JOC Article

Tandem Pummerer/Mannich Cyclization Cascade of α-Sulfinylamides as a Method To Prepare Aza-Heterocycles‡

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Received February 4, 2002

A series of α-sulfinylenamides was conveniently prepared by the condensation of a primary amine with a ketone, followed by reaction of the resulting imine with ethylsulfenylacetyl chloride and subsequent oxidation with sodium periodate. When treated with *p*-TsOH, cyclization occurred to produce fused isoquinoline lactams by a mechanism that involves an initial Pummerer reaction followed by a subsequent cyclization of the resulting *N*-acyliminium ion onto the tethered aromatic ring. The isolation of a single diastereomer was rationalized in terms of a Nazarov-type 4π-electrocyclic reaction followed by π-cyclization onto the least hindered side of the *N*-acyliminium ion. Another method that was used to generate the α-acylthionium ion intermediate involved the reaction of bis(ethylsulfenylacetyl)acetamides with dimethyl(methyl)thiosulfonium tetrafluoroborate (DMTSF). Treatment of several bis-ethylsulfenylenamides with DMTSF delivered novel spiro-heterocycles as single diastereomers in good yield by a related process. The convergency and stereochemical control associated with this cascade sequence make it particularly suited for the assembly of natural product scaffolds. Some preliminary studies were directed toward both mesembrine and deethylibophyllidine. When the model *Z*-enamido sulfoxide **33** was heated with *p*-TsOH, a 80% yield of tosylate **34** was obtained as a single diastereomer. In this case, the carbocation intermediate derived from cyclization onto the terminal π-bond was trapped with *p*-TsOH from the least hindered face, opposite the angular carbomethoxy and methyl groups. Related cyclization cascades were also found to occur with systems containing tethered indole rings.

Nitrogen-containing heterocycles are abundant in nature and exhibit diverse and important biological properties.[1,2] Accordingly, novel strategies for the stereoselective synthesis of azapolycyclic ring systems continue to receive considerable attention in the field of synthetic organic chemistry.[3−9] A variety of preparative methods have been developed, and many reviews, monographs, and reports have been released.[1] The elaboration of ring-fused heterocycles based upon tandem cyclizations are among the most powerful strategic tools available to the synthetic organic chemist, because they rapidly increase the complexity of a substrate while at the same time making economical use of available functional groups.[10−21]

‡ This paper is dedicated to Waldemar Adam on the occasion of his 65th birthday, for his significant contributions to the field of mechanistic organic chemistry.

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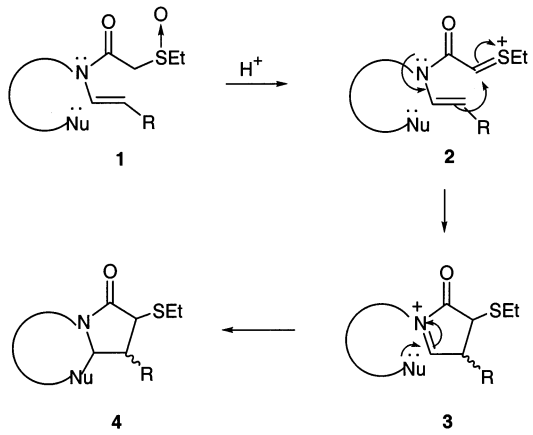
10.1021/jo020083x CCC: $22.00
Published on Web 07/20/2002

Tandem cationic reactions are featured in the biosynthesis of important natural products, and synthetic applications of both biomimetic and nonbiomimetic tandem cationic reactions[22] have been widely developed. The reaction or *N*-acyliminium ions with tethered π-bonds represents one of the most important methods for preparing complex nitrogen heterocycles.[23−26] In recent years, the Pummerer reaction followed by a π-cyclization has also been found to be a very effective and general method for the preparation of many diverse azapolycyclic skeletons.[27−29] The combination of a Pummerer/Mannich ion cyclization sequence offers unique opportunities for the assemblage of complex target molecules.[30,31] In an earlier communication we described a route to various azapolycyclic systems that involved the tandem thionium/*N*-acyliminium ion cyclization cascade depicted in Scheme 1.[32]

SCHEME 1



Application of this tandem sequence to alkaloid synthesis is potentially very broad. Among the great variety of skeletal types of monoterpenoid indole alkaloids, the ibophyllidene alkaloids are characterized structurally by the presence of a 2,3,3-trisubstituted indole.[33] The pentacyclic pyrrolizino[1,7-*cd*]carbazole unit present constitutes the core of this intriguing family of natural products.[34] We came to recognize that the cascade sequence outlined in Scheme 1 could possibly be used for a concise and stereocontrolled synthesis of deethylibophyllidine (**5**).[35] The retrosynthetic analysis is outlined in Scheme 2. The key step in our plan involves the acid-catalyzed cyclization of indole **8** into **7**. The stereochemical outcome of this cyclization is assumed to proceed by a syn delivery of the nucleophilic tether to the initially formed *N*-acyliminium ion. Raney nickel desulfurization followed by amide reduction should deliver **6**, which had already been converted to deethylibophyllidene (**5**) by Bonjoch and co-workers.[36] In this paper, we report an account of our efforts dealing with this unique tandem cyclization sequence.

Results and Discussion

The strategy delineated in Scheme 2 for the synthesis of deethylibophyllidene (**5**) relies on a tandem Pummerer/

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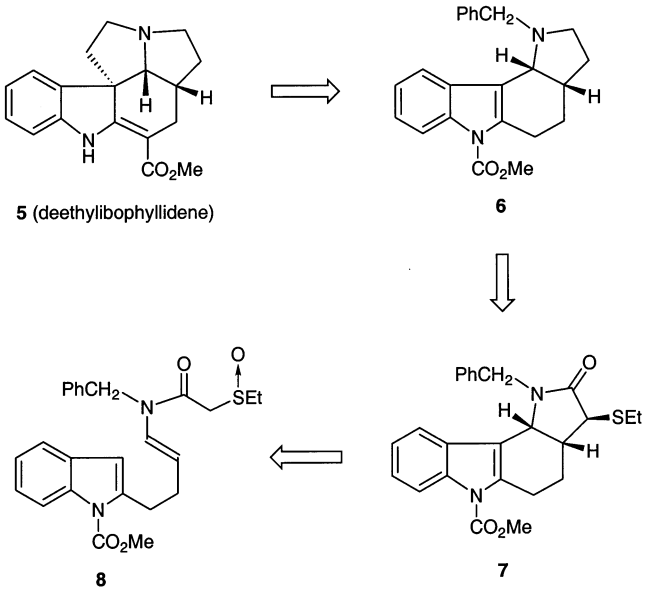
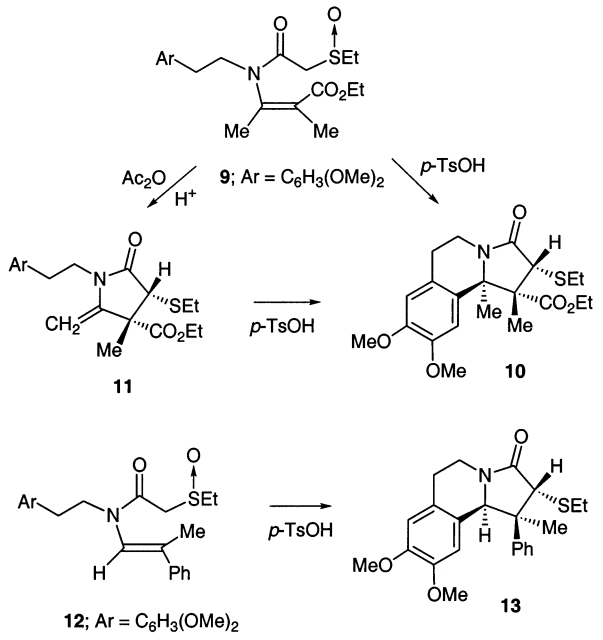
SCHEME 2



Mannich cyclization cascade.[37] To pursue this approach, we decided it was necessary to first probe several issues related to the following questions: (1) will α-sulfinylenamides of type **1** undergo ready 5-ring cyclization, (2) what is the propensity for the indole π-bond to cyclize onto the resulting *N*-acyliminium ion, (3) will the cyclization proceed in a stereoselective manner, and (4) how easy will it be to remove the ethylthio group from the resulting lactam. Our initial foray into this tandem cyclization chemistry involved substrates **9** and **12**. These compounds were conveniently prepared in 60−80% yield from the condensation of 3,4-dimethoxyphenethylamine with the appropriate aldehyde or ketone followed by reaction of the resulting imine with ethylsulfenylacetyl chloride[38] and subsequent $NaIO_4$ oxidation. The olefin geometry was assigned on the basis of NOE studies. In the case of **9**, irradiation of the methyl singlet at δ 1.88 enhanced (8%) the other methyl singlet at δ 1.96. Treatment of **9** with 2 equiv of *p*-TsOH in refluxing benzene afforded **10** in 78% yield (Scheme 3). It is important to note that only one of several possible diastereomers of the fused isoquinoline lactam **10** was observed under the reaction conditions, as indicated by ^{1}H and ^{13}C NMR spectral data (vide infra). The stereochemical assignment was unequivocally established by X-ray crystallographic analysis, which revealed a syn relationship between the ethylthio, carbethoxy, and methyl groups.[39] Interestingly, when **9** was treated with acetic anhydride (10 equiv) in refluxing toluene that contained a catalytic amount of *p*-TsOH, the only product isolated corresponded to the terminally substituted enamide **11**. Further heating of **11** in the presence of 2 equiv of *p*-TsOH afforded **10** in 78% yield. In the presence of excess acetic anhydride, the initially formed *N*-acylimin-

SCHEME 3



ium ion derived from **9** prefers to undergo deprotonation rather than cyclization.

