8*H*-ANHYDRO-4-HYDROXY-2-OXO-1,3-THIAZINIUM HYDROXIDES AS MESOIONIC 1,4-DIPOLES‡

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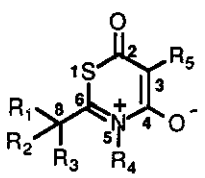
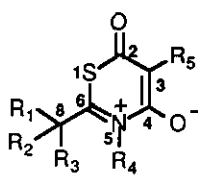
Abstract - The previously unknown 8*H*-anhydro-4-hydroxy-2-oxo-1,3-thiazinium hydroxides (1) were prepared and their 1,4-dipolar cycloaddition behavior was examined. In most cases, elimination of the proton in the 8-position of the mesoionic ring was observed to occur unless extremely reactive dipolarophiles were used. The *S,N*-ketene acetals were converted to the corresponding α-diazo ketones for further study.

Mesoionic compounds have been known for many years and have been extensively utilized as substrates for 1,3-dipolar cycloaddition.[1-7] The term mesoionic is generally restricted to five membered heterocycles that cannot be represented satisfactorily by normal covalent structures and are best described as a resonance hybrid of all possible charged forms.[8,9] The 1,3-dipole embedded within most mesoionic systems readily participates in dipolar cycloaddition reactions with various dipolarophiles. The cycloaddition chemistry of these systems has proven to be quite valuable in natural product synthesis and for the construction of novel heterocyclic systems.[10] In contrast, much less is known about the cycloaddition behavior of 1,4-dipoles whose transient existence was first postulated in 1967.[11] This class of reactive intermediates, while of considerable theoretical interest, attracted little synthetic attention until the elements of a 1,4-dipole were incorporated into a cross-conjugated heteroaromatic betaine[12] by the cyclocondensation of an appropriately substituted monoprotic amidine or thioamide with a 1,3-bielectrophile derived from malonic acid.[13] In connection with our long standing interest dealing with the chemistry of mesoionic compounds,[14] we initiated a study of the cycloaddition behavior of a series of anhydro-4-hydroxy-6-oxo-1,3-thiazinium hydroxides of type (1). The ease with which these dipoles can be prepared and their subsequent dipolar cycloaddition chemistry alerted us to the synthetic value of these mesoionic compounds. Work in our laboratory[15] as well as others[16,17] has shown that these heterocyclic betaines



1a; (R_1, R_2, R_3= alkyl)

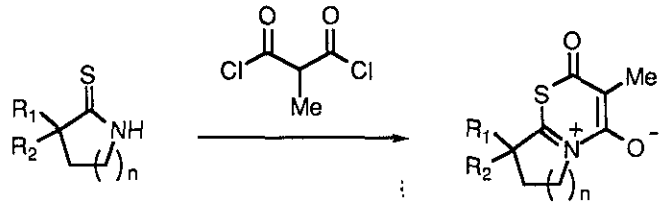


1b; (R_1, R_2, or R_3=H)

‡ Dedicated to Arnold Brossi on the occasion of his 70th birthday.

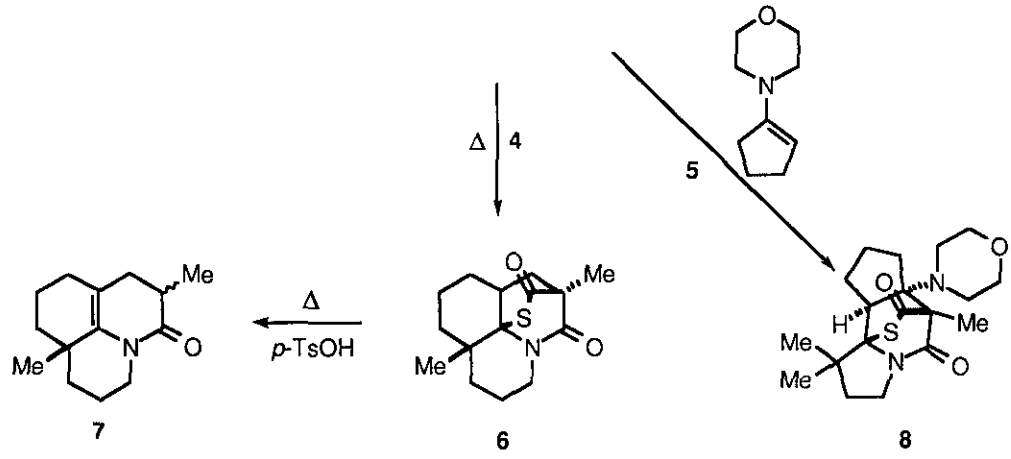
act as classic type II dipoles,[18] providing high yields of cycloadducts with both electron rich and electron deficient dipolarophiles.

Betaines (**1 a**) are highly colored compounds which are easily prepared by cyclocondensation of an appropriate thiolactam with a substituted malonyl dichloride derivative or with carbon suboxide.[15] For example, the sequential treatment of *thiolactams* (**2**) *and* (**3**) *with methyl malonyl dichloride*[19] *in* CH_2Cl_2 at 25°C afforded 1,4-dipoles (**4**) and (**5**) in excellent yield.



2; R_1 = Me; R_2 = $(CH_2)_3CH{=}CH_2$; n = 2
3; R_1 = R_2 = Me; n = 1

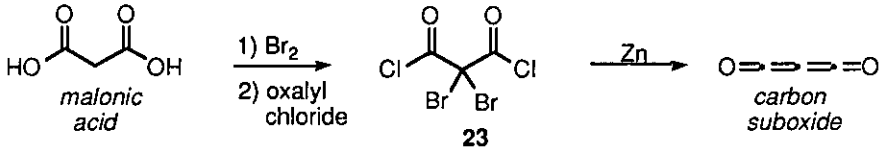
4; R_1 = Me; R_2 = $(CH_2)_3CH{=}CH_2$; n = 2
5; R_1 = R_2 = Me; n = 1



7 **6** **8**

These intensely yellow compounds were found to be stable to flash silica gel chromatography and could be recovered unchanged after months of refrigeration. Heating betaine (**4**) in toluene afforded the intramolecular dipolar cycloadduct (**6**) in 80% isolated yield (see Experimental Section). The formation of **6** is the consequence of *endo* cycloaddition with regard to the dipole and this is in full accord with the lowest energy transition state. The stereochemical assignment was based on comparison to an analogous cycloadduct whose structure had been deduced by X-ray crystallography.[15] Further heating of **6** in the presence of *p*-toluenesulfonic acid produced **7** in near quantitative yield. In a related manner, 1,4-dipole (**5**) underwent bimolecular cycloaddition with 4-(1-cyclopenten-1-yl)morpholine at room temperature to give cycloadduct (**8**) in 87% isolated yield. The regiochemical outcome of the cycloaddition is that predicted by *frontier molecular orbital theory* (FMO).[20] The high *endo* selectivity encountered

At this point in time we turned our attention to the reaction of the 3*H*-thiolactam system with carbon suboxide. Our initial apprehension in using carbon suboxide was a consequence of the harsh conditions used for its generation which traditionally involves the pyrolysis of *O*-acetyltartaric anhydride.[22] A subsequent review of the literature[23] indicated that carbon suboxide could also be obtained from dibromomalonyl dichloride (**23**).[24] Dibromomalonyl dichloride (**23**) was prepared in excellent yield by the sequential treatment of malonic acid with bromine and oxalyl chloride. The procedure was easily executed on a multi-hundred gram scale and the carbon suboxide precursor (**23**) was found to be stable for months under refrigeration. In a typical experiment, carbon suboxide was generated by the addition of an ethereal solution of **23** to zinc dust in refluxing ether. Carbon suboxide (bp 7°C) codistilled with the ether and was efficiently collected using a dry ice acetone condenser. The condenser was directly attached to the flask which contained a magnetically stirred ethereal solution of the appropriate thiolactam at -78°C.



We had previously noted that pyrrolidine-2-thione derived 1,4-dipoles were significantly more stable and well behaved in dipolar cycloaddition chemistry than the corresponding piperidine-2-thione derived dipoles.[15] With this in mind, we subjected 3-methyl-pyrrolidine-2-thione (**13**) to an ethereal solution of carbon suboxide at -78°C. The mixture was allowed to slowly warm to room temperature. The solution remained colorless with no visible reaction occurring until room temperature was achieved. At that time, a bright yellow solid which consisted of dipole (**26**) precipitated from the reaction mixture. All attempts to purify and characterize dipole (**26**) resulted in the formation of *S,N*-ketene acetal (**22**).

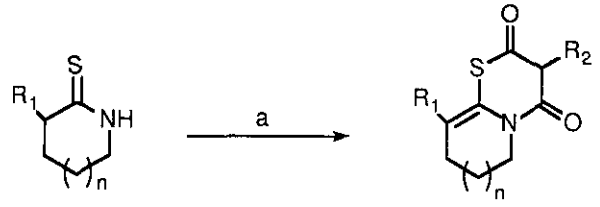
Treatment of the crude betaine (**26**) with *N*-phenylmaleimide, 4-(1-cyclopenten-1-yl)morpholine, or 1-diethylamino-1-propyne as the trapping agent failed to give any characterizable product. However, when the extremely reactive 4-phenyl-1,2,4-triazoline-3,5-dione was used as the dipolarophile, compound (**30**) was isolated in quantitative yield. The formation of **30** can be rationalized in terms of an initial 1,4-dipolar cycloaddition reaction of **26** followed by loss of carbonyl sulfide. It should be noted that the generation of **30** involves an operationally simple, one pot procedure, that consists of the making and breaking of eight bonds in a sequential fashion.

In a related fashion the reaction of 3-methyl-piperidine-2-thione (**10**) with carbon suboxide gave dipole (**25**) which was also found to undergo clean 1,4-dipolar cycloaddition producing **29** in good yield. Betaine (**25**) was found to be even more prone to undergo proton elimination producing **19** and therefore required

can be understood by noting that in the transition state leading to the *exo* isomer, severe nonbonding interactions exist between the α-methyl group of the betaine and the allylic hydrogens on the enamine. In both of the above examples, the initially formed betaine (*i.e.* **1 a**) is trisubstituted in the 8-position of the ring. With this substitution pattern, proton loss to quench the 1,4-dipole can not occur. As part of our continuing effort in this area, we thought it worthwhile to determine whether simple 8*H*-anhydro-4-hydroxy-2-oxo-1,3-thiazinium hydroxides of type (**1 b**) (R_1, R_2 or R_3=H) could be formed and whether a subsequent 1,4-dipolar cycloaddition would occur. The results of these investigations are reported herein.

