diastereomer), 3.24 (s, 1H, major diastereomer), 3.20−3.47 (m, 1H, major diastereomer), 3.33 (s, 1H, minor diastereomer), and 3.94−4.08 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.0, 16.4, 21.1, 21.3, 26.0, 26.1, 26.2, 27.4, 31.7, 32.4, 32.4, 36.5, 40.0, 40.4, 40.8, 42.5, 54.4, 55.1, 108.8, 109.3, 134.3, 136.0, 168.1, 168.4, 201.9, and 202.3. Anal. Calcd for $C_{13}H_{17}NO_2S$: C, 62.12; H, 6.82; N, 5.57. Found: C, 62.00; H, 6.87; N, 5.40.

2,3,4,5,6,9,10,11-Octahydro-2-(methylthio)-6-oxo-8*H*-2,-12-metheno-3*aH*-furo[2,3-*k*]pyrido[1,2-*a*]azepine (45). To an oven-dried, heavy-walled, high-pressure tube equipped with a magnetic stirring bar and rubber septum was added a solution of 0.1 g (0.4 mmol) of furan **38** in toluene (4 mL). Argon was bubbled through the solution for 15 min, and the septum was replaced with a threaded Teflon cap containing a rubber O-ring seal. The vessel was heated at 150 °C behind a protective shield for 4 h. The reaction mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.08 g (75%) of **45** as a white solid: mp 97−98 °C; IR (KBr) 1666, 1410, 1339, and 1176 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.28−1.38 (m, 1H), 1.48−1.70 (m, 2H), 1.72−1.95 (m, 7H), 2.18 (s, 3H), 2.27−2.36 (m, 1H), 2.36−2.52 (m, 2H), 2.82 (t, 1H, J = 12.8 Hz), 4.30 (dd, 1H, J = 14.2 and 4.6 Hz), and 5.89 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.2, 25.7, 26.8, 29.1, 29.8, 32.5, 38.1, 42.0, 44.4, 90.1, 99.3, 132.0, 151.7, and 170.4. Anal. Calcd for $C_{14}H_{19}NO_2S$: C, 63.37; H, 7.22; N, 5.28. Found: C, 63.24; H, 7.09; N, 5.14.

2,3,4,5,8,9-Hexahydro-2-(methylthio)-5-oxo-7*H*-2,10-metheno-3*aH*-furo[2,3-*i*]indolizine-3*a*-carboxylic Acid Methyl Ester (46). To a 0.5 g (1.3 mmol) sample of **29** in CH_2Cl_2 (15 mL) at −40 °C was added 0.3 g (1.3 mmol) of DMTSF. The mixture was stirred at −40 °C for 30 min before warming to 0 °C. After the mixture was stirred for 3 h at 0 °C, 0.9 mL (6.4 mmol) of triethylamine 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 diethyl ether. The combined organic layer was dried over anhydrous K_2CO_3, and the solvent was removed under reduced pressure. The residue was purified by recrystallization from hexane/CH_2Cl_2 to provide 0.3 g (77%) of **46** as a colorless solid: mp 95−96 °C; IR (film) 1729, 1482, 1306, and 1160 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.82−1.90 (m, 2H), 2.14−2.20 (m, 1H), 2.24 (s, 3H), 2.25 (d, 1H, J = 11.6 Hz), 2.50−2.56 (m, 1H), 2.59 (d, 1H, J = 11.6 Hz), 2.76 (d, 1H, J = 15.6 Hz), 2.82 (d, 1H, J = 15.6 Hz), 3.34−3.40 (m, 1H), 3.66 (s, 3H), 3.68−3.75 (m, 1H), and 6.05 (dd, 1H, J = 2.8 and 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1, 21.8, 21.9, 39.9, 41.2, 42.5, 52.8, 58.3, 92.7, 100.5, 130.7, 144.5, 172.5, and 178.0. Anal. Calcd for $C_{14}H_{17}NO_4S$: C, 56.93; H, 5.80; N, 4.74. Found: C, 56.82; H, 5.75; N, 4.82.

