Intramolecular 1,4-Dipolar Cycloadditions of Cross-Conjugated Heteroaromatic Betaines. Synthesis of Hexahydrojulolidines and Related *Peri*- and *Ortho*-Fused Ring Systems

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3-Alkenyl 2-lactams react with (chlorocarbonyl)phenylketene to give nonisolable anhydro-4-hydroxy-2-oxo-1,3-oxazinium hydroxides which undergo regio- and stereospecific 1,4-dipolar cycloaddition in moderate yields to produce cycloadducts containing a carbon dioxide bridge. Thermolysis of the cycloadduct led to extrusion of carbon dioxide *via* a nonconcerted 1,5-hydrogen shift to give julolidine-type derivatives. Two of the cycloadducts were characterized by single-crystal X-ray determinations. A significant enhancement in the overall yield of the cycloaddition occurred in related reactions using anhydro-4-hydroxy-2-oxo-1,3-thiazinium hydroxides obtained from 3-alkenyl-3-ethyl(or methyl) 2-thiolactams and a variety of 1,3-bielectrophiles such as (chlorocarbonyl)phenylketene, carbon suboxide, substituted malonyl dichlorides, and ethyl (chlorocarbonyl)acetate. The thiazinium betaines were often isolable, and in one instance, a single-crystal X-ray characterization was possible. Cycloaddition of the thiazinium betaines occurred in a regiospecific manner. The initially formed cycloadducts which retained the carbonyl sulfide bridge could be induced to lose COS on further heating. Julolidine-type derivatives were obtained principally *via* a nonconcerted process. Variation in lactam ring size, coupled with tether length and substituent in the 1,3-bielectrophile, enabled control of ring size, substituents, and whether an *ortho*- or *peri*-fused tricyclic system resulted from the overall cycloaddition. In contrast to the lactam system, the thiolactams require disubstitution in the 3-position to avoid proton loss in the intermediate betaine with formation of a 1,3-thiazoline-4,6-dione.

Inter- and intramolecular dipolar cycloadditions have found wide application in the synthesis of a variety of heterocyclic systems, with those of the bimolecular 1,3-dipolar type being the most extensively studied.[1] During the last decade, a new impetus has been given to research in this field when it was found that mesoionic compounds undergo 1,3-dipolar cycloaddition with various dipolarophiles.[2-17] Mesoionic dipoles constructed in a manner which allows for intramolecular cycloaddition often lead to cycloadducts that are difficult to convert into useful structures since subsequent elimination of a small stable fragment is not easily accomplished.[2] This can be avoided to some extent by using a suitably structured 1,4-dipole where the fragment being eliminated from the cycloadduct is, for example, cyanic acid,[18] carbon dioxide,[19] or carbonyl sulfide.[19] Although a variety of intermolecular 1,4-dipolar cycloadditions have been described in the literature,[20] applications of the intramolecular type are still rare but have significant synthetic potential. We recently described a convenient procedure which led to the formation of a *peri*-fused tricyclic heterocycle by an intramolecular 1,4-cycloaddition of an aryl-substituted anhydro-4-hydroxy-2-oxooxazinium or thiazinium hy-

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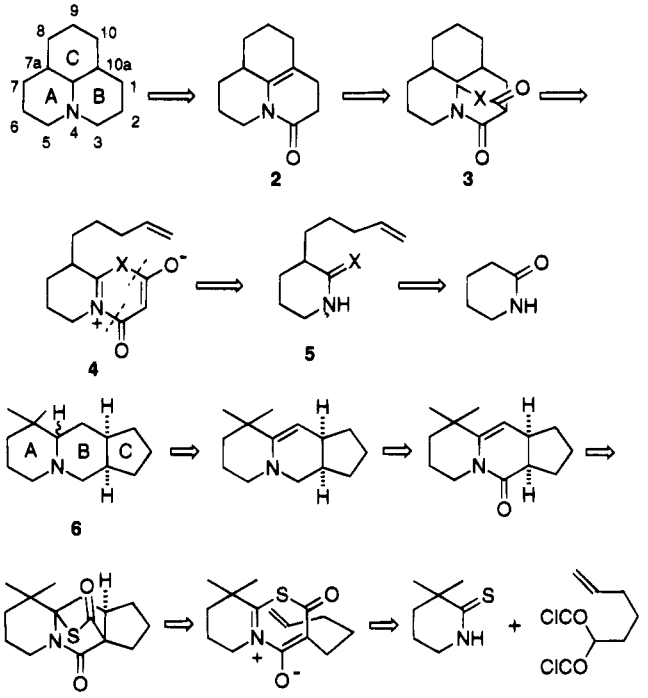
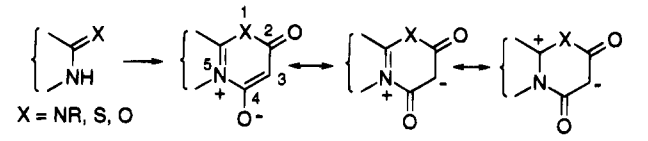
Scheme 1. Retrosynthetic Analysis of Hexahydrojulolidine (1) and the Linear Tricylic System 6 Using a 1,4-Dipolar Cycloaddition Approach (X = O, S)



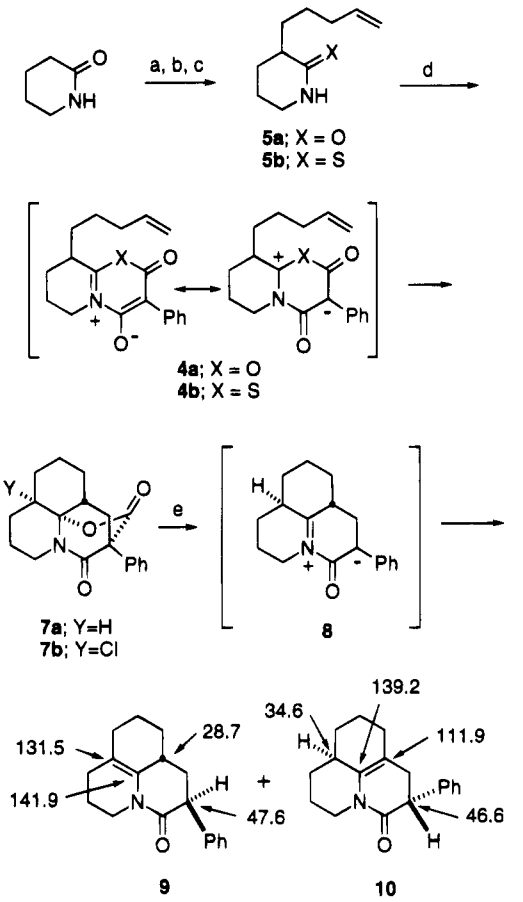
droxide.[21] These heteroaromatic betaines contain a "masked" 1,4-dipole within their framework.[22] We now report further applications of this chemistry which readily lead to saturated, tricyclic ring systems of the julolidine type which are useful intermediates for a variety of alkaloid syntheses.



Results and Discussion

Hexahydrojulolidine (**1**) represents the basic ring skeleton of many Lycopodium alkaloids,[23] and numerous synthetic routes toward this class of compound have been described in the literature.[24] This alkaloidal family represents a particularly attractive target for a 1,4-dipolar cycloaddition approach since this reaction always leads to six-membered heterocyclic rings. We have studied this cycloaddition process in some detail, paying particular attention to variation in ring size and the nature of the substituent groups present on the backbone

Scheme 2. Reaction of 3-(Penten-5-yl)-2(1*H*)-piperidinone (5a) with (Chlorocarbonyl)phenylketene



Key:
(a) 2 eq. *n*-BuLi / THF / O°C. (b) 5-Bromopentene. (c) H_2O.
(d) (Chlorocarbonyl)phenyl ketene / toluene / Et_3N / 110°C / 2 h.
(e) Toluene / 110°C / 2h or xylene 150°C / 24 h

of the 1,4-dipole. A retrosynthetic analysis of the hexahydrojulolidine ring system (**1**) using this approach is illustrated in Scheme 1. Fragmentation of the B/C ring junction bond and the 2,3-bond in ring B are the essential steps in the process. Hexahydrojulolidine (**1**) would be available from **2** by reduction of the lactam and the double bond, and **2** is the product obtained by thermal extrusion of CO_2 (or COS) from cycloadduct **3**. Intramolecular cycloaddition of betaine **4** would result in **3**, and **4** could be prepared from **5** by reaction with an appropriate 1,3-bielectrophile. Compound **5** could, in turn, be prepared from commercially available 2(1*H*)-piperidinone and 5-bromopentene. The linear, tricyclic *ortho*-fused system[25] represented by **6** may also be obtained by an analogous cycloaddition route with the principal variation being the position of the dipolarophilic tether in the betaine.

Lactam Functionalization. 1,3-Oxazinium Betaines. Using an alkylation procedure initially described by Durst and Labelle,[26] 2(1*H*)-piperidinone was treated with 2 equiv of *n*-butyllithium at 0 °C, and the resulting enolate dianion was allowed to react with 5-bromopentene to give 3-(penten-5-yl)-2(1*H*)-piperidinone (**5a**) in

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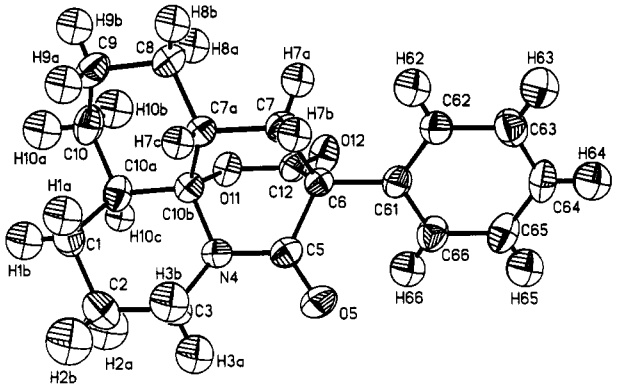


Figure 1. Ortep representation of cycloadduct **7a**.

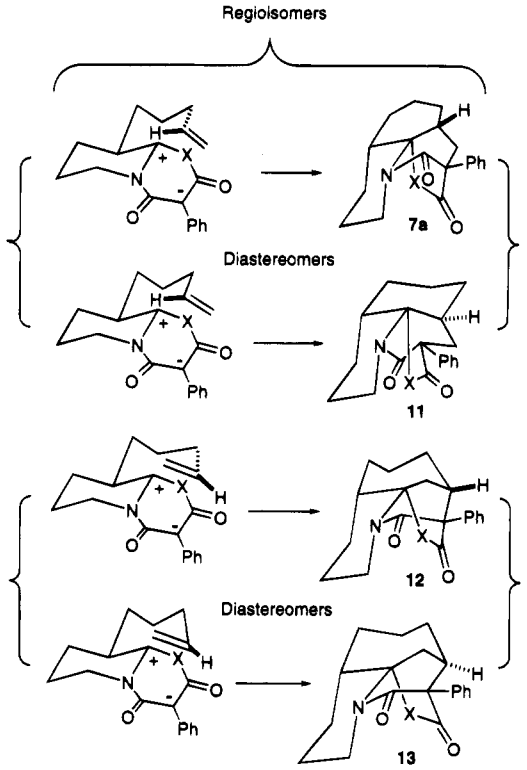


Figure 2. Possible transition states involved in the cycloaddition of heteroaromatic betaines.

