precursor (55 kcal/mol instead of 64 kcal/mol).

4. Cyl 2 Analogues[39] **(Aoe Replaced by Leu) (Table IX).** If the absolute configuration of the N-terminal amino acid is inverted, in the case of D-Tyr, the transition state is the least strained (109 kcal/mol instead of 129 kcal/mol for the L-Tyr compound). Also the ΔE value is the lowest, being 7 kcal/mol for this precursor while it is 46 kcal/mol for the other one.

Conclusion

The limiting factor for small peptide cyclization is the transition-state energy. Calculations performed using the GenMol program on five cyclotetrapeptides (chlamydocin, HC-toxin, cyclotetrapeptides of sarcosine in combination with glycine, 4-Ala-chlamydocin, and Cyl analogues) clearly indicate that the best precursor is the linear peptide which is the least strained in the transition state, thus corresponding to the lowest energy barrier to be crossed in order to bring the geometry of the molecule from the preferred conformation to the transition-state geometry. Our model can predict which precursor must be chosen for obtaining the best cyclization yield. To check if the model can be generalized, we are now performing calculations on larger peptides.

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(40) Note: the energy values are approximate (+2), and in this work we only discuss the significant differences.

Registry No. 1, 143429-86-1; **1** (dimer), 143430-04-0; **2**, 143429-87-2; **2** (dimer), 143430-05-1; **3**, 143429-88-3; **3** (dimer), 143430-06-2; **4**, 143429-89-4; **4** (dimer), 143430-07-3; **5**, 143429-90-7; 6, 143429-91-8; 7, 143429-92-9; **8**, 143429-93-0; **9**, 143429-94-1; **10**, 143429-95-2; **11**, 143429-96-3; **12**, 143429-97-4; **13**, 143429-98-5; **14**, 143429-99-6; **15**, 143430-00-6; **16**, 143430-01-7; **17**, 143445-99-2; **18**, 143430-02-8; **19**, 143430-03-9.

Molecular Design and Chemical Synthesis of Potent Enediynes. 1. Dynemicin Model Systems Equipped with N-Tethered Triggering Devices

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Abstract: In this article the molecular design and chemical synthesis of a series of enediynes (**12–19**, Chart I) related to the dynemicin A structure and carrying N-tethered triggering devices are described. The design envisioned the [(arylsulfonyl)ethoxy]carbonyl group attached at the nitrogen atom as a triggering device for the Bergman cycloaromatization reaction because of its ability to undergo β-elimination under basic conditions, liberating the labile free amine intermediate. A number of tethering groups on the aromatic ring were also installed in these systems for future incorporation of other desirable moieties such as delivery systems and solubility enhancers. The chemical synthesis of the designed systems proceeded from the corresponding quinoline intermediates **46**, **49**, and **52** (Scheme VII) through acetylide additions to quinoline (intermolecular) and carbonyl (intramolecular) functionalities as the key steps. Bergman cycloaromatization experiments under basic and acidic conditions demonstrated the abilities of these compounds to generate benzenoid diradicals. A number of potent DNA-cleaving compounds and cytotoxic agents emerged from these studies.

Introduction

The emergence of the enediyne anticancer antibiotics (Scheme I) as an exceptionally potent class of bioactive substances combining unprecedented molecular architecture and mechanism of action elicited intensive investigations in chemistry, biology, and medicine.[1] With the exception of the neocarzinostatin chromophore (**4**),[2] whose structure and mode of action represent slight variations from those of the other members of the class [calicheamicin γ_1^1 (**2**),[3] esperamicin A_1 (**3**),[4] dynemicin A (**1**)[5]], these naturally occurring substances possess a conjugated enediyne moiety embedded in a 10-membered-ring skeleton, a delivery system (carbohydrate chains or intercalating groups), and a sensitive triggering device. Upon suitable activation, these molecules enter a fascinating cascade of reactions, central to which is a Bergman cycloaromatization (**5** → **6**, Scheme II)[6] leading to a highly reactive benzenoid diradical. The potent anticancer activity of these compounds is a consequence of DNA damage by the generated reactive species which have the ability to abstract hydrogen atoms from the deoxyribose framework of one or both strands of the genetic material. The mode of action[7] of dynemicin

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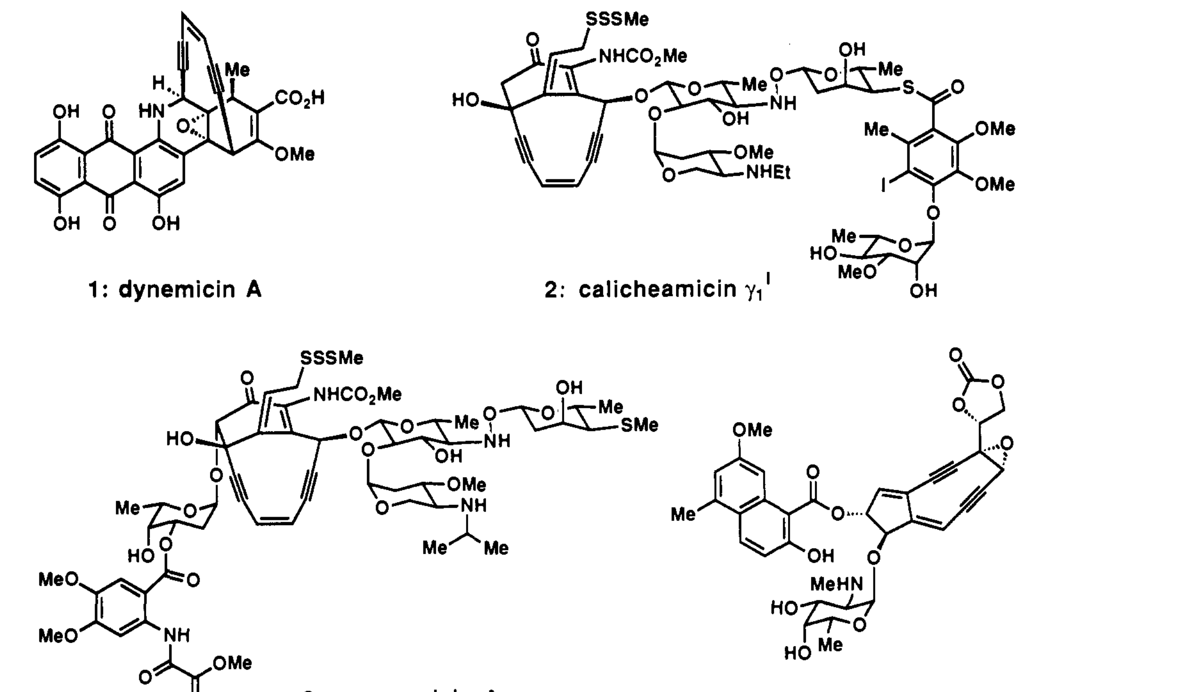
Scheme I. Structures of Naturally Occurring Enediyne Anticancer Antibiotics



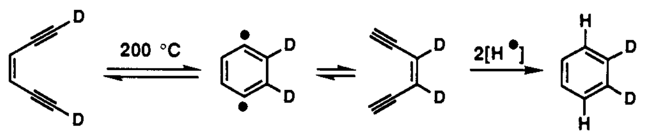
1: dynemicin A

2: calicheamicin $\gamma_1{}^I$

3: esperamicin A_1

4: neocarzinostatin chromophore

Scheme II. The Bergman Cyclization Reaction



5 6

A (**1**), depicted in Scheme III, demonstrates the key role of a bioreduction process (**1** → **7**) in the triggering of these substances toward radical generation and amplifies the importance of the "epoxide lock" in the stabilization of this particular type of enediynes. Challenged by the need for new DNA-cleaving molecules and cytotoxic agents, and taking the opportunity provided by these natural products, we initiated[8] a program directed toward the molecular design, chemical synthesis, and investigation of a series of novel enediynes. In a previous article[9] we described our initial studies involving simple monocyclic enediynes representing the parent 10-membered-ring skeleton of the naturally occurring compounds. In this and the following article in this issue,[10] we discuss the design, chemical synthesis, and chemistry of a series of biologically active dynemicin A (**1**) models. The biological actions of these systems are described elsewhere.[11]

Molecular Design

Inspired by the molecular architecture and mode of action of dynemicin A (**1**)[7] and the other naturally occurring enediyne antibiotics, and extending our initial[8] studies on simple mimics of these molecules, we set out to design a new set of enediyne compounds that would fulfill a number of requirements as discussed elsewhere.[11] The design of these molecules was based on basic chemical principles, and the expectation was that, following these design guidelines, compounds would emerge that would possess useful and adjustable biological properties, particularly DNA-cleaving properties and cytotoxic activity. Several molecular variations were considered in order to test various hypotheses pertaining to reactivity issues of the systems.[12] The synthesis and chemistry of the designed enediynes listed in Chart I are described in the following sections.

Substitutions at Nitrogen and at C-10. The Discovery of the [(Phenylsulfonyl)ethoxy]carbonyl Triggering Device and the Stabilizing Effect of Oxygen Substituents at C-10

Initial attempts to install triggering devices and other desirable groups on the basic enediyne skeleton focused on nitrogen and C-10 substitutions. Scheme IV outlines the synthesis of a series of compounds and their chemistry, including studies with the parent enediyne **34**. The previously described[13,14] compounds **20** and **21** served as starting materials. Alkylation of compound **21** on oxygen using Cs_2CO_3/18-crown-6 and excess MeI or $BrCH_2COOEt$ in acetonitrile proceeded smoothly to afford **22** (49%) or **23** (92%), respectively. Hydrolysis of ethyl ester **23** with LiOH led to carboxylic acid **24**, which was converted to its 2-pyridinethiol ester **25** by reaction with $(2\text{-PyS})_2/Ph_3P$ in 96% overall yield. Reduction of **25** with $NaBH_4$ led to the ethylene glycol derivative **26** (68% yield). Compounds **20**–**27** were used for biological investigations and chemical manipulations. Thus, compound **20** was reacted with $PhSCH_2CH_2ONa$ in THF furnishing sulfide **28** in 96% yield. This sulfide (**28**) was then converted to sulfoxide **29** (86% yield, ca. 1:1 mixture of diastereoisomers by ^1H NMR) upon treatment with stoichiometric

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Scheme III. Proposed Mechanism of Action of Dynemicin A

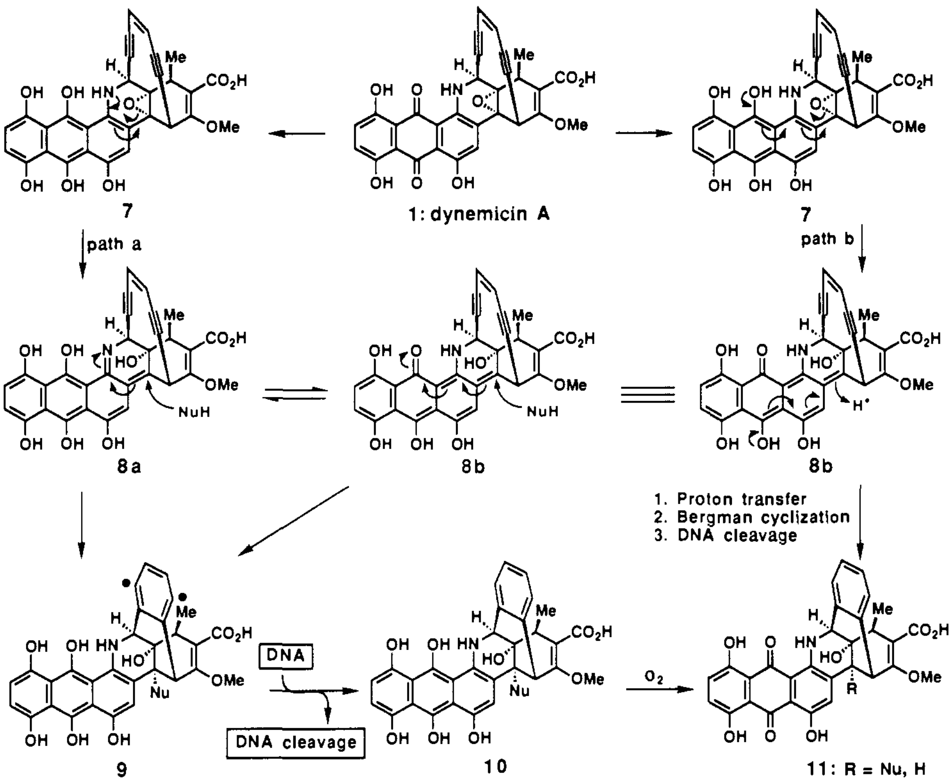
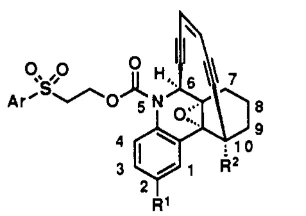


Chart I



12: $R^1 = R^2 = H$, Ar = Ph
13: $R^1 = H$, $R^2 = OMe$, Ar = Ph
14: $R^1 = H$, $R^2 = OCH_2CH_2OH$, Ar = Ph
15: $R^1 = OMe$, $R^2 = H$, Ar = Ph
16: $R^1 = OMe$, $R^2 = H$, Ar = 1-naphthyl
17: $R^1 = OMe$, $R^2 = H$, Ar = 2-naphthyl
18: $R^1 = OCH_2CH_2OH$, $R^2 = H$, Ar = Ph
19: $R^1 = C{\equiv}CCH_2OH$, $R^2 = H$, Ar = Ph

amounts of *m*-CPBA (−78 → 0 °C) and to sulfone **12** (80% yield) upon exposure to an excess amount of *m*-CPBA at ambient temperature. Similarly, compounds **22** and **27** were sequentially transformed to derivatives **30**, **31**, and **13** and **32**, **33**, and **14**, respectively.

Sulfone **12** served as an excellent precursor to the previously described[13,15] labile enediyne **34** on exposure to DBU in benzene at 5 °C or Cs_2CO_3/18-crown-6 in acetonitrile at 25 °C. When sulfone **13** was exposed to the above reaction conditions, the stable methoxy aniline derivative **35** was isolated as a crystalline solid, mp 88–89 °C (ethyl ether) (97%). The stability of this compound relative to the parent system **34** may be explained by the electron-withdrawing effect of the methoxy substituent as discussed elsewhere.[11] Addition of PhOH or PhSH to **34** generated in situ led to the formation of the cycloaromatized products **36** or **37**, respectively (Scheme IV). Compound **35** was induced to undergo Bergman cycloaromatization to **38** under acidic conditions. Figure 1 presents ORTEP drawings for compounds **13** and **35** together with some structural parameters derived from X-ray crystallographic analysis.

The parent enediyne **34** was trapped as its bis(organocobalt) complex **39** (Scheme V) by treatment with excess $Co_2(CO)_8$ as

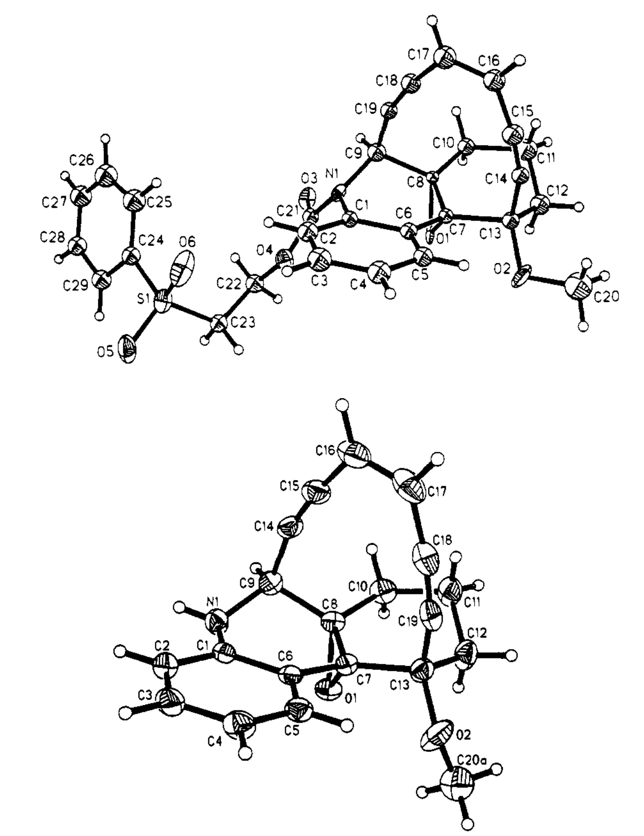


Figure 1. ORTEP drawings of compounds **13** (top) and **35** (bottom). **13**: cd distance [*r*(C14–C19)], 3.66 Å; angles at acetylenic carbons, C14 160.4°, C15 170.2°, C18 170.0°, C19 162.4°. **35**: cd distance [*r*(C14–C19)], 3.63 Å; angles at acetylenic carbons, C14 163.2°, C15 173.0°, C18 169.3°, C19 160.5°.

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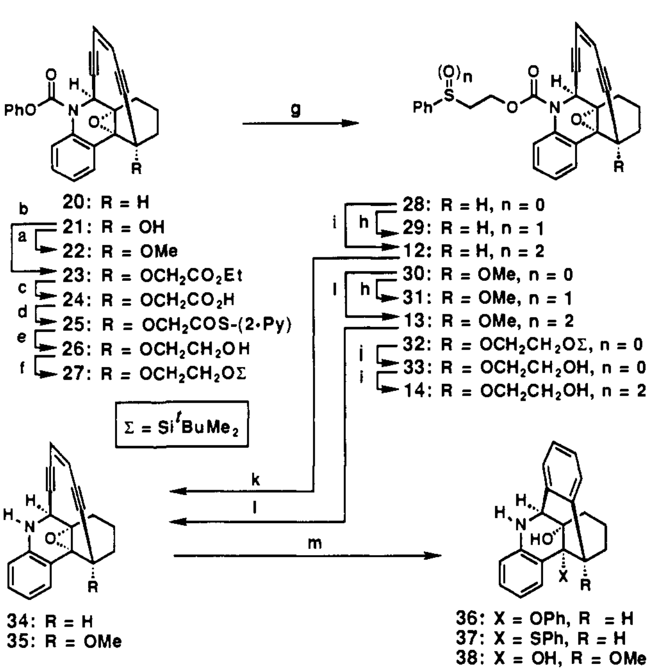
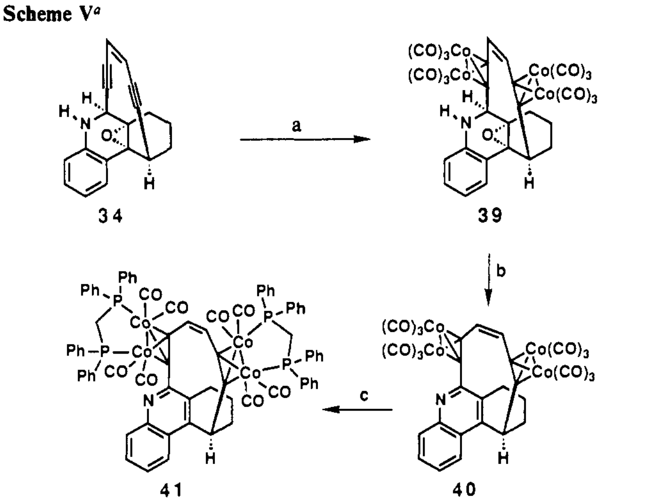
Scheme IV[a]



[a] Reagents and conditions: (a) 2.0 equiv of Cs_2CO_3, excess MeI, 0.6 equiv of 18-crown-6, CH_3CN, 25 °C, 6 h, 49%; (b) 2.0 equiv of Cs_2CO_3, 3.0 equiv of $BrCH_2CO_2Et$, 0.6 equiv of 18-crown-6, CH_3CN, 25 °C, 10 h, 92%; (c) 3.0 equiv of LiOH, THF/H_2O (1:1), 0 °C, 30 min; (d) 1.9 equiv of (2-PyS)$_2$, 1.9 equiv of PPh_3, CH_2Cl_2, 0 °C, 30 min, 96% (2 steps); (e) 10.3 equiv of $NaBH_4$, CH_2Cl_2/^{i}PrOH (1:1), 0 °C, 30 min, 68%; (f) 3.0 equiv of 2,6-lutidine, 2.3 equiv of ^{t}BuMe$_2$SiOTf, −78 → 0 °C, 1 h, 99%; (g) (for **20** → **28**, **22** → **30**, and **27** → **32**) 2.0 equiv of $PhSCH_2CH_2ONa$, THF, 25 °C, 10 min, **28** 96%, **30** 90%, or **32** 98%; (h) 1.0 equiv of *m*-CPBA, CH_2Cl_2, 0 °C, 30 min, **29** 86% or **31** 90%; (i) 2.5 equiv of *m*-CPBA, CH_2Cl_2, 25 °C, 30 min, **12** 80%, **13** 79%, or **14** 82%; (j) 1.7 equiv of ^{n}Bu$_4$NF, THF, 0 °C, 30 min, 96%; (k) excess Cs_2CO_3, 0.5 equiv of 18-crown-6, dioxane, 25 °C, 1 h, **34**, high yield; (l) 1.2 equiv of DBU, PhH, 5 °C, 30 min, **35** 97%; (m) (for **34** → **36**) 2.0 equiv of PhOH, 1,4-cyclohexadiene, 25 °C, 2 h, 25%, (for **34** → **37**) 2.0 equiv of PhSH, 1,4-cyclohexadiene, 25 °C, 2 h, 33%, (for **35** → **38**) 0.5 equiv of TsOH·H_2O, dioxane/H_2O/1,4-cyclohexadiene (4:1:1), 60 °C, 2 h, 20%.

Scheme V[a]



[a] Reagents and conditions: (a) see ref 13; (b) SiO_2, PhH, 25 °C, 1 h, 90%; (c) 10 equiv of $Ph_2PCH_2PPh_2$, PhMe, 80 °C, 5 h, 76%.

previously described.[13] This species (**39**) was observed to suffer epoxide opening and concomitant dehydration upon exposure to silica gel in benzene, leading to compound **40**. Ligand exchange with $Ph_2PCH_2PPh_2$ converted species **40** to the more crystalline compound **41** (mp > 300 °C dec, CH_2Cl_2), whose X-ray crystallographic analysis was carried out in order to confirm its

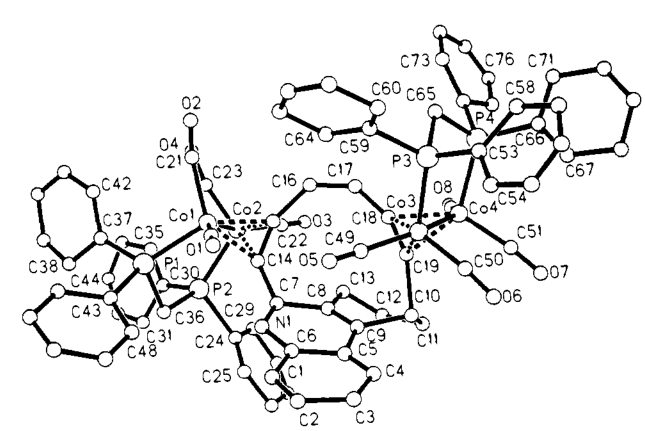
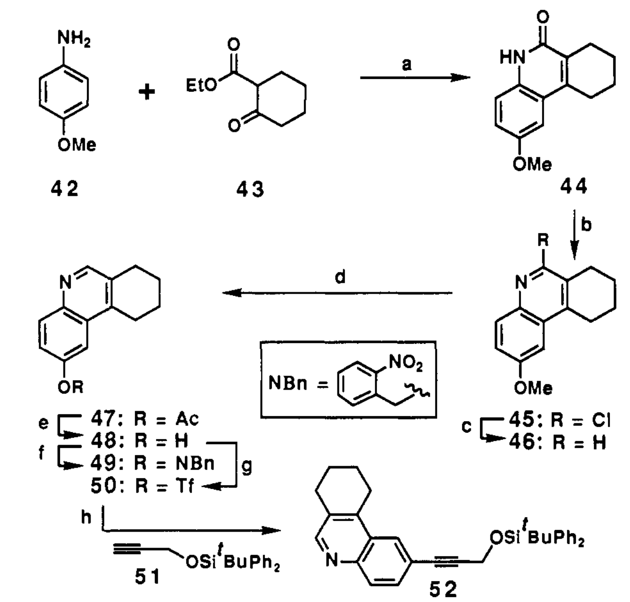


Figure 2. ORTEP drawing of cobalt complex **41**.