5-Hydroxycyclopent-1-enecarboxylic Acid Methyl Ester. A modification of the procedure of Ogasawara[64] was used to prepare this ester. A mixture containing 13.0 mL (100 mmol) of 2,5-dimethoxytetrahydrofuran and 80 mL of 0.6 N HCl was stirred at 70 °C for 3 h. After it was cooled to 0 °C, the mixture was neutralized with a 10% $KHCO_3$ solution and 16.4 mL (100 mmol) of trimethyl phosphonoacetate and 32 mL (200 mmol) of a 6.4 M aqueous solution of K_2CO_3 were added. The mixture was stirred at room temperature for 48 h and then extracted with EtOAc. The extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was distilled under high vacuum to furnish 7.6 g (54%) of the title compound as a colorless oil: IR (neat) 3447, 1721, 1634, and 1296 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.81−1.88 (m, 1H), 2.27−2.42 (m, 2H), 2.58−2.67 (m, 1H), 2.91 (br s, 1H), 3.75 (d, 3H, J = 2.0 Hz), 5.03−5.06 (m, 1H), and 6.88−6.90 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 31.1, 32.1, 51.8, 75.6, 137.9, 146.9, and 165.6; HRMS calcd for $C_7H_{10}O_3$ 142.0630, found 142.0633.

5-Acetoxycyclopent-1-enecarboxylic Acid Methyl Ester. To 3.3 g (23 mmol) of the above alcohol in 40 mL of CH_2Cl_2 at 0 °C was consecutively added 2.8 mL (34.8 mmol) of pyridine, 4.6 mL (48.7 mmol) of acetic anhydride, and 0.3 g (2.3 mmol) of DMAP. The mixture was stirred at 0 °C for 2 h and then diluted with diethyl ether and washed with 10% $CuSO_4$. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude residue was subjected to flash silica gel chromatography to give 3.4 g (80%) of the title compound as a colorless oil: IR (neat) 1731, 1639, 1240, and 1040 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.84−1.91 (m, 1H), 2.00 (s, 3H), 2.32−2.49 (m, 2H), 2.60−2.69 (m, 1H), 3.71 (s, 3H), 5.93−5.96 (m, 1H), and 7.08 (t, 1H, J = 2.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.3, 31.3, 31.5, 51.7, 77.5, 134.9, 150.3, 164.2, and 170.8; HRMS calcd for $C_9H_{12}O_4$ 184.0736, found 184.0737.

5-((*tert*-Butoxycarbonyl)methyl)cyclopent-1-enecarboxylic Acid Methyl Ester. A solution of LDA was prepared by the addition of 2.8 mL (5.5 mmol) of *n*-BuLi (2.0 M in hexane) to a solution of 0.8 mL (5.7 mmol) of diisopropylamine in 10 mL of THF at −78 °C. The solution was warmed to 0 °C for 30 min and then cooled to −30 °C, and 0.7 mL (5.3 mmol) of *tert*-butyl acetate in 5 mL of THF was added. After it was stirred for 30 min, the solution was cooled to −78 °C and 0.75 g (4.1 mmol) of the above cyclopentenyl acetate in 5 mL of THF was added dropwise. After it was stirred for 1.5 h, the solution was warmed to room temperature, quenched with a saturated aqueous NH_4Cl solution, and extracted with EtOAc. The organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.84 g (87%) of the title compound as a colorless oil: IR (neat) 2980, 1726, 1367, and 1147 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.43 (s, 9H), 1.70−1.78 (m, 1H), 2.17−2.27 (m, 2H), 2.36−2.56 (m, 2H), 2.70−2.78 (m, 1H), 3.26−3.34 (m, 1H), 3.72 (s, 3H), and 6.78−6.80 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 28.3, 29.7, 31.7, 39.8, 41.3, 51.6, 80.4, 138.3, 145.2, 165.5, and 172.3; HRMS calcd for $C_{13}H_{20}O_4$ 240.1362, found 240.1368.

