Using the Pummerer Cyclization−Deprotonation−Cycloaddition Cascade of Imidosulfoxides for Alkaloid Synthesis

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The Pummerer reaction of imidosulfoxides bearing tethered alkenyl groups has been employed for the synthesis of several alkaloids. The required imidosulfoxides necessary for the cascade sequence were easily obtained by heating the appropriate amide with (ethylsulfenyl)acetyl chloride followed by sodium periodate oxidation. The initially formed thionium ion, obtained by treating the imidosulfoxide with acetic anhydride and *p*-toluenesulfonic acid, reacts with the neighboring imido group, and the resulting oxonium ion undergoes subsequent deprotonation to produce an isomünchnone dipole. This mesoionic betaine intermediate undergoes ready intramolecular dipolar cycloaddition across the neighboring π-bond. Exposure of the resulting cycloadducts to additional acetic anhydride leads to ring opening and formation of a 5-acetoxy-substituted 2(1*H*)-pyridone. This six-ring heterocyclic system constitutes a valuable building block for the synthesis of a variety of pyridine, quinolizidine, and clavine alkaloids. The cyclization−deprotonation−cycloaddition cascade has been successfully applied to the synthesis of the naturally occurring alkaloids onychnine, dielsiquinone, (±)-lupinine, (±)-anagyrine, (±)-pumiliotoxin C, and (±)-costaclavine.

Six-membered nitrogen-containing heterocycles are abundant in nature and exhibit diverse and important biological properties.[1] Alkaloids that contain the piperidine ring continue to be the targets of extensive synthetic interest, partly because there are many biologically active natural products of this type and also because this cyclic framework is found in many rigid structures that show substantial selectivity in their interaction with enzymes or receptors.[2,3] Accordingly, novel strategies for the stereoselective synthesis of piperidine ring systems continue to receive considerable attention in the field of synthetic organic chemistry.[4−7] Among the reactions available for the preparation of six-ring heterocycles, nitrogen versions of the Diels−Alder reaction are particularly attractive.[8] Well-known and extensively studied for many decades, these 4+2-cycloadditions are frequently employed for the construction of six-membered aza ring systems.[9] The comprehensive review by Boger and Weinreb contains numerous examples demonstrating the broad application of 4+2-cycloadditions with heteroatom containing dienes and dienophiles.[8]

A strategy that we have found to be of some importance in the design of new processes for the synthesis of piperidines is to make use of 1,3-dipolar cycloaddition chemistry.[10] The prominent role that dipolar-cycloaddition reactions play in the elaboration of a variety of five-ring heterocyclic systems has become increasingly apparent in recent years.[11−13] The ease of cycloaddition, the rapid accumulation of polyfunctionality in a relatively small molecular framework, the high stereochemical control of the cycloaddition, and the fair predictability of its regiochemistry have contributed to the popularity of the reaction.[10] In the realm of synthesis, in which a premium is put on the rapid construction of polyfunctionality, the 1,3-dipolar cycloaddition reaction has now emerged as a prominent synthetic method. When the reacting components are themselves cyclic or have ring substituents, complex multicyclic arrays, such as those

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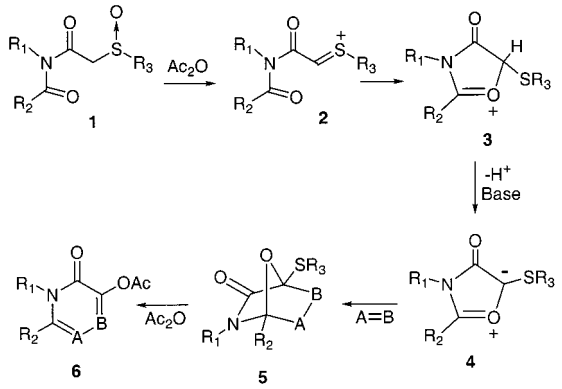
Scheme 1



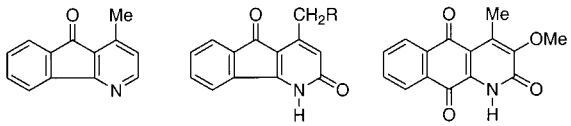
contained in drugs and natural products, can be constructed in a single step. Often the syntheses of molecules of this complexity are more difficult and lengthy by other routes.

Several years ago our laboratory initiated a study dealing with the intramolecular cycloaddition chemistry of mesoionic betaines as a method for the construction of a variety of piperidine ring systems.[14] Our interest in the chemistry of mesoionic dipoles stems from earlier investigations dealing with the rhodium(II)-catalyzed reactions of α-diazo carbonyl compounds in the presence of various heteroatoms.[15] The isomünchnone class of mesoionics is easily available from the Rh(II)-catalyzed reaction of α-diazo imides.[16,17] This mesoionic dipole[18] was found to undergo cycloadditions with both electron-rich and electron-deficient dipolarophiles and represents an efficient way to synthesize complex polyheterocyclic ring systems. More recently, we described a new approach toward a variety of 2(1*H*)-pyridones employing isomünchnone dipoles obtained from the *Pummerer-induced cyclization−cycloaddition cascade* of imidosulfoxides as outlined in Scheme 1.[19]

α-Acyl thionium ions generated from α-acyl sulfoxides under Pummerer conditions are powerful electrophiles and react efficiently with a variety of nucleophilic species.[20−23] When imidosulfoxides of type **1** are used, the initially formed thionium ion **2** derived from **1** rapidly reacts with the neighboring imido group and the resulting oxonium ion **3** undergoes subsequent deprotonation to produce isomünchnone **4**. Since **4** contains a carbonyl ylide dipole within its framework, it readily undergoes 1,3-dipolar cycloaddition with various dipolarophiles. Exposure of the resulting cycloadducts **5** to acetic anhydride in the presence of a trace of *p*-toluenesulfonic acid results in ring opening to give 5-acetoxy-substituted 2(1*H*)-pyridones **6**. This six-ring heterocyclic system represents a valuable building block in natural product synthesis, as it can act as a common intermediate for the preparation of a wide variety of piperidine, pyridine, quinolizidine, and indolizidine alkaloids.[24] To highlight the method, the above synthetic strategy was applied to the synthesis of several different classes of alkaloids. The present paper documents the results of these studies.

Results and Discussion

Azafluorenone and Azaanthraquinone Alkaloids Isolated from the Trunkwood of *Guatteria Dielsiana*. The 4-azafluorenone alkaloids comprise a small but biologically intriguing group of alkaloids. Onychnine (**7**),



7; Onychine

8; R = H; dielsine
9; R = OH; dielsinol

10; dielsiquinone

the simplest member of this family, was first isolated from the Brazilian *Annonaceae* species (*onychopetalum amazonicum*, *Guatteria dielsiana*) in 1976 and was shown to have anticandidal activity.[25] Together with dielsine (**8**), dielsinol (**9**), and the related azaanthraquinone dielsiquinone (**10**),[26] this class of alkaloids is speculated to be derived from aporphine precursors.[27] A considerable number of onychine derivatives bearing hydroxy and/or methoxy groups in the benzene ring have also been isolated from *Annonaceae*.[28] Subsequent to an initial misassignment,[25] the structure of onychine and related 4-azafluorenones have been confirmed by independent syntheses.[29] Several approaches toward this class of alkaloids were developed including an oxidative thermal rearrangement of 2-indanone oxime *O*-allyl ethers[30] and cyclization of 2-aryl-3-methylpyridines and 2-aryl-3-nicotinic acids[31,32] as well as a Pd(0)-catalyzed

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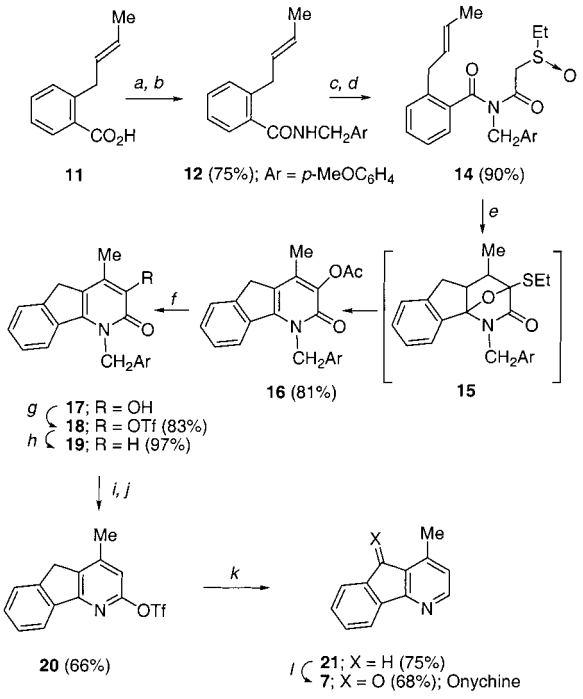
Scheme 2

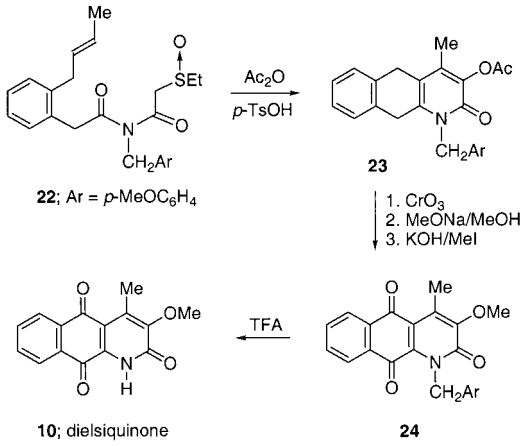


Reagents: (a) ClCOCOCl; (b) *p*-methoxybenzylamine; (c) $EtSCH_2COCl$ (**13**); (d) $NaIO_4$;(e) Ac_2O, *p*-TsOH (trace); (f) K_2CO_3, MeOH; (g) $(TfO)_2NPh$, NEt_3; (h) $Pd(PPh_3)Cl_2$, HCO_2H, NEt_3; (i) TFA, Δ; (j) Tf_2O, pyridine; (k) $Pd(PPh_3)_2Cl_2$, HCO_2H, NEt_3; (l) $KMnO_4$, acetone

cross coupling of arylboronic acids with 2-halopyridines.[33] Although a number of strategies are available for the synthesis of substituted azafluorenone derivatives, these methods often bear the disadvantage of giving rise to mixtures of isomers.[32,34,35]

Given our success in forming a variety of substituted 5,6-fused acetoxy pyridones from the Pummerer-induced reaction of imidosulfoxides,[19] it seemed to us that this approach could well prove to be adaptable to the synthesis of both onychnine (**7**) and dielsiquinone (**10**). The starting material for the synthesis of onychnine was the known 2-(2-butenyl)benzoic acid (**11**).[36] Conversion of **11** to the corresponding *p*-methoxybenzyl amide **12** followed by reaction with (ethylsulfenyl)acetyl chloride (**13**)[37] and subsequent oxidation with sodium periodate gave imidosulfoxide **14** in 68% overall yield. The Pummerer-induced dipolar cycloaddition of **14** occurred smoothly when a mixture of toluene and acetic anhydride which also contained a catalytic quantity of *p*-toluenesulfonic acid (*p*-TsOH) was used.[38] These conditions, whereby the sulfoxide is slowly added to a refluxing mixture of toluene, acetic anhydride (10 equiv), and *p*-TsOH (catalyst), gave pyridone **16** in 81% isolated yield. The formation of **16** is consistent with the sequence of events proposed in Scheme 2. The critical steps involve (a) isomünchnone formation, (b) intramolecular dipolar cycloaddition, and (c) oxabicyclic ring cleavage (i.e., **15** → **16**). Base-induced hydrolysis of the acetoxy group in **16** gave the 3-hydroxy-substituted pyridone **17** which was immediately converted into the corresponding triflate **18** in 83% overall yield by reaction with *N*-phenyltrifluoromethanesulfonimide.[39] A Pd(0)−formate reduction[40] gave pyridone **19** in 97% yield. The *p*-methoxybenzyl group was easily removed by heating **19** in trifluoroacetic acid at 100 °C for 1 h.[41] The resulting NH-pyridone was immediately treated with triflic anhydride in pyridine at 0 °C to give **20** as a crystalline solid in 66% yield. Removal of the triflate functionality was accomplished by a Pd(0)−formate reduction to furnish 4-methyl-5*H*-indeno[1,2-*b*]pyridine (**21**) in 75% yield. Subsequent oxidation of **21** with potassium permanganate (68%) afforded onychnine (**7**) in 11 steps in 15.3% overall yield starting from 2-(2-butenyl)benzoic acid.

