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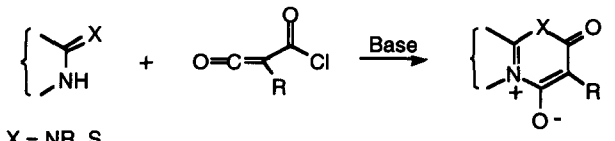
Details Associated with the Bimolecular 1,4-Dipolar Cycloaddition Reaction of Cross-Conjugated Heteroaromatic Betaines

Albert Padwa, Steven J. Coats and Mark A. Semones*
Department of Chemistry, Emory University, Atlanta, Georgia 30322

Abstract: A series of 3,3-disubstituted bicyclic anhydro-4-hydroxy-2-oxo-1,3-thiazinium hydroxides are easily prepared from the reaction of 3H-thiolactams with 1,3-bielectrophiles. These cross-conjugated heteroaromatic betaines undergo regio- and diastereospecific 1,4-dipolar cycloaddition with electron-rich and electron-deficient π-bonds to produce 1,4-cycloadducts containing a carbonyl sulfide bridge. A representative betaine dipole and a 1,4-cycloadduct were characterized by single crystal X-ray determinations. In certain cases, the initially formed cycloadduct can be induced to lose COS on further heating. The frontier orbital coefficients of the thiazinium betaine were determined by semi-empirical MOPAC calculations with the PM3 Hamiltonian. The HOMO of the 1,4-dipole is dominant for reactions with electron-deficient dipolarophiles such as N-phenylmaleimide, while the LUMO becomes important for cycloaddition to more electron-rich species such as ynamines or vinyl ethers.

The prominent role that 1,3-dipolar cycloaddition reactions play in the elaboration of a variety of organic molecules has become increasingly apparent in recent years.[1-4] The ease of the cycloaddition, the rapid accumulation of polyfunctionality in a relatively small molecular framework, the high stereochemical control of the cycloaddition, and the fair predictability of its regiochemistry have contributed to the popularity of the reaction. In the realm of synthesis, in which a premium is put on the rapid construction of polyfunctional, highly bridged carbon and heteroatom networks, the 1,3-dipolar cycloaddition reaction has now emerged as a prominent synthetic method.[5-12] When the reacting components are themselves cyclic or have ring substituents, complex multicyclic arrays, such as those contained in drugs and natural products, can be constructed in a single step. Often the syntheses of molecules of this complexity are more difficult and lengthy by other routes.[12]

In contrast to 1,3-dipoles, much less is known about the cycloaddition behavior of 1,4-dipoles. 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 by the cyclocondensation of an appropriately substituted monoprotic amidine or thioamide with a 1,3-bielectrophile derived from malonic acid.[13,14] Although a few examples of intramolecular 1,4-dipolar cycloadditions have been reported in the literature, little is known about the bimolecular behavior of this class of reactive intermediates.[15-24] Moreover, the range of their structural variation has remained somewhat narrow. In most instances, at least one of the substituents present on the betaine backbone has been an aryl group (R=Ar), presumably selected to facilitate dipole formation.[15-21] In order to broaden



X = NR, S

1

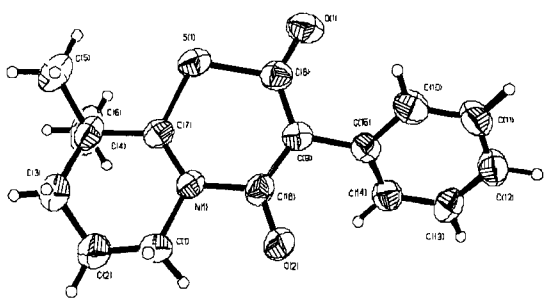
the utility of these cross conjugated betaines for synthesis, we thought it worthwhile to study the bimolecular 1,4-cycloaddition reaction in greater detail paying particular attention to the nature of the dipolarophile used. The present paper documents the results of our studies in this area.

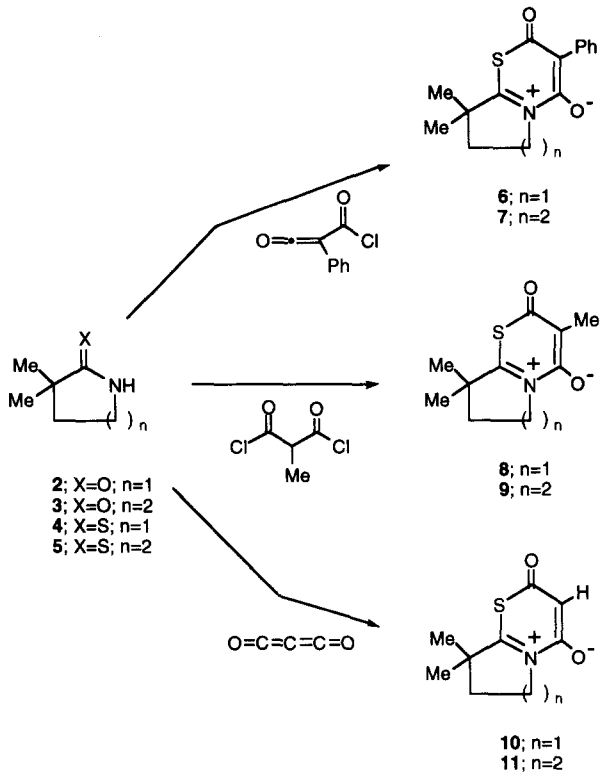
Results and Discussion

The anhydro-4-hydroxy-2-oxo-1,3-thiazinium hydroxide dipoles were synthesized by three different procedures depending on the nature of the substituent group at the 3-position of the ring. Sulfuration of a 3,3-disubstituted lactam such as **2** or **3** with Lawesson's reagent[25] gave the starting thiolactams **4** and **5**. Simply mixing these compounds with (chlorocarbonyl)phenyl ketene[26] in CH_2Cl_2 at 25°C for 5 min produced the 3-phenyl substituted betaines **6** and **7** in high yield as crystalline orange solids which were quite stable and could be stored in a refrigerator for at least a year without significant decomposition. An X-ray crystal analysis of betaine **7** was carried out and an ORTEP representation of this dipole is given in Figure 1.[27] The presence of a phenyl substituent in the 3-position of the 1,3-thiazinium betaine would be anticipated to stabilize the *"masked"* 1,4-dipole by charge delocalization. Use of carbon suboxide[28] as the 1,3-bielectrophile allows the introduction of a hydrogen at this position. The reaction of the 3H-thiolactam with methyl malonyl dichloride[29] provides an effective way of introducing a methyl group, thus extending the generality of the process.