70% yield (Scheme 2). A number of 3-substituted 2-lactams were prepared in this general manner, and details are given in the Experimental Section. Treatment of **5a** with (chlorocarbonyl)phenylketene[27] in toluene/Et_3N afforded cycloadduct **7a** (24%) (Scheme 2). The mass spectrum of **7a** exhibits an $[M^+ + 1]$ ion at m/z 312 (40%), and the most abundant ion has m/z 267, $[M^+ - 44]$, corresponding to the loss of carbon dioxide. These fragmentations, together with the analytical data, established the molecular formula as $C_{19}H_{21}NO_3$. Although the complexity of the ^1H NMR spectrum of **7a** precluded any definitive structural assignment, the absence of alkene protons at δ 5.8 and 5.0 which were present in **5a**, and the ^{13}C NMR spectrum which showed two carbonyl groups at 169.6 (lactam) and 170.0 ppm (ester) (ν_{CO} 1760 and 1680 cm^{-1}), were consistent with this structure. A single-crystal X-ray determination (Figure 1) unequivocally established that the cycloadduct corresponded to the *endo*-isomer, with the carbon dioxide bridge and the methine proton at the B/C ring junction being *trans* to each other.[28] Isolation of cycloadducts with carbon dioxide bridges is a rare event in dipolar cycloaddition chemistry, and this is especially so in this instance in view of the relatively high temperatures required for betaine formation.

The possible transition states involved in the cycloaddition process (Figure 2) indicate that, in addition to the *exo*-isomer **11**, two alternate regioisomers **12** and **13** are possible. Molecular mechanics calculations[29] for all four isomers showed that structure **7a** has the lowest total energy (45.93 kcal mol^{-1}), consistent with **7a** being the major product of the cycloaddition. The remaining residue consisted of a complex mixture of products whose ^1H NMR spectrum still showed chemical shifts at δ 5.8 and 5.0 for the alkene protons. More than likely, the mixture contains products arising from both intramolecular charge neutralization from betaine **4a** and from bis-alkylation of the lactam by the ketene to form a disubstituted malonamide. A similar mixture of products resulted when **5a** was allowed to react with (chlorocarbonyl)phenylketene in boiling benzene. A very minor product that was isolated under these reaction conditions was shown to be **7b**. This structure was established by X-ray data[28] and is most likely formed by a radical chlorination process, as it was absent when toluene was used as the reaction solvent. Carbon suboxide or substituted malonyl dichlorides failed to produce 1,4-dipolar cycloadducts with lactam **5a** under analogous reaction conditions.

When cycloadduct **7a** was heated in xylene at 150 °C for 24 h, compound **9** was isolated in 76% yield and is easily accounted for by the extrusion of carbon dioxide from the original cycloadduct followed by a H-rearrangement. Its ^{13}C NMR spectrum indicated two newly formed, fully substituted alkenic carbon atoms at 141.9 and 131.5 ppm and a carbonyl carbon atom at 168.1 ppm. A methine proton α to the carbonyl group appeared as a triplet at δ 3.9, and decoupling showed that it was coupled to the methylene protons β to the carbonyl group at δ 1.9. On irradiation of the δ 3.9 chemical shift, the chemical shift at δ 1.9 appeared as a doublet being coupled to the γ proton with J = 0.9 Hz. These data indicate that the location of the double bond is between rings A and C. A single-crystal X-ray determination (Figure 3) of **9** further verified this assignment and showed that the stereochemistry at C-10a was identical with that present in **7a**.[28]

Under the above reaction conditions, only compound **9** was obtained. The other double-bond regioisomer **10** (double bond between rings B and C) was ultimately obtained by a slight variation of the thermal conditions. Heating cycloadduct **7a** in refluxing toluene for 2 h afforded two products in equal amounts, together with recovered starting material. Separation was effected using preparative TLC (silica gel), and structure **10** was obtained as a clear oil. Its mass spectrum was identical with that of **9**, with the $[M^+ + 1]$ ion appearing at m/z 268 (100%). Its ^1H NMR spectrum, however, was distinctly different from that of **9** with respect to the aromatic region. In addition, the methine proton α to

(27) Nakanishi, S.; Butler, K. *Org. Prep. Proc. Intl.* **1975**, *7*, 155.

(28) The authors have deposited coordinates for structures **7a**, **7b**, **9**, and **36** with the Cambridge Data Centre. The coordinates can be obtained from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

(29) PC Model and MMX Program, Serena Software, Inc., Bloomington, IN.

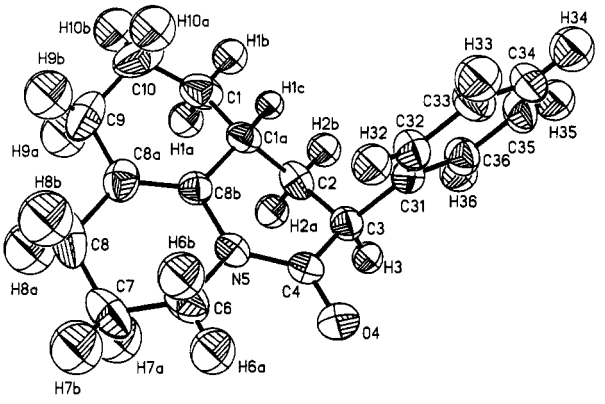


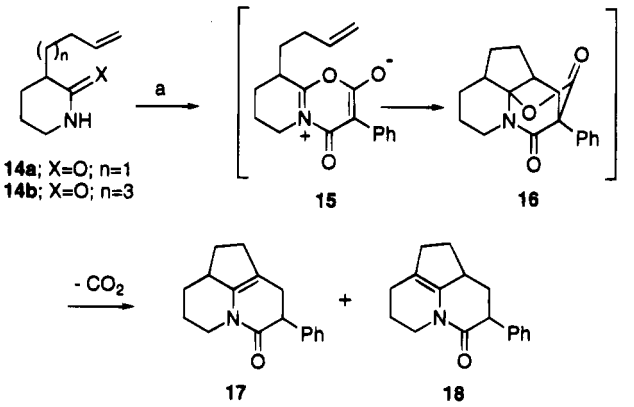
Figure 3. Ortep representation of cycloadduct **9**.

the amide carbonyl group appears as a doublet of doublets slightly upfield at δ 3.7. This is in sharp contrast to the multiplicity of this proton in **9** where it appeared as a triplet at δ 3.9. Further evidence for **10** being a regioisomer of **9** was obtained from its ^{13}C NMR spectrum. In compound **10**, the chemical shifts for the newly formed alkene carbon atoms appeared at 111.9 and 139.2 ppm, while in compound **9**, these were found at 131.5 and 141.9 ppm. In addition, the chemical shift of the carbon atom at the ring junction with the methine proton in compound **10** was found at 34.6 ppm, while in compound **9**, the chemical shift of the corresponding carbon atom was at 28.7 ppm.

The formation of **9** and **10** involves thermal cycloreversion of the initial cycloadduct **7a** with the extrusion of carbon dioxide to produce a highly unstable zwitterionic species (**8**). This is followed by a symmetry-allowed 1,5-hydrogen shift,[30] with the migrating proton being either H-7a or H-10a to give compounds **9** and **10**, respectively (Scheme 2). For this process to be symmetry allowed under thermal conditions, the 1,5-hydrogen shift should be suprafacial,[31] but geometrical constraints within the molecule may obviate such a process. In compound **9**, the stereochemistry of the proton α to the lactam carbonyl group is the same as that of H-7a in **7a**. On this basis, we may safely predict that the stereochemistry of the proton at the 2-position of **10** will be different from that of **9**, in agreement with the ^1H NMR data.

Variation in the Dipolarophilic Chain Length. Control of ring size in the final product of the cycloaddition by variation of the dipolarophilic chain length is of appreciable interest. Introduction of a four-carbon chain was readily achieved by treating 2(1*H*)-piperidinone with 2 equiv of *n*-butyllithium followed by reaction with 4-bromobutene to give 3-(buten-4-yl)-2(1*H*)-piperidinone (**14a**) in 63% yield. A mixture of **14a** and (chlorocarbonyl)phenylketene was allowed to reflux in xylene for 12 h, and the major product isolated was assigned structure **18** (Scheme 3) on the basis of the following evidence. The mass spectrum of **18** showed a molecular ion [M^+], *m/z* 253 (100%), and the ν_{CO} 1638 cm^{-1} corresponding to the amide carbonyl group was similar to that present in cycloadduct **9**. The ^1H NMR spectrum of **18** showed the phenyl protons as a well-

Scheme 3. Cycloadditions with Variable Dipolarophilic Chain Length



(a) (Chlorocarbonylphenyl) ketene / xylene / 150°C / 12 h

defined multiplet at δ 7.2. In addition, in its ^{13}C NMR spectrum, the olefinic carbon atoms were at 141.5 and 136.0 ppm, suggesting that the double bond is located between rings A and C. In an attempt to isolate the initially formed cycloadduct **16**, the reaction temperature was maintained at 110 °C for 2 h. However, TLC and ^1H NMR spectral data showed that the reaction produced a complex mixture of the difficultly separable regioisomers **17** and **18** (1:1 mixture), as well as products arising from intramolecular charge neutralization of betaine **15**. It appears that the highly strained nature of cycloadduct **16** precludes its isolation at the reaction temperatures needed to initiate the cycloaddition and that it undergoes a rapid cycloreversion at the elevated temperature with the loss of carbon dioxide to give **17** and **18**. The highly strained nature of **16** was evident from Dreiding models of this system, and this strain was also reflected in its calculated minimized energy[29] of 49.97 kcal mol^{-1}. An increase in the dipolarophilic tether to a six-carbon chain would allow the introduction of a seven-membered ring. Treatment of 2(1*H*)-piperidinone with 2 equiv of *n*-butyllithium in the usual manner, followed by the addition of 6-bromohexene, gave lactam **14b** (Scheme 3). When **14b** was treated with (chlorocarbonyl)phenylketene in refluxing toluene for 2 h, a complex mixture of products was observed (TLC, ^1H NMR). The mixture showed olefinic protons at δ 5.8 and 5.0, indicating that cycloaddition had not occurred. Apparently, with an increase of the dipolarophilic chain to six carbon atoms, it was no longer possible to achieve adequate orbital overlap of the double bond with the 1,4-dipole in the transition state (Figure 2). This type of behavior with increase in chain length has been observed in other 1,4-dipolar intramolecular cycloadditions.[19]

Variation in the Size of the Parent Lactam Ring. The effect of varying the initial lactam ring size on the 1,4-cycloaddition was also evaluated. Treatment of 2(1*H*)-azepinone with 2 equiv of *n*-butyllithium followed by the addition of 5-bromopentene gave 3-(penten-5-yl)-2(1*H*)-azepinone (**19**) in 35% yield. Reaction of lactam **19** with (chlorocarbonyl)phenylketene gave the expected cycloadduct **21** (25%), the intermediate betaine **20** not being isolated. The IR spectrum of cycloadduct **21** showed ν_{CO} at 1770 and 1680 cm^{-1}, indicative of the carbon dioxide bridge and the lactam carbonyl group, respectively. Its ^{13}C NMR spectrum showed the carbonyl carbon atom of the CO_2 bridge at 170 ppm, with the

(30) For related examples of 1,5-hydrogen shift, see: (a) Lenz, G. R. *J. Org. Chem.* **1976**, *41*, 2201. (b) Ninomiya, I.; Naito, T.; Mori, T. *J. Chem. Soc., Perkin Trans. I* **1973**, *1*, 505. (c) Ninomiya, I.; Naito, T. *Heterocycles* **1981**, *15*, 1433.

