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An Approach toward Azacycles Using Photochemical and Radical Cyclizations of *N*-Alkenyl Substituted 5-Thioxopyrrolidin-2-ones

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The photochemical reactions of a series of cyclic *N*-alkenyl-substituted thioimides have been examined. Irradiation of *N*-3-methylbut-3-enyl-5-thioxo-pyrrolidin-2-one (**16**) results in intramolecular [2 + 2] cycloaddition to give the highly strained thietane **17**, whose structure was confirmed on the basis of its X-ray analysis. Treatment of cycloadduct **17** with dimethyl(methylthio)sulfonium tetrafluoroborate gave 2,5,6,7-tetrahydropyrrolizin-3-one (**20**) in good yield. Further reduction of **20** with Raney-Ni afforded 5,5-dimethylhexahydro-pyrrolizin-1-one (**21**). This sequence of reactions demonstrates the facility with which the 2 + 2 photoadduct can be converted into the pyrrolizidine alkaloid core skeleton. The photochemistry of the closely related *N*-butenyl thioxopyrrolidin-one (**22**) proceeded in a slightly different fashion and produced 7-mercaptomethyl tetrahydropyrrolizin-3-one (**24**) in 68% yield. In contrast to the above results, irradiation of the thioxaphthalimido system containing an *N*-cycloalkenyl group in the side chain gave rise to products derived by γ-hydrogen abstraction from the n−π* triplet excited state. The photobehavior of the related *N*-3-alkenyl pyrrolidine-2,5-dithione system (**62**) was also studied and found to give products derived from both a 2 + 2 cycloaddition (**63**) and hydrogen atom transfer (**64**). Finally, the reaction of several *N*-alkenyl substituted thioimides (**71**−**73**) with tributylstannane in the presence of AIBN gave cyclized products derived from transient radical intermediates.

Introduction

Thiocarboxamides are widely used in both agriculture and medicine[1] and represent useful precursors for the preparation of a variety of organic compounds.[2] This functional group undergoes an assortment of chemical transformations that makes it attractive for synthetic applications.[3] Thioenolate anions of thioamides have been employed in a variety of condensation reactions,[4] and stereoselective Michael additions to α,β-unsaturated ketones are also known to occur.[5] Numerous heterocycles have been generated from thioamides by virtue of their dipolar nature.[6] Thiocarboxamides have been oxidized to carbonyl compounds,[7] reduced to amines,[8] and converted to nitriles,[9] thioimidates,[10] and amidines.[11] Radical cyclization of 2-alkenylthioanilides has been used to prepare 2,3-disubstituted indoles.[12] Other cyclization reactions include electrophile-induced additions to olefins[13] and the Rh(II)-catalyzed reaction of thioamido-substituted α-diazomethyl vinyl ketones.[14] As a consequence of their broad synthetic utility, it is not surprising that there are numerous procedures for the preparation of thioamides from amides and lactams.[15]

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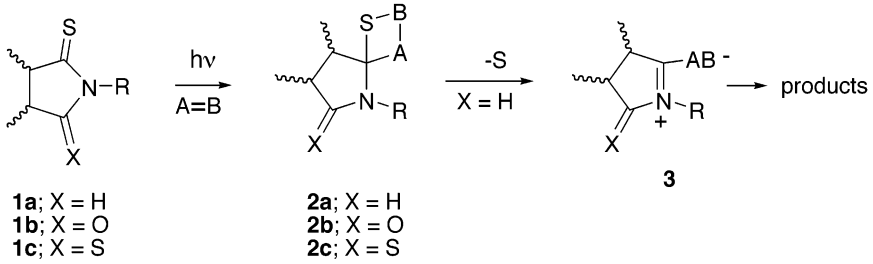
SCHEME 1

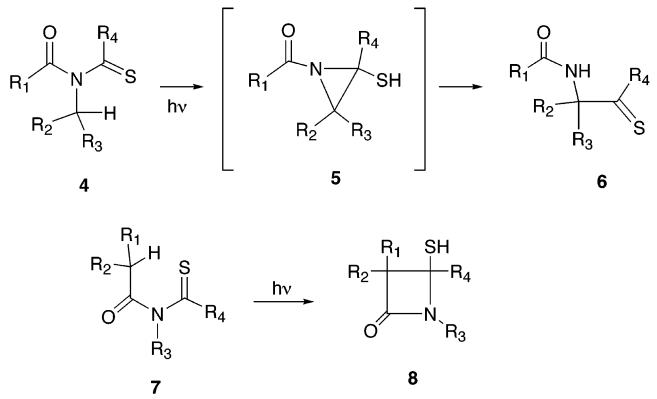


1a; X = H
1b; X = O
1c; X = S

2a; X = H
2b; X = O
2c; X = S

Photochemical cyclizations of nitrogen-containing thiocarbonyl compounds have also been studied in some detail[16] and represent a potentially important method for the synthesis of various heterocyclic ring systems. Most simple thioamides were found to be inert to both the Norrish type I (α-cleavage) and Norrish type II (hydrogen abstraction) reactions[17] in contrast to the behavior of their oxygen and nitrogen counterparts.[18] However, many aliphatic and aromatic monothioimides of type **1a** (X = H) undergo both inter- and intramolecular Paterno−Büchi-like photocycloadditions with olefins[19] to give various imido-thietanes **2a** (X = H) as primary products that can undergo further fragmentation (Scheme 1). Simple aminothietanes of type **2a** (X = H) are generally too labile to be isolated, except for one example in the literature.[20] The facility with which the subsequent fragmentation occurs can be ascribed to the participation of the lone pair of electrons on the nitrogen atom that facilitates C−S cleavage in the thietane ring leading to the formation of a zwitterionic intermediate (**3**). This transient species can give rise to a plethora of photoproducts. The [2 + 2] photocycloaddition of various thioimides,[21] thiouracils,[22] and 2-thioparabanic acids[23] (i.e., **1b** or **1c**) furnishes isolable thietanes (**2b** or **2c**) since the availability of the lone-pair electrons on the nitrogen atom is reduced by conjugation with the second carbonyl group. Most thioimides of type **1b** (X = O) react from their n−π* triplet excited state, whereas it is known that

SCHEME 2



thioketones react from both their n−π* triplet and long-lived upper singlet excited state (π−π* singlet).[24] For thiocarboxamides **1a** (X = H), π donation by a nitrogen atom is more efficient than σ withdrawal and thus they are predicted to have nucleophilic n−π* states. Simple resonance theory suggests that the addition of a second carbonyl or thiocarbonyl group to the nitrogen atom should lead to delocalization of the nitrogen lone-pair electrons, making the chromophore more reactive during photochemical excitation. Indeed, introduction of another carbonyl group onto the thioamide renders the thiocarbonyl group quite reactive toward photochemical hydrogen abstraction from the β-, γ-, and δ-positions and leads to nitrogen-containing heterocycles such as lactams and rearranged amides (Scheme 2).[25,26]

Work by the Kanaoka and Machida groups has also shown that, in contrast to thiocarboxamides, photochemical excitation of aromatic thioimides possessing a benzylic hydrogen at the δ- and ϵ-positions of the *N*-alkyl side chain gives rise to photocyclization products (i.e., **9** → **10**, Scheme 3).[27] Certain cyclic thioimides that contain an *N*-ω-(phenylalkyl) substituent also undergo the Norrish type II cyclization. For example, the photolysis of the monothioimide **11** resulted in the formation of bicyclic γ-lactams **13** (27−84% yield) and enethiols **14** and **15** (37−51% yield), which are formed by disproportionation of the initially generated biradical intermediate **12**.[28]

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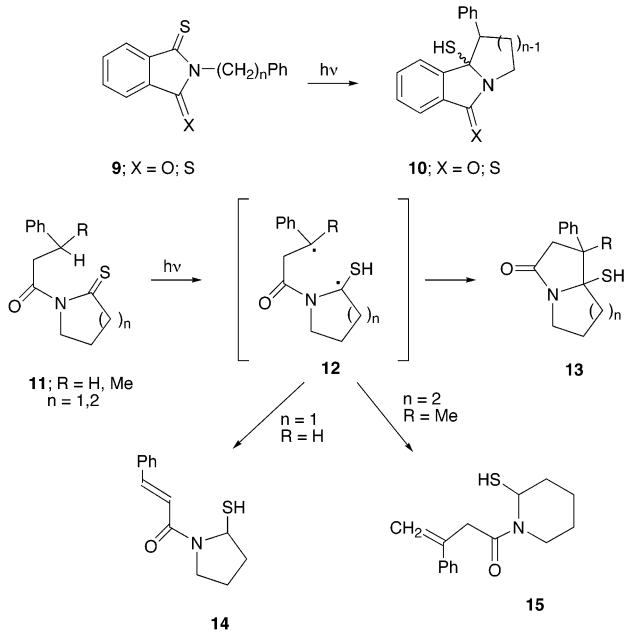
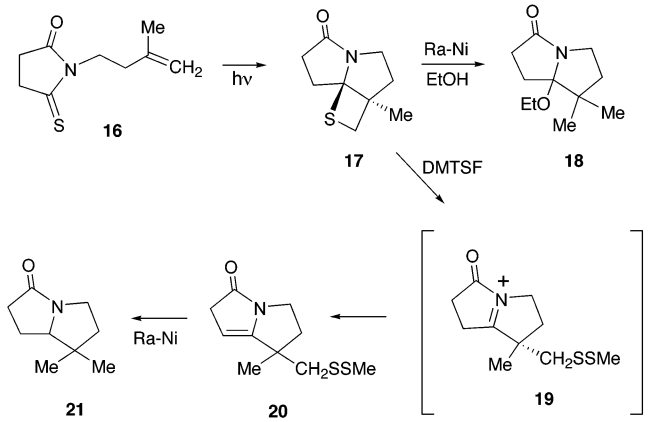
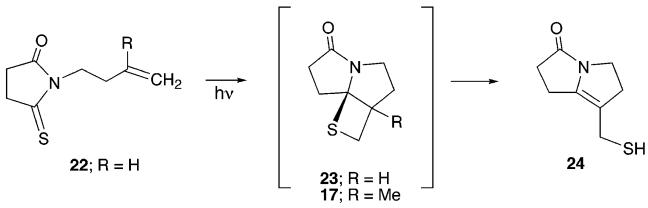
SCHEME 3



SCHEME 4



SCHEME 5



In the course of our own studies dealing with the cyclization chemistry of thiocarboxamides,[29] we became interested in using the intramolecular [2 + 2] photocycloaddition as a method for preparing various azabicyclic ring systems commonly found in pyrrolizidine alkaloids. We reasoned that loss of sulfur from the initially formed thietane cycloadduct (i.e., **2**) might represent an efficient approach for the synthesis of fused heterocycles. In this paper, we report an account of our efforts dealing with the intramolecular photocycloaddition reactions of several cyclic thioimides.[30]

Results and Discussion

A series of *N*-alkenyl-substituted thioxopyrrolidinones were easily prepared by an N-alkylation reaction of succinimide followed by thiation using Lawesson's reagent.[15] We began our investigation of their photochemical behavior by first irradiating a sample of *N*-3-methylbut-3-enyl-5-thioxopyrrolidin-2-one (**16**) in benzene using a 450-W Hanovia medium-pressure lamp under an argon atmosphere with a Pyrex filter sleeve for 2 h (Scheme 4). Silica gel chromatography of the crude reaction mixture afforded the highly strained thietane **17** in 73% yield whose structure was assigned on the basis of its spectral and analytical data. The assignment of structure **17** was further validated by single-crystal X-ray analysis.[31] Compound **17** was treated with Raney-Ni in ethanol for 2 h to give the ethoxy substituted hexahydropyrrolizin-3-one (**18**).

We also carried out a ring-opening reaction on cycloadduct **17** by treating it with dimethyl(methylthio)sulfonium tetrafluoroborate (DMTSF).[32] The ease with which the S−S bond of (dimethylthio)sulfonium salts are cleaved by nucleophilic reagents was first documented by Helmkamp and co-workers in their work on the preparation of DMTSF and its addition to alkenes and alkynes.[33] These reactions, and related studies by Meerwein,[34] indicate that reagents such as DMTSF may be regarded as sulfanyl derivatives and can function as a potential source of alkylsulfanyl ions.[35] 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.[36] It follows, therefore, that the conversion of **17** to **20** upon treatment with DMTSF proceeds by the pathway outlined in Scheme **4**. Methylthiolation of the thietane sulfur with DMTSF produces a transient alkylthiosulfonium salt that easily dissociates to *N*-acyliminium ion **19**. Once formed, **19** readily undergoes loss of a proton to give **20**. Subjection of **20** to Raney-Ni afforded hexahydropyrrolizinone **21** in good yield. The above transformations clearly demonstrate the facility with which the resulting photoadduct **17** can be converted into the pyrrolizidine core skeleton.