α-Sulfinylenamide **12** underwent an analogous cyclization, affording the fused isoquinoline lactam **13** in 69% yield. The olefin geometry in **12** rests on the absence of a NOE between the vinylic hydrogen and the methyl group. This cyclization reaction also proceeded with high diastereospecificity and led to a single diastereomer where the methyl and ethylthio groups are on the same side of the ring. The NOE enhancement between the tertiary hydrogen adjacent to the nitrogen atom of the lactam ring and the vicinal methyl group further defines the stereochemical relationship of the substituent groups present in **13**.

A plausible mechanism that nicely rationalizes the stereochemical results involves initial formation of an α-acylthionium ion (i.e., **14**) followed by a Nazarov-type[40] 4π-electrocyclic ring closure, which occurs in a conrotatory fashion to give *N*-acyliminium ion **15** (Scheme 4). The final cyclization step proceeds in a stereoselective manner by attack of the proximal aromatic ring from the less hindered side of the iminium ion framework.

A rather interesting rearrangement was encountered when a monosubstituted enamide (i.e., **16**) was used. Subjection of **16** to the acidic conditions resulted in the formation of 2*H*-benzo[*c*]azocin-3-one **19** as the only isolable product in 42% yield (Scheme 5). More than likely, the thionium/*N*-acyliminium ion cascade first produces tetrahydropyrrolo[2,1-*a*]isoindol-3-one **17** as a transient intermediate. Under the reaction conditions the tricyclic amide undergoes an acid-catalyzed ring opening to give **18**, which is subsequently isomerized to give the thermodynamically more stable 2*H*-benzoazocinone **19**.

Another method that has occasionally been used to generate α-acylthionium ions involves the reaction of thioketals with dimethyl(methylthio)sulfonium tetrafluo-

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(39) The authors have deposited coordinates for stuctures **10**, **34**, and **38** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, B2 1EZ, UK.

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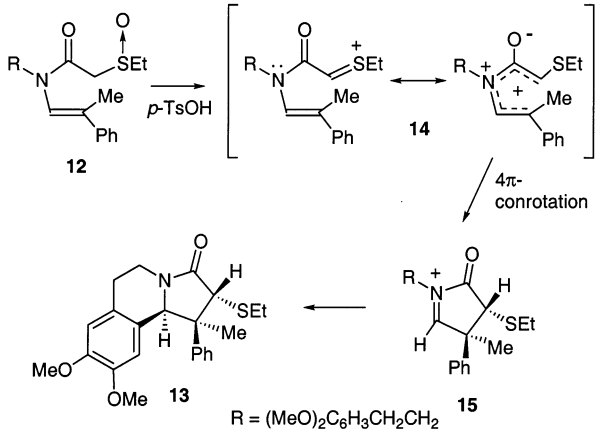
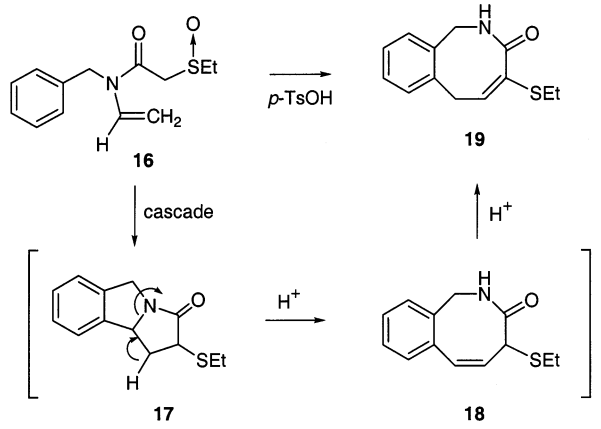
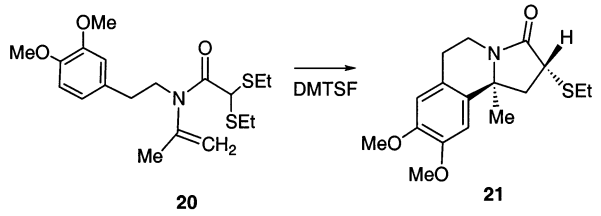
SCHEME 4



SCHEME 5



SCHEME 6



roborate (DMTSF).[41,42] This reagent exhibits a remarkable high reactivity toward thioketals and causes the carbon−sulfur bond to become labile upon methylthiolation.[43,44] The initially formed alkylthiosulfonium ion easily dissociates to produce a thionium ion and ethyl methyl disulfide. Indeed, we found that the reaction of bis(ethylsulfenyl)acetamide **20** with DMTSF afforded isoquinolinone **21** in 82% yield (Scheme 6).

Several types of α-sulfinylenamides were examined so as to establish the scope and generality of the process.

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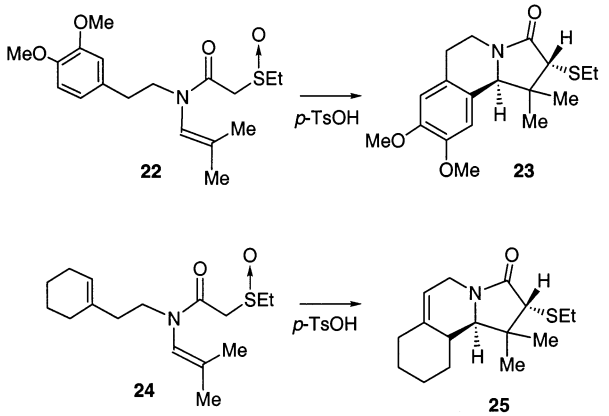
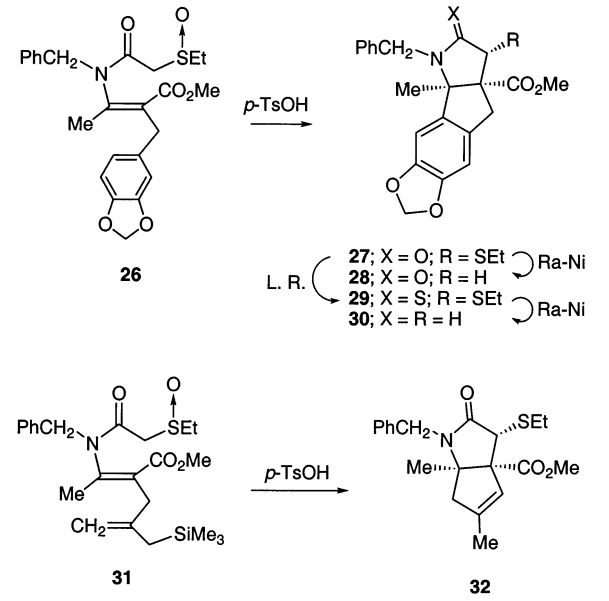
SCHEME 7



SCHEME 8



As illustrated in Scheme 7, the cyclization of enamide **22** furnished isoquinolinone **23** in 65% yield. Because all of the previous examples involved aromatic π-bond cyclizations, we decided to study several systems that possess a simple olefinic tether. We found that treatment of the cyclohexenyl substituted enamide **24** with *p*-TsOH also caused a thionium ion induced Mannich reaction to occur, ultimately producing **25** in 58% yield.