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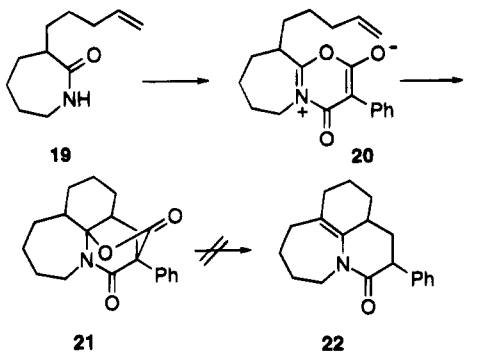


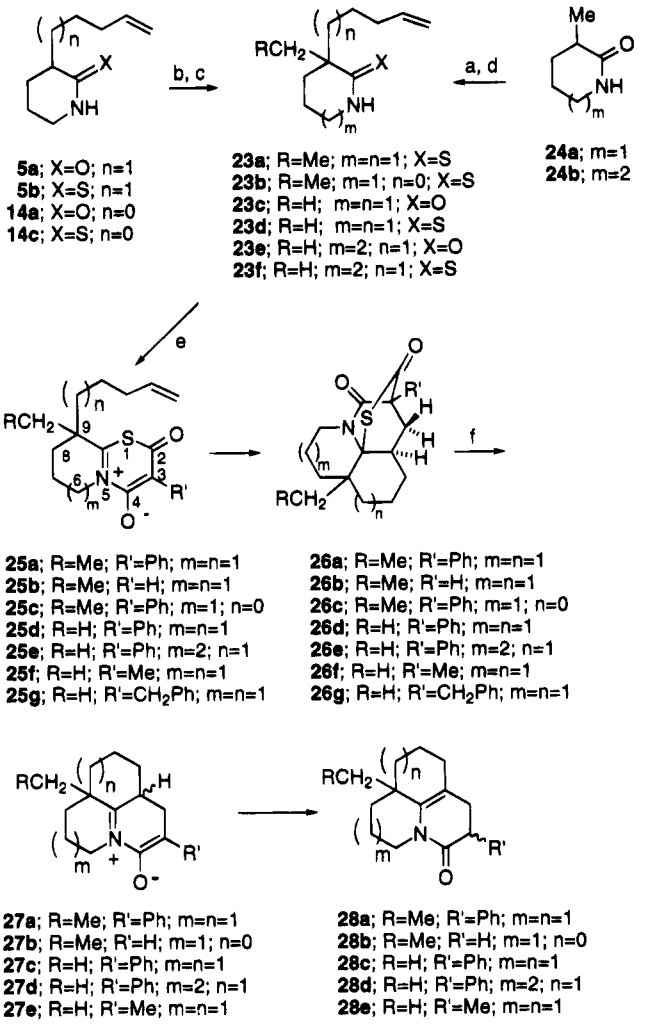
lactam carbonyl carbon atom at 167.9 ppm, but its ^{1}H NMR spectrum was extremely complex, making definitive structural assignments very difficult. Analytical and mass spectral data were consistent with structure **21**. This cycloadduct was more thermally stable than cycloadduct **7a**, requiring an increase of 34 °C with respect to the temperature necessary for compound **7a** to undergo extrusion of carbon dioxide. Thermolysis of **21** under these more forcing conditions resulted in a complex mixture of products with no signs of the expected extrusion product **22**.

1,3-Thiazinium Betaines. The modest yields obtained in the above cycloaddition reactions may be due to low conversion of the 2-lactams into the oxazinium betaines, as well as partial loss of the betaine structure by intramolecular charge neutralization. Our inability to induce cyclocondensation of the 2-lactam with carbon suboxide and related three-carbon reagents represents a significant drawback to the use of oxazinium betaines. However, the corresponding 1,3-thiazinium betaines, readily available from the more nucleophilic 2-thiolactam system by cyclocondensation with a variety of 1,3-bielectrophiles, were found to readily undergo intramolecular cycloaddition. Despite the additional step in the precursor synthesis, these betaines were found to be extremely attractive reactive intermediates. Our overall synthetic approach leading to *peri* ring-fused systems is shown in Scheme 4. The 1,4-dipolar cycloaddition of these betaines always resulted in a ring-fused 3,4-dihydopyridin-2-one. Three variables were introduced into our reaction sequences which allowed appreciable control over the nature of the final products. Variation of the ring size in the initial 2-thiolactam, the position and length of the dipolarophilic tether in the betaine relative to the thiazinium sulfur atom, and the nature of the 1,3-bielectrophilic species used to generate the thiazinium betaine have all been successfully exploited in our synthetic work.

The 3,3-disubstituted 2-thiolactams **23** were synthesized by two procedures. For example, starting with 2(1*H*)-piperidinone (**5a**), it was possible to introduce the alkenyl side chain at the 3-position of the lactam ring. Sulfuration of the 3-substituted 2-lactam with Yokoyama's reagent[32] (or Lawesson's reagent[33]) gave **5b**, and this was followed by introduction of the ethyl group to produce **23a**, employing essentially the same alkylation conditions utilized for the introduction of the alkenyl group. No *S*-alkylation product was observed, and the complete removal of the methine proton in this alkylation procedure was evident from the absence of its characteristic multiplet at δ 2.7. In addition, the ^{13}C-APT NMR spectrum of **23a** clearly showed the new quaternary center at 48.5 ppm. An alternative, complementary procedure started with the 3-methyl-substituted 2-lactam **24**.[34] Introduction of the alkenyl side chain was carried out essentially as above, and the resultant 3,3-disubstituted 2-lactam was converted into **23c** or **23d** by sulfuration with Lawesson's reagent. Full descriptions of the 2-lactams and 2-thiolactams prepared by these procedures are found in the Experimental Section.

Reaction of the 3,3-disubstituted 2-thiolactams with 1,3-bielectrophiles occurred readily under a variety of reaction conditions, leading ultimately to [6,6,6] *peri*-fused ring systems. 3-Ethyl-3-(penten-5-yl)-2(1*H*)-piperidinethione (**23a**) was heated in toluene/triethylamine with (chlorocarbonyl)phenylketene at 110 °C for 2 h, producing cycloadduct **26a** as a mixture of *exo* and *endo* isomers, the intermediate betaine **25a** not being isolated under these reaction conditions.

Scheme 4. Cycloadditions with 1,3-Thiazinium Betaines



(a) 2 x *n*-BuLi, Et_2O, 0° C, 5-Br-pent-1-ene. (b) Yokoyama's reagent, THF, rt, 24 h. (c) 2 x *n*-BuLi, THF, 0° C, EtI. (d) Lawesson's reagent, benzene, rt. (e) (chlorocarbonyl)phenyl ketene, toluene or xylene, reflux. (f) toluene, or xylene, reflux.

(32) Yokoyama, M.; Hasegawa, Y.; Hatenaka, H.; Kawazoe, Y.; Imamoto, T. *Synthesis* **1984**, 827.

(33) Lawesson, S. O.; Shabana, R.; Scheibye, S.; Clausen, K.; Oleseh, S. O. *Nouv. J. Chem.* **1980**, *47*, 4. Lawesson, S. O.; Thompson, I.; Clausen, K.; Scheibye, S. *Org. Syn.* **1990**, *7*, 372.

(34) Kariyone, K. *Chem. Pharm. Bull.* **1960**, *8*, 1110.

Further heating of cycloadduct **26a** in xylene resulted in the loss of carbonyl sulfide,[35] and the two epimeric products present in the crude reaction mixture in a 1:2 ratio were isolated by silica gel chromatography. The minor product was assigned as epimer **28a-β** (β-R′, 12%), and the major product as epimer **28a-α** (α-R′, 24%). These structures were assigned on the basis of their analytical data as well as their characteristic ^{1}H NMR data, especially a comparison with the ^{1}H NMR data for cycloadducts **9** and **10**. In the α-epimer, the phenyl protons occurred as a well-defined multiplet at δ 7.2, whereas in the β-epimer, they appeared essentially as a singlet. Other slight differences in both their ^{1}H and ^{13}C NMR spectra were found, and these are listed in the Experimental Section. In contrast to the thermal decomposition of the corresponding cycloadduct in the oxazinium betaine series, cycloadduct **26a** has only a single hydrogen atom eligible for the 1,5-sigmatropic shift. Since this shift occurs with retention of configuration of the migrating proton for a concerted process, the two epimers of **28a** must have originated from either of the two diastereomers, leading to the conclusion that, under these reaction conditions, the intramolecular cycloaddition of the intermediate thiazinium betaine was not stereospecific or, alternatively, the rearrangement was not concerted. Rearrangements of similarly substituted cycloadducts of 1,3-thiazinium betaines have been shown to be substituent dependent and usually involve a two-step process.[19] Further evidence on this apparent dichotomy is discussed below.

Cyclocondensation of thiolactam **23a** with carbon suboxide occurred at room temperature over a 3 day period. The intermediate betaine **25b** was not isolated under these reaction conditions, as cycloaddition occurred readily to give **26b**. The ethyl triplet in **26b** was unsymmetrical and suggestive of two ethyl groups being present in the reaction product, indicating that the cycloaddition was not stereospecific. Attempts to separate these products were unsuccessful.

Entry to [6,6,5] *peri*-fused ring systems started with 2-thiolactam **14c**, obtained from the reaction of 2(1*H*)-piperidinone with 4-bromobutene as above, followed by treatment with Yokoyama's reagent.[32] Introduction of the ethyl substituent gave 3-(buten-4-yl)-3-ethyl-2(1*H*)-piperidinethione (**23b**). Treatment of this thioamide with (chlorocarbonyl)phenylketene in toluene/triethylamine for 2 h at 110 °C gave, without isolation of the intermediate betaine **25c**, cycloadduct **26c**. Use of refluxing xylene as the solvent over 12 h and purification of the reaction mixture by silica gel chromatography gave both the minor epimer of **28b-β** (β-R′, 12%) as well as the major epimer **28b-α** (α-R′, 33%). The structural assignments were made on the basis of their spectral characteristics (Experimental Section) which were consistent with those of related cycloadducts discussed above. Extension of these reactions to the 2(1*H*)-azepinone system were unsuccessful, due to the failure of the 2(1*H*)-azepinone to undergo dialkylation under the general reaction conditions. Attempts to trap the resonance-stabilized zwitterionic intermediate **27** with a variety of added reactive dipolarophiles (*e.g.*, *N*-phenylmaleimide, dimethyl acetylenedicarboxylate, and reactive enamines) did not result in the isolation of a characterizable bimolecular cycloadduct.

(35) Carbonyl sulfide may be conveniently identified by trapping in an alcoholic solution of piperidine where it formed the corresponding salt. See: Seibert, W. *Angew. Chem.* **1959**, *71*, 194.