5-(Carboxymethyl)cyclopent-1-enecarboxylic Acid Methyl Ester. The above diester was stirred with 10 mL of a 10% TFA solution of CH_2Cl_2 at room temperature for 3 h. The solvent was evaporated under reduced pressure, and the crude residue was subjected to flash silica gel chromatography to afford 0.4 g (67%) of the title compound as a colorless oil: IR (neat) 3508 (br), 1710, 1629, and 1439 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.70−1.78 (m, 1H), 2.23−2.34 (m, 2H), 2.39−2.58 (m, 2H), 2.93 (ddd, 1H, J = 16.0, 4.0, and 1.2 Hz), 3.31−3.40 (m, 1H), 3.73 (d, 3H, J = 0.8 Hz), and 6.84−6.86 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 30.1, 31.7, 38.5, 40.8, 51.7, 137.8, 146.1, 165.6, and 179.3; HRMS calcd for $C_9H_{12}O_4$ 184.0736, found 184.0734.

5-(2-[3-(1-Acetoxy-2,2-bis(methylsulfanyl)ethyl)-2-oxopiperidin-1-yl]-2-oxoethyl)cyclopent-1-enecarboxylic Acid Methyl Ester. To a 0.34 g (1.8 mmol) sample of the above acid in 10 mL of CH_2Cl_2 was added 0.2 mL (2.2 mmol) of oxalyl chloride followed by 1 drop of DMF. The reaction mixture was stirred at room temperature for 1 h and then concentrated under reduced pressure to give the corresponding acid chloride as a yellow oil. The acid chloride was immediately taken up in 3 mL of CH_2Cl_2 and slowly added to a solution containing 0.3 g (1.0 mmol) of lactam **25** and 1.0 g of 4 Å powdered molecular sieves in 10 mL of CH_2Cl_2. The reaction mixture was vigorously stirred at room temperature for 12 h and then filtered over a pad of Celite. The filtrate was washed with a saturated $NaHCO_3$ solution, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to afford 0.42 g (96%) of the title compound as a mixture of two major diastereomers: IR (neat) 1751, 1716, 1690, 1623, and 1372 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) (diastereomer A) δ 1.55−1.65 (m, 1H),

(64) Yamane, T.; Takahashi, M.; Ogasawara, K. *Synthesis* **1995**, 444.

1.67−1.80 (m, 2H), 1.89−1.95 (m, 1H), 2.03−2.10 (m, 1H), 2.05 (s, 3H), 2.11 (s, 3H), 2.16 (s, 3H), 2.21−2.29 (m, 1H), 2.37−2.49 (m, 2H), 2.91 (ddd, 1H, J = 18.0, 14.0, and 10.4 Hz), 3.18−3.27 (m, 2H), 3.36−3.41 (m, 1H), 3.68 (s, 3H), 3.66−3.79 (m, 2H), 3.86 (dd, 1H, J = 8.0 and 1.6 Hz), 5.65 (dt, 1H, J = 8.0 and 4.0 Hz), and 6.75−6.80 (m, 1H); ^{1}H NMR ($CDCl_3$, 400 MHz) (diastereomer B) δ 1.56−1.65 (m, 1H), 1.67−1.77 (m, 1H), 1.91−2.06 (m, 3H), 2.07 (s, 3H), 2.09 (s, 3H), 2.11 (s, 3H), 2.23−2.30 (m, 1H), 2.35−2.48 (m, 2H), 2.91 (ddd, 1H, J = 18.0, 13.2, 10.4 Hz), 3.11−3.17 (m, 1H), 3.28 (dt, 1H, J = 18.0 and 4.0 Hz), 3.38−3.46 (m, 1H), 3.59−3.66 (m, 1H), 3.69 (s, 3H), 3.79−3.84 (m, 1H), 4.20 (t, 1H, J = 9.6 Hz), 5.36 (dt, 1H, J = 9.6 and 3.2 Hz), and 6.77−6.79 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) (diastereomer A) δ 13.1, 13.9, 20.9, 21.6, 30.6, 31.6, 40.6, 43.2, 43.8, 43.9, 45.8, 51.4, 56.7, 71.9, 138.5, 145.0, 165.4, 169.8, 173.5, and 175.7; ^{13}C NMR ($CDCl_3$, 100 MHz) (diastereomer B) δ 13.0, 13.4, 21.9, 23.7, 28.2, 30.7, 31.6, 40.7, 43.6, 43.9, 46.2, 51.5, 56.4, 73.6, 138.6, 145.1, 165.4, 170.3, 172.2, and 176.0; HRMS calcd for $C_{18}H_{26}NO_4S_2$ [M − CH_3COO] 383.1225, found 383.1210.