RESULTS AND DISCUSSION

Our study commenced with an examination of simple cyclic 3*H*-thiolactams as mesoionic precursors. Initial efforts involved exposing the 3*H*-thiolactam to conditions similar to that used for the formation of 1,4-dipoles (**4**) and (**5**). Our earlier experience[15] had indicated that 1,4-dipoles containining phenyl substituents in the 3-position of the ring are not only the most stable but are the most easily formed. This is presumably due to stabilization of the dipole by the phenyl group. Our first attempts to form the 8*H*-anhydro-4-hydroxy-2-oxo-1,3-thiazinium hydroxide system (**1 b**) involved treating thiolactams (**9-12**) with (chlorocarbonyl)phenylketene.[21] Although the reaction afforded highly colored solutions, all attempts to isolate a 1,4-dipole or its corresponding cycloadduct were unsuccessful. The only product that was formed corres-ponded to the *S,N*-ketene acetal (*i.e.* **14-17**).



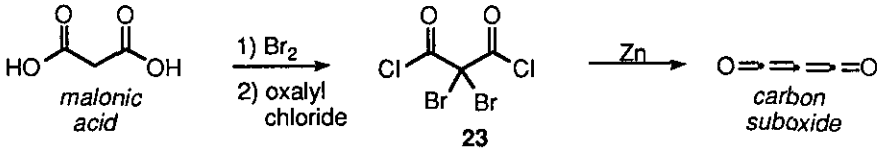
9; R_1 = H; n = 1
10; R_1 = Me; n = 1
11; R_1 = H; n = 2
12; R_1 = Me; n = 2
13; R_1 = Me; n = 0

14; R_1 = H; R_2 = Ph; n = 1
15; R_1 = Me; R_2 = Ph; n = 1
16; R_1 = H; R_2 = Ph; n = 2
17; R_1 = Me; R_2 = Ph; n = 2
18; R_1 = R_2 = H; n = 1
19; R_1 = Me; R_2 = H; n = 1
20; R_1 = R_2 = H; n = 2
21; R_1 = Me; R_2 = H; n = 2
22; R_1 = Me; R_2 = H; n = 0

a = malonyl dichloride or (chlorocarbonyl)phenylketene

Similarly, when malonyl dichloride was used to generate the betaine, only the related *S,N*-ketene acetals (**18-22**) were obtained. Apparently, the initially formed betaine (**1 b**) is unstable to the reaction conditions and readily loses a proton.

At this point in time we turned our attention to the reaction of the 3*H*-thiolactam system with carbon suboxide. Our initial apprehension in using carbon suboxide was a consequence of the harsh conditions used for its generation which traditionally involves the pyrolysis of *O*-acetyltartaric anhydride.[22] A subsequent review of the literature[23] indicated that carbon suboxide could also be obtained from dibromomalonyl dichloride (**23**).[24] Dibromomalonyl dichloride (**23**) was prepared in excellent yield by the sequential treatment of malonic acid with bromine and oxalyl chloride. The procedure was easily executed on a multi-hundred gram scale and the carbon suboxide precursor (**23**) was found to be stable for months under refrigeration. In a typical experiment, carbon suboxide was generated by the addition of an ethereal solution of **23** to zinc dust in refluxing ether. Carbon suboxide (bp 7°C) codistilled with the ether and was efficiently collected using a dry ice acetone condenser. The condenser was directly attached to the flask which contained a magnetically stirred ethereal solution of the appropriate thiolactam at -78°C.



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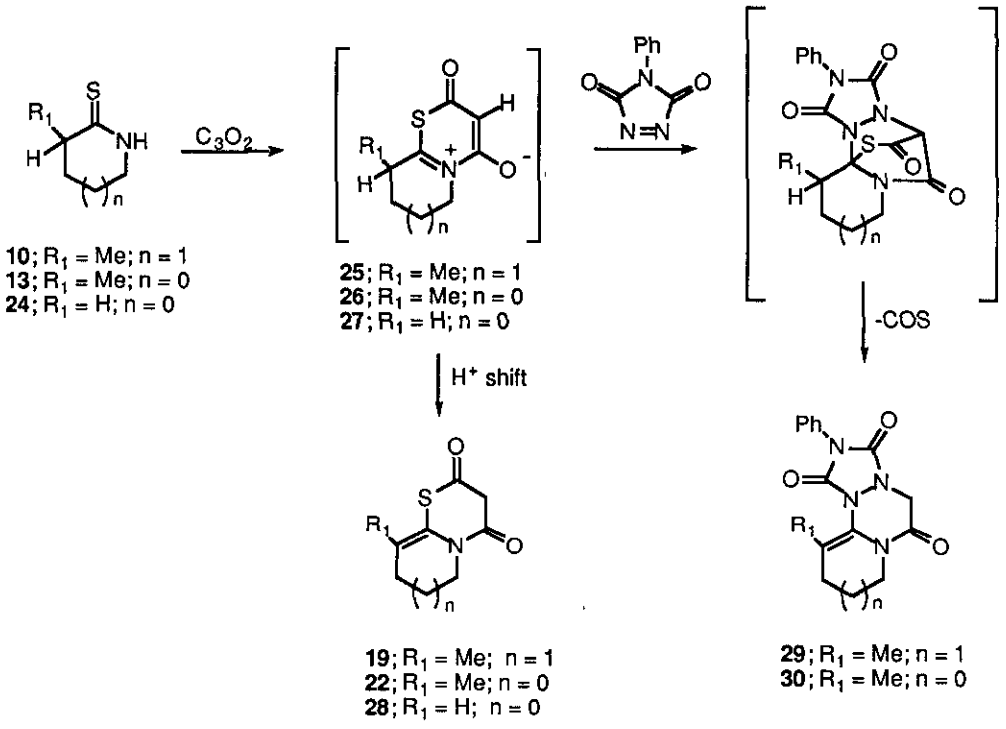


10; R_1 = Me; n = 1
13; R_1 = Me; n = 0
24; R_1 = H; n = 0

25; R_1 = Me; n = 1
26; R_1 = Me; n = 0
27; R_1 = H; n = 0

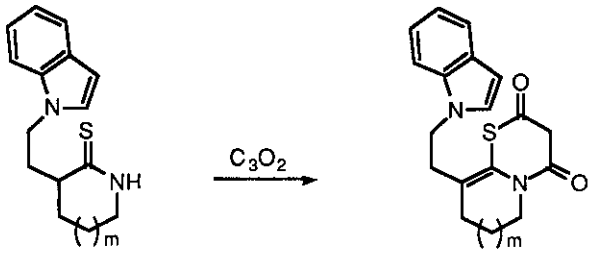
19; R_1 = Me; n = 1
22; R_1 = Me; n = 0
28; R_1 = H; n = 0

29; R_1 = Me; n = 1
30; R_1 = Me; n = 0

enhanced stability of betaine (**26**) relative to **25** is probably the result of a higher energy of activation for proton loss since the resulting 5-membered ring ketene acetal (**22**) is more highly strained than the corresponding 6-membered ring ketene acetal (**19**). The reaction of several acyclic 3*H*-thiolactams with carbon suboxide gave no indication of dipole formation. In all cases, the corresponding *S,N*-ketene acetals were formed in excellent yield. When the unsubstituted pyrrolidine-2-thione (**24**) was treated with carbon suboxide, the resulting 1,4-dipole (**27**) and its elimination product (**28**) were both unstable, and all of our attempts to isolate a product failed.

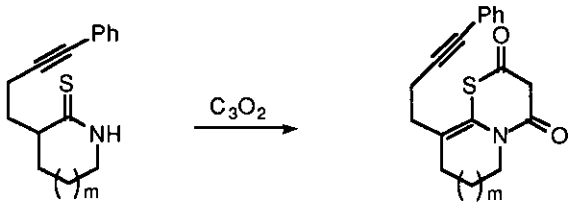
Our earlier studies[15] dealing with the intramolecular 1,4-dipolar cycloaddition reaction has shown that 1,4-dipoles such as **1b** (R_5=H) are reluctant to undergo reaction across an unactivated tethered olefin. Consequently, we chose to examine only those 1,4-dipoles which had undergone successful cycloaddition in the trisubstituted betaine series (**1a**).[25] In this vein, the reaction of 3*H*-thiolactams (**31-34**) with carbon suboxide was examined since both the indole and acetylenic units had undergone successful intramolecular cycloadditon. However, with these systems, only the corresponding *S,N*-ketene acetals (**35-38**) were obtained in high yield. Betaine formation first occurred as evidenced by the formation of a bright yellow precipitate in the early stages of the reaction. Extended reaction times or further heating afforded only the proton eliminated products (**35-38**). Apparently, proton loss from the betaine to generate the *S,N*-ketene acetal is faster than intramolecular cycloaddition across the modestly activated

π-system. Studies are underway to ascertain whether the use of more highly electron rich or electron deficient π-bonds might enhance the FMO interactions and thereby facilitate the rate of dipolar cycloaddition relative to proton elimination.



31; m = 1
32; m = 0

35; m = 1
36; m = 0

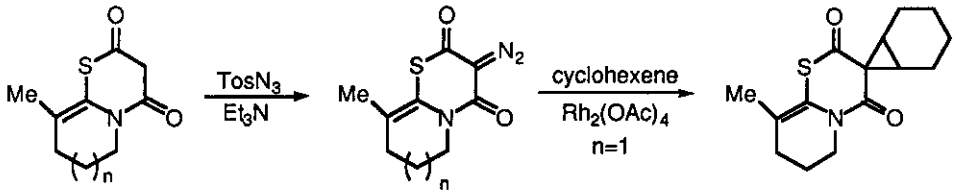


33; m = 1
34; m = 0

37; m = 1
38; m = 0

The 1,3-diketone functionality present in the resulting *S,N*-ketene acetals provided an opportunity to study the behavior of the corresponding distabilized diazo ketones. Indeed, it was quite easy to prepare a series of these diazoketones by using the standard diazo transfer reaction[26] with tosyl azide. In all of the cases investigated, the resulting diazoketone displayed much greater stability than the corresponding 1,3-diketone from which it was derived. For example, the *S,N*-ketene acetal (**22**) was too unstable to be fully characterized. However, conversion of **22** to the corresponding diazo ketone (**41**) provided a highly stable, easily characterizable compound.