Attention was next turned to the acid-induced cyclization of enamides **26** and **31** where the point of attachment of the interacting π-bond was switched from nitrogen to carbon. Treatment of **26** with *p*-TsOH under identical conditions used for the cyclization of **9** gave **27** as a single diastereomer in 79% yield (Scheme 8). The ethylthio group of **27** was reductively cleaved with Raney nickel to afford lactam **28** in 98% yield. Heating a sample of **27** with Lawesson's reagent furnished thioamide **29** in 86% yield, which, in one-step, gave indacene **30** (70%) upon treatment with Raney nickel. The well-documented reactivity of allyl silanes toward electrophiles[45] suggested

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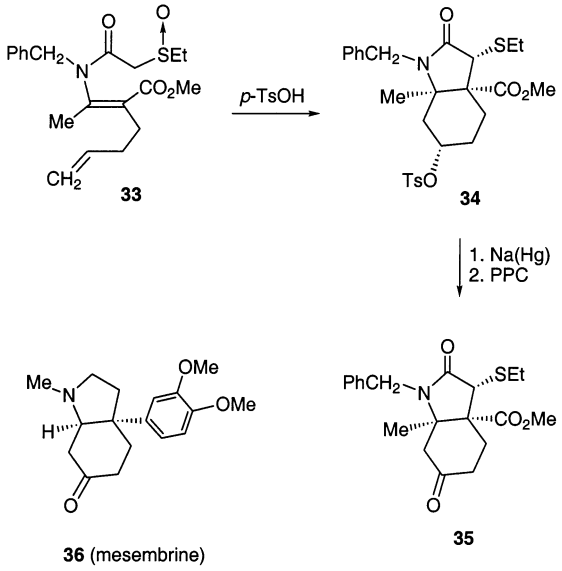
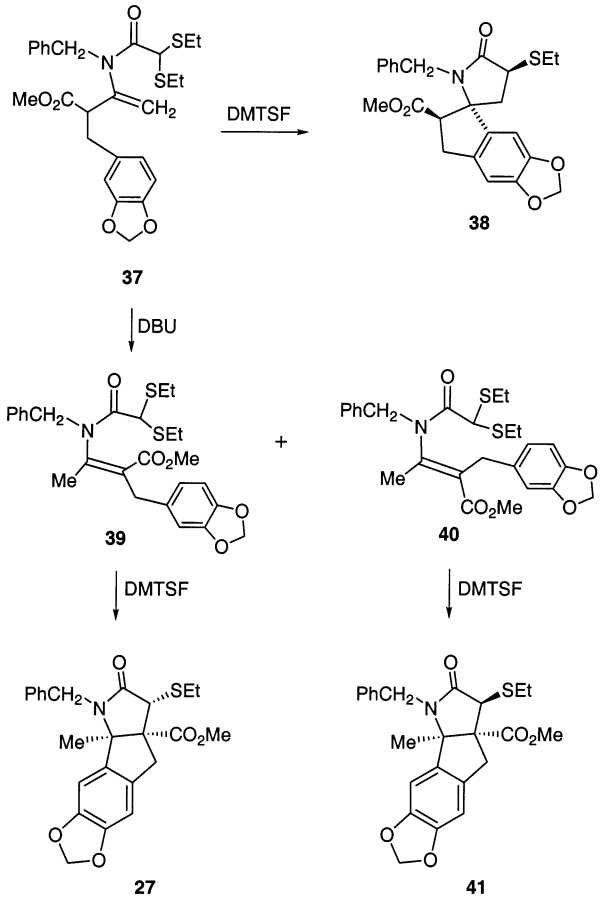
SCHEME 9



SCHEME 10



that the acid-promoted reaction of sulfinylenamide **31** should provide access to a bicyclic lactam. Indeed, treatment of **31** with *p*-TsOH afforded the cyclized product **32** in 61% yield. We suspect that the initially formed lactam, which possesses an exocyclic double bond, is isomerized under the reaction conditions. The structure and stereochemistry of products **27** and **32** follow from analysis of their NMR spectroscopic data, and their formation is perfectly consistent with the tandem thionium/iminium ion cascade sequence outlined in Scheme 4.

The convergency and stereochemical control associated with this cascade sequence make it particularly suited for the assembly of natural product scaffolds. With this in mind, some preliminary studies were directed toward mesembrine (**36**), a well-known member of the *Scelectium* class of alkaloids.[46] When the model *Z*-enamido sulfoxide **33** was heated with *p*-TsOH, an 80% yield of tosylate **34** was obtained as a single diastereomer (Scheme 9). The stereochemistry of **34** was established by a single-crystal X-ray analysis,[39] and its formation is consistent with the proposed 4π-electrocyclic ring closure. In this case, the carbocation intermediate derived from cyclization onto the terminal π-bond was trapped with tosic acid from the least hindered face, opposite the angular carbomethoxy and methyl groups. Reduction of **34** with Na(Hg) followed by PCC oxidation afforded **35** in 82% overall yield. Further studies are aimed at extending this model cascade reaction toward the synthesis of the *Sceletium* class of alkaloids.

To further explore the scope and generality of the tandem cyclization process, we carried out another variation of the Pummerer initiation reaction using dithioacetal-substituted enamides as thionium ion precursors.[41] Sequential treatment of benzylamine with 2-benzo[1,3]-dioxol-5-ylmethyl-3-oxobutyric acid methyl ester[47] followed by reaction with bis-ethylsulfenylacetyl chloride[48] produced enamide **37** in 63% yield. Interestingly, only the methylene-substituted enamide **37** was formed in this reaction. The DMSTF cyclization of **37** provided access to the unusual spiro-heterocycle **38** whose stereochemistry was also established by single-crystal X-ray analysis (Scheme 10).[39] When enamide **37** was allowed to stir with 2 equiv of DBU at 25 °C for 12 h, complete isomerization to the tetrasubstituted alkenes **39** and **40** (1:1 mixture) occurred in quantitative yield. Silica gel chromatography easily separated the two geometrical isomers. The olefin geometry was assigned on the basis of NOE studies. In the case of **39**, irradiation of the methylene protons enhanced the methyl singlet at δ 2.09. Similarly, irradiation of the vinylic methyl group at δ 2.06 resulted in an enhancement of the carbomethoxy signal at δ 3.60 for the *E*-isomer **40**. As we anticipated from the 4π-conrotatory mechanism outlined in Scheme 4, cyclization of each olefin (i.e., **39** and **40**) afforded single diastereomers epimeric at the ethylthio position without any cross contamination (Scheme 10).

Given the success in forming azapolycyclic ring systems from enamides possessing simple aromatic and olefinic tethers, it seemed to us that a related cyclization cascade might also occur with systems containing a tethered indole ring. This was particularly important for our planned approach to deethylibophyllidine. To test this

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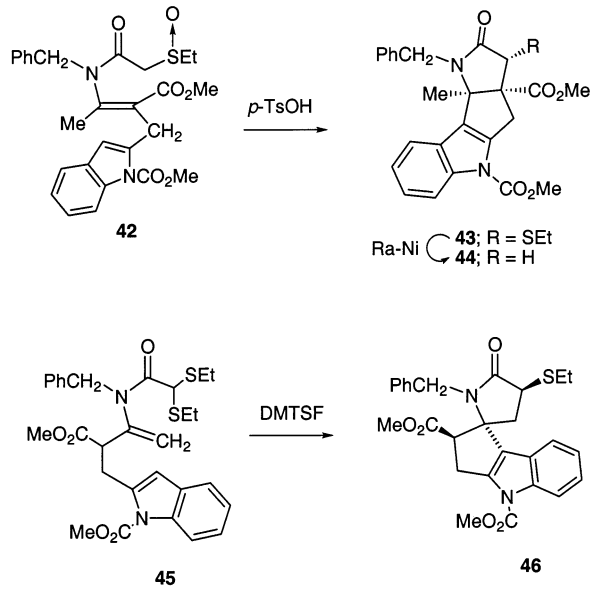
(47) Barry, R. H.; Mattocks, A. M.; Hartung, W. H. *J. Am. Chem. Soc.* **1948**, *70*, 693.

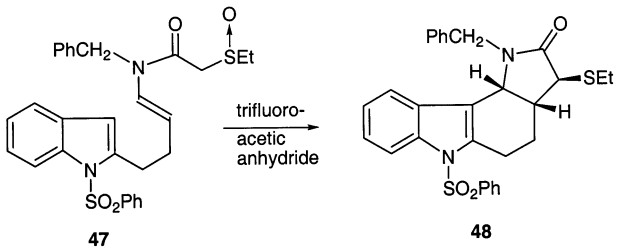
(48) Bellus, D. *Helv. Chim. Acta* **1975**, *58*, 2509.