Scheme VI[a]



[a] Reagents and conditions: (a) 190 °C, 30 min, H_2SO_4 (concentrated), 100 °C, 30 min, 30%; (b) 10.8 equiv of $POCl_3$, 100 °C, 1 h, 94%; (c) H_2 Pd/C, MeOH, 55 °C, 60 h, 94%; (d) (for **46** → **47**) 2.0 equiv of EtSNa, DMF, 160 °C, 4 h; 3.0 equiv of Ac_2O, 25 °C, 30 min, 86%; (e) Dowex 1X8-200 hydroxide form (catalytic), ^{n}Bu$_4$NI (catalytic), MeOH, 60 °C, 24 h, 98%; (f) 1.1 equiv of 2-nitrobenzyl bromide, 2.0 equiv of K_2CO_3, 0.02 equiv of ^{n}Bu$_4$NI, DMF, 25 °C, 3 h, 94%; (g) 1.3 equiv of Tf_2O/Pyr, 0 °C, 36 h, 78%; (h) 1.3 equiv of **51**, 0.05 equiv of $PdCl_2(PPh_3)_2$, 2.0 equiv of Et_2NH, 0.1 equiv of CuI, DMF, 25 °C, 11 h, 97%.

molecular structure. Figure 2 depicts the ORTEP drawing of **41** as derived from such a study. As expected, attempts to remove the metals oxidatively led to rapid decomposition.

Substitution at C-2. The Neutral Position, Ideal for Tethering

To test the ideas discussed in the design section regarding the C-2 position of this class of enediynes, the 2-methoxy series of compounds was targeted for synthesis. Confirmation of the expected chemical and biological profiles of the final target compound **15** (Chart I) encouraged us to also target compounds **18** and **19** (Chart I) equipped with both the sulfone triggering device and a tether for coupling to suitable moieties. Schemes VI–XI outline the syntheses of these molecules. The requisite starting key intermediates **46**, **49**, and **52** for these constructions were obtained quite rapidly and efficiently from 4-methoxyaniline (**42**) and ethyl 2-oxocyclohexanecarboxylate (**43**), as shown in Scheme VI. Thus, condensation of **42** with **43** under the influence of heat and concentrated H_2SO_4[16] produced compound **44** in 30% yield.

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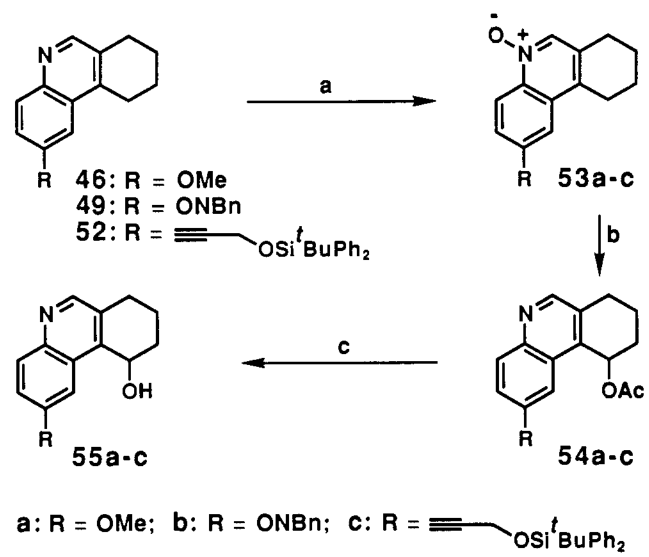
Scheme VII[a]



[a] Reagents and conditions: (a) 1.2 equiv of *m*-CPBA, CH_2Cl_2, 25 °C, 1 h, **53** 90% from **46**, **53b** 87% from **49**, **53c** 91% from **52**; (b) Ac_2O, 70 °C, 1 h, **54a** 57%, **54b** 74%, **54c** 91%; (c) for **54a,b**, Dowex 1×8-200 hydroxide form (catalytic), MeOH, 60 °C, 24 h, **55a** 84%, **55b** 89%, or for **54c**, 0.1 equiv of NaOMe, MeOH, 25 °C, 30 min, **55c** 69%.

Reaction of **44** with $POCl_3$ at 100 °C furnished chloride **45** (94%), which was subjected to catalytic hydrogenolysis to afford the requisite compound **46**[17] (94%). The latter compound served well as a precursor to both **49** and **52**. Thus, demethylation of **46** with NaSEt at 160 °C followed by cooling and in situ acetylation (for isolation purposes) produced **47** (86% overall yield). The phenol **48** was then conveniently generated from **47** by exposure to NaOMe in MeOH at 60 °C (98%) and was smoothly converted to its *o*-nitrobenzyl ether **49** (94%) and triflate **50** (78%) by standard chemistry. Coupling of triflate **50** with the acetylenic unit of **51** under the catalytic action of $PdCl_2(PPh_3)_2$ and CuI furnished the desired target **52** in 97% yield.

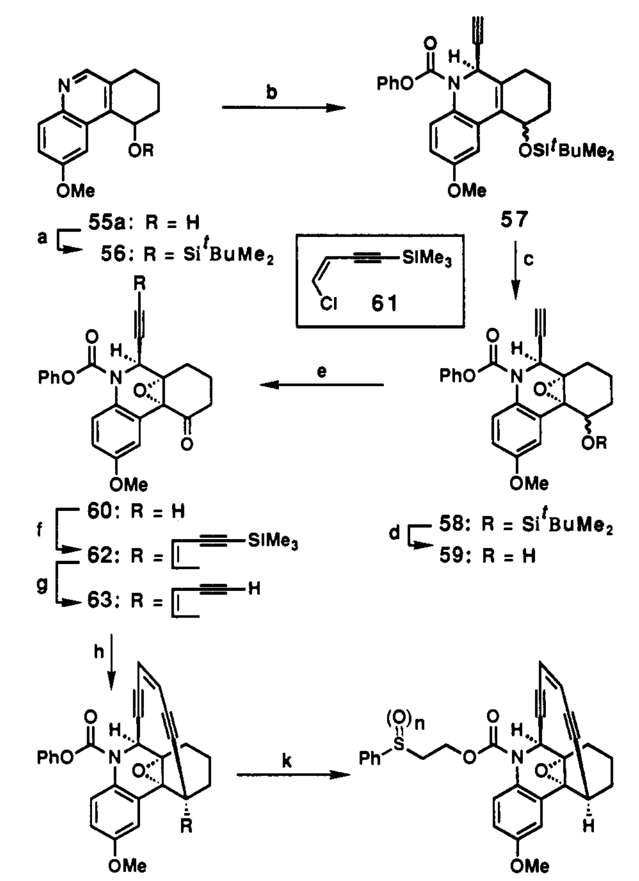
Functionalization of the C-10 position in these systems (**46**, **49**, and **52**) was achieved according to Scheme VII. Oxidation with *m*-CPBA led to *N*-oxides **53a–c** (87–91%), which upon heating in acetic anhydride at 70 °C gave the corresponding acetates **54a–c** in 57–91% yield. Deacetylation with NaOMe in MeOH then furnished the hydroxy compounds **55a–c** in 69–89% yield.

Scheme VIII summarizes the synthesis of 2-methoxy enediynes **64–67** and **15** by a sequence resembling that used for the synthesis of enediynes **20**, **21**, **28**, and **12** (Scheme IV and ref 13). The chemistry, DNA-cleaving properties, and cytotoxic activity of these systems were, as expected, similar to those of the parent compounds lacking the 2-methoxy group.[11,15] The naphthyl sulfone analogs **16** and **17** were prepared in a similar manner (Scheme IX) and showed DNA-cleaving and cytotoxic profiles comparable to those of compound **15**.

Scheme X outlines the construction of enediynes **77–83** and **18** following chemistry similar to that established above for the 2-methoxy series. A notable new tactic in this scheme was the utilization of the *o*-nitrobenzyl protecting group for the phenolic group, a choice that led to highly crystalline intermediates and a photodeprotection at the right stage (**77** → **78**, MeOH:$CHCl_3$ = ca. 3:1, 76% yield). Pivaloate formation led selectively to **79** in high yield, whereas exposure to excess thiocarbonyldiimidazole furnished compound **80** in 100% yield. Treatment of **80** with *n*BuSnH/AIBN in benzene at 70 °C gave **81** (90% yield). Exposure of **81** to $PhSCH_2CH_2OH/Cs_2CO_3$/18-crown-6 in CH_3CN at 25 °C accomplished exchange of the PhO with the $PhSCH_2CH_2O$ group as well as removal of the pivaloate group from the phenol. In situ trapping of the phenoxide anion with the ethylene glycol derivative ^{t}BuMe$_2$SiOCH$_2$CH$_2$OTs afforded compound **82** in 70% overall yield from **81**. Finally, removal of the silyl ether followed by *m*-CPBA oxidation furnished **18** via **83** in 99% overall yield from **82**. Compound **18** exhibited the expected chemical and DNA-cleaving profiles[11] and showed remarkably high potency in cytotoxicity tests against a variety of tumor cell lines.[11] Figure 3 shows the crystal structure of sulfide **82** and lists some of the interesting parameters of the enediyne core.

The 2-acetylene-substituted enediyne systems **91–95** and **19** were synthesized from key intermediate **55c** as summarized in Scheme XI. As before, the synthesis of this series of compounds proceeded smoothly and in high overall yield. The key ring-closure reaction (**90** → **91**, Scheme XI) proceeded in 90% yield under basic conditions. The final steps included the standard deoxygenation, carbamate side chain exchange, deprotection of the primary hydroxyl group, and oxidation of the sulfur. The final target **19** designed for the rigidity of its tether exhibited the

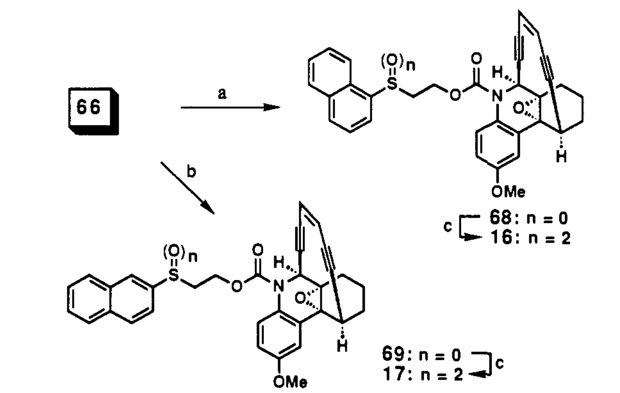
Scheme VIII[a]



[a] Reagents and conditions: (a) 1.2 equiv of ^{t}BuMe$_2$SiOTf, 1.5 equiv of 2,6-lutidine, CH_2Cl_2, 20 °C, 1 h, 91%; (b) 1.2 equiv of ethynylmagnesium bromide, 1.2 equiv of PhOCOCl, THF, −78 → 25 °C, 1 h, 100%; (c) 2.0 equiv of *m*-CPBA, CH_2Cl_2, 25 °C, 2 h, 99%; (d) 1.25 equiv of ^{n}Bu$_4$NF, THF, 0 °C, 1 h, 99%; (e) 2.0 equiv of PCC, 4-Å molecular sieves, CH_2Cl_2, 25 °C, 2 h, 87%; (f) 1.6 equiv of **61**, 0.06 equiv of $Pd(PPh_3)_4$, 0.24 equiv of CuI, 2.0 equiv of ^{n}BuNH$_2$, PhH, 25 °C, 2 h, 73%; (g) 4.0 equiv of $AgNO_3$, THF/EtOH/H_2O (1:1:1), 25 °C, 15 min; 7.0 equiv of KCN, 25 °C, 1 h, 88%; (h) 1.1 equiv of LDA, PhMe, −78 °C, 1 h, 66% along with 14% recovery of **63**; (i) 3.0 equiv of thiocarbonyldiimidazole, 0.65 equiv of DMAP, CH_2Cl_2, 25 °C, 72 h, 100%; (j) 2.1 equiv of ^{n}Bu$_3$SnH, 0.24 equiv of AIBN, PhH, 75 °C, 1 h, 86%; (k) 2.0 equiv of $PhSCH_2CH_2OH$, 5.0 equiv of Cs_2CO_3, 1.0 equiv of 18-crown-6, CH_3CN, 25 °C, 45 h, 91%; (l) 2.0 equiv of *m*-CPBA, CH_2Cl_2, 25 °C, 2 h, 88%.

(17) Hollingsworth, B. L.; Petrow, V. *J. Chem. Soc.* **1948**, 1537.

Scheme IX[a]



[a] Reagents and conditions: (a) 2.0 equiv of 2-(1-naphthylthio)ethanol, 5.0 equiv of Cs_2CO_3, 1.0 equiv of 18-crown-6, CH_3CN, 25 °C, 45 h, 92%; (b) 2.0 equiv of 2-(2-naphthylthio)ethanol, 5.0 equiv of Cs_2CO_3, 1.0 equiv of 18-crown-6, CH_3CN, 25 °C, 45 h, 85%; (c) 3.0 equiv of *m*-CPBA, CH_2Cl_2, 25 °C, 1 h, **16** 85%, **17** 92%.

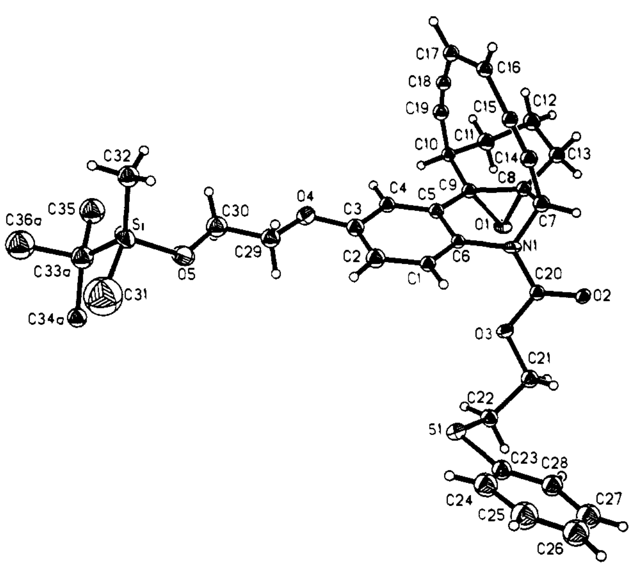


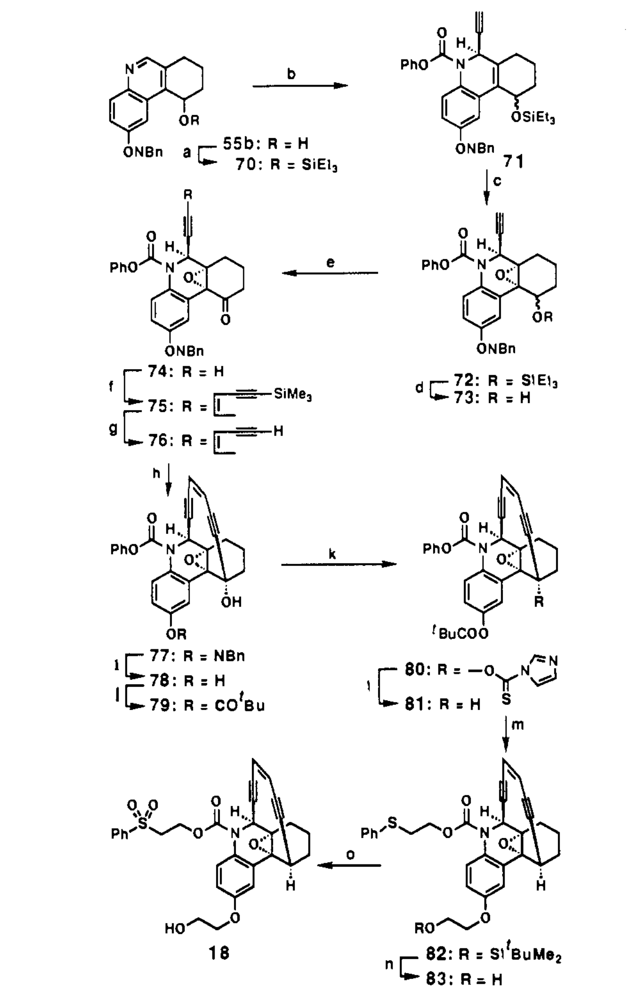
Figure 3. ORTEP drawings of compound **82**. cd distance [*r*(C14–C19)]: 3.67 Å. Angles at acetylenic carbons: C14, 164.0°; C15, 167.5°; C18, 172.2°; C19, 161.9°.

anticipated chemical, biochemical, and most significantly, potent and selective cytotoxicity against a variety of cancer cells.[11] Bergman cycloaromatizations were demonstrated with a number of these compounds including **81** and **98** (Scheme XII). Thus **81**, upon treatment with excess $TsOH{\cdot}H_2O$ at 80 °C in wet benzene/1,4-cyclohexadiene (3:1), gave compound **96** in 80% yield. On the other hand, exchange of the pivaloate with the $CH_2CH_2OSi^tBuMe_2$ group led to **98** (via **97**, Scheme XII), which upon exposure to the above acidic conditions at 70 °C led to the cyclized product **99** in 71% yield.

Conclusion

A series of enediyne model systems patterned after the dynemicin A structure (**1**) was designed and synthesized. The molecular design of these systems projected relatively simple structures for accessibility purposes. These systems were equipped with the necessary functionality for biological action. Of particular importance were the design and installation of triggering devices capable of activation and triggering of the Bergman cyclization reaction generating benzenoid diradicals. On the basis of chemical principles first, this rational approach initially focused on substitutions at the nitrogen atom, the oxygen atom at C-10, and the aromatic carbon C-2. To complete the study, substitutions at the aromatic carbon C-3 were also considered, as will be discussed in the following article in this issue.[10]

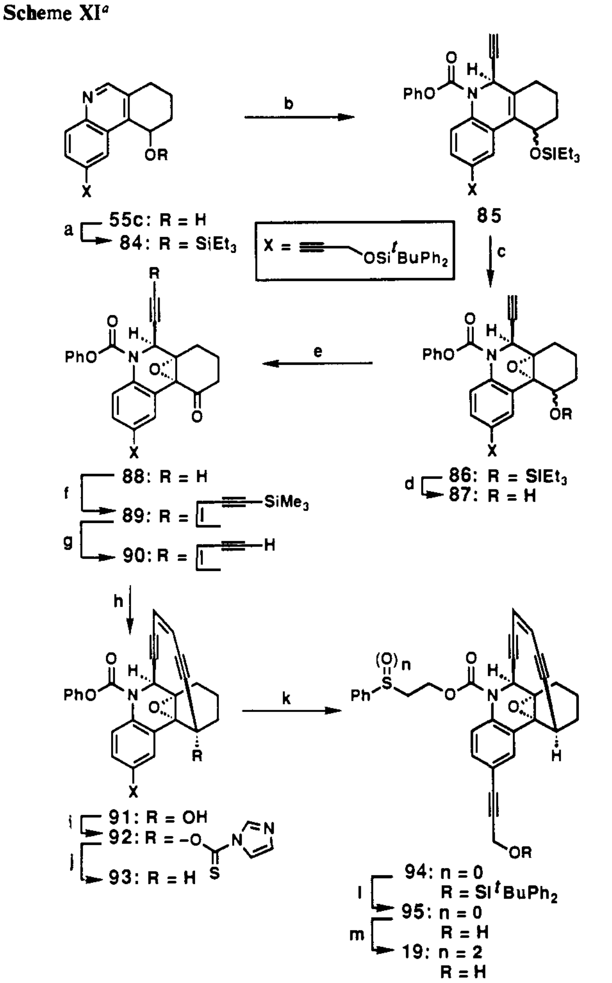
Scheme X[a]



[a] Reagents and conditions: (a) 1.1 equiv of Et_3SiOTf, 1.3 equiv of 2,6-lutidine, CH_2Cl_2, 20 °C, 1 h, 95%; (b) 1.3 equiv of ethynylmagnesium bromide, 1.3 equiv of PhOCOCl, THF, −78 → 25 °C, 1 h, 100%; (c) 2.0 equiv of *m*-CPBA, CH_2Cl_2, 25 °C, 2 h, 95%; (d) 1.05 equiv of $^nBu_4NF$, 1.6 equiv of ^tBuSH, THF, 20 °C, 30 min, 88%; (e) 2.0 equiv of PCC, 4-Å molecular sieves, CH_2Cl_2, 25 °C, 3 h, 100%; (f) 1.6 equiv of 61, 0.01 equiv of $Pd(PPh_3)_4$, 0.02 equiv of CuI, 2.0 equiv of $^nBuNH_2$, CH_2Cl_2, 25 °C, 2 h, 78%; (g) 4.0 equiv of $AgNO_3$, THF/EtOH/H_2O (1:1:1), 25 °C, 1 h; 7.0 equiv of KCN, 25 °C, 30 min, 96%; (h) 1.1 equiv of LDA, PhMe, −78 °C, 1 h, 86%; (i) sunlight, $MeOH/CH_2Cl_2$ (4:1), 28 °C, 4 h, 76%; (j) 1.1 equiv of ^tBuCOCl, 1.5 equiv of Et_3N, CH_2Cl_2, 20 °C, 30 min, 90%; (k) 3.0 equiv of thiocarbonyldiimidazole, 1.0 equiv of DMAP, CH_2Cl_2, 25 °C, 48 h, 100%; (l) 2.2 equiv of $^nBu_3SnH$, 0.01 equiv of AIBN, PhH, 70 °C, 1 h, 95%; (m) 4.0 equiv of $PhSCH_2CH_2OH$, 16.0 equiv of Cs_2CO_3, 5.0 equiv of 18-crown-6, CH_3CN, 25 °C, 40 h, 4.0 equiv of $^tBuMe_2SiOCH_2CH_2OTs$, 25 °C, 40 h, 70%; (n) 1.1 equiv of $^nBu_4NF$, THF, 20 °C, 20 min, 100%; (o) 2.0 equiv of *m*-CPBA, CH_2Cl_2, 25 °C, 1 h, 99%.