5-[2-(2-(Methylsulfanyl)-5,6-dihydro-4*H*-furo[2,3-*b*]pyridin-7-yl)-2-oxoethyl]cyclopent-1-enecarboxylic Acid Methyl Ester (47). To a solution of 0.11 g (0.24 mmol) of the above mixture of diastereomers in 8 mL of CH_3CN at −40 °C was added 0.05 g (0.24 mmol) of DMTSF. The reaction mixture was stirred at −40 °C for 1 h and then quenched with 5 equiv of Et_3N and diluted with diethyl ether. The organic layer was washed with a saturated $NaHCO_3$ solution, dried over K_2CO_3, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 0.05 g (62%) of **47** as a colorless oil: IR (neat) 1710, 1664, 1618, and 1511 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.68−1.76 (m, 1H), 1.84−1.90 (m, 2H), 2.24−2.39 (m, 2H), 2.32 (s, 3H), 2.41−2.44 (m, 2H), 2.48−2.58 (m, 1H), 2.72−2.79 (m, 1H), 3.23 (dt, 1H, J = 16.8 and 3.2 Hz), 3.40−3.48 (m, 1H), 3.70 (s, 3H), 3.72−3.78 (m, 1H), 3.83−3.89 (m, 1H), 6.33 (s, 1H), and 6.82 (dd, 1H, J = 4.0 and 2.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.0, 20.6, 23.3, 30.5, 31.7, 39.9, 41.0, 43.0, 51.5, 105.2, 117.6, 138.6, 140.8, 145.4, 146.5, 165.5, and 170.2. Anal. Calcd for $C_{17}H_{21}NO_4S$: C, 60.87; H, 6.31; N, 4.18. Found: C, 60.53; H, 6.09; N, 4.11.

8-(Methylsulfanyl)-4,9-dioxo-1,2,2*a*,3,4,6,7,8,9,9*a*-decahydro-5*H*-4*a*-azacyclopenta[*cd*]phenalene-9*b*-carboxylic Acid Methyl Ester (48). A solution of 0.9 g (0.25 mmol) of furan **47** in 4 mL of toluene was heated at 110 °C for 2 h. The solvent was removed under reduced pressure, and the residue was subjected to flash silica gel chromatography to afford 0.7 g (80%) of **48** as a pale yellow solid: mp 134−135 °C; IR (neat) 1726, 1701, 1665, 1639, and 1383 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.40−1.50 (m, 1H), 1.80−1.90 (m, 3H), 1.91−2.00 (m, 1H), 2.07 (s, 3H), 2.08−2.14 (m, 1H), 2.34−2.40 (m, 1H), 2.42−2.54 (m, 4H), 3.35 (s, 1H), 3.55−3.61 (m, 1H), 3.71 (s, 3H), 3.80 (dd, 1H, J = 11.6 and 7.6 Hz), and 4.02−4.08 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.4, 21.3, 27.1, 28.5, 30.4, 32.4, 40.9, 42.9, 52.5, 53.3, 53.9, 54.5, 112.6, 132.2, 166.2, 174.5, and 203.0. Anal. Calcd for $C_{17}H_{21}NO_4S$: C, 60.87; H, 6.31; N, 4.18. Found: C, 60.58; H, 6.30; N, 4.08.