Scheme 3



The *Annonaceae* species is a large family comprising over 130 genera and is recognized as being the center of benzyl isoquinoline alkaloid production in plants.[42] The co-ocurrence of onychnine (**7**) and dielsiquinone (**10**) in the same trunkwood of *Gutteria dielsiana* suggests their biogenetic relationship. Loss of CO would convert an azaanthraquinone into an azafluorenone derivative. As an extension of the above studies, we initiated a synthesis of dielsiquinone (**10**) that employs an intramolecular isomünchnone cycloaddition as the key synthetic strategy. This approach is based on the earlier methodology used to prepare oncychnine (**7**). Thus, the pyridone ring system was to be constructed by treating imidosulfoxide **22** with Ac_2O and trapping the resulting dipole with the tethered π-bond (Scheme 3). On the basis of our earlier model studies,[19] we expected that the initially formed cycloadduct would spontaneously rearrange to give an acetoxy-substituted pyridone (i.e., **23**). Indeed, treatment of the 2-(butenyl)phenylacetyl imidosulfoxide **22** under the standard Pummerer conditions afforded pyridone **23** in 68% yield. Oxidation of the benzylic positions with CrO_3 followed by a base-induced hydrolysis/methylation sequence afforded anthraquinone **24** in 54% overall yield. The *p*-methoxybenzyl group was readily removed by

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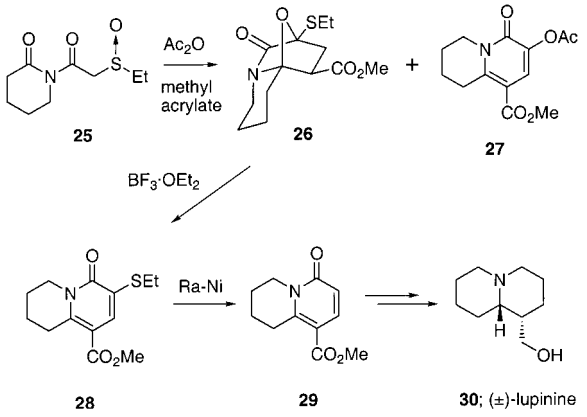
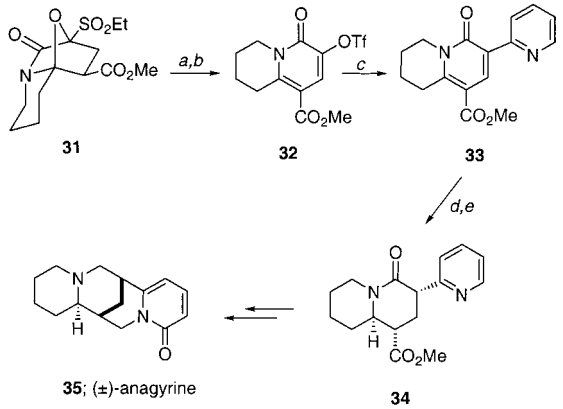
Scheme 4



Scheme 5



Reagents: (a) BF_3•OEt_2; (b) $(TfO)_2NPh$, NEt_3; (c) 2-tri-*n*-butyltinpyridine, $Pd_2(dba)_3$, TFP (d) H_2, PtO_2 (e) NaOMe, MeOH

heating **24** in trifluoroacetic acid at 100 °C for 45 min which resulted in the formation of dielsiquinone (**10**) in 93% yield. The above route constitutes the first total synthesis of this alkaloid and provides support for the original structural assignment based on comparison of the physical data with those reported in the literature.[26]

Synthesis of the Quinolizidine Alkaloids (±)-Lupinine and (±)-Anagyrine. The quinolizidine alkaloids represent a relatively large class of natural products[43] whose importance stems from the potent and useful biological activity of certain of its members.[44] The common structural feature of these compounds is a six-membered nitrogen heterocycle incorporated into a bicyclic ring system. Our interest in establishing imidosulfoxides as useful building blocks for quinolizidine alkaloid synthesis prompted us to use this methodology for the preparation of (±)-lupinine (**30**). A short synthesis of this alkaloid was carried out as depicted in Scheme 4. The Pummerer-induced reaction of imidosulfoxide **25** with methyl acrylate gave rise mainly to cycloadduct **26** (61%) together with lesser quantities of pyridone **27** (10%). The directionality of ring opening of cycloadduct **26** was found to be markedly dependent on the nature of the electrophilic agent used to induce oxabicyclic cleavage. Acetoxy-substituted pyridone **27** was the exclusive product formed when **26** was heated in the presence of acetic anhydride. Treatment of **26** with BF_3•OEt_2, on the other hand, furnished the thioethyl substituted pyridone **28** (62%), which upon Raney-nickel reduction provided the desulfurated pyridone **29** (85%). The preparation of **29** constitutes a formal synthesis of (±)-lupinine (**30**), as Boekelheide had previously reported the conversion of **29** into **30**.[45] We suspect that BF_3•OEt_2 coordinates with both the amido carbonyl and oxa bridge atoms thereby lessening the availability of the amido nitrogen lone pair for ring cleavage. Consequently, the sulfur atom lone pair of electrons controls the regioselectivity of ring cleavage when BF_3•OEt_2, is used as the electrophile. This results in the formation of the thioethyl-substituted pyridone **28**.

As shown in Scheme 5, cycloadduct **26** may also be used for a short synthesis of (±)-anagyrine (**35**), a member of the lupinine family of quinolizidine alkaloids.[46] Oxidation of **26** with $NaIO_4/RuCl_3$ furnished sulfone **31** (91%), which, when treated with BF_3•OEt_2 followed by reaction with *N*-phenyltrifluoromethanesulfonimide,[40] gave triflate **32** in 80% overall yield. Stille cross-coupling[47] of **32** with (tri-*n*-butylstannyl)pyridine provided **33** in 70% yield. Catalytic hydrogenation of **33** over PtO_2 followed by a base-induced equilibration delivered **34** in 85% isolated yield. The present sequence constitutes a formal synthesis of (±)-anagyrine, based on the successful conversion of lactam **34** into **35** by Goldberg and Lipkin.[48]

Application of the Method toward the Synthesis of (±)-Pumiliotoxin C. Extracts from the skin of certain poison frogs and toads have yielded many pharmacologically active alkaloids,[49] including a variety of quinolizidines such as pumiliotoxin C (**36**).[50] Several imaginative syntheses of this *cis*-decahydroquinoline alkaloid have already been reported in the literature.[51] Our approach to the skeleton of pumiliotoxin C is shown in antithetic format in Scheme 6 and is centered on the construction of the key oxabicyclic intermediate **39**. We reasoned that isomünchnone **38**, formed by a *Pummerer-induced cyclization−deprotonation* sequence from imidosulfoxide **37**, should undergo intramolecular dipolar cycloaddition. The resultant cycloadduct **39** is expected to undergo ready ring-opening. Our synthetic plan called for a controlled reduction of the pyridone derived from **39** to generate the *cis*-decahydroquinoline system of **36**. Indeed, a short

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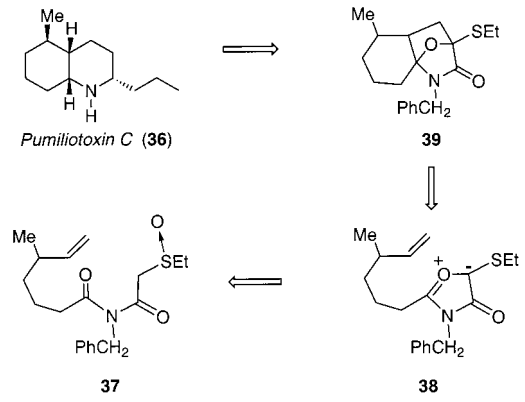
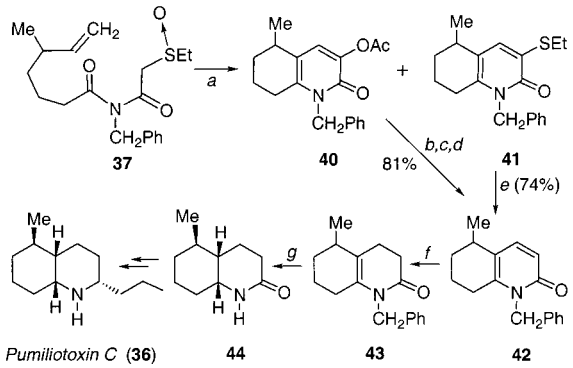
Scheme 6



Scheme 7

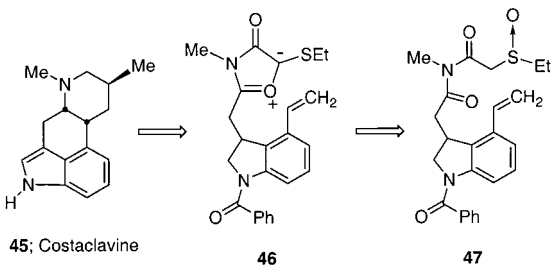


Reagents: (a) Ac_2O, *p*-TsOH (trace), Δ (b) K_2CO_3, MeOH; (c) $(TfO)_2NPh$, NEt_3; (d) $Pd(OAc)_2$, Ph_3P, HCO_2H, Et_3N; (e) Ra-Ni, EtOH (65 °C); (f) $LiB[CH(CH_3)C_2H_5]_3H$; (g) H_2, PtO_2

synthesis of pumiliotoxin C was carried out along these lines and is depicted in Scheme 7. The Pummerer-induced reaction of imidosulfoxide **37** gave mainly 5-acetoxypyridone **40** together with lesser quantities of **41** (13%). Both compounds were independently converted to pyridone **42** *via* the procedure outlined in Scheme 7. Selective reduction of **42** with L-Selectride[52] afforded the ene−lactam **43** in 77% yield. Catalytic hydrogenation of **43** over PtO_2 furnished **44** (86%) with a high degree of diastereoselectivity.[53] The preparation of **44** constitutes a formal synthesis of (±)-pumiliotoxin C, as **44** had previously been converted into the natural product.[54]

Application of the Method to the Ergot Alkaloid (±)-Costaclavine. The successful synthesis of pumiliotoxin C by the *Pummerer cyclization−deprotonation* route prompted us to use a similar methodology for the preparation of (±)-costaclavine (**45**). The clavine ergot alkaloids have received increasing attention in recent years,[55] since many members of this family exhibit diverse pharmacodynamic properties and present a formidable challenge for synthetic chemists.[56] Costaclavine was first isolated from the saprophytic culture of the

Scheme 8



agropyrum-type ergot fungus[57] and was later obtained chemically by the reduction of both agroclavine and elymoclavine.[58] This alkaloid was first synthesized in 1976 by Ninomiya[59] and more recently in the Oppolzer laboratory using an intramolecular nitrone−olefin cycloaddition reaction.[60] The cornerstone of our strategy (Scheme 8) involves the cycloaddition of an isomünchnone dipole (**46**) generated from imidosulfoxide **47**.