The synthetic sequences to prepare the targeted enediynes were based, for the most part, on methodology previously developed in these laboratories[13] but included a number of new and notable tactics, extensions, and modifications. Among the most interesting features of the described syntheses are the following: (a) the high-yielding palladium(0)-mediated coupling reactions involving terminal acetylenes; (b) the efficient, base-induced construction of the 10-membered-ring enediyne moiety; (c) the utilization of the *o*-nitrobenzyl protecting group as a photolytically removable group characterized with high crystallinity; and (d) the highly efficient final stages for deoxygenation and appendage attachment. The synthetic routes described are practical in terms of overall yields and number of steps, and the targeted enediynes may be produced in multigram quantities. Options for enantioselective syntheses are also available at several stages along the defined

Scheme XI[a]



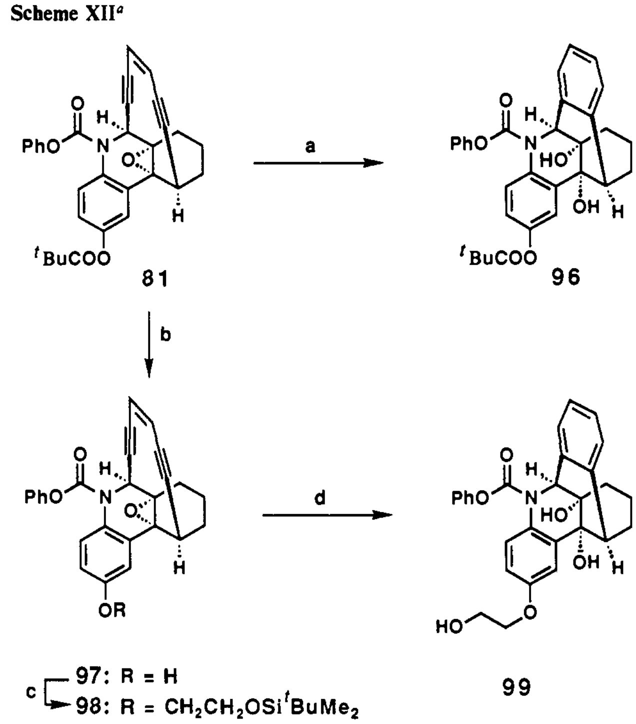
[a] Reagents and conditions: (a) 1.5 equiv of Et_3SiOTf, 2.0 equiv of 2,6-lutidine, CH_2Cl_2, 0 °C, 15 min, 88%; (b) 1.8 equiv of ethynylmagnesium bromide, 1.2 equiv of PhOCOCl, THF, −78 → 0 °C, 2 h, 83%; (c) 1.5 equiv of *m*-CPBA, CH_2Cl_2 buffer solution (pH 7.5) (1:1.7), 25 °C, 2 h, 87%; (d) 1.0 equiv of HF/Pyr, THF, 25 °C, 24 h, 92%; (e) 2.0 equiv of PCC, 4-Å molecular sieves, CH_2Cl_2, 25 °C, 3 h, 90%; (f) 1.6 equiv of **61**, 0.06 equiv of $Pd(PPh_3)_4$, 2.0 equiv of $^nBuNH_2$, 0.24 equiv of CuI, THF, 25 °C, 3.5 h, 67%; (g) 4.0 equiv of $AgNO_3$, THF/EtOH/H_2O (2:1:1), 25 °C, 45 min; 9.6 equiv of KCN, 25 °C, 1 h, 90%; (h) 1.1 equiv of LDA, PhMe, −78 °C, 30 min, 90%; (i) 3.0 equiv of thiocarbonyldiimidazole, 10.3 equiv of DMAP, CH_2Cl_2, 25 °C, 60 h, 76% (16% of **74** recovered); (j) 2.0 equiv of $^nBu_3SnH$, 0.01 equiv of AIBN, PhH, 55 °C, 1.5 h, 77% (10% of **74** obtained); (k) 2.0 equiv of $PhSCH_2CH_2ONa$, THF, 25 °C, 10 min, 92%; (l) 1.5 equiv of $^nBu_4NF$, THF, 0 °C, 15 min, 81%; (m) 2.0 equiv of *m*-CPBA, CH_2Cl_2, 25 °C, 30 min, 82%.

pathways for production of pure enantiomers of either sense.

In addition to the development of efficient routes to these biologically interesting enediynes, the present study established (a) the [(phenylsulfonyl)ethoxy]carbonyl substituent on nitrogen as an excellent and unique triggering device activated by chemical and biological means both in vitro and in vivo,[11] and (b) the ethylene glycol unit at the C-2 aromatic position as an appropriate and convenient tether for coupling these systems to other moieties without compromising their chemical and biological properties. In fact compound **18**, containing both of these functionalities, was found to be among the most in vitro potent cytotoxic agents described.[11]

Most significantly, these designed enediynes, while chemically stable under neutral conditions, undergo the Bergman cycloaromatization reaction upon chemical (basic or acidic) or biological activation. They, therefore, constitute a unique class of DNA-cleaving molecules and cytotoxic agents with prodrug profiles. Targeting them to specific DNA or RNA sequences and tumor cells by attaching them to suitable delivery systems may enhance

Scheme XII[a]



[a] Reagents and conditions: (a) 1.7 equiv of $TsOH{\cdot}H_2O$, wet PhH/1,4-cyclohexadiene (3:1), 80 °C, 20 min, 80%; (b) 0.2 equiv of Cs_2CO_3, MeOH, 65 °C, 2 h, 93%; (c) 3.0 equiv of Cs_2CO_3, 0.5 equiv of 18-crown-6, 2.0 equiv of $^tBuMe_2SiOCH_2CH_2OTs$, CH_3CN, 25 °C, 16 h, 66%; (d) 1.7 equiv of $TsOH{\cdot}H_2O$, wet PhH/1,4-cyclohexadiene (3:1), 70 °C, 1 h, 71%.

their potential value in biotechnology and medicine.

Experimental Section

General Techniques. Melting points were recorded on a Thomas-Hoover capillary melting point apparatus and are not corrected. NMR spectra were recorded on a Bruker AM-300 or AMX-500 instrument. IR spectra were recorded on a Perkin-Elmer 1600 FTIR spectrophotometer. Low-resolution mass spectra (MS) and high-resolution mass spectra (HRMS) were recorded on a VG ZAB-ZSE mass spectrometer under positive fast atom bombardment (FAB^+) conditions. Elemental analyses were performed by Robertson Microlit Laboratories, Inc., Madison, NJ.

All reactions were monitored by thin-layer chromatography carried out on 0.25-mm E. Merck silica gel plates (60F-254) using UV light, 7% ethanolic phosphomolybdic acid, or 5% ethanolic *p*-anisaldehyde and heat as the developing agent. Preparative thin-layer chromatography (preparative TLC) was performed on 0.5 mm × 20 cm × 20 cm E. Merck silica gel plates (60F-254). E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography.

All reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions unless otherwise noted. Yields refer to chromatographically and spectroscopically (^1H NMR) homogeneous materials, unless otherwise stated.

Compound 23. To a mixture of **21** (300 mg, 0.73 mmol), cesium carbonate (480 mg, 1.46 mmol), and methyl bromoacetate (0.21 mL, 2.19 mmol) in acetonitrile (9 mL) was added 18-crown-6 (117 mg, 0.44 mmol) at 0 °C. The cooling bath was then removed, and the mixture was stirred at ambient temperature for 10 h. The reaction mixture was diluted with ethyl acetate (40 mL), washed sequentially with saturated ammonium chloride (10 mL), saturated sodium bicarbonate (10 mL), and brine (10 mL), and dried ($MgSO_4$). The solvent was removed in vacuo, and the residue was purified by flash column chromatography (silica, 5% ethyl acetate in benzene) to give 323 mg (92%) of **23**: colorless crystals, mp 198–200 °C dec (from dichloromethane); R_f = 0.55 (silica, 40% ethyl acetate in petroleum ether); IR (film) ν_{max} 3081, 3048, 3016, 2949, 2194, 1757, 1712, 1599, 1488, 1206, 1125 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, *J* = 8.1 Hz, 1 H, aromatic), 7.36 (br s, 1 H, aromatic), 7.31–7.20 (m, 3 H, aromatic), 7.19–7.10 (m, 2 H, aromatic), 7.08–7.02 (m, 2 H, aromatic), 5.74 (d, *J* = 10.0 Hz, 1 H, olefinic), 5.59 (dd, *J* = 10.0, 1.4 Hz, 1 H, olefinic), 5.45 (br s, 1 H, NC*H*C≡C), 4.30 (d, *J* = 15.5 Hz, 1 H, CH_2COOCH_3), 4.21 (d, *J* = 15.5 Hz, 1 H, CH_2COOCH_3), 3.72 (s, 3 H, OCH_3), 2.25 (dd, *J* = 15.0, 8.2 Hz, 1 H, CH_2), 2.22–2.06 (m, 2 H, CH_2), 1.96–1.85 (m, 1 H, CH_2), 1.82 (br d, J = 12.5 Hz, 1 H, CH_2), 1.73–1.66 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7, 135.5, 130.8, 129.3, 129.2, 128.0, 127.6, 125.6, 125.6, 123.8, 122.4, 121.5, 98.3, 95.7, 93.9, 88.4, 79.8, 72.9, 63.0, 62.6, 52.0, 50.3, 29.2, 23.1, 18.9; MS (FAB$^+$) m/e (relative intensity) 614 (M + Cs, 100), 526 (13); HRMS for $C_{29}H_{23}NO_6Cs$ (M + Cs) calcd 614.0580, found 614.0574.

Compound 25. A solution of **23** (323 mg, 0.67 mmol) in THF (4 mL) was treated with 0.5 N lithium hydroxide (4 mL) at 0 °C for 0.5 h. Acidification with 5% aqueous hydrochloric acid, extraction with ethyl acetate (5 mL), and drying over $MgSO_4$ provided the corresponding crude acid **24** as a white foam. This material was immediately treated in CH_2Cl_2 (15 mL) with 2,2'-dipyridyl disulfide (266 mg, 1.26 mmol) and triphenylphosphine (330 mg, 1.26 mmol) at 0 °C for 0.5 h. The organic solvent was removed in vacuo, and the residue was purified by flash column chromatography (silica, 20% ethyl acetate in benzene) to give 368 mg (96%) of **25**: pale yellow foam; R_f = 0.45 (silica, 10% ethyl acetate in benzene); IR (film) ν_{max} 3051, 2950, 2200, 1721, 1571, 1451, 1420, 1378, 1320, 1278, 1202, 1115 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (br d, J = 4.0 Hz, 1 H, aromatic), 8.42 (br d, J = 7.9 Hz, 1 H, aromatic), 7.63 (td, J = 7.7, 1.3 Hz, 1 H, aromatic), 7.52–7.48 (d, J = 7.9 Hz, 1 H, aromatic), 7.38 (br s, 1 H, aromatic), 7.28–7.03 (m, 8 H, aromatic), 5.75 (d, J = 10.0 Hz, 1 H, olefinic), 5.59 (dd, J = 10.0, 0.8 Hz, 1 H, olefinic), 5.45 (br s, 1 H, NC*H*C≡C), 4.50 (d, J = 15.8 Hz, 1 H, CH_2COS), 4.37 (d, J = 15.8 Hz, 1 H, CH_2COS), 2.30–2.07 (m, 2 H, CH_2), 2.12 (dt, J = 17.0, 10.0 Hz, 1 H, CH_2), 1.98–1.88 (m, 2 H, CH_2), 1.75–1.68 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.8, 150.4, 149.3, 137.3, 137.2, 135.5, 130.6, 130.5, 129.2, 128.2, 128.0, 127.3, 126.3, 125.6, 125.6, 123.6, 122.6, 121.4, 121.0, 97.9, 96.1, 93.8, 88.4, 80.0, 73.1, 69.8, 62.9, 50.2, 29.2, 23.0, 18.9; MS (FAB$^+$) m/e (relative intensity) 693 (M + Cs, 100), 600 (30), 561 (12), 221 (29); HRMS for $C_{33}H_{24}N_2O_5SCs$ (M + Cs) calcd 693.0460, found 693.0467.

Compound 26. To a mixture of **25** (368 mg, 0.65 mmol) and sodium borohydride (260 mg, 6.7 mmol) in dichloromethane (10 mL) was added 2-propanol (10 mL) dropwise at 0 °C. After being stirred for 0.5 h, the reaction mixture was diluted with ethyl acetate (20 mL) and washed with saturated sodium bicarbonate (10 mL) and brine (10 mL). The organic layer was dried ($MgSO_4$) and evaporated in vacuo, and the residue was purified by flash column chromatography (silica, 10% ethyl acetate in benzene) to give 200 mg (68%) of **26**: R_f = 0.29 (silica, 40% ethyl acetate in petroleum ether); IR (film) ν_{max} 3504, 2939, 2187, 1721, 1595, 1490, 1458, 1379, 1321, 1203, 1148, 1107 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (dd, J = 8.1, 1.4 Hz, 1 H, aromatic), 7.36 (br s, 1 H, aromatic), 7.32–7.02 (m, 7 H, aromatic), 5.74 (d, J = 10.0 Hz, 1 H, olefinic), 5.58 (dd, J = 10.0, 1.7 Hz, 1 H, olefinic), 5.45 (br s, 1 H, NC*H*C≡C), 3.82–3.65 (m, 4 H, CH_2CH_2OH), 2.22 (dd, J = 15.0, 9.0 Hz, 1 H, CH_2), 2.22–2.07 (m, 3 H, CH_2, O*H*), 1.95–1.82 (m, 2 H, CH_2), 1.72–1.63 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.9, 135.9, 130.7, 129.3, 127.9, 127.9, 126.4, 125.7, 125.3, 123.9, 122.3, 121.5, 99.1, 95.6, 93.8, 88.5, 78.8, 73.1, 65.9, 63.3, 61.8, 50.3, 29.3, 23.2, 18.8; MS (FAB$^+$) m/e (relative intensity) 586 (M + Cs, 100), 552 (6), 434 (10); HRMS for $C_{28}H_{23}NO_5Cs$ (M + Cs) calcd 586.0631, found 586.0637.

Compound 27. A solution of **26** (200 mg, 0.44 mmol) in dichloromethane (8 mL) cooled at −78 °C was treated with 2,6-lutidine (0.16 mL, 1.34 mmol) and *tert*-butyldimethylsilyl triflate (0.23 mL, 1.01 mmol). The mixture was then allowed to warm to 0 °C over 1 h, diluted with ethyl ether (15 mL), washed with brine (10 mL), and dried ($MgSO_4$). The solvent was removed in vacuo, and the residue was purified by flash column chromatography (silica, 20% ethyl ether in petroleum ether) to give 252 mg (99%) of **27**: colorless foam; R_f = 0.37 (silica, 10% ethyl acetate in petroleum ether); IR (film) ν_{max} 3051, 2932, 2204, 1724, 1595, 1491, 1462, 1378, 1320, 1277, 1245, 1203, 1097 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (dd, J = 8.1, 1.2 Hz, 1 H, aromatic), 7.45 (br s, 1 H, aromatic), 7.40–7.12 (m, 7 H, aromatic), 5.83 (d, J = 10.0 Hz, 1 H, olefinic), 5.67 (dd, J = 10.0, 1.7 Hz, 1 H, olefinic), 5.54 (br s, 1 H, NC*H*C≡C), 3.94–3.72 (m, 4 H, CH_2CH_2OTBS), 2.33 (dd, J = 15.1, 8.6 Hz, 1 H, CH_2), 2.28–2.17 (m, 2 H, CH_2), 2.05–1.93 (m, 2 H, CH_2), 1.82–1.73 (m, 1 H, CH_2), 0.94 (s, 9 H, $SiC(CH_3)_3$), 0.12 (s, 6 H, $Si(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.0, 135.6, 131.2, 129.3, 128.1, 127.8, 126.3, 125.6, 125.4, 124.1, 122.1, 121.5, 99.7, 95.1, 93.9, 88.5, 78.8, 72.9, 66.4, 63.3, 62.4, 50.4, 29.3, 25.9, 23.3, 18.4, −5.2, −5.3; MS (FAB$^+$) m/e (relative intensity) 700 (M + Cs, 100); HRMS for $C_{34}H_{37}NO_5SiCs$ (M + Cs) calcd 700.1495, found 7006.1488.

Compound 28. Representative Procedure. To a suspension of NaH (60%, 16.0 mg, 0.40 mmol) in THF (1 mL) cooled at 0 °C was added 2-(phenylthio)ethanol (61.7 mg, 0.40 mmol) followed by stirring at 0 °C for 10 min. To the resultant solution cooled at 0 °C was added a solution of **20** (80.0 mg, 0.20 mmol) in THF (1 mL). After stirring at 0 °C for 5 min, the reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with ethyl acetate, washed with saturated brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography (silica, 15% ethyl acetate in benzene) to give 87.1 mg (96%) of **28**: pale yellow gum; R_f = 0.47 (silica, 40% ethyl ether in petroleum ether); IR ($CDCl_3$) ν_{max} 2920, 1710, 1350 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (dd, J = 8.0, 1.0 Hz, 1 H, aromatic), 7.42–7.16 (m, 8 H, aromatic), 5.57 (dd, J = 10.0, 1.5 Hz, 1 H, olefinic), 5.63 (dd, J = 10.0, 1.5 Hz, 1 H, olefinic), 5.41 (br s, 1 H, NC*H*), 4.40–4.15 (m, 2 H, SCH_2CH_2), 3.78 (two sets of br s, 1 H, C≡CC*H*CH_2), 3.15 (m, 2 H, SCH_2), 2.37 (dd, J = 15.0, 8.5 Hz, 1 H, CH_2), 2.20 (ddd, J = 15.5, 9.5, 9.5 Hz, 1 H, CH_2), 1.93 (m, 2 H, CH_2), 1.78 (dd, J = 13.0, 3.5 Hz, 1 H, CH_2), 1.58 (m, 1 H, CH_2); HRMS for $C_{28}H_{23}NO_3SCs$ (M + Cs) calcd 586.0453, found 586.0453.

Compound 29. Representative Procedure. A solution of **28** (16.6 mg, 0.0366 mmol) in CH_2Cl_2 cooled at 0 °C was treated with *m*-CPBA (6.9 mg, 0.0403 mmol) followed by stirring at 0 °C for 30 min. The reaction mixture was quenched with dimethyl sulfide, diluted with CH_2Cl_2 (30 mL), and washed with saturated aqueous $NaHCO_3$ (2 × 30 mL). The organic layer was dried over anhydrous Na_2SO_4, concentrated in vacuo, and purified by flash column chromatography (silica, 100% ethyl ether) to give 15.1 mg (86%) of **29**: pale yellow gum; R_f = 0.25 (silica, 100% ethyl ether); IR (film) ν_{max} 2930, 1713, 1494, 1392, 1321, 1272, 1230, 1048 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (m, 9 H, aromatic), 5.76 (d, J = 10.0 Hz, 1 H, olefinic), 5.64 (d, J = 10.0 Hz, 1 H, olefinic), 5.39 (br s, 1 H, NC*H*), 4.63–4.31 (m, 2 H, $SOCH_2CH_2$), 3.76 (s, 1 H, C≡CC*H*CH_2), 3.18–2.98 (m, 2 H, $SOCH_2$), 2.38 (dd, J = 15.0, 8.5 Hz, 1 H, CH_2), 2.22 (m, 1 H, CH_2), 1.96 (m, 2 H, CH_2), 1.79 (m, 1 H, CH_2), 1.59 (m, 1 H, CH_2); HRMS for $C_{28}H_{23}NO_4SCs$ (M + Cs) calcd 602.0402, found 602.0426.

Compound 12. Representative Procedure. A solution of **28** (126.0 mg, 0.278 mmol) in CH_2Cl_2 (3 mL) was treated with *m*-CPBA (119.0 mg, 0.695 mmol) at 0 °C followed by stirring at 25 °C for 30 min. The reaction mixture was quenched with dimethyl sulfide, diluted with CH_2Cl_2 (70 mL), and washed with saturated aqueous $NaHCO_3$ (2 × 70 mL). The organic layer was dried over anhydrous Na_2SO_4, concentrated in vacuo, and purified by flash column chromatography (silica, 70% ethyl ether in petroleum ether) to give 108.0 mg (80%) of **12**: colorless gum; R_f = 0.23 (silica, 70% ethyl ether in petroleum ether); IR ($CDCl_3$) ν_{max} 2975, 2950, 1715, 1360, 1300, 1150 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92–7.10 (m, 9 H, aromatic), 5.73 (dd, J = 10.0, 1.5 Hz, 1 H, olefinic), 5.63 (dd, J = 10.0, 1.0 Hz, 1 H, olefinic), 5.45–4.85 (br s, 1 H, NC*H*), 4.65–4.22 (m, 2 H, $SO_2CH_2CH_2$), 3.73 (br s, 1 H, C≡CC*H*CH_2), 3.60–3.36 (m, 2 H, SO_2CH_2), 2.34 (m, 1 H, CH_2), 2.18 (ddd, J = 15.5, 9.5, 9.5 Hz, 1 H, CH_2), 2.02–1.84 (m, 2 H, CH_2), 1.78 (m, 1 H, CH_2), 1.58 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.0, 129.3, 128.5, 128.1, 127.9, 127.1, 125.2, 124.8, 121.9, 101.7, 93.7, 91.2, 88.6, 70.1, 60.9, 59.3, 55.0, 49.4, 29.3, 32.1, 22.3, 15.6; HRMS for $C_{28}H_{23}NSO_5Cs$ (M + Cs) calcd 618.0351, found 618.0352.

Compound 30. Prepared in 90% yield in a similar manner as that described for **28**. **30**: pale yellow gum; R_f = 0.32 (silica, 40% ethyl ether in petroleum ether); IR (film) ν_{max} 2952, 1714 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (d, J = 8.3 Hz, 1 H, aromatic), 7.43–7.13 (m, 8 H, aromatic), 5.82 (d, J = 10.0 Hz, 1 H, olefinic), 5.66 (dd, J = 10.0, 2.0 Hz, 1 H, olefinic), 5.41 (br s, 1 H, NC*H*), 4.42–4.12 (m, 2 H, SCH_2CH_2), 3.47 (s, 3 H, OCH_3), 3.13 (m, 2 H, SCH_2), 2.38–1.68 (m, 6 H, CH_2); HRMS for $C_{29}H_{26}NO_4S$ (M + H) calcd 484.1582, found 484.1582.

Compound 31. Prepared in 90% yield in a similar manner as that described for **29**. **31**: pale yellow gum; R_f = 0.25 (silica, 100% ethyl ether); IR (film) ν_{max} 2929, 1711, 1492, 1393, 1321, 1276, 1242, 1090, 1090, 1048, 737 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36 (dd, J = 7.5, 2.5 Hz, 1 H, aromatic), 7.70–7.13 (m, 1 H, aromatic), 5.83 (d, J = 10.0 Hz, 1 H, olefinic), 5.65 (dd, J = 10.0, 2.0 Hz, 1 H, olefinic), 5.42 (br s, 1 H, NC*H*), 4.62–4.30 (m, 2 H, $SOCH_2CH_2$), 3.48 (s, 3 H, OCH_3), 3.18–2.85 (m, 2 H, $SOCH_2$), 2.30 (dd, J = 15.0, 8.5 Hz, 1 H, CH_2), 2.17 (m, 2 H, CH_2), 1.93 (m, 2 H, CH_2), 1.76 (m, 1 H, CH_2); HRMS for $C_{29}H_{25}NO_5SCs$ (M + Cs) calcd 632.0508, found 632.0494.

Compound 13. Prepared in 79% yield in a similar manner as that described for **12**. **13**: white crystalline solid, mp 183–184 °C (from CH_2Cl_2/petroleum ether); R_f = 0.26 (silica, 70% ethyl ether in petroleum ether); IR ($CDCl_3$) ν_{max} 2930, 1710, 1410, 1325, 1145 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36–7.00 (m, 9 H, aromatic), 5.81 (d, J = 10.0 Hz, 1 H, olefinic), 5.64 (d, J = 10.0 Hz, 1 H, olefinic), 5.47 (br s, 1 H, NC*H*), 4.55–4.42 (two sets of br singlets due to rotamers, 2 H, $SO_2CH_2CH_2$), 3.47 (br s, 5 H, OCH_3 and SO_2CH_2), 2.66 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.1, 130.8, 129.4, 127.9, 127.8, 126.2, 125.2, 123.9, 122.2, 99.3, 95.2, 93.8, 88.3, 79.2, 72.8, 59.3, 55.1, 52.0, 50.0, 28.2, 23.1, 18.8; HRMS for $C_{29}H_{26}NO_6S$ (M + H) calcd 516.1481, found 516.1470.