α-Diazo ketones have enjoyed an extremely rich history and are well recognized as valuable intermediates for the preparation of a variety of heterocyclic and carbocyclic rings.[27] Ring contraction,[28] Wolff rearrangement,[29] cyclopropanation,[30] X-H insertion (X=C,N,O)[31,32], and ylide formation[33] represent some of the most common reactions of α-diazo ketones. As part of our efforts in this area, we thought it worthwhile to investigate the chemistry of the α-diazo ketones derived from the *S,N*-ketene acetals in light of their interesting array of functionality. To our delight, when α-diazo ketone (**39**) was heated in cyclohexene in the presence of a catalytic amount of rhodium acetate, the cyclopropanated product (**42**) was isolated in near quantitative yield. Further studies along these lines are continuing and will be reported at a future date.



19; n = 1
21; n = 2
22; n = 0

39; n = 1
40; n = 2
41; n = 0

42

In conclusion, we have prepared and investigated the 1,4-dipolar cycloaddition behavior of several 8*H*-anhydro-4-hydroxy-2-oxo-1,3-thiazinium hydroxides. These reactive dipoles readily lose a proton to give *S,N*-ketene acetals unless extremely reactive trapping agents are used. The rapid assembly and interesting combination of functionality found in α-diazo ketones derived from the *S,N*-ketene acetals provide fertile ground for future studies.

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 oven dried glassware under an atmosphere of extra dry nitrogen. Solutions were evaporated under reduced pressure with a rotary evaporator and the residue was chromatographed on a silica gel column using an ethyl acetate-hexanes mixture as the eluent unless specified otherwise.

General Procedure for Alkylation of Lactams:

Piperidones - To a 0.2 M solution of the appropriate lactam in dry THF at 0°C was added 2.14 equivalent of *n*-butyllithium (1.6 M in hexane) dropwise *via* syringe. The resulting solution was stirred for 2 h at 0°C, cooled to -78°C, and 1.1 equiv. of the appropriate alkylating reagent was added in one portion *via* syringe. The reaction mixture was stirred overnight while slowly warming to room temperature. The solution was quenched with a saturated NH_4Cl solution and the organic phase was washed with brine. The combined aqueous layer was extracted with CH_2Cl_2 and the combined organic phase was dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash silica gel chromatography.

Pyrrolidinones - To a 1.0 M solution containing 1.0 equiv. of diisopropylamine in dry THF at 0°C was added 1.0 equiv. of *n*-butyllithium (1.6 M) in hexane. The solution was stirred for 30 min, cooled to -78°C, and 0.95 equiv. of the appropriate *N*-benzyl-2-pyrrolidinone in dry THF (1 g/1 ml) was added *via* syringe. After stirring for 30 min, the resulting yellow solution was treated with 1.2 equiv. of the alkylating reagent. The reaction mixture was stirred for 12 h while slowly warming to room temperature. The solution was quenched with a saturated NH_4Cl solution and extracted with CH_2Cl_2. The organic layer was dried over

anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography.

To a flame dried 250 ml three neck round bottom flask equipped with two rubber septa and a dry-ice condenser was added 100 ml of liquid ammonia at -78°C. To the liquid ammonia was added 30.0 mmol of the appropriate 3-substituted *N*-benzyl-2-pyrrolidinone in 20 ml of dry THF, 30.0 mmol of absolute ethanol, and 115 mmol of lithium wire portionwise. When the solution remained dark blue, no more lithium was added and the mixture was stirred for an additional 15 min. The solution was slowly quenched with solid NH_4Cl. The ammonia was allowed to evaporate overnight in a fume hood and the residue was taken up in ether and water. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography.

General Procedure for the Preparation of Thiolactams. A solution of the appropriate lactam and 0.5 equiv. of Lawesson's reagent[34] in dry toluene (15 ml/1 g of lactam) was heated at reflux until the reaction was complete (*ca.* 30 min). The solvent was removed under reduced pressure and the crude product was purified by flash silica gel chromatography. An eluent mixture containing 1-5% EtOAc/ CH_2Cl_2 was used to separate the Lawesson's reagent byproducts from the thiolactams.

4-Hydroxy-3,9-dimethyl-2-oxo-9-(4-pentenyl)-6,7,8,9-tetrahydro-2*H*-pyrido[2,1-*b*][1,3]thiazinium hydroxide Inner Salt (4). A sample of 3-methyl-3-(4-pentenyl)-piperidin-2-one was prepared from 10.0 g (89.2 mmol) of 3-methyl piperidin-2-one and 14.6 g (98.1 mmol) of 5-bromo-1-pentene. Purification gave 15.7 g (97%) of the alkenyl substituted amide as a white solid; mp 55-56°C; ir (KBr) 3189, 3068, 2940, and 1645 cm-1; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.09 (s, 3H), 1.15-1.75 (m, 8H), 1.90 (q, 2H, J=6.9 Hz), 3.17 (m, 2H), 4.91-4.98 (m, 2H), 5.62-5.75 (m, 1H) and 6.95 (br s, 1H) ; ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 19.3, 23.3, 25.6, 32.3, 34.1, 39.0, 40.9, 42.5, 114.3, 138.6, and 178.1.

A sample of 3-methyl-3-(4-pentenyl)-piperidine-2-thione (**2**) was prepared from 10.0 g (55.2 mmol) of the above lactam and 11.1 g (27.6 mmol) of Lawesson's reagent. Purification gave 8.3 g (76%) of **2** as a light yellow solid; mp 36-37°C; ir (neat) 2865, 1555, and 1351 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.30-1.40 (m, 2H), 1.30 (s, 3H), 1.47-1.68 (m, 2H), 1.71-2.07 (m, 6H), 3.14-3.40 (m, 2H), 4.91 (dd, 1H, J=10.3 and 0.8 Hz), 4.97 (dd, 1H, J=17.3 and 1.3 Hz), 5.68-5.88 (m, 1H), and 9.24 (br s, 1H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 18.5, 23.5, 29.6, 31.1, 34.1, 42.1, 45.0, 45.2, 114.5, 138.6, and 211.5; Anal. Calcd for $C_{11}H_{19}NS$: C, 66.95; H, 9.70; N, 7.10; S, 16.25. Found: C, 66.86; H, 9.76; N, 7.12; S, 16.20.

A sample of 4-hydroxy-3,9-dimethyl-2-oxo-9-(4-pentenyl)-6,7,8,9-tetrahydro-2*H*-pyrido[2,1-*b*][1,3]thiazinium hydroxide inner salt (**4**) was prepared by dropwise addition of 320 mg (2.5 mmol) of methyl malonyl dichloride[19] to a stirred solution containing 400 mg (2.0 mmol) of thiolactam (**2**) in 20ml of CH_2Cl_2 at 0°C. The resulting mixture was allowed to warm slowly to room temperature over 24 h.

Removal of the solvent under reduced pressure provided a bright yellow residue that was purified by flash silica gel chromatography (60% EtOAc/hexane) to give 400 mg (71%) of **4** as a yellow oil; ir (neat) 2860, 1690, and 1610 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.10-1.40 (m, 2H), 1.49 (s, 3H), 1.60-1.90 (m, 6H), 1.98 (s, 3H), 2.05-2.15 (m, 2H), 3.84-3.94 (m, 1H), 4.34-4.43 (m, 1H), 4.96-5.04 (m, 2H), and 5.65-5.79 (m, 1H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 10.3, 18.1, 23.1, 29.1, 30.7, 33.4, 42.2, 45.2, 48.9, 97.5, 115.4, 137.2, 161.1, 166.0, and 191.4; HRMs Calcd for $C_{15}H_{22}NO_2S$: $[M+H]^+$ 280.1371. Found: 280.1373.

Preparation of 2,7a-Dimethyl-1-thia-2,3,6,7,7a,8,9,10,10a,10b-decahydro-10b,2-epithiomethano-1*H*,5*H*-benzo[*ij*]quinolizine-3,12-dione (6) and 2,7a-Dimethyl-2,3,6,7,7a,8,9,10-octahydro-1*H*,5*H*-benzo[*ij*]quinolizin-3-one (7). A solution containing 500 mg (1.8 mmol) of 1,4-dipole (**4**) in 25 ml of toluene was heated at reflux for 2 h. The solvent was removed under reduced pressure and the residue was purified by flash silica gel chromatography (20% EtOAc/hexane) to give 400 mg (80%) of cycloadduct (**6**) as a white crystalline solid; mp 99-100°C; ir (KBr) 2933, 1690, and 1670 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.32 (s, 3H), 1.35 (s, 3H), 1.36-1.70 (m, 7H), 1.75-1.85 (m, 1H), 1.85-2.00 (m, 2H), 2.05-2.15 (m, 2H), 2.25-2.40 (m, 1H), 3.29-3.39 (m, 1H), and 4.07-4.16 (m, 1H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 15.6, 17.7, 20.5, 27.8, 28.9, 31.1, 36.2, 36.8, 36.9, 37.9, 40.6, 57.4, 78.4, 170.0, and 200.2; Anal. Calcd for $C_{15}H_{21}NO_2S$: C, 64.49; H, 7.57; N, 5.01; S, 11.48. Found: C, 64.22; H, 7.65, N, 4.96; S, 11.39.