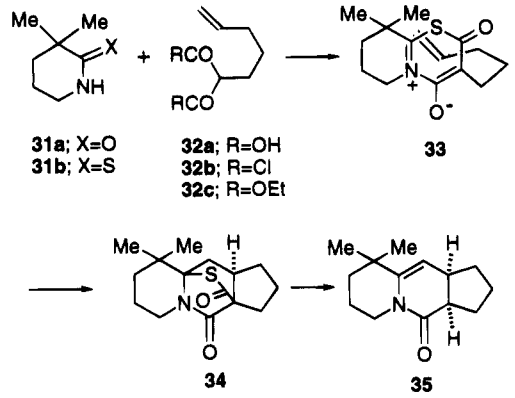
Treatment of 2-thiolactam **23d** with (chlorocarbonyl)-phenylketene in benzene at 25 °C gave betaine **25d**. Characterization of the betaine was by spectral data (see the Experimental Section) and the consistency of these data with those of a related betaine whose structure was established by a single-crystal X-ray determination (*vide infra*). When betaine **25d** was heated under reflux in toluene for 20 h, cycloadduct **26d** was accompanied by an equal amount of 2,3-dihydropyridinone **28c** (β-R′, 48%) which corresponds to the carbonyl sulfide elimination product. Elevation of the reaction temperature to that of boiling xylene (1 h) resulted in the conversion of **25d** or **26d** into **28c** in quantitative yield. Analytical and spectral data were used to assign the structure of **28c**, the α-configuration of the 2-proton following from the chemical shift of the 2-phenyl-substituted protons which were consistent with others in this configuration. The isolation of only one product in this "cycloaddition–extrusion–rearrangement" sequence suggests that, with this substituent pattern, the intermediate 1,3-thiazinium betaine undergoes a regio- and stereospecific cycloaddition and that the final 1,5-hydrogen shift occurred *via* a concerted path.

Entry to the [7,6,6] *peri*-fused ring system was possible using a methyl-substituted 2(1*H*)-azepinone. Under analogous reaction conditions, 3-methyl-2(1*H*)-azepinone[36] (**24b**) was converted into the corresponding 3-methyl-3-(penten-5-yl)-2(1*H*)-azepinone (**23e**) and then to the 2-thiolactam **23f**. This 2-thiolactam, on treatment with (chlorocarbonyl)phenylketene in benzene at 25 °C, gave betaine **25e** in excellent yield. Heating **25e** in toluene for 20 h afforded cycloadduct **26e** (14%) as the minor product, together with an inseparable 1:1-diastereomeric mixture of **28d** (71%) as the major product.

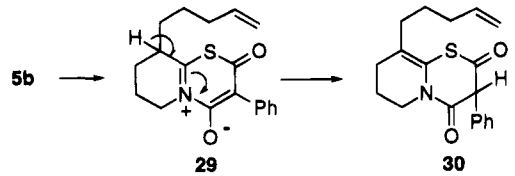
The presence of a phenyl substituent in the 3-position of the 1,3-thiazinium betaine would be anticipated to stabilize the "masked" 1,4-dipole by charge delocalization. Carbon suboxide[37] allows the introduction of a hydrogen at this position, and substituted malonyl dichlorides have provided[19] an effective way of introducing alkyl substituents, thus extending the generality of the reaction and leading to intermediates likely to provide evidence on whether the 1,5-hydrogen shift (concerted *vs* nonconcerted) is substituent dependent. Betaine **25f** was prepared in excellent yield by the dropwise addition of methylmalonyl dichloride to 3-methyl-3-(penten-5-yl)-2(1*H*)-piperidinethione (**23d**). Heating **25f** in toluene at 120 °C for 2 h afforded an excellent yield of cycloadduct **26f** whose spectral data indicated that it was a homogeneous product. This cycloadduct lost carbonyl sulfide on thermolysis, and by rearrangement of the intermediate zwitterion **27e**, cycloadduct **28e** was produced in excellent yield as a 5:1 mixture of diastereomers. The predominant formation of one stereoisomer strongly suggests that the final 1,5-sigmatropic rearrangement occurred principally *via* a concerted path, in keeping with earlier observations of the effect of methyl substituents on this rearrangement.[19] Use of benzyl malonyl dichloride[38] as the 1,3-bielectrophile gave the corresponding benzyl-substituted betaine **25g** which, on heating at reflux in toluene for 20 h, produced cycloadduct **26g**.

(36) Schäffler, A.; Ziegenbein, W. *Chem. Ber.* **1955**, *88*, 1374.
(37) Birkoffer, L.; Sommer, P. *Chem. Ber.* **1976**, *109*, 1701. Hopf, H.; Sommer, P. *Helv. Chim. Acta* **1961**, *44*, 201. Crombie, L. *J. Chem. Soc., Chem. Commun.* **1968**, 130.
(38) Kappe, T.; Golser, W. *Synthesis* **1972**, 312.

Scheme 5. Cycloaddition Route to a [6,6,5] *Ortho*-Fused Ring System



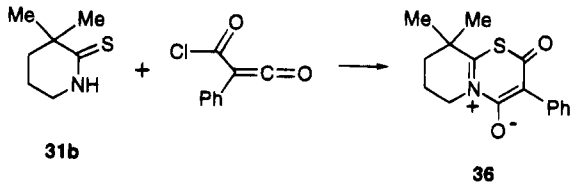
In the above cycloadditions, the intermediate betaines **25** had two substituents in the 9-position of the bicyclic ring system. With only one substituent, the reaction takes an entirely different course. (Chlorocarbonyl)-phenylketene and 3-(penten-5-yl)-2(1*H*)-piperidinethione (**5b**) in refluxing toluene gave, instead of a cycloadduct, a product assigned structure **30** on the basis of its molecular ion [$M^+ + 1$] (*m/z* 328), alkenic protons at δ 5.8 and 5.0, and two different carbonyl carbon atoms at 193.6 and 164.7 ppm, with the more downfield chemical shift being assigned to that of the 2-carbonyl group adjacent to the sulfur atom. The ^{13}C NMR spectrum also showed two new quaternary carbon atoms at 137.6 and 131.9 ppm, corresponding to the original 2- and 3-positions of the thiolactam ring. The formation of **30** is consistent with proton loss at the 9-position of the bicyclic 1,3-thiazinium betaine **29**. This pathway was found to be quite general with thiazinium betaines of this type and independent of the nature of the 3-substituent group. Once formed, the 1,3-thiazolinedione **30** was unresponsive to the cycloaddition conditions. While this deprotonation reaction is always possible in betaine systems of this type when one (or more) of the substituents at the position α to the positively charged atom corresponds to a hydrogen atom, this is the first instance in which it has been observed (*cf.* the oxazinium system above). This ready rearrangement is no doubt a function of the acidity of the 9-proton and the ease of formation of the ketene thioaminal structure present in thiazolinedione **30**.



Scheme 5 shows an extension of the above cycloaddition for the preparation of a [6,6,5] *ortho*-fused ring system. 3,3-Dimethyl-2(1*H*)-piperidinethione[39] (**31b**) was prepared by the alkylation–sulfuration procedure described above and, when treated with (penten-5-yl)-malonyl dichloride (**32b**), gave the betaine **33**, which was characterized by its analytical and spectral data. When heated in xylene at 150 °C for 22 h, loss of carbonyl sulfide followed by rearrangement to **35** occurred, the *cis*-ring junction being assigned on the basis of the NMR data and steric considerations.

(39) Stamm, H.; Worderer, A.; Wiesert, W. *Chem. Ber.* **1981**, *114*, 32.

It should also be noted that treatment of thiolactam **31b** with (chlorocarbonyl)phenylketene gave the corresponding betaine **36** as nicely crystalline orange needles sufficiently stable to undergo single-crystal X-ray determination.[28] Betaine **36** provided an opportunity for unambiguous spectral characterization of the 1,3-thiazinium betaine moiety which was of considerable use in the characterization of the other isolated betaines.



In conclusion, we have developed an efficient ring annulation procedure leading to hexahydrojulolidines and related ring systems. The intramolecular 1,4-dipolar cycloaddition of bicyclic anhydro-1,3-thiazinium hydroxides can now be exploited to prepare a variety of azapolycyclic ring systems found in nature. Work along these lines is in progress and will be reported in due course.

Experimental Section[40]

3-(Penten-5-yl)-2(1*H*)-piperidinone (5a). The following preparation illustrates the general procedure used for the synthesis of the substituted lactams. 2(1*H*)-Piperidinone (10.0 g, 0.101 mol) and THF (500 mL) were added to a flame-dried, 1L three-neck flask equipped with a magnetic stirring bar, a pressure-equalizing addition funnel, and a nitrogen inlet valve. The resultant mixture was stirred at 0 °C for 1 h, and to this mixture was added dropwise *n*-butyllithium (92 mL of 2.2 M, 0.20 mol) in hexane. The resultant reaction mixture was stirred for an additional 1 h at 0 °C, after which 5-bromopentene (16.0 g, 0.101 mol) was injected rapidly into the stirred mixture. After being stirred for an additional h at 0 °C, the reaction mixture was poured into a saturated sodium chloride solution (300 mL). The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and evaporated to a brown syrup which was purified by vacuum distillation to give **5a** as colorless, irregular prisms: 11.8 g (70%), bp 119–120 °C/0.1 mm (mp 40–41 °C); IR ($CHCl_3$) ν_{NH} 3300, ν_{CO} 1650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.3 (s, 1H), 5.8 (m, 1H), 5.0 (m, 2H), 3.3 (m, 2H), 2.3 (m, 1H), 2.2–1.1 (m, 10H); MS [$M^+ + 1$] 168 (100%).

Anal. Calcd for $C_{10}H_{17}NO$: C, 71.85; H, 10.17; N, 8.38. Found: C, 71.85; H, 10.27; N, 8.37.

3-(Buten-4-yl)-2(1*H*)-piperidinone (14a). Compound **14a** was prepared in a similar fashion from 2(1*H*)-piperidinone (10.0 g, 0.101 mol) in THF (500 mL) by treatment with *n*-butyllithium (100 mL of 2.06 M in hexane, 0.20 mol) at 0 °C followed by the addition of 4-bromobutene (15.0 g, 0.11 mol).

(40) Spectral characterizations were carried out on the following instruments: ^1H NMR spectra, Varian XL-200 operating at 200 MHz with tetramethylsilane as an internal standard; ^{13}C NMR spectra, IBM WP-100 at 25.2 MHz with tetramethylsilane or deuterated chloroform (77.0 ppm) as the internal standard; infrared spectra, Perkin-Elmer Model 298 spectrophotometer; mass spectra, Hewlett-Packard GC-MS system Model 5987A. Separations were performed using silica gel or alumina, gravity or flash columns, or preparative thin layer plates. Analytical HPLC were carried out using a Waters Model 6000A solvent delivery system, and compounds were detected using a Waters Model 440 nm UV absorbance detector. The column used was μ-Poracil. All melting points were determined in capillaries on a Melt-Temp apparatus and are uncorrected. Microanalyses were performed by Atlantic Microlab Inc., Atlanta, GA, or Robertson Laboratory Inc., Madison, NJ.

(41) Carbon suboxide was prepared by the thermal dehydration of malonic acid with phosphorus pentoxide see: Diels, O. *Ber.* **1907**, *40*, 353 and ref 19.