SCHEME 11



42 **45**

SCHEME 12



47 **48**

possibility, two differently substituted indolyl enamides (i.e., **42** and **45**) were synthesized from the appropriate ketones. Treatment of **42** with 2 equiv of *p*-TsOH in refluxing benzene afforded the crystalline polycycle **43** in 80% yield (Scheme 11). Raney nickel reduction of **43** furnished **44** in quantitative yield. Likewise, treatment of enamide **45** with DMTSF initiated a clean cyclization to deliver spirocycle **46** in 69% yield as a single diastereomer. A possible rationale to account for the formation of **46** involves a facile equilibration of the carbomethoxy-bearing stereogenic center via tautomerization of the *N*-acyliminium ion intermediate prior to the final ring closure. Alternatively, the direction of conrotatory closure may be influenced by the presence of the neighboring carbomethoxy group. Most importantly, these two examples clearly demonstrate the facility with which the thionium/iminium ion cascade occurs with enamides possessing tethered indole rings.

The potential of further employing this methodology for the synthesis of various ibophyllidene alkaloids prompted us to carry out a model study to probe the likelihood of using the cascade sequence for a synthesis of deethylibophyllidene (**5**). Initial feasibility studies were conducted with enamidosulfoxide **47**. Gratifyingly, the reaction of **47** with trifluoroacetic anhydride gave azacycle **48** in 60% yield (Scheme 12). Further application of this method to deethylibophyllidene and related alkaloids is currently underway in our laboratories and will be reported in due course.

In conclusion, the acid-catalyzed reaction of a series of α-sulfinylenamides furnished fused isoquinoline lactams by a mechanism that involves an initial Pummerer reaction followed by a subsequent cyclization of the resulting *N*-acyliminium ion onto the tethered aromatic ring. The isolation of a single diastereomer can be rationalized in terms of a Nazarov-type 4π-electrocyclic reaction followed by π-cyclization onto the least hindered side of the *N*-acyliminium ion. The convergency and stereochemical control associated with this cascade sequence make it particularly suited for the assembly of natural product scaffolds. Further utilization of this sequence for the stereocontrolled synthesis of several pyrrolizino[1,7-*cd*]carbazole alkaloids is under current investigation.

Experimental Section

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70 eV. Unless otherwise noted, all reactions were performed in flame-dried glassware under an atmosphere of dry 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.

1-[2-(3,4-Dimethoxyphenyl)ethyl]-4-ethylsulfenyl-3-methyl-2-methylene-5-oxopyrrolidine-3-carboxylic Acid Ethyl Ester (11). To a solution containing 0.4 g (4.0 mmol) of acetic anhydride and 2 mg of *p*-toluenesulfonic acid in 50 mL of toluene at reflux was added dropwise 0.18 g (0.4 mmol) of 3-([2-(3,4-dimethoxyphenyl)ethyl]ethylsulfinylacetylamino)-2-methylbut-2-enoic acid ethyl ester (**9**) in 2 mL of toluene. After heating at reflux for 1 h, the reaction mixture was concentrated under reduced pressure, and the residue was subjected to silica gel chromatography to give 0.14 g (78%) of **11** as a colorless oil: IR (neat) 1730, 1645, 1517, 1388, and 1260 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.21 (t, 3H, J = 7.2 Hz); 1.30 (t, 3H, J = 7.4 Hz), 1.61 (s, 3H), 2.76 (m, 5H), 3.29 (s, 1H), 3.54 (m, 1H), 3.87 (s, 3H), 3.89 (s, 3H), 4.13 (q, 2H, J = 7.2 Hz), 4.35 (d, 1H, J = 2.7 Hz), and 4.41 (d, 1H, J = 2.7 Hz), 6.79 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.9, 14.9, 21.1, 28.1, 31.6, 42.2, 53.2, 54.4, 55.8, 61.5, 85.3, 111.2, 111.8, 120.6, 130.6, 147.7, 148.0, 148.9, 150.0, 170.4, and 171.9. Anal. Calcd for $C_{21}H_{29}NO_5S$: C, 61.89; H, 7.17; N, 3.44. Found: C, 61.72; H, 7.03; N, 3.22.

***N*-Benzyl-2-ethylsulfinyl-*N*-vinylacetamide (16).** To a 2.6 g (0.24 mol) sample of benzylamine at 0 °C was added 1.1 g of acetaldehyde (0.24 mol). The reaction mixture was stirred at 0 °C for 2 h and at room temperature for 1 h. After this time, solid potassium hydroxide pellets were added, and the reaction mixture was allowed to sit overnight. The mixture was filtered and the solvent was removed under reduced pressure to leave behind a yellow oil, which was taken up in 5 mL of CH_2Cl_2. To this solution was added 2.3 g (17 mmol) of ethylsulfenylacetyl chloride in 50 mL of CH_2Cl_2 followed by 1 mL of pyridine. The mixture was allowed to stir for 30 min at 0 °C and then at 25 °C for 3.5 h. The solution was concentrated under reduced pressure and the residue was chromatographed on a silica gel column to give 1.3 g (48%) of *N*-benzyl-2-ethylsulfenyl-*N*-vinylacetamide as a pale yellow oil, which was used in the next step without further purification: IR (neat) 1658, 1559, 1566, and 1457 cm^{-1};^1H NMR ($CDCl_3$, 400 MHz) δ 1.23 (t, 3H, J = 7.5 Hz), 2.60 (q, 2H, J = 7.5 Hz), 3.47 (s, 2H), 4.29−4.52 (m, 2H), 4.84 (s, 2H), 6.86 (dd, 1H, J = 15 and 9.3 Hz), and 7.14−7.30 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 26.6, 33.4, 45.8, 96.1, 125.8, 126.9, 127.2, 128.7, 129.2, 133.4, 137.1, and 168.6.

To a 0.3 g (1 mmol) sample of the above enamide in 20 mL of MeOH was added 0.4 g (1.6 mmol) of $NaIO_4$. After stirring for 3 h at room temperature, the mixture was diluted with water and extracted with CH_2Cl_2. The organic layers were combined, washed with a saturated NaCl solution, and dried

with $MgSO_4$. The mixture was concentrated under reduced pressure and the residue was chromatographed on silica gel to give 0.25 g (88%) of *N*-benzyl-2-ethylsulfinyl-*N*-vinylacetamide (**16**) as a pale yellow oil: IR (neat) 1624, 1457, 1182, and 1019 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.37 (t, 3H, J = 7.6 Hz), 2.74−2.87 (m, 1H), 2.93−3.06 (m, 1H), 3.99 (s, 2H), 4.49−4.64 (m, 2H), 4.87 (s, 2H), 6.89 (dd, 1H, J = 15.2 and 9.2 Hz), and 7.16−7.34 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 6.8, 46.7, 48.7, 55.2, 99.0, 125.8, 127.0, 127.5, 128.9, 129.4, 132.6, 136.2, and 164.2. Anal. Calcd for $C_{13}H_{17}NO_2S$: C, 62.13; H, 6.82; N, 5.58. Found: C, 62.05; H, 6.78; N, 5.47.

4-Ethylsulfenyl-1,6-dihydro-2*H*-benzo[*c*]azocin-3-one (19). To a 0.24 g (0.9 mmol) sample of sulfoxide **16** in 15 mL of toluene was added 0.9 mL (10 mmol) of acetic anhydride and 20 mg of *p*-TsOH. The resulting solution was heated at reflux for 3 h. The solution was cooled and concentrated under reduced pressure, and the residue was subjected to silica gel chromatography to give 0.1 g (42%) of **19** as a pale yellow oil: IR (neat) 1684, 1559, and 1457 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.35 (t, 3H, J = 7.2 Hz), 1.65 (brs, 1H), 2.89 (q, 2H, J = 7.2 Hz), 3.81 (d, 2H, J = 2.4 Hz), 4.64 (s, 2H), 6.44 (t, 1H, J = 2 Hz), and 7.22−7.31 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.9, 25.3, 46.8, 51.5, 127.9, 128.3, 128.6, 128.9, 129.1, 129.7, 136.5, 137.2, and 168.9. Anal. Calcd for $C_{13}H_{15}NOS$: C, 66.93; H, 6.49; N, 6.01. Found: C, 6.72; H, 6.34; N, 5.97.

***N*-[2-(3,4-Dimethoxyphenyl)ethyl]-2-bis(ethylsulfenylacetyl)-*N*-isopropenylacetamide (20).** To a solution of 3,4-dimethoxyphenethylamine (10 mL, 60 mmol) in benzene (60 mL) was added 6.5 mL (90 mmol) of anhydrous acetone, followed by 24 g of 4 Å molecular sieves. The reaction mixture was stirred at room temperature for 24 h before filtering through a plug of Celite. The plug was rinsed with diethyl ether, and the combined filtrates were concentrated under reduced pressure to give 11 g (84%) of 4-(3-aza-4-methylpent-3-enyl)-1,2-dimethoxybenzene as a yellow oil, which was used in the next step without further purification: IR (neat) 1659, 1588, 1509, 1253, and 1139 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.62 (s, 3H), 1.92 (s, 3H), 2.81 (t, 2H, J = 8.0 Hz), 3.71 (t, 2H, J = 7.6 Hz), 3.76 (s, 3H), 3.78 (s, 3H), and 6.70 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.0, 29.0, 36.6, 53.3, 55.4, 55.5, 110.8, 111.9, 120.3, 132.9, 146.9, 148.3, 167.2.