The photochemistry of the closely related *N*-butenyl thioxopyrrolidinone (**22**) (R = H) proceeded in a slightly different fashion and produced 7-mercaptomethyl-1,2,5,6-tetrahydropyrrolizin-3-one (**24**) in 68% yield (Scheme 5).

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(31) We have deposited atomic coordinates for compounds **17** and **47b** with the Cambridge Data Centre. The coordinates can be obtained on the request from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, CB2 1EZ, U.K.

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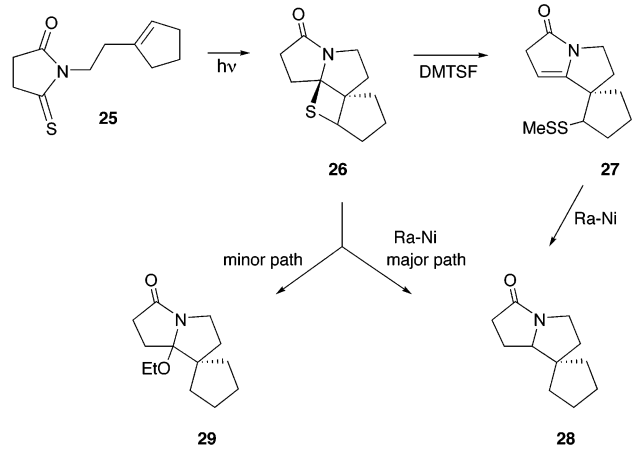
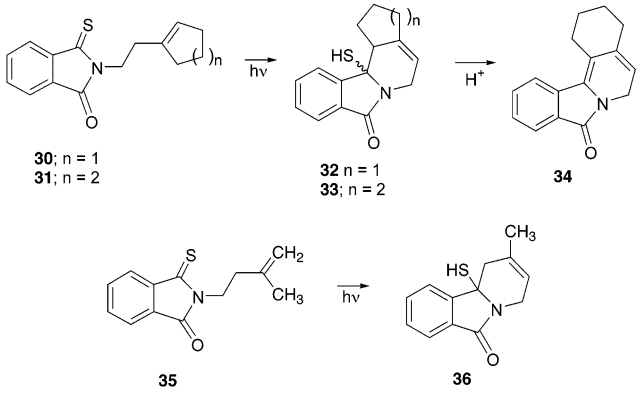
SCHEME 6



25 **26** **27** **29** **28**

SCHEME 7



30; n = 1
31; n = 2
32 n = 1
33; n = 2
34
35
36

More than likely, the photoreaction also proceeds by a Paterno−Büchi-like cycloaddition. With this system, however, the initially formed cycloadduct readily undergoes ring opening followed by a subsequent deprotonation to give **24** as a consequence of the available hydrogen atom (i.e., R = H). This ring-opening reaction does not occur with the related 3-methylbutenyl system **17** (i.e., R = Me).

Photolysis of the *N*-cyclopentenyl derivative **25** was also carried out and, in a similar fashion, produced the tetracyclic thietane **26** as the major photoproduct in 68% yield based on recovered starting material (Scheme 6). The ^{1}H NMR and ^{13}C NMR spectra indicate that the cycloadduct was obtained as a single stereoisomer. As was the case with photoadduct **17**, treatment of **26** with DMTSF afforded the related tetrahydropyrrolizinone **27** in 92% yield. Further reduction of **27** with Raney-Ni gave spiro pyrrolizinone **28** in 95% yield. The direct reduction of cycloadduct **26** with Raney-Ni also afforded **28**, but in this case lesser quantities (7%) of the ethoxy-substituted spiro pyrrolizinone **29** were also formed. Compound **29** is presumably derived by the trapping of an initially produced *N*-acyliminium ion with ethanol.

In contrast to the above results, irradiation of the thioxaphthalimide systems **30** and **31** containing an *N*-cycloalkenylalkyl group in the side chain produced the mercapto-substituted pyridoisoindolones **32** and **33** as a 1:1 mixture of diastereomers in 64 and 73% yields, respectively. Further treatment of **33** with *p*-toluenesulfonic acid resulted in the loss of H_2S and afforded dihydropyridine **34** in 91% yield. Photolysis of the closely related *N*-but-3-enyl thioxaphthalimide (**35**) furnished the analogous pyridoisoindolone **36** in 73% yield (Scheme 7).

In an earlier report,[37] Oda had suggested that in certain cases, apparent Norrish type II products such as **32** (or **36**) are actually derived from a Paterno−Büchi photocycloaddition reaction, which is subsequently converted into the mercapto pyridoisoindolone system. However, we were unable to detect such an intermediate in the photolysis of **30**, **31**, or **35**. The fact that **36** is the major product formed from the irradiation of **35** may be rationalized by γ-hydrogen abstraction from the n−π* triplet state of the thioxaphthalimido chromophore.[38] The adjacent phthalimido ring apparently enhances the ability of the n−π* excited state to abstract a γ-hydrogen relative to undergoing [2 + 2] cycloaddition across the tethered π bond.

Over a period of years, several research groups have worked on the photochemistry of phthalimide systems. These molecules exhibit diverse photochemical behavior, including electron-transfer reactions,[39] photoreductions,[40] Paterno−Büchi cycloadditions,[41] and the addition of alkenes to form benzazepine-diones[42] (i.e., **37** → **38**). In related studies, Booker-Millburn and co-workers showed that the photolysis of a number of *N*-alkenyl-substituted maleimide derivatives also led to the formation of complex perhydroazaazulenes in excellent yield (i.e., **39** → **41**).[43] Some of the polycyclic ring systems that were prepared by this method constitute the core skeleton of a number of complex alkaloids.[44] The overall process has been considered as a formal intramolecular [5 + 2] cycloaddition.[43] Although the mechanism of this novel cycloaddition is not known with certainty, it has been postulated[43] from the earlier work of Mazzocchi[45] that the reaction proceeds by a direct [2 + 2] cycloaddition

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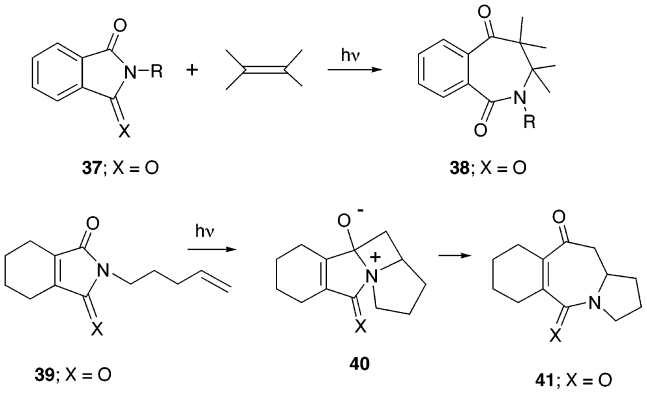
(42) (a) Mazzocchi, P. H.; Bowen, M. J.; Narain, N. K. *J. Am. Chem. Soc.* **1977**, *99*, 7063. (b) Mazzocchi, P. H.; Minamikawa, S.; Bowen, M. *J. Org. Chem.* **1978**, *43*, 3079. (c) Maruyama, K.; Kubo, Y. *Chem. Lett.* **1978**, 769.

(43) (a) Booker-Milburn, K. I.; Costin, N. J.; Dainty, R. F.; Patel, D.; Sharpe, A. *Tetrahedron Lett.* **1998**, *39*, 7423. (b) Booker-Milburn, K. I.; Anson, C. E.; Clissold, C.; Costin, N. J.; Dainty, R. F.; Murray, M.; Patel, D.; Sharpe, A. *Eur. J. Org. Chem.* **2001**, 1473. (c) Booker-Milburn, K. I.; Cowell, J. K.; Sharpe, A.; Delgado Jiménez. F. *Chem. Commun.* **1996**, 249. (d) Booker-Milburn, K. I.; Gulten, S.; Sharpe, A. *Chem. Commun.* **1997**, 1385.

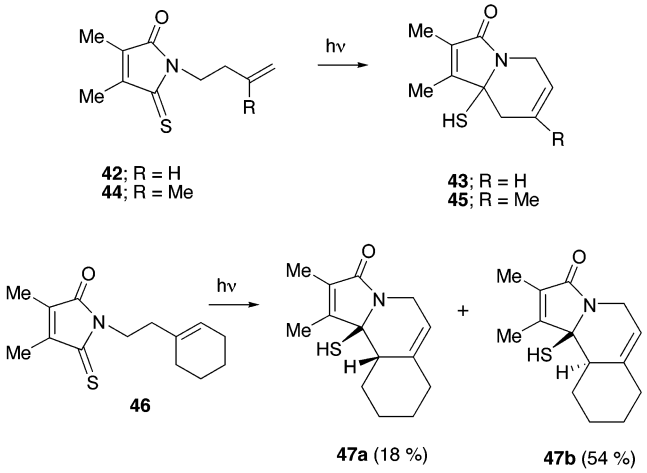
(44) Booker-Milburn, K. I.; Dudin, L. F.; Anson, C. E.; Guile, S. D. *Org. Lett.* **2001**, *3*, 3005.

(45) (a) Mazzocchi, P. H.; Khachik, F.; Wilson, P. *J. Am. Chem. Soc.* **1981**, *103*, 6498. (b) Mazzocchi, P. H.; Wilson, P.; Khachik, F.; Klingler, L.; Minamikana, S. *J. Org. Chem.* **1983**, *48*, 2981. (c) Mazzocchi, P. H.; Minamikana, S.; Wilson, P.; Bowen, M.; Narain, N. *J. Org. Chem.* **1981**, *46*, 4846.

SCHEME 8



SCHEME 9

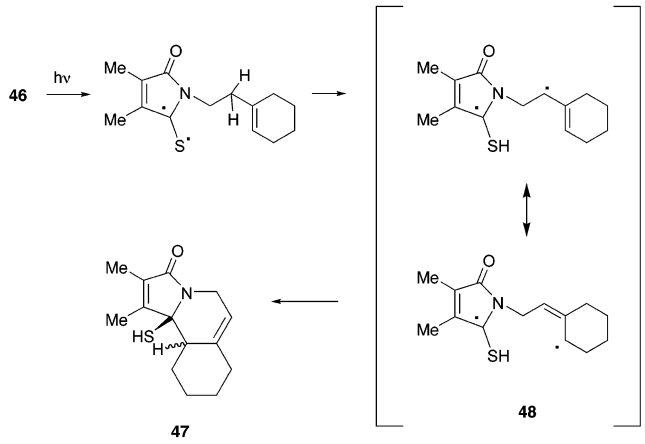


onto the excited amide resonance structure to give a zwitterionic tricyclic species (i.e., **40**), which then undergoes a spontaneous fragmentation to the product (Scheme 8).