A 100 mg sample of cycloadduct (**6**) was heated at reflux for 1.5 h in 1 ml of toluene containing 5 mg of *p*-toluenesulfonic acid. The solvent was removed under reduced pressure and the residue was purified by flash silica gel chromatography (15% EtOAc/hexane) to give 78 mg (95%) of **7** as a colorless oil which consisted of a 5:1 inseparable mixture of diastereomers; ir (neat) 2930, 1640, and 1520 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.10 (s, 3H), 1.14 (d, 3H, J=6.9 Hz), 1.49-1.95 (m, 7H), 2.00-2.45 (m, 4H), 2.75-2.85 (m, 2H), and 4.41-4.48 (m, 2H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 14.9, 18.3, 19.9, 25.7, 29.5, 32.5, 34.6, 34.8, 37.5, 38.5, 41.9, 114.9, 136.7, and 173.8; HRMs Calcd for $C_{14}H_{21}NO$: 219.1623. Found: 219.1623.

Preparation of 4-Hydroxy-3,8,8-trimethyl-2-oxo-3,4,6,7-tetrahydro-2*H*,6*H*-pyrrolo[2,1-*b*][1,3]-thiazinium hydroxide Inner Salt (5). A sample of 3,3-dimethyl-pyrrolidine-2-thione (**3**)[35] was prepared from 5.0 g (44.3 mmol) of 3,3-dimethyl-pyrrolidin-2-one and 8.9 g (22.0 mmol) of Lawesson's reagent. Purification gave 3.6 g (82%) of **3** as white crystals; mp 83-84°C; ir (CCl_4) 3200-3100, 2950, and 1520 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.14 (s, 6H), 1.93 (t, 2H, J=6.9 Hz), 3.41 (t, 2H, J=6.9 Hz), and 9.23 (br s, 1H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 26.9, 33.1, 37.0, 45.3, and 213.4.

To a solution containing 1.2 g (9.3 mmol) of thiolactam (**3**) in 50 ml of dry CH_2Cl_2 at 5°C was added dropwise 2.2 g (14.0 mmol) of methyl malonyl dichloride[19]. The bright yellow solution was allowed to warm to 25°C and was stirred for 12 h. The solution was concentrated under reduced pressure. Nmr analysis of the residue established the presence of 1,4-dipole (**5**) and chlorocarbonylmethylthioacetic acid *S*-(3,3-

dimethyl-4,5-dihydro-3*H*-pyrrol-2-yl) ester. This mixture was converted to 1,4-dipole (**5**) by dissolving the residue in THF, cooling to -78°C, and adding 1.2 equiv. of triethylamine for each equiv. of chlorocarbonylmethylthioacetic acid *S*-(3,3-dimethyl-4,5-dihydro-3*H*-pyrrol-2-yl) ester present. The reaction mixture was allowed to warm to room temperature and the solvent was removed under reduced pressure. The residue was subjected to silica gel chromatography to give 1.8 g (91%) of 1,4-dipole (**5**) as a yellow solid; mp 123-124°C; ir (KBr) 2930, 1731, 1600, and 1531 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.47 (s, 6H), 1.98, (s, 3H), 2.17 (t, 2H, J=6.0 Hz), and 4.53 (t, 2H, J=6.0 Hz); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 10.1, 26.4, 33.5, 52.8, 53.4, 96.8, 159.3, 167.1, and 190.4; Anal. Calcd for $C_{10}H_{13}NO_2S$: C, 56.85; H, 6.20; N, 6.63; S, 15.18. Found: C, 56.93; H, 6.23; N, 6.68; S, 15.07.

Preparation of 1,1,6-Trimethyl-6a-morpholino-2,3,5,6,6a,7,8,9,9a,9b-decahydro-9b,6-epithiomethano-1*H*-cyclopent[*g*]indolizine-5,11-dione (8). A 171 mg (1.1 mmol) sample of 4-(1-cyclopenten-1-yl)morpholine was added dropwise to a 5°C solution containing 200 mg (1.0 mmol) of 1,4-dipole (**5**) in 4 ml of dry CH_2Cl_2. The resulting solution was allowed to reach room temperature and was stirred at this temperature for 18 h. Removal of the solvent under reduced pressure followed by flash silica gel chromatography (25% EtOAc/hexane) gave 300 mg (87%) of cycloadduct (**8**) as a white solid; mp 189-190°C; ir (KBr) 2969, 1701, and 1661 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.21 (s, 3H), 1.29 (s, 3H), 1.41 (s, 3H), 1.63-2.27 (m, 8H), 2.69 (m, 4H), 2.85 (t, 1H, J=9.0 Hz), 3.43-3.50 (m, 1H), 3.59 (m, 4H), and 3.73 (m, 1H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 12.4, 23.4, 24.4, 25.4, 30.4, 34.2, 37.7, 43.4, 45.2, 46.7, 49.4, 67.8, 70.5, 76.0, 83.6, 170.8, and 200.8; Anal. Calcd for $C_{19}H_{28}N_2O_3S$: C, 62.61; H, 7.74; N, 7.69. Found: C, 62.56; H, 7.77; N, 7.62.

General Procedure for the Reaction of Malonyl Dichloride or (Chlorocarbonyl)phenylketene with 3*H*-Thiolactams. To a solution containing the appropriate thiolactam (5 mmol/20 ml CH_2Cl_2) was added malonyl dichloride or (chlorocarbonyl)phenylketene[21] (1.3 equiv.) at 25°C. The resulting solution was stirred at 25°C for 2 h and the solvent was removed under reduced pressure. Flash silica gel chromatography (EtOAc/hexane) of the residue gave purified product.

Preparation of 3-Phenyl-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3]thiazine-2,4-dione (14). A sample of piperidine-2-thione (**9**) was prepared from 1.0 g (10.0 mmol) of piperidin-2-one and 2.1 g (5.0 mmol) of Lawesson's reagent. Purification gave 1.1 g (96%) of **9**[36] as white needles; mp 92-93°C; ir (CCl_4) 3220-3100, 2950, 1570, and 1530 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.56-1.62 (m, 4H), 2.66-2.70 (m, 2H), 3.14-3.17 (m, 2H), and 9.62 (br s, 1H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 19.4, 20.0, 38.4, 43.8, and 201.0.

A sample of 3-phenyl-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3]thiazine-2,4-dione (**14**) was prepared from 580 mg (5.0 mmol) of thiolactam (**9**) and 1.1 g (6.3 mmol) of (chlorocarbonyl)phenylketene. Purification gave 750 mg (57%) of **14** as white crystals; mp 83-84°C; ir (CCl_4) 2920, 1685, 1660, and 1620

cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.58-1.82 (m, 2H), 2.07-2.12 (m, 2H), 3.25-3.33 (m, 1H), 4.18-4.25 (m, 1H), 4.76 (s, 1H), 5.28 (t, 1H, J=3.9 Hz), and 7.21-7.23 (m, 5H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 21.8, 24.0, 42.2, 66.7, 118.2, 124.6, 127.7, 128.2, 128.9, 132.3, 164.6, and 193.4; Anal. Calcd for $C_{14}H_{13}NO_2S$: C, 64.84; H, 5.05; N, 5.40; S, 12.36. Found: C, 64.92; H, 5.07; N, 5.36; S, 12.47.

Preparation of 9-Methyl-3-phenyl-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3]thiazine-2,4-dione (15). A sample of 3-methyl-piperidine-2-thione (**10**) was prepared from 8.0 g (71.0 mmol) of 3-methyl-piperidin-2-one[37] and 14.3 g (34.5 mmol) of Lawesson's reagent. Purification gave 7.7 g (84%) of **10** as white crystals; mp 61-62°C; ir (CCl_4) 3240-3100, 2920, 1550, and 1520 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.34 (d, 3H, J=7.2 Hz), 1.39-1.87 (m, 4H), 2.63-2.69 (m, 1H), 3.23 (br s, 2H), and 9.48 (br s, 1H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 19.2, 21.7, 27.7, 41.3, 44.8, and 207.5; Anal. Calcd for $C_6H_{11}NS$: C, 55.77; H, 8.58; N, 10.84. Found: C, 55.62; H, 8.41; N, 10.59.

A sample of 9-methyl-3-phenyl-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3]thiazine-2,4-dione (**15**) was prepared from 650 mg (5.04 mmol) of thiolactam (**10**) and 1.1 g (6.3 mmol) of (chlorocarbonyl)phenyl ketene. Purification gave 1.0 g (73%) of **15** as white crystals; mp 86-87°C; ir (CCl_4) 2940, 1690, and 1665 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.77 (s, 3H), 1.81-1.93 (m, 2H), 2.18-2.26 (m, 2H), 3.42 (ddd, 1H, J=12.5, 9.8 Hz, and 3.4 Hz), 4.30 (ddd, 1H, J=12.5, 5.4 Hz, and 4.1 Hz), 4.85 (s, 1H), and 7.21-7.35 (m, 5H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 19.6, 22.4, 30.5, 42.1, 66.8, 119.2, 127.6, 127.8, 128.2, 128.9, 132.0, 164.6, and 193.5; Anal. Calcd for $C_{15}H_{15}NO_2S$: C, 65.91; H, 5.52; N, 5.13; S, 11.73. Found: C, 66.00; H, 5.56; N, 5.07; S, 11.80.

Preparation of 3-Phenyl-3,4,6,7,8,9-hexahydro-2*H*-azepino[2,1-*b*][1,3]thiazine-2,4-dione (16). A sample of azepane-2-thione[38] (**11**) was prepared from 10.0 g (88.0 mmol) of azepan-2-one and 17.8 g (44.0 mmol) of Lawesson's reagent. Purification gave 8.5 g (74%) of **11** as white needles; mp 106-107°C; ir (CCl_4) 3220-3140, 2920, and 1560 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.51-1.64 (m, 6H), 2.81-2.84 (m, 2H), 3.21-3.26 (m, 2H), and 9.57 (br s, 1H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 23.7, 27.2, 29.5, 44.3, 46.2, and 208.7.