To a solution of 0.5 g (2.4 mmol) of the above imine in CH_2Cl_2 (12 mL) was added 0.2 mL (2.4 mmol) of pyridine, followed by 0.5 g (2.4 mmol) of bis-ethylsulfenylacetyl chloride. The reaction mixture was stirred at this temperature for 2 h before quenching with a saturated solution of $NaHCO_3$. The organic layer was separated and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the crude oil was purified by silica gel chromatography to furnish 0.44 g (65%) of enamide **20** as a colorless oil: IR (neat) 1638, 1510, 1389, and 1261 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.22 (t, 6H, J = 7.2 Hz), 1.94 (s, 3H), 2.63−2.84 (m, 6H), 3.59 (t, 2H, J = 7.6 Hz), 3.83 (s, 3H), 3.86 (s, 3H), 4.86 (s, 1H), 4.98 (s, 1H), 5.09 (s, 1H), 6.76 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 20.9, 24.0, 33.4, 47.5, 49.0, 55.8, 111.0, 112.0, 115.8, 120.7, 131.2, 144.2, 147.4, 148.7, and 167.6. Anal. Calcd for $C_{19}H_{29}NO_3S_2$: C, 59.51; H, 7.63; N, 3.65. Found: C, 59.36; H, 7.21; N, 3.60.

2-Ethylsulfenyl-8,9-dimethoxy-10*b*-methyl-1,5,6,10*b*-tetrahydro-2*H*-pyrrolo[2,1-*a*]isoquinolin-3-one (21). To a 0.25 g (0.7 mmol) sample of enamide **20** in 15 mL of CH_2Cl_2 at −40 °C was added 0.2 g (1.0 mmol) of dimethyl(methylthio)-sulfonium tetrafluoroborate (DMTSF).[49] The mixture was stirred for 15 min at −40 °C before warming to 0 °C for 30 min. The reaction mixture was quenched with a saturated solution of $NaHCO_3$. The organic layer was dried over anhydrous $MgSO_4$, the solvent was removed under reduced pressure, and the crude residue was subjected to column chromatography to give 0.17 g (82%) of the title compound as a colorless oil: IR (neat) 1681, 1610, 1417, and 1247 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, 3H, J = 7.2 Hz), 1.51 (s, 3H), 2.02 (dd, 1H, J = 12.0 and 11.2 Hz), 2.64−2.92 (m, 5H), 3.08 (dt, 1H, J = 12.4 and 4.4 Hz), 3.73 (dd, 1H, J = 10.0 and 9.2 Hz), 3.84 (s, 3H), 3.86 (s, 3H), 4.29 (dd, 1H, J = 13.2 and 6.4 Hz), 6.52 (s, 1H), and 6.55 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 24.9, 27.6, 28.0, 34.5, 42.7, 43.7, 55.8, 56.0, 58.9, 107.5, 111.4, 124.2, 133.8, 147.8, 148.0, and 170.5. Anal. Calcd for $C_{17}H_{23}NO_3S$: C, 63.52; H, 7.22; N, 4.36. Found: C, 63.45; H, 7.08; N, 4.31.

***N*-[2-(3,4-Dimethoxyphenyl)ethyl]-2-ethylsulfinyl-*N*-(2-methylpropenyl)acetamide (22).** To 5 mL (30 mmol) of dimethoxyphenethylamine in a round-bottom flask at 0 °C was added 2.7 mL (30 mmol) of 2-methyl propionaldehyde. The solution was allowed to stir for 30 min at 0 °C and at 25 °C for 1 h. The reaction mixture was filtered over Na_2SO_4 and concentrated under reduced pressure to give 5.6 g (80%) of [2-(3,4-dimethoxyphenyl)ethyl]isobutylideneamine as a pale yellow oil, which was used in the next step without further purification: IR (neat) 1669, 1516, 1465, 1262, and 1030 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.97 (d, 6H, J = 9.2 Hz), 2.32 (m, 1H), 2.81 (t, 2H, J = 9.6 Hz), 3.54 (t, 2H, J = 9.6 Hz), 3.81 (s, 3H), 3.84 (s, 3H), 6.65−6.76 (m, 3H), and 7.35 (d, 1H, J = 6.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.5, 34.1, 37.1, 55.9, 59.1, 63.1, 112.3, 112.6, 121.1, 132.8, 147.5, 148.8, and 170.5.

A 2.3 g (16.7 mmol) sample of ethylsulfenyl-acetyl chloride in 50 mL of CH_2Cl_2 at 0 °C was added to 2.6 g (11 mmol) of the above imine, followed by the addition of 1 mL of pyridine (12 mmol). The mixture was stirred at 0 °C for 30 min and then at 25 °C for 12 h. The solution was concentrated under reduced pressure and the residue was chromatographed on silica gel to give 2.3 g (62%) of *N*-[2-(3,4-dimethoxyphenyl)-ethyl]-2-ethylsulfenyl-*N*-(2-methylpropenyl)acetamide as a pale yellow oil, which was used in the next step without purification: IR (neat) 1644, 1516, 1417, 1146, and 1029 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.23 (t, 3H, J = 7.2 Hz), 1.59 (d, 3H, J = 1.6 Hz), 1.71 (d, 3H, J = 1.6 Hz), 2.60 (q, 2H, J = 7.2 Hz), 2.75 (t, 2H, J = 8 Hz), 3.16 (s, 2H), 3.61 (t, 2H, J = 8 Hz), 3.84 (s, 3H), 3.87 (s, 3H), 5.87 (m, 1H), and 6.74 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6, 17.9, 22.1, 26.5, 33.4, 33.5, 49.8, 56.1, 111.3, 112.2, 120.9, 124.1, 131.8, 136.4, 147.7, 149.0, and 170.1.

To a 2.0 g (6.0 mmol) sample of the above sulfide in 50 mL of MeOH was added 1.9 g (9 mmol) of $NaIO_4$. To this mixture was added 50 mL of water and the solution was stirred at room temperature for 3 h. The solution was extracted with CH_2Cl_2, and the organic extracts were combined, washed with a saturated NaCl solution, and dried with $MgSO_4$. The solution was filtered and the solvent was removed under reduced pressure. The residue was chromatographed on silica gel to give 1.5 g (72%) of sulfoxide **22** as a pale yellow oil: IR (neat) 1516, 1261, 1235, and 1028 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.34 (t, 3H, J = 7.6 Hz), 1.62 (d, 3H, J = 0.8 Hz), 1.76 (d, 3H, J = 0.8 Hz), 2.75 (t, 2H, J = 8.4 Hz), 2.71 (m, 1H), 2.97 (m, 1H), 3.60−3.65 (m, 3H), 3.77 (m, 1H), 3.84 (s, 3H), 3.88 (s, 3H), 5.83 (m, 1H), and 6.71−6.78 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 6.6, 18.1, 22.2, 33.3, 46.5, 49.4, 55.9, 56.1, 111.4, 112.1, 120.9, 132.2, 131.2, 138.4, 147.8, 149.1, and 164.8. Anal. Calcd for $C_{18}H_{27}NO_4S$: C, 61.16; H, 7.70; N, 3.97. Found: C, 61.04; H, 7.58; N, 4.06.

2-Ethylsulfenyl-8,9-dimethoxy-1,1-dimethyl-1,5,6,10*b*-tetrahydro-2*H*-pyrrolo[2,1-*a*]isoquinolin-3-one (23). To a mixture containing 1.8 mL (19 mmol) of acetic anhydride, 10 mg of *p*-TsOH, and 15 mL of toluene was added 0.7 g (1.8 mmol) of sulfoxide **22** in 5 mL of toluene, and the mixture was heated at reflux for 30 min and then left to stir overnight at room temperature. The solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography to give 0.34 g (56%) of **23** as a yellow oil: IR (neat) 1689, 1515, 1423, 1255, and 1112 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.59 (s, 3H), 1.24 (t, 3H, J = 7.4 Hz), 1.35 (s, 3H), 2.57 (m, 1H), 2.71−2.83 (m, 4H), 3.03 (s, 1H), 3.79 (s, 3H), 3.82 (s,

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3H), 4.30 (brs, 1H), 4.64 (brs, 1H), and 6.48−6.56 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.5, 22.6, 23.1, 25.5, 29.3, 37.1, 44.6, 55.8, 55.9, 56.2, 64.1, 108.5, 112.1, 124.7, 127.7, 147.8, 147.9, 172.3. Anal. Calcd for $C_{18}H_{27}NO_4S$: C, 64.45; H, 7.52; N, 4.18. Found: C, 64.27; H, 7.44; N, 4.01.