Compound 32. Prepared in 98% yield in a similar manner as that described for **28**. **32**: R_f = 0.17 (silica, 10% ethyl acetate in petroleum ether); IR (film) ν_{max} 3055, 2931, 2192, 1708, 1581, 1489, 1460, 1393, 1320, 1277, 1246, 1102, 1026 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.51 (br d, J = 7.2 Hz, 1 H, aromatic), 7.42 (br d, J = 7.5 Hz, 1 H, aromatic), 7.40–7.26 (m, 5 H, aromatic), 7.25–7.16 (m, 2 H, aromatic), 5.82 (d, J = 10.0 Hz, 1 H, olefinic), 5.66 (dd, J = 10.0, 1.2 Hz, 1 H, olefinic), 5.46 (br s, 1 H, NCH*C*≡C), 4.39 (dt, J = 11.0, 7.1 Hz, 1 H, OC*H*$_2$CH$_2$SPh), 4.25 (br s, 1 H, OC*H*$_2$CH$_2$SPh), 3.92–3.69 (m, 4 H, C*H*$_2$C*H*$_2$OTBS), 3.24–3.10 (m, 2 H, CH$_2$C*H*$_2$SPh), 2.30 (dd, J = 15.0, 8.2 Hz, 1 H, C*H*$_2$), 2.26–2.13 (m, 2 H, C*H*$_2$), 2.23–1.92 (m, 2 H, C*H*$_2$), 1.79–1.73 (m, 1 H, C*H*$_2$), 0.95 (s, 9 H, SiC(C*H*$_3$)$_3$), 0.12 (s, 6 H, Si(C*H*$_3$)$_2$); ^{13}C NMR (125 MHz, CDCl$_3$) δ 154.5, 135.7, 134.9, 131.1, 129.9, 129.0, 127.9, 127.6, 126.5, 126.1, 125.0, 123.9, 122.1, 99.7, 94.9, 94.1, 88.3, 78.8, 73.0, 66.3, 64.6, 62.4, 62.4, 50.0, 32.3, 29.2, 25.9, 23.3, 18.8, –5.2, –5.3; MS (FAB$^+$) m/e (relative intensity) 760 (M + Cs, 100); HRMS for $C_{36}H_{41}NO_5SiSCs$ (M + Cs) calcd 760.1529, found 760.1529.

Compound 33. A solution of **32** (320 mg, 0.51 mmol) in THF (10 mL) was treated with tetra-*n*-butylammonium fluoride (0.87 mL, 1.0 M solution in THF, 0.87 mmol) at 0 °C for 0.5 h. The solvent was evaporated in vacuo, and the residue was purified by flash column chromatography (silica, 20% ethyl acetate in benzene) to give 252 mg (96%) of **33**: white foam; R_f = 0.63 (silica, 30% ethyl acetate in benzene); IR (film) ν_{max} 3482, 3055, 2936, 2198, 1705, 1581, 1490, 1455, 1395, 1321, 1278, 1108, 1060 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.29 (dd, J = 8.1, 1.2 Hz, 1 H, aromatic), 7.35–7.07 (m, 8 H, aromatic), 5.72 (d, J = 10.0 Hz, 1 H, olefinic), 5.57 (dd, J = 10.0, 1.7 Hz, 1 H, olefinic), 5.38 (br s, 1 H, NCH*C*≡C), 4.29 (dt, J = 11.0, 7.2 Hz, 1 H, PhSCH$_2$C*H*$_2$O), 4.14 (br s, 1 H, PhSCH$_2$C*H*$_2$O), 3.82–3.71 (m, 3 H, C*H*$_2$C*H*$_2$OH), 3.68–3.62 (m, 1 H, C*H*$_2$CH$_2$OH), 3.14–3.00 (m, 2 H, PhSC*H*$_2$), 2.21 (dd, J = 14.8, 7.8 Hz, 1 H, C*H*$_2$), 2.18–2.04 (m, 2 H, C*H*$_2$), 2.00 (br s, 1 H, O*H*), 1.92–1.82 (m, 2 H, C*H*$_2$), 1.72–1.63 (m, 1 H, C*H*$_2$); ^{13}C NMR (125 MHz, CDCl$_3$) δ 154.5, 135.8, 134.9, 130.6, 129.9, 129.9, 129.1, 127.8, 126.6, 126.4, 125.0, 123.7, 122.3, 99.1, 95.6, 94.1, 88.3, 78.8, 73.3, 65.9, 64.6, 63.2, 61.9, 50.0, 32.3, 29.3, 23.3, 18.9; MS (FAB$^+$) m/e (relative intensity) 646 (M + Cs, 100), 539 (12); HRMS for $C_{30}H_{27}NO_5SCs$ (M + Cs) calcd 646.0664, found 646.0651.

Compound 14. Prepared in 82% yield in a similar manner as that described for **12**. **14**: R_f = 0.30 (silica, 30% ethyl acetate in benzene); IR (film) ν_{max} 3519, 2932, 2188, 1710, 1492, 1450, 1400, 1320, 1290, 1145, 1108, 1068 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.28–8.22 (m, 1 H, aromatic), 7.82–7.74 (m, 2 H, aromatic), 7.53–7.37 (m, 3 H, aromatic), 7.15–7.00 (m, 3 H, aromatic), 5.68 (dd, J = 10.0, 5.0 Hz, 1 H, olefinic), 5.54–5.49 (m, 1 H, olefinic), 5.20 (br s, 1 H, NCH*C*≡C), 4.46–4.38 (m, 1 H, OC*H*$_2$CH$_2$SO$_2$Ph), 4.37–4.27 (m, 1 H, OC*H*$_2$CH$_2$SO$_2$Ph), 3.78–3.60 (m, 4 H, C*H*$_2$C*H*$_2$OH), 3.40–3.12 (m, 2 H, CH$_2$C*H*$_2$SO$_2$Ph), 2.22–2.18 (m, 4 H, C*H*$_2$, O*H*), 1.90–1.78 (m, 2 H, C*H*$_2$), 1.67–1.60 (m, 1 H, C*H*$_2$); ^{13}C NMR (125 MHz, CDCl$_3$) δ 154.1, 138.8, 135.4, 134.0, 133.3, 130.6, 129.4, 128.3, 127.9, 127.8, 125.2, 123.8, 122.3, 98.9, 95.6, 93.8, 88.4, 78.7, 73.1, 65.9, 63.2, 61.9, 59.4, 55.1, 50.0, 29.3, 23.1, 18.8; MS (FAB$^+$) m/e (relative intensity) 678 (M + Cs, 100); HRMS for $C_{30}H_{27}NO_7SCs$ (M + Cs) calcd 678.0563, found 678.0563.

Compound 35. A solution of **13** (30.0 mg, 0.058 mmol) in benzene (0.5 mL) was treated with DBU (10.6 mg, 0.069 mmol) at 5 °C for 30 min. The reaction mixture was diluted with CH$_2$Cl$_2$ (40 mL), washed with saturated aqueous NaHCO$_3$ (40 mL), dried over anhydrous Na$_2$SO$_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (silica, 50 → 60% ethyl ether in petroleum ether) to give 17.0 mg (97%) of **35**: crystalline solid, mp > 300 °C; R_f = 0.61 (silica, 70% ethyl ether in petroleum ether); IR (CDCl$_3$) ν_{max} 3400, 2950, 2850, 1100, 1080 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.32 (d, J = 7.3 Hz, 1 H, aromatic), 7.11 (dd, J = 7.3, 7.3 Hz, 1 H, aromatic), 6.82 (dd, J = 7.3, 7.3 Hz, 1 H, aromatic), 6.55 (d, J = 7.3 Hz, 1 H, aromatic), 5.83 (d, J = 8.8 Hz, 1 H, olefinic), 5.73 (dd, J = 8.8, 1.7 Hz, 1 H, olefinic), 4.32 (d, J = 1.7 Hz, 1 H, NC*H*), 4.00 (br s, 1 H, N*H*), 3.50 (s, 3 H, OC*H*$_3$), 2.36–1.68 (m, 6 H, C*H*$_2$); ^{13}C NMR (125 MHz, CDCl$_3$) δ 142.2, 131.0, 128.3, 123.1, 122.5, 122.0, 119.3, 115.9, 100.2, 96.9, 94.6, 87.3, 79.6, 72.9, 62.9, 29.0, 24.6, 19.0; HRMS for $C_{20}H_{17}NO_2$ (M$^+$) calcd 303.1337, found 303.1348.

Trapping of Free Amino Epoxide 34 with Nucleophiles. Compound 36. Representative Procedure. A solution of **12** (9.5 mg, 0.0196 mmol) in a 4:1 mixture of dioxane/water (1 mL) was treated with Cs$_2$CO$_3$ (19.0 mg, 0.059 mmol) and 18-crown-6 (3.1 mg, 0.012 mmol) at 0 °C followed by stirring at 25 °C for 1 h to generate a crude solution of **34** (high yield as checked by TLC). Phenol (3.7 mg, 0.039 mmol) was added to the above solution, and stirring was continued for another 2 h at 25 °C. The reaction mixture was diluted with ethyl acetate (50 mL), washed with saturated aqueous NaHCO$_3$ (1 × 50 mL), dried over anhydrous Na$_2$SO$_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (silica, 40 → 60% ethyl ether in petroleum ether) to give 2.5 mg (25%) of **36**: R_f = 0.35 (silica, 70% ethyl ether in petroleum ether); IR (CDCl$_3$) ν_{max} 3250, 3400, 2940 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.31 (dd, J = 7.5, 1.5 Hz, 1 H, aromatic), 7.16 (m, 3 H, aromatic), 7.05 (m, 2 H, aromatic), 6.98 (ddd, J = 7.5, 7.5, 1.5 Hz, 1 H, aromatic), 6.93 (d, J = 7.5 Hz, 1 H, aromatic), 6.80 (m, 3 H, aromatic), 6.72 (ddd, J = 7.5, 7.5, 1.0 Hz, 1 H, aromatic), 6.46 (dd, J = 8.0, 1.0 Hz, 1 H, aromatic), 4.17 (br s, 1 H, O*H* or N*H*, exchangeable with D$_2$O), 4.12 (s, 1 H, NC*H*), 3.60 (s, 1 H, O*H* or N*H*, exchangeable with D$_2$O), 3.55 (dd, J = 3.0, 3.0 Hz, 1 H, C≡CC*H*CH$_2$), 2.65 (dddd, J = 13.0, 13.0, 4.5, 4.5 Hz, 1 H, C*H*$_2$), 2.30 (ddd, J = 14.0, 14.0, 6.5 Hz, 1 H, C*H*$_2$), 1.70 (dd, J = 14.0, 5.0 Hz, 1 H, C*H*$_2$), 1.50 (m, 1 H, C*H*$_2$), 1.38 (m, 1 H, C*H*$_2$), 0.90 (m, 1 H, C*H*$_2$); HRMS for $C_{25}H_{23}NO_2Cs$ (M + Cs) calcd 502.0783, found 502.0772.

Compound 37. Prepared in 33% yield from **12** and thiophenol in a similar manner as that described for **36**. **37**: R_f = 0.40 (silica, 70% ethyl ether in petroleum ether); IR (CDCl$_3$) ν_{max} 3450, 3390, 3070, 2930, 2870, 1490, 1470 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.63 (d, J = 7.5 Hz, 1 H, aromatic), 7.35 (m, 2 H, aromatic), 7.18 (d, J = 7.0 Hz, 1 H, aromatic), 7.14 (t, J = 7.0 Hz, 1 H, aromatic), 7.09 (t, J = 7.0 Hz, 1 H, aromatic), 7.03 (m, 3 H, aromatic), 6.87 (d, J = 7.0 Hz, 1 H, aromatic), 6.80 (t, J = 7.0 Hz, 1 H, aromatic), 6.61 (t, J = 7.0 Hz, 1 H, aromatic), 6.31 (d, J = 7.5 Hz, 1 H, aromatic), 4.12 (two sets of singlets, 2 H, N*H* and NC*H*), 3.73 (s, 1 H, O*H*), 3.62 (t, J = 2.8 Hz, 1 H, ArC*H*CH$_2$), 2.80 (ddd, J = 12.8, 12.8, 5.6 Hz, 1 H, C*H*$_2$), 2.41 (dddd, J = 12.8, 12.8, 4.5, 4.5 Hz, 1 H, C*H*$_2$), 1.75 (dd, J = 13.2, 4.9 Hz, 1 H, C*H*$_2$), 1.54 (m, 1 H, C*H*$_2$), 1.39 (br d, J = 13.2 Hz, 1 H, C*H*$_2$), 0.90 (m, 1 H, C*H*$_2$); ^{13}C NMR (125 MHz, CDCl$_3$) δ 141.6, 139.2, 137.1, 135.1, 133.7, 130.6, 128.1, 127.8, 127.4, 127.0, 126.8, 126.4, 119.9, 115.8, 70.4, 62.1, 55.6, 33.3, 29.8, 28.0, 18.8; HRMS for $C_{25}H_{23}NOS$ (M$^+$) calcd 385.1500, found 385.1500.

Acid-Induced Bergman Cycloaromatization of Free Amino Epoxide 35. Compound 38. A solution of **35** (10.0 mg, 0.033 mmol) in a 4:1:1 mixture of dioxane, water, and 1,4-cyclohexadiene (0.5 mL) was treated with TsOH·H$_2$O (3.1 mg, 0.016 mmol) at 60 °C for 5 min. The reaction mixture was diluted with ethyl acetate, washed with saturated aqueous NaHCO$_3$, dried over anhydrous Na$_2$SO$_4$, and concentrated in vacuo. The residue was purified by flash column chromatography (silica, 5 → 10% ethyl ether in petroleum ether) to give 2.1 mg (20%) of **38**: yellowish gum; R_f = 0.37 (silica, 70% ethyl ether in petroleum ether); IR (film) ν_{max} 3380, 29234, 2854, 1082 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.63 (dd, J = 8.0, 1.5 Hz, 1 H, aromatic), 7.39 (m, 1 H, aromatic), 7.19 (m, 3 H, aromatic), 6.89 (ddd, J = 7.5, 7.5, 1.5 Hz, 1 H, aromatic), 6.38 (dd, J = 8.0, 1.0 Hz, 1 H, aromatic), 4.16 (s, 1 H, NC*H*), 3.90 (s, 3 H, OC*H*$_3$), 3.66 (s, 1 H, O*H* or N*H*, exchangeable with D$_2$O), 2.78 (s, 1 H, O*H* or N*H*, exchangeable with D$_2$O), 2.75 (ddd, J = 13.0, 13.0, 4.5 Hz, 1 H, C*H*$_2$), 2.30 (m, 1 H, C*H*$_2$), 2.23 (ddd, J = 14.0, 14.0, 6.5 Hz, 1 H, C*H*$_2$), 2.0 (m, 1 H, C*H*$_2$), 1.57 (m, 1 H, C*H*$_2$), 1.65 (dd, J = 13.5, 5.0 Hz, 1 H, C*H*$_2$); HRMS for $C_{20}H_{21}NO_3Cs$ (M + Cs) calcd 456.0576, found 456.0603.

Cobalt Complex 40. A solution of **39**[13] (10.1 mg, 0.012 mmol) in benzene (0.5 mL) was treated with SiO$_2$ (0.25 g) followed by stirring at 25 °C for 1 h. The reaction mixture was filtered through Celite and concentrated in vacuo to give a residue which was purified by flash column chromatography (silica, 1 → 2.5% ethyl acetate in benzene) to give 8.9 mg (90%) of **40**: green solid, mp > 300 °C (from CH$_2$Cl$_2$); R_f = 0.72 (silica, 10% ethyl ether in petroleum ether); IR (CDCl$_3$) ν_{max} 2870, 2830, 2080, 2060, 2025 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.95 (d, J = 8.5 Hz, 1 H, aromatic), 7.93 (d, J = 8.0 Hz, 1 H, aromatic), 7.61 (dd, J = 8.0, 8.0 Hz, 1 H, aromatic), 7.49 (dd, J = 8.0, 8.0 Hz, 1 H, aromatic), 6.42 (s, 2 H, olefinic), 4.83 (d, J = 7.0 Hz, 1 H, C*H*CH$_2$), 3.51 (br s, 1 H, N*H*), 3.31 (ddd, J = 17.0, 12.5, 6.0 Hz, 1 H, C*H*$_2$), 2.94 (ddd, J = 17.0, 6.0, 2.2 Hz, 1 H, C*H*$_2$), 2.74 (m, 1 H, C*H*$_2$), 2.41 (m, 1 H, C*H*$_2$), 1.65 (m, 1 H, C*H*$_2$); ^{13}C NMR (125 MHz, CDCl$_3$) δ 200.0, 199.5, 199.0, 198.0, 156.1, 146.8, 144.4, 136.4, 129.3, 128.8, 128.0, 125.9, 124.9, 124.2, 108.4, 91.0, 88.2, 84.0, 42.2, 32.6, 28.5, 19.5; MS (FAB$^+$) m/e (relative intensity) 960 (40), 771 (46), 687 (46), 659 (58), 631 (100), 603 (40), 575 (28), 547 (49), 519 (21), 491 (12); HRMS for $C_{31}H_{15}NO_{13}Co_4Cs$ (M + Cs) calcd 959.6820, found 959.6887.

Cobalt Complex 41. A solution of **40** (8.9 mg, 0.0108 mmol) in toluene (0.5 mL) was treated with bis(diphenylphosphino)methane (41.4 mg, 0.108 mmol) followed by stirring at 80 °C for 5 h. The reaction mixture was concentrated in vacuo, and the residue was purified by flash column chromatography (silica, 10 → 20% ethyl ether in petroleum ether) to give 12.2 mg (76%) of **41**: green solid, mp > 300 °C dec (from CH$_2$Cl$_2$/petroleum ether); R_f = 0.31 (silica, 30% ethyl ether in petroleum ether); IR (CDCl$_3$) ν_{max} 2927, 2002, 1963 cm^{-1}; MS (FAB$^+$) m/e (relative intensity) 1484 (30), 1456 (37), 1428 (32), 1399 (23), 1372 (31), 1344 (23), 1316 (49), 1288 (100), 1260 (50), 1201 (23); HRMS for $C_{77}H_{57}NO_8P_4Co_4$ (M$^+$) calcd 1484.0441, found 1484.0500.

2-Acetoxy-7,8,9,10-tetrahydrophenanthridine (47). A mixture of 2-methoxy-7,8,9,10-tetrahydrophenanthridine (**46**, 48.17 g, 226 mmol) and sodium ethanethiolate (43.69 g, 520 mmol) in dry DMF was heated at 160 °C for 4 h. After the reaction mixture was cooled to 0 °C, acetic anhydride (63.9 mL, 678 mmol) was added and the reaction mixture was stirred for 30 min. The resulting thick white slurry was poured into 0.1 M (pH 7.5) phosphate buffer (1.6 L) and extracted with ethyl ether (3 × 400 mL). The combined organic layers were washed with water (3 × 300 mL) and brine (300 mL), dried ($MgSO_4$), filtered through a 3 × 3 cm plug of silica, and evaporated in vacuo. The residue was purified by recrystallization from ethyl acetate/hexanes to give 45.70 g (86%) of **47**: white crystalline solid, mp 118–119 °C; R_f = 0.39 (silica, 50% ethyl acetate in dichloromethane); IR ($CHCl_3$) ν_{max} 3018, 2938, 2861, 1758, 1507, 1369, 1193, 1174 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.60 (s, 1 H, H6), 8.06 (d, J = 9.0 Hz, 1 H, H4), 7.61 (d, J = 2.5 Hz, 1 H, H1), 7.36 (dd, J = 9.0, 2.5 Hz, 1 H, H3), 3.03 (t, J = 6.0 Hz, 2 H, H7 or H10), 2.89 (t, J = 6.0 Hz, 2 H, H7 or H10), 2.37 (s, 3 H, $OCOCH_3$), 1.98–1.86 (m, 4 H, H8 and H9); ^{13}C NMR (125 Mz, $CDCl_3$) δ 169.5, 152.3, 148.4, 144.3, 140.9, 131.3, 130.1, 128.0, 122.9, 113.8, 27.0, 24.8, 22.2, 22.1, 21.1; MS (FAB$^+$) m/e (relative intensity) 242 (M + H, 100), 200 (25); HRMS for $C_{15}H_{16}NO_2$ (M + H) calcd 242.1181, found 242.1181. Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.80. Found: C, 74.66; H, 6.37; N, 5.64.

2-Hydroxy-7,8,9,10-tetrahydrophenanthridine (48). To a solution of **47** (26.50 g, 110 mmol) in dry methanol (150 mL) were added Dowex 1×8-200 in the hydroxide form (0.40 g, catalytic) and tetra-n-butylammonium bromide (50 mg, catalytic), and the resulting mixture was stirred at 60 °C for 24 h. The reaction mixture was cooled, diluted with ethyl ether (100 mL), and filtered to give 21.47 g (98%) of **48**: white crystalline solid, mp 284–286 °C dec; R_f = 0.25 (silica, 50% ethyl acetate in dichloromethane); IR ($CHCl_3$) ν_{max} 2933, 2906, 2850, 2582, 1627, 1503, 1421 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 9.92 (s, 1 H, OH), 8.34 (s, 1 H, H6), 7.77 (d, J = 9.0 Hz, 1 H, H4), 7.19 (dd, J = 9.0, 2.6 Hz, 1 H, H3), 7.12 (d, J = 2.6 Hz, 1 H, H1), 2.88 (t, J = 6.1 Hz, 2 H, H7 or H10), 2.78 (t, J = 6.1 Hz, 2 H, H7 or H10), 1.87–1.74 (m, 4 H, H8 and H9); ^{13}C NMR (125 MHz, DMSO-d_6) δ 155.5, 148.8, 141.1, 138.5, 130.9, 129.4, 128.4, 120.0, 104.0, 26.5, 24.3, 22.1, 21.9; MS (FAB$^+$) m/e (relative intensity) 200 (M + H, 100), 124 (8), 107 (14); HRMS for $C_{13}H_{14}NO$ (M + H) calcd 200.1075, found 200.1079. Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.49; H, 6.88; N, 7.00.

2-[(2-Nitrobenzyl)oxy]-7,8,9,10-tetrahydrophenanthridine (49). A mixture of **48** (57.17 g, 287 mmol), 2-nitrobenzyl bromide (68.19 g, 316 mmol), powdered potassium carbonate (142.0 g, 1.03 mol), and tetra-n-butylammonium iodide (3.18 g, 8.61 mmol) in dry DMF (400 mL) was stirred at 25 °C for 3 h and then poured into a mixture of ethyl ether (200 mL), dichloromethane (1500 mL), and water (200 mL) with stirring. After this mixture was allowed to settle, the aqueous layer was discarded. The organic layer was washed with water (3 × 1500 mL), dried ($MgSO_4$), and filtered through an 8 × 8 cm plug of silica, rinsing with ethyl ether (300 mL). The combined filtrates were evaporated in vacuo, and the residue was purified by recrystallization from chloroform/ethyl ether to give 90.41 g (94%) of **49**: off-white crystalline solid, mp 153–154 °C; R_f = 0.48 (silica, 40% ethyl acetate in dichloromethane); IR ($CHCl_3$) ν_{max} 2939, 1619, 1526, 1508, 1433, 1342 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.50 (s, 1 H, H6), 8.19 (dd, J = 7.4, 1.0 Hz, 1 H, aromatic), 7.99 (d, J = 9.1 Hz, 1 H, H4), 7.97 (dd, J = 7.4, 1.0 Hz, 1 H, aromatic), 7.71 (td, J = 7.4, 1.0 Hz, 1 H, aromatic), 7.52 (td, J = 7.4, 1.0 Hz, 1 H, aromatic), 7.39 (dd, J = 9.1, 2.8 Hz, 1 H, H3), 7.24 (d, J = 2.8 Hz, 1 H, H1), 5.61 (s, 2 H, benzylic), 2.99 (t, J = 6.1 Hz, 2 H, H7 or H10), 2.88 (t, J = 6.1 Hz, 2 H, H7 or H10), 2.01–1.84 (m, 4 H, H8 and H9); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 150.3, 146.9, 142.4, 140.0, 134.0, 133.9, 133.4, 131.5, 130.1, 128.5, 128.4, 124.9, 119.8, 102.7, 66.7, 27.1, 24.9, 22.3, 22.2; MS (FAB$^+$) m/e (relative intensity) 335 (M + H, 100), 200 (13); HRMS for $C_{20}H_{19}N_2O_3$ (M + H) calcd 335.1396, found 335.1394. Anal. Calcd for $C_{20}H_{18}N_2O_3$: C, 71.84; H, 5.43; N, 8.38. Found: C, 71.45; H, 5.62; N, 8.01.