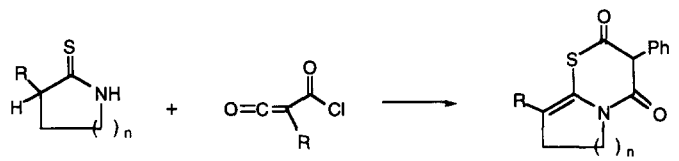
Attempts to form the 8H-anhydro-4-hydroxy-2-oxo-1,3-thiazinium hydroxide system from 3-monosubstituted thiolactams failed to give the 1,4-dipole. Although the reaction afforded highly colored

Figure 1. *ORTEP Representation of Betaine 7.*



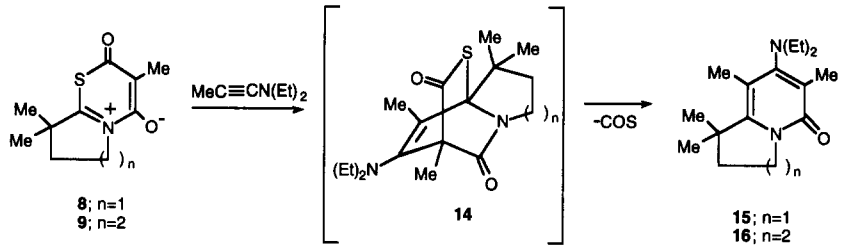


solutions, all attempts to isolate a 1,4-dipole were unsuccessful. The only product that was formed corresponded to an S,N-ketene acetal. Apparently, the initially formed betaine is unstable to the reaction conditions and readily loses a proton.

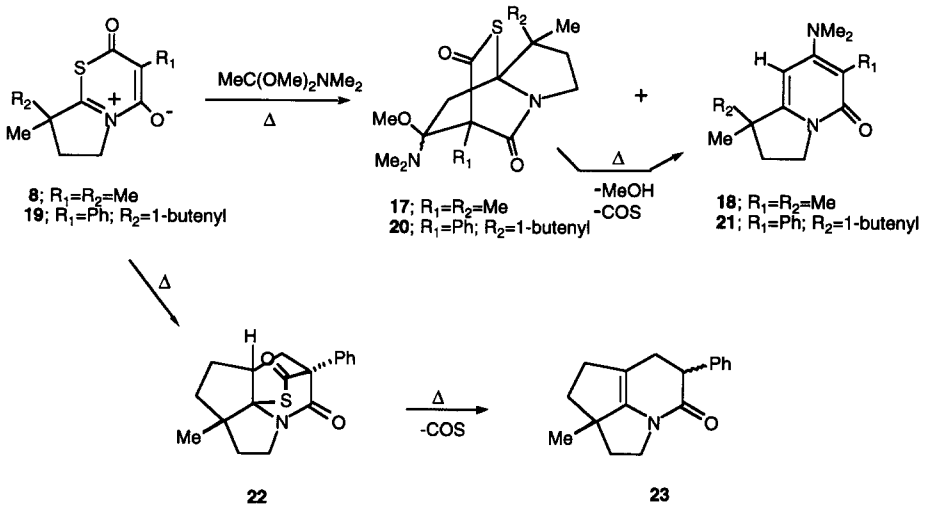


12 13

Our bimolecular cycloaddition studies commenced by studying the reaction of betaine **8** with 1-diethylamino-1-propyne. The 1,4-dipolar cycloaddition proceeded readily at 0°C (10 min) in CH_2Cl_2 producing α-pyridone **15** in quantitative yield. An analogous reaction occurred with the homologous betaine **9** producing cycloadduct **16** in 90% yield. Formation of the pyridone ring presumably involves 1,4-dipolar cycloaddition of the betaine across the triple bond to give the initial cycloadduct **14**, which undergoes a rapid cheletropic extrusion of carbonyl sulfide.[16] No signs of the initial adduct **14** could be detected, even at temperatures as low as -20°C.



When the reaction of **8** was carried out in the presence of N,N-dimethylacetamide dimethyl acetal in CH_2Cl_2 at 40°C for 2 h, two compounds were isolated in a combined 85% yield. The major product corresponded to α-pyridone **18** (75%) while the minor component was the dipolar cycloadduct **17**. When **17** was allowed to stand in solution at 25°C, it was slowly converted to **18** over a period of several hours. The extrusion of COS was accelerated by heating **17** in CH_2Cl_2. The formation of cycloadduct **17** can be accounted for by an initial loss of methanol from N,N-dimethylacetamide dimethyl acetal to give (1-methoxyvinyl)dimethylamine[30] which undergoes a subsequent bimolecular cycloaddition with betaine **8** to produce **17**.

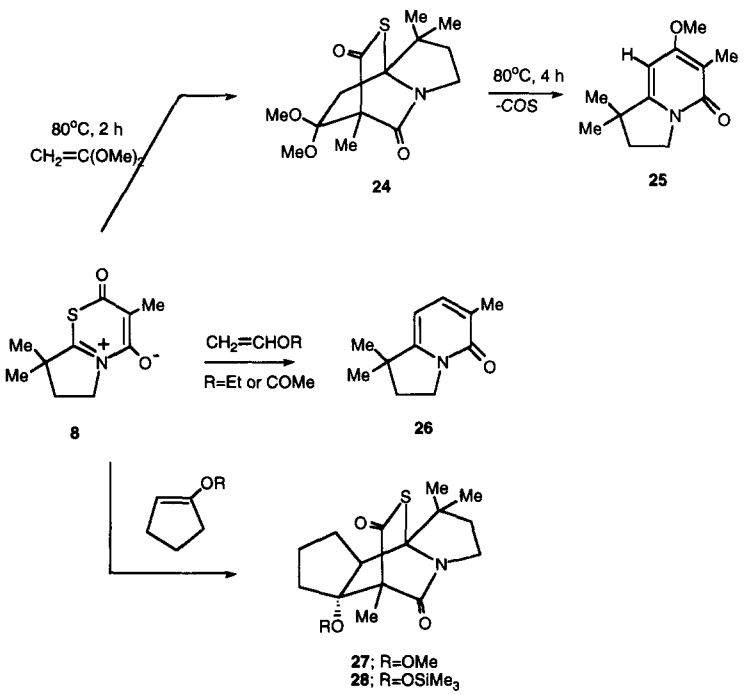


Work in our laboratory together with Pott's group has shown that the intramolecular 1,4-dipolar cycloaddition of bicyclic thiazinium hydroxides with tethered alkenyl π-bonds is a very efficient process and provides an easy route toward a variety of 5,5,6-fused heterocyclic ring systems.[23] Thus, heating betaine **19** in xylene for 30 min afforded cycloadduct **22** in 98% yield which extruded carbonyl sulfide[31] on further heating (240°C) to produce **23** as a 5:1-mixture of diastereomers. Interestingly, when the thermolysis of **19** was carried out in the presence of N,N-dimethylacetamide dimethyl acetal, the only product isolated corresponded to pyridone **21**, the intermediate cycloadduct **20** not being isolated. This observation clearly points out the high reactivity of electron rich π-systems as dipolarophiles in these 1,4-

dipolar cycloaddition reactions *(vide infra).*

We also became interested in the possibility of using the resulting α-pyridone **21** for a further intramolecular 4+2-cycloaddition. 2-Pyridones have been employed in normal electron demand bimolecular Diels-Alder reactions with electron deficient π-systems.[32,33] The intramolecular Diels-Alder reaction of 2-pyridones would provide a convenient route to complex polyazaheterocycles and remains an almost totally unexplored reaction.[34] Unfortunately, all of our attempts to induce pyridone **21** to undergo internal cycloaddition across the butenyl π-bond failed to lead to any characterizable products and further work with this system was abandoned.