The reaction mixture was stirred for an additional 1 h and was then poured into a saturated sodium chloride solution (300 mL) and worked up as above. The final syrup was purified by distillation under vacuum to give **14a** as colorless, irregular prisms: 10.7 g (63%), bp 117–118 °C/0.17 mm, (mp 53–55 °C); IR ($CHCl_3$) ν_{NH} 3300, ν_{CO} 1650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.7 (s, 1H), 5.8 (m, 1H), 5.0 (m, 2H), 3.3 (m, 2H), 2.2–1.2 (m, 9H); MS [M^+ + 1] 154 (100%).

Anal. Calcd for $C_9H_{15}NO$: C, 70.58; H, 9.80; N, 9.15. Found: C, 70.63; H, 9.89; N, 9.13.

3-(Hexen-6-yl)-2(1*H*)-piperidinone (14b). 2(1*H*)-Piperidinone (10.0 g, 0.1 mol) in THF (500 mL) was treated with *n*-butyllithium (95 mL of 2.32 M in hexane, 0.22 mol) at 0 °C. After the addition of 6-bromohexene (19.8 g, 0.12 mol), the reaction mixture was stirred for an additional 1 h. The reaction mixture was then poured into a saturated sodium chloride solution (300 mL) and worked up as above. The final brown oil was purified by distillation under vacuum to give compound **14b** as colorless, irregular prisms: 11.4 g (62%), bp 133–135 °C/0.6 mm (mp 32–33 °C); IR ($CHCl_3$) ν_{NH} 3300, ν_{CO} 1650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.9 (s, 1H), 5.8 (m, 1H), 5.0 (m, 2H), 3.3 (m, 2H), 2.3 (m, 1H), 2.2–1.2 (m, 12H); MS [M^+ + 1] 182 (100%).

Anal. Calcd for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.72. Found: C, 72.65; H, 10.39; N, 7.70.

3-(Penten-5-yl)-2(1*H*)-azepinone (19). 2(1*H*)-Azepinone (10.0 g, 0.08 mol) in THF (500 mL) was treated with *n*-butyllithium (90 mL of 2.06 M in hexane, 0.18 mol) at 0 °C. After the addition of 5-bromopentene (14.0 g, 0.09 mol), the reaction mixture was stirred for an additional 1 h and was then poured into a saturated sodium chloride solution (300 mL) and worked up as above. The final oil was purified by vacuum distillation to give compound **19** as a colorless syrup: 5.6 g (35%), bp 108–110 °C/0.01 mm; IR ($CHCl_3$) ν_{NH} 3250, ν_{CO} 1660 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.8 (s, 1H), 5.8 (m, 1H), 4.9 (m, 2H), 3.3 (m, 2H), 2.3 (m, 1H), 2.2–1.2 (m, 12H); MS [M^+] 181 (3%).

Anal. Calcd for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.72. Found: C, 72.75; H, 10.69; N, 7.68.

Preparation of Cycloadduct 7a. This preparation illustrates the general procedure used for the synthesis of the initial cycloadducts in the oxazinium betaine series. 3-(Penten-5-yl)-2(1*H*)-piperidinone (**5a**) (2.0 g, 0.01 mol) in toluene (25 mL) and triethylamine (3 mL) were added to a flame-dried 100 mL 3-neck flask equipped with a condenser, a pressure-equalizing addition funnel, and a nitrogen inlet valve. The mixture was heated under reflux for 5 min. (Chlorocarbonyl)-phenylketene (2.2 g, 0.01 mol) in toluene (25 mL) was added dropwise, followed by refluxing the mixture for an additional 2 h. When cooled, triethylamine hydrochloride was removed from the reaction mixture by filtration through Celite, and the filtrate was evaporated to a burgundy syrup. Trituration of the syrup with methanol/diethyl ether resulted in the separation of compound **7a** as yellow, irregular prisms. These were recrystallized from CH_2Cl_2/diethyl ether, giving colorless microneedles of **7a**: 0.9 g (24%), mp 160–161 °C dec; IR (KBr) $\nu_{C=O}$ 1760, 1680 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.4 (m, 5H, phenyl), 3.8 (m, 1H), 3.2 (m, 1H), 2.7 (dd, 1H, J = 10.2, 10.1 Hz), 2.4–1.2 (m, 13H); ^{13}C NMR (25 MHz, $CDCl_3$) δ 170.0, 169.6, 132.4, 129.3 (2C), 128.2, 127.9 (2C), 91.3, 57.3, 41.2, 36.7 (2C), 31.3, 30.5, 26.8, 24.7, 22.2, 19.9; MS (CI pos) [M^+ + 1] 312 (40%).

Anal. Calcd for $C_{19}H_{21}NO_3$: C, 73.32; H, 6.74; N, 4.49. Found: C, 73.21; H, 6.83; N, 4.42.

Thermolysis of Cycloadduct 7a. Compound **7a** (0.37 g, 1.18 mmol) in toluene (25 mL) was heated at 110 °C for 3 h. After the reaction mixture was cooled, the solvent was evaporated and the resulting brown syrup was purified by preparative thin layer chromatography (silica gel) using hexane/ethyl acetate (3:1) as the eluant. The first fraction was identified as compound **10** and was obtained as a colorless oil: 0.05 g (16%); IR (neat) ν_{CO} 1640 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.2 (m, 5H, phenyl), 4.2 (m, 1H), 3.7 (dd, 1H, J = 3.7, 3.5 Hz), 3.2 (m, 1H), 2.7 (m, 1H), 2.3–1.1 (m, 12H); ^{13}C NMR (25 MHz, $CDCl_3$) δ 170.2, 139.2, 128.3 (2C), 127.2, 126.7 (2C), 111.9, 106.5, 46.6, 40.6, 34.6, 32.7, 30.7, 29.9, 29.3, 23.2, 21.8; MS (CI pos) [M^+ + 1] 268 (100%).

The second fraction, identified as compound **9**, was obtained as a yellow oil which crystallized from hexane/ethyl acetate as colorless, irregular prisms: 0.03 g (10%), mp 139–140 °C; IR (KBr) $\nu_{C=O}$ 1630 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.2 (m, 5H, phenyl), 4.6 (m, 1H), 3.9 (t, 1H, J = 3.8, 3.7 Hz), 3.2 (m, 1H), 2.3–1.2 (m, 13H); ^{13}C NMR (25 MHz, $CDCl_3$) δ 168.1, 141.9, 131.5, 128.5 (2C), 128.0, 126.5 (2C), 113.2, 47.6, 40.5, 35.5, 30.3, 30.0, 28.7, 28.1, 21.8 (2C); MS (CI pos) [M^+ + 1] 268 (100%).

Anal. Calcd for $C_{18}H_{21}NO$: C, 80.89; H, 7.86; N, 5.24. Found: C, 80.92; H, 7.93; N, 5.17.

In the initial experiment, compound **7a** (0.5 g, 1.6 mmol) in xylene (20 mL) was heated at 150 °C for 24 h. Evaporation of the solvent followed by column chromatography (silica gel) of the residue using hexane/ethyl acetate (10:1) as the elutant gave compound **9** as colorless, irregular prisms from hexane/ethyl acetate: 0.3 g (76%), mp 139-140 °C. Spectral data were identical to that obtained above.

Anal. Calcd for $C_{18}H_{21}NO$: C, 80.89; H, 7.86; N, 5.24. Found: C, 80.76; H, 7.97; N, 5.20.

Preparation of Cycloadduct 18. A sample of 3-(buten-4-yl)-2(1*H*)-piperidinone (**14a**) (3.2 g, 0.02 mol) in xylene (20 mL) was heated to 110 °C for 5 min. (Chlorocarbonyl)-phenylketene (4.2 g, 0.02 mol) in xylene (20 mL) was added, and the resultant mixture was stirred under reflux for an additional 12 h. After the reaction mixture was cooled, the xylene was evaporated to give a dark-brown syrup which was purified by column chromatography (silica gel) using hexane/ethyl acetate 10:1 as the eluant. This afforded product **18** as a yellow syrup which crystallized on standing. Recrystallization from hexane/ethyl acetate gave colorless, irregular prisms: 0.59 g (11%), mp 124–126 °C; IR (KBr) $\nu_{C=O}$ 1638 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.3 (m, 5H, phenyl), 4.0 (m, 2H), 3.7 (m, 1H), 2.8 (m, 1H), 2.5–2.1 (m, 10H); ^{13}C NMR (25 MHz, $CDCl_3$) δ 167.9, 141.5, 136.0, 128.5 (2C), 127.9, 126.5 (2C), 114.6, 48.3, 39.9, 35.3, 35.1, 33.5, 29.2, 22.9, 22.0; MS (EI) [M^+] 253 (100%).

Anal. Calcd for $C_{17}H_{19}NO$: C, 80.63; H, 7.57; N, 5.53. Found: C, 80.69; H, 7.57; N, 5.48.

Preparation of Cycloadduct 21. 3-(Penten-5-yl)-2(1*H*)-azepinone (**19**) (2.0 g, 0.01 mol), toluene (30 mL), and triethylamine (3 mL) were heated at 110 °C for 5 min, and (chlorocarbonyl)phenylketene (2.0 g, 0.01 mol) in toluene (25 mL) was then added. The resultant mixture was heated under reflux for 2 h, and after the reaction mixture was cooled, the triethylamine hydrochloride was filtered using Celite and the filtrate was evaporated to a burgundy syrup. Addition of methanol/diethyl ether caused the separation of compound **21** as yellow, irregular prisms. These were recrystallized using CH_2Cl_2/diethyl ether, giving colorless, irregular prisms: 0.89 g (25%), mp 194–195 °C dec; IR (KBr) $\nu_{C=O}$ 1770, 1680 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.3 (m, 5H, phenyl), 4.6 (m, 1H), 2.7 (m, 2H), 2.2–1.2 (m, 15H); ^{13}C NMR (25 MHz, $CDCl_3$) δ 170.0, 167.9, 132.8, 129.3 (2C), 128.0, 127.7 (2C), 93.7, 57.1, 42.4, 41.6, 41.2, 31.6, 31.0, 30.6, 30.3, 30.1, 28.7, 24.5; MS (EI) [M^+] 325 (3%), *m/z* 281 (100%) ($M^+ - CO_2$).

Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.66; H, 7.21; N, 4.19.

3-(Penten-5-yl)-2(1*H*)-piperidinethione (5b). The following procedure is illustrative of thionation using Yokoyama's reagent. 3-(Penten-5-yl)-2(1*H*)-piperidinone (**5a**) (2.0 g, 0.01 mol), THF (20 mL), and Yokoyama's reagent (2.5 g, 6.1 mmol) were stirred at room temperature for 24 h. The solvent was evaporated, and the residue was purified by column chromatography (silica gel) using CH_2Cl_2 as the eluting solvent. Compound **5b** was obtained as a colorless syrup which crystallized on standing to give colorless, irregular prisms: 1.8 g (82%), mp 49–50 °C; IR ($CHCl_3$) $\nu_{C=S}$ 1210 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.8 (s, 1H, NH), 5.8 (m, 1H, C=CH), 5.0 (m, 2H, $C=CH_2$), 3.37 (m, 2H), 2.7 (m, 1H), 2.2–1.2 (m, 10H); ^{13}C NMR (25 MHz, $CDCl_3$) δ 207.6, 138.5, 114.5, 46.3, 44.7, 34.7, 33.6, 26.4, 24.5, 19.1; MS (CI pos) [M^+ + 1] 184 (100%).