As part of our studies in this area, we thought it would be of interest to determine whether the photochemistry of the related thiomaleimide system would undergo an analogous [5 + 2] cycloaddition or possibly proceed by some alternate photochemical pathway. We found that the irradiation of the parent thiomaleimide **42** resulted in the complete disappearance of the starting material after 2.5 h, and after chromatographic purification, a new product was obtained in 62% yield. The structure of this compound was assigned as the mercapto-substituted indolizinone **43** on the basis of its spectral properties. Similarly, photolysis of the related *N*-3-methyl-but-3-enyl thiomaleimide (**44**) gave the analogous product **45** in 64% yield after 2.5 h of irradiation using a 450-W Hanovia medium-pressure lamp (Scheme 9). We then turned our attention to the investigation of the more complex cyclohexenyl substituted system **46** with a view to testing the limits of the photoreaction. Irradiation of a sample of **46** for 2.5 h afforded a 72% yield of **47** as a 1:3 mixture of two diastereomers which could be separated by column chromatography. The structure of the major diastereomer **47b** was established as the trans stereoisomer on the basis of an X-ray crystal structure analysis.[31]

We considered two mechanistic possibilities to account for the observed transformation with these systems. Path

SCHEME 10. Path A

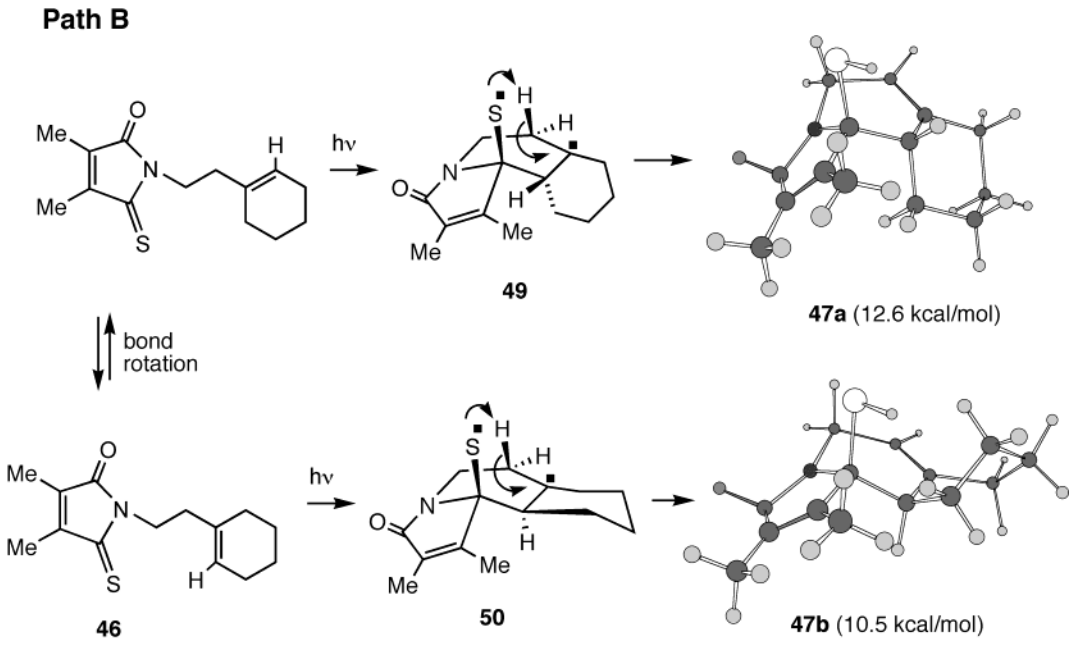


A involves γ-hydrogen abstraction from the n$-\pi^*$ triplet state of the thiomaleimide chromophore and is analogous to that suggested to occur with the thiophthalimido systems **30** and **31**. The initially formed diradical intermediate **48** undergoes subsequent coupling at the remote allylic site to preferentially afford the thermodynamically more stable six-membered ring rather than the more highly strained four-membered azetidine ring. Although this pathway seems reasonable, we believe that the formation of a 3:1 mixture of diastereomers is inconsistent with the hydrogen transfer mechanism (path A, Scheme 10). A stepwise abstraction-coupling mechanism would be more likely to produce a 1:1 mixture of diastereomers since the activation energy associated with diradical coupling is less than 3 kcal. Consequently, there should be little selectivity encountered in the coupling step and the diastereomeric ratio would only depend on whether the amido radical attacks the top or bottom face of the allylic π radical. The alternate mechanistic possibility (path B, Scheme 11) differs in its timing from path A and proceeds by initial addition of the electronically excited carbon atom of the n$-\pi^*$ excited state of the thiocarbonyl group onto the adjacent cyclohexenyl π bond. The resulting diradical intermediate (**49** or **50**) would then undergo a subsequent transannular 1,5-hydrogen abstraction[46] to give the diastereomeric photoproducts **47a** or **47b**. The fact that a 3:1 mixture of stereoisomers is obtained would certainly support this type of mechanism. Stepwise addition to the π bond will result in two distinctly different diradical intermediates (i.e., **49** vs **50**), which in turn would deliver the cis (**47a**) and trans (**47b**) tricyclic diastereomers. Furthermore, one would expect that the preferred diastereomer would reflect the strain energy of the resulting tricyclic ring systems.[47] In recent years, molecular mechanics calculations have developed into an important technique for calculation of molecular properties.[48a] The stability of the diastereomeric tricyclic compounds **47a** and **47b** can be determined by calcula-

(46) Serebryakov, E. P. *Bull. Acad. Sci. USSR* **1984**, *33*, 120.

(47) Another possibility to account for the preference of the trans diastereomer was suggested by one of the referees. The trans product could form from an exo approach of the cycloalkene ring to the electronically excited heterocyclic ring and the cis product from an endo approach of the two reacting sites. The difference in energy of the respective transition states would also explain the preference for the trans diastereomer.

SCHEME 11. Path B

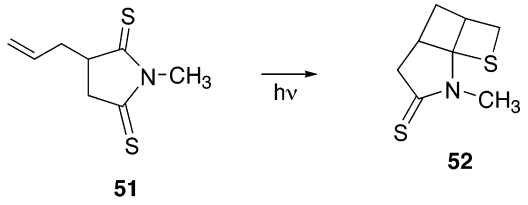


tion of their steric energies, the direct sum of the force-field increments.[48b] We assume that the relative energy differences of the lowest-energy conformation of compounds **47a** and **47b** will parallel the energy differences of the diradical intermediates **49** and **50** and also the energy differences in the transition state for their formation. The MMX calculations reveal a 2.1 kcal difference between the two diastereomeric products but only a 0.1 kcal difference between the conformations of the starting thiomaleimides. The lower-energy tricyclic diastereomer (**47b**) corresponds to the trans isomer, which was the major product formed. Thus, path B successfully predicts the observed stereochemistry of the obtained major (trans) isomer of **47** and lends further weight to this mechanistic interpretation.

As a logical extension of our photochemical program dealing with intramolecular thietane formation, the photoreaction of several *N*-3-alkenyl pyrrolidine-2,5-dithiones was investigated. The change of an oxygen to a sulfur atom in the cyclic imide chromophore is known to result in unique photochemistry.[16] For example, the excited state of dithiosuccinimides reacts with olefins only by photoaddition.[49] Other photoreactions such as the Norrish type I and type II reactions, which are common to the parent thione and imide families,[38] are less important with dithioimides. The inertness of dithioimides to the undesired Norrish I reaction suggests that these substrates may have some interesting synthetic capabilities. For example, thiosuccinimides such as **51** have been reported to undergo smooth intramolecular cycloaddition to give the highly strained thietane **52** (Scheme 12).[49]

We opted to study the photochemistry of the related *N*-alkenyl dithio-succinimide system and, in the course

SCHEME 12



of our investigations, encountered some interesting differences. Thus, the irradiation of the straight chain *N*-3-butenyl dithione **53** afforded a 4:1 mixture (64%) of thietane **54** and pyrrolizine-3-thione **55**

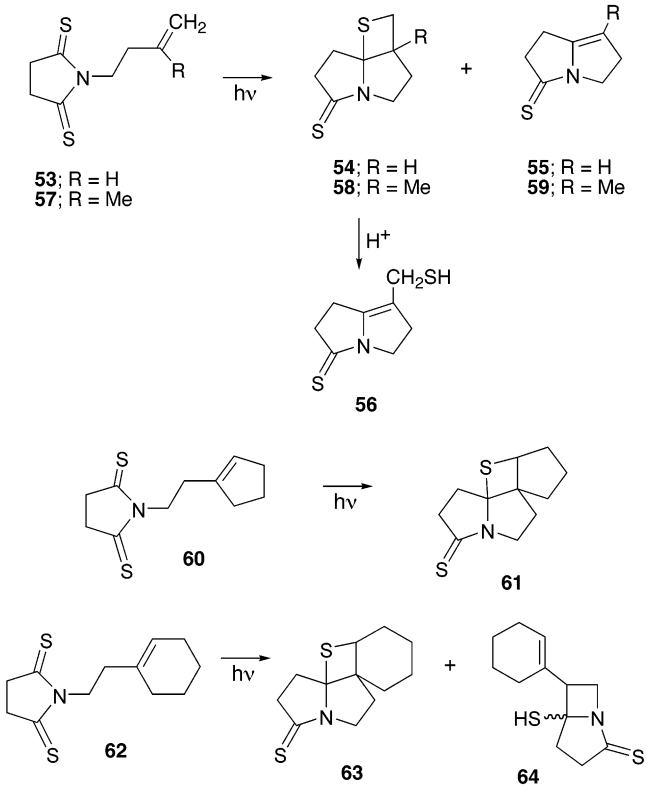
(Scheme 13). It would appear that the excited thioamido group undergoes [2 + 2] cycloaddition and partial fragmentation of thioformaldehyde from **54** to give **55**. Treatment of a sample of **54** with a trace of acid gave the ring-opened mercaptan **56** in high yield. An analogous photocycloaddition reaction also occurred with dithione **57**, which gave the novel 3-thione **58** as well as 1*H*-pyrrolizine **59** in 72 and 10% yield, respectively. Irradiation of the *N*-2-cyclopentenyl-ethyl pyrrolidine dithione (**60**) afforded the Paterno−Büchi cycloadduct **61**. Interestingly, when the homologous cyclohexenyl system **62** was used, bicyclic azetidine **64** (30%) was obtained in addition to the expected [2 + 2] photoadduct **63** (28%). We suspect that **64** is derived from a competitive hydrogen transfer reaction. No signs of a photoproduct related to **64** were observed with the cyclopentenyl thione **60**. It is well known that [2 + 2] photocycloaddition of the n−π* state of a carbonyl compound to an unsaturated substrate proceeds via a biradical intermediate.[50] Presumably the formation of thietane **61** (or **63**) also proceeds by a related biradical intermediate (i.e., **65**) derived by addition of the

(48) (a) For a review, see: Burkert, U.; Allinger, N. L. *Molecular Mechanics*; American Chemical Society: Washington, DC, 1982. (b) We have used the UNIX version of PCModel operating on a G4-Macintosh computer (OSX 10.2) for these calculations.

(49) Oda, K.; Machida, M.; Aoe, K.; Nisibata, K.; Sato, Y.; Kanaoka, Y. *Chem. Pharm. Bull.* **1986**, *34*, 1411.

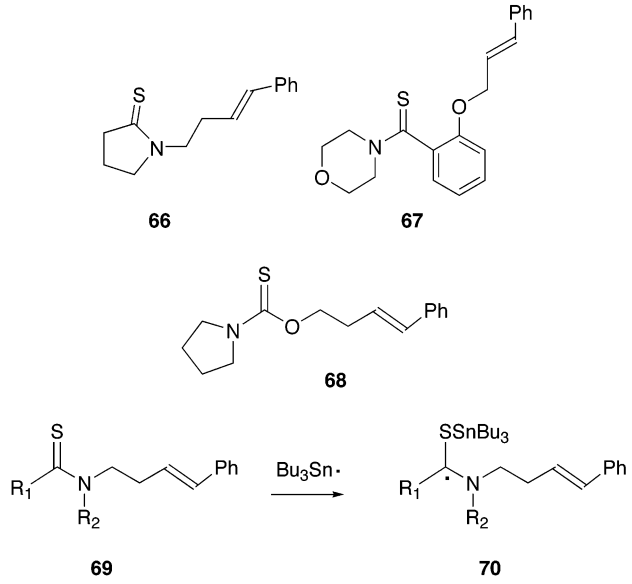
(50) Turro, N. J. *Modern Molecular Photochemistry*; The Benjamin/Cummings Publishing Co., Inc.: Menlo Park, CA, 1978; p 432.