Betaine **8** was found to require higher temperatures and prolonged reaction times for bimolecular cycloadditions with less activated π-systems.[34-36] For example, it was necessary to heat a sample of **8** with 1,1-dimethoxyethylene in benzene at 80°C for 2 h in order for cycloaddition to occur. The initial cycloadduct **24** was isolated in 83% yield which on further heating (80°C, 4 h) extruded carbonyl sulfide to give α-pyridone **25**. In order to induce cycloaddition of **8** with ethyl vinyl ether or vinyl acetate, it was necessary to carry out the reaction in toluene (sealed tube) at 135°C for 16 h. Under these conditions, only α-pyridone **26** was isolated in 60 or 65% yield, respectively. The initially formed 1,4-cycloadduct apparently undergoes a facile *elimination-extrusion* reaction producing the stable pyridone ring. An analogous cycloaddition reaction occurred with both the methyl and silyl enol ethers of cyclopentanone giving the 1,4-cycloadducts **27** (75%) and **28** (90%) as stable crystalline solids.

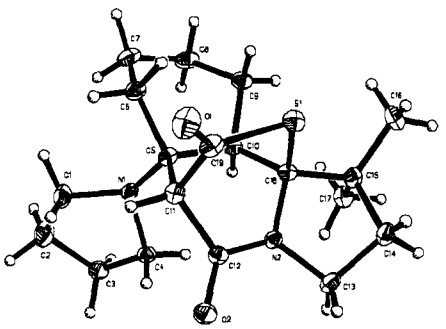


24 **25** **8** **26**

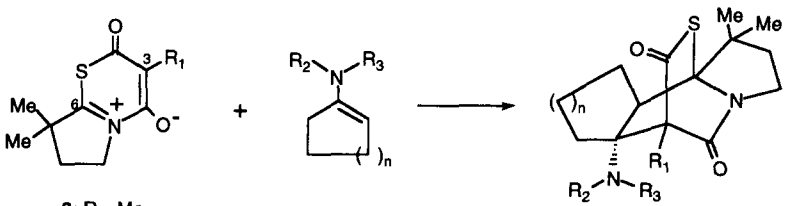
27; R=OMe
28; R=OSiMe$_3$

High yields of bimolecular cycloadducts (*ca* 85%) were also obtained when betaine **8** (or **10**) was allowed to react with several cyclic enamines. Structural assignments were made on the basis of their analytical and spectral properties. In the case of cycloadduct **31**, its structure was unequivocally established by an X-ray crystal analysis (see Figure 2).[27] Cycloadducts **29-31** were resistant to the loss of carbonyl sulfide under a variety of forcing thermal conditions. These bimolecular 1,4-dipolar cycloadditions can proceed either through *exo*- or *endo*-transition states. The exclusive *endo* selectivity

Figure 2. *ORTEP Representation of Cycloadduct* ***31***.



(relative to the pyrrolidine ring) encountered with these systems can be understood by noting that, in the transition state leading to the *exo* isomer, there is a severe nonbonding interaction between the α-methyl group on the betaine with the allylic hydrogens on the enamine. This interaction is absent in the transition state leading to cycloadduct **31**.



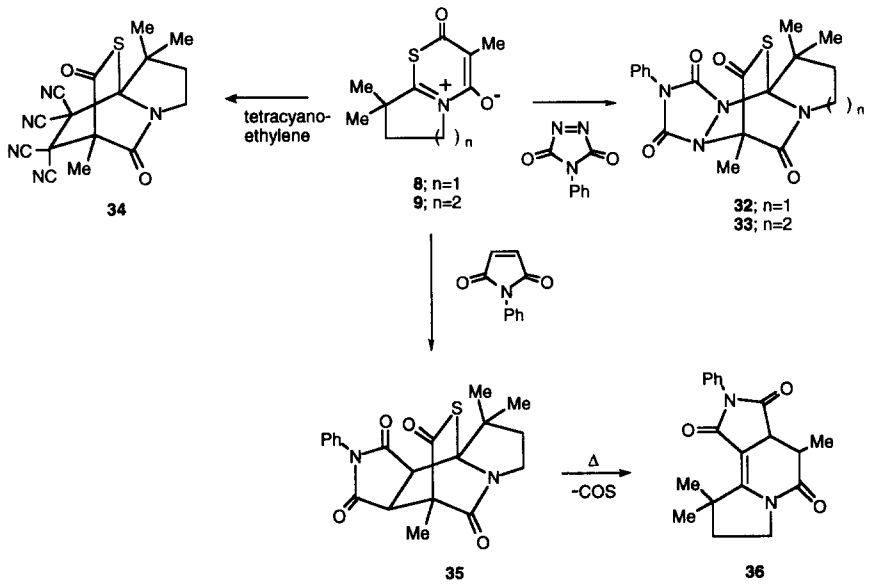
8; R_1=Me
10; R_1=H

29; R_1=Me; R_2=R_3=$(CH_2)_2$; n=2
30; R_1=Me; R_2=$(CH_2)_2$; R_3=$O(CH_2)_2$; n=1
31; R_1=H; R_2=R_3=$(CH_2)_2$; n=2

Anhydro-4-hydroxy-2-oxo-1,3-thiazinium hydroxides (*i.e.*, **1**; X=S) contain a 1,4-dipole within their framework and are therefore willing participants in cycloaddition chemistry. Of the three categories described by Sustmann,[37] the type II classification seems to best fit the 1,4-dipolar cycloadditions of these cyclic betaines (*i.e.*, **6-11**). Indeed, the regioselectivity observed using electron rich π-systems is perfectly consistent with frontier molecular orbital theory.[38] With these betaines, the dominant interaction is the *LUMO*$_{(dipole)}$ (-1.86 ev)-*HOMO*$_{(dipolarophile)}$ (type III). The frontier orbital coefficients at the reacting centers of the betaine were calculated using the MOPAC program with the PM3 Hamiltonian. MNDO

calculations indicate that the atomic coefficient at the thioamide carbonyl center (*i.e.*, C_6) is larger (0.73) than the enolate substituted center (*i.e.*, C_3 (0.18)) in the LUMO (See Table I). It is well known that the C_β-coefficient of the HOMO of an electron rich alkene is larger than the C_α-coefficient[39] and consequently cycloadducts related to **31** are predicted to be the major regioisomers.