Anal. Calcd for $C_{10}H_{17}NS$: C, 65.59; H, 9.28; N, 7.64. Found: C, 65.50; H, 9.36; N, 7.56.

3-(Buten-4-yl)-2(1*H*)-piperidinethione (14c). 3-(Buten-4-yl)-2-(1*H*)-piperidinone (**14a**) (3.0 g, 0.02 mol), THF (30 mL), and Yokoyama's reagent (4.0 g, 9.8 mmol) were stirred together at room temperature for 24 h. The solvent was evaporated, and the residue was purified by column chromatography (silica gel) using hexane/ethyl acetate (10:1) as the eluting solvent. Product **14c** was obtained as colorless, irregular prisms: 2.3 g (71%), mp 52–53 °C; IR ($CHCl_3$) $\nu_{C=S}$ 1210 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.0 (s, 1H, NH), 5.8 (m, 1H, C=CH), 5.0 (m, 2H, $C=CH_2$), 3.3 (m, 2H, CH_2), 2.6 (m, 1H, CH), 2.3–1.5 (m, 8H); ^{13}C NMR (25 MHz, $CDCl_3$) δ 207.9, 138.0, 115.1, 45.8, 44.8, 34.3, 31.2, 24.5, 19.3; MS (CI pos) [M^+ + 1] 170 (100%).

Anal. Calcd for $C_9H_{15}NS$: C, 63.85; H, 8.93; N, 8.27. Found: C, 63.64; H, 8.99; N, 8.21.

3-Ethyl-3-(penten-5-yl)-2(1*H*)-piperidinethione (23a). The following illustrates the procedure used for the introduction of the 3-ethyl substituent. 3-(Penten-5-yl)-2(1*H*)-piperidinethione (**5b**) (1.8 g, 9.83 mmol) in THF (100 mL) was stirred at 0 °C for 1 h in the apparatus described above. *n*-Butyllithium (9 mL of 2.23 M in hexane, 0.02 mol) was then added dropwise, and the resultant mixture was stirred at 0 °C for an additional 1 h. Ethyl bromide (1.5 g, 0.013 mol) was injected rapidly into the mixture, which was stirred for an additional 1 h. The reaction was quenched with brine (200 mL), the organic phase was separated, and the aqueous phase was extracted with ethyl acetate (3 × 100 mL). These extracts were combined with the organic phase. The combined extracts were dried ($MgSO_4$) and filtered, and the solvent was evaporated to give a brown oil. This oil was purified by column chromatography (silica gel) using CH_2Cl_2 as the eluting solvent. Product **23a** was obtained as a yellow oil: 1.7 g (80%); IR ($CHCl_3$) $\nu_{C=S}$ 1210 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.6 (s, 1H, NH), 5.8 (m, 1H, C=CH), 5.0 (m, 2H, C=CH), 3.2 (m, 2H), 2.1–1.2 (m, 12H), 0.9 (t, 3H, J = 7.5, 7.3 Hz, CH_3); ^{13}C NMR (25 MHz, $CDCl_3$) δ 210.9, 138.6, 114.5, 48.7, 45.1, 41.9, 35.1, 34.3, 27.6, 23.9, 19.6, 8.7; MS (CI pos) [M^+ + 1] 212 (100%).

Anal. Calcd for $C_{12}H_{21}NS$: C, 68.18; H, 10.10; N, 6.62. Found: C, 68.28; H, 10.05; N, 6.61.

3-(Buten-4-yl)-3-ethyl-2(1*H*)-piperidinethione (23b). 3-(Buten-4-yl)-2(1*H*)-piperidinethione (**14c**) (1.8 g, 0.01 mol) in THF (100 mL) was treated with *n*-butyllithium (12 mL of 2.06 M in hexane, 0.02 mol) at 0 °C for 1 h. Ethyl bromide (1.5 g, 0.013 mol) was injected rapidly into the mixture, which was stirred for an additional 1 h. The reaction was quenched with brine (200 mL), the organic phase was separated, and the aqueous phase was next extracted with ethyl acetate (3 × 100 mL). These extracts were combined with the organic phase. The combined extracts were dried ($MgSO_4$) and filtered, and the solvent was evaporated to give a brown oil. This oil was purified by column chromatography (silica gel) using CH_2Cl_2 as the eluting solvent. Product **23b** was obtained as a yellow oil: 1.2 g (60%); IR ($CHCl_3$) $\nu_{C=S}$ 1210 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.7 (s, 1H, NH), 5.8 (m, 1H, C=CH), 5.0 (m, 2H, $C=CH_2$), 3.3 (m, 2H), 2.2–1.5 (m, 11H), 0.9 (t, 3H, J = 7.5, 7.3 Hz, CH_3); ^{13}C NMR (25 MHz, $CDCl_3$) δ 210.4, 139.7, 114.3, 48.5, 45.0, 41.3, 35.1, 28.7, 27.6, 19.5, 8.7; MS (CI pos) [M^+ + 1] 198 (100%).

3-Methyl-3-(penten-5-yl)-2(1*H*)-piperidinethione (23d). This procedure illustrates the alternative route into the 2-thiolactams. 3-Methyl-3-(penten-5-yl)-2(1*H*)-piperidinone (**23c**) (5.27 g, 97%) was prepared from 3-methyl-2(1*H*)-piperidinone (**24a**) (3.40 g, 30 mmol) and 5-bromo-1-pentene (4.50 g, 30 mmol) using essentially the same conditions as described for similar alkylations above. This lactam (2.72 g, 15.03 mmol) was converted into 3-methyl-3-(penten-5-yl)-2(1*H*)-piperidinethione (**23d**) with Lawesson's reagent (3.04 g, 7.52 mmol) in dry benzene (100 mL): 2.24 g (76%), mp 36–37 °C; IR (neat) 2865, 1555, 1351 cm^{-1}; ^1H 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, 0.8 Hz), 4.97 (dd, 1H, J = 17.3, 1.3 Hz), 5.68–5.88 (m, 1H), and 9.24 (brs, 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, 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.

Similarly, 3-methyl-3-(penten-5-yl)-2(1*H*)-azepinone (**23e**) was prepared from 3-methyl-2(1*H*)-azepinone (**24b**) (2.54 g, 20 mmol) and 5-bromo-1-pentene (4.0 g, 27 mmol) at 0 °C as above: 1.2 g (31%); IR (CCl_4) 3240–3160, 2920, 1640, 1480, and 1230 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.06 (s, 3H), 1.12–1.71 (m, 10H), 1.92–1.99 (m, 2H), 2.99–3.19 (m, 2H), 4.83–4.93 (m, 2H), 5.63–5.76 (m, 1H) and 6.71 (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.3, 24.2, 25.2, 29.2, 34.2, 35.4, 36.1, 42.2, 45.0, 114.5, 138.6, 181.1; HRMS Calcd for $C_{12}H_{21}NO$: 195.1623; found: 195.1621. Conversion of **23e** into 3-methyl-3-(penten-5-yl)-2(1*H*)-azepinethione (**23f**) occurred readily when the above lactam (1.20 g, 6.15 mmol) was treated with Lawesson's reagent (1.25 g, 3.09 mmol) in dry benzene (50 mL): 0.70 g (54%); ^1H NMR (300 MHz, $CDCl_3$) δ 1.24 (s, 3H), 1.28–1.95 (m, 12H), 3.20–3.35 (m, 2H), 4.78–4.89 (m, 2H), 5.60–5.68 (m, 1H), and 9.82 (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.5, 23.2, 23.7, 27.4, 30.4, 31.4, 34.1, 35.8, 46.6, 49.0, 114.5, 138.3, 215.6.

In a similar fashion 3,3-dimethyl-2(1*H*)-piperidinone (**31a**) (3.40 g , 26.77 mmol) and Lawesson's reagent (5.40 g, 13.39 mmol) in dry benzene (100 mL) gave 3,3-dimethyl-2(1*H*)-piperidinethione (**31b**) as colorless, irregular prisms: 3.74 g (98%), mp 96–97 °C; IR (CCl_4) 3200–3100, 2920, 1545, 1340, and 1080 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 (75 MHz, $CDCl_3$) δ 18.5, 30.8, 34.8, 41.7, 45.1, 211.5.

Preparation of Cycloadduct 26a. 3-Ethyl-3-(penten-5-yl)-2(1*H*)-piperidinethione (**23a**) (1.66 g, 7.86 mmol) in toluene (40 mL) and triethylamine (3 mL) were heated at 110 °C for 5 min. (Chlorocarbonyl)phenylketene (1.44 g, 8.0 mmol) in toluene (30 mL) was then added dropwise. The resultant mixture was stirred at 110 °C for an additional 2 h, and after the reaction mixture was cooled, the solvent was evaporated and the residue was triturated with a small amount of methanol and diethyl ether. Compound **26a** separated as yellow irregular prisms which on recrystallization from CH_2Cl_2/diethyl ether formed colorless, irregular prisms: 0.63 g (22%), mp 167–169 °C dec; IR (KBr) ν_{CO} 1690, 1650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.2 (m, 5H), 3.9 (m, 1H), 3.5 (m, 1H) 2.8 (dd, 1H, J = 13.5, 11.0 Hz), 2.5 (m, 1H), 2.2–1.3 (m, 13H), 0.9 (t, 3H, J = 7.4 Hz); [M^+ + 1] 356 (45%).

Anal. Calcd for $C_{21}H_{25}NO_2S$: C, 70.94; H, 7.08; N, 3.44). Found: C, 70.82; H, 7.16; N, 3.93.

Preparation of Cycloadduct 26b. 3-Ethyl-3-(penten-5-yl)-2(1*H*)-piperidinethione (**23a**) (0.5 g, 2.44 mmol) in diethyl ether (30 mL) was cooled to −88 °C, and freshly prepared carbon suboxide[37] (0.22 g, 3.26 mmol) in similarly cooled diethyl ether (25 mL) was added all at once. The reaction mixture was allowed to warm slowly to room temperature while being stirred, and stirring was continued for an additional 72 h. The solvent was then evaporated and replaced with toluene (30 mL), and the resultant reaction mixture was heated under reflux for 2 h. After the reaction mixture was cooled, the solvent was evaporated and the residue was purified by column chromatography (silica gel) using hexane/ethyl acetate (6:1) as the solvent. A major fraction identified as the starting material (NMR, TLC) was first eluted from the column. Further elution with CH_2Cl_2 gave product **26b** as a yellow oil which crystallized from hexane/ethyl acetate as colorless, irregular prisms: 0.03 g (18%), mp 145–147 °C dec; IR (KBr) $\nu_{C=O}$1690, 1665 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.0 (m, 1H), 3.9 (m, 1H), 3.6 (m, 1H), 2.4 (m, 1H), 2.1–1.2 (m, 14H),).9 (t, 3H, J = 7.4 Hz); [M^+ + 1] 280 (100%).

Anal. Calcd for $C_{15}H_{21}NO_2S$: C, 64.51; H, 7.52; N, 5.01. Found: C, 64.54; H, 7.70; N, 4.84.