Exploiting the ready accessibility of 4-substituted indolines, we chose the known amide **48**[61] as our bifunctional starting material since this permits the facile generation of the desired mesoionic betaine intermediate **46**. Treatment of **48** with (ethylsulfenyl)acetyl chloride (**13**) followed by sodium periodate gave imidosulfoxide **47**. When **47** was subjected to the *Pummerer-deprotonation* conditions, a-mixture of α-acetoxy and α-thioethyl pyridones **49** and **50** was obtained in 64% and 11% yield, respectively. Both of these compounds are derived from the transient cycloadduct obtained by intramolecular cycloaddition of isomünchnone **46** across the tethered vinyl group. Pyridone **49** was then converted to the corresponding triflate **52** in 81% yield by hydrolysis of the acetoxy group with K_2CO_3 (i.e., **49** → **51**) followed by reaction with *N*-(5-chloro-2-pyridyl)triflimide[62] (Scheme 9). Stille cross-coupling of **52** with tetramethyl tin[47] in the presence of $Pd(PPh_3)_2Cl_2$ provided the methyl-substituted pyridone **53** in 73% yield. Catalytic hydrogenation of **53** in acetic acid at 5 atm pressure of hydrogen followed by removal of the protective benzoyl group with aqueous HCl afforded **54** as a 4:1 mixture of diastereomers in 85% yield. The major isomer was separated, reduced with LAH, and oxidized with manganese dioxide according to the procedure of Ninomiya[59] to give (±)-costaclavine (**45**). Thus, starting from amido indoline **48**, (±)-costaclavine was obtained in 12 steps with an overall yield of 17% which compares very favorably with the other two syntheses of racemic **45**.[59,60]

In summary, a new route to several 4-azafluorenone, quinolizidine, and clavine ergot alkaloids has been developed. An important finding from this study is that the Pummerer reaction of imidosulfoxides represents a highly efficient method for the synthesis of azapolycyclic ring systems. The subsequent ring cleavage reaction of the

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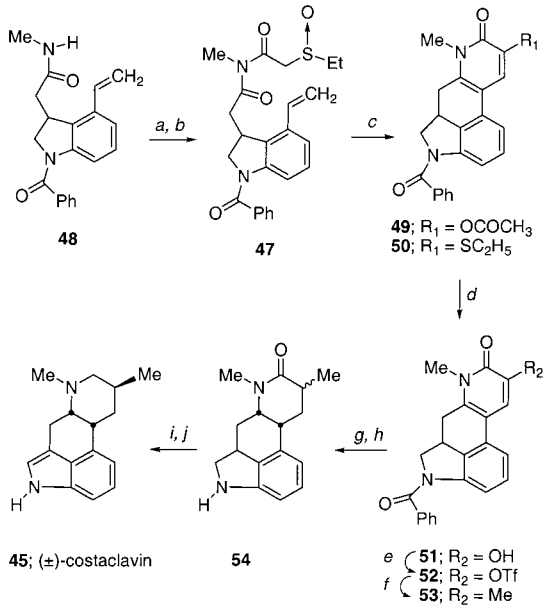
(62) In this case, the yield of triflate **52** was much higher when *N*-(5-chloro-2-pyridyl)triflimide was used as the triflating agent; see: Comins, D. L.; Dehghani, A. *Tetrahedron Lett.* **1992**, *33*, 6299.

Scheme 9



Reagents: (a) **13**, Δ; (b) $NaIO_4$; (c) Ac_2O, *p*-TsOH (trace); (d) K_2CO_3, MeOH; (e) *N*-(5-chloro-2-pyridyl)triflimide, NEt_3; (f) $Pd(PPh_3)_2Cl_2$, Me_4Sn, LiCl; (g) H_2, PtO_2; (h) H_3O^+; (i) LAH; (j)MnO_2

initially formed isomünchnone cycloadducts gives rise to acetoxy-substituted pyridones which can be further utilized for natural product synthesis. The foregoing examples help to define the scope of the *cyclization−deprotonation−cycloaddition cascade* of imidosulfoxides and validate their potential in natural product synthesis. The use of this methodology for the synthesis of other alkaloidal skeletons is currently under 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.

General Procedure for the Preparation of Imidosulfoxides. A solution containing 10 mmol of the appropriate amide and 13 mmol of (ethylsulfenyl)acetyl chloride (**13**)[37] in 100 mL of anhydrous benzene was heated at reflux for 12 h. The reaction mixture was cooled, diluted with ether, and washed with 10% NaOH solution. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography.

To a solution of 5.5 mmol of sodium periodate in a 2:1 mixture of methanol−H_2O was added 5.0 mmol of the appropriate imidosulfide. The resulting mixture was stirred for 3 h, diluted with water, extracted with chloroform, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was subjected to silica gel chromatography to give the pure imidosulfoxide.

2-But-2-enyl-*N*-(4-methoxybenzyl)benzamide (12). To a stirred solution of 5.0 g (28 mmol) of *trans*-2-(2-butenyl)-benzoic acid (**11**)[36] in 100 mL of benzene was added 7.2 g (57 mmol) of oxalyl chloride followed by 1 drop of DMF. The resulting mixture was stirred for 2 h at rt (room temperature), concentrated under reduced pressure, dissolved in 25 mL of CH_2Cl_2, and added to a stirred solution of 9.0 g (65 mmol) of *p*-methoxybenzylamine in 100 mL of CH_2Cl_2. After stirring for 1 h at rt, the mixture was diluted with water, extracted with CH_2Cl_2, and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by silica gel chromatography afforded 6.3 g (75%) of **12** as a white solid: mp 79−80 °C; IR (CCl_4) 3288, 1637, 1509, and 1246 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.57 (d, 3H, J = 6.6 Hz), 3.42 (d, 2H, J = 6.2 Hz), 3.74 (s, 3H), 4.52 (d, 2H, J = 5.6 Hz), 5.51 (m, 1H), 5.97 (m, 1H), 6.11 (brs, 1H), 6.82 (d, 2H, J = 8.6 Hz), and 7.23 (m, 6H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 12.8, 30.5, 43.1, 55.1, 113.2, 124.9, 125.7, 125.8, 126.4, 127.1, 128.7, 129.6, 136.1, 139.0, 158.8, and 169.6. Anal. Calcd for $C_{19}H_{21}NO_2$: C, 77.25; H, 7.15; N, 4.74. Found: C, 77.19; H, 7.03; N, 4.68.

2-But-2-enyl-*N*-((ethylsulfinyl)acetyl)-*N*-(4-methoxybenzyl)benzamide (14). Following the general procedure, treatment of 6.1 g (21 mmol) of the above amide with 3.7 g (27 mmol) of (ethylsulfenyl)acetyl chloride (**13**) afforded 7.5 g (91%) of 2-but-2-enyl-*N*-((ethylsulfenyl)acetyl)-*N*-(4-methoxybenzyl)benzamide as a clear oil: IR (neat) 1694, 1509, 1346, and 1246 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.19 (t, 3H, J = 7.5 Hz), 1.65 (d, 3H, J = 3.8 Hz), 2.45 (q, 2H, J = 7.5 Hz), 3.30 (m, 2H), 3.57 (s, 2H), 3.76 (s, 3H), 4.83 (s, 2H), 5.46 (m, 2H), 6.77 (d, 2H, J = 8.6 Hz), 7.05 (d, 2H, J = 8.3 Hz), and 7.29 (m, 4H). Without further purification, this sulfide was subjected to oxidation.

Treatment of 7.5 g (19 mmol) of the above sulfide with 4.8 g (23 mmol) of sodium periodate gave 7.5 g (99%) of **14** as a colorless oil: IR (neat) 1687, 1509, 1346, and 1246 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.33 (t, 3H, J = 7.5 Hz), 1.64 (m, 3H), 2.81 (m, 2H), 3.20 (d, 2H, J = 7.5 Hz), 3.76 (s, 3H), 3.97 (d, 1H, J = 14.6 Hz), 4.10 (d, 1H, J = 14.6 Hz), 4.82 (m, 2H), 5.42 (m, 2H), 6.75 (d, 2H, J = 8.6 Hz), 6.98 (d, 2H, J = 8.2 Hz), 7.29 (m, 3H), and 7.43 (m, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 6.5, 12.8, 17.8, 30.1, 35.8, 55.1, 60.0, 113.8, 125.9, 126.2, 127.0, 127.7, 128.3, 129.3, 130.2, 131.2, 134.1, 139.5, 159.0, 168.4, and 173.9. Anal. Calcd for $C_{23}H_{27}NO_4S$: C, 66.80; H, 6.59; N, 3.39. Found: C, 66.71; H, 6.48; N, 3.25.

Acetic Acid 1-(4-Methoxybenzyl)-4-methyl-2-oxo-2,5-dihydro-1*H*-indeno[1,2-*b*]pyridin-3-yl Ester (16). To a refluxing solution of 2.0 g (19 mmol) of acetic anhydride and 2 mg of *p*-toluenesulfonic acid in 50 mL of toluene was added dropwise 0.8 g (1.9 mmol) of sulfoxide **14** in 2 mL of toluene. After being heated at reflux for 1 h, the mixture was concentrated under reduced pressure, and the residue was subjected to silica gel chromatography to give 0.6 g (81%) of **16** as a white solid: mp 200−201 °C; IR (CCl_4) 1758, 1652, 1509, and 1196 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 2.18 (s, 3H), 2.37 (s, 3H), 3.47 (s, 2H), 3.65 (s, 3H), 5.60 (brs, 2H), 6.77 (d, 2H, J = 8.6 Hz), 7.09 (d, 2H, J = 8.6 Hz), 7.23 (m, 2H), 7.45 (d, 1H, J = 7.1 Hz), and 7.55 (d, 1H, J = 7.6 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 13.0, 20.3, 33.7, 47.2, 54.9, 113.9, 120.6, 121.9, 124.9, 126.9, 127.0, 127.5, 135.7, 136.7, 136.8, 141.9, 143.9, 157.5, 158.4, and 168.5. Anal. Calcd for $C_{23}H_{21}NO_4$: C, 73.58; H, 5.64; N, 3.73. Found: C, 73.49; H, 5.71; N, 3.65.