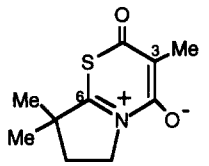
The cycloaddition reaction of betaine **8** with several alkyl- and aryl-substituted ethylenes failed and this is undoubtedly related to the large energy gap between the frontier molecular orbitals. MO calculations indicate that the cycloaddition of these 1,4-dipoles with electron-deficient olefins should switch over to a $HOMO_{(1,4\text{-dipole})}$-$LUMO_{(dipolarophile)}$ controlled process (type I). In order to probe this point, we examined the cycloaddition reactions of betaines **8** and **9** with several electron-deficient alkenes. When the extremely reactive 4-phenyl-1,2,4-triazoline-3,5-dione was used as the dipolarophile, cycloadducts **32** and **33** were isolated in excellent yield. As anticipated, tetracyanoethylene also underwent ready cycloaddition with betaine **8** at 25°C to give cycloadduct **34** in 98% yield. N-Phenylmaleimide was also found to react with betaine **8** producing cycloadduct **35** as a 2:1-mixture of diastereomers in high yield. Further heating of **35** (240°C) produced compound **36** which is the consequence of COS extrusion. Other π-systems whose frontier MO gap was greater than 8.5 ev failed to cycloadd. Interestingly, dimethyl acetylenedicarboxylate and quinone did not undergo cycloaddition. With these π-systems, we suspect that the reason is the instability of these reagents to the thermal conditions (180°C) necessary to induce the reaction.



The high yield encountered (98%) when N-phenylmaleimide was allowed to react with betaine **8** led us to explore whether the bimolecular cycloaddition would occur preferentially across an electron-rich

or electron-deficient dipolarophile if both pathways were available. In order to probe this point, the reaction of betaine **8** in the presence of a 1:1-mixture of N-phenylmaleimide and N,N-dimethylacetamide dimethyl

Table I. *HOMO and LUMO Energies and Coefficients for Betaine* ***8***



atom no.	C_3	C_6
HOMO coeff.	-0.77	+0.11
LUMO coeff.	+0.18	+0.73

Energy Separation
ΔE ev

dipolarophile	*type I*[a]	*type III*[b]
1-morphilino-1-cyclopentene	9.81	6.56
1-diethylamino-1-propyne	10.60	6.77
N,N-dimethylacetamide dimethylacetal[c]	9.75	6.96
1-methoxycyclopentene	9.95	7.12
ethyl vinyl ether	10.01	7.73
1,1-dimethoxyethylene	9.47	8.30
cyclopentene	9.95	8.65
N-phenylmaleimide	7.22	7.44
maleic anhydride	7.25	9.84
N-phenyl-1,2,4-triazoline-3,5-dione	7.01	7.93
tetracyanoethylene	6.12	9.53

[a][$HOMO_{(dipole)}$-$LUMO_{(dipolarophile)}$]

[b][$HOMO_{(dipolarophile)}$-$LUMO_{(dipole)}$]

[c][(1-methoxyvinyl)-dimethyl amine as the dipolarophile]

acetal was carried out. The only product isolated from the reaction corresponded to cycloadduct **18** derived from the cycloaddition of **8** with N,N-dimethylacetamide dimethyl acetal. MNDO calculations indicate that the smaller energy gap (ΔE=6.96) corresponds to the type III process and consequently the reaction of betaine **8** occurs preferentially with (1-methoxyvinyl)-dimethylamine (see Table I). In a separate experiment, betaine **8** was also allowed to react with a 1:1-mixture of N-phenylmaleimide and 1,1-dimethoxyethylene. In this case, the only cycloadduct obtained (*i.e.* **35**) corresponded to cycloaddition across the electron-deficient π-bond (type I process). A similar trend was also noted in several other competition experiments. In all the cases examined, we have found that the rate of cycloaddition of a particular dipolarophile with betaine **8**, can be nicely accommodated in terms of perturbation theory.

In conclusion, the bimolecular 1,4-cycloaddition of bicyclic anhydro-2-oxo-4-hydroxy-1,3-thiazinium hydroxides proceeds smoothly with a very high degree of regio- and diastereoselectivity. Other aspects of this reaction and its application to more complex natural product synthesis will be reported in due course.

General Experimental

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-hexane mixture as the eluent unless specified otherwise.

Preparation of Anhydro-8,8-dimethyl-4-hydroxy-2-oxo-3-phenyl-7,8-dihydropyrrolo[2,1-*b*][1,3]-thiazinium Hydroxide (6). To a solution containing 370 mg (2.90 mmol) of 3,3-dimethyl-pyrrolidin-2-thione (**4**)[40] in 50 mL of dry CH_2Cl_2 at rt was added 670 mg (3.7 mmol) of (chlorocarbonyl)phenylketene[26] in one portion. The resulting mixture was stirred for 10 min at rt and then the solvent was removed under reduced pressure. Purification of the orange residue by flash chromatography on silica gel gave 751 mg (96%) of the 1,4-dipole **6**; mp 199-200°C; IR (CCl_4) 3000, 1610, and 1500 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.34 (s, 6H), 1.97-2.01 (m, 2H), 4.30-4.35 (m, 2H), and 7.18-7.47 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 26.4, 33.4, 53.1, 53.7, 102.0, 126.5, 127.8, 130.9, 133.4, 159.0, 167.7, and 192.0; Anal. Calcd. for $C_{15}H_{15}NO_2S$: C, 65.91; H, 5.49; N, 5.13; S, 11.73. Found: C, 65.86; H, 5.59; N, 5.12; S, 11.80.

Preparation of Anhydro-9,9-dimethyl-4-hydroxy-2-oxo-3-phenyl-tetrahydropyrido[2,1-*b*][1,3]-thiazinium Hydroxide (7). To a solution containing 18.6 g (164.4 mmol) of 3-methyl-piperidin-2-one in 600 mL of THF at 0°C was added 226 mL of *n*-butyllithium (1.6 M in hexane) dropwise *via* a syringe. The resulting solution was stirred for 2 h at 0°C, cooled to -78°C, and 23.3 g (164.4 mmol) of methyl iodide was added in one portion *via* syringe. The reaction mixture was stirred overnight while slowly warming to rt.

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 to give 19.9 g (95%) of 3,3-dimethyl-piperidin-2-one as a white solid; mp 102-103°C; IR ($CHCl_3$) 3270, 3180, and 1640 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.11 (s, 6H), 1.53-1.58 (m, 2H), 1.63-1.70 (m, 2H), 3.18 (dt, 2H, J=6.0 and 2.2 Hz), and 7.10 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 19.2, 27.0, 35.8, 37.5, 42.6, and 178.7; Anal. Calcd. for $C_7H_{13}NO$: C, 66.05; H, 10.30; N, 11.01. Found: C, 66.13; H, 10.38; N, 11.03.

A sample of 3,3-dimethyl-piperidin-2-thione (**5**) was prepared by heating 9.2 g (72.3 mmol) of 3,3-dimethyl-piperidin-2-one and 14.6 g (36.1 mmol) of Lawesson's reagent[25] in 100 mL of refluxing toluene for 30 min. Removal of the solvent under reduced pressure followed by flash silica gel chromatography to give 9.5 g (92%) of **5** as a white solid; mp 96-97°C; IR (CCl_4) 3200-3100, 2920, and 1545 cm^{-1}; ^1H-NMR (300 MHz, $CDCl_3$) δ 1.23 (s, 6H), 1.53-1.57 (m, 2H), 1.64-1.77 (m, 2H), 3.15-3.17 (m, 2H), and 9.59 (brs, 1H); ^{13}C-NMR (75MHz, $CDCl_3$) δ 18.5, 30.8, 34.8, 41.7, 45.1, and 211.5.