When 3-(buten-4-yl)-3-ethyl-2(1*H*)-piperidinethione (**23b**) (0.35 g, 1.79 mmol) in diethyl ether (30 mL) cooled to −88 °C was treated with freshly prepared carbon suboxide[37] (0.22 g, 3.26 mmol) in similarly cooled diethyl ether (25 mL) and the reaction mixture was worked up as above followed by purification by column chromatogaphy (silica gel) using hexane/ethyl acetate/CH_2Cl_2 (5:1:1) as solvent and recrystallization from hexane/ethyl acetate, the related *peri*-fused [6,6,5] cycloadduct was obtained as colorless, irregular prisms: 0.13 g (35%), mp

158–160 °C dec; IR (KBr) $\nu_{C=O}$ 1690, 1670 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.9 (m, 1H), 3.6 (m, 1H), 2.7 (m, 1H), 2.3 (m,-1H), 2.0–1.3 (m, 12H), 0.9 (t, 3H, J = 7.1 Hz); MS [M$^+$ + 1] 266 (100%).

Anal. Calcd for $C_{14}H_{19}NO_2S$: C, 63.36; H, 7.16; N, 5.28. Found: C, 63.19; H, 7.12; N, 5.16.

Preparation of Cycloadduct 26c. 3-(Buten-4-yl)-3-ethyl-2(1*H*)-piperidinethione (**23b**) (0.44 g, 2.2 mmol) in toluene (30 mL) and triethylamine (3 mL) were heated at 110 °C for 5 min. (Chlorocarbonyl)phenylketene (0.40 g, 2.2 mmol) in toluene (25 mL) was then added dropwise, and the reaction mixture was heated for an additional 2 h at 110 °C. After the reaction mixture was cooled, the solvent was evaporated and the residue was triturated with methanol/diethyl ether to give compound **26c** as a yellow solid. Recrystallization from CH_2Cl_2/diethyl ether gave **26c** as colorless, irregular prisms: 0.09 g (12%), mp 157–158 °C dec; IR (KBr) $\nu_{C=O}$ 1670, 1650 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.4 (m, 5H), 3.9 (m, 1H), 3.4 (m, 1H), 2.9 (dd, 1H, J = 7.1 Hz), 2.3–1.3 (m, 12H), 0.9 (t, 3H, J = 7.1, 7.0 Hz); [M$^+$ + 1] 342 (65%).

Anal. Calcd for $C_{20}H_{23}NO_2S$: C, 70.34; H, 6.78; N, 4.10. Found: C, 70.07; H, 6.96; N, 3.92.

Preparation of Cycloadducts 28a. 3-Ethyl-3-(penten-5-yl)-2(1*H*)-piperidinethione (**23a**) (1.37 g, 6.49 mmol) in xylene (25 mL) was heated at 110 °C for 5 min, and (chlorocarbonyl)-phenylketene (1.26 g, 7.0 mmol) in xylene (25 mL) was added dropwise. The reaction mixture was heated at 150 °C for 24 h, and the solvent was then evaporated from the cooled reaction mixture. The residue was purified by column chromatography (silica gel) using hexane/ethyl acetate (6:1) as the eluting solvent. The first fraction was identified as compound **28a-β** (β-R′) on the basis of its spectral characteristics. It was recrystallized from hexane/ethyl acetate, giving colorless, irregular prisms: 0.23 g (12%), mp 129–130 °C; IR (KBr) $\nu_{C=O}$ 1655 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.3 (m, 5H, phenyl), 4.4 (m, 1H), 3.5 (dd, 1H, J = 5.7, 5.7 Hz), 3.0 (m, 1H), 2.6 (m, 1H), 2.3–1.1 (m, 12H), 0.8 (t, 3H, J = 7.6, 7.3 Hz); ^{13}C NMR (25 MHz, $CDCl_3$) δ 171.4, 139.4, 139.0, 128.9 (2C), 128.2 (2C), 126.8, 115.6, 47.2, 42.1, 35.4, 34.3, 33.5, 32.1, 29.4, 28.1, 18.0, 7.6; MS (CI pos) [M$^+$ + 1] 296 (100%).

Anal. Calcd for $C_{20}H_{25}NO$: C, 81.36; H, 8.46; N, 4.74. Found: C, 81.33; H, 8.57; N, 4.70.

The second fraction, obtained as a yellow oil, was identified as compound **28a-α** (α-R′) on the basis of its spectral data: 0.47 g (24%); IR (neat) $\nu_{C=O}$ 1660 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.3 (m, 5H, phenyl), 4.4 (m, 1H), 3.8 (m, 1H), 2.9 (m, 2H), 2.3–0.9 (m, 13H), 0.6 (t, 3H, J = 7.6, 7.3 Hz); ^{13}C NMR (25 MHz, $CDCl_3$) δ 171.4, 138.8, 137.0, 128.1 (2C), 126.9 (2C), 126.6, 112.8, 46.1, 41.8, 35.1, 33.0, 31.5, 31.4, 29.9, 26.5, 19.4, 17.6, 7.1; MS (CI pos) [M$^+$ + 1] 296 (30%).

Preparation of Cycloadducts 28b. 3-(Buten-4-yl)-3-ethyl-2(1*H*)-piperidinethione (**23b**) (4.37 g, 0.02 mol) in xylene (70 mL) was heated at 150 °C for 5 min, and (chlorocarbonyl)-phenylketene (4.0 g, 0.02 mol) in xylene (50 mL) was added dropwise. The resultant mixture was heated at 150 °C for a further 12 h. The solvent was evaporated from the cooled reaction mixture, and the residue was purified by column chromatography (silica gel) using hexane/ethyl acetate (20:1) as the eluting solvent. The first fraction eluted was identified as compound **28b-β** (β-R′) on the basis of its spectral characteristics. After recrystallization from hexane/ethyl acetate, it was obtained as colorless irregular prisms: 0.74 g (12%), mp 86–88 °C; IR (KBr) $\nu_{C=O}$ 1660 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.2 (m, 5H, phenyl), 4.0 (m, 1H, H-5), 3.7 (dd, 1H, J = 7.7, 7.6 Hz, H-2), 3.0 (m, 1H, H-5′), 2.7–1.1 (m, 12H), 0.9 (t, 3H, J = 7.6, 7.3 Hz); ^{13}C NMR (25 MHz, $CDCl_3$) δ 171.0, 139.6, 129.0 (2C), 128.3, 126.8 (2C), 114.9, 106.6, 48.4, 45.6, 41.6, 36.4, 32.6, 30.0, 29.9, 27.1, 19.8, 9.0; MS (CI pos) [M$^+$ + 1] 282 (100%).

Anal. Calcd for $C_{19}H_{23}NO$: C, 81.09; H, 8.23; N, 4.97. Found: C, 80.83; H, 8.23; N, 4.97.

The second fraction from the column was obtained as a yellow oil, and on the basis of its spectral characteristics, it was identified as compound **28b-α** (α-R′): 1.89 g (33%); IR (neat) $\nu_{C=O}$ 1660 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.2 (m, 5H, phenyl), 4.0 (m, 1H, H-5), 3.8 (d, 1H, J = 7.1 Hz), 2.8 (m, 2H), 2.4–1.1 (m, 11H), 0.7 (t, 3H, J = 7.5, 7.3 Hz); ^{13}C NMR (25 MHz, $CDCl_3$) δ 171.2, 140.0, 128.6, 128.2 (2C), 126.8 (2C), 112.6, 47.3, 45.8, 41.2, 36.0, 31.7, 29.7, 27.2, 25.4, 19.4, 8.6; MS (CI pos) [M$^+$ + 1] 282 (100%).

Preparation and Thermal Cycloaddition of Anhydro-1,3-thiazinium Hydroxide 25d. The anhydro-1,3-thiazinium hydroxide **25d** was prepared from the thiolactam **23d** (480 mg, 2.44 mmol) and (chlorocarbonyl)phenylketene (500 mg, 2.77 mmol): 770 mg (93%); IR (CCl_4) 2930, 1670, 1610 1440, 1320, 1120 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.20–1.88 (m, 8H), 1.34 (s, 3H), 1.97–2.04 (m, 2H), 3.71–3.81 (m, 1H), 4.11–4.18 (m, 1H), 4.95–5.03 (m, 2H), 5.65–5.78 (m, 1H), 7.13–7.18 (m, 1H), 7.26–7.31 (m, 2H), and 7.45–7.48 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.2, 23.3, 29.8, 30.6, 33.6, 42.2, 45.6, 49.2, 102.6, 115.7, 126.4, 127.7, 130.9, 134.0, 137.4, 161.0, 166.5, 193.1.

Anal. Calcd for $C_{20}H_{23}NO_2S$: C, 70.35; H, 6.79; N, 4.10. Found: C, 70.19; H, 6.52; N, 4.03.

A solution of the betaine **25d** (780 mg, 2.29 mmol) in toluene (10 mL) was heated under reflux for 20 h. Standard workup gave a mixture of two compounds which were separated by column chromatography on silica gel. The initial fraction contained cycloadduct **26d**, obtained as colorless, irregular prisms: 330 mg (42%), mp 168–169 °C; IR (CCl_4) 2940, 1690, 1655, 1440, 1380, 1250 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28–2.13 (m, 11H), 1.36 (s, 3H), 2.46–2.51 (m, 1H), 2.86 (dd, 1H, J = 13.2, 10.2 Hz), 3.40–3.50 (m, 1H), 3.96–4.05 (m, 1H), and 7.26–7.41 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.9, 20.5, 28.1, 29.1, 31.4, 33.1, 36.1, 37.8, 38.0, 40.8, 65.3, 77.0, 127.3, 127.7, 130.0, 133.2, 168.9, 198.2.

Anal. Calcd for $C_{20}H_{23}NO_2S$: C, 70.35; H, 6.79; N, 4.10; S, 9.39. Found: C, 70.07; H, 6.82; N, 4.04; S, 9.29.

The other major product was cycloadduct **28c** obtained as a yellow oil in 48% yield; IR (CCl_4) 2940, 1655, 1500, 1390, 1370 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.75 (s, 3H), 1.19–1.28 (m, 1H), 1.35–1.38 (m, 3H), 1.49–1.54 (m, 3H), 1.69–1.85 (m, 2H), 2.03–2.17 (m, 2H), 2.68 (dd, 1H, J = 16.4, 5.3 Hz), 2.81 (dd, 1H, J = 12.8, 4.4 Hz), 3.65 (d, 1H, J = 5.3 Hz), 4.40 (d, 1H, J = 12.8 Hz), and 7.14 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.9, 19.8, 24.6, 30.0, 31.7, 32.5, 37.1, 38.4, 41.6, 46.2, 112.7, 126.6, 126.8, 128.0, 135.9, 138.3, 171.1; HRMS calcd for $C_{19}H_{23}NO$ 281.1779, found 281.1778. Cycloadduct **26d** was converted in quantitative yield into **28c** by refluxing in xylene for 1 h.