Trifluoromethanesulfonic Acid 1-(4-Methoxybenzyl)-4-methyl-2-oxo-2,5-dihydro-1*H*-indeno[1,2-*b*]pyridin-3-yl Ester (18). To a stirred solution of 1.8 g (4.8 mmol) of **16** in 50 mL of methanol was added 2 mL of a saturated solution of potassium carbonate. The resulting mixture was stirred for 3 h at rt, diluted with water, extracted with $CHCl_3$, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude 3-hydroxypyridone **17** was dissolved in 50 mL of CH_2Cl_2. To this was added 1.0 g (10 mmol) of triethylamine followed by 2.6 g (7.2 mmol) of *N*-phenyltrifluoromethanesulfonimide. The resulting mixture was stirred for 12 h, diluted with water, extracted with CH_2Cl_2, and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel chromatography afforded 1.9 g (83%) of **18** as a bright yellow solid: mp 166−167 °C; IR (CCl_4) 1652, 1509, 1417, and 1211 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 2.42 (s, 3H), 3.71 (s, 2H), 3.73 (s, 3H), 5.76 (brs, 2H), 6.82 (d, 2H, J = 8.6 Hz), 7.11 (d, 2H, J = 8.6 Hz), 7.32 (m, 2H), 7.58 (d, 1H, J = 7.4 Hz), and 7.66 (d, 1H, J = 7.9 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 13.8, 34.2, 47.9, 55.2, 114.4, 119.9, 122.8, 125.4, 126.9, 127.1, 127.6, 128.3, 135.4, 138.9, 144.6, 144.7, 157.4, and 158.9. Anal. Calcd for $C_{22}H_{18}F_3NO_5S$: C, 56.77; H, 3.90; N, 3.01. Found: C, 56.85; H, 3.92; N, 3.03.

1-(4-Methoxybenzyl)-4-methyl-1,5-dihydroindeno[1,2-*b*]pyridin-2-one (19). To a stirred solution of 0.5 g (1.1 mmol) of triflate **18** in 25 mL of DMF was added 0.16 g (0.2 mmol) of $Pd(PPh_3)_2Cl_2$, 0.34 g (3.4 mmol) of triethylamine, and 0.1 g (2.1 mmol) of formic acid. The reaction was heated to 110 °C for 1 h. The reaction was cooled to rt, diluted with water, extracted with ethyl acetate, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.35 g (97%) of **19** as a white solid: mp 164−165 °C; IR (CCl_4) 1652, 1524, 1246, and 1033 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.32 (s, 3H), 3.62 (s, 2H), 3.73 (s, 3H), 5.71 (brs, 2H), 6.48 (s, 1H), 6.82 (d, 2H, J = 8.6 Hz), 7.12 (d, 2H, J = 8.6 Hz), 7.29 (m, 2H), 7.54 (d, 1H, J = 7.1 Hz), and 7.62 (d, 1H, J = 7.6 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 19.0, 33.6, 46.8, 55.2, 114.2, 116.6, 121.9, 122.5, 125.2, 127.1, 127.2, 127.4, 128.2, 136.3, 144.4, 145.7, 147.4, 158.6, and 163.7. Anal. Calcd for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03; N, 4.41. Found: C, 79.39; H, 6.07; N, 4.34.

Trifluoromethanesulfonic Acid 4-Methyl-5*H*-indeno-[1,2-*b*]pyridin-2-yl Ester (20). A solution of 0.1 g (0.3 mmol) of **19** in 7 mL of trifluoroacetic acid was heated at 100 °C in a sealed tube for 1 h. The mixture was concentrated under reduced pressure, and the residue was dissolved in ethyl acetate and filtered over a plug of silica gel. The solvent was removed under reduced pressure, the resulting oil was dissolved in 5 mL of pyridine and cooled to 0 °C, and 0.13 g (0.47 mmol) of triflic anhydride was added dropwise. The resulting mixture was stirred for 2 h and concentrated under reduced pressure, and the residue was chromatographed on a silica gel column to give 0.7 g (66%) of **20** as a white solid: mp 92−93 °C; IR (CCl_4) 1602, 1566, 1424, 1203, and 1139 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.47 (s, 3H), 3.75 (s, 2H), 6.86 (s, 1H), 7.44 (m, 2H), 7.56 (m, 1H), and 8.00 (m, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 18.8, 33.0, 112.6, 121.7, 125.2, 127.5, 129.5, 136.4, 139.5, 143.8, 147.8, 156.1, and 159.3. Anal. Calcd for $C_{14}H_{10}F_3O_3S$: C, 51.07; H, 3.06; N, 4.25. Found: C, 51.37; H, 3.24; N, 3.93.

4-Methyl-5*H*-indeno[1,2-b]pyridine (21). To a stirred solution of 0.06 g (0.2 mmol) of **20** in 5 mL of DMF was added 0.03 mg (0.03 mmol) of $Pd(PPh_3)_2Cl_2$, 0.05 g (0.5 mmol) of triethylamine, and 0.01 g of formic acid. The mixture was heated to 110 °C for 1 h, cooled to rt, diluted with water, extracted with ethyl acetate, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.02 g (75%) of 4-methyl-5*H*-indeno[1,2-*b*]pyridine as a white solid: mp 97−98 °C (lit.[29] mp 97−99 °C); IR (neat) 1606, 1455, 1388, and 1077 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.42 (s, 3H), 3.77 (s, 2H), 7.01 (d, 1H, J = 5.0 Hz), 7.37 (m, 2H), 7.58 (d, 1H, J = 7.0 Hz), 8.09 (d, 1H, J = 7.0 Hz), and 8.47 (d, 1H, J = 5.0 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 18.5, 33.3, 120.9, 122.4, 125.1, 127.2, 128.4, 136.0, 141.2, 143.0, 143.3, and 148.4. Anal. Calcd for $C_{13}H_{11}N$: C, 86.15; H, 6.12; N, 7.73. Found: C, 86.22; H, 6.13; N, 7.79.

Onychnine (7). To a stirred solution of 0.02 g (0.1 mmol) of the above indenopyridine **21** in 10 mL of acetone was added 0.08 g (0.5 mmol) of potassium permanganate. After being stirred at rt for 3 h, the reaction was diluted with EtOH, filtered over a pad of Celite, and concentrated under reduced pressure. The residue was chromatgraphed on silica gel to afford 0.02 g (68%) of onychine (**7**) as a pale yellow solid: mp 127−129 °C (lit.[29] mp 125−127 °C); IR (neat) 2935, 1703, 1600, 1565, and 920 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.52 (s, 3H), 6.75 (d, 1H, J = 6.0 Hz), 7.00−7.90 (m, 4H), and 8.29 (d, 1H, J = 6.0 Hz). Anal. Calcd for $C_{13}H_9NO$: C, 79.98; H, 4.65; N, 7.17. Found: C, 79.75; H, 4.61; N, 7.19.

(*E*)-2-(But-2-enyl-phenyl)acetonitrile. To a mixture of 1.4 g (5.3 mmol) of phosphorus tribromide in 8 mL of benzene at 0 °C was added 0.3 g (4 mmol) of pyridine in 4 mL of benzene. After stirring of the mixture for 15 min, 2.0 g (13 mmol) of 2-((*E*)-but-2-en-1-yl)benzyl alcohol[63] in 3 mL of benzene was added *via* syringe. After being stirred for 10 min, the mixture was treated with 20 mL of a 5% HCl solution, extracted with chloroform, and dried over $MgSO_4$. Filtration through a plug of silica gel gave 2.8 g (76%) of (*E*)-1-(bromomethyl)-2-but-2-enylbenzene as a colorless oil which was immediately used in the next step: IR (neat) 3018, 1485, 1450, and 1245 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.70 (d, 3H, J = 6.2 Hz) 3.48 (d, 2H, J = 6.2 Hz) 4.55 (s, 2H), 5.51−5.66 (m, 2H), and 7.18−7.35 (m, 4H); ^{13}C-NMR ($CDCl_3$, 75 MHz) 617.9, 31.7, 35.5, 126.5, 126.6, 126.8, 128.1, 129.2, 130.1, 130.5, and 139.7.

To a solution of 5.4 g (24 mmol) of the above bromide in 30 mL of DMSO was added 1.5 g (31 mmol) of NaCN. The mixture was stirred for 20 min at rt, diluted with water, and extracted with ether. After drying over $MgSO_4$, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography to give 3.9 g (94%) of (2-but-2-enyl-phenyl)acetonitrile as a 4:1-mixture of *E* and *Z* isomers: IR (neat) 2244, 1491, and 1451 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.68 (d, 3H, J = 5.7 Hz), 3.32 (d, 2H, J = 5.1 Hz), 3.70 (s, 2H), 5.38−5.66 (m, 2H), and 7.19−7.40 (m, 4H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 17.7, 30.7, 36.1, 117.7, 125.9, 126.8, 127.0, 127.8, 127.9, 128.3, 129.6, and 130.0; HRMS calcd for $C_{12}H_{13}N$ 171.1048, found 171.1054.

(*E*)-2-(2-But-2-enyl-phenyl)-*N*-(4-methoxybenzyl)acetamide. To a solution of 2.0 g (12 mmol) of the above nitrile in 100 mL of 95% ethanol was added 6.5 g (120 mmol) of KOH. The mixture was heated at reflux for 15 h and cooled to rt, and the solvent was removed under reduced pressure. To the resulting mixture was added 50 mL of water. The mixture was acidified with 2 N HCl and extracted with ether. The ether extracts were dried over $MgSO_4$, and the solvent was removed under reduced pressure. Chromatography on silica gel gave 4.0 g (93%) of (*E*)-(2-but-2-enyl-phenyl)acetic acid as a colorless oil which was immediately used in the next step: IR (neat) 3018, 2662, 1709, and 1410 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.65 (d, 3H, J = 6.0 Hz), 3.36 (d, 2H, J = 5.8 Hz), 3.69 (s, 2H), 5.42−5.57 (m, 2H), 7.21−7.23 (m, 4H), and 11.1−12.1 (brs, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 17.8, 30.8, 36.3, 38.3, 125.2, 126.4, 126.7, 127.8, 128.1, 129.0, 129.4, 129.8, 130.7, 131.8, 139.8, and 178.3.

To a solution of 1.5 g (7.6 mmol) of the above carboxylic acid in 75 mL of benzene was added 1.5 g (11 mmol) of oxalyl chloride followed by 1 drop of DMF. The resulting mixture was stirred for 2 h, concentrated under reduced pressure, and dissolved in 80 mL of methylene chloride, and this was added to a stirred solution of 2.2 g (16 mmol) of *p*-methoxybenzylamine. After being stirred for 20 min at rt, the reaction mixture was diluted with water, extracted with $CHCl_3$, and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by chromatography on silica gel gave 0.49 g (87%) of the titled compound as a white solid: mp 81−82 °C; IR (KBr) 3288, 1643, 1512, and 1446 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.64 (d, 3H, J = 5.2 Hz), 3.30 (d, 2H, J = 3.2 Hz), 3.64 (s, 2H), 3.77 (s, 3H), 4.32 (d, 2H), 5.44−5.48 (m, 2H), 5.71 (brs, 1H), 6.82, (d, 2H, J = 8.6 Hz), 7.09 (d, 2H, J = 8.6 Hz), and 7.21−7.25 (m, 4H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 17.8, 36.1, 41.1, 42.9, 55.1, 113.9, 126.8, 127.8, 127.9, 128.6, 128.7, 128.8, 128.9, 130.1, 130.2, 130.7, 132.9, 139.6, and 170.7. Anal. Calcd for $C_{20}H_{23}NO_2$: C, 77.64: H, 7.49; N, 4.53. Found: C, 77.48: H, 7.53; N, 4.50.