To a solution containing 1.0 g (7.0 mmol) of 3,3-dimethyl-piperidin-2-thione (**5**) in 50 mL of dry CH_2Cl_2 at rt was added 1.5 g (8.3 mmol) of (chlorocarbonylphenyl)ketene[26] in one portion. The resulting mixture was stirred for 10 min at rt and then the solvent was removed under reduced pressure. Purification of the orange residue by flash chromatography on silica gel gave 1.3 g (66%) of the 1,4-dipole **7** as orange needles; mp 155-156°C; IR (CCl_4) 3000, 1605, and 1500 cm^{-1}; ^1H-NMR (300 MHz, $CDCl_3$) δ 1.18 (s, 6H), 1.39-1.42 (m, 2H), 1.64 (brs, 2H), 3.76-3.80 (m, 2H), 7.05-7.07 (m, 1H), 7.16-7.21 (m, 2H), and 7.37 (d, 2H, J=7.5 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 18.0, 30.6, 33.6, 41.9, 49.0, 102.2, 126.1, 127.4, 130.9, 134.3, 160.9, 166.4, and 193.2; Anal. Calcd. for $C_{16}H_{17}NO_2S$: C, 66.87; H, 5.96; N, 4.88; S, 11.16. Found: C, 66.97; H, 5.96; N, 4.91; S, 11.09.

Preparation of Anhydro-3,8,8-trimethyl-4-hydroxy-2-oxo-7,8-dihydropyrrolo[2,1-*b*][1,3]-thiazinium Hydroxide (8). To a solution containing 1.2 g (9.3 mmol) of thiolactam **4** in 50 mL of dry CH_2Cl_2 at 5°C was added dropwise 2.2 g (14.2 mmol) of methyl malonyl dichloride[29]. The bright yellow solution was allowed to warm to 25°C and was stirred at rt for 12 h. The solution was concentrated under reduced pressure and the resulting residue was subjected to silica gel chromatography to give 1.8 g (91%) of 1,4-dipole **8**; mp 123-124°C; IR (KBr) 2930, 1731, 1600, and 1531 cm^{-1}; ^1H-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 Anhydro-3,9,9-trimethyl-4-hydroxy-2-oxo-tetrahydropyrido[2,1-*b*][1,3]-thiazinium Hydroxide (9). A sample of 1,4-dipole **9** was prepared in the same manner outlined for dipole **8**. A 400 mg (2.79 mmol) sample of 3,3-dimethyl-piperidin-2-thione (**5**) in 20 mL of dry CH_2Cl_2 at 5°C was allowed to react with 651 mg (4.20 mmol) of methyl malonyl dichloride.[29] Workup as outlined for dipole **8** provided 600 mg (95%) of 1,4-dipole **9** as yellow crystals; mp 129-130°C; IR (KBr) 2946, 1659, and 1595 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.53 (s, 6H), 1.83-1.87 (m, 2H), 1.99 (s, 3H), 2.04-2.12 (m, 2H), and 4.17 (t, 2H, J=6.3 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 10.3, 18.1, 30.8, 34.1, 41.8, 48.8, 97.9, 161.2, 166.1, and 191.5; Anal. Calcd. for $C_{11}H_{16}NO_2S$: C, 58.38; H, 7.13; N, 6.19. Found: C, 58.21; H, 7.05; N, 6.07.

Preparation of Anhydro-8,8-dimethyl-4-hydroxy-2-oxo-7,8-dihydropyrrolo[2,1-*b*][1,3]-thiazinium Hydroxide (10). A sample of carbon suboxide[41] was prepared by the dropwise addition of 1.4 g (4.7 mmol) of dibromomalonyl dichloride in 10 mL of ether *via* an addition funnel to a slurry of zinc dust 0.9 g (13.8 mmol) in 3 mL of distilling ether. The carbon suboxide produced (bp 7°C) codistills with ether and was condensed with a dry ice acetone condenser. The condenser was attached to a flask containing a magnetically stirred mixture of 200 mg (1.5 mmol) of 3,3-dimethyl-pyrrolidin-2-thione (**4**) in 5 mL of ether at -78°C. After the addition of dibromomalonyl dichloride was complete, the addition funnel was washed with several 5 mL portions of ether. The reaction mixture was stirred at -78°C under positive argon pressure and then allowed to slowly warm to rt. After stirring several hours at rt, the solvent was removed under reduced pressure to give 305 mg (100%) of 1,4-dipole **10** as red crystals; mp 152-153°C; IR (KBr) 2968, 1675, and 1625 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.47 (s, 6H), 2.18 (t, 3H, J=7.2 Hz), 4.40 (t, 3H, J=7.2 Hz), and 5.20 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 26.4, 33.6, 52.2, 53.7, 86.7, 159.7, 167.8, and 194.8; Anal. Calcd. for $C_9H_{11}NO_2S$: C, 54.80; H, 5.62; N, 7.10; S, 16.26. Found: C, 54.89; H, 5.66; N, 7.13; S, 16.16.

Preparation of Anhydro-9,9-dimethyl-4-hydroxy-2-oxo-tetrahydropyrido[2,1-*b*][1,3]-thiazinium Hydroxide (11). A sample of 1,4-dipole **11** was prepared in the same manner outlined for dipole **10** from 500 mg (3.49 mmol) of 3,3-dimethyl-piperidin-2-thione (**5**), 3.1 g (10.4 mmol) of dibromomalonyl dichloride, and 2.1 g (32.2 mmol) of zinc dust. Removal of the solvent at 16 h resulted in the quantitative formation of 1,4-dipole **11**; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.55 (s, 6H), 1.84-1.88 (m, 2H), 2.04-2.12 (m, 2H), 4.14 (t, 2H, J=6.3 Hz), and 5.30 (s, 1H).

Preparation of 7-Diethylamino-1,1,6,8-tetramethyl-2,3-dihydro-1*H*-indolizin-5-one (15). A 69 mg (0.62 mmol) sample of 1-diethylamino-1-propyne was added in one portion to a -20°C solution containing 66 mg (0.31 mmol) of 1,4 dipole **8** in 1 mL of CH_2Cl_2. The resulting solution was stirred for 10 min at -20°C. Removal of the solvent under reduced pressure followed by chromatography on silica gel gave 73 mg (90%) of **15** as a yellow oil; IR (neat) 2968, 2868, 1730, and 1630 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.06 (t, 6H, J=7.0 Hz), 1.39 (s, 6H), 1.98 (t, 2H, J=7.0 Hz), 2.06 (s, 6H), 3.06 (q, 4H, J=7.0 Hz), and 4.09

(t, 2H, J=7.0 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 12.2, 13.3, 14.2, 26.1, 38.8, 45.0, 45.3, 46.2, 110.8, 121.6, 149.2, 158.9, and 162.3; HRMS Calcd. for $C_{16}H_{26}N_2O$: 262.2045. Found: 262.2045.