Preparation and Thermal Cycloaddition of Anhydro-1,3-thiazinium Hydroxide 25e. The anhydro-1,3-thiazinium hydroxide **25e** was prepared from the thioamide **23f** (400 mg, 1.90 mmol) and (chlorocarbonyl)phenylketene (400 mg, 2.22 mmol): 630 mg (94%); IR (CCl_4) 2980, 1605, 1440, 1235, and 1110 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36–1.85 (m, 10H), 1.43 (s, 3H), 1.97–2.05 (m, 2H), 4.01–4.08 (m, 1H), 4.84–4.88 (m, 1H), 4.95–5.01 (m, 2H), 5.65–5.76 (m, 1H), 7.11–7.17 (m, 1H), 7.26–7.31 (m, 2H), and 7.47 (d, 2H, J = 7.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0, 23.5, 25.0, 28.8, 33.7, 37.3, 39.8, 47.3, 51.6, 103.0, 115.8, 126.4, 127.7, 130.7, 134.0, 137.4, 161.0, 167.0, 193.6.

Anal. Calcd for $C_{21}H_{25}NO_2S$: C, 70.95; H, 7.09; N, 3.94. Found: C, 70.86; H, 6.98; N, 3.71.

A solution of the betaine **25e** (510 mg, 1.44 mmol) in toluene (20 mL) was heated under reflux for 20 h. Standard reaction workup gave a mixture of two compounds which were separated by column chromatography on silica gel. The minor fraction isolated contained cycloadduct **26e** as colorless, irregular prisms: 70 mg (14%), mp 180–181 °C; IR (CCl_4) 2940, 1695, 1660, 1380, 1280, 1220 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19–2.07 (m, 12H), 1.43 (s, 3H), 2.28–2.38 (m, 1H), 2.69–2.76 (m, 1H), 2.95 (dd, 1H, J = 13.0 and 10.4 Hz), 3.23 (dd, 1H, J = 14.9 and 12.0 Hz), 4.90 (dd, 1H, J = 14.9 and 5.8 Hz), and 7.24–7.41 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.9, 24.1, 26.9, 30.4, 33.0, 33.2, 36.8, 40.5, 41.1, 43.1, 43.3, 64.7, 81.0, 127.2, 127.7 130.0, 133.5, 169.2, 198.9.

Anal. Calcd for $C_{21}H_{25}NO_2S$: C, 70.95; H, 7.09; N, 3.94; S, 9.02. Found: C, 70.89; H, 7.12; N, 3.96; S, 9.08.

The major fraction contained the cycloadduct **28d** as a 1:1-diasteromeric mixture: 300 mg (71%); IR (CCl_4) 2920, 1655,

1450, 1380, 1310, 1250 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.08 (3H), 1.16 (s, 3H), 1.19–2.47 (m, 14H), 2.93–3.08 (m, 1H), 3.53–3.60 (m, 1H), 4.64–4.71 (m, 1H), and 7.14–7.30 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.3, 18.4, 24.6, 24.7, 24.8, 25.1, 28.2, 28.6, 30.8, 30.8, 32.7, 32.8, 36.2, 36.3, 40.7, 41.1, 43.0, 43.8, 44.3, 47.0, 47.3, 116.4, 117.3, 126.6, 127.6, 127.8, 128.1, 128.2, 138.8, 138.9, 171.6, 171.7; HRMS calcd for $C_{20}H_{25}NO$ 295.1936, found 295.1936.

Preparation and Thermal Cycloaddition of Anhydro-1,3-thiazinium Hydroxide (25f). The betaine **25f** was prepared by the dropwise addition of methylmalonyl dichloride (320 mg, 2.54 mmol) to a solution containing 3-methyl-3-(penten-5-yl)-2(1*H*)-piperidinethione (**23d**) (400 mg, 2.03 mmol) in toluene at −20 °C for 24 h: 400 mg (71%); IR (neat) 2860, 1690, and 1610 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 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, 1H), 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 (75 MHz, $CDCl_3$) δ 10.3, 18.1, 23.1, 29.1, 30.7, 33.4, 42.2, 45.3, 48.9, 97.5, 115.4, 137.2, 161.1, 166.0, 191.4.

A solution of the betaine **25f** (500 mg, 1.8 mmol) in toluene (25 mL) was heated under reflux for 2 h. Standard workup of the reaction mixture gave cycloadduct **26f** as colorless, irregular prisms: 400 mg (80%), mp 99–100 °C; IR (KBr) 2933, 1690, 1670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 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 (75 MHz, $CDCl_3$) 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, 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.

The cycloadduct **26f** (100 mg) was heated under reflux for 60 h in toluene (1 mL) containing *p*-toluenesulfonic acid (5 mg). Standard workup of the reaction mixture gave the carbonyl sulfide extruded cycloadduct **28e** as a colorless oil: 78 mg (95%); IR (neat) 2930, 1640, and 1520 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.10 (s, 3H), 1.14 (d, 3H), 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 (75 MHz, $CDCl_3$) δ 14.9, 18.3, 19.9, 25.7, 29.5, 32.5, 34.6, 34.8, 38.5, 41.9, 114.9, 136.7, 173.8.

Anal. Calcd for $C_{14}H_{21}NO$: C, 76.66; H, 9.66; N, 6.39. Found: C, 76.51; H, 9.48, N, 6.27.

Anhydro-3-benzyl-4-hydroxy-9-methyl-2-oxo-9-(pent-4-yl)tetrahydropyrido[2,1-*b*][1,3]thiazinium Hydroxide (25g). Compound **25a** was prepared by the dropwise addition of 660 mg (3.04 mmol) of benzylmalonyl dichloride[38] to a solution of 500 mg (2.54 mmol) of thiolactam **5b** in CH_2Cl_2 at 0 °C. The resulting mixture was allowed to slowly warm to rt over 24 h. Removal of the solvent under reduced pressure provided a bright yellow residue that was purified by flash silica gel chromatography, giving 710 mg (79%) of **25g** as a yellow oil: IR (CCl_4) 2940, 1610, and 1440 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 3H), 1.53–2.00 (m, 10H), 3.71 (s, 2H), 3.70–3.78 (m, 1H), 4.13–4.20 (m, 1H), 4.90–4.96 (m, 2H), 5.58–5.72 (m, 1H), 6.99–7.14 (m, 3H), and 7.32 (d, 2H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.2, 20.9, 23.2, 29.9, 30.8, 33.5, 42.2, 45.4, 48.9, 102.1, 115.7, 125.6, 127.9, 128.9, 137.2, 141.4, 161.1, 166.4, and 192.4; HRMS calcd for $C_{21}H_{25}NO_2S$ 355.1606, found 355.1604.

Preparation of 2-Benzyl-7a-methyl-1-thiadecahydropyrido[3,2,1-*ij*]quinoline-2,4-dione (26g). A solution containing 650 mg (1.83 mmol) of 1,4-dipole **25g** in 25 mL of toluene was heated at reflux for 20 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel to give 420 mg (65%) of cycloadduct **26g** as a white crystalline solid: mp 169–170 °C; IR (CCl_4) 2920, 1690, and 1660 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.08–2.25 (m, 13H), 1.31 (s, 3H), 3.28–3.37 (m, 1H), 3.37 (s, 2H), 4.11–4.20 (m, 1H), and 7.16–7.36 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.7, 20.5, 27.7, 28.8, 31.1, 32.7, 33.8, 36.1, 36.6, 38.0, 40.6, 61.2, 77.5, 126.3, 127.9, 131.6, 137.4, 169.4, and 200.0.

Anal. Calcd for $C_{21}H_{25}NO_2S$: C, 70.95; H, 7.09; N, 3.94; S, 9.02. Found: C, 70.94; H, 7.10; N, 3.96; S, 9.12.

Preparation and Thermal Cycloaddition of Anhydro-1,3-thiazinium Hydroxide (33). 2-(Penten-5-yl)malonic acid (**32a**) was prepared by hydrolysis of diethyl (penten-5-yl)malonate[19] (**32c**) (6.0 g, 26 mmol) with potassium hydroxide (2.95 g, 0.053 mol) in absolute ethanol (60 mL): 4.40 g (97%), mp 83–84 °C; IR (CCl_4) 3500–3400, 2960, 2920, 1700, 1630, and 1380 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.45–1.54 (m, 2H), 1.95 (dd, 2H, J = 15.4 and 7.3 Hz), 2.09 (dd, 2H, J = 13.6, 6.7 Hz), 3.44 (t, 1H, J = 7.3 Hz), 4.96–5.05 (m, 2H), 5.73–5.81 (m, 1H), 11.72 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.3, 28.1, 33.1, 51.5, 115.1, 137.6, 174.5.

Anal. Calcd for $C_8H_{12}O_4$: C, 55.81, H, 7.02. Found: C, 55.65, H, 6.94.

(Penten-5-yl)malonyl dichloride (**32b**) was prepared from the diacid[19] **32a** (4.40 g, 25.6 mmol) and phosphorus pentachloride (10.6 g, 50.8 mmol). It was obtained as a colorless oil by vacuum distillation: 4.0 g (75%), bp 72–74 °C (0.35 mm); IR (CCl_4) 2920, 1780, 1640, 1300, 1010, and 910 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.42–1.53 (m, 2H), 2.02–2.12 (m, 3H), 4.16–4.22 (m, 1H), 4.35–4.42 (m, 1H), 4.93–5.04 (m, 2H), 5.64–5.78 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.4, 28.8, 32.8, 72.1, 115.9, 136.8, 167.6; HRMS calcd for $C_8H_{10}Cl_2O_2$ 208.0058, found 208.0055.

The betaine **33** was prepared from 3,3-dimethyl-2(1*H*)-piperidinethione (**31b**) (140 mg, 0.98 mmol) and (penten-5-yl)-malonyl dichloride (**32b**) (500 mg, 2.39 mmol): 100 mg (37%); ^1H NMR (300 MHz, $CDCl_3$) δ 1.19–1.58 (m, 4H), 1.49 (s, 6H), 1.79–1.87 (m, 2H), 2.00–2.07 (m, 3H), 2.43–2.47 (m, 1H), 4.11 (t, 2H, J = 6.2 Hz), 4.85–4.99 (m, 2H), 5.74–4.86 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.3, 25.1, 27.0, 31.0, 33.8, 34.3, 41.9, 48.8, 103.0, 114.0, 139.1, 161.2, 166.4, 191.9. A solution of the betaine **33** (290 mg, 0.98 mmol) in xylene (25 mL) was heated at 150 °C for 22 h. Standard workup of the reaction mixture gave cycloadduct **35** as a yellow oil: 135 mg (62%); IR (CCl_4) 2940, 1660, 1450, 1380, and 1260 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.06 (s, 3H), 1.10 (s, 3H), 1.36–1.97 (m, 10H), 2.47–2.55 (m, 1H), 2.66–2.77 (m, 1H), 3.14–3.23 (m, 1H), 3.89–3.97 (m, 1H), and 4.75–4.76 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.9, 22.8, 28.9, 29.3, 29.6, 33.1, 33.9, 36.6, 36.7, 41.6, 45.3, 106.1, 144.4, 174.0; HRMS calcd for $C_{14}H_{21}NO$ 219.1623, found 219.1623.

Preparation of Anhydro-9,9-dimethyl-4-hydroxy-2-oxo-3-phenyltetrahydropyrido[2,1-*b*][1,3]thiazinium Hydroxide (36). A sample of betaine **36** was prepared from thiolactam **31b** as orange needles (66%); 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.

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Supplementary Material Available: ^1H NMR and ^{13}C NMR spectra for new compounds lacking analyses (5 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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