***N*-[(2-But-2-enylphenyl)acetyl]-2-(ethylsulfanyl)-*N*-(4-methoxybenzyl)acetamide.** Following the general procedure, treatment of 0.42 g (1.4 mmol) of the above amide with 0.23 g (1.6 mmol) of acid chloride **13** gave 0.49 g (87%) of the titled compound as a clear oil: IR (neat) 1694, 1609, and 1509 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.21−1.27 (m, 3H), 1.57−1.62 (m, 3H), 2.5−2.60 (m, 2H), 3.10 (d, 2H, J = 5.2 Hz), 3.78 (s, 3H), 3.95 (s, 2H), 3.97 (s, 2H), 4.98 (s, 2H), 5.19−5.24 (m, 1H), 5.34−5.41 (m, 1H), 6.84−6.89 (m, 2H), and 7.03−7.25 (m, 6H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 17.8, 26.2, 36.2, 37.9, 41.7, 46.7, 55.3, 114.3, 126.3, 126.4, 127.5, 127.6, 128.8, 128.9, 129.7, 130.3, 132.3, 139.3, 159.0, 172.7, and 174.4; HRMS calcd for $C_{24}H_{29}NO_3S$ 411.1868, found 411.1867.

***N*-[(2-But-2-enylphenyl)acetyl]-2-(ethylsulfinyl)-*N*-(4-methoxybenzyl)acetamide (22).** Treatment of 0.33 g (0.8

(63) Semmelhack, M. F.; Zask, A. *J. Am. Chem. Soc.* **1983**, *105*, 2034.

mmol) of the above sulfide with 0.42 g (1.9 mmol) of sodium periodate in a 4:1 H_2O/methanol mixture gave 0.3 g (96%) of **22** as a clear oil: IR (neat) 1690, 1610, 1514, and 1349 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.29 (t, 3H, J = 7.5 Hz), 1.52−1.56 (m, 3H), 2.72−2.79 (m, 2H), 2.97 (d, 2H, J = 5.9 Hz), 3.74 (s, 3H), 3.89 (s, 2H), 4.10 (d, 1H, J = 14.8 Hz), 4.35 (d, 1H, J = 14.8 Hz), 5.15 (m, 3H), 5.35 (m, 1H), 6.86 (m, 2H), and 7.15 (m, 6H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 6.4, 17.6, 35.9, 40.9, 45.9, 46.7, 55.0, 60.5, 114.2, 126.1, 126.2, 127.4, 127.6, 127.7, 127.8, 128.6, 129.6, 130.1, 131.4, 158.9, 168.4, and 174.6. Anal. Calcd for $C_{24}H_{29}NO_4S$: C, 67.42; H, 6.84; N, 3.28. Found: C, 67.29; H, 6.73; N, 3.17.

Acetic Acid 1-(4-Methoxybenzyl)-4-methyl-2-oxo-1,2,5,10-tetrahydrobenzo[*g*]quinolin-3-yl Ester (23). To a refluxing solution of 2.4 g (2.3 mmol) of acetic anhydride and 2 mg of *p*-toluenesulfonic acid in 60 mL of *m*-xylene was added dropwise 1.0 g (2.3 mmol) of the above amide in 2 mL of *m*-xylene. After being heated at reflux for 1.5 h, the mixture was concentrated under reduced pressure and the residue subjected to silica gel chromatography to give 0.6 g (68%) of **23** as a white solid: mp 170−171 °C; IR (KBr) 1755, 1663, 1613, and 1546 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.14 (s, 3H), 2.37 (s, 3H), 3.72 (s, 3H), 3.77 (s, 2H), 3.93 (s, 2H), 5.39 (brs, 2H), 6.81 (m, 2H), and 7.14 (m, 6H); ^{13}C-NMR δ 12.8, 20.5, 30.2, 31.6, 46.6, 55.2, 111.5, 114.2, 126.5, 126.8, 127.8, 127.9, 127.8, 127.9, 131.0, 132.3, 137.3, 137.4, 138.7, 156.0, 158.8, and 168.7. Anal. Calcd for $C_{24}H_{23}NO_4$: C, 74.02; H, 5.95; N, 3.60. Found: C, 73.92; H, 6.03; N, 3.63.

Acetic Acid 1-(4-Methoxybenzyl)-4-methyl-2,5,10-trioxo-1,2,5,10-tetrahydrobenzo[*g*]quinolin-3-yl Ester. To a stirred solution of 0.3 g (0.8 mmol) of pyridone **23** in 25 mL of acetic acid at rt was added 0.3 g (3 mmol) of chromium trioxide followed by 7 drops of water. The oxidation was complete after 15 min, and the solution was extracted with ether. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography to give 0.22 g (62%) of the titled compound as a yellow solid: mp 94−95 °C; IR (KBr) 1773, 1661, 1608, and 1278 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.42 (s, 3H), 2.59 (s, 3H), 3.72 (s, 3H), 5.94 (s, 2H), 6.78 (d, 2H, J = 8.6 Hz), 7.16 (d, 2H, J = 9.4 Hz), 7.68−7.75 (m, 2H), 7.94 (d, 1H, J = 7.1 Hz), and 8.04 (d, 1H, J = 9.4 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 15.0, 20.4, 48.1, 55.1, 113.9, 119.7, 126.6, 126.5, 128.2, 128.9, 129.0, 132.1, 132.2, 133.7, 134.4, 138.5, 140.8, 157.1, 158.8, 167.9, 180.3, and 182.3. Anal. Calcd for $C_{24}H_{19}NO_6$: C, 69.04; H, 4.59; N, 3.36. Found: C, 68.80: H, 4.65; N, 3.32.

3-Methoxy-1-(4-methoxybenzyl)-4-methyl-1*H*-benzo[*g*]-quinoline-2,5,10-trione (24). To a solution of 0.16 g (0.1 mmol) of the above azaanthraquinone in 10 mL of methanol was added 25 mg of sodium methoxide at 25 °C. After stirring of the solution for 20 min, 2 mL of an aqueous NH_4Cl solution and 5 mL of brine were added. The mixture was extracted with chloroform, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give 0.03 g (91%) of 3-hydroxy-1-(4-methoxybenzyl)-4-methyl-1*H*-benzo[*g*]quinoline-2,5,10-trione: IR (neat) 1662, 1626, and 1279 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.63 (s, 3H), 3.73 (s, 3H), 6.03 (s, 2H), 6.78−6.80 (m, 2H), 7.16−7.19 (m, 2H), 7.69 (brs, 2H), 7.98 (brs, 2H), and 8.05 (brs, 2H). This compound was used in the next step without further purification.

To a solution of 0.1 g (0.3 mmol) of the above alcohol in 2 mL of dimethyl sulfoxide was added 0.25 g (4.5 mmol) of KOH in 5 mL of DMSO. To this mixture was immediately added an excess of iodomethane. After being stirred for 25 min, the mixture was diluted with water, extracted with ether, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel to give 0.08 g (74%) of **24** as a yellow solid: mp 211−212 °C; IR (KBr) 1649, 1588, 1509, 1358 and 1279 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.63 (s, 3H), 3.73 (s, 3H), 4.02 (s, 3H), 6.00 (s, 2H), 6.78 (d, 2H, J = 8.6 Hz), 7.17 (d, 2H, J = 8.6 Hz), 7.70 (m, 2H), 7.95 (dd, 1H, J = 6.0 and 1.5 Hz), and 8.05 (dd, 1H, J = 6.0 and 1.5 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 47.6, 55.2, 59.8, 113.9, 121.1, 126.2, 126.4, 128.7, 128.8, 129.6, 132.3, 133.5, 134.1, 135.9, 138.8, 151.1, 158.5, 158.7, 180.2, and 182.9. Anal. Calcd for $C_{23}H_{19}NO_5$: C, 70.93; H, 4.92; N, 3.60. Found: C, 70.85: H, 4.88; N, 3.52.

Dielsiquinone (10). A solution of 0.03 g (6 mmol) of the above amide in 12 mL of trifluoroacetic acid was heated in a sealed tube at 100 °C for 45 min. The mixture was cooled, the solvent was removed under reduced pressure, and the residue was chromatographed on silica gel to give **10** as a light yellow solid: mp 252−254 °C; IR (neat) 1652, 1591, 1478, 1327, 1297, and 1131 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 2.66 (s, 3H), 4.06 (s, 3H), 7.76 (t, 1H, J = 7.6 Hz), 7.83 (t, 1H, J = 7.6 Hz), 8.16 (d, 1H, J = 7.6 Hz), 8.21 (d, 1H, J = 7.6 Hz), and 9.75 (brs, 1H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 15.0, 61.0, 118.5, 127.5, 128.6, 131.0, 134.6, 134.7, 135.8, 136.5, 138.8, 153.8, 157.9, 178.4, and 183.0. Anal. Calcd for $C_{15}H_{11}NO_4$: C, 66.90; H, 4.12; N, 5.20. Found: C, 66.81: H, 4.06; N, 5.14.

8-(Ethylsulfenyl)-7-oxo-11-oxa-6-aza-tricyclo[6.2.1.0^{1,6}]-undecane-10-carboxylic Acid Methyl Ester (26). A solution containing 0.3 g (1.2 mmol) of 1-((ethylsulfinyl)acetyl)-piperidin-2-one (**25**),[19] 1.0 g (9.8 mmol) of acetic anhydride, 1.9 g (22 mmol) of methyl acrylate, and 2 mg of *p*-toluenesulfonic acid in 30 mL of toluene was heated at 90 °C for 15 min. The reaction mixture was cooled and concentrated under reduced pressure, and the resulting residue was purified by silica gel chromatography. The major product eluted from the column (51%) was identified as cycloadduct **26**: mp 93−94 °C; IR (CCl_4) 1727, 1402, and 1172 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.32 (t, 3H, J = 7.5 Hz), 1.61 (m, 2H), 1.98 (m, 5H), 2.51 (dd, 1H, J = 12.6 and 4.6 Hz), 2.80 (m, 3H), 3.09 (dd, 1H, J = 8.3 and 4.6 Hz), 3.76 (s, 3H), and 3.82 (m, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.9, 20.2, 23.2, 24.0, 27.5, 35.9, 39.0, 48.3, 52.4, 92.8, 94.0, and 170.7. Anal. Calcd for $C_{13}H_{19}NO_4S$: C, 54.72; H, 6.71; N, 4.91. Found: C, 54.72; H, 6.75; N, 4.84.

The minor product (10%) isolated from the above chromatographic separation was identified as 3-acetoxy-4-oxo-6,7,8,9-tetrahydro-4*H*-quinolizine-1-carboxylic acid methyl ester (**27**): mp 122−123 °C; IR (CCl_4) 2953, 1772, 1717, 1661, and 1198 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.88 (m, 4H), 2.33 (s, 3H), 3.39 (t, 2H, J = 6.6 Hz), 3.82 (s, 3H), 4.09 (t, 2H, J = 6.2 Hz), and 7.77 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 18.0, 20.5, 21.2, 26.7, 43.3, 51.9, 105.9, 129.5, 136.6, 148.5, 153.2, 165.1, and 168.6. Anal. Calcd for $C_{13}H_{15}NO_5$: C, 58.86; H, 5.70; N, 5.28. Found: C, 58.92; H, 5.63; N, 5.01.

3-(Ethylsulfenyl)-4-oxo-6,7,8,9-tetrahydro-4*H*-quinolizine-1-carboxylic Acid Methyl Ester (28). To a stirred solution containing 0.13 g (0.5 mmol) of cycloadduct **26** in 35 mL of CH_2Cl_2 was added 0.32 g (2.3 mmol) of boron trifluoride etherate. The resulting mixture was stirred at rt for 3 h, quenched with water, and extracted with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to silica gel chromatography to give 0.12 g (62%) of thiopyridone **28** as a white solid: mp 71−72 °C; IR (CCl_4) 1715, 1634, 1265, and 1146 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) $\boldsymbol{\delta}$ 1.34 (t, 3H, J = 7.4 Hz), 1.81 (m, 2H), 1.94 (m, 2H), 2.91 (q, 2H, J = 7.4 Hz), 3.35 (t, 2H, J = 6.6. Hz), 3.84 (s, 3H), 4.09 (t, 2H, J = 6.2 Hz), and 7.77 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) $\boldsymbol{\delta}$ 13.5, 18.2, 21.4, 25.1,26.6, 43.0, 51.8, 107.7, 124.8, 134.1, 151.5, 160.8, and 165.6. Anal. Calcd for $C_{13}H_{17}NO_3S$: C, 58.40; H, 6.41; N, 5.24. Found: C, 58.19; H, 6.34; N, 5.08.