SCHEME 13



excited n−π* state of the thiocarbonyl group onto the terminal position of the tethered alkene.[51]

As a further continuation of our studies in this area, we thought it worthwhile to use the *N*-alkenyl 5-thioxopyrrolidinone ring system as a precursor for radical cyclizations. During the past decade, the synthesis of heterocyclic rings by radical cyclization has been extensively investigated and this trend is showing no sign of abating.[52] Most of the effort in this area has focused on carbon centered radicals,[53] but oxygen[54a] and especially nitrogen radicals[54b] are attracting an increasing amount of attention since these species can provide access to a variety of important heterocyclic systems. Recently, there have been several examples of radical cyclizations of various thionoesters and thioamides, which involve the addition of tri-butylstannyl radical to a thiocarbonyl group and intramolecular addition of the resulting radical to a carbon−carbon multiple π bond.[12,55] Bachi and coworkers' attempts to induce radical cyclizations of thioamides **66**−**68** by reaction with tri-*n*-butylstannyl radical failed, however, to give cyclized products.[56] The inert nature of these compounds was attributed to the radical stabilizing power of the nitrogen atom.[56] Apparently, the initially formed adduct radical **70** derived from thioamide **69** is not sufficiently reactive to maintain a viable chain reaction by addition to the neighboring double bond. In an earlier report we had demonstrated that the radical stabilizing effect of the nitrogen atom can be significantly reduced by the incorporation of an electron-withdrawing substituent and that it becomes possible to induce radical cyclization under these conditions.[57]



Since we had a supply of various *N*-alkenyl-substituted 5-thioxopyrrolidinones on hand from our photochemical studies, we decided to investigate their radical cyclization behavior. For our initial exploratory work, thioimide **71** was chosen as the substrate. Treatment of this compound with 1.1 equiv of *n*-Bu_3SnH in boiling benzene under the standard conditions afforded 7-methyl-tetrahydropyrrolizin-3-one (**77**) but in only 28% yield (Scheme 14). More than likely this reaction proceeds by an initial and reversible addition of *n*-$Bu_3Sn^{\bullet}$ onto the thiono sulfur atom. The resulting adduct radical **74** undergoes a subsequent 5-*exo* trig addition to the tethered π bond to give the cyclic radical **75**, which then abstracts a hydrogen atom from *n*-Bu_3SnH to furnish the cyclized lactam **76**. On elimination of tributylstannyl mercaptan, tetrahydro-pyrrolizinone **77** is obtained.

Incorporating an electron withdrawing group (R = SO_2-Me or CO_2Me) on the π bond did not significantly enhance the cyclization process. Thus, the tin-mediated reaction was not particularly efficient in these two cases since the

(51) We assume that the conversion of **25** to **26** also occurs via a similar diradical intermediate.

(52) (a) Curran, D. P. *Synthesis* **1988**, 489. (b) Cid, M. M.; Dominguez, D.; Castedo, L.; Vazquez-Lopez, E. *Tetrahedron* **1999**, *55*, 5599. (c) Fallis, A. G.; Brinza, I. M. *Tetrahedron* **1997**, *53*, 17543. (d) Boivin, J.; Schiano, A. M.; Zard, S. Z.; Zhang, H. *Tetrahedron Lett.* **1999**, *40*, 4531. (e) Lin, X.; Stien, D.; Weinreb, S. M. *Org. Lett.* **1999**, *4*, 637.

(53) (a) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon−Carbon Bonds*; Pergamon Press: Oxford, 1986. (b) Curran, D. P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 4, pp 715−831.

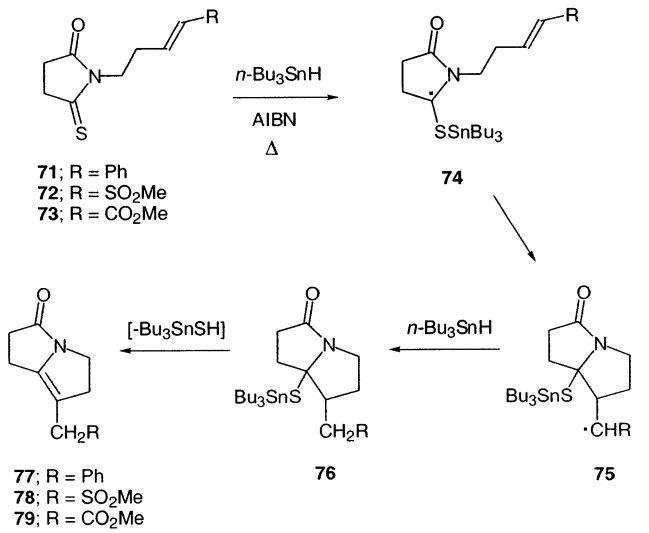
(54) (a) Russell Bowman, W.; Stephenson, P. T.; Young, A. R. *Tetrahedron Lett.* **1995**, *36*, 5623 and references therein. (b) Boivin, J.; Callier-Dublauchet, A. C.; Quiclet-Sire, B.; Schiano, A. M.; Zard, S. Z. *Tetrahedron* **1995**, *51*, 6517.

(55) (a) Reding, M. T.; Fukuyama, T. *Org. Lett.* **1999**, *7*, 973. (b) Feldman, K. S.; Schildknegt, K. *J. Org. Chem.* **1994**, *59*, 1129. (c) Bachi, M. D.; Bosch, E. *J. Org. Chem.* **1992**, *57*, 4696.

(56) Bachi, M. D.; Bosch, E.; Denenmark, D.; Girsh, D. *J. Org. Chem.* **1992**, *57*, 6803.

(57) Padwa, A.; Nimmesgern, H.; Wong, G. S. K. *J. Org. Chem.* **1985**, *50*, 5620.

SCHEME 14



resulting pyrrolizinones **78** and **79** were only obtained in 50% yield. These experiments do demonstrate the feasibility of radical cyclizations using *N*-alkenyl-substituted thioimides and opens the way to the construction of various pyrrolizidine alkaloids.

In conclusion, the photolysis of various thioxapyrrolidinones and thiophthal-imides affords novel [2 + 2] cycloadducts as well as cyclized photoadducts derived from hydrogen transfer chemistry. Ring opening to relieve angle strain occurs readily, and this [2 + 2] photocycloaddition/ring cleavage sequence should prove useful for the preparation of various azapolycyclic rings. The preliminary radical cyclizations also show the potential of using *N*-alkenyl thioimides for the synthesis of five-membered nitrogen heterocycles. Further variations and synthetic applications of this methodology will be reported in due course.

Experimental Section

1-(3-Methyl-but-3-enyl)-5-thioxo-pyrrolidin-2-one (16). A 6.0 g (36 mmol) sample of 1-(3-methyl-but-3-enyl)-pyrrolidine-2,5-dione[58] and 7.3 g (18 mmol) of Lawesson's reagent were suspended in 120 mL of toluene, and the mixture was heated at reflux for 30 min. The solvent was removed under reduced pressure, and the resulting residue was purified by flash silica gel chromatography to give 4.2 g (63%) of thiosuccinimide **16** as a yellow oil: IR (neat) 1753, 1441, and 1397 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.79 (s, 3H), 2.33 (t, 2H, J = 7.4 Hz), 2.67−2.72 (m, 2H), 3.09−3.15 (m, 2H), 4.00 (t, 2H, J = 7.4 Hz), 4.68 (s, 1H), and 4.76 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.5, 28.9, 34.4, 38.9, 40.8, 112.8, 142.3, 178.8, and 210.8. Anal. Calcd for $C_9H_{13}NOS$: C, 58.98; H, 7.15; N, 7.64. Found: C, 58.89; H, 7.18; N, 7.60.

4-Methyl-2-thia-7-aza-tricyclo[5.3.0.0^{1,4}]deca-8-one (17). A 1.1 g (1.8 mmol) sample of thiosuccinimide **16** was dissolved in 100 mL of benzene, and the mixture was deoxygenated by bubbling argon through the solution for 15 min. The solution was irradiated through a Pyrex filter with a 450-W Hanovia high-pressure Hg lamp for 1 h. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.82 g (74%) of thietane **17** as a white solid: mp 49−51 °C; IR (neat) 2953, 1700, and 1398 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.31 (s, 3H), 1.53−1.61 (m, 1H), 1.94−2.00 (m, 1H), 2.28−2.43 (m, 3H), 2.61−2.70 (m, 1H), 2.77 (d, 1H, J = 9.1 Hz), 2.90 (d, 1H, J = 9.1 Hz), 3.51−3.59 (m, 1H), and 4.00−4.13 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.1, 30.7, 31.3, 32.9, 40.2, 41.4, 56.6, 82.4, and 172.7. Anal. Calcd for $C_9H_{13}NOS$: C, 58.98; H, 7.15; N, 7.64. Found: C, 58.77; H, 7.18; N, 7.45.

7a-Ethoxy-7,7-dimethyl-hexahydropyrrolizin-3-one (18). To a stirred suspension containing 1.0 g of Raney-Ni in 3 mL of ethanol was added 0.16 g (0.9 mmol) of thietane **17** in one portion. The reaction mixture was heated at reflux for 6 h, cooled to room temperature, and filtered over Celite. The solvent was removed under reduced pressure, and the crude residue was purified by flash silica gel chromatography to give 0.13 g (74%) of pyrrolizidinone **18** as a colorless oil: IR (neat) 1711, 1468, 1395, and 1157 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.81 (s, 3H), 1.06 (s, 3H), 1.16 (dt, 3H, J = 7.0 and 0.6 Hz), 1.68−1.73 (m, 1H), 1.87−1.94 (m, 1H), 2.05−2.11 (m, 1H), 2.20−2.32 (m, 1H), 2.38−2.46 (m, 1H), 2.72−2.76 (m, 1H), 3.05 (dd, 1H, J = 11.7 and 10.3 Hz), and 3.37−3.49 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 15.6, 20.5, 21.6, 24.1, 34.2, 39.1, 39.5, 43.7, 57.0, 103.6, and 172.1. HRMS Calcd for $C_{11}H_{19}NO_2$: 197.1416. Found: 197.1416.

7-Methyl-7-methyldisulfanylmethyl-2,5,6,7-tetrahydropyrrolizin-3-one (20). A 0.33 g (1.8 mmol) sample of thietane **17** in 6 mL of acetonitrile was cooled to −40 °C and was treated with 0.36 g (1.8 mmol) of DMTSF. After the solution was stirred for 10 min at −40 °C, 1.3 mL (9.1 mmol) of triethylamine was added dropwise. After the solution was warmed to 0 °C, the reaction mixture was diluted with ether and a saturated sodium bicarbonate solution was added. The layers were separated, and the aqueous layer was extracted with ether. The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography to give 0.27 g (65%) of disulfide **20** as a colorless oil: IR (neat) 1699, 1380, 1270, and 958 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.33 (s, 3H), 2.05−2.14 (m, 1H), 2.34−2.45 (m, 1H), 2.42 (s, 3H), 3.02 (s, 2H), 3.14 (d, 2H, J = 2.4 Hz), 3.49−3.54 (m, 2H), and 4.85 (t, 1H, J = 2.4 Hz); ^{13}C NMR ($CDCl_3$ 100 MHz) δ 23.6, 24.1, 39.2, 40.4, 41.9, 43.0, 49.8, 93.4, 154.4, and 174.8; HRMS Calcd for $C_{10}H_{15}NOS_2$: 229.0595. Found: 229.0599.

7,7-Dimethyl-hexahydro-pyrrolizin-3-one (21). To a stirred suspension containing 1.0 g of Raney-Ni in 3 mL of ethanol was added 0.16 g (0.9 mmol) of disulfide **11** in one portion. The mixture was heated at reflux for 6 h, cooled to room temperature, and filtered over Celite. The solvent was removed under reduced pressure, and the crude residue was purified by flash silica gel chromatography to give 0.14 g of pyrrolizin-3-one **21**: IR (neat) 2958, 2871, 1690, 1142, and 1280 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.77 (s, 3H), 1.00 (s, 3H), 1.72−2.07 (m, 4H), 2.40−2.44 (m, 1H), 2.59−2.2.62 (m, 1H), 3.10−3.11 (m, 1H), 3.37−3.43 (m, 1H), and 3.60 (t, 1H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.3, 20.2, 24.7, 34.6, 38.5, 39.9, 41.9, 70.2, and 175.0. Anal. Calcd for $C_9H_{14}NO$: C, 71.02; H, 9.27; N, 9.20. Found: C, 70.78; H, 9.11; N, 9.06.