***N*-(2-Cyclohex-1-enylethyl)-2-ethylsulfinyl-*N*-(2-methylpropenyl)acetamide (24).** To 5 mL (44 mmol) of 2-cyclohex-1-enylethylamine at 0 °C was added 4 mL of 2-methylpropionaldehyde. The mixture was allowed to stir for 30 min at 0 °C and then warmed to 25 °C and stirred for an additional 30 min. The solution was dried over Na_2SO_4, the solvent was removed under reduced pressure, and the residue was distilled to give 4.9 g (61%) of (2-cyclohex-1-enylethyl)isobutylidenamine as a pale yellow oil, which was used in the next step without further purification: IR (neat) 1671, 1459, 1438, and 1365 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.99 (d, 6H, J = 6.8 Hz), 1.52 (m, 4H), 1.91 (m, 4H), 2.13 (t, 2H, J = 7.2 Hz), 2.35 (m, 1H), 3.35 (t, 2H, J = 7.2 Hz), 5.34 (brs, 1H), and 7.37 (d, 1H, J = 5.2 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.6, 22.7, 23.1, 25.4, 28.7, 34.2, 39.4, 59.8, 122.9, 135.4, and 169.9.

A 1.2 g (8.3 mmol) sample of ethylsulfenyl-acetyl chloride in 50 mL of CH_2Cl_2 at 0 °C was added to 1.0 g (5.5 mmol) of the above imine followed by the addition of 0.5 mL (6.2 mmol) of pyridine. The reaction mixture was stirred at 0 °C for 30 min, warmed to room temperature, and stirred overnight. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel to give 1.3 g (81%) of *N*-(2-cyclohex-1-enylethyl)-2-ethylsulfenyl-*N*-(2-methylpropenyl)acetamide as a yellow oil, which was used in the next step without purification: IR (neat) 1650 and 1449 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.14 (t, 3H, J = 7.2 Hz), 1.39−1.49 (m, 4H), 1.51 (d, 3H, J = 1.2 Hz), 1.63 (d, 3H, J = 1.2 Hz), 1.83 (m, 4H), 2.01 (t, 2H, J = 7.2 Hz), 2.53 (q, 2H, J = 7.2 Hz), 3.06 (s, 2H), 3.39 (t, 2H, J = 7.2 Hz), 5.31 (brs, 1H), and 5.83 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.5, 17.9, 22.0, 22.5, 23.0, 25.4, 26.3, 28.2, 33.4, 35.8, 46.4, 123.0, 124.1, 135.1, 135.7, and 169.7.

To a 0.9 g (3.4 mmol) sample of the above sulfide in 25 mL of MeOH was added 1.2 g (5.6 mmol) of $NaIO_4$. Sufficient water (10 mL) was added to the mixture until it became cloudy and then the mixture was allowed to stir at 25 °C for 3 h. The mixture was further diluted with 25 mL of water and extracted with CH_2Cl_2. The organic extracts were combined, washed with a saturated NaCl solution, and dried over $MgSO_4$. The solution was filtered and the solvent was removed under reduced pressure. The residue was chromatographed on silica gel to give 0.7 g (72%) of **24** as a yellow oil: IR (neat) 1643, 1416, 1050, and 1019 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.34 (t, 3H, J = 7.6 Hz), 1.41−1.57 (m, 4H), 1.60 (d, 3H, J = 1.2 Hz), 1.73 (d, 3H, J = 1.2 Hz), 1.89−1.93 (m, 4H), 2.08 (t, 2H, J = 7.6 Hz), 2.72−2.78 (m, 1H), 3.01−3.06 (m, 1H), 3.46 (t, 2H, J = 7.6 Hz), 3.58 (d, 1H, J = 14 Hz), 3.77 (d, 1H, J = 14 Hz), 5.37 (brs, 1H), and 5.84 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 6.6, 18.0, 22.2, 22.5, 23.0, 25.5, 28.2, 35.8, 46.3, 46.5, 55.9, 123.2, 123.4, 134.9, 137.9, and 164.5. Anal. Calcd for $C_{16}H_{27}NO_2S$: C, 64.61; H, 9.16; N, 4.71. Found: C, 64.55; H, 9.03; N, 4.66.

2-Ethylsulfenyl-1,1-dimethyl-1,5,7,8,9,10,10*a*,*10b*-octahydro-2*H*-pyrrolo[2,1-*a*]isoquinolin-3-one (25). To a mixture containing 0.7 mL (6.8 mmol) of acetic anhydride and 10 mg of *p*-TsOH in 10 mL of toluene at 120 °C was added 0.2 g (0.6 mmol) of sulfoxide **24** in 3 mL of toluene. The resulting mixture was stirred for 30 min at 120 °C and then the solution was concentrated under reduced pressure. The residue was subjected to silica gel chromatography to give 0.09 g (51%) of **25** as a pale yellow oil: IR (neat) 1702 and 1418 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.98 (s, 3H), 1.25 (t, 3H, J = 7.2 Hz), 1.28 (s, 3H), 1.31 (m, 1H), 1.39 (m, 1H), 1.69 (m, 1H), 1.90−2.18 (m, 6H), 2.56 (dd, 1H, J = 12.8 and 4.0 Hz), 2.76 (t, 2H, J = 9.4 Hz), 2.81 (m, 1H), 3.01 (brs, 1H), 4.09 (brs, 1H), and 5.62 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.9, 18.2, 21.2, 25.1, 27.1, 27.3, 27.5, 33.3, 37.7, 41.3, 41.5, 58.8, 70.3, 124.0, 135.4, and 172.8. Anal. Calcd for $C_{16}H_{25}NOS$: C, 68.78; H, 9.03; N, 5.02. Found: C, 68.59; H, 8.87; N, 4.95.

1-Benzyl-3-ethylsulfenyl-7*a*-methyl-2,6-dioxooctahydroindole-3*a*-carboxylic Acid Methyl Ester (35). To a cooled suspension containing 0.02 g (0.4 mmol) of **34** in 7 mL of a 1:1 mixture of THF/MeOH was added 0.8 g (6 mmol) of Na_2HPO_4 followed by 1.0 g of 5% Na(Hg). The mixture was stirred at 0 °C for 3 h and then poured into water. The solution was extracted with chloroform and dried over anhydrous $MgSO_4$. Silica gel chromatography provided 0.12 g (83%) of 1-benzyl-3-ethylsulfenyl-6-hydroxy-7*a*-methyl-2-oxooctahydroindole-3*a*-carboxylic acid methyl ester as a white solid: mp 165−166 °C; IR (neat) 1738, 1681, 1410, and 1062 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (s, 3H), 1.28 (t, 3H, J = 7.3 Hz), 1.37 (m, 2H), 1.84 (br s, 1H), 1.98−2.21 (m, 4H), 2.70 (q, 2H, J = 7.5 Hz), 3.49 (s, 1H), 3.55 (s, 3H), 3.62 (m, 1H), 4.10 (d, 1H, J = 15.4 Hz), 4.72 (d, 1H, J = 15.6 Hz), and 7.23 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.2, 21.7, 23.3, 28.5, 30.4, 43.4, 45.9, 50.6, 51.7, 56.9, 63.1, 65.7, 127.2, 127.8, 128.2, 138.3, 171.9 and 172.2. Anal. Calcd. for $C_{20}H_{27}NO_4S$: C, 63.63; H, 7.21; N, 3.71. Found: C, 63.62; H, 7.12; N, 3.69.

To a solution containing 0.04 g (0.1 mmol) of the above alcohol in 6 mL of CH_2Cl_2 was added 0.04 g (0.2 mmol) of pyridinium chlorochromate. The reaction mixture was stirred at room temperature for 5 h and the solvent was removed under reduced pressure. The residue was subjected to silica gel chromatography to give 0.04 g (97%) of **35** as a colorless oil: IR (neat) 1730, 1695, 1403, and 1204 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.11 (s, 3H), 1.31 (t, 3H, J = 7.3 Hz), 2.16 (m, 1H), 2.42 (m, 2H), 2.48 (s, 2H), 2.66 (m, 1H), 2.78 (q, 2H, J = 7.3 Hz), 3.48 (s, 1H), 3.66 (s, 3H), 4.25 (d, 1H, J = 15.4 Hz), 4.60 (d, 1H, J = 15.6 Hz), and 7.25 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.2, 24.0, 28.0, 29.0, 35.9, 43.6, 50.0, 52.0, 52.8, 56.4, 65.1, 127.4, 127.7, 128.4, 137.7, 170.8, 171.7, and 206.5. Anal. Calcd for $C_{20}H_{25}NO_4S$: C, 63.97; H, 6.72; N, 3.73. Found: C, 63.85; H, 6.71; N, 3.69.