2-[[(Trifluoromethyl)sulfonyl]oxy]-7,8,9,10-tetrahydrophenanthridine (50). To a solution of **48** (23.6 g, 118.4 mmol) in dry pyridine (236 mL) was added trifluoromethanesulfonic anhydride (24.0 mL, 142.1 mmol) at −30 °C over 15 min. After being stirred at 0 °C for 24 h, the mixture was diluted with dichloromethane (800 mL) and washed with saturated aqueous sodium bicarbonate (400 mL × 2), saturated aqueous copper sulfate (400 mL × 3), and brine (400 mL). The organic layer was dried (Na_2SO_4) and evaporated in vacuo, and the residue was purified by flash column chromatography (silica, 10% ethyl acetate in dichloromethane) to give 40.7 g (100%) of **50**: white crystalline solid, mp 80–81 °C (from ethyl ether/petroleum ether); R_f = 0.39 (silica, 10% ethyl acetate in dichloromethane); IR (film) ν_{max} 2934, 2865, 1614, 1597, 1504, 1416, 1208, 1004, 928 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.65 (s, 1 H, H6), 8.11 (d, J = 9.2 Hz, 1 H, H4), 7.78 (d, J = 2.7 Hz, 1 H, H1), 7.49 (dd, J = 9.2, 2.7 Hz, 1 H, H3), 3.04 (t, J = 6.2 Hz, 2 H, H10), 2.89 (t, J = 6.2 Hz, 2 H, H7), 2.00–1.93 (m, 2 H, CH_2), 1.92–1.87 (m, 2 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.7, 147.1, 145.1, 141.4, 132.6, 131.3, 128.0, 121.3, 117.5, 114.7, 27.0, 24.8, 22.0, 21.9; MS (FAB$^+$) m/e (relative intensity) 332 (M + H, 100), 199 (13), 171 (8), 133 (7); HRMS for $C_{14}H_{13}F_3NO_3S$ (M + H) calcd 332.0568, found 332.0568.

2-[3-[(*tert*-Butyldiphenylsilyl)oxy]propynyl]-7,8,9,10-tetrahydrophenanthridine (52). To a mixture of **50** (1.28 g, 3.86 mmol), 3-[(*tert*-butyldiphenylsilyl)oxy]propyne (**51**, 1.48 g, 5.02 mmol), and diethylamine (800 μL, 7.73 mmol) in dry degassed N,N-dimethylformamide (7.7 mL) was added copper(I) iodide (74 mg, 0.39 mmol), followed by bis(triphenylphosphine)palladium(II) chloride (135 mg, 0.19 mmol). After being stirred in the dark for 11 h under argon, the mixture was diluted with ethyl acetate (50 mL) and washed with saturated aqueous sodium bicarbonate (20 mL × 2) and brine (20 mL). The organic layer was dried (Na_2SO_4) and evaporated in vacuo, and the residue was purified by flash column chromatography (silica, 10% ethyl ether in dichloromethane) to give 1.78 g (97%) of **52**: R_f = 0.39 (silica, 10% ethyl acetate in dichloromethane); IR (film) ν_{max} 3048, 2932, 2857, 2227, 1589, 1568, 1502, 1428, 1370, 1112 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.59 (s, 1 H, H6), 7.95 (d, J = 8.6 Hz, 1 H, H4), 7.92 (d, J = 1.5 Hz, 1 H, H1), 7.84–7.78 (m, 4 H, aromatic), 7.53 (dd, J = 8.6, 1.5 Hz, 1 H, H3), 7.48–7.39 (m, 6 H, aromatic), 4.62 (s, 2 H, C≡CCH_2O), 3.04 (t, J = 5.8 Hz, 2 H, H10), 2.87 (t, J = 5.8 Hz, 2 H, H7), 2.01–1.93 (m, 2 H, CH_2), 1.93–1.85 (m, 2 H, CH_2), 1.12 (s, 9 H, t-Bu); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.8, 145.6, 141.0, 135.6, 133.1, 130.6, 130.2, 129.7, 129.6, 127.6, 127.5, 127.2, 120.7, 88.4, 85.3, 53.2, 27.0, 26.7, 24.8, 22.2, 22.1, 19.2; MS (FAB$^+$) m/e (relative intensity) 476 (M + H, 100), 418 (9), 388 (12), 220 (11), 197 (9); HRMS for $C_{32}H_{34}NOSi$ (M + H) calcd 476.2410, found 476.2410.

2-Methoxy-7,8,9,10-tetrahydrophenanthridine *N*-Oxide (53a). Representative Procedure. To a solution of **46** (91.80 g, 430 mmol) in dichloromethane (500 mL) cooled at 0 °C was added a solution of m-CPBA (55%, 161.7 g, 516 mmol) in dichloromethane (900 mL), and the resulting mixture was stirred at 25 °C for 1 h. Dimethyl sulfide (6.95 mL, 94.6 mmol) was added, and stirring was continued for 15 min followed by addition of saturated aqueous sodium bicarbonate solution (1000 mL). The organic layer was separated, and the aqueous layer was extracted with dichloromethane (500 mL). The combined organic layers were dried ($MgSO_4$), filtered through a 3 × 3 cm plug of silica, and evaporated in vacuo. The residue was purified by recrystallization from benzene/cyclohexane to give a total of 88.34 g (90%) of the N-oxide **53**: off-white crystalline solid, mp 167–169 °C; R_f = 0.31 (silica, 20% methanol in ethyl acetate); IR ($CHCl_3$) ν_{max} 2943, 1617, 1512, 1459, 1428, 1379, 1108 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.65 (d, J = 9.5 Hz, 1 H, H4), 8.18 (s, 1 H, H6), 7.30 (dd, J = 9.5, 2.6 Hz, 1 H, H3), 7.10 (d, J = 2.6 Hz, 1 H, H1), 2.95 (t, J = 6.2 Hz, 2 H, H10), 2.77 (t, J = 6.2 Hz, 2 H, H7), 1.99–1.94 and 1.89–1.85 (m, 2 H each, H8 and H9); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1, 134.8, 134.3, 131.4, 130.8, 121.7, 120.3, 101.8, 55.5, 27.0, 24.7, 22.1, 21.8; MS (FAB$^+$) m/e (relative intensity) 230 (M + H, 100), 213 (10); HRMS for $C_{14}H_{16}NO_2$ (M + H) calcd 230.1181, found 230.1194. Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.00; H, 6.51; N, 6.46.

2-[(2-Nitrobenzyl)oxy]-7,8,9,10-tetrahydrophenanthridine *N*-Oxide (53b). Prepared in 87% yield in same manner as described for **53a**. **53b**: off-white crystalline solid, mp 181–181.5 °C (from chloroform/ethyl acetate/ethyl ether); IR ($CHCl_3$) ν_{max} 2944, 1616, 1526, 1432, 1383 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.70 (d, J = 9.5 Hz, 1 H, H4), 8.19 (dd, J = 7.7, 1.2 Hz, 1 H, aromatic), 8.19 (s, 1 H, H6), 7.93 (dd, J = 7.7, 1.2 Hz, 1 H, aromatic), 7.72 (td, J = 7.7, 1.2 Hz, 1 H, aromatic), 7.53 (td, J = 7.7, 1.2 Hz, 1 H, aromatic), 7.41 (dd, J = 9.5, 2.6 Hz, 1 H, H3), 7.23 (d, J = 2.6 Hz, 1 H, H1), 5.59 (s, 2 H, benzylic), 2.92 (t, J = 6.3 Hz, 2 H, H7 or H10), 2.77 (t, J = 6.3 Hz, 2 H, H7 or H10), 1.99–1.85 (m, 4 H, H8 and H9); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.6, 146.8, 135.2, 134.7, 134.1, 132.7, 131.4, 131.1, 130.8, 128.6, 128.5, 125.0, 122.1, 120.3, 103.5, 66.9, 27.1, 24.7, 22.1, 21.8; MS (FAB$^+$) m/e (relative intensity) 351 (M + H, 100), 335 (8), 216 (7), 124 (6), 107 (10); HRMS for $C_{20}H_{19}N_2O_4$ (M + H) calcd 351.1345, found 351.1345. Anal. Calcd for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.32; H, 5.13; N, 7.88.

2-[3-[(*tert*-Butyldiphenylsilyl)oxy]propynyl]-7,8,9,10-tetrahydrophenanthridine *N*-Oxide (53c). Prepared in 91% yield in same manner as described for **53a**. **53c**: R_f = 0.61 (silica, 15% methanol in ethyl acetate); IR (film) ν_{max} 3070, 2932, 2857, 2232, 1588, 1568, 1428, 1372, 1301, 1237, 1112 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, J = 8.9 Hz, 1 H, H4), 8.27 (s, 1 H, H6), 7.87 (br s, 1 H, H1), 7.80–7.74 (m, 4 H, aromatic), 7.52 (br d, J = 8.9 Hz, 1 H, H3), 7.46–7.38 (m, 6 H, aromatic) 4.59 (s, 2 H, C≡CCH_2O), 2.96 (t, J = 6.2 Hz, 2 H, H10), 2.77 (t, J = 6.2 Hz, 2 H, H7), 2.00–1.91 (m, 2 H, CH_2), 1.91–1.84 (m, 2 H, CH_2), 1.09 (s, 9 H, *t*-Bu); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.6, 136.6, 135.6, 132.9, 132.2, 131.5, 131.0, 129.8, 129.2, 127.7, 126.5, 123.3, 120.2, 90.0, 84.3, 53.0, 27.0, 26.6, 24.6, 22.0, 21.9, 19.1; MS (FAB^+) *m/e* (relative intensity) 492 (M + H, 100), 434 (12), 404 (21), 388 (11), 197 (13); HRMS for $C_{32}H_{34}NO_2Si$ (M + H) calcd 492.2359, found 492.2364.

10-Acetoxy-2-methoxy-7,8,9,10-tetrahydrophenanthridine (54a). Representative Procedure. A mixture of the *N*-oxide **53a** (10.00 g, 43.4 mmol) and acetic anhydride (150 mL) was heated at 70 °C for 1 h and then evaporated in vacuo to dryness. The residue was dissolved in dichloromethane (700 mL) and saturated aqueous sodium bicarbonate (400 mL) was added. After the mixture was stirred for 15 min, the aqueous layer was separated and extracted with dichloromethane (2 × 200 mL). The combined organic extracts were washed with brine (400 mL), dried ($MgSO_4$), and filtered through a 3 × 3 cm plug of silica. The silica plug was rinsed with a 1:1 mixture of dichloromethane/ethyl acetate (400 mL). The combined filtrates were concentrated in vacuo, and the residue was dissolved in methanol (50 mL). After standing in the refrigerator at 0 °C for 15 h, the crystalline precipitate was filtered and washed with ice-cooled methanol (30 mL) to give, after drying under vacuum (0.02 Torr, 20 h), the acetate **54a** (6.73 g, 57%): white crystalline solid, mp 116.5–117 °C; R_f = 0.48 (silica, ethyl ether); IR ($CHCl_3$) ν_{max} 2935, 1725, 1647, 1620, 1506 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (s, 1 H, H6), 7.97 (d, *J* = 9.1 Hz, 1 H, H4), 7.30 (dd, *J* = 9.1, 2.7 Hz, 1 H, H3), 7.09 (d, *J* = 2.7 Hz, 1 H, H1), 6.60 (br s, 1 H, H10), 3.88 (s, 3 H, OCH_3), 3.04 (br d, *J* = 17.6 Hz, 1 H, H7), 2.89–2.82 (m, 1 H, H7), 2.25 (br d, *J* = 14.3 Hz, 1 H, H9), 2.09 (s, 3 H, $COCH_3$), 2.01–1.95 (m, 3 H, H8 and H9); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4, 158.3, 149.7, 142.9, 135.5, 131.4, 131.3, 127.6, 120.7, 100.6, 64.4, 55.4, 29.0, 26.7, 21.1, 17.2; MS (FAB^+) *m/e* (relative intensity) 272 (M + H, 100), 230 (33), 212 (28); HRMS for $C_{16}H_{18}NO_3$ (M + H) calcd 272.1287, found 272.1288. Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.75; H, 6.39; N, 5.10.

10-Acetoxy-2-[(2-nitrobenzyl)oxy]-7,8,9,10-tetrahydrophenanthridine (54b). Prepared in 74% yield in same manner as described for **54a**. **54b**: white crystalline solid, mp 125–127 °C (from dichloromethane/ethyl ether); R_f = 0.43 (silica, 4% methanol in dichloromethane); IR ($CHCl_3$) ν_{max} 3019, 2948, 2870, 1728, 1619, 1527, 1507, 1438, 1367, 1341 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (s, 1 H, H6), 8.24 (dd, *J* = 7.7, 0.8 Hz, 1 H, aromatic), 8.00 (d, *J* = 9.1 Hz, 1 H, H4), 7.81 (dd, *J* = 7.7, 0.8 Hz, 1 H, aromatic), 7.64 (td, *J* = 7.7, 0.8 Hz, 1 H, aromatic), 7.48 (td, *J* = 7.7, 0.8 Hz, 1 H, aromatic), 7.40 (dd, *J* = 9.1, 2.6 Hz, 1 H, H3), 7.09 (d, *J* = 2.6 Hz, 1 H, H1), 6.43 (t, *J* = 6.0 Hz, 1 H, H10), 5.61 and 5.59 (AB q, *J* = 15.8 Hz, 2 H, benzylic), 2.99 (m, 1 H, H7), 2.80 (m, 1 H, H7), 2.15 (m, 1 H, H9), 1.91 (s, 3 H, $OCOCH_3$), 1.93–1.79 (m, 3 H, H8 and H9); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 156.7, 150.2, 147.0, 143.1, 135.8, 133.9, 133.4, 131.8, 131.6, 128.4, 128.3, 127.6, 125.2, 120.7, 102.5, 67.3, 64.1, 29.0, 26.7, 20.8, 17.2. Anal. Calcd for $C_{22}H_{20}N_2O_5$: C, 67.34; H, 5.14; N, 7.14. Found: C, 67.34; H, 5.19; N, 7.20.

10-Acetoxy-2-[3-[(*tert*-butyldiphenylsilyl)oxy]propynyl]-7,8,9,10-tetrahydrophenanthridine (54c). Prepared in 91% yield in same manner as described for **54a**. **54c**: R_f = 0.37 (silica, 30% ethyl acetate in petroleum ether); IR (film) ν_{max} 2931, 2856, 2227, 1734, 1500, 1427, 1370, 1228, 1112, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (s, 1 H, H6), 7.99 (d, *J* = 8.6 Hz, 1 H, H4), 7.81 (br s, 1 H, H1), 7.80–7.75 (m, 4 H, aromatic), 7.78 (br d, *J* = 8.6 Hz, 1 H, H3), 7.48–7.39 (m, 6 H, aromatic), 6.49 (br s, 1 H, H10), 4.59 (s, 2 H, $C\equiv CCH_2O$), 3.04 (br d, *J* = 16.7 Hz, 1 H, H7), 2.86 (ddd, *J* = 16.7, 9.8, 6.7 Hz, 1 H, H7), 2.31 (br d, *J* = 12.0 Hz, 1 H, H9), 2.08 (s, 3 H, $COCH_3$), 2.00–1.88 (m, 3 H, H9 and H8), 1.11 (s, 9 H, *t*-Bu); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 152.9, 146.3, 136.5, 135.6, 133.1, 131.8, 131.2, 130.1, 129.8, 127.7, 126.3, 125.8, 121.9, 89.0, 84.9, 64.4, 53.2, 28.5, 26.8, 26.7, 21.2, 19.2, 17.1; MS (FAB^+) *m/e* (relative intensity) 534 (M + H, 100), 474 (45), 218 (53), 197 (28), 154 (30); HRMS for $C_{34}H_{36}NO_3Si$ (M + H) calcd 534.2464, found 534.2443.

10-Hydroxy-2-methoxy-7,8,9,10-tetrahydrophenanthridine (55a). Representative Procedure. To a solution of **54a** (7.10 g, 26.2 mmol) in dry methanol (200 mL) was added Dowex 1×8-200 in the hydroxide form (1.00 g), and the resulting mixture was heated at 60 °C for 24 h. The warm reaction mixture was filtered, and the filtrate was distilled until 100 mL remained. Ethyl ether (100 mL) was added to the residue, and the resulting solution was allowed to stand in the refrigerator at 0 °C for 16 h. The crystalline precipitate was filtered off and washed with ethyl ether (50 mL) to give 5.03 g (84%) of **55a**: white crystalline solid, mp 189.5–190.5 °C; R_f = 0.21 (silica, ethyl ether); IR ($CHCl_3$) ν_{max} 3156, 2931, 1621, 1508 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.45 (s, 1 H, H6), 7.96 (d, *J* = 9.2 Hz, 1 H, H4), 7.50 (d, *J* = 2.6 Hz, 1 H, H3), 7.31 (dd, *J* = 9.2, 2.6 Hz, 1 H, H1), 5.37 (br s, 1 H, H10), 3.97 (s, 3 H, OCH_3), 2.97–2.75 (m, 2 H, H7), 2.75–2.30 (br s, 1 H, O*H*), 2.30 (br d, *J* = 10.6 Hz, 1 H, H9), 2.07–1.96 (m, 3 H, H8 and H9); ^{13}C NMR (125 MHz, DMSO-d_6) δ 157.1, 149.7, 142.5, 140.2, 130.2, 129.7, 128.1, 119.7, 103.0, 61.0, 55.3, 31.8, 26.6, 16.7; MS (FAB^+) *m/e* (relative intensity) 230 (M + H, 100), 212 (10); HRMS for $C_{14}H_{16}NO_2$ (M + H) calcd 230.1181, found 230.1189. Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.16; H, 6.73; N, 6.08.

10-Hydroxy-2-[(2-nitrobenzyl)oxy]-7,8,9,10-tetrahydrophenanthridine (55b). Prepared in 89% yield in same manner as described for **55a**. **55b**: white crystalline solid, mp 181–183 °C (from methanol/ethyl ether); R_f = 0.22 (silica, 40% ethyl acetate in dichloromethane); IR ($CHCl_3$) ν_{max} 3018, 2943, 2866, 1619, 1508, 1335 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.49 (s, 1 H, H6), 8.13 (dd, *J* = 7.7, 1.0 Hz, 1 H, aromatic), 7.89 (d, *J* = 9.1 Hz, 1 H, H4), 7.87 (dd, *J* = 7.7, 1.0 Hz, 1 H, aromatic), 7.80 (td, *J* = 7.7, 1.0 Hz, 1 H, aromatic), 7.68 (d, *J* = 2.7 Hz, 1 H, H1), 7.63 (td, *J* = 7.7, 1.0 Hz, 1 H, aromatic), 7.38 (dd, *J* = 9.1, 2.7 Hz, 1 H, H3), 5.60 and 5.57 (AB q, *J* = 14.6 Hz, 2 H, benzylic), 5.39 (d, *J* = 6.6 Hz, 1 H, O*H*), 5.12 (br dt, *J* = 6.3, 3.1 Hz, H10), 2.88 (m, 1 H, H7), 2.71 (ddd, *J* = 17.2, 10.5, 5.5 Hz, 1 H, H7), 2.06–1.90 (m, 2 H, H9), 1.85–1.74 (m, 2 H, H8); ^{13}C NMR (125 MHz, DMSO-d_6) δ 155.8, 150.2, 147.6, 142.7, 140.3, 134.0, 132.1, 130.9, 129.9, 129.6, 129.3, 128.0, 124.8, 119.7, 104.8, 66.6, 61.0, 31.7, 26.6, 16.7; MS (FAB^+) *m/e* (relative intensity) 351 (M + H, 100), 333 (7), 216 (10); HRMS for $C_{20}H_{19}N_2O_4$ (M + H) calcd 351.1345, found 351.1345. Anal. Calcd for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.27; H, 5.20; N, 7.93.

2-[3-[(*tert*-Butyldiphenylsilyl)oxy]propynyl]-10-hydroxy-7,8,9,10-tetrahydrophenanthridine (55c). Prepared in 69% yield in same manner as described for **55a**. **55c**: white crystalline solid, mp 132–133 °C (from ethyl ether/petroleum ether); R_f = 0.17 (silica, 30% ethyl acetate in petroleum ether); IR (film) ν_{max} 3398, 3070, 2932, 2857, 2232, 1588, 1568, 1428, 1372, 1196, 1112 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (s, 1 H, H6), 8.23 (d, *J* = 1.1 Hz, 1 H, H1), 7.88 (d, *J* = 8.6 Hz, 1 H, H4), 7.81–7.78 (m, 4 H, aromatic), 7.49 (dd, *J* = 8.6, 1.1 Hz, 1 H, H3), 7.48–7.39 (m, 6 H, aromatic), 5.31 (br s, 1 H, H10), 4.59 (s, 2 H, $C\equiv CCH_2O$), 3.05 (br, 1 H, O*H*), 2.83 (br d, *J* = 11.5 Hz, 1 H, H7), 2.72 (ddd, *J* = 17.3, 11.5, 5.6 Hz, 1 H, H7), 2.25 (br d, *J* = 12.7 Hz, 1 H, H9), 2.08–1.98 (m, 1 H, H9), 1.93–1.84 (m, 2 H, H8), 1.11 (s, 9 H, *t*-Bu); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.8, 146.1, 140.3, 135.6, 133.0, 130.9, 130.3, 129.8, 129.5, 127.7, 127.1, 126.5, 121.4, 88.8, 85.1, 62.3, 53.2, 31.3, 27.0, 26.7, 19.2, 16.7; MS (FAB^+) *m/e* (relative intensity) 492 (M + H, 100), 434 (8), 236 (8), 199 (11), 154 (7); HRMS for $C_{32}H_{34}NO_2Si$ (M + H) calcd 492.2359, found 492.2359.

10-[(*tert*-Butyldimethylsilyl)oxy]-2-methoxy-7,8,9,10-tetrahydrophenanthridine (56). To a stirred suspension of **55a** (6.15 g, 26.8 mmol) and 2,6-lutidine (4.69 mL, 40.2 mmol) in dichloromethane (80 mL) at 10 °C was added *tert*-butyldimethylsilyl triflate (7.40 mL, 32.2 mmol). After stirring at 20 °C for 1 h, methanol (5 mL) was added, stirring was continued for 5 min, and the reaction mixture was evaporated to dryness in vacuo. The residue was purified by flash column chromatography (silica, 10% ethyl acetate in dichloromethane), and the product was recrystallized from cyclohexane/hexanes to give 8.42 g (91%) of **56**: white crystalline solid, mp 127–127.5 °C; R_f = 0.53 (silica, 20% ethyl acetate in dichloromethane); IR ($CHCl_3$) ν_{max} 2954, 2855, 1622, 1507 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (s, 1 H, H6), 7.96 (d, *J* = 8.8 Hz, 1 H, H4), 7.29 (m, 2 H, H1 and H3), 5.40 (t, *J* = 2.8 Hz, 1 H, H10), 3.95 (s, 3 H, OCH_3), 3.00 (dd, *J* = 17.5, 4.8 Hz, 1 H, H7), 2.81 (ddd, *J* = 17.5, 11.5, 5.9 Hz, 1 H, H7), 2.27–2.13 (m, 2 H, CH_2), 1.87–1.75 (m, 2 H, CH_2), 0.86 (s, 9 H, *t*-Bu), 0.23 (s, 6 H, $Si(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 150.3, 143.1, 140.0, 131.2, 129.7, 128.0, 120.0, 102.0, 63.5, 55.5, 31.6, 27.0, 25.9, 18.2, 16.3, −3.5, −4.3; MS (FAB^+) *m/e* (relative intensity) 344 (M + H, 100), 286 (24), 212 (16); HRMS for $C_{20}H_{30}NO_2Si$ (M + H) calcd 344.2046, found 344.2052. Anal. Calcd for $C_{20}H_{29}NO_2Si$: C, 69.92; H, 8.51; N, 4.08. Found: C, 70.02; H, 8.71; N, 3.98.