1-But-3-enyl-5-thioxo-pyrrolidin-2-one (22). To a solution of 5.5 g (36 mmol) of 1-but-3-enyl-pyrrolidine-2,5-dione[59] in 120 mL of toluene was added 8.1 g (20 mmol) of Lawesson's reagent, and the suspension was heated at reflux for 45 min. The solvent was removed under reduced pressure, and the orange residue was purified by flash silica gel chromatography to give 4.2 g (68%) of thiosuccinimide **22** as a yellow oil: IR (neat) 1748, 1439, 1397, and 1197 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.35−2.43 (m, 2H), 267−2.72 (m, 2H), 3.08−3.13 (m, 2H), 3.95 (t, 2H, J = 7.4 Hz), 5.00−5.07 (m, 2H), and 5.78−5.81 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.8, 30.9, 38.8, 41.5, 117.6, 134.4, 178.8, and 210.8. HRMS Calcd for $C_8H_{11}NOS$: 169.0561. Found: 169.0568.

7-Mercaptomethyl-1,2,5,6-tetrahydro-pyrrolizin-3-one (24). A 0.28 g (6.2 mmol) sample of thiosuccinimide **22**

(58) Burnett, D. A.; Choi, J.-K.; Hart, D. J.; Tsai, Y.-M. *J. Am. Chem. Soc.* **1984**, *106*, 8201.

(59) Gesson, J. P.; Jacquesy, J. C.; Rambaud, D. *Bull. Soc. Chim. Fr.* **1992**, *129*, 227.

was dissolved in 20 mL of benzene, and the mixture was deoxygenated by bubbling argon through the solution for 15 min. The solution was irradiated in a Pyrex test tube with a 450-W Hanovia high-pressure Hg lamp for 1 h. The solvent was removed under reduced pressure, and the orange residue was purified by flash silica gel column chromatography to give 0.035 g (13%) of thiol **24**: IR (neat) 2927, 2858, 1678, 1407, and 1367 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.52 (t, 1H, J = 7.3 Hz), 2.56−2.60 (m, 2H), 2.74−2.78 (m, 2H), 2.96−3.00 (m, 2H), 3.25 (d, 2H, J = 7.3 Hz), and 3.67 (t, 2H, J = 8.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.8, 21.4, 34.7, 34.8, 40.2, 109.7, 141.7, and 170.7. HRMS Calcd for $C_8H_{11}NOS$: 169.0561. Found: 169.0560.

1-(2-Cyclopent-1-enyl-ethyl)-5-thioxo-pyrrolidin-2-one (25). A 3.9 g (20 mmol) sample of 1-(2-cyclopent-1-enyl-ethyl)-pyrrolidine-2,5-dione[60] and 4.1 g (10 mmol) of Lawesson's reagent were suspended in 100 mL of toluene, and the mixture was heated at reflux for 30 min. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 3.3 g (78%) of thiosuccinimide **25** as a pale-yellow oil: IR (neat) 1748, 1440, 1396, and 1178 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.77−1.87 (m, 2H), 2.24−2.31 (m, 4H), 2.38 (t, 2H, J = 7.4 Hz), 2.66−2.71 (m, 2H), 3.08−3.13 (m, 2H), 3.96−4.02 (m, 2H), and 5.36 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.6, 28.0, 28.9, 32.7, 35.2, 38.9, 40.9, 126.2, 140.7, 178.7, and 210.7. Anal. Calcd for $C_{11}H_{15}NOS$: C, 63.12; H, 7.22; N, 6.69. Found: C, 63.27; H, 7.20; N, 6.65.

2-Thia-10-aza-tetracyclo[8.3.0^{1,7}.0^{3,7}]trideca-11-one (26). A 1.3 g (6.2 mmol) sample of thiosuccinimide **25** was dissolved in 100 mL of benzene, and the mixture was deoxygenated by bubbling argon through the solution for 15 min. The solution was irradiated for 1 h through a Pyrex filter with a 450-W Hanovia high-pressure Hg lamp. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.97 g (74%) of thietane **26** as a white solid: mp 95−97 °C; IR (neat) 1701, 1398, 1327, and 1156 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.39 (dt, 1H, J = 13.6 and 6.0 Hz), 1.59−1.69 (m, 1H), 1.73−1.93 (m, 5H), 2.20−2.37 (m, 4H), 2.58−2.70 (m, 1H), 3.45−3.56 (m, 2H), and 4.02 (dd, 1H, J = 9.8 and 7.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.0, 31.6, 32.8, 33.5, 34.6, 37.1, 40.4, 42.6, 67.6, 78.7, and 172.8. Anal. Calcd. for $C_{11}H_{15}NOS$: C, 63.12; H, 7.22; N, 6.69. Found: C, 62.94; H, 7.24; N, 6.64.

7,7-Spiro-cyclopentyl-hexahydro-pyrrolizin-3-one (28). A 0.18 g (0.9 mmol) sample of thietane **26** was added in one portion to a slurry of 2.0 g of Raney-Ni in 15 mL of ethanol at room temperature, and the mixture was heated for 6 h at 80 °C. The mixture was allowed to cool to room temperature, filtered through a pad of Celite, and washed with ethanol, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel column chromatography to give 0.086 g (55%) of lactam **28** as an oil: IR (neat) 2951, 2869, 1693, 1411, and 1278 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.16−1.22 (m, 1H), 1.48−1.80 (m, 8H), 1.88−2.07 (m, 3H), 2.41 (ddd, 1H, J = 16.7, 9.9 and 2.9 Hz), 2.68 (dt, 1H, J = 16.8 and 9.5 Hz), 3.11−3.17 (m, 1H), 3.35−3.42 (m, 1H), and 3.79 (t, 1H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.9, 24.8, 25.0, 30.8, 34.5, 34.7, 35.1, 40.4, 40.8, 50.3, 68.9, and 174.7. Anal. Calcd. for $C_{11}H_{17}NO$: C, 73.69; H, 9.56; N, 7.82. Found: C, 73.42; H, 9.51; N, 7.78.

7a-Ethoxy-7,7-spiro-cyclopentyl-hexahydropyrrolizin-3-one (29). The minor component isolated from the above silica gel column contained 0.011 g (7%) of aminal **29**, which was obtained as a very labile oil; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.13−1.28 (m, 1H), 1.16 (t, 3H, J = 7.2 Hz), 1.28−1.48 (m, 1H), 1.50−1.82 (m, 5H), 1.83−2.17 (m, 4H), 2.29−2.48 (m, 2H), 2.69−2.83 (m, 1H), 3.04−3.11 (m, 1H), and 3.34−3.47 (m, 3H).

2,5,6,7-Tetrahydro-pyrrolizin-3-one (27). A 0.11 g (0.5 mmol) sample of thietane **26** in 3 mL of acetonitrile was cooled to −40 °C and was treated with 0.1 g (0.5 mmol) of DMTSF. After the solution was stirred for 10 min at −40 °C, 0.3 mL (2.5 mmol) of triethylamine was added dropwise. After the solution was warmed to 0 °C, the solution was diluted with ether and 10 mL of a saturated sodium bicarbonate was added. The layers were separated, and the aqueous layer was extracted with ether. The combined organic layer was dried over $MgSO_4$, concentrated under reduced pressure, and purified by flash silica gel chromatography to give 0.12 g (92%) of disulfide **27** as a colorless oil: IR (neat) 1701, 1445, 1345, and 953 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.64−1.99 (m, 6H), 2.01−2.40 (m, 2H), 2.31 (s, 3H), 3.08 (t, 1H, J = 7.7 Hz), 3.19 (dd, 2H, J = 5.4 and 2.4 Hz), 3.27−3.49 (m, 2H), and 4.77 (t, 1H, J = 2.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 23.6, 32.9, 37.0, 39.1, 39.8, 42.5, 52.0, 59.6, 94.7, 151.0, and 173.9. HRMS Calcd for $C_{12}H_{17}NOS_2$: 255.0752. Found: 255.0746.

Further reduction of **27** with Raney-Ni in ethanol afforded lactam **28** in 95% yield.

2-(2-Cyclopent-1-enyl-ethyl)-3-thioxo-2,3-dihydro-isoindol-1-one (30). A sample containing 0.85 g of 2-(2-cyclopent-1-enyl-ethyl)-isoindole-1,3-dione[61] was dissolved in 40 mL of toluene and was treated with 0.7 g of Lawesson's reagent. After the solution was heated for 30 min at reflux, the solvent was removed under reduced pressure and the residue was purified by flash silica gel chromatography to give 0.46 g (51%) of thiophthalimide **30** as a pale-yellow oil: IR (neat) 2838, 1752, 1598, and 1460 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.86 (m, 2H), 2.25 (m, 2H), 2.33 (m, 2H), 2.49 (m, 2H), 4.17 (t, 2H, J = 7.3 Hz), 5.38 (s, 1H), 7.69 (m, 2H), 7.76 (dd, 1H, J = 5.5 and 3.2 Hz), and 7.95 (dd, 1H, J = 5.5 and 3.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.5, 29.4, 32.6, 35.1, 39.5, 122.6, 123.8, 126.0, 127.3, 133.1, 134.0, 137.1, 140.7, 169.5, and 196.7. HRMS Calcd for $C_{15}H_{15}NOS$: 257.0874. Found: 257.0865

10b-Mercapto-1,2,3,5,10b,10c-hexahydro-5a-aza-cyclopenta[*c*]fluoren-6-one (32). A sample of 0.3 g of thiophthalimide **30** was dissolved in 25 mL of CH_2Cl_2, and the mixture was deoxygenated by bubbling argon through the solution for 15 min. The solution was irradiated with a 450-W Hanovia high-pressure Hg lamp for 1 h in a Pyrex test tube. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.19 g (64%) of photoproduct **32** as a white solid: mp 104−105 °C; IR (neat) 2954, 1689, 1466 and 1390 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.56−1.68 (m, 1H), 1.86−2.16 (m, 4H), 2.41−2.43 (m, 3H), 3.80−3.88 (m, 1H), 4.61−4.70 (m, 1H), 5.64 (d, 1H, J = 2.4 Hz), 7.47−7.51 (m, 1H), 7.53−7.63 (m, 2H), and 7.86 (d, 1H, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.2, 29.23, 30.6, 37.8, 51.0, 70.6, 113.8, 122.4, 123.9, 129.1, 130.9, 132.1, 140.8, 149.5, and 165.1. HRMS Calcd for $C_{15}H_{15}NOS$: 257.0874. Found: 257.0872.

2-(2-Cyclohex-1-enyl-ethyl)-3-thioxo-2,3-dihydro-isoindol-1-one (31). A 5.1 g (20 mmol) sample of 2-(2-cyclohex-1-enyl-ethyl)-isoindole-1,3-dione[61] and 8.1 g (20 mmol) of Lawesson's reagent were suspended in 45 mL of toluene, and the mixture was heated at reflux for 20 min. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 5.0 g of thiophthalimide **31** as an orange solid: mp 48−49 °C; IR (neat) 2858, 1731, 1603, 1470, and 1347 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.51 (m, 2H), 1.62 (m, 2H), 1.87 (m, 2H), 2.04 (m, 2H), 2.32 (t, 2H, J = 7.3 Hz), 4.11 (t, 2H, J = 7.3 Hz), 5.54 (s, 1H), 7.67 (m, 2H), 7.75 (ddd, 1H, J = 8.1, 4.8, and 3.6 Hz), 7.95 (ddd, 1H, J = 6.3, 3.6, and 0.7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.1, 22.7, 25.2, 28.1, 35.9, 39.6, 122.5, 123.6, 123.7, 127.2, 132.9, 133.8, 134.1, 137.0, 169.5, and 196.7. Anal. Calcd for $C_{16}H_{17}NOS$: C, 70.81; H, 6.31; N, 5.16. Found: C, 70.74; H, 6.31; N, 5.17.