Preparation of 2-Diethylamino-3,9,9-trimethyl-6,7,8,9-tetrahydroquinolizin-4-one (16). A 148 mg (1.33 mmol) sample of diethylamino-1-propyne was added dropwise to a -78°C solution containing 200 mg (0.88 mmol) of 1,4-dipole **9** in 5 mL of dry CH_2Cl_2. The resulting dark solution was allowed to reach rt and was stirred at this temperature for 8 h. Removal of the solvent under reduced pressure followed by distillation (110-120°C, 10^{-4} mm) provided 210 mg (86%) of cycloadduct **16** as a yellow oil; IR (neat) 2969, 1690, 1632, and 1580 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.00 (t, 6H, J=6.9 Hz), 1.43 (s, 6H), 1.64-1.67 (m, 2H), 1.85-1.93 (m, 2H), 2.05 (s, 3H), 2.20 (s, 3H), 3.05 (q, 4H, J=6.9 Hz), and 3.94 (t, 2H, J=6.6 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 13.6, 14.0, 16.1, 18.6, 28.5, 35.5, 40.4, 46.1, 46.2, 115.4, 121.3, 147.6, 157.6, and 164.2; HRMS Calcd. for $C_{17}H_{29}N_2O$: $[M+H]^+$ 277.2280. Found: 227.2280.

Preparation of 7-Dimethylamino-1,1,6-trimethyl-2,3-dihydro-1*H*-indolizin-5-one (18). A solution containing 100 mg (0.47 mmol) of 1,4 dipole **8** and 914 mg (6.71 mmol) of N,N-dimethylacetamide dimethyl acetal in 4.5 mL of CH_2Cl_2 was heated at 40°C for 3 h. Removal of the solvent under reduced pressure followed by chromatography on silica gel gave 88 mg (85%) of **18** as a yellow oil; IR (neat) 2954, 1637, and 1588 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.28 (s, 6H), 1.91 (t, 2H, J=7.1 Hz), 2.11 (s, 3H), 2.78 (s, 6H), 4.08 (t, 2H, J=7.1 Hz), and 5.80 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 13.2, 27.2, 37.0, 42.7, 43.9, 45.7, 92.0, 110.3, 154.7, 160.7, and 162.7; HRMS Calcd. for $C_{13}H_{20}N_2O$: 220.1575. Found: 220.1572.

The very labile 1,4-dipolar cycloadduct **17** could be obtained in modest yield by flash chromatography of the crude reaction mixture on silica gel; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.19 (s, 3H), 1.21 (s, 3H), 1.59 (s, 3H), 1.75-1.82 (m, 1H), 1.95-2.21 (m, 1H), 2.20 (s, 6H), 2.21-2.39 (m, 2H), 3.30 (s, 3H), 3.47-3.52 (m, 1H), and 3.62-3.71 (m, 1H).

Preparation of 1-But-3-enyl-7-dimethylamino-1-methyl-6-phenyl-2,3-dihydro-1*H*-indolizin-5-one (21). A solution containing 300 mg (0.86 mmol) of 1,4 dipole **19**[42] and 229 mg (1.68 mmol) N,N-dimethylacetamide dimethyl acetal in 15 mL of CH_2Cl_2 was heated at reflux for 2 h. Removal of the solvent under reduced pressure followed by chromatography on silica gel gave 224 mg (81%) of **21** as white crystals; mp 148-149°C; IR (neat) 2958, 1644, and 1587 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.31 (s, 3H), 1.60-1.80 (m, 2H), 1.83-1.92 (m, 2H), 2.00-2.19 (m, 2H), 2.57 (s, 6H), 4.00 (t, 2H J=7.0 Hz), 4.90-5.10 (m, 2H), 5.76 (s, 1H), 5.75-8.82 (m, 1H), and 7.10-7.41 (m, 5H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 25.5, 28.9, 34.3, 39.1, 42.2, 45.9, 47.5, 92.2, 109.9, 114.8, 125.9, 127.7, 131.0, 137.7, 137.9, 155.1, 158.4, and 161.6; Anal. Calcd. for $C_{21}H_{26}N_2O$: C, 78.21; H, 8.13; N, 8.69. Found: C, 78.14; H, 8.09; N, 8.48.

Preparation of 11,11-Dimethoxy-2,2,7-trimethyl-9-thia-5-aza-tricyclo[5.2.2.0^{1,5}]undecane-6,8-dione (24). A solution containing 100 mg (0.47 mmol) of 1,4 dipole **8** and 83 mg (0.95 mmol) of 1,1-

dimethoxyethylene in 3 mL of benzene was heated at reflux for 2 h. Removal of the solvent under reduced pressure followed by chromatography on silica gel gave 117 mg (83%) of **24** as a white solid; mp 80-82°C; IR (neat) 2968, 1701, and 1666 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.18 (s, 3H), 1.23 (s, 3H), 1.58 (s, 3H), 1.84 (ddd, 1H, J=12.6, 3.1, and 3.0 Hz), 2.15 (dt, 1H, J=12.6 and 9.0 Hz), 2.48 (AB quartet, 2H, J=13.3 Hz), 3.30 (s, 3H), 3.36 (s, 3H), 3.55 (ddd, 1H, J=18.5, 9.5, and 9.4 Hz), and 3.64 (ddd, 1H, J=18.5, 8.7, and 8.5 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 9.6, 9.7, 23.4, 23.8, 37.3, 43.7, 44.2, 50.4, 51.0, 51.1, 70.0, 102.1, 166.7, and 197.5; Anal. Calcd. for $C_{14}H_{22}NO_4S$: C, 55.98; H, 7.39; N, 4.67. Found: C, 55.81; H, 7.42; N, 4.58.

A solution containing 100 mg (0.47 mmol) of cycloadduct **24** in 3 mL of benzene was heated at reflux for 4 h. Removal of the solvent under reduced pressure followed by chromatography on silica gel gave 90 mg (93%) of **25** as white crystals; mp 126-127°C; IR (neat) 2958, 1644, and 1587 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.31 (s, 6H), 1.95 (s, 3H), 1.96 (t, 2H, J=7.0 Hz), 3.81 (s, 3H), 4.09 (t, 2H, J=7.0 Hz), and 3.55 (s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 8.4, 21.1 36.9, 44.1, 45.8, 55.7, 87.1, 107.7, 156.1, 162.4, and 164.9; Anal. Calcd. for $C_{12}H_{17}NO_2$: C, 69.52; H, 8.27; N, 6.76. Found: C, 69.43; H, 8.02; N, 6.69.