4-Oxo-6,7,8,9-tetrahydro-4*H*-quinolizine-1-carboxylic Acid Methyl Ester (29). To a suspension of 0.1 g of Raney nickel in 15 mL of ethanol was added 0.07 g (0.3 mmol) of pyridone **28** in 2 mL of ethanol. The mixture was heated at reflux for 0.5 h, cooled to rt, and filtered through a pad of Celite. Concentration under reduced pressure followed by silica gel chromatography afforded 0.5 g (85%) of **29**: mp 143−144 °C; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.85 (m, 2H), 1.94 (m, 2H), 3.37 (t, 2H, J = 6.6 Hz), 3.83 (s, 3H), 4.06 (t, 2H, J = 6.2 Hz), 6.41 (d, 1H, J = 9.6 Hz), and 7.90 (d, 1H, J = 9.6 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 18.1,21.3, 26.8, 42.4, 51.7, 107.4, 115.3, 139.6, 155.7, 162.8, and 165.6. Anal. Calcd for $C_{11}H_{13}NO_3$: C, 63.76; H, 6.32; N, 6.76. Found: C, 63.53; H, 6.28; N, 6.72.

8-(Ethylsulfonyl)-7-oxo-11-oxa-6-azatricyclo[6.2.1.0^{1,6}]-undecane-10-carboxylic Acid Methyl Ester (31). To a

stirred solution of 0.9 g (3.2 mmol) of cycloadduct **26** in 50 mL of a 3:1 mixture of acetonitrile/dioxane was added 2.0 g (9.4 mmol) of sodium periodate followed by 0.03 g (0.2 mmol) of $RuCl_3$. The resulting mixture was stirred at rt for 4 h, quenched with water, and extracted with CH_2Cl_2. The organic extracts were washed with a saturated $NaHCO_3$, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography to give 0.91 g (91%) of **31** as a white solid: mp 125−126 °C; IR (CCl_4) 1731, 1401, 1326, and 1162 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.34 (t, 3H, J = 7.5 Hz), 1.49 (m, 2H), 1.90 (m, 4H), 2.21 (m, 1H), 2.69 (m, 1H), 2.86 (dd, 1H, J = 12.6 and 4.3 Hz), 3.20 (m, 3H), 3.67 (s, 3H), and 3.74 (m, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 4.9, 19.7, 22.7, 27.0, 30.1, 38.9, 47.6, 52.4, 66.6, 93.8, 95.9, 166.6, and 169.5. Anal. Calcd for $C_{13}H_{19}NO_6S$: C, 49.20; H, 6.03; N, 4.41. Found: C, 49.45; H, 6.07; N, 4.34.

3-Hydroxy-4-oxo-6,7,8,9-tetrahydro-4*H*-quinolizine-1-carboxylic Acid Methyl Ester. To a solution of 0.7 g (2.2 mmol) of the above sulfone in 100 mL of CH_2Cl_2 was added 1.5 g (11 mmol) of boron trifluoride etherate. The mixture was stirred at rt for 5 h, quenched with water, and extracted with CH_2Cl_2. The extracts were dried over $MgSO_4$ and concentrated under reduced pressure, and the residue was subjected to silica gel chromatography to give 0.41 g (85%) of 3-hydroxy-4-oxo-6,7,8,9-tetrahydro-4*H*-quinolizine-1-carboxylic acid methyl ester as a colorless solid: mp 162−163 °C; IR (CCl_4) 3420, 1717, 1645, 1622, and 1213 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) ***δ*** 1.82 (m, 2H), 1.95 (m, 2H), 3.32 (t, 2H, J = 6.5 Hz), 3.83 (s, 3H), 4.13 (t, 2H, J = 6.5 Hz), 7.11 (brs, 1H), and 7.40 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) ***δ*** 18.3, 21.2, 25.9, 43.1, 51.8, 107.8, 114.7, 142.2, 144.7, 159.3, 165.8. Anal. Calcd for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; N, 6.27. Found: C, 59.06; H, 5.86; N, 6.22.

4-Oxo-3-(trifluoromethylsulfonyloxy)-6,7,8,9-tetrahydro-4*H*-quinolizine-1-carboxylic Acid Methyl Ester (32). To a stirred solution of 0.33 g (1.5 mmol) of the above hydroxypyridone in 45 mL of CH_2Cl_2 was added 0.23 g (2.2 mmol) of triethylamine. After stirring of the mixture for 30 min, 0.79 g (2.2 mmol) of *N*-phenyltrifluoromethanesulfonimide was added, and the resulting mixture was allowed to stir at 25 °C for 3 h. At the end of this time, water was added and the reaction mixture was extracted with CH_2Cl_2, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on a silica gel column to give 0.5 g (95%) of **32** as a colorless solid: mp 105−106 °C; IR (CCl_4) 1724, 1676, 1426, and 1208 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.73 (m, 2H), 1.97 (m, 2H), 3.43 (t, 2H, J = 6.7 Hz), 3.86 (s, 3H), 4.13 (t, 2H, J = 6.2 Hz) and 7.96 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 17.8, 21.0, 27.1, 43.9, 52.3, 105.6, 116.5, 120.7, 130.7, 135.4, 156.0, 157.1, and 164.3. Anal. Calcd for $C_{12}H_{12}F_3NO_6S$: C, 40.57; H, 3.40; N, 3.94. Found: C, 40.49; H, 3.43; N, 3.91.

4-Oxo-3-(pyridin-2-yl)-6,7,8,9-tetrahydro-4*H*-quinolizine-1-carboxylic Acid Methyl Ester (33). A solution containing 0.25 g (0.7 mmol) of the above triflate, 0.36 g (1.0 mmol) of 2-(tri-*n*-butylstannyl)pyridine, 0.24 g (5.7 mmol) of lithium chloride, 0.07 g (0.07 mmol) of $Pd_2(dba)_3$, and 0.03 g (0.14 mmol) of tris(2-furyl)phosphine in 40 mL of THF was heated at reflux for 14 h. The mixture was cooled to rt, an aqueous KF solution was added, and the mixture was stirred at rt for an additional 1h. The mixture was extracted with chloroform, washed with water, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude residue was purified by silica gel chromatography to give 0.14 g (70%) of **33** as a bright yellow solid: mp 153−154 °C; IR (CCl_4) 1713, 1646, 1527, 1436, and 1224 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) ***δ*** 1.86 (m, 2H), 2.00 (m, 2H), 3.45 (t, 2H, J = 6.7 Hz), 3.86 (s, 3H), 4.16 (t, 2H, J = 6.2 Hz), 7.21 (m, 1H), 7.73 (m, 1H), 8.46 (d, 1H, J = 8.2 Hz), 8.66 (m, 1H), and 8.91 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) ***δ*** 18.1, 21.6, 27.1, 43.1, 51.8, 107.9, 122.3, 123.4, 123.8, 136.2, 139.5, 149.1, 153.2, 155.9, 161.6, and 165.9. Anal. Calcd for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.34; H, 5.66; N, 9.63.

(11)*R*-(1*R*,3*R*,10*S*)-1-Carbomethoxy-3-(2-pyridyl)-4-quinolizidinone (34). A mixture containing 0.05 g (0.2 mmol) of the above pyridone and 10 mg of PtO_2 in 25 mL of methanol was hydrogenated at rt under an atmosphere of 75 psi of hydrogen for 18 h. The reaction mixture was filtered through a pad of Celite, concentrated under reduced pressure, and subjected to silica gel chromatography to give 0.04 g (85%) of a mixture of diastereomers which could be equilibrated to a single isomer **34** by refluxing the mixture in NaOMe/methanol. The methanolic solution was diluted with water, extracted with ether, and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by silica gel chromatography gave a pure sample of **34** as a pale yellow solid: mp 145−146 °C (lit.[48] mp 143−145 °C); IR ($CHCl_3$) 3000, 1740, 1635, 1600, 1575, and 1170 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.70 (m, 7.H), 2.50 (m, 4H), 3.65 (s, 3H), 3.70 (m, 1 H), 4.78 (m, 1H), 7.12 (m, 2H), 7.55 (m, 1H), and 8.45 (m, 1H). Anal. Calcd for $C_{16}H_{20}N_2O_3$: C, 66.65; H, 6.99; N, 9.72. Found: C, 66.51; H, 6.84; N, 9.53.

5-Methylhept-6-enoic Acid Benzylamide. To a solution of 9.0 g (79 mmol) of 4-methylhex-5-en-1-ol[64] in 150 mL of CH_2Cl_2 at 0 °C was added 10.9 g (95 mmol) of methanesulfonyl chloride followed by 9.6 g (95 mmol) of triethylamine. The solution was allowed to warm to rt and was stirred for an additional 1 h. Concentration under reduced pressure followed by silica gel chromatography afforded 15.2 g (100%) of methanesulfonic acid 4-methylhex-5-enyl ester which was used in the next step without further purification: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.01 (d, 3H, J = 6.7 Hz), 1.41 (m, 2H), 1.74 (m, 2H), 2.15 (m, 1H), 3.00 (s, 3H), 4.21 (t, 2H, J = 6.6 Hz), 4.97 (m, 2H), and 5.65 (m, 1H).

To a solution of 15 g (78 mmol) of the above mesylate in 100 mL of DMSO was added 5.8 g (117 mmol) of NaCN. The mixture was heated to 90 °C for 2 h, diluted with water, extracted with ether, and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product distilled to give 7.0 g (73%) of 5-methylhept-6-enenitrile: bp 87−90 °C (21 mm); IR (neat) 2243, 1636, 1455, and 1420 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.02 (d, 3H, J = 6.7 Hz), 1.45 (m, 2H), 1.65 (m, 2H), 2.14 (m, 1H), 2.33 (t, 2H, J = 7.1 Hz), 4.98 (m, 2H), and 5.65 (m, 1H).

A mixture of 7.0 g (57 mmol) of the above nitrile and 32 g (570 mmol) of KOH in 100 mL of an ethanol/water mixture was heated at reflux for 12 h. The mixture was cooled to rt, washed with ether, and acidified with concentrated HCl. The mixture was extracted with ether, dried over $MgSO_4$, and concentrated under reduced pressure. The crude acid was distilled to give 7.2 g (89%) of 5-methylhept-6-enoic acid: bp 132−135 °C (20 mm); IR (neat) 1713, 1416, 1293, and 912 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.00 (d, 3H, J = 6.7 Hz), 1.33 (m, 2H), 1.62 (m, 2H), 2.13 (m, 1H), 2.34 (m, 2H), 4.95 (m, 2H), 5.67 (m, 1H), and 11.30 (brs, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 20.1, 22.4, 34.1, 35.8, 37.6, 112.9, 144.0, and 180.4.