A sample of 3-phenyl-3,4,6,7,8,9-hexahydro-2*H*-azepino[2,1-*b*][1,3]-thiazine-2,4-dione (**16**) was prepared from 500 mg (3.9 mmol) of thiolactam (**11**) and 700 mg (4.9 mmol) of (chlorocarbonyl)phenyl ketene. Purification gave 650 mg (61%) of **16** as a viscous oil; ir (neat) 2935, 1688, and 1632 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.43-1.80 (m, 4H), 2.01-2.18 (m, 2H), 3.49-3.58 (m, 1H), 3.92-4.00 (m, 1H), 4.85 (s, 1H), 5.64 (t, 1H, J=5.8 Hz), and 7.16-7.28 (m, 5H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 23.7, 27.6, 27.9, 47.0, 67.6, 128.0, 128.1, 128.6, 128.9, 130.4, 131.1, 165.4, and 195.5; HRMs Calcd for $C_{15}H_{15}NO_2S$: 273.0824. Found: 273.0819.

Preparation of 10-Methyl-3-phenyl-3,4,6,7,8,9-hexahydro-2*H*-azepino[2,1-*b*][1,3]thiazine-2,4-dione (17). A sample of 3-methylazepane-2-thione (**12**) was prepared from 3.8 g (30.0 mmol)

of 3-methylazepan-2-one and 6.1 g (15.0 mmol) of Lawesson's reagent. Purification gave 4.1 g (96%) of **12** as white needles; mp 98-99°C; ir (CCl_4) 3200-3100, 2905, and 1530 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.18 (d, 3H, J=6.8 Hz), 1.25-1.65 (m, 5H), 1.79-2.84 (m, 1H), 2.75 (t, 1H, J=7.6 Hz), 3.21-3.41 (m, 2H), and 9.59 (br s, 1H); Anal. Calcd for $C_7H_{13}NS$: C, 58.69; H, 9.14; N, 9.78; S, 22.38. Found: C, 58.75; H, 9.15; N, 9.76; S, 22.34.

A sample of 10-methyl-3-phenyl-3,4,6,7,8,9-hexahydro-2H-azepino[2,1-b][1,3]thiazine-2,4-dione (**17**) was prepared from 500 mg (3.5 mmol) of thiolactam (**12**) and 700 mg (3.9 mmol) of (chlorocarbonyl)phenyl ketene. Purification gave 950 mg (95%) of **17** as a colorless oil; ir (CCl_4) 2920, 1685, 1660, and 1630 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.42-1.44 (m, 2H), 1.68 (d, 3H, J=6.3 Hz), 1.68-1.75 (m, 2H), 1.93-2.10 (m, 2H), 3.46-3.88 (m, 2H), 4.85 (s, 1H), and 7.09-7.27 (m, 5H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 22.4, 23.1, 27.8, 34.9, 46.8, 67.9, 122.9, 128.0, 128.2, 128.4, 131.4, 141.6, 165.5, and 195.3; HRMs Calcd for $C_{16}H_{17}NO_2S$: 287.0980. Found: 287.0979.

3,4,7,8-Tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3]thiazine-2,4-dione (18) was prepared from 580 mg (5.0 mmol) of thiolactam (**9**) and 880 mg (6.3 mmol) of malonyl dichloride. Purification gave 910 mg (99%) of **18** as white needles; mp 97-98°C; ir (CCl_4) 2940, 1690, 1665, and 1615 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.71-1.79 (m, 2H), 2.13-2.19 (m, 2H), 3.51 (s, 2H), 3.68 (t, 2H, J=5.6 Hz), and 5.36 (t, 1H, J=3.9 Hz); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 21.9, 24.0, 41.6, 52.0, 118.5, 125.3, 162.7, and 191.9; Anal. Calcd for $C_8H_9NO_2S$: C, 52.44; H, 4.95; N, 7.65; S, 17.50. Found: C, 52.52; H, 4.95; N, 7.64; S, 17.51.

9-Methyl-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3]thiazine-2,4-dione (19) was prepared from 520 mg (4.0 mmol) of thiolactam (**10**) and 704 mg (5.0 mmol) of malonyl dichloride. Purification gave 570 mg (72%) of **19** as white crystals; mp 67-68°C; ir (CCl_4) 2940, 1690, 1660, and 1630 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.69 (s, 3H), 1.72 (t, 2H, J=5.8 Hz), 2.13 (t, 2H, J=6.5 Hz), 3.47 (s, 2H), and 3.62 (t, 2H, J=5.6 Hz); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 19.5, 22.4, 30.4, 41.4, 52.4, 119.7, 128.2, 162.5, and 191.9; Anal. Calcd for $C_9H_{11}NO_2S$: C, 54.80; H, 5.62; N, 7.10; S, 16.25. Found: C, 54.87; H, 5.64; N, 7.10; S, 16.17.

3,4,6,7,8,9-Hexahydro-2*H*-azepino[2,1-*b*][1,3]thiazine-2,4-dione (20) was prepared from 650 mg (5.0 mmol) of thiolactam (**11**) and 880 mg (6.3 mmol) of malonyl dichloride. Purification gave 990 mg (94%) of **20** as white needles; mp 86-87°C; ir (CCl_4) 2940, 1710, 1690, and 1630 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.36-1.38 (m, 2H), 1.50-1.52 (m, 2H), 2.03-2.05 (m, 2H), 3.35 (s, 2H), 3.45 (t, 2H, J=5.4 Hz), and 5.60 (t, 1H, J=5.5 Hz); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 23.8, 27.4, 27.8, 46.3, 53.1, 129.6, 130.8, 163.6, and 193.8; HRMs Calcd for $C_9H_{11}NO_2S$: 197.0511. Found: 197.0509.

10-Methyl-3,4,6,7,8,9-hexahydro-2*H*-azepino[2,1-*b*][1,3]thiazine-2,4-dione (21) was prepared from 2.7 g (18.9 mmol) of thiolactam (**12**) and 3.3 g (23.6 mmol) of malonyl dichloride. Purification gave 3.6 g (90%) of **21** as white crystals; mp 57-58°C; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.57-1.59 (m, 2H),

1.77 (t, 2H, J=6.1 Hz), 1.86 (s, 3H), 2.29-2.32 (m, 2H), and 3.55 (br s, 4H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 22.4, 23.2, 27.6, 35.1, 46.5, 53.5, 124.1, 141.3, 164.3, and 193.9; HRMs Calcd for $C_{10}H_{13}NO_2S$: 211.0667. Found: 211.0664.

Preparation of 8-Methyl-3,4,6,7-tetrahydro-2H-pyrrolo[2,1-*b*][1,3]thiazine-2,4-dione (22). A sample of 3-methylpyrrolidine-2-thione (**13**) was prepared from 5.0 g (50.4 mmol) of 3-methyl pyrrolidin-2-one and 10.2 g (25.2 mmol) of Lawesson's reagent. Purification gave 5.6 g (97%) of **13** as white needles; mp 84-85°C; ir (CCl_4) 3240-3080, 2940, 2860, and 1520 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.24 (d, 3H, J=7.0 Hz), 1.66-1.76 (m, 1H), 2.30-2.38 (m, 1H), 2.71-2.78 (m, 1H), 3.46-3.49 (m, 2H), and 9.23 (br s, 1H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 18.6, 30.9, 47.1, 47.5, and 209.9.

A sample of 8-methyl-3,4,6,7-tetrahydro-2*H*-pyrrolo[2,1-*b*][1,3]thiazine-2,4-dione (**22**) was prepared from 1.2 g (10.0 mmol) of thiolactam (**13**) and 1.8 g (12.5 mmol) of malonyl dichloride. The solvent was removed under reduced pressure. Compound (**22**) was found to readily decompose when subjected to silica gel chromatography or distillation; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.76 (s, 3H), 2.68 (t, 2H, J=8.4 Hz), 3.61 (s, 2H), and 4.07 (t, 2H, J=8.4 Hz). Direct conversion to 3-diazo-8-methyl-3,4,6,7-tetrahydro-2*H*-pyrrolo[2,1-*b*][1,3]thiazine-2,4-dione (**41**) allowed for full characterization.

Preparation of Carbon Suboxide. A sample of dibromomalonic acid[39] was prepared by the dropwise addition of 310 g (1.9 mol) of bromine to a mechanically stirred solution of 100 g (961.0 mmol) of malonic acid in 100 ml of 5% HBr at 5°C. The resulting heterogeneous mixture was allowed to warm to room temperature and was stirred for an additional 12 h. The solid was removed by filtration through a glass funnel, washed with pentane, and dried for 5 days in a vacuum oven (40°C (5 mm) in the presence of NaOH) until all of the complexed HBr had been removed as judged by the absence of color and odor. The resulting white solid (mp 141-142°C (lit.[39] 147°C)) contained 220 g (88%) and was used in the next step without further purification.

A sample of dibromomalonyl dichloride (**23**)[24] was prepared by the addition of 29.0 g (228.5 mmol) of oxalyl chloride to a solution of 20.0 g (76.0 mmol) of dibromomalonic acid in 30 ml of dry CH_2Cl_2 at room temperature. The addition of one drop of DMF generally caused the reaction to proceed to completion within several hours. The mixture was distilled and the fraction boiling between 75-85°C (20 mm) was collected and used in the next step without further purification. The light yellow solid was stable for months under refrigeration and gentle heating allowed for delivery as a liquid; mp 39-42°C; ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 62.1 and 161.0.

A sample of carbon suboxide[24] was prepared by the dropwise addition of 3 equiv. of dibromomalonyl dichloride (**23**) in dry ether (20 ml/1 g of acid chloride) *via* an addition funnel to a slurry of 9 equiv. of zinc dust in refluxing ether (1 g zinc/5 ml ether). The carbon suboxide produced (bp 7°C) codistills with the ether and was condensed using a dry ice acetone condenser. The condenser was attached to a flask

containing a magnetically stirred mixture of the appropriate thiolactam in ether at -78°C. After the addition of dibromomalonyl dichloride (**23**) was complete, the addition funnel was washed with several small portions of ether. The reaction flask was removed from the dry ice condenser and the mixture was stirred at -78°C under positive argon pressure. The reaction mixture was allowed to warm slowly to room temperature.

Preparation of 4-Hydroxy-9-methyl-2-oxo-6,7,8,9-tetrahydro-2*H*-pyrido[2,1-*b*][1,3]thiazinium Hydroxide Inner Salt (25). A sample of **25** was prepared from 100 mg (0.8 mmol) of 3-methylpiperidine-2-thione (**10**), 689 mg (2.3 mmol) of dibromomalonyl dichloride (**23**), and 460 mg (6.9 mmol) of zinc dust. After stirring for 16 h at 30°C, the reaction mixture consisted of 15% 1,4-dipole (**25**) and 85% of 9-methyl-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3]thiazine-2,4-dione (**19**). The 1,4-dipole (**25**) was cleanly converted to **19** by careful removal of the solvent under reduced pressure followed by dissolution in $CDCl_3$.