2-Benzo[1,3]dioxol-5-ylmethyl-3-[benzyl(bis(ethylsulfenyl)acetyl)amino]but-3-enoic Acid Methyl Ester (37). To a solution containing 13 g (51 mmol) of 2-benzo[1,3]-dioxol-5-ylmethyl-3-oxobutyric acid methyl ester[47] in 100 mL of toluene was added 5.6 mL (51 mmol) of benzylamine. The solution was heated at reflux in a flask equipped with a Dean−Stark trap for 8 h. The solvent was removed under reduced pressure and the crude enamide was taken up in 170 mL of CH_2Cl_2. To this solution was added 4.6 mL (56 mmol) of pyridine followed by 10 g (51 mmol) of bis(ethylsulfenyl)acetyl chloride.[48] The reaction mixture was stirred at room temperature for 2 h and was then washed with a saturated $NaHCO_3$ solution. The organic layer was dried over anhydrous $MgSO_4$. Removal of the solvent under reduced pressure left a crude oil, which was purified by silica gel chromatography. The major fraction contained 16 g (63%) of enamide **37** as a clear oil: IR (neat) 1745, 1645, 1453, and 1204 cm^{-1}; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.16 (m, 6H), 2.68 (m, 4H), 2.95 (m, 1H), 2.98 (m, 1H), 3.56 (m, 4H), 4.74 (m, 2H), 4.80 (s, 1H), 5.16 (s, 1H), 5.45 (s, 1H), 5.95 (s, 2H), 6.62 (d, 1H, J = 8.0 Hz), 6.76 (m, 2H), 7.18 (m, 2H), and 7.28 (m, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 13.8, 13.9, 23.3, 23.5, 36.2, 48.2, 49.1, 51.4, 51.9, 100.6, 107.8, 108.9, 117.8, 121.6, 126.9, 127.6, 128.0, 131.5, 136.9, 143.4, 145.7, 147.1, 167.7, and 171.6. Anal. Calcd for $C_{26}H_{31}NO_5S_2$: C, 62.26; H, 6.23; N, 2.79. Found: C, 66.24; H, 6.08; N, 2.85.

Methyl 3-Ethylthio-15,17-dioxa-2-oxo-1-benzylspiro-[pyrrolidine-5,6′-tricyclo[7.3.0.0^{3,7}]dodecane]*a*-6(7),8(12),-13-triene-10-carboxylate (38). To a 0.6 g (1.1 mmol) sample of enamide 37 in 20 mL of CH_2Cl_2 at −40 °C was added 0.3 g (1.7 mmol) of DMTSF. The mixture was stirred for 1 h at −40 °C before warming to 0 °C for 30 min. After this time, the solution was quenched with a saturated $NaHCO_3$ solution and the aqueous layer was extracted with ether. The combined organic phase was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the crude residue was crystallized to give **38** as a

white solid: mp 90−91 °C; IR (neat) 1730, 1695, 1247, and 941 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.30 (t, 3H, J = 7.6 Hz), 1.79 (dd, 1H, J = 14.4 and 10.0 Hz), 2.77−2.91 (m, 4H), 3.08 (dd, 1H, J = 15.6 and 9.6 Hz), 3.19 (dd, 1H, J = 9.6 and 8.4 Hz), 3.57 (dd, 1H, J = 11.2 and 9.6 Hz), 3.63 (s, 3H), 4.09 (d, 1H, J = 15.2 Hz), 4.74 (d, 1H, J = 15.2 Hz), 5.92 (s, 1H), 5.96 (s, 1H), 6.35 (s, 1H), 6.62 (s, 1H), and 7.16−7.23 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.3, 25.3, 31.5, 38.6, 41.8, 44.3, 51.2, 51.8, 74.7, 101.4, 103.3, 104.9, 127.3, 128.2, 133.0, 135.7, 137.6, 147.7, 148.6, 172.4, and 174.5. Anal. Calcd for $C_{24}H_{25}NO_5S$: C, 65.58; H, 5.74; N, 3.19. Found: C, 65.52; H, 5.69; N, 3.08.

2-Benzo[1,3]dioxol-5-ylmethyl-3-[benzyl(bis(ethylsulfenyl)acetyl)amino]but-2-enoic Acid Methyl Ester (39). To a solution containing 0.65 g (1.3 mmol) of **37** was added 0.4 mL (2.6 mmol) of DBU. The reaction mixture was stirred at room temperature for 2 h. The solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography to separate the 1:1 mixture of stereoisomers. Compound **39** showed the following properties: IR (neat) 1738, 1709, 1659, 1240, and 1033 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.08 (t, 3H, J = 7.6 Hz), 1.22 (t, 3H, J = 7.2 Hz), 2.09 (s, 3H), 2.53−2.85 (m, 4H), 3.48 (s, 3H), 3.58 (s, 2H), 4.58 (d, 1H, J = 14.4 Hz), 4.69 (s, 1H), 4.74 (d, 1H, J = 14.4 Hz), 5.92 (s, 2H), 6.53 (d, 1H, J = 7.6 Hz), 6.58 (s, 1H), 6.69 (d, 1H, J = 7.6 Hz), and 7.28 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 14.1, 20.0, 22.8, 24.0, 35.3, 50.3, 51.3, 52.2, 100.9, 108.3, 108.6, 121.1, 127.6, 128.3, 129.2, 131.4, 132.1, 136.7, 141.8, 146.2, 147.8, 166.5, and 167.61. Anal. Calcd for $C_{26}H_{31}NO_5S_2$: C, 62.26; H, 6.23; N, 2.79. Found: C, 62.07; H, 6.16; N, 2.70.

The isomeric *E*-alkene **40** exhibited the following spectral properties: IR (neat) 1723, 1652, 1481, 1247, and 1040 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, 3H, J = 7.6 Hz), 1.29 (t, 3H, J = 7.2 Hz), 2.06 (s, 3H), 2.71−2.93 (m, 4H), 3.43 (s, 2H), 3.60 (s, 3H), 4.52 (d, 1H, J = 14.4 Hz), 4.66 (s, 1H), 4.78 (d, 1H, J = 14.4 Hz), 5.90 (s, 1H), 6.28 (s, 1H), 6.31 (d, 1H, J = 8.0 Hz), 6.62 (d, 1H, J = 8.0 Hz), 7.28 (m, 4H), and 7.34 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 14.1 20.6, 23.2, 24.1, 35.1, 49.9, 50.0, 51.9, 100.8, 108.0, 108.9, 121.3, 127.8, 128.6, 129.0, 130.9, 133.1, 136.7, 141.5, 146.0, 147.5, 167.7, and 168.2; HRMS calcd for $C_{26}H_{31}NO_5S_2$ 501.1644, found 501.1656.

3-Benzyl-1-ethylsulfenyl-3*a*-methyl-2-oxo-2,3,3*a*,3*b*,8*a*,9-hexahydro-1*H*-5,7-dioxa-3-aza-cyclopenta[*a*]-*s*-indacene-9*a*-carboxylic Acid Methyl Ester (41). To a 0.12 g (0.2 mmol) sample of enamide **40** in 5 mL of CH_2Cl_2 was added 0.06 g (0.28 mmol) of DMTSF. The reaction mixture was stirred at −40 °C for 10 min before warming to room temperature and stirring for an additional 1.5 h. After this time, the solution was quenched with a saturated solution of $NaHCO_3$ and the aqueous layer was extracted with CH_2Cl_2. The combined organic phase was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the crude residue was chromatographed to give 0.07 g (68%) of **41** as a colorless oil: IR (neat) 1723, 1688, 1304, and 1026 cm^{-1}; ^{1}H NMR (300 Mz, $CDCl_3$) δ 1.23 (s, 3H), 1.37 (t, 3H, J = 7.3 Hz), 2.86−2.95 (m, 2H), 3.14 (d, 1H, J = 16.4 Hz), 3.34 (d, 1H, J = 16.4 Hz), 3.67 (s, 3H), 4.09 (d, 1H, J = 15.6 Hz), 4.49 (s, 1H), 4.63 (d, 1H, J = 15.4 Hz), 5.92 (d, 1H, J = 1.5 Hz), 5.97 (d, 1H, J = 1.3 Hz), 6.64 (s, 1H), 6.69 (s, 1H), and 7.11−7.40 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.8, 19.9, 27.4, 37.4, 43.7, 50.4, 52.7, 64.6, 74.0, 101.4, 104.6, 105.2, 127.1, 127.4, 128.4, 133.6, 136.7, 138.0, 146.7, 148.7, 170.8, and 172.3. Anal. Calcd for $C_{24}H_{25}NO_5S$: C, 65.58; H, 5.74; N, 3.19. Found: C, 65.44; H, 75.78; N, 3.21.