12b-Mercapto-2,3,4,6,12b,12c-hexahydro-1*H*-isoindolo-[1,2-a]isoquin-olin-8-one (33). A 0.3 g sample of thiophthalimide **31** was dissolved in 25 mL of CH_2Cl_2 in a Pyrex test

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tube, and the mixture was deoxygenated by bubbling argon through the solution for 15 min. The solution was irradiated with a 450-W Hanovia high-pressure Hg lamp for 1.5 h. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel to give 0.22 g (73%) of photoproduct **33** as a white solid: mp 174−175 °C; IR (neat) 2459, 1690, 1614, 1404 and 1260 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.27−1.35 (m, 2H), 1.74−1.83 (m, 2H) 1.90−2.00 (m, 3H), 2.29−2.43 (m, 2H), 2.46 (d, 1H, J = 2.9 Hz), 3.86 (dd, 1H, J = 18.1 and 1.6 Hz), 4.59 (ddd, 1H, J = 18.1, 6.7 and 3.8 Hz), 5.55 (t, 1H, J = 2.1 Hz), 7.49 (t, 1H, J = 7.5 Hz), 7.58 (t, 1H, J = 7.5 Hz), 7.73 (d, 1H, J = 7.5 Hz), and 7.85 (d, 1H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.3, 25.7, 29.0, 34.1, 36.5, 46.9, 70.8, 116.9, 123.0, 124.0, 129.1, 130.4, 131.9, 135.6, 150.0, and 164.2. Anal. Calcd for $C_{16}H_{17}NOS$: C, 70.82; H, 6.32; N, 5.17. Found: C, 70.76; H, 6.29; N, 5.05.

2,3,4,6-Tetrahydro-1*H*-isoindolo[1,2-a]isoquinolin-8-one (34). A 0.047 g sample of lactam **33** was dissolved in 4 mL of methanol, and 0.03 g of *p*-toluenesulfonic acid was added. The reaction mixture was allowed to stir for 24 h at room temperature. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give (64%) of compound **34** as a white solid: mp 95−96 °C; IR (neat) 2931, 2862, 1690, 1404, and 1112; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.86−1.92 (m, 2H) 2.25−2.31 (m, 2H), 2.56−59 (m, 2H), 2.89−2.91 (m, 2H), 3.83−3.86 (m, 2H), 5.85 (t, 1H, J = 4.5 Hz), 7.43 (dt, 1H, J = 7.63 and 1.0 Hz), 7.53 (dt; 1H, J = 7.9 and 1.0 Hz), 7.82 (d, 1H, J = 7.6 Hz), and 7.88 (d, 1H, J = 1.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.7, 25.4, 25.5, 29.2, 38.1, 119.4, 123.3, 123.6, 128.1, 128.2, 128.4, 130.7, 130.8, 131.4, 135.2, and 165.3. Anal. Calcd for $C_{16}H_{15}NO$: C, 80.97; H, 6.38; N, 5.91. Found: C, 80.73; H, 6.24; N, 5.85.

2-(3-Methyl-but-3-enyl)-3-thioxo-2,3-dihydro-isoindol-1-one (35). A 1.0 g (4.5 mmol) sample of 2-(3-methyl-but-3-enyl)-isoindole-1,3-dione[62] and 1.2 g (2.9 mmol) of Lawesson's reagent were suspended in 80 mL of toluene, and the mixture was heated at reflux for 20 min. The solvent was removed under reduced pressure, and the resulting residue was purified by flash silica gel chromatography to give 0.69 g (69%) of thioimide **35** as an orange oil: IR (neat) 2971, 1737, 1644, and 1465 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.83 (s, 3H), 2.43 (t, 2H, J = 7.3 Hz), 4.17 (t, 2H, J = 7.3 Hz), 4.69 (s, 1H), 4.75 (s, 1H), 7.68 (m, 2H), 7.76 (dd, 1H, J = 5.6 and 3.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.4, 35.7, 39.4, 112.7, 122.7, 123.7, 127.2, 133.1, 134.0, 137.1, 142.1, 169.6, and 196.7. Anal. Calcd for $C_{13}H_{13}NOS$: C, 67.50; H, 5.66; N, 6.06. Found: C, 67.34; H, 5.75; N, 5.94.

10b-Mercapto-2-methyl-1,10b-dihydro-4*H*-pyrido[2,1-a]isoindol-6-one (36). A sample of 0.15 g of thiophthalimide **35** was dissolved in 25 mL of CH_2Cl_2, and the mixture was deoxygenated by bubbling argon through the solution for 15 min. The solution was irradiated with a 450-W Hanovia high-pressure Hg lamp for 1 h in a Pyrex test tube. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.11 g (73%) of photoproduct **36** as a white solid: mp 102−104 °C (lit[63] mp 101−102.5 °C); IR (neat) 2839, 1700, 1466 and 1396 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.80 (s, 3H), 2.39−2.45 (m, 1H), 2.55 (s, 1H), 2.70−2.78 (m, 1H), 3.81−3.91 (m, 1H), 4.58−4.65 (m, 1H), 5.62(d, 1H, J = 0.4 Hz), 7.47−7.59 (m, 1H), 7.62−7.69 (m, 2H), and 7.84 (dd, 1H, J = 1.0 and 6.7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.3, 37.1, 43.6, 66.3, 117.8, 122.1, 123.9, 129.2, 129.7, 130.5, 132.3, 149.9, and 164.8. Anal. Calcd for $C_{13}H_{13}NOS$: C, 67.50; H, 5.66; N, 6.06. Found: C, 67.58; H, 5.49; N, 5.89.

1-But-3-enyl-3,4-dimethyl-pyrrole-2,5-dione. A solution of 3.5 g (28 mmol) of 2,3-dimethylmaleic anhydride in 120 mL of toluene was treated with 3.2 g (44 mmol) of the known buten-3-enylamine.[64] The mixture was heated at reflux for 3 h in a Dean−Stark apparatus and then allowed to cool to room temperature. The solvent was removed under reduced pressure, and the resulting oily residue was purified by flash silica gel chromatography to give 4.7 g (94%) of the titled compound as a colorless oil: IR (neat) 3078, 2941, 1770, 1717, and 1405 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.93 (d, 6H, J = 5.1 Hz), 2.29−2.35 (m, 2H), 3.52−3.56 (m, 2H), 4.98−5.29 (m, 2H), and 5.66−5.77 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 8.8, 33.1, 37.3, 117.4, 134.8, 137.2, and 172.3.

1-But-3-enyl-3,4-dimethyl-5-thioxo-1,5-dihydro-pyrrol-2-one (42). A solution containing 2.8 g (16 mmol) of the above dione in 100 mL of toluene was treated with 2.8 g (7.0 mmol) of Lawesson's reagent. The mixture was heated at reflux for 2 h and then cooled to room temperature. The solvent was removed under reduced pressure, and the resulting oily residue was subjected to flash silica gel chromatography to give 2.2 g (73%) of monothiomaleimide **42** as a red oil: IR (neat) 3078, 2938, 1725, and 1396 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.91 (dd, 3H, J = 2.9 and 1.3 Hz), 2.07 (dd, 3H, J = 2.9 and 1.3 Hz), 2.33−2.39 (m, 2H), 3.88 (t, 2H, J = 1.3 Hz), 4.97−5.05 (m, 2H), and 5.70−5.77 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 9.1, 10.9, 32.5, 40.4, 117.3, 130.2, 134.7, 141.0, 174.3, and 202.5. HRMS Calcd for $C_{10}H_{13}NOS$: 195.0718. Found: 195.0716.

8a-Mercapto-1,2-dimethyl-8,8a-dihydro-5*H*-indolizin-3-one (43). A solution containing 0.5 g (2.6 mmol) of **42** in 100 mL of CH_2Cl_2 was deoxygenated by bubbling Ar through the solution for 15 min. The solution was irradiated with a 450-W Hanovia medium-pressure Hg lamp for 2.5 h. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.3 g (62%) of indolizidone **43** as a colorless oil: IR (neat) 3050, 2919, 2515, 1678, 1417, and 1133 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.79 (d, 3H, J = 1.1 Hz), 2.04 (d, 3H, J = 1.1 Hz), 2.12−2.21 (m, 2H), 2.44−2.50 (m, 1H), 3.69−3.77 (m, 1H), 4.06−4.44 (m, 1H), 5.70−5.74 (m, 1H), and 5.84−5.88 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 8.6, 10.5, 36.1, 37.4, 67.9, 121.0, 124.8, 127.5, 153.6, and 168.1. Anal. Calcd for $C_{10}H_{13}NOS$: C, 61.52; H, 6.72; N, 7.18. Found: C, 61.47; H, 6.50; N, 6.88.

3,4-Dimethyl-1-(3-methyl-but-3-enyl)pyrrole-2,5-dione. A solution of 3.0 g (24 mmol) of 2,3-dimethyl-maleic anhydride in 120 mL of toluene was treated with 3.2 g (38 mmol) of the known 3-methyl-but-3-enylamine.[65] The mixture was heated at reflux for 3 h in a Dean−Stark apparatus and then allowed to cool to room temperature. The solvent was removed under reduced pressure, and the resulting oily residue was purified by flash silica gel chromatography to give 4.4 g (96%) of the title compound as a colorless oil: IR (neat) 3075, 2941, 1770, 1716, and 1407 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.74 (s, 3H), 1.92 (d, 6H, J = 1.0 Hz), 2.26 (t, 2H, J = 7.3 Hz), 3.59 (t, 2H, J = 7.3 Hz), 4.63 (s, 1H), and 4.71 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 8.8, 22.2, 36.4, 36.7, 112.6, 137.1, 142.4, and 172.3.

3,4-Dimethyl-1-(3-methyl-but-3-enyl)-5-thioxo-1,5-dihydropyrrol-2-one (44). A solution of 2.9 g (15 mmol) of the above dione in 100 mL of toluene was treated with 2.7 g (6.6 mmol) of Lawesson's reagent. The mixture was heated at reflux for 2 h and then cooled to room temperature. The solvent was removed under reduced pressure, and the resulting oily residue was subjected to flash silica gel chromatography to give 2.1 g (69%) of monothiomaleimide **44** as a red oil: IR (neat) 3073, 2939, 1731, and 1350 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.77 (s, 3H), 1.92 (d, 3H, J = 1.3 Hz), 2.07 (d, 3H, J = 1.3 Hz), 2.30 (t, 2H, J = 7.0 Hz), 3.91−3.95 (m, 2H), 4.65 (d, 1H, J = 1.0 Hz), and 4.72 (d, 1H, J = 1.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 9.1, 10.9, 22.5, 39.6, 112.5, 130.2, 141.1, 142.5, 174.3, and 202.5; HRMS Calcd for $C_{11}H_{15}NOS$: 209.0874. Found: 209.0871.

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8a-Mercapto-1,2,7-trimethyl-8,8a-dihydro-5*H*-indolizin-3-one (45). A solution containing 0.5 g (2.6 mmol) of **44** in 100 mL of CH_2Cl_2 was deoxygenated by bubbling Ar through the solution for 15 min. The solution was irradiated with a 450-W Hanovia medium-pressure Hg lamp for 2.5 h. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.32 g (64%) of indolizidone **45** as a colorless oil: IR (neat) 2968, 2917, 2513, 1704, 1412, and 1126 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.73 (s, 3H), 1.80 (d, 3H, J = 1.3 Hz), 1.81 (s, 1H), 2.06 (d, 3H, J = 1.3 Hz), 2.11−2.17 (m, 1H), 2.29 (d, 1H, J = 16.8 Hz), 3.67−3.74 (m, 1H), 4.35−4.41 (m, 1H), 5.56 (d, 1H, J = 1.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 8.7, 10.6, 23.3, 37.2, 40.8, 68.5, 118.4, 127.6, 128.9, 153.3, and 168.2. Anal. Calcd for $C_{11}H_{15}NOS$: C, 63.13; H, 7.23; N, 6.70. Found: C, 63.02; H, 6.95; N, 6.49.

1-(2-Cyclohex-1-enyl-ethyl)-3,4-dimethyl-pyrrole-2,5-dione. A solution containing 2.5 g (20 mmol) of 2,3-dimethylmaleic anhydride in 120 mL of toluene was treated with 2.5 g (20 mmol) of the commercially available 2-cyclohex-1-enylethylamine. The mixture was heated at reflux for 3 h in a Dean−Stark apparatus and then allowed to cool to room temperature. The solvent was removed under reduced pressure, and the resulting oily residue was purified by flash silica gel chromatography to give 4.2 g (91%) of the titled compound as a colorless oil: IR (neat) 2931, 1770, 1716, and 1406 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.47−1.68 (m, 4H), 1.88−1.95 (m, 4H), 1.93 (d, 6H, J = 0.6 Hz), 2.13−2.17 (m, 2H), 3.54 (t, 2H, J = 7.3 Hz), and 5.34 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 8.8, 22.4, 23.0, 25.5, 28.0, 36.6, 37.0, 123.8, 134.5, 137.1, and 172.3.