4-Hydroxy-8-methyl-2-oxo-7,8-dihydro-2*H*,6*H*-pyrrolo[2,1-*b*][1,3]thiazinium Hydroxide Inner Salt (26) was prepared from 50 mg (0.4 mmol) of 3-methylpyrrolidine-2-thione (**13**), 384 mg (1.3 mmol) of dibromomalonyl dichloride (**23**), and 256 mg (3.9 mmol) of zinc dust. Best results were obtained when the resulting heterogeneous slurry was used for cycloaddition within 30 min of reaching room temperature. The dipole was stable under the reaction conditions for up to 16 h at 30°C. 1,4-Dipole (**26**) was cleanly converted to **22** by careful removal of the solvent under reduced pressure followed by dissolution in $CDCl_3$.

Preparation of 11-Methyl-2-phenyl-2,3,5,6,9,10-hexahydro-1*H*,8*H*-pyrido[2,1-*c*]-1,2,4-triazolo[1,2-*a*][1,2,4]triazine-1,3,5-trione (29). A 136 mg (0.8 mmol) sample of 4-phenyl-1,2,4-triazoline-3,5-dione was added in one portion to a -78°C solution containing 151 mg (0.4 mmol) of 1,4-dipole (**25**) in 10 ml of ether. The resulting orange solution was allowed to reach room temperature and was stirred at this temperature for 6 h. Removal of the solvent under reduced pressure provided 285 mg of a yellow solid which consisted of 80% of cycloadduct (**29**), 17% of the elimination product (**19**), and 3% of thiolactam (**10**). The structure of cycloadduct (**29**) was assigned by analogy with **30**; mp 65-70°C; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.93 (s, 3H), 2.13-2.43 (m, 4H), 3.72-3.85 (m, 2H), 4.62-4.67 (m, 2H), and 7.35-7.52 (m, 5H).

Preparation of 10-Methyl-2-phenyl-2,3,5,6,8,9-hexahydro-1*H*-pyrrolo[2,1-*c*]-1,2,4-triazolo[1,2-*a*][1,2,4]triazine-1,3,5-trione (30). A 76 mg (0.4 mmol) sample of 4-phenyl-1,2,4-triazoline-3,5-dione was added in one portion to a -78°C solution containing 79 mg (0.4 mmol) of 1,4-dipole (**26**) in 10 ml of ether. The resulting orange solution was allowed to reach room temperature and was stirred at this temperature for 6 h. Removal of the solvent under reduced pressure provided 128 mg (100%) of cycloadduct (**30**) as a yellow solid; mp 109-110°C; ir (KBr) 2969, 1721, and 1695 cm^{-1}; ^{1}H-nmr

(acetone-d_6, 300 MHz) δ 1.78 (s, 3H), 2.32 (ddd, 1H, J=12.7, 7.5, and 2.1 Hz), 2.82-2.93 (m, 1H), 3.95 (ddd, 1H, J=7.5, 7.1, and 2.3 Hz), 4.12 (d, 1H, J=16.8 Hz), 4.24 (m, 1H), 4.40 (d, 1H, J=16.8 Hz), and 7.48 (br s, 5H); ^{13}C-nmr (acetone-d_6, 75 MHz) δ 24.6, 31.2, 46.0, 49.0, 78.5, 126.9, 128.7, 129.6, 132.8, 154.2, 155.0, 168.0, 168.5, and 209.6; HRMs Calcd for $C_{15}H_{14}N_4O_3$: 315.1093. Found: 315.1094.

Attempted Preparation of 3,4,7,8-Tetrahydro-2*H*-pyrrolo[2,1-*b*][1,3]thiazine-2,4-dione (28), 4-Hydroxy-2-oxo-7,8-dihydro-2*H*,6*H*-pyrrolo[2,1-*b*][1,3]thiazinium hydroxide Inner Salt (27), and 2-Phenyl-7,8-dihydro-6*H*-2,3a,5a,9b-tetraazacyclopenta[a]naphthalene-1,3,5-trione. An attempt was made to prepare dipole (**27**) by treating 100 mg (1.0 mmol) of piperidine-2-thione (**24**),[40] 875 mg (2.9 mmol) of dibromomalonyl dichloride (**23**), and 582 mg (8.9 mmol) of zinc dust. After stirring for 15 min at 30°C, the reaction consisted a complex mixture with a low yield of **28** being present in the crude reaction mixture based on nmr analysis. A 173 mg (1.0 mmol) sample of 4-phenyl-1,2,4-triazoline-3,5-dione was added in one portion to the above cooled solution. The resulting orange solution was allowed to reach room temperature and was stirred at this temperature for 6 h. Removal of the solvent under reduced pressure provided a complex mixture that resisted purification.

Preparation of *N*-(2-Iodoethyl)indole. A solution containing 20.0 g (95.7 mmol) of tetrahydro-2-(2-bromoethoxy)-2*H*-pyran[41] in 50 ml of benzene was added to 1.1 g (2.7 mmol) of tetrabutylammonium hydrogen sulfate and 25 ml of a 50% w/w NaOH solution. To the stirred two phase solution was added 7.5 g (64.1 mmol) of indole and the resulting mixture stirred at room temperature for 72 h. The solution was diluted with 250 ml water and the organic phase was separated and washed with 10% HCl, water and dried over anhydrous $MgSO_4$. The solution was filtered and the solvent was removed under reduced pressure to yield 15.6 g (100%) of *N*-[2-(tetrahydropyranyl)oxyethyl]indole as a yellow oil which was used in the next step without further purification; ir (neat) 1613, 1512, and 1464 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.43-1.83 (m, 6H), 3.36-3.43 (m, 1H), 3.56-3.63 (m, 1H), 3.65-3.79 (m, 1H), 4.02-4.10 (m, 1H), 4.34 (t, 2H, J=5.3 Hz), 4.50 (t, 1H, J=3.2 Hz), 6.52 (d, 1H, J=3.1 Hz), 7.10-7.15 (m, 1H), 7.22 (d, 1H, J=3.1 Hz), 7.23-7.25 (m, 1H), 7.39-7.42 (m, 1H), and 7.64-7.67 (m, 1H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 19.0, 25.2, 30.3, 46.2, 61.7, 66.2, 98.6, 101.1, 109.3, 119.2, 120.7, 121.3, 128.3, 128.5, and 136.0.

To a solution containing 15.6 g (63.3 mmol) of *N*-[2-(tetrahydropyranyl)oxyethyl]indole in 500 ml of 90% aqueous methanol was added 610 mg (3.2 mmol) of *p*-toluenesulfonic acid monohydrate and the resulting solution was stirred for 14 h. The solvent was removed under reduced pressure and the residue was taken up in 250 ml of CH_2Cl_2 and washed with saturated $NaHCO_3$, brine and dried over anhydrous $MgSO_4$. The solution was filtered and the solvent was removed under reduced pressure. The residue was subjected to flach silica gel chromatography to give 9.0 g (88%) of *N*-(2-hydroxyethyl)indole as a light yellow oil; ir (neat) 3385, 2607, and 1512 cm^{-1}; ^{1}H- nmr ($CDCl_3$, 300 MHz) δ 2.29 (s, 1H), 3.69 (t, 2H, J=5.3 Hz), 4.08 (t, 2H, J=5.3 Hz), 6.55 (d, 1H, J=3.1 Hz), 7.09 (d, 1H, J=3.1 Hz), 7.18-7.37 (m, 3H), and 7.69-7.72 (m, 1H);

^{13}C-nmr ($CDCl_3$, 75 MHz) δ 48.3, 61.3, 101.0, 109.2, 119.3, 120.8, 121.4, 128.2, 128.4, and 135.8.

To a solution containing 1.0 g (6.2 mmol) of *N*-(2-hydroxyethyl)indole in 15 ml of pyridine was added 2.4 g (12.6 mmol) of *p*-toluenesulfonyl chloride portionwise at 0°C. After solution of the *p*-toluenesulfonyl chloride was complete, the flask was placed in the refrigerator for 12 h. The resulting solution was poured onto 100 g of ice water and extracted with ether. The combined ether layers were washed with a 6 N HCl solution, water and dried over anhydrous $MgSO_4$. The solution was filtered and the solvent was removed under reduced pressure to yield 1.6 g (100%) of *N*-[2-(toluenesulfonyl)oxyethyl]indole as a yellow oil which was used in the next step without further purification; ir (neat) 1599, 1464, 1360, and 1175 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 2.31 (s, 3H), 4.23 (s, 4H), 6.47 (d, 1H, J=3.1 Hz), 7.01 (d, 1H, J=3.1 Hz), 7.02-7.05 (m, 2H), 7.12-7.15 (m, 2H), 7.44-7.47 (m, 2H), and 7.61-7.64 (m, 2H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 21.2, 44.6, 67.8, 101.5, 108.6, 119.2, 120.6, 121.3, 127.1, 127.9, 128.4, 129.3, 131.4, 135.3, and 144.5.

To a solution containing 15.7 g (62.4 mmol) of the above compound in 150 ml of acetone under a N_2 was added 15.0 g (100.0 mmol) of NaI and the solution heated at reflux for 14 h. The thick solution was cooled to room temperature and most of the solvent was removed under reduced pressure. The residue was taken up in 125 ml of water and extracted with pentane. The combined organic layer was washed with 10% $Na_2S_2O_3$ solution and dried over anhydrous $MgSO_4$. The organic layer was filtered and the solvent removed under reduced pressure. The residue was subjected to flash silica gel chromatography to give 11.0 g (81%) of *N*-(2-iodoethyl)indole as a light yellow oil; ir (neat) 3100, 1887, 1512, 1464, and 1312 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 3.46, (t, 2H, J=7.5 Hz), 4.50 (t, 2H, J=7.5 Hz), 6.69 (d, 1H, J=3.2 Hz), 7.17 (d, 1H, J=3.2 Hz), 7.30-7.41 (m, 3H), and 7.82-7.84 (m, 1H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 2.3, 48.5, 101.7, 108.7, 119.7, 121.0, 121.7, 127.4, 128.5, and 135.2.