To a solution of 4.7 g (33 mmol) of the above acid in 50 mL of CH_2Cl_2 was added 6.4 g (40 mmol) of 1,1′-carbonylimidazole. The mixture was stirred at rt for 1 h and then poured into a solution of 3.9 g (37 mmol) of benzylamine in 50 mL of CH_2Cl_2. After being stirred at 25 °C for 1 h, the mixture was washed with 10% HCl and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by silica gel chromatography gave 7.1 g (93%) of 5-methylhept-6-enoic acid benzylamide as a colorless oil: IR (neat) 3288, 1651, 1557, and 1455 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.99 (d, 3H, J = 6.8 Hz), 1.32 (m, 2H), 1.65 (m, 2H), 2.12 (m, 1H), 2.19 (t, 2H, J = 7.6 Hz) 4.43 (d, 2H, J = 5.7 Hz), 4.94 (m, 2H), 5.66 (m, 1H), 5.76 (brs, 1H), and 7.31 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 20.1, 23.4, 36.1, 36.8, 37.6, 43.6, 112.8, 127.5, 127.8, 128.7, 138.4, 144.2, and 172.8. Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.74; H, 9.08; N, 6.01.

***N*-Benzyl(ethylsulfenyl)-*N*-(5-methylhept-6-enoyl)-acetamide.** Following the general procedure, treatment of 5.7 g (25 mmol) of the above amide with 4.5 g (32 mmol) of acid chloride **13** afforded 7.2 g (86%) of the titled compound as a light yellow oil: IR (neat) 1694, 1455, 1377, and 1151 cm^{-1};

(64) Beckwith, A. L. J.; Easton, C. J.; Lawerence, T.; Serelis, A. K. *Aust. J. Chem.* **1983**, *36*, 545.

^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.96 (d, 3H, J = 6.7 Hz), 1.27 (m, 5H), 1.63 (m, 2H), 2.06 (m, 1H), 2.60 (m, 4H), 3.75 (s, 2H), 4.91 (m, 2H), 5.01 (s, 2H), 5.64 (m, 1H), 7.17 (d, 2H, J = 7.2 Hz), and 7.31 (m, 3H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 20.1, 22.4, 26.2, 35.7, 37.4, 37.6, 37.7, 46.9, 112.8, 125.9, 127.4, 128.8, 136.9, 144.1, 172.5, and 176.1; HRMS calcd for $C_{19}H_{27}NO_2S$ 333.1762, found: 333.1761.

***N*-Benzyl-2-(ethylsulfinyl)-*N*-(5-methylhept-6-enoyl)-acetamide (37).** Treatment of 4.1 g (12.4 mmol) of the above sulfide with 2.9 g (13.7 mmol) of sodium periodate gave 4.1 g (94%) of **37** as a colorless oil: IR (neat) 1694, 1455, 1379, and 1161 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.95 (d, 3H, J = 6.7 Hz), 1.23 (m, 2H), 1.37 (t, 3H, J = 7.5 Hz), 1.54 (m, 2H), 2.04 (m, 1H), 2.54 (t, 2H, J = 7.3 Hz), 2.88 (m, 2H), 4.18 (d, 1H, J = 14.6 Hz), 4.40 (d, 1H, J = 14.6 Hz), 4.99 (m, 4H), 5.61 (m, 1H), 7.16 (d, 2H, J = 7.1 Hz), and 7.32 (m, 3H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 6.6, 20.1, 22.0, 35.6, 36.9, 37.6, 46.3, 47.2, 60.5, 1130, 126.0, 127.7, 129.0, 136.1, 143.9, 168.3, and 176.4. Anal. Calcd for $C_{19}H_{27}NO_3S$: C, 65.30; H, 7.79; N, 4.01. Found: C, 65.17; H, 7.63; N, 3.92.

Acetic Acid 1-Benzyl-5-methyl-2-oxo-1,2,5,6,7,8-hexahydroquinolin-3-yl Ester (40). To a refluxing solution of 3.1 g (30 mmol) of acetic anhydride and 2 mg of *p*-toluenesulfonic acid in 50 mL of toluene was added dropwise 1.1 g (3.0 mmol) of sulfoxide **37** in 2 mL of toluene. After being heated at reflux for 1 h, the mixture was concentrated under reduced pressure, and the residue was subjected to silica gel chromatography. The major product eluted from the above chromatographic separation contained 0.68 g (73%) of a colorless oil which was identified as acetoxypyridone **40**: IR (neat) 1769, 1660, 1612, and 1555 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.19 (d, 3H, J = 7.0 Hz), 1.35 (m, 1H), 1.71 (m, 3H), 2.33 (s, 3H), 2.53 (m, 2H), 2.68 (m, 1H), 5.35 (brs, 2H), 7.13 (d, 2H, J = 8.8 Hz), and 7.27 (m, 4H); ^{13}C-NMR ($CDCl_3$, 75 MHz) 619.1, 20.6, 21.7, 27.0, 29.4, 30.8, 47.0, 118.3, 126.3, 127.2, 128.7, 130.0, 136.2, 138.7, 141.0, 157.8, and 168.8; HRMS calcd for $C_{19}H_{21}NO_3$ 311.1521, found 311.1531. Anal. Calcd for $C_{19}H_{21}NO_3$: C, 73.28; H, 6.80; N, 4.50. Found: C, 73.09; H, 6.77; N, 4.32.

The minor product eluted from the column contained 0.12 g (13%) of a colorless oil which was identified as 1-benzyl-3-(ethylsulfenyl)-5-methyl-5,6,7,8-tetrahydro-1*H*-quinolin-2-one (**41**): IR (neat) 1639, 1588, 1537, and 1454 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.20 (d, 3H, J = 6.9 Hz), 1.27 (m, 2H), 1.35 (t, 3H, J = 7.3 Hz), 1.42 (m, 1 H), 1.71 (m, 3H), 2.53 (m, 1H), 2.69 (m, 1H), 2.91 (m, 2H), 5.35 (brs, 2H), 7.13 (d, 2H, J = 6.5 Hz), and 7.26 (m, 3H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 13.6, 19.0, 22.0, 25.1,26.9, 29.4, 30.9, 47.0, 119.8, 126.4, 126.5, 127.0, 128.6, 135.5, 136.6, 139.7, and 160.8; HRMS calcd for $C_{19}H_{23}NOS$ 313.1500, found: 313.1497.

Trifluoromethanesulfonic Acid 1-Benzyl-5-methyl-2-oxo-1,2,5,6,7,8-hexahydroquinolin-3-yl Ester. To a stirred solution of 0.7 g (2.2 mmol) of pyridone **40** in 50 mL of methanol was added 1 mL of a saturated aqueous solution of potassium carbonate. The mixture was stirred for 30 min, diluted with water, extracted with $CHCl_3$, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude hydroxypyridone was dissolved in 50 mL of CH_2Cl_2. To this was added 0.44 g (4.4 mmol) of triethylamine followed by 1.2 g (3.3 mmol) of *N*-phenyltrifluoromethanesulfonimide. The resulting mixture was stirred for 2 h, diluted with water, extracted with $CHCl_3$, and dried over $MgSO_4$. Removal of the solvent under reduced pressure followed by silica gel chromatography afforded 0.77 g (87%) of the titled compound as a white solid: mp 97−98 °C; IR (CCl_4) 1667, 1614, 1548, and 1427 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.19 (d, 3H, J = 6.9 Hz), 1.35 (m, 1H), 1.73 (m, 3H), 2.63 (m, 3H), 5.37 (m, 2H), 7.12 (d, 2H, J = 6.9 Hz), and 7.27 (m, 4H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 18.8, 21.6, 27.2, 29.1, 30.8, 47.3, 118.0, 126.3, 127.4, 128.8, 131.1, 135.4, 137.6, 144.6, and 157.1. Anal. Calcd for $C_{18}H_{18}F_3NO_4S$: C, 53.86; H, 4.52; N, 3.49. Found: C, 53.85; H, 4.61; N, 3.44.

1-Benzyl-5-methyl-5,6,7,8-tetrahydro-1*H*-quinolin-2-one (42). To a stirred solution of 0.9 g (2.1 mmol) of the above triflate in 25 mL of DMF was added 0.08 g (0.1 mmol) of Pd(PPh$_3$)$_2$(OAc)$_2$, 0.7 mg (6.4 mmol) of triethylamine, and 0.2 mg (4.3 mmol) of 95% formic acid. The mixture was heated at 100 °C for 1 h, cooled to rt, diluted with water, extracted with ethyl acetate, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.54 g (99%) of **42** as a white solid: mp 87−88 °C; IR (CCl_4) 1661, 1589, 1538, and 1455 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.19 (d, 3H, J = 7.0 Hz), 1.35 (m, 1H), 1.71 (m, 3H), 2.61 (m, 3H), 5.35 (m, 2H), 6.58 (d, 1H, J = 9.3 Hz), 7.12 (d, 2H, J = 7.2 Hz), and 7.27 (m, 4H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 19.1, 21.8, 27.2, 29.4, 30.8, 46.4, 117.7, 119.9, 126.2, 127.1,128.7, 136.7, 140.7, 143,6, and 163.1. Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.35; H, 7.61; N, 5.48.

This same compound was also prepared by the Raney-nickel desulfurization of thioethyl pyridone **41** using standard reductive conditions.

1-Benzyl-5-methyl-3,4,5,6,7,8-hexahydro-1*H*-quinolin-2-one (43). To a solution of 0.2 g (0.8 mmol) of **42** in 25 mL of THF at −40 °C was added dropwise 1.6 mL of a 1 M solution of L-Selectride in THF. The reaction mixture was stirred for 1 h, allowed to warm to 0 °C, and quenched with brine. The organic layer was washed with an aqueous solution of 30% H_2O_2 and a 10% NaOH solution and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.16 g (77%) of **43** as a colorless oil: IR (neat) 1666, 1388, and 1182 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.01 (d, 3H, J = 7.0 Hz), 1.23 (m, 1H), 1.54 (m, 1 H), 1.67 (m, 2H), 2.06 (m, 3H), 2.21 (m, 2H), 2.56 (m, 2H), 4.82 (d, 1H, J = 16.3 Hz), 4.92 (d, 1H, J = 16.3 Hz), and 7.22 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 19.3, 20.1, 23.5, 25.8, 30.3, 31.9, 32.6, 43.8, 120.3,126.2,126.7,128.5, 131.7, 138.5, and 170.5. Anal. Calcd for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N, 5.49. Found: C, 80.14; H, 8.26; N, 5.53.

(4*aR*,5*S*,8*aS*)-5-Methyldecahydroquinolin-2-one (44). To a solution containing 0.08 g of **43** in 10 mL of EtOH was added a catalytic amount of PtO_2. The resulting mixture was hydrogenated at 50 psi for 10 h, filtered through a pad of Celite, and concentrated under reduced pressure. The residue was chromatographed on silica gel to afford 0.07 g (86%) of **44** as a white solid: mp 148−149 °C (lit.[54] mp 150−152 °C); IR (neat) 3190, 2950, 1670, and 1600 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.93 (d, 3H, J = 6.5 Hz), 1.30−2.65 (m, 12H), 3.60 (m, 1H), and 6.53 (brs, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 19.2, 20.1, 23.2, 27.4, 27.7, 31.7, 33.8, 39.7, 52.2, and 172.3. Anal. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.25; N, 8.37. Found: C, 71.69; H, 10.22; N, 8.36.