1-(2-Cyclohex-1-enyl-ethyl)-3,4-dimethyl-5-thioxo-1,5-dihydropyrrol-2-one (46). A solution containing 3.5 g (15 mmol) of the above dione in 100 mL of toluene was treated with 3.0 g (7.5 mmol) of Lawesson's reagent. The mixture was heated at reflux for 2 h and then cooled to room temperature. The solvent was removed under reduced pressure, and the resulting oily residue was subjected to flash silica gel chromatography to give 2.7 g (68%) of monothiomaleimide **46** as a red oil; IR (neat) 3025, 2932, 1728, and 1396 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.46−1.61 (m, 4H), 1.92−2.02 (m, 4H), 1.92 (d, 3H, J = 1.0 Hz), 2.07 (d, 3H, J = 1.0 Hz), 2.19 (t, 2H, J = 7.3 Hz), 3.88 (t, 2H, J = 7.3 Hz), and 5.35 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 9.1, 22.4, 23.0, 25.5, 28.3, 36.3, 39.9, 123.8, 130.2, 134.5, 141.0, 174.3, and 202.5. HRMS Calcd for $C_{14}H_{19}NOS$: 249.1187. Found: 249.1184.

10b-Mercapto-1,2-dimethyl-7,8,9,10,10a,10b-hexahydro-5*H*-pyrrolo[2,1-a]-isoquinolin-3-one (47). A solution of 0.5 g (2.0 mmol) of **46** in 100 mL of CH_2Cl_2 was deoxygenated by bubbling Ar through the solution for 15 min. The solution was irradiated with a 450-W Hanovia medium-pressure Hg lamp for 2.5 h, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.36 g (72%) of indolizidone **47** as a 1:3 mixture of diastereomers. The minor diastereomer **47a** was isolated as a white solid: mp 104−105 °C; IR (neat) 2929, 2851, 1693, 1410, and 1125 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.82 (dq, 1H, J = 12.4 and 3.8 Hz), 1.16−1.25 (m, 1H), 1.35−1.48 (m, 2H), 1.71−1.75 (m, 1H), 1.80 (d, 3H, J = 1.3 Hz), 1.82−1.84 (m, 1H), 1.93−2.00 (m, 1H), 2.05 (d, 3H, J = 1.3 Hz), 2.13−2.17 (m, 1H), 2.31−2.36 (m, 2H), 3.69 (dd, 1H, J = 17.8 and 2.2 Hz), 4.39 (dd, 1H, J = 17.8 and 4.4 Hz), 5.47 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 8.7, 11.7, 26.5, 29.9, 30.8, 36.6, 36.8, 48.8, 71.7, 114.1, 129.2, 139.4, 151.2, and 168.3. Anal. Calcd for $C_{14}H_{19}NOS$: C, 67.44; H, 7.69; N, 5.62. Found: C, 67.25; H, 7.40; N, 5.33.

The major diastereomer **47b** was obtained as a white solid; dec 155 °C; IR (neat) 2923, 2855, 2493, 1677, and 1420 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.20−1.46 (m, 3H), 1.48 (s, 1H), 1.69−2.00 (m, 3H), 1.80 (d, 3H, J = 1.0 Hz), 2.03−2.22 (m, 2H), 2.14 (d, 3H, J = 1.0 Hz), 3.68 (dd, 1H, J = 117.8 and 1.3 Hz), 4.31−4.38 (m, 1H), and 5.50 (dd, 1H, J = 4.4 and 2.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 8.7, 12.3, 25.6, 26.0, 30.3, 34.6, 36.2, 45.0, 73.0, 117.2, 127.2, 135.6, 155.0, and 167.3. Anal. Calcd for $C_{14}H_{19}NOS$: C, 67.44; H, 7.69; N, 5.62. Found: C, 67.30; H, 7.55; N, 5.38.

1-But-3-enyl-pyrrolidine-2,5-dithione (53). To a solution containing 2.1 g (14 mmol) of the known 1-(but-3-enyl)-pyrrolidine-2,5-dione[59] in 50 mL of toluene was added 8.2 g (20 mmol) of Lawesson's reagent, and the mixture was heated at reflux for 30 min. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.98 g (40%) of dithiosuccinimide **53** as a pale-yellow oil: IR (neat) 1639, 1419, and 1363 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.41 (m, 2H), 3.16 (s, 4H), 4.36 (t, 2H, J = 7.6 Hz), 5.12 (m, 2H), and 5.80 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 29.8, 41.1, 44.6, 117.3, 133.9, and 211.9. HRMS Calcd for $C_8H_{11}NS_2$: 185.0333. Found: 185.0331.

2-Thia-7-aza-tricyclo[5.3.0.0^{1,4}]deca-8-thione (54). A 0.19 g (1.0 mmol) sample of dithiosuccinimide **53** was dissolved in 50 mL of benzene, and the mixture was deoxygenated by bubbling argon through the solution for 15 min. The solution was irradiated through a Pyrex filter with a 450-W Hanovia high-pressure Hg lamp for 25 min. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.083 g (43%) of thietane **54**: IR (neat) 2942, 1476, 1323, 1122, and 1026 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.01−2.19 (m, 2H), 2.23−2.34 (m, 1H), 2.64−2.72 (m, 2H), 2.96−3.18 (m, 2H), 3.28 (t, 1H, J = 9.5 Hz), 3.65−3.72 (m, 1H), 3.79−3.90 (m, 1H), and 4.39−4.46 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.2, 33.2, 38.0, 43.5, 46.5, 50.6, 84.1, and 198.4. Anal. Calcd for $C_8H_{11}NS_2$: C, 51.88; H, 5.99; N, 7.57. Found: C, 51.80; H, 6.12; N, 7.44.

1,2,5,6-Tetrahydro-pyrrolizine-3-thione (55). The second fraction isolated from the column contained 0.036 g (19%) of thione **55**: IR (neat) 2925, 1495, 1344 and 1127 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.61−2.69 (m, 2H), 2.96−3.03 (m, 2H), 3.32 (t, 2H, J = 7.6 Hz), 3.79 (t, 2H, J = 7.9 Hz), and 5.00 (t, 1H J = 2.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.1, 33.8, 43.9, 47.3, 103.6, 150.1, and 192.7. HRMS Calcd for C_7H_9NS: 139.0456. Found: 139.0454.

7-Mercaptomethyl-1,2,5,6-tetrahydro-pyrrolizin-3-one (56). Recrystallization of a sample of **54** from ethyl acetate gave the ring-opened product **56** as a yellow solid: mp 107−108 °C; IR (neat) 2946, 1486, and 1168 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.58 (t, 3H, J = 7.6 Hz), 2.58−2.62 (m, 2H), 3.00−3.02 (m, 2H), 3.21−3.28 (m, 4H), 3.75−3.79 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.3, 2.52, 34.7, 43.8, 46.8, 116.1, 145.3, and 192.4. Anal. Calcd for $C_8H_{11}NS_2$: C, 51.85; H, 5.98; 7.56. Found: C, 51.89; H, 5.99; N, 7.54.

1-(3-Methyl-but-3-enyl)-pyrrolidine-2,5-dithione (57). A 1.4 g (8.3 mmol) sample of the known 1-(3-methylbut-3-enyl)-pyrrolidine-2,5-dione[58] and 3.8 g (9.5 mmol) of Lawesson's reagent were suspended in 75 mL of toluene, and the mixture was heated at reflux for 30 min. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.8 g (49%) of dithioimide **57**:[16b] IR (neat) 3073, 2971, 2689, 1644, 1419, and 1168 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.81 (s, 3H), 2.33 (t, J = 8.3 Hz, 2H), 3.16 (s, 4H), 4.39 (t, 2H, J = 8.3 Hz), 4.75 (s, 1H), and 4.81 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.7, 33.1, 41.2, 44.3, 112.4, 142.0, and 211.8. Anal. Calcd for $C_9H_{13}NS_2$: C, 54.26; H, 6.58; N, 7.03. Found: C, 54.42; H, 6.55; N, 6.98.

4-Methyl-2-thia-7-aza-tricyclo[5.3.0.0^{1,4}]deca-8-thione (58). A 0.1 g sample of dithiosuccinimide **57** was dissolved in 25 mL of benzene, and the mixture was deoxygenated by bubbling argon through the solution for 15 min. The solution was irradiated with a 450-W Hanovia high-pressure Hg lamp for 15 min in a Pyrex test tube. At the end of this time, the solvent was removed under reduced pressure and the resulting orange residue was purified by flash silica gel column chromatography to give 0.073 g (72%) of thietane **58**,[16b] a light-yellow oil that crystallized on standing: mp 81−82 °C; ^1H

NMR ($CDCl_3$, 300 MHz) δ 1.30 (s, 3H), 1.72 (m, 1H), 2.09 (m, 1H), 2.33 (m, 2H), 2.83 (m, 1H), 2.92 (m, 1H), 2.99 (m, 1H), 3.08 (m, 1H), 3.80 (m, 1H), and 4.32 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.0, 30.9, 33.5, 40.9, 43.6, 45.8, 55.6, 86.6, and 197.7. Anal. Calcd for $C_9H_{13}NS_2$: C, 54.26; H, 6.58; N, 7.03. Found: C, 54.07; H, 6.42; N, 6.87.

7-Methyl-1,2,5,6-tetrahydro-pyrrolizine-3-thione (59). The minor component (10%) isolated from column chromatography was identified as thioamide **59**: IR (neat) 2930, 1487, 1325, and 1109 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.69 (t, 3H, J = 1.4 Hz), 2.54−2.60 (m, 2H), 2.86−2.91 (m, 2H), 3.28−3.33 (m, 2H), and 3.76−3.82 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.5, 19.1, 38.1, 43.9, 47.1, 114.1, 143.9, and 190.6. HRMS Calcd for $C_8H_{11}NS$: 153.0612. Found: 153.0610.

1-(2-Cyclopent-1-enyl-ethyl)-pyrrolidine-2,5-dithione (60). To a solution of 0.78 g (4.0 mmol) of the known 1-(2-cyclopent-1-enyl-ethyl)-pyrrolidine-2,5-dione[60] in 50 mL of toluene was added 2.0 g (4.8 mmol) of Lawesson's reagent, and the mixture was heated at reflux for 30 min. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.5 g (58%) of dithiosuccinimide **60** as a yellow oil: IR (neat) 2843, 1419, and 1362 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.85 (m, 2H), 2.29 (m, 4H), 2.40 (t, 2H, J = 7.1 Hz), 3.16 (s, 4H), 4.41 (t, 2H, J = 7.1 Hz), and 5.42 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.4, 27.0, 32.7, 35.4, 41.3, 44.3, 125.9, 140.5, and 211.9. Anal. Calcd for $C_{11}H_{15}NS_2$: C, 58.62; H, 6.71; N, 6.21. Found: C, 58.69; H, 6.74; N, 6.21.

2-Thia-10-aza-tetracyclo[8.3.0^{1,7}.0^{3,7}]trideca-11-thione (61). A 0.24 g (1.8 mmol) sample of dithiosuccinimide **60** was dissolved in 50 mL of benzene, and the mixture was deoxygenated by bubbling argon through the solution for 15 min. The solution was irradiated with a 450-W Hanovia high-pressure Hg lamp for 20 min. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel to give 0.12 g (48%) of thietane **61** as a light-yellow solid: mp 94−96 °C; IR (neat) 2949, 1478, 1455, 1324, and 929 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.40 (dt, 1H, J = 13.7 and 5.8 Hz), 1.76−2.01 (m, 6H), 2.20−2.43 (m, 3H), 2.92−3.15 (m, 2H), 3.53 (dd, 1H, J = 4.8 and 1.2 Hz), 3.74−3.85 (m, 1H), and 4.41 (dd, 1H, J = 12.6 and 7.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.0, 33.5, 34.0, 34.6, 36.3, 42.7, 43.9, 45.6, 66.7, 83.1, and 197.9. Anal. Calcd for $C_{11}H_{15}NS_2$: C, 58.62; H, 6.71; N, 6.21. Found: C, 58.59; H, 6.84; N, 6.22.