Preparation of 9-((2-Indol-1-yl)ethyl)-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3]thiazine-2,4-dione (35). A sample of 3-(2-indol-1-yl)ethyl)piperidin-2-one was prepared from 4.0 g (40.4 mmol) of 2-piperidone and 11.4 g (41.9 mmol) of *N*-((2-indol-1-yl)ethyl)indole. Purification gave 6.5 g (66%) of 3-(2-indolylethyl)piperidin-2-one as a clear oil: ir (neat) 3288, 3212, 1667, 1489, and 1314 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.41-1.52 (m, 1H), 1.59-2.01 (m, 4H), 2.21-2.43 (m, 2H), 3.23-3.30 (m, 2H), 4.34 (t, 2H, J=7.3 Hz), 6.51 (d, 1H, J=3.1 Hz), 7.00 (s, 1H), 7.10-7.25 (m, 2H), 7.18 (d, 1H, J=3.1 Hz), 7.43-7.45 (m, 1H), and 7.64-7.67 (m, 1H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 21.3, 26.9, 32.4, 38.1, 41.9, 44.3, 100.9, 109.4, 119.0, 120.7, 121.2, 127.7, 128.4, 135.8, and 174.5.

A sample of 3-(2-indolylethyl)piperidine-2-thione (**31**) was prepared from 3.0 g (12.2 mmol) of 3-((2-indol-1-yl)ethyl)piperidin-2-one and 2.5 g (6.1 mmol) of Lawesson's reagent. Purification gave 3.0 g (94%) of 3-((2-indol-1-yl)ethyl)piperidine-2-thione as a light yellow solid; mp 79-80°C; ir (neat) 3202, 1577, 1551, and 1472 cm-1; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.40-1.53 (m, 1H), 1.63-1.88 (m, 3H), 2.15 (quin., 1H, J=7.5 Hz), 2.60-2.72 (m, 2H), 3.18-3.27 (m, 2H), 4.37 (t, 2H, J=7.2 Hz), 6.52 (d, 1H, J=3.0 Hz), 7.09-7.25 (m,

2H), 7.21 (d, 1H, J=3.0 Hz), 7.45-7.48 (m, 1H), 7.63-7.66 (m, 1H), and 9.32 (br s, 1H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 19.5, 25.6, 35.3, 43.7, 44.2, 44.3, 101.1, 109.0, 118.5, 120.7, 121.3, 127.6, 128.4, 135.8, and 205.5; Anal. Calcd for $C_{15}H_{18}N_2S$: C, 69.72; H, 7.02; N, 10.84; S, 12.41. Found: C, 69.81; H, 7.02; N, 10.79; S, 12.51.

A sample of 9-((2-indol-1-yl)ethyl)-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3]thiazine-2,4-dione (**35**) was prepared from 100 mg (0.4 mmol) of thiolactam (**31**), 250 mg (1.6 mmol) of dibromomalonyl dichloride (**23**), and 160 mg (2.5 mmol) of zinc dust. The reaction was allowed to stir at room temperature for 16 h and the solvent was removed under reduced pressure. The residue was subjected to flash silica gel chromatography to give 126 mg (100%) of **35** as a white solid; mp 139-140°C; ir (KBr) 2948, 2880, 1690, and 1512 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.82 (t, 2H, J=5.6 Hz), 2.23 (t, 2H, J=6.4 Hz), 2.66 (t, 2H, J=6.1 Hz), 2.99 (s, 2H), 3.69 (t, 2H, J=5.4 Hz), 4.30 (t, 2H, J=6.1 Hz), 6.50 (d, 1H, J=2.5 Hz), 7.06-7.23 (m, 4H), and 7.59 (d, 1H, J=8.0 Hz); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 22.4, 28.7, 35.1, 41.2, 43.9, 51.6, 101.9, 109.0, 119.5, 121.1, 121.4, 123.2, 127.8, 127.9, 128.4, 136.2, 162.9, and 191.0; HRMs Calcd for $C_{18}H_{18}N_2O_2S$: 326.1089. Found: 326.1092.

Preparation of 8-(2-(Indol-1-yl)ethyl)-3,4,6,7-tetrahydro-2*H*-pyrrolo[2,1-*b*][1,3]thiazine-2,4-dione (36). A sample of 3-(2-(indol-1-yl)ethyl)pyrrolidin-2-one was prepared from 1.0 g (11.8 mmol) of pyrrolidine and 1.0 g (11.8 mmol) of *N*-(2-(indol-1-yl)ethyl)indole. Purification gave 840 mg (31%) of 3-(2-(indol-1-yl)ethyl)pyrrolidin-2-one as a white solid. A sample of 3-(2-(indol-1-yl)ethyl)pyrrolidine-2-thione (**32**) was prepared from 200 mg (0.9 mmol) of 3-(2-(indol-1-yl)ethyl)piperidin-2-one and 177 mg (0.5 mmol) of Lawesson's reagent. Purification gave 50 mg (22%) of 32 as a clear oil; ir (neat) 3172, 2929, 1535, and 1514 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.60-1.74 (m, 1H), 1.88-2.01 (m, 1H), 2.14-2.23 (m, 1H), 2.60-2.71 (m, 2H), 3.39-3.47 (m, 2H), 4.29-4.40 (m, 2H), 6.50 (d, 1H, J=2.9 Hz), 7.07-7.23 (m, 3H), 7.41 (d, 1H, J=8.3 Hz), 7.62 (d, 1H, J=7.7 Hz), and 8.53 (br s, 1H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 29.0, 33.8, 44.3, 47.2, 49.6, 101.5, 109.4, 119.4, 121.0, 121.6, 127.7, 128.6, 136.1, and 208.1; HRMs Calcd for $C_{14}H_{16}N_2S$: 244.1034. Found: 244.1036.

A sample of 8-(2-(indol-1-yl)ethyl)-3,4,6,7-tetrahydro-2*H*-pyrrolo[2,1-*b*][1,3]thiazine-2,4-dione (**36**) was prepared from 50 mg (0.2 mmol) of 3-(2-(indol-1-yl)ethyl)pyrrolidine-2-thione, 190 mg (0.6 mmol) of dibromomalonyl dichloride (23), and 121 mg (1.9 mmol) of zinc dust. The reaction was allowed to stir at room temperature for 16 h and the solvent was removed under reduced pressure to give 65 mg (100%) of **36** as a white solid; mp 146-148°C; ir (KBr) 2917, 1651, and 1450 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 2.51 (t, 2H, J=8.5 Hz), 2.63 (t, 2H, J=6.5 Hz), 3.46 (s, 2H), 3.97 (t, 2H, J=8.5 Hz), 4.25 (t, 2H, J=6.5 Hz), 6.51 (d, 1H, J=2.9 Hz), 7.04 (d, 1H, J=2.9 Hz), 7.08-7.30 (m, 3H), and 7.62 (d, 1H, J=7.6 Hz); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 28.8, 30.7, 43.9, 45.9, 47.7, 102.2, 108.8, 119.6, 121.1, 121.3, 121.7, 124.2, 127.3, 128.8, 135.9, 160.6, and 189.3; HRMs Calcd for $C_{17}H_{16}N_2O_2S$: 313.1011. Found: 313.1010.

Preparation of 9-(4-Phenylbut-3-ynyl)-3,4,7,8-tetrahydro-2*H*, 6*H*-pyrido[2,1-*b*][1,3]thiazine-2,4-dione (37). A sample 3-(4-phenylbut-3-ynyl)piperidin-2-one was prepared from 750 mg (7.5 mmol) of 2-piperidone and 1.9 g (7.5 mmol) of 1-iodo-4-phenylbut-3-yne. Purification afforded 200 mg (12%) of a clear oil that was used in the next step. A sample of 3-(4-phenylbut-3-ynyl)piperidine-2-thione (33) was prepared from 200 mg (0.9 mmol) of 3-(4-phenylbut-3-ynyl)piperidin-2-one and 178 mg (0.5 mmol) of Lawesson's reagent. Purification gave 180 mg (84%) of 33 as a white solid; mp 108-109°C; ir (neat) 2939, 2860, and 1556 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.58-1.68 (m, 1H), 1.73-2.02 (m, 4H), 2.46-2.67 (m, 3H), 2.78-2.84 (m, 1H), 3.26-3.38 (m, 2H), 7.21-7.29 (m, 3H), 7.34-7.38 (m, 2H), and 8.57 (br s, 1H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 17.3, 19.5, 24.6, 33.8, 44.7, 45.4, 81.3, 89.0, 123.7, 127.5, 128.1, 131.5, and 207.3; HRMs Calcd for $C_{15}H_{17}NS$: 243.1082. Found: 243.1073.

A sample of 9-(4-phenylbut-3-ynyl)-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3]thiazine-2,4-dione (**37**) was prepared from 62 mg (0.3 mmol) of 3-(4-phenylbut-3-ynyl)piperidine-2-thione (**33**), 230 mg (0.8 mmol) of dibromomalonyl dichloride (**23**), and 150 mg (2.3 mmol) of zinc dust. The reaction was allowed to stir at room temperature for 16 h and the solvent was removed under reduced pressure. The residue was subjected to flash silica gel chromatography (20% EtOAc/hexane) to give 77 mg (100%) of **37** as a clear oil; ir (neat) 2935, 2890, 1700, 1670, and 1627 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.93 (t, 2H, J=5.8 Hz), 2.39 (t, 2H, J=6.5 Hz), 2.49-2.54 (m, 2H), 2.59-2.64 (m, 2H), 3.60 (s, 2H), 3.81 (t, 2H, J=5.8 Hz), 7.24-7.28 (m, 3H), and 7.30-7.33 (m, 2H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 18.1, 22.5, 28.4, 32.5, 41.8, 52.3, 82.1, 87.7, 122.2, 123.2, 127.9, 128.3, 130.6, 131.3, 162.8, and 191.9; HRMs Calcd for $C_{18}H_{17}NO_2S$: 311.0980. Found: 311.0972.