Preparation of 1,1,6-Trimethyl-2,3-dihydro-1*H*-indolizin-5-one (26) from Vinyl Acetate. A sealed tube containing 100 mg (0.47 mmol) of 1,4 dipole **6** and 780 mg (9.06 mmol) of vinyl acetate in 2.5 mL of toluene was heated at 150°C for 16 h. Removal of the solvent under reduced pressure followed by chromatography on silica gel gave 29 mg (35%) of pyridone **26** as white crystals; mp 94-95°C; IR (neat) 2966, 1642, and 1583 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.26 (s, 6H), 1.96 (t, 2H, J=7.0 Hz), 2.09 (s, 3H), 4.08 (t, 2H, J=7.0 Hz), 5.90 (d, 1H, J=6.8 Hz), and 7.17 (d, 1H, J=6.8 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 16.4, 27.1, 37.0, 43.7, 45.9, 98.1, 126.0, 137.6, 155.9, and 162.1; Anal. Calcd. for $C_{11}H_{15}NO$: C, 74.53; H, 8.54; N, 7.91. Found: C, 74.47; H, 8.36; N, 7.88.

A similar thermolysis of 1,4 dipole **8** with ethyl vinyl ether in 2.5 mL of toluene at 150°C for 16 h afforded pyridone **26** in 23% yield.

Preparation of 10a-Methoxy-1-thia-3,7,7-trimethyl-decahydro-4a-aza-as-indacen-2,4-dione (27). A sealed tube containing 120 mg (0.57 mmol) of 1,4 dipole **8** and 334 mg (3.40 mmol) of 1-methoxycyclopentene in 2 mL of benzene was heated at 180°C for 24 h. Removal of the solvent under reduced pressure followed by chromatography on silica gel gave 132 mg (75%) of **27** as white crystals; mp 130-132°C; IR (neat) 2965, 1694, and 1662 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.19 (s, 3H), 1.25 (s, 3H), 1.41 (s, 3H), 1.38-1.44 (m, 1H),1.65-1.92 (m, 5H), 2.10-2.21 (m, 2H), 2.79 (t, 1H, J=7.9 Hz), 3.19 (s, 3H), 3.52 (ddd, 1H, J=18.3, 11.4, and 11.3 Hz), and 3.77 (dd, 1H, J=11.1 and 10.9 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 10.1, 23.5, 24.2, 25.8, 30.8, 34.9, 37.9, 43.7, 44.9, 50.4, 50.8, 69.4, 83.2, 90.8, 169.5, and 199.7; Anal. Calcd. for $C_{16}H_{24}NO_3S$: C, 61.91; H, 7.80; N, 4.51. Found: C, 61.78; H, 7.73; N, 4.42.

Preparation of 5a-Trimethylsilyloxy-1,1,5-trimethyl-decahydro-3a-aza-indacen-4-one (28). A sealed tube containing 95 mg (0.45 mmol) of 1,4 dipole **8** and 106 mg (0.67 mmol) of 1-(trimethysilyloxy)cyclopentene in 3 mL of benzene was heated at 180°C for 36 h. Removal of the solvent under reduced pressure followed by chromatography on silica gel gave 158 mg (90%) of **28** as white crystals; mp 109-110°C; IR (neat) 2965, 1694, and 1662 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.09 (s, 9H), 1.15 (s, 3H), 1.21 (s, 3H), 1.37 (s, 1H), 1.30-1.41 (m, 3H), 1.70-1.88 (m, 5H), 2.10-2.25 (m, 2H), 2.65 (dd, 1H, J=8.7 and 8.6 Hz), 3.44 (ddd, 1H, J=18.2, 11.3, and 11.3 Hz), and 3.72 (dd, 1H, J=11.1 and 10.4 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 2.2, 10.3, 23.6, 24.3, 25.4, 30.5, 37.8, 37.9, 43.7, 44.6, 57.4, 70.7, 82.7, 89.6, 168.9, and 200.0; Anal. Calcd. for $C_{18}H_{30}NO_3SSi$: C, 58.67; H, 8.21; N, 3.80. Found: C, 58.62; H, 8.09; N, 3.75.

Preparation of 3,3,7-Trimethyl-11a-pyrrolidin-1-yl-1-thia-dodecahydro-pyrrolo[2,1-*a*]isoquinolin-2,4-dione (29). A 172 mg (1.14 mmol) sample of 1-pyrrolidino-1-cyclohexene was added drop-wise to a 5°C solution containing 200 mg (0.95 mmol) of 1,4-dipole **8** in 4 mL of dry CH_2Cl_2. The resulting solution was allowed to reach rt and was stirred at this temperature for 18 h. Removal of the solvent under reduced pressure was followed by flash silica gel chromatography to give 285 mg (83%) of adduct **29** as a white solid; mp 159-160°C; IR (KBr) 2950, 1684, and 1657 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.25 (s, 3H), 1.32 (s, 3H), 1.44 (s, 3H), 1.50-1.74 (m, 11H), 1.85-1.92 (m, 1H), 1.97-2.05 (m, 1H), 2.16-2.26 (m, 1H), 2.46-2.55 (m, 1H), 2.83-2.88 (m, 2H), 2.99-3.04 (m, 2H), 3.44-3.54 (m, 1H), and 3.75-3.82 (m, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 11.8, 18.6, 18.7, 21.9, 24.3, 24.5, 25.4, 27.6, 38.5, 43.6, 45.4, 45.8, 47.2, 63.5, 71.8, 82.4, 170.3, and 200.8; Anal. Calcd. for $C_{20}H_{30}N_2O_2S$: C, 66.26; H, 8.34; N, 7.73; S, 8.85. Found: C, 66.15; H, 8.40; N, 7.72; S, 8.77.

Preparation of 3,7,7-Trimethyl-10a-morpholin-4-yl-1-thia-decahydro-4a-aza-as-indacen-2,4-dione (30). A 65 mg (4.26 mmol) sample of 4-cyclopent-1-enyl-morpholine was added dropwise to a 5°C solution containing 75 mg (3.55 mmol) of 1,4-dipole **8** in 1 mL of dry CH_2Cl_2. The resulting solution was allowed to reach rt and was stirred at this temperature for 18 h. Removal of the solvent under reduced pressure was followed by flash silica gel chromatography to give 115 mg (90%) of adduct **30** 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), 2.60-2.75 (m, 4H), 2.85 (t, 1H, J=9.0 Hz), 3.43-3.50 (m, 1H), 3.53-3.60 (m, 4H), and 3.74-3.81 (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.

Preparation of 7,7-Dimethyl-11a-pyrrolidin-1-yl-1-thia-dodecahydropyrrolo[2,1-*a*]isoquinolin-2,4-dione (31). A 230 mg (1.52 mmol) sample of 1-pyrrolidino-1-cyclohexene was added dropwise to a 5°C solution of 200 mg (1.01 mmol) of 1,4-dipole **10** in 5 mL of dry CH_2Cl_2. The resulting solution was allowed

to reach rt and was stirred at this temperature for 18 h. Removal of the solvent under reduced pressure was followed by flash silica gel chromatography to give 257 mg (67%) of cycloadduct **31** as white crystals; mp 194-195°C; IR (KBr) 2954, 2867, 1687, and 1667 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.26 (s, 3H), 1.32 (s, 3H), 1.31-1.85 (m, 13H), 2.18-2.30 (m, 1H), 2.52-2.57 (m, 1H), 2.73-2.85 (m, 4H), 3.38-3.50 (m, 1H), 3.73-3.82 (m, 1H), and 3.88 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 16.6, 18.6, 22.2, 24.0, 24.3, 24.6, 29.2, 38.7, 42.8, 45.0, 45.5, 45.6, 61.4, 65.8, 85.7, 168.2, and 198.0; Anal. Calcd. for $C_{19}H_{29}N_2O_2S$: C, 65.29; H, 8.37; N, 8.02. Found: C, 65.14; H, 8.15; N, 8.24.