Acetic Acid 2,2-Bis(methylsulfanyl)-1-(2-oxo-1-pent-4-ynoylpiperidin-3-yl) Ethyl Ester. To a 1.0 g (3.7 mmol) sample of **25** in CH_2Cl_2 (18 mL) was added 3.6 g of oven-dried 4 Å powdered molecular sieves and 0.85 g (7.3 mmol) of pent-4-ynoyl chloride.[65] The mixture was stirred at room temperature for 15 h, followed by filtration through a plug of silica with diethyl ether. The filtrate was washed with a saturated aqueous $NaHCO_3$ solution and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.8 g (59%) of the title compound as a yellow oil consisting of a 1:1 mixture of diastereomers: IR (neat) 1744, 1687, 1369, and 1156 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.64−1.81 (m, 4H), 1.95 (t, 1H, J = 2.6 Hz), 2.00 (t, 1H, J = 2.6 Hz), 2.08 (s, 3H), 2.11 (s, 6H), 2.14 (s, 6H), 2.19 (s, 3H), 2.49−2.62 (m, 8H), 3.11−3.19 (m, 5H), 3.20−3.28 (m, 1H), 3.58−3.64 (m, 1H), 3.73−3.80 (m, 2H), 3.86−3.90 (m, 1H), 3.89 (d, 1H, J = 8.0 Hz), 4.21 (d, 1H, J = 9.6 Hz), 5.40 (dd, 1H, J = 9.2 and 3.2 Hz), and 5.69 (dd, 1H, J = 8.0 and 4.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.9, 13.1, 13.6, 14.0, 14.4, 14.5, 20.9, 21.0, 21.2, 21.7, 21.9, 23.7, 38.8, 38.9, 43.5, 43.9, 45.0, 46.3, 56.4, 56.8, 68.8, 69.3, 72.1, 73.6, 83.5, 83.6, 169.9, 170.3, 172.4, 173.7, 174.8, and 175.0; HRMS calcd for $C_{14}H_{19}NO_2S_2$ [M − AcOH]$^+$ 297.0857, found 297.0857.

***N*-(2-(Methylsulfanyl)-5,6-dihydro-4*H*-furo[2,3-*b*]pyridin-7-yl)pent-4-ynamide (49).** To a 0.5 g (1.4 mmol) sample of the above compound in CH_2Cl_2 (10 mL) at −40 °C was added 0.4 g (1.8 mmol) of DMTSF. The mixture was stirred at −40 °C for 30 min before warming to 0 °C. After the mixture was stirred for 3 h at 0 °C, 1.0 mL (7 mmol) of triethylamine 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 diethyl ether. The combined organic layer was dried over anhydrous K_2CO_3, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.15 g (42%) of furan **49** as a clear oil: IR (neat) 2115, 1666, 1510, and 1344 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.87−1.93 (m, 2H), 1.97 (t, 1H, J = 2.8 Hz), 2.38 (s, 3H), 2.45 (t, 2H, J = 6.4 Hz), 2.57−2.61 (m, 2H), 3.02 (t, 2H, J = 7.4 Hz), 3.83−3.86 (m, 2H), and 6.37 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 20.1, 20.6, 23.2, 35.2, 43.2, 68.8, 83.7, 105.3, 117.7, 141.1, 146.2, and 169.0. Anal. Calcd for $C_{13}H_{15}NO_2S$: C, 62.63; H, 6.07; N, 5.62. Found: C, 62.55; H, 5.91; N, 5.55.

9-Hydroxy-8-(methylsulfanyl)-1,2,6,7-tetrahydro-5*H*-pyrido[3,2,1-*ij*]quinolin-3-one (52). To an oven-dried, heavy-walled, high-pressure tube equipped with a magnetic stirring bar and rubber septum was added a solution of 0.05 g (0.18 mmol) of furan **49** in toluene (2 mL). Argon was bubbled through the solution for 15 min, and the septum was replaced with a threaded Teflon cap containing a rubber O-ring seal. The vessel was heated at 170 °C behind a protective shield for 2 days. The reaction mixture was cooled, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.05 g (100%) of a tan solid consisting of a 1:1 mixture of thiomethyl isomers **52** and **53**. Compound **52** was obtained as a pale yellow oil: IR (film) 1727, 1632, 1393, 1180, and 1154 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.92−1.98 (m, 2H), 2.20 (s, 3H), 2.59−2.63 (m, 2H), 2.82−2.85 (m, 2H), 3.02 (t, 2H, J = 6.2 Hz), 3.84−3.87 (m, 2H), 6.73 (s, 1H), and 6.84 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.6, 21.8, 25.9, 26.4, 31.5, 40.4, 112.0, 118.0, 129.4, 129.8, 130.1, 152.6, and 169.2. Anal. Calcd for $C_{13}H_{15}NO_2S$: C, 62.63; H, 6.07; N, 5.62. Found: C, 62.69; H, 6.12; N, 5.48.