***N*-[(Phenyloxy)carbonyl]-10-[(*tert*-butyldimethylsilyl)oxy]-6-ethynyl-2-methoxy-5,6,7,8,9,10-hexahydrophenanthridine (57).** A solution of **56** (7.84 g, 22.8 mmol) in dry THF (110 mL) was cooled at −78 °C and treated with ethynylmagnesium bromide (55.36 mL, 0.5 M solution in THF, 27.7 mmol). The solution was briefly warmed to 0 °C and then cooled again to −78 °C, and phenyl chloroformate (4.36 mL, 27.7 mmol) was added. The reaction mixture was allowed to slowly warm to 25 °C over 1 h, quenched with saturated aqueous ammonium chloride (100 mL), poured into saturated aqueous sodium bicarbonate (100 mL), and extracted with dichloromethane (2 × 100 mL). The combined organic layers were dried ($MgSO_4$) and evaporated in vacuo, and the residue was purified by flash column chromatography (silica, 10% ethyl ether in petroleum ether) to give 11.15 g (100%) of **57**: white foam (ca. 3:1 mixture of diastereomers as determined by ^{1}H NMR); R_f = 0.34 (silica, 20% ethyl ether in petroleum ether); IR ($CHCl_3$) ν_{max} 3302, 2948, 2933, 2896, 2855, 1716, 1593, 1493, 1385, 1303 cm^{-1}; ^{1}H

NMR (500 MHz, $CDCl_3$) δ 7.90–7.10 (m, 6 H, aromatic), 6.94 (br s, 1 H, aromatic), 6.80 (dd, *J* = 8.9, 2.9 Hz, 1 H, aromatic), 5.64 and 5.60 (2 s, 1 H, H6), 4.96 and 4.67 (2 br s, 1 H, H10), 3.83 and 3.82 (2 s, 3 H, OCH_3), 2.51–1.61 (m, 7 H, H7, H8, H9, and C≡C*H*), 0.95 and 0.82 (2 s, 9 H, *t*-Bu), 0.28, 0.20, and 0.08 (singlets, 6 H, $Si(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.0, 129.7, 129.3, 125.7, 121.7, 111.8, 111.6, 109.8, 79.9, 71.6, 64.9, 64.0, 55.6, 55.5, 48.8, 32.6, 31.4, 28.2, 27.8, 26.0, 25.9, 18.4, 18.1, 18.0, −3.1, −3.6, −4.1, −4.3; MS (FAB^+) *m/e* (relative intensity) 489 (M^+, 47), 464 (29), 432 (100), 396 (15), 358 (62), 344 (10), 236 (29), 212 (16), 151 (15); HRMS for $C_{29}H_{35}NO_4Si$ (M^+) calcd 489.2335, found 489.2349.

***N*-[(Phenyloxy)carbonyl]-10-[(*tert*-butyldimethylsilyl)oxy]-6a,10a-epoxy-6-ethynyl-2-methoxy-5,6,6a,7,8,9,10,10a-octahydrophenanthridine (58).** A solution of **57** (9.26 g, 18.9 mmol) in dichloromethane (125 mL) was treated with *m*-CPBA (97%, 6.53 g, 36.8 mmol) and stirred at 35 °C for 2 h. After cooling to 20 °C, dimethyl sulfide (22.77 mL, 37.8 mmol) was added and stirring was continued for 20 min. The reaction mixture was poured into saturated aqueous sodium bicarbonate (200 mL) and extracted with ethyl ether (300 mL). The combined organic layers were washed with brine (100 mL), dried ($MgSO_4$), and evaporated in vacuo. The residue was purified by recrystallization from ethyl ether/petroleum ether to give 9.50 g (99%) of **58**: white crystalline solid (ca. 3:1 mixture of diastereomers as determined by ^{1}H NMR), mp 116–119 °C; R_f = 0.29 (silica, 20% ethyl ether in petroleum ether); IR ($CHCl_3$) ν_{max} 3303, 2950, 2932, 2883, 2855, 1722, 1585, 1503, 1384, 1300 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47–7.07 (m, 7 H, aromatic), 6.86 and 6.83 (two sets of dd, *J* = 8.8, 2.9 Hz, 1 H, aromatic), 5.51 (m, 1 H, H6), 4.88 (m, 1 H, H10, minor isomer), 4.77 (dd, *J* = 9.9, 5.6 Hz, 1 H, H10, major isomer), 3.81 and 3.80 (2 s, 3 H, OCH_3), 2.38 (dd, *J* = 14.4, 7.2 Hz, 1 H, CH_2, minor isomer), 2.31 (dd, *J* = 14.4, 5.6 Hz, 1 H, CH_2, major isomer), 2.07 (s, 1 H, C≡C*H*), 1.91–1.61 (m, 5 H, H7, H8 and H9), 0.88 and 0.80 (2 s, 9 H, *t*-Bu), 0.27, 0.20, 0.15, 0.08, 0.03, and −0.02 (singlets, 6 H, $Si(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.8, 151.2, 129.2, 128.5, 128.1, 125.5, 121.8, 121.6, 115.3, 115.0, 113.3, 112.1, 78.6, 73.4, 72.7, 70.0, 55.6, 55.5, 48.1, 29.4, 26.4, 26.0, 25.7, 24.0, 22.4, 20.4, 18.2, 18.1, 13.5, −2.8, −2.9, −3.4, −5.2; MS (FAB^+) *m/e* (relative intensity) 638 (M + Cs, 100), 506 (14), 448 (43); HRMS for $C_{29}H_{35}NO_5SiCs$ (M + Cs) calcd 638.1339, found 638.1360. Anal. Calcd for $C_{29}H_{35}NO_5Si$: C, 68.88; H, 6.98; N, 2.77. Found: C, 68.88; H, 7.21; N, 2.66.

***N*-[(Phenyloxy)carbonyl]-6a,10a-epoxy-6-ethynyl-10-hydroxy-2-methoxy-5,6,6a,7,8,9,10,10a-octahydrophenanthridine (59).** A solution of **58** (9.56 g, 18.9 mmol) in THF (100 mL) was treated with tetra-*n*-butylammonium fluoride (TBAF) (23.6 mL, 1.0 M in THF, 23.6 mmol) at 0 °C for 1 h and evaporated to dryness in vacuo. The residue was purified by flash column chromatography (silica, 7% ethyl acetate in dichloromethane) to give 7.35 g (99%) of **59**: white foam (ca. 3:1 mixture of diastereomers as determined by ^{1}H NMR); R_f = 0.40 (silica, 70% ethyl ether in petroleum ether); IR ($CHCl_3$) ν_{max} 3600, 3300, 2950, 1720, 1590, 1500, 1490, 1385, 1300 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 2.8 Hz, 1 H, aromatic, major isomer), 7.44–7.09 (m, 6 H, aromatic, major isomer, 7 H, aromatic, minor isomer), 6.91 (dd, *J* = 8.8, 2.8 Hz, 1 H, aromatic, minor isomer), 6.90 (dd, *J* = 8.8, 2.8 Hz, 1 H, aromatic, major isomer), 5.59 (d, *J* = 2.0 Hz, 1 H, H6, major isomer), 5.57 (d, *J* = 2.0 Hz, 1 H, H6, minor isomer), 4.87 (br s, 1 H, H10, minor isomer), 4.67 (br dd, *J* = 14.5, 6.0 Hz, 1 H, H10, major isomer), 3.84 (s, 3 H, OCH_3), 2.45 (dd, *J* = 15.0, 7.5 Hz, 1 H, CH_2, minor isomer), 2.34 (dt, *J* = 14.7, 4.6 Hz, 1 H, CH_2, major isomer), 2.11–1.40 (m, 7 H, CH_2); MS (FAB^+) *m/e* (relative intensity) 391 (M^+, 100), 374 (18), 254 (13); HRMS for $C_{23}H_{21}NO_5$ (M^+) calcd 391.1420, found 391.1450.

***N*-[(Phenyloxy)carbonyl]-6a,10a-epoxy-6-ethynyl-2-methoxy-10-oxo-5,6,6a,7,8,9,10,10a-octahydrophenanthridine (60).** A solution of **59** (1.15 g, 2.93 mmol) in dichloromethane (25 mL) was treated with powdered, activated 4-Å molecular sieves (1.0 g) and pyridinium chlorochromate (1.26 g, 5.85 mmol). The suspension was stirred at 25 °C for 2 h, diluted with ethyl ether (25 mL), and filtered through a 3 × 3 cm plug of silica. The silica plug was rinsed with ethyl ether (100 mL), and the combined filtrates were concentrated in vacuo. The residue was purified by recrystallization from ethyl acetate/benzene/petroleum ether to give 0.98 g (87%) of **60**: white crystalline solid, mp 186.5–187.5 °C; R_f = 0.48 (silica, 50% ethyl ether in petroleum ether); IR ($CHCl_3$) ν_{max} 3303, 2960, 1717, 1609, 1493, 1380, 1311, 1299 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 2.9 Hz, 1 H, aromatic), 7.40–7.08 (m, 6 H, aromatic), 6.93 (dd, *J* = 8.8, 2.9 Hz, 1 H, aromatic), 5.70 (d, *J* = 2.3 Hz, 1 H, H6), 3.84 (s, 3 H, OCH_3), 2.76 (dt, *J* = 15.5, 5.0 Hz, 1 H, H9), 2.59 (ddd, *J* = 15.5, 10.2, 6.0 Hz, 1 H, H9), 2.36–2.28 (m, 2 H, H7), 2.22 (s, 1 H, C≡C*H*), 2.00–1.90 (m, 2 H, H8); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.3, 157.3, 154.1, 151.0, 129.3, 128.5, 127.6, 125.7, 124.0, 121.4, 114.9, 114.8, 77.7, 74.6, 74.3, 57.3, 55.5, 47.5, 38.8, 23.7, 18.3; MS (FAB^+) *m/e* (relative intensity) 389 (M^+, 88), 358 (21), 307 (88), 286 (100), 167 (30); HRMS for $C_{23}H_{19}NO_5$ (M^+) calcd 389.1263, found 389.1266. Anal. Calcd for $C_{23}H_{19}NO_5$: C, 70.94; H, 4.92; N, 3.60. Found: C, 70.94; H, 4.70; N, 3.63.

***N*-[(Phenyloxy)carbonyl]-6-[6-(trimethylsilyl)-3(*Z*)-hexene-1,5-diynyl]-6a,10a-epoxy-2-methoxy-10-oxo-5,6,6a,7,8,9,10,10a-octahydrophenanthridine (62).** A solution of **60** (5.69 g, 14.6 mmol) in dry degassed benzene (120 mL) was added to copper(I) iodide (0.666 g, 3.51 mmol), and to the resulting mixture was added chloro (*Z*)-enyne **61** (3.69 g, 23.4 mmol) followed by *n*-butylamine (2.89 mL, 29.2 mmol) and tetrakis(triphenylphosphine)palladium(0) (1.01 g, 0.877 mmol) in dry degassed benzene (60 mL). The reaction mixture was stirred at 25 °C for 2 h, diluted with ethyl ether (200 mL), poured into saturated aqueous ammonium chloride (200 mL), and extracted with ethyl ether (2 × 70 mL). The combined organic layers were dried ($MgSO_4$) and evaporated in vacuo. The residue was purified by flash column chromatography (silica, 25% ethyl ether in petroleum ether) to give 5.43 g (73%) of **62**: white foam; R_f = 0.29 (silica, 30% ethyl ether in petroleum ether); IR ($CHCl_3$) ν_{max} 2958, 2836, 1717, 1609, 1590, 1493, 1380, 1299, 1251 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, *J* = 3.0 Hz, 1 H, aromatic), 7.38–7.06 (m, 6 H, aromatic), 6.89 (dd, *J* = 8.9, 3.0 Hz, 1 H, aromatic), 5.92 (d, *J* = 1.6 Hz, 1 H, H6), 5.86 (d, *J* = 11.0 Hz, 1 H, olefinic), 5.65 (br d, *J* = 11.0 Hz, 1 H, olefinic), 3.81 (s, 3 H, OCH_3), 2.78–2.62 (m, 2 H, H9), 2.37–2.25 (m, 2 H, H7), 2.05–1.85 (m, 2 H, H8), 0.20 (s, 9 H, $Si(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.2, 157.2, 154.1, 151.0, 129.3, 128.6, 128.5, 125.7, 124.0, 121.4, 120.7, 118.9, 114.8, 114.8, 103.5, 101.5, 90.5, 83.0, 74.6, 57.4, 55.4, 48.4, 38.8, 23.8, 18.2, −0.17; MS (FAB^+) *m/e* (relative intensity) 511 (M^+, 100), 390 (8), 362 (9), 176 (11), 120 (10); HRMS for $C_{30}H_{29}NO_5Si$ (M^+) calcd 511.1815, found 511.1815.

***N*-[(Phenyloxy)carbonyl]-6-[3(*Z*)-hexene-1,5-diynyl]-6a,10a-epoxy-2-methoxy-10-oxo-5,6,6a,7,8,9,10,10a-octahydrophenanthridine (63).** Silver nitrate (1.43 g, 8.44 mmol) was added to a solution of **62** (1.08 g, 2.11 mmol) in 48 mL of H_2O/EtOH/THF (1:1:1) at 25 °C followed by stirring for 15 min. Potassium cyanide (0.962 g, 14.8 mmol) was then added, and the mixture was stirred for 1 h, concentrated in vacuo to 20 mL, poured into saturated aqueous sodium bicarbonate (30 mL), and extracted with dichloromethane (3 × 40 mL). The combined organic layers were dried ($MgSO_4$) and evaporated in vacuo, and the residue was purified by flash column chromatography (silica, 35% ethyl ether in petroleum ether) to give 0.807 g (99%) of **63**: white foam; R_f = 0.22 (silica, 40% ethyl ether in petroleum ether); IR ($CHCl_3$) ν_{max} 3299, 2947, 1716, 1609, 1590, 1501, 1493, 1380, 1299, 1253 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 2.9 Hz, 1 H, aromatic), 7.38–7.07 (m, 6 H, aromatic), 6.89 (dd, *J* = 8.9, 2.9 Hz, 1 H, aromatic), 5.88 (s, 1 H, H6), 5.77 and 5.74 (AB q, *J* = 11.2 Hz, 2 H, olefinic), 3.81 (s, 3 H, OCH_3), 3.16 (d, *J* = 1.5 Hz, 1 H, C≡C*H*), 2.74 (dt, *J* = 15.3, 5.0 Hz, 1 H, H9), 2.67 (ddd, *J* = 15.3, 10.1, 6.1 Hz, 1 H, H9), 2.36–2.26 (m, 2 H, H7), 1.99–1.89 (m, 2 H, H8); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.5, 157.2, 154.1, 151.0, 129.3, 128.7, 128.5, 125.7, 124.1, 121.4, 120.4, 120.3, 114.8, 114.7, 90.6, 85.1, 82.7, 80.3, 74.9, 57.4, 55.5, 48.3, 38.8, 23.8, 18.6; MS (FAB^+) *m/e* (relative intensity) 439 (M^+, 100), 364 (8), 176 (19), 120 (10); HRMS for $C_{27}H_{21}NO_5$ (M^+) calcd 439.1420, found 439.1434.

Compound 64. A solution of **63** (575 mg, 1.31 mmol) in dry toluene (100 mL) was cooled to −78 °C and treated with lithium diisopropylamide (1.40 mL, 1.0 M solution in THF) followed by stirring for 1 h at −78 °C. The reaction mixture was quenched with saturated aqueous ammonium chloride (30 mL). The resultant mixture was allowed to warm to room temperature, poured into saturated aqueous sodium bicarbonate (100 mL), and extracted with ethyl ether (50 mL). The combined organic layers were dried ($MgSO_4$) and evaporated in vacuo. The residue was purified by flash column chromatography (silica, 30 → 60% ethyl ether in petroleum ether) to give recovered **63** (79 mg, 14%) and 378 mg (66%) of **64**: white crystalline solid, mp 157–159 °C dec (ethyl ether); R_f = 0.25 (silica, 50% ethyl ether in petroleum ether); IR ($CHCl_3$) ν_{max} 3444, 2954, 1717, 1610, 1592, 1505, 1493, 1383, 1321, 1301 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (d, *J* = 2.9 Hz, 1 H, aromatic), 7.34–7.12 (m, 6 H, aromatic), 6.84 (dd, *J* = 8.9, 2.9 Hz, 1 H, aromatic), 5.83 (d, *J* = 10.0 Hz, 1 H, olefinic), 5.67 (dd, *J* = 10.0, 1.4 Hz, 1 H, olefinic), 5.50 (br s, 1 H, NC*H*C≡C), 3.78 (s, 3 H, OCH_3), 2.73 (br s, 1 H, O*H*), 2.31 (dd, *J* = 15.1, 8.3 Hz, 1 H, CH_2), 2.18–2.13 (m, 2 H, CH_2), 1.98 (m, 1 H, CH_2), 1.88 (dt, *J* = 12.0, 2.8 Hz, 1 H, CH_2), 1.70 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.6, 153.9, 151.1, 129.3, 128.9, 128.8, 127.1, 125.6, 124.1, 122.1, 121.5, 116.4, 113.8, 100.5, 94.1, 88.7, 73.7, 73.1, 65.8, 64.4, 55.4, 50.5, 35.2, 23.1, 19.2; MS (FAB^+) *m/e* (relative intensity) 439 (M^+, 100), 379 (25); HRMS for $C_{27}H_{21}NO_5$ (M^+) calcd 439.1420, found 439.1419. Anal. Calcd for $C_{27}H_{21}NO_5$: C, 73.79; H, 4.82; N, 3.19. Found: C, 73.99; H, 4.70; N, 3.90.

Compound 65. Thiocarbonyldiimidazole (1.26 g, 7.09 mmol) was added to a solution of **64** (1.04 g, 2.36 mmol) and DMAP (0.188 g, 1.53 mmol) in dry dichloromethane (5 mL) at 25 °C. After stirring at 25 °C for 72 h, the solution was concentrated in vacuo, and the residue was purified by flash column chromatography (silica, 6% ethyl ether in dichloromethane) to give 1.30 g (100%) of **75**: white foam; R_f = 0.39 (silica, 10% ethyl ether in dichloromethane); IR ($CHCl_3$) ν_{max} 2932, 1722, 1610, 1587, 1502, 1463, 1383, 1321, 1244, 1198; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (s, 1 H, imidazole), 7.65 (s, 1 H, imidazole), 7.40–7.13 (m, 7 H, aromatic and imidazole), 7.02 (d, J = 0.9 Hz, 1 H, aromatic), 6.85 (dd, J = 8.9, 2.9 Hz, 1 H, aromatic), 5.94 (d, J = 10.0 Hz, 1 H, olefinic), 5.73 (dd, J = 10.0, 1.6 Hz, 1 H, olefinic), 5.54 (d, J = 1.6 Hz, 1 H, NC*H*C≡C), 3.54 (s, 3 H, OC*H*$_3$), 3.04 (dt, J = 12.1, 3.2 Hz, 1 H, C*H*$_2$), 2.41 (dt, J = 15.2, 8.2 Hz, 1 H, C*H*$_2$), 2.29–2.08 (m, 3 H, C*H*$_2$), 1.82 (m, 1 H, C*H*$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.1, 153.7, 151.0, 137.2, 131.1, 129.4, 129.3, 129.1, 127.9, 125.8, 124.0, 123.4, 121.5, 117.7, 114.8, 113.9, 100.8, 94.3, 89.0, 85.6, 74.4, 63.7, 55.5, 55.1, 50.9, 50.5, 28.6, 22.6, 18.5; MS (FAB$^+$) m/e (relative intensity) 550 (M + H, 40), 422 (100), 369 (39), 273 (52), 258 (30), 243 (44), 219 (40), 178 (66); HRMS for $C_{31}H_{24}N_3O_5S$ (M + H) calcd 550.1437, found 550.1437.

Compound 66. A solution of **65** (230 mg, 0.418 mmol) in dry benzene (8 mL) was treated with n-Bu_3SnH (250 μL, 0.929 mmol) and AIBN (15 mg, catalytic) at 75 °C for 1 h. The solution was concentrated in vacuo, and the residue was purified by flash column chromatography (silica, 10 → 30% ethyl ether in petroleum ether) to give 152 mg (86%) of **66**: white crystalline solid, mp 126–128 °C dec (from ethyl ether); R_f = 0.31 (silica, 30% ethyl ether in petroleum ether); IR ($CHCl_3$) ν_{max} 2926, 1721, 1502, 1380, 1297, 1271, 1200 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.10 (m, 7 H, aromatic), 6.84 (dd, J = 8.8, 2.8 Hz, 1 H, aromatic), 5.77 (dd, J = 9.9, 1.6 Hz, 1 H, olefinic), 5.66 (dd, J = 9.9, 1.6 Hz, 1 H, olefinic), 5.47 (d, J = 1.6 Hz, 1 H, NC*H*C≡C), 3.81 (s, 3 H, OC*H*$_3$), 3.72 (br s, 1 H, C≡CC*H*C), 2.39 (dd, J = 15.2, 8.1 Hz, 1 H, C*H*$_2$), 2.23 (m, 1 H, C*H*$_2$), 2.05–1.89 (m, 2 H, C*H*$_2$), 1.58 (m, 1 H, C*H*$_2$), 1.20 (m, 1 H, C*H*$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.9, 153.9, 151.1, 129.8, 129.3, 128.7, 127.4, 125.6, 125.0, 121.9, 121.5, 113.3, 113.0, 101.6, 94.1, 91.4, 88.9, 70.0, 61.0, 55.5, 50.0, 29.5, 23.3, 22.5, 15.6; MS (FAB$^+$) m/e (relative intensity) 424 (M + H, 100), 341 (44); HRMS for $C_{27}H_{22}NO_4$ (M + H) calcd 424.1549, found 424.1532.

Compound 67. A mixture of **66** (40 mg, 0.094 mmol), 2-(phenylthio)ethanol (29 mg, 0.19 mmol), cesium carbonate (153 mg, 0.47 mmol), and 18-crown-6 (25 mg, 0.094 mmol) in dry acetonitrile (8 mL) was stirred at 25 °C for 45 h and evaporated in vacuo. The residue was dissolved in dichloromethane (10 mL), filtered through a 5 × 5 mm plug of silica, and evaporated in vacuo. The residue was purified by flash column chromatography (silica, 20% ethyl ether in petroleum ether) to give 44 mg (91%) of **67**: white crystalline solid, mp 163–165 °C dec (from ethyl ether); R_f = 0.43 (silica, 40% ethyl ether in petroleum ether); IR ($CHCl_3$) ν_{max} 2932, 1700, 1502, 1392, 1229, 1270; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40–7.18 (m, 6 H, aromatic), 7.10 (d, J = 2.7 Hz, 1 H, aromatic), 6.82 (dd, J = 8.8, 2.7 Hz, 1 H, aromatic), 5.77 (dd, J = 9.9, 1.5 Hz, 1 H, olefinic), 5.65 (dd, J = 9.9, 1.5 Hz, 1 H, olefinic), 5.42 (br s, 1 H, NC*H*C≡C), 4.38–4.21 (m, 2 H, PhSCH$_2$C*H*$_2$O), 3.87 (s, 3 H, OC*H*$_3$), 3.70 (s, 1 H, C≡CC*H*), 3.18–2.12 (m, 2 H, PhSC*H*$_2$CH$_2$O), 2.36 (m, 1 H, C*H*$_2$), 2.24–1.57 (m, 5 H, C*H*$_2$); MS (FAB$^+$) m/e (relative intensity) 483 (M$^+$, 100), 440 (21), 425 (28); HRMS for $C_{29}H_{25}NO_4S$ (M$^+$) calcd 483.1504, found 483.1511.