1-(2-Cyclohex-1-enyl-ethyl)-pyrrolidine-2,5-dithione (62). A 6.7 g (32 mmol) sample of the known 1-(2-cyclohex-1-enyl-ethyl)-pyrrolidine-2,5-dione[60] and 13 g (32 mmol) of Lawesson's reagent were suspended in 60 mL of toluene, and the mixture was heated at reflux for 30 min. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography to give 4.4 g (57%) of dithiosuccinimide **62** as a yellow oil that crystallized on standing: mp 44−45 °C; IR (neat) 2853, 1419, 1358, and 1086 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.53 (m, 2H), 1.60 (m, 2H), 1.95 (m, 2H), 2.03 (m, 2H), 2.23 (t, 2H, J = 7.8 Hz), 3.15 (s, 4H), and 4.35 (t, 2H, J = 7.8 Hz), and 5.44 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.4, 23.0, 25.5, 28.6, 33.6, 41.4, 44.8, 124.0, 134.3, and 212.1. Anal. Calcd for $C_{12}H_{17}NS_2$: C, 60.20; H, 7.16; N, 5.85. Found: C, 60.26; H, 7.18; N, 5.74.

2-Thia-11-aza-tetracyclo[9.3.0^{1,8}.0^{3,8}]tetradeca-12-thione (63). A 0.2 g sample of dithiosuccinimide **62** was dissolved in 25 mL of benzene, and the mixture was deoxygenated by bubbling argon through the solution for 15 min. The solution was irradiated with a 450-W Hanovia high-pressure Hg lamp for 30 min at room temperature in a Pyrex test tube. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography to give 0.056 g (30%) of thietane **63** as a light-yellow solid: mp 78−79 °C; IR (neat) 2933, 2863, 1478, 1319, 1158, and 1026 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.41 (m, 2H), 1.60 (m, 1H), 1.77 (m, 4H), 1.98 (m, 2H), 2.18 (m, 1H), 2.45 (m, 2H), 2.95 (m, 1H), 3.09 (m, 1H), 3.41 (t, 1H, J = 5.1 Hz), 3.80 (m, 1H), and 4.30 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.8, 18.5, 28.0, 28.8, 34.4, 40.3, 41.5, 43.2, 45.9, 57.7, 85.8, and 197.4. HRMS Calcd for $C_{12}H_{17}NS_2$: 239.0802. Found: 239.0802.

6-Cyclohex-1-enyl-5-mercapto-1-aza-bicyclo[3.2.0]-heptane-2-thione (64). The second compound isolated from silica gel column chromatography contained 0.056 g (30%) of **64** as a colorless oil, which consisted of a mixture of a 1:1 mixture of diasteromers: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.66 (m, 5H), 1.95 (m, 1H), 2.14 (m, 1H), 2.42 (dd, 1H, J = 13.4 and 8.7 Hz), 2.60 (dd, 1H, J = 13.4 and 7.3 Hz), 2.94 (dd, 1H, J = 17.8 and 8.5 Hz), 3.30 (ddd, 1H, J = 17.1, 8.1 Hz, and 4.4 Hz), 3.32 (t, 1H, J = 7.8 Hz), 4.08 (dd, 1H, J = 10.3 and 7.8 Hz), 4.36 (dd, 1H, J = 10.3 and 7.8 Hz), and 5.66 (dd, 1H, J = 3.4 and 1.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.2, 22.4, 25.3, 28.6, 43.4, 45.5, 53.4, 56.9, 87.5, 126.3, 133.4, and 207.3. HRMS Calcd for $C_{12}H_{17}NS_2$: 239.0802. Found: 239.0800.

1-(4-Methanesulfonyl-but-3-enyl)-pyrrolidine-2,5-dione. A solution containing 1.9 g (8.2 mmol) of methanesulfonylmethyl-phosphonic acid diethyl ester[66] in 40 mL of THF at −78 °C was treated with 3.4 mL (8.2 mmol) of 2.4 M *n*-butyllithium in hexane, and the mixture was allowed to stir for 30 min. A solution of 1.28 g (8.2 mmol) of the known 3-(2,5-dioxo-pyrrolidin-1-yl)-propionaldehyde[67] in 10 mL of THF was added dropwise to the reaction mixture. The solution was allowed to warm gradually to room temperature and was stirred continuously overnight. The mixture was quenched by the addition of 15 mL of an aqueous NH_4Cl solution and extracted with ethyl acetate. The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude mixture was purified by flash silica gel column chromatography to give 1.9 g (45%) of the titled compound as a white solid: mp 127−128 °C; IR (neat) 1772, 1697, 1403, 1306, and 1132 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.57 (dq, 2H, J = 7.0 and 1.2 Hz), 2.72 (s, 4H), 2.91 (s, 3H), 3.80 (t, 2H, J = 7.0 Hz), 6.45 (d, 1H, J = 15.1 Hz), and 6.83 (dt, 1H, J = 15.1 and 6.7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.3, 29.7, 36.7, 42.8, 132.0, 143.7, and 177.1. Anal. Calcd for $C_9H_{13}NO_4S$: C, 46.74; H, 5.67; N, 6.06. Found: C, 46.73; H, 5.69; N, 6.03.

1-(4-Methanesulfonyl-but-3-enyl)-5-thioxo-pyrrolidin-2-one (72). A 0.65 g (1.6 mmol) sample of Lawesson's reagent was added to 0.75 g (3.2 mmol) of the above succinimide in 50 mL of toluene, and the mixture was heated at reflux. After cooling to room temperature, the solvent was evaporated under reduced pressure and the oily residue was purified by flash silica gel column chromatography to afford 0.32 g (40%) of thiosuccinimide **72** as a yellow oil which solidified on standing: mp 64−66 °C; IR (neat) 1751, 1638, 1344, 1299, and 1132 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.62 (m, 2H, J = 7.2 and 1.4 Hz), 2.71−2.76 (m, 2H), 2.91 (s, 3H), 3.11−3.16 (m, 2H), 4.04 (t, 2H, J = 7.2 Hz), 6.42 (d, 1H, J = 15.1 Hz), and 6.85 (dt, J = 15.4 and 7.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.6, 28.8, 38.9, 40.1, 42.7, 132.0, 143.7, 178.7, and 210.7; Anal. Calcd for $C_9H_{13}NO_3S_2$: C, 43.70; H, 5.30; N, 5.66. Found: C, 43.74; H, 5.35; N, 5.65.

5-(2-Oxo-5-thioxo-pyrrolidin-1-yl)-pent-2-enoic Acid Methyl Ester (73). A 3.2 g (7.9 mmol) sample of Lawesson's reagent was added to 3.7 g of methyl 5-(2,5-dioxo-1-pyrrolidino)-2-pentenoate[67] in dry toluene, and the mixture was heated at reflux for 1 h. The solvent was removed under reduced pressure, and the oily residue was subjected to flash silica gel column chromatography to give 2.1 g (53%) of the monothiosuccinimide **73** as a yellow oil: IR (neat) 2842, 1761, 1725, 829, and 717 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.54 (dq, 2H, J = 7.2 and 1.2 Hz), 2.70−2.75 (m, 2H), 3.11−3.16 (m, 2H), 3.72 (s, 3H), 4.02 (t, 2H, J = 7.2 Hz), 5.86 (dd, 1H, J = 15.6 and 1.44 Hz), and 6.89 (dt, 1H, J = 15.6 and 8.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.6, 29.2, 38.7, 40.4, 51.6, 123.2,

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144.2, 166.4, 178.6, and 210.6. HRMS Calcd for $C_{10}H_{13}NO_3S$: 227.0616. Found: 227.0623.

7-Benzyl-1,2,5,6-tetrahydro-pyrrolizin-3-one (77). To a solution of 0.16 g (0.64 mmol) of 1-(4-phenyl-but-3-enyl)-5-thioxo-pyrrolidin-2-one (**71**)[55c] in 50 mL of toluene was added 0.18 g (0.73 mmol) of tris-trimethylsilylsilane[68] and 0.02 g (0.13 mmol) of AIBN. The mixture was heated at reflux, and additional quantities of AIBN were added at 30 min intervals. The mixture was heated for an additional 30 min after the last addition of AIBN. The solution was cooled to room temperature and concentrated under reduced pressure, and the crude residue was purified by flash silica gel column chromatography to give 0.03 g (28%) of the known pyrrolizidine **77**[55c] as a colorless oil: IR (neat) 1685, 1431, 1408, 1364, 1264, and 702 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.35−2.40 (m, 2H), 2.68−2.73 (m, 2H), 2.77−2.83 (m, 2H), 3.33 (s, 2H), 3.61 (t, 2H, J = 8.9 Hz), and 7.15−7.33 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.9, 33.5, 34.8, 36.3, 40.0, 110.5, 126.5, 128.7, 128.8, 129.3, 140.5, and 170.5.

Methanesulfonylmethyl-1,2,5,6-tetrahydro-pyrrolizin-3-one (78). A 0.2 g (0.8 mmol) sample of the monothioimide **72** was dissolved in 50 mL of toluene and was treated with 0.28 g (0.95 mmol) of tributyltin hydride and 0.027 g (0.16 mmol) of AIBN. The resulting mixture was heated at reflux for 2 h and cooled to room temperature, and the solvent was evaporated under reduced pressure. The oily residue was subjected to flash silica gel chromatography to afford 0.085 g (48%) pyrrolizidone **78** as a colorless oil: IR (neat) 1721, 1670, 1434, 1260, and 994 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.63−2.66 (m, 2H), 2.74−2.79 (m, 2H), 2.89 (s, 3H), 3.01−3.11 (m, 2H), 3.65−3.72 (m, 2H), and 3.72 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.1, 34.4, 36.3, 40.3, 40.5, 53.8, 97.3, 148.9, and 170.9. FAB HRMS $[(C_9H_{13}NO_3S) + Li]^+$ Calcd: 222.0776. Found: 222.0786.

Pyrrolizidone **78** was also prepared in the following manner. A 0.19 g (0.8 mmol) sample of monothioimide **72** was dissolved in 50 mL of toluene and was treated with 0.23 g (0.92 mmol) of tris(trimethylsilyl)silane and 0.025 g (0.15 mmol) of AIBN, and the mixture was heated at reflux. At 30 min intervals, a total of four additional 0.023 g samples of AIBN were added to the refluxing mixture. After the last addition, the mixture was allowed to stir for an additional 30 min and was allowed to cool to room temperature. The solvent was evaporated under reduced pressure, and the resulting residue was purified by flash column chromatography to give 0.11 g (68%) of pyrrolizidone **78** as a colorless oil.

(5-Oxo-2,5,6,7-tetrahydro-3H-pyrrolizin-1-yl)-acetic Acid Methyl Ester (79). A 0.17 g (0.75 mmol) sample of monothioimide **75** was dissolved in 50 mL of toluene and was treated with 0.25 g (0.87 mmol) tributyltin hydride and 0.025 g (0.15 mmol) of AIBN. The resulting solution was heated at reflux for 2 h. The reaction mixture was allowed to cool to room temperature and was evaporated under reduced pressure. The oily residue was subjected to flash silica gel chromatography to afford 0.099 g (67%) of pyrrolizidinone **79** as a white solid: mp 64−65 °C; IR (neat) 1721, 1670, 1434, 1260, and 994 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.49−2.54 (m, 2H), 2.69−2.75 (m, 2H), 2.88−2.94 (m, 2H), 3.01 (s, 2H), 3.59−3.66 (m, 2H), and 3.66 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.8, 32.3, 34.6, 36.4, 40.1, 52.0, 103.5, 143.0, 170.6, and 171.4. HRMS Calcd for $C_{10}H_{13}NO_3$: 195.0895. Found: 195.09012.

An alternative method that was also used involved dissolving a 0.18 g (0.8 mmol) sample of monothioimide **75** in 50 mL of toluene. The solution was treated with 0.24 g (0.95 mmol) of tris(trimethylsilyl)silane and 0.026 g (0.16 mmol) of AIBN, and the mixture was heated at reflux. At 30 min intervals, a total of four additional 0.026 g samples of AIBN were added to the refluxing mixture. After the last addition was complete, the mixture was allowed to stir for 30 min and was then allowed to cool to room temperature. The solvent was evaporated under reduced pressure, and the resulting oily residue was purified by flash column chromatography to give 0.12 g (75%) of pyrrolizidone **79**.

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Supporting Information Available: ^1H NMR and ^{13}C NMR spectra for new compounds lacking analyses together with ORTEP drawings for compounds **17** and **47b** in PDF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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