9-Hydroxy-10-(methylsulfanyl)-1,2,6,7-tetrahydro-5*H*-pyrido[3,2,1-*ij*]quinolin-3-one (53). Extensive silica gel chromatography of the above mixture gave the isomeric phenol **53** as a clear oil: IR (film) 1727, 1632, 1393, 1180, and 1154 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.87−1.96 (m, 2H), 2.17 (s, 3H), 2.58−2.63 (m, 2H), 2.73−2.76 (m, 2H), 3.13−3.18 (m, 2H), 3.82−3.85 (m, 2H), 6.68 (s, 1H) and 6.88 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.9, 21.6, 23.7, 27.7, 31.3, 40.8, 113.0, 117.3, 128.7, 129.3, 130.4 152.5, and 169.0. Anal. Calcd for $C_{13}H_{15}NO_2S$: C, 62.63; H, 6.07; N, 5.62. Found: C, 62.48; H, 5.89; N, 5.37.

3-[1-(Bis(methylsulfanyl)methyl)-1-hydroxypropyl]piperidin-2-one (54). To a solution of 9.8 mL (70 mmol) of diisopropylamine in THF (150 mL) at 0 °C was added *n*-butyllithium (70 mmol, 46 mL of a 1.5 M solution in hexane). The reaction mixture was stirred at 0 °C for 30 min, and 13.5 g (70 mmol) of 1-(trimethylsilanyl)piperidin-2-one[66] in THF (100 mL) was added dropwise. The mixture was stirred at 0 °C for an additional 30 min and then cooled to −78 °C. A solution of 12 g (70 mmol) of 1,1-bis(methylsulfanyl)butan-2-

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one[67] dissolved in THF (100 mL) was added dropwise. After the addition was complete, the reaction mixture was stirred for an additional 30 min before being poured into a saturated aqueous solution of NH_4Cl. The organic phase was separated, and the aqueous phase was washed with EtOAc. The combined organic layers were dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to yield 13 g (65%) of **54** as a yellow oil consisting of a 5:1 mixture of inseparable diastereomers: IR (neat) 1641, 1488, 1442, and 1409 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, 3H, J = 7.6 Hz, minor diastereomer), 0.94 (t, 3H, J = 7.6 Hz, major diastereomer), 1.34−1.43 (m, 1H), 1.57−1.70 (m, 2H), 1.82−1.89 (m, 1H), 1.94−2.01 (m, 1H), 2.03−2.09 (m, 1H), 2.18 (s, 6H, minor diastereomer), 2.22 (s, 3H, major diastereomer), 2.23 (s, 3H, major diastereomer), 3.19−3.33 (m, 3H), 3.51 (s, 1H, major diastereomer), 3.67 (s, 1H, minor diastereomer), 6.74 (s, 1H, major diastereomer), 6.95 (s, 1H, minor diastereomer), and 7.18 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (major diastereomer) δ 8.6, 15.6, 16.7, 22.5, 23.1, 30.0, 42.2, 47.0, 64.1, 64.1, 81.6, and 176.9; (minor diastereomer) δ 8.2, 13.7, 15.2, 23.2, 30.3, 42.1, 44.1, 64.8, 82.7, and 176.9. Anal. Calcd for $C_{11}H_{21}NO_2S_2$: C, 50.15; H, 8.04; N, 5.32. Found: C, 50.26; H, 8.07; N, 5.24.