Compound 15. Prepared from **67** in 88% yield in a similar manner as that described for **12**. **15**: white foam; R_f = 0.40 (silica, 5% ethyl ether in dichloromethane); IR ($CHCl_3$) ν_{max} 3056, 3017, 2933, 2190, 1708, 1503, 1446, 1397, 1321, 1144 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09–7.08 (m, 7 H, aromatic), 6.80 (br s, 1 H, aromatic), 5.76 (d, J = 9.9 Hz, 1 H, olefinic), 5.64 (d, J = 9.9 Hz, 1 H, olefinic), 5.36–4.98 (m, 1 H, NC*H*C≡C), 4.53–4.34 (m, 2 H, SO$_2$CH$_2$C*H*$_2$O), 3.82 (s, 3 H, OC*H*$_3$), 3.68 (s, 1 H, C≡CC*H*), 3.53–3.44 (m, 2 H, SO$_2$C*H*$_2$CH$_2$O), 2.32 (br s, 1 H, C*H*$_2$), 2.17 (dt, J = 15.3, 9.3 Hz, 1 H, C*H*$_2$), 2.00–1.86 (m, 2 H, C*H*$_2$), 1.77 (m, 1 H, C*H*$_2$), 1.57 (m, 1 H, C*H*$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.8, 134.0, 133.7, 130.2, 129.8, 129.4, 128.3, 128.0, 127.4, 124.9, 121.9, 113.2, 112.8, 101.5, 93.9, 91.4, 69.9, 65.8, 59.4, 55.5, 55.1, 49.8, 29.4, 23.2, 22.4, 15.6, 15.2; HRMS (FAB$^+$) for $C_{29}H_{26}NO_6S$ (M + H) calcd 516.1481, found 516.1499.

Compound 68. Prepared from **66** and 2-(1-naphthylthio)ethanol in 92% yield in a similar manner as that described for **67**. **68**: white crystalline solid, mp 190–192 °C dec (from ethyl ether); R_f = 0.41 (silica, 40% ethyl ether in petroleum ether); IR ($CDCl_3$) ν_{max} 3051, 2920, 2849, 1707, 1501, 1454, 1391, 1275, 1208 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (br d, J = 6.3 Hz, 1 H, aromatic), 7.85 (d, J = 8.0 Hz, 1 H, aromatic), 7.77 (d, J = 8.0 Hz, 1 H, aromatic), 7.68 (br s, 1 H, aromatic), 7.57 (br t, J = 6.3 Hz, 1 H, aromatic), 7.52 (td, J = 7.0, 1.1 Hz, 1 H, aromatic), 7.41 (br t, J = 7.5 Hz, 1 H, aromatic), 7.30 (br s, 1 H, aromatic), 7.09 (d, J = 2.8 Hz, 1 H, aromatic), 6.79 (br d, J = 6.3 Hz, 1 H, aromatic), 5.76 (dd, J = 9.9, 1.6 Hz, 1 H, olefinic), 5.65 (dd, J = 9.9, 1.6 Hz, 1 H, olefinic), 5.42–5.22 (br s, 1 H, NC*H*C≡C), 4.35–4.17 (m, 2 H, OC*H*$_2$CH$_2$S), 3.81 (s, 3 H, OC*H*$_3$), 3.69 (br s, 1 H, CH$_2$C*H*C≡C), 3.23–3.16 (m, 2 H, OCH$_2$C*H*$_2$S), 2.35 (m, 1 H, C*H*$_2$), 2.19 (m, 1 H, C*H*$_2$), 2.04–1.87 (m, 2 H, C*H*$_2$), 1.77 (m, 1 H, C*H*$_2$), 1.61 (m, 1 H, C*H*$_2$); HRMS (FAB$^+$) for $C_{33}H_{27}NO_4SCs$ (M + Cs) calcd 666.0715, found 666.0715.

Compound 16. Prepared from **68** in 85% yield in a similar manner as that described for **12**. **16**: white foam; R_f = 0.39 (silica, 5% ethyl ether in dichloromethane); IR ($CDCl_3$) ν_{max} 3055, 2919, 2849, 1708, 1503, 1455, 1398, 1292, 1212, 1152, 1125, 1026, 809, 771 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73–8.68 (m, 1 H, aromatic), 8.66–8.29 (m, 1 H, aromatic), 8.12 (m, 1 H, aromatic), 7.97 (br d, J = 7.7 Hz, 1 H, aromatic), 7.70 (m, 1 H, aromatic), 7.63 (br t, J = 7.7 Hz, 1 H, aromatic), 7.58 (m, 1 H, aromatic), 7.17–6.96 (m, 1 H, aromatic), 7.05 (br s, 1 H, aromatic), 6.79–6.67 (m, 1 H, aromatic), 5.76 (br d, J = 9.6 Hz, 1 H, olefinic), 5.64 (m, 1 H, olefinic), 5.31–4.76 (br s, 1 H, NC*H*C≡C), 4.58–4.32 (m, 2 H, OC*H*$_2$CH$_2$SO$_2$), 3.80 (s, 3 H, OC*H*$_3$), 3.70–3.65 (m, 3 H, OCH$_2$C*H*$_2$SO$_2$ and CH$_2$C*H*C≡C), 2.32 (m, 1 H, C*H*$_2$), 2.13 (m, 1 H, C*H*$_2$), 1.98–1.84 (m, 2 H, C*H*$_2$), 1.75 (m, 1 H, C*H*$_2$), 1.56 (m, 1 H, C*H*$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.7, 135.6, 134.2, 130.8, 129.4, 129.0, 128.7, 127.4, 127.1, 124.9, 124.5, 123.9, 123.8, 121.9, 113.2, 112.8, 101.5, 97.8, 94.0, 91.4, 88.6, 69.9, 65.8, 59.4, 55.5, 55.4, 54.7, 49.7, 29.4, 23.2, 22.3, 15.6, 15.2; HRMS (FAB$^+$) for $C_{33}H_{27}NO_6SCs$ (M + Cs) calcd 698.0613, found 698.0627.

Compound 69. Prepared from **66** and 2-(2-naphthylthio)ethanol in 85% yield in a similar manner as that described for **67**. **69**: white crystalline solid, mp 206–208 °C dec (from ethyl ether); R_f = 0.40 (silica, 40% ethyl ether in petroleum ether); IR ($CDCl_3$) ν_{max} 3052, 2937, 1707, 1501, 1452, 1393, 1276, 1209 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (br s, 1 H, aromatic), 7.79–7.75 (m, 3 H, aromatic), 7.49–7.42 (m, 3 H, aromatic), 7.26 (br s, 1 H, aromatic), 7.08 (d, J = 2.8 Hz, 1 H, aromatic), 6.78 (br s, 1 H, aromatic), 5.75 (dd, J = 9.9, 1.7 Hz, 1 H, olefinic), 5.64 (dd, J = 9.9, 1.7 Hz, 1 H, olefinic), 5.43–5.15 (br s, 1 H, NC*H*C≡C), 4.43–4.27 (m, 2 H, OC*H*$_2$CH$_2$S), 3.79 (s, 3 H, OC*H*$_3$), 3.68 (br s, 1 H, CH$_2$C*H*C≡C), 3.31–3.22 (m, 2 H, OCH$_2$C*H*$_2$S), 2.35 (m, 1 H, C*H*$_2$), 2.20 (m, 1 H, C*H*$_2$), 2.04–1.87 (m, 2 H, C*H*$_2$), 1.77 (m, 1 H, C*H*$_2$), 1.58 (m, 1 H, C*H*$_2$); HRMS (FAB$^+$) for $C_{33}H_{27}NO_4SCs$ (M + Cs) calcd 666.0715, found 666.0715.

Compound 17. Prepared from **69** in 92% yield in a similar manner as that described for **12**. **17**: white foam; R_f = 0.39 (silica, 5% ethyl ether in dichloromethane); IR ($CDCl_3$) ν_{max} 3056, 2922, 2851, 1709, 1503, 1452, 1400, 1268, 1213, 1153, 1126 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55–8.44 (m, 1 H, aromatic), 8.07–7.26 (m, 4 H, aromatic), 7.67 (td, J = 8.1, 1.2 Hz, 1 H, aromatic), 7.62 (td, J = 8.1, 1.2 Hz, 1 H, aromatic), 7.05–6.60 (m, 3 H, aromatic), 5.73 (d, J = 9.7 Hz, 1 H, olefinic), 5.61 (d, J = 9.7 Hz, 1 H, olefinic), 5.30–4.48 (br s, 1 H, NC*H*C≡C), 4.55–4.44 (m, 2 H, OC*H*$_2$CH$_2$SO$_2$), 3.78 (s, 3 H, OC*H*$_3$), 3.61–3.53 (m, 3 H, OCH$_2$C*H*$_2$SO$_2$, CH$_2$C*H*C≡C), 2.30 (m, 1 H, C*H*$_2$), 2.10 (m, 1 H, C*H*$_2$), 1.98–1.82 (m, 2 H, C*H*$_2$), 1.73 (m, 1 H, C*H*$_2$), 1.53 (m, 1 H, C*H*$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.6, 135.8, 135.3, 133.5, 132.1, 130.0, 129.9, 129.6, 129.3, 128.0, 127.5, 127.1, 124.9, 122.5, 121.8, 113.2, 112.4, 101.4, 93.9, 91.3, 88.7, 69.8, 65.8, 60.7, 59.7, 55.4, 55.3, 49.7, 29.4, 23.1, 22.2, 15.5, 15.2; HRMS (FAB$^+$) for $C_{33}H_{27}NO_6Cs$ (M + Cs), calcd 698.0613, found 698.0620.

2-[(2-Nitrobenzyl)oxy]-10-[(triethylsilyl)oxy]-7,8,9,10-tetrahydrophenanthridine (70). Prepared in 95% yield in a similar manner as that described for **56**. **70**: white crystalline solid, mp 110–111 °C (from cyclohexane/hexanes); R_f = 0.54 (silica, 40% ethyl acetate in dichloromethane); IR ($CHCl_3$) ν_{max} 2953, 2908, 2875, 1619, 1526, 1506 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (s, 1 H, H6), 8.22 (dd, J = 7.7, 1.2 Hz, 1 H, aromatic), 8.01 (d, J = 9.1 Hz, 1 H, H4), 7.99 (dd, J = 7.7, 1.2 Hz, 1 H, aromatic), 7.71 (td, J = 7.7, 1.2 Hz, 1 H, aromatic), 7.52 (td, J = 7.7, 1.2 Hz, 1 H, aromatic), 7.51 (d, J = 2.7 Hz, 1 H, H1), 7.40 (dd, J = 9.1, 2.7 Hz, 1 H, H3), 5.67 and 5.63 (AB q, J = 15.3 Hz, 2 H, benzylic), 5.40 (t, J = 3.1 Hz, 1 H, H10), 3.02–2.97 (m, 1 H, H7), 2.81 (ddd, J = 17.3, 11.5, 5.8 Hz, 1 H, H7), 2.26–2.11 (m, 2 H, H9), 1.90–1.81 (m, 2 H, H8), 0.98 (t, J = 7.9 Hz, 9 H, OSi(CH$_2$C*H*$_3$)$_3$), 0.73 (q, J = 7.9 Hz, 6 H, OSi(C*H*$_2$CH$_3$)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.2, 150.8, 146.8, 143.4, 140.1, 134.1, 133.7, 131.6, 130.0, 128.4, 128.3, 128.1, 125.0, 120.0, 103.7, 66.9, 63.7, 32.0, 27.2, 16.6, 7.1, 5.6; MS (FAB$^+$) m/e (relative intensity) 465 (M + H, 100), 435 (8), 330 (11), 198 (10); HRMS for $C_{26}H_{33}N_2O_4Si$ (M + H) calcd 465.2209, found 465.2209. Anal. Calcd for $C_{26}H_{32}N_2O_4Si$: C, 67.21; H, 6.98; N, 6.03. Found: C, 66.99; H, 7.00; N, 5.94.

***N*-[(Phenyloxy)carbonyl]-6-ethynyl-2-[(2-nitrobenzyl)oxy]-10-[(triethylsilyl)oxy]-5,6,7,8,9,10-hexahydrophenanthridine (71).** Prepared in 100% yield in a similar manner as that described for **57**. **71**: white foam (ca. 3:1 mixture of diastereomers as determined by ^{1}H NMR); R_f = 0.37

(silica, 20% ethyl ether/petroleum ether); IR ($CDCl_3$) ν_{max} 3299, 3014, 2950, 2908, 2874, 1718, 1526, 1493, 1384, 1341, 1303 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (dd, J = 7.7, 1.3 Hz, 1 H, aromatic), 7.93 (dd, J = 7.7, 1.3 Hz, 1 H, aromatic), 7.70 (td, J = 7.7, 1.3 Hz, 1 H, aromatic), 7.50 (td, J = 7.7, 1.3 Hz, 1 H, aromatic), 7.38 (br t, J = 7.2 Hz, 1 H, aromatic), 7.24–7.17 (m, 6 H, aromatic), 6.85 (dd, J = 8.8, 2.8 Hz, 1 H, H3), 5.66 (d, J = 1.9 Hz, 1 H, H6, major isomer), 5.61 (d, J = 1.9 Hz, 1 H, H6, minor isomer), 5.53 (s, 2 H, benzylic), 4.98 (br s, 1 H, H10, major isomer), 4.69 (br s, 1 H, H10, minor isomer), 2.52–2.44 (m, 1 H, CH_2), 2.30–2.19 (m, 1 H, CH_2), 2.00–1.92 (m, 3 H, CH_2), 1.75–1.64 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.1, 150.9, 146.8, 136.7, 134.1, 134.0, 129.4, 129.3, 128.4, 128.2, 128.1, 125.7, 125.0, 121.7, 112.7, 112.4, 111.1, 110.9, 79.8, 71.8 and 71.7, 67.1 and 67.0, 65.1 and 64.2, 48.8, 32.7 and 31.9, 28.2, 27.9, 7.1 and 7.0, 5.7 and 5.5; MS (FAB$^+$) m/e (relative intensity) 610 (M$^+$, 100), 581 (25), 517 (13), 479 (86), 343 (7), 222 (18); HRMS for $C_{35}H_{38}N_2O_6Si$ (M$^+$) calcd 610.2499, found 610.2495. Anal. Calcd for $C_{35}H_{38}N_2O_6Si$: C, 68.83; H, 6.27; N, 4.59. Found: C, 68.83; H, 6.39; N, 4.78.

***N*-[(Phenyloxy)carbonyl]-6a,10a-epoxy-6-ethynyl-2-[(2-nitrobenzyl)oxy]-10-[(triethylsilyl)oxy]-5,6,6a,7,8,9,10,10a-octahydrophenanthridine (72).** Prepared in 95% yield in a similar manner as that described for **58**. **72**: white crystalline solid (ca. 3:1 mixture of diastereomers as determined by ^{1}H NMR), mp 135–137 °C (from dichloromethane/cyclohexane/hexanes); R_f = 0.44 (silica, 30% ethyl ether in petroleum ether); IR ($CHCl_3$) ν_{max} 3303, 2953, 2912, 2874, 2252, 1718, 1612, 1502, 1302 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (dd, J = 7.7, 1.3 Hz, 1 H, aromatic), 7.93–7.91 (m, 1 H, aromatic), 7.69 (t, J = 7.7 Hz, 1 H, aromatic), 7.63–7.61 (m, 1 H, aromatic), 7.50 (t, J = 7.7 Hz, 1 H, aromatic), 7.42–7.31 (m, 3 H, aromatic), 7.19–7.10 (m, 3 H, aromatic), 6.96 (dd, J = 8.8, 2.7 Hz, 1 H, H3, major isomer), 6.93 (dd, J = 8.8, 2.7 Hz, 1 H, H3, minor isomer), 5.55 (d, J = 2.1 Hz, 1 H, H6), 5.52 (s, 2 H, benzylic), 4.93 (br s, 1 H, H10, minor isomer), 4.80 (dd, J = 9.9, 5.6 Hz, 1 H, H10, major isomer), 2.43 (dd, J = 13.9, 6.8 Hz, 1 H, CH_2, minor isomer), 2.34 (dd, J = 14.8, 5.7 Hz, 1 H, CH_2, major isomer), 2.11 (d, J = 2.0 Hz, 1 H, C≡CH), 2.18–1.87 (m, 2 H, CH_2), 1.76–1.65 (m, 2 H, CH_2), 1.48–1.33 (m, 1 H, CH_2), 1.00 (t, J = 7.9 Hz, 9 H, Si(CH_2CH_3)$_3$), 0.71 (q, J = 7.9 Hz, 6 H, Si(CH_2CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.8, 153.9, 151.1, 146.8, 134.0, 133.8, 129.4, 129.2, 128.3, 128.2, 125.5, 125.0, 121.5, 116.3, 116.0, 113.8, 113.2, 78.5 and 78.4, 73.3, 72.8, 70.3 and 69.9, 67.1 and 67.0, 60.4 and 58.8, 48.4 and 47.9, 29.4 and 27.2, 24.0 and 23.9, 20.4 and 20.2, 7.0 and 6.9, 5.8 and 5.5; MS (FAB$^+$) m/e (relative intensity) 627 (M + H, 40), 626 (M$^+$, 100), 597 (52), 581 (10), 490 (26); HRMS for $C_{35}H_{38}N_2O_7Si$ (M$^+$) calcd 626.2448, found 626.2450. Anal. Calcd for $C_{35}H_{38}N_2O_7Si$: C, 67.07; H, 6.11; N, 4.47. Found: C, 66.91; H, 6.14; N, 4.36.

***N*-[(Phenyloxy)carbonyl]-6a,10a-epoxy-6-ethynyl-10-hydroxy-2-[(2-nitrobenzyl)oxy]-5,6,6a,7,8,9,10,10a-octahydrophenanthridine (73).** A solution of **72** (45.27 g, 72.3 mmol) and *tert*-butyl mercaptan (5.70 mL, 50.6 mmol) in THF (250 mL) was treated at 0 °C with tetra-*n*-butylammonium fluoride (TBAF, 75.9 mL, 1.0 M solution in THF, 75.9 mmol). The reaction mixture was stirred at 20 °C for 30 min, diluted with ethyl ether (750 mL), poured into water (1500 mL), and separated. The organic layer was washed with water (2 × 2000 mL), dried over anhydrous $MgSO_4$, and evaporated in vacuo. The residue was purified by suspending it in hot acetonitrile (500 mL), cooling to 10 °C, and filtering. The white solid was washed with acetonitrile (100 mL) and ethyl ether (200 mL) to give 32.70 g (88%) of **73**: white crystalline solid (ca. 3:1 mixture of diastereomers as determined by ^{1}H NMR), mp 207–209 °C (acetonitrile); R_f = 0.46 (silica, 10% ethyl acetate in dichloromethane); IR ($CDCl_3$) ν_{max} 3469, 3196, 2950, 2922, 1689, 1521, 1495, 1386 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.13 (dd, J = 7.8, 1.2 Hz, 1 H, aromatic), 7.84 (br dd, J = 7.8, 1.2 Hz, 1 H, aromatic), 7.79 (td, J = 7.8, 1.2 Hz, 1 H, aromatic), 7.63 (td, J = 7.8, 1.2 Hz, 1 H, aromatic), 7.60 (d, J = 2.7 Hz, 1 H, H1, major isomer), 7.55 (d, J = 2.7 Hz, 1 H, H1, minor isomer), 7.49–7.13 (m, 6 H, aromatic), 7.04 (dd, J = 8.8, 2.7 Hz, 1 H, H3, major isomer), 7.01 (dd, J = 8.8, 2.7 Hz, 1 H, H3, minor isomer), 5.65–5.44 (m, 2 H, benzylic, 1 H, OH, 1 H, H6, minor isomer), 5.31 (m, 1 H, H6, major isomer), 4.67 (br s, 1 H, H10, minor isomer), 4.48 (dt, J = 9.0, 6.5 Hz, 1 H, H10, major isomer), 2.27 (dd, J = 14.1, 6.7 Hz, 1 H, CH_2, minor isomer), 2.22 (dd, J = 14.8, 5.4 Hz, 1 H, CH_2, major isomer), 1.80–1.20 (m, 5 H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 155.6, 153.3, 150.8, 147.6, 134.0, 132.2, 129.5, 129.4, 129.3, 128.5, 128.2, 125.8, 124.8, 121.7, 115.8, 115.4, 114.1, 78.5, 76.0, 72.8, 67.0 and 66.7, 66.0, 62.4 and 60.2, 47.5, 29.1 and 27.3, 25.1 and 23.7, 22.4 and 19.8; MS (FAB$^+$) m/e (relative intensity) 513 (M + H, 100), 391 (86); HRMS for $C_{29}H_{25}N_2O_7$ (M + H) calcd 513.1662, found 513.1662. Anal. Calcd for $C_{29}H_{24}N_2O_7$: C, 67.96; H, 4.72; N, 5.47. Found: C, 67.71; H, 4.84; N, 5.36.

***N*-[(Phenyloxy)carbonyl]-6a,10a-epoxy-6-ethynyl-2-[(2-nitrobenzyl)oxy]-10-oxo-5,6,6a,7,8,9,10,10a-octahydrophenanthridine (74).** Prepared in 100% yield in a similar manner as that described for **60**. **74**: white crystalline solid, mp 128–130 °C (from dichloromethane/benzene/pentane); R_f = 0.28 (silica, dichloromethane); IR ($CHCl_3$) ν_{max} 3300, 2945, 2252, 1717, 1493, 1380, 1342, 1308, 1252 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (dd, J = 7.8, 1.2 Hz, 1 H, aromatic), 8.11 (d, J = 2.7 Hz, 1 H, H1), 7.91 (dd, J = 7.8, 1.2 Hz, 1 H, aromatic), 7.69 (td, J = 7.8, 1.2 Hz, 1 H, aromatic), 7.49 (td, J = 7.8, 1.2 Hz, 1 H, aromatic), 7.43–7.32 (m, 4 H, aromatic), 7.20 (br t, J = 7.2 Hz, 1 H, aromatic), 7.09 (br d, J = 7.2 Hz, 1 H, aromatic), 7.00 (dd, J = 8.9, 2.7 Hz, 1 H, H3), 5.71 (d, J = 2.4 Hz, 1 H, H6), 5.50 (s, 2 H, benzylic), 2.75 (dt, J = 15.1, 5.1 Hz, 1 H, H9), 2.59 (ddd, J = 15.1, 10.0, 6.0 Hz, 1 H, H9), 2.36–2.28 (m, 2 H, H7), 2.23 (br s, 1 H, C≡CH), 2.03–1.88 (m, 2 H, H8); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.1, 155.9, 154.0, 151.0, 146.9, 134.0, 133.4, 129.3, 129.3, 128.7, 128.6, 128.3, 125.8, 125.0, 124.4, 121.4, 116.9, 115.0, 77.5, 74.7, 74.4, 67.2, 57.2, 47.5, 38.7, 23.7, 18.3; MS (FAB$^+$) m/e (relative intensity) 511 (M + H, 100), 375 (20); HRMS for $C_{29}H_{23}N_2O_7$ (M + H) calcd 511.1505, found 511.1525. Anal. Calcd for $C_{29}H_{23}N_2O_7 \cdot {}^1/_2(C_6H_6)$: C, 69.94; H, 4.59; N, 5.10. Found: C, 69.81; H, 4.53; N, 4.88.