Indacene **27** was also prepared from the DMTSF-induced reaction of the analogous dithiane **39**. To a cooled (−40 °C) solution containing 0.04 g (0.08 mmol) of dithiane **39** in 2 mL of CH_2Cl_2 was added 0.02 g (0.11 mmol) of DMTSF. The solution was allowed to warm to 0 °C for 2 h before quenching with a saturated solution of $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2, and the combined organic phases were washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography to afford 0.03 g (72%) of indacene **27**, which was identical in every detail with a sample obtained from the acid-catalyzed reaction of sulfoxide **26**.

4-(1-Benzenesulfonyl-1*H*-indol-2-yl)butyraldehyde. To a solution of 1.8 g (9.4 mmol) of $AgBF_4$ in 25 mL of DMSO was added 2.8 g (7.3 mmol) of 1-benzenesulfonyl-2-(4-bromobutyl)-1*H*-indole.[50] The reaction mixture was stirred at room temperature for 18 h and then 1.2 mL (8.7 mmol) of Et_3N was added. After stirring for 20 min, the mixture was diluted with H_2O and extracted with diethyl ether. The combined organic layers were dried over anhydrous $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel chromatography to give 1.6 g (69%) of the titled compound as a white solid: mp 126−128 °C; IR (KBr) 1724 and 1448 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.09 (q, 2H, J = 7.4 Hz), 2.53−2.57 (m, 2H), 3.04 (t, 2H, J = 7.4 Hz), 6.41 (s, 1H), 7.36−7.52 (m, 6H), 7.69−7.72 (m, 2H), 8.15 (d, 1H, J = 8.2 Hz), and 9.78 (t, 1H, J = 1.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.7, 28.5, 43.3, 109.9, 115.1, 120.5, 123.9, 124.4, 129.9, 133.9, 137.5, 139.0, 141.1, and 202.1. Anal. Calcd for $C_{18}H_{17}O_3NS$: C, 66.03; H, 5.23; N, 4.28. Found: C, 66.15; H, 5.06; N, 4.18.

***N*-[4-(1-Benzenesulfonyl-1*H*-indol-2-yl)but-1-enyl]-*N*-benzyl-2-ethylsulfenylacetamide**. To a solution of 0.7 g (2.3 mmol) of the above aldehyde in 10 mL of CH_2Cl_2 was added 0.3 mL (2.4 mmol) of benzylamine and 1.6 g of anhydrous $MgSO_4$. The reaction mixture was stirred at room temperature for 2 h and then filtered. To the filtrate was added 0.5 mL (5.7 mmol) of pyridine followed by 4.6 mmol of ethylsulfenyl acetyl chloride. The reaction mixture was stirred at room temperature for 3 h and then poured into a saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layer was washed with a saturated NH_4Cl solution and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel chromatography to give 0.9 g (80%) of the titled compound as a 2:1 mixture of inseparable *Z*/*E* isomers: IR (neat) 1641, 1448, 1366, and 686 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.24−1.28 (m, 2H), 2.43−2.50 (m, 2H), 2.59−2.68 (m, 2H), 2.97−3.01 (m, 2H), 3.26 (s, 2H, minor isomer), 3.43 (s, 2H, major isomer), 4.83 (s, 2H, major isomer), 4.85 (s, 2H, minor isomer), 4.97−5.05 (m, 1H, minor isomer), 5.05−5.11 (m, 1H, major isomer), 6.17 (s, 1H, major isomer), 6.21 (s, 1H, minor isomer), 6.62 (d, 1H, J = 13.7 Hz, major isomer), 7.10−7.52 (m, 11H), 7.65−7.70 (m, 2H), and 8.12−8.16 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.4, 14.5, 26.6, 29.8, 29.9, 30.1, 33.4, 33.8, 47.1, 49.3, 109.7, 110.2, 111.9, 113.7, 115.0, 120.4, 123.08, 123.7, 124.2, 124.3, 125.8, 126.3, 127.0, 127.1, 127.4, 127.6, 128.7, 129.1, 129.4, 129.9, 133.8, 136.3, 137.3, 137.4, 139.1, 139.2, 140.1, 140.8, 168.2, and 168.3; HRMS calcd for $C_{29}H_{30}N_2O_3S_2$ 518.1698, found 518.1698.

***N*-[4-(1-Benzenesulfonyl-1*H*-indol-2-yl)but-1-enyl]-*N*-benzyl-2-ethanesulfinylacetamide (47).** To a solution of 0.4 g (0.7 mmol) of the above enamide in 10 mL of a 4:1 mixture of dioxane and H_2O was added 0.6 g (2.7 mmol) of sodium periodate. The reaction mixture was stirred at room temperature for 12 h, diluted with H_2O, and extracted with EtOAc. The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash silica gel chromatography to give 0.25 g (68%) of **47** as a 2:1 mixture of inseparable *Z*/*E* isomers: IR (neat) 1645 and 1449 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.21−1.25 (m, 3H), 2.44−2.56 (m, 2H), 2.72−3.04 (m, 4H), 3.71−3.96 (m, 2H), 4.81 (s, 2H, major isomer), 4.85 (s, 2H, minor isomer), 5.07−5.15 (m, 1H, minor isomer), 5.20−5.27 (m, 1H, major isomer), 6.17 (s, 1H,

(50) Padwa, A.; Hertzog, D. L.; Nadler, W. R. *J. Org. Chem.* **1994**, *59*, 7072.

major isomer), 6.21 (s, 1H, minor isomer), 6.57 (d, 1H, J = 13.8 Hz, major isomer), 7.08−7.52 (m, 11H), 7.66−7.72 (m, 2H), and 8.14−8.17 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 6.6, 29.4, 29.6, 29.8, 29.9, 46.2, 46.3, 47.9, 49.4, 55.1, 55.2, 110.1, 109.6, 113.2, 114.8, 114.9, 117.5, 120.3, 120.4, 123.7, 123.8, 124.1, 124.2, 125.6, 126.2, 126.6, 127.1, 127.3, 127.7, 127.8, 128.6, 129.1, 129.3, 129.7, 133.7, 133.8, 135.4, 136.3, 137.2, 138.7, 138.9, 140.8, 140.5, 163.7, and 163.8; HRMS calcd for $C_{29}H_{30}N_2O_4S_2$ 534.1647, found 534.1653.

6-Benzenesulfonyl-1-benzyl-3-ethylsulfenyl-3,3*a*,4,5,6,-10*c*-hexahydro-1H-pyrrolo[3,2-*c*]carbazol-2-one (48). To a solution of 0.08 g (0.4 mmol) of trifluoroacetic anhydride in 10 mL of CH_2Cl_2 was added 0.1 g (0.2 mmol) of **47**. The reaction mixture was stirred at room temperature for 15 min and then poured into a saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with EtOAc, and the combined organic layers were dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash silica gel chromatography to give 0.06 g (60%) of **48** as a clear oil: IR (neat) 1688, 1451, 1373, and 1174 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.35−1.39 (t, 3H, J = 7.4 Hz), 1.81−1.98 (m, 1H), 1.99−2.08 (m, 1H), 2.26−2.35 (m, 1H), 2.79−3.04 (m, 3H), 3.30 (dd, 1H, J = 18.6 and 3.6 Hz), 3.36 (s, 1H), 4.02 (d, 1H, J = 3.6 Hz), 4.80 (1H, J = 3.6 Hz), and 5.10 (d, 1H, J = 4.7 Hz), ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.8, 23.6, 25.1, 25.5, 39.4, 43.8, 48.2, 52.0, 113.8, 114.4, 118.8, 123.7, 124.9, 126.5, 126.6, 127.2, 128.7, 129.6, 129.7, 134.2, 136.3, 137.2, 138.8, 139.1, and 173.1; HRMS calcd for $C_{29}H_{28}N_2O_3S_2$ 516.1541, found 516.1535.

Acknowledgment. This research was supported by the National Science Foundation (grant CHE-0132651). The authors wish to thank Dr. M. Diana Danca for helpful discussions.

Supporting Information Available: Spectroscopic and experimental procedures for compounds **9**, **10**, **12**, **13**, **26**−**34**, and **42**−**46**. ^{1}H and ^{13}C NMR spectra for new compounds lacking elemental analyses together with ORTEP drawings for structures **10**, **34**, and **38**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO020083X