3-[1-(Bis(methylsulfanyl)methyl)-1-hydroxypropyl]-1-but-3-enoylpiperidin-2-one (55). To a 9.5 g (36 mmol) sample of **54** in CH_2Cl_2 (200 mL) was added 36 g of oven-dried 4 Å powdered molecular sieves and 5.6 g (54 mmol) of but-3-enoyl chloride.[60] The mixture was stirred at room temperature for 15 h, followed by filtration through a plug of silica with diethyl ether. The filtrate was washed with a saturated aqueous $NaHCO_3$ solution and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 10 g (86%) of **55** as a yellow oil consisting of a single diastereomer: IR (neat) 1808, 1701, and 1384 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.97 (t, 3H, J = 7.6 Hz), 1.53 (qd, 1H, J = 11.8 and 4.2 Hz), 1.66−1.76 (m, 1H), 1.73 (hept, 1H, J = 7.4 Hz), 1.94−2.12 (m, 3H), 2.27 (s, 3H), 2.28 (s, 3H), 3.47 (dd, 1H, J = 11.8 and 7.0 Hz), 3.50 (m, 1H), 3.63−3.70 (m, 2H), 3.72 (d, 1H, J = 0.8 Hz), 3.88−3.94 (m, 1H), 5.11−5.18 (m, 3H), and 5.95−6.05 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.9, 16.2, 16.9, 22.1, 23.1, 30.0, 44.5, 50.5, 64.6, 81.9, 118.5, 131.3, 174.9, and 178.3. Anal. Calcd for $C_{15}H_{25}NO_3S_2$: C, 54.36; H, 7.61; N, 4.23. Found: C, 54.19; H, 7.55; N, 4.09.

***N*-(3-Ethyl-2-(methylsulfanyl)-5,6-dihydro-4*H*-furo[2,3-*b*]pyridin-7-yl)but-3-enamide (56).** To a 0.5 g (1.5 mmol) sample of **55** in CH_3CN (10 mL) at −40 °C was added 0.3 g (1.5 mmol) of DMTSF. The reaction mixture was stirred at −40 °C for 3 h, and then 1.0 mL (7 mmol) of triethylamine 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 diethyl ether. The combined organic layer was dried over anhydrous K_2CO_3, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.2 g (60%) of furan **56** as a colorless oil: IR (film) 1673, 1625, 1373, 1308, and 1175 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.13 (t, 3H, J = 7.4 Hz), 1.88−1.94 (m, 2H), 2.30 (s, 3H), 2.41−2.49 (m, 4H), 3.56−3.58 (m, 2H), 3.82−3.84 (m, 2H), 5.15−5.22 (m, 2H), and 5.96−6.07 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 18.5, 19.8, 20.5, 23.1, 41.2, 43.0, 105.1, 118.3, 131.7, 133.3, 136.6, 145.6, and 169.1. Anal. Calcd for $C_{14}H_{19}NO_2S$: C, 63.36; H, 7.22; N, 5.28. Found: C, 63.17; H, 7.08; N, 5.13.

7-Ethyl-7-(methylsulfanyl)-5,6,9,9*a*-tetrahydro-1*H*,4*H*,7*H*-pyrrolo[3,2,1-*ij*]quinoline-2,8-dione (57). A solution of 0.2 g (0.9 mmol) of furan **56** in toluene (5 mL) was heated at reflux for 1 h. The reaction mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.2 g (70%) of **57** as a white solid: mp 117−118 °C; IR (film) 1729, 1682, 1351, and 1180 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.75 (t, 3H, J = 7.5 Hz), 1.62−1.70 (m, 1H), 1.79−1.88 (m, 1H), 1.91 (s, 3H), 1.93−1.99 (m, 1H), 2.06−2.31 (m, 5H), 2.72 (dd, 1H, J = 17.1 and 9.2 Hz), 3.02 (dd, 1H, J = 17.1 and 5.8 Hz), 3.30−3.45 (m, 2H), and 3.55−3.60 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.1, 13.1, 20.5, 21.4, 25.2, 29.9, 37.2, 38.8, 44.0, 56.7, 105.0, 141.6, 173.2, and 201.6. Anal. Calcd for $C_{14}H_{19}NO_2S$: C, 63.36; H, 7.22; N, 5.28. Found: C, 63.08; H, 7.15; N, 5.24.

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Supporting Information Available: Figures giving ^1H and ^{13}C NMR spectra for new compounds lacking elemental analyses together with ORTEP drawings for structures **46**, **48**, and **57** and text giving experimental details for the preparation of **20** and **66** and their spectroscopic properties. This material is available free of charge via the Internet at http://pubs.acs.org. The authors have deposited atomic coordinates for these structures with the Cambridge Crystallographic Data Centre.

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