Preparation of 8-(4-Phenylbut-3-ynyl)-3,4,6,7-tetrahydro-2*H*-pyrrolo[2,1-*b*][1,3]thiazine-2,4-dione (38). A sample of 1-*tert*-butyldimethylsilylpyrrolidin-2-one was prepared by the dropwise addition of 26.6 g (176.2 mmol) of TBDMSCl in 300 ml of CH_2Cl_2 to a solution containing 10.0 g (117.5 mmol) of pyrroildin-2-one, 40.9 ml (294.0 mmol) of Et_3N, and a catalytic amount of DMAP in 300 ml of CH_2Cl_2. The resulting solution was stirred at room temperature for 1 h; washed with H_2O, brine, and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by distillation (77°C (0.2 mm)) gave 22.0 g (94%) of 1-*tert*-butyldimethylsilylpyrrolidin-2-one as a colorless oil.

To a solution containing of 4.2 ml (24.0 mmol) of diisopropylamine in 15 ml of dry THF at 0°C was added 15.0 ml (24.0 mmol) of *n*-butyllithium (1.6 M) in hexane. The solution was stirred for 30 min, cooled to -78°C, and 4.4 g (22.1 mmol) of 1-*tert*-butyldimethylsilylpyrrolidin-2-one in 30 ml THF was added via syringe. The resulting solution was stirred at -78°C for 1 h and 5.6 g (21.9 mmol) of 4-iodobut-1-ynylbenzene in 10 ml of THF was added dropwise. The reaction mixture was stirred at room temperature for 1 h and then quenched with a saturated aqueous NH_4Cl solution. The layers were separated and the organic phase was washed with brine. The combined aqueous layer was extracted with CH_2Cl_2 and the

combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was subjected to flash silica gel chromatography to give 6.5 g (90%) of 3-(4-phenylbut-3-ynyl)-1-*tert*-butyldimethylsilylpyrrolidin-2-one which was used in the next step without further purification.

To a solution of 6.5 g (19.8 mmol) of 3-(4-phenylbut-3-ynyl)-1-*tert*-butyldimethylsilylpyrrolidin-2-one in 120 ml of THF at 0°C was added 22.0 ml (22.0 mmol; 1M solution in THF) of TBAF in one portion. The resulting solution was stirred for 1 h. Removal of the solvent under reduced pressure followed by chromatography on silica gel (20% EtOAc/hexane) gave 2.1 g (50%) of 3-(4-phenylbut-3-ynyl)pyrrolidin-2-one as a white solid; mp 84-85°C; ir (neat) 3195, 2860, 1680, and 1490 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.65 (m, 1H), 1.85 (ddd, 1H, J=10.7, 8.9, and 5.5 Hz), 2.18 (ddd, 1H, J=7.6, 5.2, and 4.9 Hz), 2.35-2.45 (m 1H), 2.45-2.65 (m 3H), 3.30-3.35 (m, 2H), 6.01 (br s, 1H), 7.25-7.27 (m, 3H), and 7.34-7.38 (m, 2H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 17.5, 27.5, 30.0, 40.3, 40.5, 81.2, 89.2, 123.8, 127.6, 128.2, 131.5, and 180.6; HRMs Calcd for $C_{14}H_{15}NO$: 213.1154. Found: 213.1155.

A sample of 3-(4-phenylbut-3-ynyl)pyrrolidine-2-thione (**34**) was prepared from 1.0 g (4.7 mmol) of 3-(4-phenylbut-3-ynyl)pyrrolidin-2-one and 950 mg (2.3 mmol) of Lawesson's reagent. Purification gave 1.1 g (100%) of 34 as a white solid; mp 130-131°C; ir (neat) 3148, 2881, and 1541 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.62-1.72 (m, 1H), 1.92 (ddd, 1H, J=10.7, 8.8, and 5.1 Hz), 2.45-2.69 (m, 4H), 2.88-2.98 (m, 1H), 3.57 (m, 2H), 7.25-7.27 (m, 3H), 7.35-7.38 (m, 2H), and 7.86 (br s, 1H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 17.6, 28.6, 32.2, 47.3, 51.6, 81.4, 89.0, 123.7, 127.7, 128.2, 131.5, and 208.5; HRMs Calcd for $C_{14}H_{15}NS$: 229.0925. Found: 229.0916.

A sample of 8-(4-phenylbut-3-ynyl)-3,4,6,7-tetrahydro-2*H*-pyrrolo[2,1-*b*][1,3]thiazine-2,4-dione (**38**) was prepared from 100 mg (0.4 mmol) of 3-(4-phenyl-but-3-ynyl)pyrrolidine-2-thione (**34**), 390 mg (1.3 mmol) of dibromomalonyl dichloride (**23**), and 260 mg (3.9 mmol) of zinc dust. The reaction was allowed to stir at room temperature for 16 h and the solvent was removed under reduced pressure. The residue was subjected to flash silica gel chromatography (5% EtOAc/CH_2Cl_2) to give 130 mg (99%) of **38** as a clear oil; ir (neat) 2920, 2856, 1689, 1654, and 1490 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 2.42 (t, 2H, J=6.8 Hz), 2.56 (t, 2H, J=6.8 Hz), 2.78 (t, 2H, J=8.5 Hz), 3.69 (s, 2H), 4.08 (t, 2H, J=8.5 Hz), 7.24-7.27 (m, 3H), and 7.32-7.40 (m, 2H); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 18.0, 27.0, 29.7, 30.4, 46.0, 47.9, 82.0, 88.2, 122.9, 123.3, 127.9, 128.3, 131.4, 160.4, and 189.7; HRMs Calcd for $C_{17}H_{16}NO_2S$: $[M+H]^+$ 298.0902. Found: 298.0901.

Preparation of 3-Diazo-9-methyl-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3]thiazine-2,4-dione (39). To an ice cooled solution containing 220 mg (1.1 mmol) of 9-methyl-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3]thiazine-2,4-dione (**19**) and 220 mg (1.1 mmol) of *p*-tosyl azide in 50 ml of MeCN was added 120 mg (1.2 mmol) of triethylamine. The resulting mixture was stirred for 4 h at 0°C. The solvent was removed under reduced pressure and the residue was purified by flash silica gel chromatog-

raphy to give 180 mg (72%) of **39** as a red oil; ir (CCl_4) 2960, 2125, and 1630 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.74 (s, 3H), 1.81 (t, 2H, J=5.6 Hz), 2.19 (t, 2H, J=6.2 Hz), and 3.80 (t, 2H, J=5.6 Hz); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 19.4, 21.9, 30.8, 41.9, 114.7, 117.9, 124.5, 157.3, and 178.4.

Preparation of 3-Diazo-10-Methyl-3,4,6,7,8,9-hexahydro-2*H*-azepino[2,1-*b*][1,3]thiazine-2,4-dione (40). To a solution containing 1.5 g (6.9 mmol) of **21** and 1.4 g (6.9 mmol) of *p*-tosyl azide in 30 ml of MeCN was added 700 mg (6.9 mmol) of triethylamine. The resulting mixture was stirred for 4 h at 0°C. Removal of the solvent under reduced pressure followed by silica gel chromatography gave 1.3 g (77%) of **40** as a red oil; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.38-1.46 (m, 2H), 1.60-1.64 (m, 2H), 1.62 (s, 3H), 2.09 (t, 2H, J=5.6 Hz), and 3.47 (t, 2H, J=6.1 Hz); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 21.9, 22.8, 26.7, 35.0, 48.2, 77.2, 120.6, 138.7, 159.0, and 180.6.

Preparation of 3-Diazo-8-methyl-3,4,6,7-tetrahydro-2*H*-pyrrolo[2,1-*b*][1,3]thiazine-2,4-dione (41). A sample of **41** was prepared from 1.2 g (10.0 mmol) of 3-methylpyrrolidine-2-thione (**13**) and 1.8 g (12.5 mmol) of malonyl dichloride. The solvent and excess malonyl dichloride was removed under reduced pressure. The oily residue was dissolved in 100 ml of MeCN and 2.0 g (10.0 mmol) of *p*-tosyl azide was added. To the ice cooled solution was added 1.0 g (10.0 mmol) of triethylamine and the resulting mixture was stirred for 4 h at 0°C. Removal of the solvent under reduced pressure followed by purification of the resulting residue by flash silica gel chromatography (CH_2Cl_2) gave 1.1 g (50%) of **41** as a red oil; ir (CCl_4) 2940, 2080, and 1610 cm^{-1}; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 1.53 (s, 3H), 2.47 (t, 2H, J=8.7 Hz), and 3.84 (t, 2H, J=8.7 Hz); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 12.7, 32.2. 45.8, 76.6, 119.6, 129.3, 153.9, and 176.3.

Reaction of 3-Diazo-9-methyl-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3]thiazine-2,4-dione (39) with Cyclohexene. A solution containing 200 mg (89.0 mmol) of 3-diazo-9-methyl-3,4,7,8-tetrahydro-2*H*,6*H*-pyrido[2,1-*b*][1,3]thiazine-2,4-dione (**39**) and 2 mg of $Rh_2(OAc)_4$ in 1.0 ml of cyclohexene was heated at reflux for 2 h. Removal of the solvent under reduced pressure followed by chromatography on silica gel gave 240 mg (97%) of **42** as a colorless oil; ^{1}H-nmr ($CDCl_3$, 300 MHz) δ 0.87-0.97 (m, 1H), 1.04-1.17 (m, 2H), 1.38-1.46 (m, 1H), 1.49-1.56 (m, 2H), 1.59 (s, 2H), 1.73-1.82 (m, 2H), 1.99-2.06 (m, 4H), 2.69-2.79 (m, 1H), 3.36-3.45 (m, 1H), 3.54-3.62 (m, 1H), and 4.07 (t, 1H, J=9.2 Hz); ^{13}C-nmr ($CDCl_3$, 75 MHz) δ 18.4, 20.6, 20.7, 22.0, 22.1, 26.8, 28.6, 34.5, 41.7, 53.4, 57.0, 77.9, 106.4, 123.0, 167.2, and 200.7.

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