***N*-[(1-Benzoyl-4-vinyl-2,3-dihydro-1*H*-indol-3-yl)acetyl]-2-(ethylsulfenyl)-*N*-methylacetamide.** Following the general procedure, treatment of 1.4 g (4.3 mmol) of 2-(1-benzoyl-4-vinyl-2,3-dihydro-lH-indol-3-yl)-*N*-methylacetamide (**48**)[61] with 0.66 g (4.8 mmol) of acid chloride **13** gave 1.8 g (98%) of the titled compound as a colorless oil: IR (neat) 1690, 1646, 1449, and 1383 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) $\boldsymbol{\delta}$ 1.21 (t, 3H, J = 7.4 Hz), 2.52 (q, 2H, J = 7.4 Hz), 2.93 (m, 2H), 3.16 (s, 3H), 3.61 (m, 2H), 3.92 (m, 2H), 4.28 (dd, 1H, J = 11.5 and 8.4 Hz), 5.35 (d, 1 H, J = 11 .1 Hz), 5.77 (d, 1H, J = 17.5 Hz), 6.72 (dd, 1H, J = 17.5 and 11.1 Hz), 7.22 (m, 1H), and 7.42 (m, 7H); ^{13}C-NMR ($CDCl_3$, 75 MHz) $\boldsymbol{\delta}$ 14.2, 26.0, 31.2, 35.0, 37.1, 42.2, 56.4, 116.4, 120.5, 127.1, 128.2, 128.3, 130.3, 131.9, 132.4, 133.7, 136.2, 142.4, 168.8, 171.8, and 173.8; HRMS calcd for $C_{24}H_{26}N_2O_3S$ 422.1664, found 422.1662.

***N*-[(1-Benzoyl-4-vinyl-2,3-dihydro-1*H*-indol-3-yl)acetyl]-2-(ethylsulfinyl)-*N*-methylacetamide (47).** Treatment of 0.5 g (1.1 mmol) of the above amide with 0.3 g (1.2 mmol) of sodium periodate afforded 0.5 g (96%) of **47** as a colorless oil: IR (neat) 2929, 1690, 1646, 1449, and 1383 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.31 (t, 3H, J = 7.4 Hz), 2.80 (m, 4H), 3.13 (s, 3H), 3.83 (m, 2H), 4.04 (m, 1H), 4.25 (m, 2H), 5.37 (d, 1H, J = 11.1 Hz), 5.78 (d, 1H, J = 17.4 Hz), 6.71 (dd, 1H, J = 17.4 and 11.1 Hz), 7.22 (m, 1H), and 7.43 (m, 7H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 6.3, 30.9, 34.5, 41.3, 45.7, 56.0, 59.8, 116.5, 120.4, 126.9, 128.1,128.3, 130.2, 130.3, 132.2, 133.6, 136.0, 136.1, 142.3, 167.5, 168.6, and 173.8. Anal. Calcd for $C_{24}H_{26}N_2O_4S$: C, 65.73; H, 5.98; N, 6.39. Found: C, 65.58; H, 5.81; N, 6.36.

Acetic Acid 4-Benzoyl-7-methyl-8-oxo-4,5,5a,6,7,8-hexahydroindolo[4,3-*fg*]quinolin-9-yl Ester (49). To a refluxing solution of 2.3 g (23 mmol) of acetic anhydride and 2 mg of *p*-toluenesulfonic acid in 50 mL of xylene was added dropwise 1.0 g (2.3 mmol) of sulfoxide **47** in 2 mL of xylene. After being heated at reflux for 3 h, the reaction mixture was cooled to rt and concentrated under reduced pressure, and the residue was subjected to silica gel chromatography. The major product eluted from the chromatographic separation contained 0.6 g (64%) of **49** as a white solid: mp 269−270 °C; IR (CCl_4) 1766, 1659, 1623, 1388, and 1196 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.36 (s, 3H), 2.67 (t, 1 H, J = 15.2 Hz), 3.30 (m, 1 H), 3.67 (s, 3H), 3.72 (m, 1 H), 3.91 (t, 1H, J = 10.8 Hz), 4.60 (m, 1 H), 7.02 (m, 1H), and 7.53 (m, 8H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 20.6, 30.7, 32.0, 34.1, 58.3, 112.0, 116.1, 124.6, 127.3, 128.7, 129.1, 129.2,.129.3, 129.5, 130.8, 136.1,139.6, 140.9, 141.8, 157.6, 168.7, and 168.8. Anal. Calcd for $C_{24}H_{20}N_2O_4$: C, 71.99; H, 5.03; N, 7.00. Found: C, 72.06; H, 5.08; N, 6.94.

The minor product eluted from the column contained 0.1 g (11%) of 4-benzoyl-9-(ethylsulfenyl)-7-methyl-4,5,5*a*,7-tetrahydro-6*H*-indolo[4,3-*fg*]quinolin-8-one (**50**): IR (CCl_4) 1645, 1616, 1460, and 1396 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.37 (t, 3H, J = 7.5 Hz), 2.67 (t, 1 H, J = 15.2 Hz), 2.91 (q, 2H, J = 7.5 Hz), 3.29 (m, 1 H), 3.65 (s, 3H), 3.69 (m, 1H), 3.91 (t, 1H, J = 10.7 Hz), 4.33 (m, 1H), 7.08 (m, 1H), and 7.53 (m, 8H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 13.3, 24.9, 30.4, 31.9, 33.9, 57.7, 113.2, 115.9, 116.1, 127.2, 128.2, 128.4, 128.6, 129.0, 130.7, 136.1,140.3, 141.0, 160.5, and 168.7. Anal. Calcd for $C_{24}H_{22}N_2O_2S$: C, 71.62; H, 5.51; N, 6.96. Found: C, 71.55; H, 5.49; N, 7.01.

Trifluoromethanesulfonic Acid 4-Benzoyl-7-methyl-8-oxo-4,5,5*a*,6,7,8-hexahydroindolo[4,3-*fg*]quinolin-9-yl Ester (52). To a stirred solution of 0.4 g (0.9 mmol) of **49** in 35 mL of methanol was added.2 mL of a saturated solution of potassium carbonate. The resulting mixture was stirred for 3 h at rt, diluted with water, extracted with $CHCl_3$, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the resulting hydroxypyridone **51** was dissolved in 35 mL of CH_2Cl_2. To this was added 0.2 g (1.7 mmol) of triethylamine followed by 0.5 g (1.3 mmol) of *N*-(5-chloro-2-pyridyl)triflimide. The resulting mixture was stirred for 12 h, diluted with water, extracted with CH_2Cl_2, and dried over $MgSO_4$. Concentration under reduced pressure followed by silica gel chromatography afforded 0.4 g (81%) of **52** as a colorless solid: mp 219−220 °C; IR (CCl_4) 2875, 1666, 1424, and 1218 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.72 (t, 1H, J = 15.2 Hz), 3.37 (m, 1H), 3.68 (s, 3H), 3.75 (m, 1H), 3.92 (t, 1H, J = 10.7 Hz), 4.52 (m, 1H), 7.13 (m, 1H), 7.52 (m, 7H), and 7.73 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 30.8, 32.3, 33.6, 57.8, 111.6, 115.9, 116.4, 120.7, 125.5, 127.2, 128.6, 129.4, 130.8, 135.9, 138.6, 141.1, 145.2, 156.8, and 168.7. Anal. Calcd for $C_{23}H_{17}F_3N_2O_5S$: C, 56.33; H, 3.49; N, 5.71. Found: C, 56.39; H, 3.56; N, 5.69.

4-Benzoyl-7,8-dimethyl-4,5,5*a*,7-tetrahydro-6*H*-indolo[4,3-*fg*]quinolin-8-one (53). A solution containing 0.1 g (0.2 mmol) of **52**, 0.04 g (0.2 mmol) of tetramethyltin, 0.03 mg (0.6 mmol) of lithium chloride, and 0.01 g (0.02 mmol) of $Pd(PPh_3)_2Cl_2$ in 20 mL of DMF was heated to 100 °C for 2 h. The mixture was cooled to rt, diluted with water, extracted with ethyl acetate, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel chromatography to give 0.05 g (73%) of **53** as a white solid: mp 237−238 °C; IR (CCl_4) 1645, 1609, 1460, and 1396 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.23 (s, 3H), 2.65 (t, 1H, J= 15.0 Hz), 3.30 (m, 1H), 3.65 (s, 3H), 3.68 (m, 1H), 3.90 (t, 1H, J = 10.8 Hz), 4.55 (m, 1H), 7.10 (m, 1H), and 7.56 (m, 8H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 17.5, 30.7, 31.7, 34.1, 58.3, 112.6, 115.9, 127.2, 127.3, 128.6, 129.0, 130.7, 132.8, 136.2, 136.3, 140.9, 141.7, 163.3, and 168.8. Anal. Calcd for $C_{23}H_{20}N_2O_2$: C, 77.51; H, 5.66; N, 7.86. Found: C, 77.60; H, 5.82; N, 7.69.

(5*β*,10*β*)-2,3-Dihydro-6,8-dimethylergolin-7-one (54). To a solution of 0.04 g (0.13 mmol) of **53** in 2 mL of acetic acid was added 3 mg of PtO_2. The resulting mixture was hydrogenated at 1000 psi of hydrogen for 8 h and was filtered over a pad of Celite. A few drops of concentrated hydrochloric acid were added, and the mixture was heated at reflux for 3 h. The solution was cooled to rt, diluted with aqueous ammonia, and extracted with $CHCl_3$. After drying over $MgSO_4$, the solvent was removed under reduced pressure and the residue was purified by silica gel chromatography to give 0.04 g (85%) of **54** as a 4:1 mixture of diastereomers. A pure sample of the major diastereomer **54** was obtained as a white solid by silica gel chromatography: mp 247−248 °C (lit.[59,60] mp 246−248 °C); IR (KBr) 3400 and 1620 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.20 (d, 3H, J = 6.5 Hz), 3.30, (s, 3H), 2.6−4.7 (m, 11H), 6.9−7.7 (m, 3H). Anal. Calcd for $C_{16}H_{20}N_2O$: C, 74.97; H, 7.86; N, 10.93. Found: C, 74.85; H, 7.74; N, 10.78.

(±)Costaclavine (45). To a solution containing 0.04 g (0.15 mmol) of lactam **54** in 5 mL of ether was added 0.03 g (0.66 mmol) of LAH in small portions. After heating of the mixture at reflux for 1 h, water was added to decompose the excess hydride. The aqueous layer was extracted with ether, and the combined ether layer was washed with brine, dried, and concentrated under reduced pressure. The resulting oil was taken up in 5 mL of $CHCl_3$, and 0.04 g (0.46 mmol) of MnO_2 was added. The mixture was heated at 60 °C for 10 h, filtered, and concentrated under reduced pressure. The resulting oil was purified by preparative TLC to give 0.02 g (49%) of costaclavine (**45**) as a white solid: mp 220−222 °C (lit.[60] mp 222−224 °C); IR (KBr) 1620, 1610, 1560, 1130 and 1040 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.95 (d, 3H, J = 6.5 Hz), 1.45 (m, 1H), 1.87 (m, 2H), 2.27 (s, 3H), 2.50 (m, 1H), 2.65 (brs, 1H), 2.75 (1H, J = 8.0 Hz), 2.90 (d, 1H, J = 15.7 Hz), 3.30 (dd, 1H, J = 15.7 and 3.0 Hz), 3.37 (brs, 1H), 6.90−7.45 (m, 4H), and 7.80 (brs, 1H). Anal. Calcd for $C_{16}H_{20}N_2$: C, 79.96; H, 8.39; N, 11.66. Found: C, 79.87; H, 8.75; N, 11.51.

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Supporting Information Available: ^{1}H- and ^{13}C-NMR spectra for new compounds lacking elemental analyses. This material is available free of charge via the Internet at http://pubs.acs.org.

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