Preparation of 9-Phenyl-1-thia-3,7,7-trimethyl-octahydro-4a,7b,9,10a-tetraaza-as-indacen-2,4,8,-10-tetraone (32). A 91 mg (0.52 mmol) sample of 4-phenyl-1,2,4-triazoline-3,5-dione was added in one portion to a -40°C solution containing 110 mg (0.52 mmol) of 1,4-dipole **8** in 5 mL of dry CH_3CN. The cooling bath was removed and the solution was allowed to stir for 10 min. Removal of the solvent under reduced pressure provided cycloadduct **32** (100%) as a yellow solid; mp 117-118°C; IR (KBr) 2966, 1786, 1730, 1690, and 1600 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.60 (s, 3H), 1.63 (s, 3H), 1.96-2.03 (m, 1H), 2.15 (s, 3H), 2.17-2.29 (m, 1H), 3.60-3.70 (m, 1H), 3.82-3.89 (m, 1H), and 7.39-7.51 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 12.7, 22.2, 22.8, 38.6, 44.0, 48.3, 71.9, 93.2, 125.9, 129.1, 129.2, 130.2, 150.6, 152.1, 162.0, and 188.7; Anal. Calcd. for $C_{18}H_{18}N_4O_4S$: C, 55.94; H, 4.70; N, 14.51. Found: C, 55.82; H, 4.61; N, 14.43.

Preparation of 10-Phenyl-1-thia-3,8,8-trimethyl-octahydro-2,3a,5a,9b-tetraaza-cyclopenta[a]-naphthalen-2,4,9,11-tetraone (33). A 78 mg (0.44 mmol) sample of 4-phenyl-1,2,4-triazoline-3,5-dione was added in one portion to a -40°C solution containing 100 mg (0.44 mmol) of 1,4-dipole **9** in 5 mL of dry CH_3CN. The cooling bath was removed and the solution was allowed to stir for 10 min. Removal of the solvent under reduced pressure provided cycloadduct **33** (90%) as a yellow solid; mp 102-103°C; IR (KBr) 2958, 1782, 1727, 1685 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.22-1.39 (m, 2H), 1.56 (s, 3H), 1.72 (s, 3H), 1.81-1.99 (m, 2H), 2.14 (s, 3H), 3.58-3.72 (m, 1H), 3.82-3.95 (m, 1H), and 7.39-7.50 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 13.2, 17.0, 22.8, 27.7, 35.3, 37.8, 40.0, 70.2, 93.5, 126.3, 127.0, 129.2, 130.5, 148.1, 149.7, 164.7, and 188.8; Anal. Calcd. for $C_{19}H_{20}N_4O_4S$: C, 56.98; H, 5.04; N, 14.01. Found: C, 56.78; H, 4.97; N, 14.23.

Preparation of 2,2,7-Trimethyl-6,8-dioxo-9-thia-5-aza-tricyclo[5.2.2.0 1,5]undecane-10,10,11,11-tetracarbonitrile (34). A 72 mg (0.56 mmol) sample of tetracyanoethylene was added in one portion to a solution containing 100 mg (0.47 mmol) of 1,4-dipole **8** in 4 mL CH_3CN at rt. The resulting black solution was allowed to stir at rt for 30 min. Removal of the solvent under reduced pressure followed by recrystallization of the residue from ethyl acetate/hexane gave 160 mg (98%) of cycloadduct **34** as tan crystals; mp 180-181°C; IR (KBr) 2988, 1726, and 1697 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.50 (s, 3H),

1.81 (s, 3H), 1.91 (s, 3H), 2.05-2.12 (m, 1H), 2.60-2.72 (m, 1H), 3.60-3.70 (m, 1H), and 3.99-4.06 (m, 1H); Anal. Calcd. for $C_{16}H_{13}N_5O_2S$: C, 56.63; H, 3.86; N, 20.64. Found: C, 56.38; H, 3.82; N, 20.52.

Preparation of 9-Phenyl-1-thia-3,7,7-trimethyl-decahydro-4a,9-diaza-as-indacen-2,4,8,10-tetra-one (35). A solution containing 81 mg (0.47 mmol) of N-phenylmaleimide and 100 mg (0.47 mmol) of 1,4-dipole **8** in 100 μL of dry CH_3CN was heated at 85°C for 6 h. Removal of the solvent under reduced pressure followed by trituration with ethyl acetate gave 175 mg (98%) of cycloadduct **35** as a tan solid; mp 239-240°C; IR (KBr) 2965, 1720, 1715, and 1670 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.44 (s, 3H), 1.54 (s, 3H), 1.79 (s, 3H), 1.87-1.93 (m, 1H), 2.20-2.32 (m, 1H), 3.40 (d, 1H, J=9.3 Hz), 3.45-3.55 (m, 1H), 3.75-3.86 (m, 1H), 3.93 (d, 1H, J=9.6 Hz), 7.18-7.22 (m, 2H), and 7.40-7.50 (m, 3H); Anal. Calcd. for $C_{20}H_{20}N_2O_4S$: C, 62.48; H, 5.24; N, 7.29. Found: C, 62.19; H, 5.20; N, 7.09.

A 50 mg (0.13 mmol) sample of cycloadduct **35** was heated at 240°C for 5 min. Silica gel chromatography of the residue provided 38 mg (90%) of 4,8,8-trimethyl-2-phenyl-3a,6,7,8-tetrahydro-4*H*-2,5a-diaza-as-indacene-1,3,5-trione (**36**) as white crystals; mp 219-220°C; IR (KBr) 2967, 1755, 1704, and 1646 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.41 (s, 3H), 1.55 (s, 3H), 1.63 (d, 3H, J=7.8 Hz), 1.88-2.02 (m, 2H), 2.57-2.69 (m, 1H), 3.42 (d, 1H, J=15.0 Hz), 3.73-3.87 (m, 2H), 7.28-7.38 (m, 3H), and 7.41-7.48 (m, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 13.4, 24.6, 26.1, 37.5, 38.1, 44.1, 44.4, 44.9, 77.1, 97.0, 126.5, 128.2, 128.9, 132.0, 158.8, 171.3, and 173.4; Anal. Calcd. for $C_{19}H_{20}N_2O_3$: C, 70.34; H, 6.22; N, 8.64. Found: C, 70.25; H, 6.08; N, 8.55.

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