***N*-[(Phenyloxy)carbonyl]-6-[6-(trimethylsilyl)-3(*Z*)-hexene-1,5-diynyl]-6a,10a-epoxy-2-[(2-nitrobenzyl)oxy]-10-oxo-5,6,6a,7,8,9,10,10a-octahydrophenanthridine (75).** Prepared in 78% yield in a similar manner as that described for 62. **75**: white foam; R_f = 0.40 (silica, dichloromethane); IR ($CHCl_3$) ν_{max} 2956, 1718, 1526, 1493, 1380, 1342, 1308, 1250, 1203, 844 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (dd, J = 7.9, 1.2 Hz, 1 H, aromatic), 8.09 (d, J = 3.0 Hz, 1 H, H1), 7.90 (br d, J = 7.9 Hz, 1 H, aromatic), 7.69 (td, J = 7.9, 1.2 Hz, 1 H, aromatic), 7.51–7.06 (m, 7 H, aromatic), 6.97 (dd, J = 8.8, 3.0 Hz, 1 H, H3), 5.93 (d, J = 1.6 Hz, H6), 5.82 (d, J = 11.1 Hz, olefinic), 5.66 (br d, J = 11.1 Hz, olefinic), 5.49 (s, 2 H, benzylic), 2.77–2.62 (m, 2 H, H9), 2.38–2.25 (m, 2 H, H7), 2.01–1.90 (m, 2 H, H8), 0.20 (s, 9 H, SiC(CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.1, 155.8, 153.9, 151.0, 146.9, 134.0, 133.4, 129.3, 128.7, 128.6, 128.4, 125.7, 125.0, 124.3, 121.5, 121.4, 120.8, 118.9, 116.9, 115.0, 103.6, 101.5, 90.4, 83.1, 74.7, 67.2, 57.2, 48.3, 38.7, 23.8, 18.2, 0.16; MS (FAB$^+$) m/e (relative intensity) 632 (M$^+$, 100), 496 (14), 376 (10), 319 (7); HRMS for $C_{36}H_{32}N_2O_7Si$ (M$^+$) calcd 632.1979, found 632.1999. Anal. Calcd for $C_{36}H_{32}N_2O_7Si$: C, 68.34; H, 5.10; N, 4.43. Found: C, 68.30; H, 5.10; N, 4.41.

***N*-[(Phenyloxy)carbonyl]-6-[3(*Z*)-hexene-1,5-diynyl]-6a,10a-epoxy-2-[(2-nitrobenzyl)oxy]-10-oxo-5,6,6a,7,8,9,10,10a-octahydrophenanthridine (76).** Prepared in 96% yield in a similar manner as that described for 63. **76**: unstable white foam; R_f = 0.52 (silica, 60% ethyl ether in petroleum ether); IR ($CDCl_3$) ν_{max} 3300, 2945, 1717, 1582, 1492, 1380, 1309 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (dd, J = 7.8, 1.0 Hz, 1 H, aromatic), 7.99 (d, J = 2.8 Hz, 1 H, H1), 7.78 (br d, J = 7.8 Hz, 1 H, aromatic), 7.58 (td, J = 7.8, 1.0 Hz, 1 H, aromatic), 7.41–6.97 (m, 7 H, aromatic), 6.86 (dd, J = 8.8, 2.8 Hz, 1 H, H3), 5.78 (s, 1 H, H6), 5.70 and 5.63 (AB q, J = 11.0 Hz, 2 H, olefinic), 5.38 (s, 2 H, benzylic), 3.07 (d, J = 0.8 Hz, C≡CH), 2.68–2.54 (m, 2 H, H9), 2.27–2.21 (m, 2 H, H7), 1.89–1.80 (m, 2 H, H8); HRMS (FAB$^+$) for $C_{33}H_{25}N_2O_7$ (M + H) calcd 561.1662, found 561.1641.

Compound 77. Prepared in 86% yield in a similar manner as that described for **64**. **77**: white crystalline solid, mp 196–197 °C (from dichloromethane/ethyl ether/petroleum ether); R_f = 0.35 (silica, 60% ethyl ether in petroleum ether); IR ($CHCl_3$) ν_{max} 3430, 2955, 2252, 1718, 1689, 1523, 1492, 1386, 1340, 1325, 1274 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, J = 2.8 Hz, 1 H, H1), 8.15 (dd, J = 7.8, 1.2 Hz, 1 H, aromatic), 7.88 (d, J = 7.8, 1.2 Hz, 1 H, aromatic), 7.64 (td, J = 7.8, 1.2 Hz, 1 H, aromatic), 7.46 (td, J = 7.8, 1.2 Hz, 1 H, aromatic), 7.36–7.12 (m, 6 H, aromatic), 6.95 (dd, J = 8.9, 2.8 Hz, 1 H, H3), 5.81 (d, J = 10.0 Hz, 1 H, olefinic), 5.67 (dd, J = 10.0, 1.4 Hz, 1 H, olefinic), 5.51 (s, 2 H, benzylic), 5.50 (br s, 1 H, NCHC≡C), 2.31 (dd, J = 15.1, 8.3 Hz, 1 H, CH_2), 2.21 (s, 1 H, OH), 2.20–2.14 (m, 2 H, CH_2), 1.97 (m, 1 H, CH_2), 1.88 (dt, J = 12.1, 3.0 Hz, 1 H, CH_2), 1.73 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.0, 147.0, 134.0, 133.9, 129.6, 129.3, 129.2, 129.0, 128.7, 128.1, 127.3, 126.7, 124.9, 124.1, 124.0, 122.0, 121.5, 117.7, 114.7, 100.4, 94.0, 93.9, 88.7, 73.6, 73.0, 67.0, 64.2, 50.5, 35.1, 23.0, 19.1; HRMS (FAB$^+$) for $C_{33}H_{24}N_2O_7$ (M$^+$) calcd 560.1584, found 560.1584. Anal. Calcd for $C_{33}H_{24}N_2O_7 \cdot {}^1/_2(H_2O)$: C, 69.59; H, 4.42; N, 4.92. Found: C, 69.57; H, 4.32; N, 4.72.

Compound 78. A solution of **77** (809 mg, 1.44 mmol) in a mixture of dichloromethane (60 mL), methanol (240 mL), and triethylamine (0.02 mL) was distributed into 20 test tubes (16 × 20 mm, Fisher disposable borosilicate culture tubes) and exposed to sunlight at 28 °C for 4 h. The combined solutions were evaporated in vacuo, and the residue was purified by flash column chromatography (silica, 15% ethyl acetate in dichloromethane) to give a tan crystalline solid, which was further purified by recrystallization from ethyl acetate/dichloromethane/ethyl ether/petroleum ether to give 469 mg (76%) of **78**: white crystalline solid, mp 205–206 °C; R_f = 0.23 (silica, 15% ethyl acetate in dichloromethane); IR ($CHCl_3$) ν_{max} 3412, 3209, 2945, 1690, 1500, 1385, 1328 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.43 (s, 1 H, ArO*H*), 8.13 (d, *J* = 2.7 Hz, 1 H, aromatic), 7.39 (br t, *J* = 7.7 Hz, 2 H, aromatic), 7.25–7.10 (m, 4 H, aromatic), 6.62 (dd, *J* = 8.7, 2.7 Hz, 1 H, aromatic), 6.24 (s, 1 H, O*H*), 6.10 (d, *J* = 10.0 Hz, olefinic), 5.89 (dd, *J* = 10.0, 1.6 Hz, olefinic), 5.41 (br s, 1 H, NC*H*C≡C), 2.23 (dd, *J* = 15.3, 8.5 Hz, CH_2), 2.06–2.00 (m, 2 H, CH_2), 1.83–1.74 (m, 2 H, CH_2), 1.66–1.62 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 154.2, 150.8, 129.4, 127.2, 127.1, 125.7, 125.1, 122.1, 121.6, 117.9, 114.7, 102.6, 94.3, 92.6, 88.9, 72.5, 71.8, 64.9, 63.8, 50.3, 34.2, 22.9, 18.7; MS (FAB$^+$) *m/e* (relative intensity) 425 (M$^+$, 100), 255 (86); HRMS for $C_{26}H_139NO_5$ (M$^+$) calcd 425.1263, found 425.1281. Anal. Calcd for $C_{26}H_{19}NO_5$: C, 73.40; H, 4.50; N, 3.29. Found: C, 73.06; H, 4.81; N, 3.21.

Compound 79. A suspension of **78** (469 mg, 1.10 mmol) in dichloromethane (4.0 mL) was treated with triethylamine (184 mL, 1.32 mmol) and freshly distilled pivaloyl chloride (149 μL, 1.21 mmol) followed by stirring at 20 °C for 30 min to give a clear solution, which was diluted with ethyl ether (15 mL), poured into water (30 mL), and extracted with ethyl ether (10 mL). The combined organic layers were washed with water (30 mL), saturated aqueous sodium bicarbonate (30 mL), and brine (30 mL), dried ($MgSO_4$), and filtered through a 2 × 2 cm plug of silica, rinsing with ethyl ether (20 mL). The combined filtrates were evaporated in vacuo, and the residue was purified by recrystallization from dichloromethane/ethyl ether/petroleum ether to give 505 mg (90%) of **79**: white crystalline solid, mp 245–247 °C dec; R_f = 0.32 (silica, 50% ethyl ether in petroleum ether); IR ($CHCl_3$) ν_{max} 3464, 2969, 2870, 1723, 1492, 1381, 1316, 1203, 1177, 1118 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36 (d, *J* = 2.7 Hz, 1 H, aromatic), 7.45–7.11 (m, 6 H, aromatic), 7.02 (dd, *J* = 8.7, 2.7 Hz, 1 H, aromatic), 5.88 (d, *J* = 10.0 Hz, 1 H, olefinic), 5.69 (dd, *J* = 10.0, 1.3 Hz, 1 H, olefinic), 5.53 (d, *J* = 1.3 Hz, 1 H, NC*H*C≡C), 2.61 (br s, 1 H, O*H*), 2.32 (dd, *J* = 14.7, 7.9 Hz, 1 H, CH_2), 2.24–1.68 (m, 5 H, CH_2), 1.35 (s, 9 H, *t*-Bu); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.2, 151.3, 148.0, 133.1, 129.3, 129.0, 127.1, 127.0, 125.8, 124.4, 124.3, 122.2, 121.5, 121.2, 100.1, 94.4, 93.6, 88.9, 73.9, 73.2, 64.1, 50.3, 39.1, 35.2, 27.1, 23.1, 19.2; HRMS (FAB$^+$) for $C_{31}H_{27}NO_6$ (M$^+$) calcd 509.1838, found 509.1838.

Compound 80. Prepared in 100% yield in a similar manner as that described for **65**. **80**: white crystalline solid, mp 108–110 °C dec (from dichloromethane/benzene/cyclohexane); R_f = 0.20 (silica, 50% ethyl ether/petroleum ether); IR ($CHCl_3$) ν_{max} 2971, 2871, 1750, 1724, 1494, 1384, 1316, 1283, 1244, 1229, 1208, 1106 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (br s, 1 H, aromatic), 7.61–7.16 (m, 9 H, aromatic), 7.05 (dd, *J* = 8.8, 2.6 Hz, 1 H, aromatic), 6.00 (d, *J* = 10.1 Hz, 1 H, olefinic), 5.78 (dd, *J* = 10.1, 1.5 Hz, 1 H, olefinic), 5.61 (d, *J* = 1.5 Hz, 1 H, NC*H*C≡C), 3.08 (br d, *J* = 12.2 Hz, 1 H, CH_2), 2.48–1.81 (m, 5 H, CH_2), 1.17 (s, 9 H, *t*-Bu); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.1, 176.6, 150.8, 148.1, 137.4, 133.2, 131.1, 129.4, 128.3, 127.8, 127.5, 125.9, 124.2, 123.4, 122.6, 121.6, 121.4, 117.4, 100.8, 93.9, 93.8, 89.2, 85.6, 74.6, 63.4, 50.2, 38.9, 28.6, 26.8, 22.5, 18.5; MS (FAB$^+$) *m/e* (relative intensity) 620 (M + H, 9), 560 (12), 492 (32), 372 (6), 289 (17), 258 (9), 246 (12), 235 (29), 213 (10), 179 (100); HRMS for $C_{35}H_{30}N_3O_6S$ (M + H) calcd 620.1855, found 620.1832. Anal. Calcd for $C_{35}H_{30}N_3O_6S$: C, 67.84; H, 4.72; N, 6.78. Found: C, 67.44; H, 4.88; N, 4.80.

Compound 81. Prepared in 95% yield in a similar manner as that described for **66**. **81**: white crystalline solid, mp > 300 °C dec (from dichloromethane/ethyl ether/pentane); R_f = 0.43 (silica, 30% ethyl ether in petroleum ether); IR ($CHCl_3$) ν_{max} 3052, 2966, 2934, 2870, 1748, 1723, 1494, 1377, 1315, 1284, 1264, 1204, 1116 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51–7.11 (m, 7 H, aromatic), 7.03 (dd, *J* = 8.8, 2.6 Hz, 1 H, aromatic), 5.83 (dd, *J* = 9.9, 1.5 Hz, 1 H, olefinic), 5.69 (dd, *J* = 9.9, 1.5 Hz, 1 H, olefinic), 5.52 (d, *J* = 1.5 Hz, 1 H, NC*H*C≡C), 3.74 (s, 1 H, C≡C*H*C), 2.42 (dd, *J* = 15.2, 8.7 Hz, 1 H, CH_2), 2.30–1.59 (m, 5 H, CH_2), 1.20 (s, 9 H, *t*-Bu); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.8, 150.9, 148.2, 132.8, 129.9, 129.3, 127.3, 127.2, 125.7, 125.2, 122.0, 121.5, 121.2, 120.3, 101.3, 93.6, 91.5, 89.0, 70.2, 60.8, 49.8, 39.1, 29.5, 27.1, 23.2, 22.5, 15.6; MS (FAB$^+$) *m/e* (relative intensity) 494 (M + H, 100), 409 (6), 288 (7), 272 (10), 260 (7), 246 (9), 233 (7); HRMS for $C_{31}H_{28}NO_5$ (M + H) calcd 494.1967, found 494.1967. Anal. Calcd for $C_{31}H_{27}NO_5$: C, 75.44; H, 5.51; N, 2.84. Found: C, 75.66; H, 5.55; N, 2.91.

Compound 82. Cesium carbonate (9.00 g, 27.6 mmol) was flame dried under vacuum for 10 min and cooled. To the cesium carbonate was added 18-crown-6 (2.36 g, 8.93 mmol), 2-(phenylthio)ethanol (0.968 mL, 7.17 mmol), and dry acetonitrile (200 mL). After the mixture was stirred for 10 min at 25 °C, **81** (885 mg, 1.79 mmol) was added and stirring was continued for another 40 h at 25 °C. A solution of $tBuMe_2SiOCH_2CH_2OTs$ (2.66 g, 7.17 mmol) in dry benzene (5 mL) was added followed by stirring at 25 °C for another 40 h. The reaction mixture was filtered through a short pad of Celite and evaporated in vacuo. The residue was diluted with ethyl ether (120 mL), filtered from the precipitated 18-crown-6·CH_3CN complex, and evaporated in vacuo. The residue was purified by flash column chromatography (silica, 17:6:2 petroleum ether/benzene/ethyl ether) to give an off-white crystalline solid, which was further purified by recrystallization from benzene/pentane to give 785 mg (70%) of **82**: white crystalline solid, mp 146–147 °C; R_f = 0.47 (silica, 20% ethyl ether in petroleum ether); IR ($CDCl_3$) ν_{max} 3053, 2949, 2928, 2853, 1706, 1503, 1392, 1271, 1132 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.17 (m, 6 H, aromatic), 7.07 (d, *J* = 2.8 Hz, 1 H, aromatic), 6.81 (dd, *J* = 8.8, 2.8 Hz, 1 H, aromatic), 5.74 (dd, *J* = 9.9, 1.5 Hz, 1 H, olefinic), 5.63 (dd, *J* = 9.9, 1.5 Hz, 1 H, olefinic), 5.41–5.18 (m, 1 H, NC*H*C≡C), 4.36–4.16 (m, 2 H, $PhSCH_2CH_2O$), 4.02 (t, *J* = 5.0 Hz, 2 H, $ArOCH_2CH_2OTBS$), 3.95 (t, *J* = 5.0 Hz, 2 H, $ArOCH_2CH_2OTBS$), 3.66 (br s, 1 H, C*H*C≡C), 3.17–3.10 (m, 2 H, $PhSCH_2CH_2O$), 2.34 (m, 1 H, CH_2), 2.16 (dt, *J* = 15.1, 9.3 Hz, 1 H, CH_2), 2.03–1.84 (m, 2 H, CH_2), 1.75 (m, 1 H, CH_2), 1.53 (m, 1 H, CH_2), 0.90 (s, 9 H, *t*-Bu), 0.09 (s, 6 H, Si(CH_3)$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 135.0, 129.9, 129.5, 129.1, 128.8, 127.4, 127.3, 126.6, 124.9, 121.9, 113.8, 113.6, 101.5, 94.3, 91.3, 88.6, 70.1, 69.5, 64.6, 61.9, 60.9, 49.7, 32.4, 29.5, 25.9, 23.2, 22.5, 18.4, 15.6, –5.2; HRMS (FAB$^+$) for $C_{36}H_{41}NO_5SSi$ (M$^+$) calcd 627.2475, found 627.2485. Anal. Calcd for $C_{36}H_{41}NO_5SSi$: C, 68.87; H, 6.58; N, 2.23; S, 5.10; Si, 4.47. Found: C, 68.78; H, 6.59; N, 2.15; S, 5.14; Si, 4.34.

Compound 83. A solution of **82** (758 mg, 121 mmol) in THF (20 mL) was treated with tetra-*n*-butylammonium fluoride (TBAF) (1.33 mL, 1.0 M solution in THF, 1.33 mmol) followed by stirring at 20 °C for 20 min. The reaction mixture was evaporated in vacuo, and the residue was purified by flash column chromatography (silica, 75% ethyl ether in petroleum ether) to give 617 mg (100%) of **83**: white foam; R_f = 0.42 (silica, 90% ethyl ether in petroleum ether); IR ($CHCl_3$) 3586, 2936, 1702, 1502, 1394, 1319, 1271, 1230, 1206 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.19 (m, 6 H, aromatic), 7.12 (d, *J* = 2.8 Hz, 1 H, aromatic), 7.84 (dd, *J* = 8.8, 2.8 Hz, 1 H, aromatic), 7.77 (dd, *J* = 9.9, 1.4 Hz, 1 H, olefinic), 7.65 (dd, *J* = 9.9, 1.4 Hz, 1 H, olefinic), 5.43–5.18 (m, 1 H, NC*H*C≡C), 4.38–4.20 (m, 2 H, $PhSCH_2CH_2O$), 4.09 (t, *J* = 4.4 Hz, 2 H, $ArOCH_2CH_2OH$), 3.97 (br t, *J* = 4.4 Hz, 2 H, $ArOCH_2CH_2OH$), 3.68 (br s, 1 H, C*H*C≡C), 3.19–3.12 (m, 2 H, $PhSCH_2CH_2O$), 2.36 (m, 1 H, CH_2), 2.19 (dt, *J* = 15.3, 9.4 Hz, 1 H, CH_2), 2.08 (br s, 1 H, O*H*), 2.02–1.85 (m, 2 H, CH_2), 1.77 (m, 1 H, CH_2), 1.58 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.7, 135.0, 129.9, 129.7, 129.2, 129.1, 127.6, 127.5, 126.6, 124.9, 122.0, 113.8, 113.7, 101.5, 94.2, 91.4, 88.6, 70.2, 69.5, 64.6, 61.4, 60.9, 49.7, 32.4, 29.5, 23.2, 22.5, 15.6; HRMS (FAB$^+$) for $C_{30}H_{27}NO_5S$ (M$^+$) calcd 513.1610, found 513.1619.

Compound 18. Prepared in 99% yield in a similar manner as that described for **12**. **18**: white foam; R_f = 0.16 (silica, ethyl ether); IR ($CDCl_3$) ν_{max} 3520, 2934, 2870, 1707, 1503, 1399, 1320, 1292, 1206 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88–7.10 (m, 7 H, aromatic), 6.82 (br s, 1 H, aromatic), 5.76 (br d, *J* = 9.7 Hz, 1 H, olefinic), 5.64 (br d, *J* = 9.7 Hz, 1 H, olefinic), 5.36–4.99 (m, 1 H, NC*H*C≡C), 4.52–4.33 (m, 2 H, $SO_2CH_2CH_2O$), 4.08 (br s, 2 H, $ArOCH_2CH_2OH$), 3.96 (br s, 2 H, $ArOCH_2CH_2OH$), 3.66 (s, 1 H, C*H*C≡C), 3.50–3.42 (m, 2 H, $SO_2CH_2CH_2O$), 2.33 (br s, 1 H, CH_2), 2.20–2.13 (m, 2 H, CH_2 and O*H*), 1.99–1.84 (m, 2 H, CH_2), 1.77 (m, 1 H, CH_2), 1.57 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.9, 138.9, 134.0, 129.7, 129.4, 128.7, 128.0, 127.8, 127.6, 125.0, 121.9, 113.8, 101.4, 93.9, 91.4, 88.8, 70.0, 69.5, 61.4, 60.8, 59.3, 55.1, 49.7, 29.7, 29.4, 23.2, 22.4, 15.6; HRMS (FAB$^+$) $C_{30}H_{28}NO_7S$ (M + H) calcd 546.1586, found 546.1598.

2-[3-[(*tert*-Butyldiphenylsilyl)oxy]propynyl]-10-[(triethylsilyl)oxy]-7,8,9,10-tetrahydrophenanthridine (84). Prepared in 88% yield in a similar manner as that described for **56**. **84**: R_f = 0.66 (silica, 30% ethyl acetate in petroleum ether); IR (film) ν_{max} 2953, 2875, 1499, 1427, 1370, 111, 1085, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.86 (s, 1 H, H6), 8.22 (br s, 1 H, H1), 7.97 (d, *J* = 8.6 Hz, 1 H, H4), 7.82–7.77 (m, 4 H, aromatic), 7.56 (br d, *J* = 8.6 Hz, 1 H, H3), 7.48–7.39 (m, 6 H, aromatic), 5.54 (br s, 1 H, H10), 4.61 (s, 2 H, C≡CH_2O), 2.98 (br d, *J* = 17.0 Hz, 1 H, H7), 2.80 (ddd, *J* = 17.0, 11.4, 5.7 Hz, 1 H, H7), 2.21 (br d, *J* = 12.7 Hz, 1 H, H9), 2.17–2.09 (m, 1 H, H9), 1.93–1.84 (s, 2 H, H8), 1.12 (s, 9 H, ^{t}Bu), 1.01 (t, *J* = 8.0 Hz, 9 H, Si(CH_2CH_3)$_3$), 0.76 (q, *J* = 8.0 Hz, 6 H, Si(CH_2CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.2, 146.4, 140.8, 135.6, 133.1, 130.6, 130.2, 129.8, 129.7, 127.7, 127.4, 126.6, 120.9, 88.4, 84.9, 63.5, 53.1, 32.0, 27.1, 26.7, 19.2, 16.8, 6.9, 5.4; MS (FAB$^+$) *m/e* (relative intensity) 606 (M + H, 100), 474 (8), 220 (15), 197 (19), 181 (6); HRMS for $C_{38}H_{48}NO_2Si_2$ (M + H) calcd 606.3224, found 606.3230.

***N*-[(Phenyloxy)carbonyl]-2-[3-[(*tert*-butyldiphenylsilyl)oxy]propynyl]-6-ethynyl-10-[(triethylsilyl)oxy]-5,6,7,8,9,10-hexahydrophenanthridine (85).** Prepared in 83% yield in a similar manner as that described for **57**. **85**: R_f = 0.55 (silica, 50% ethyl ether in petroleum ether); IR (film) ν_{max} 3283, 2954, 2229, 2117, 1722, 1659, 1592, 1494, 1383, 1322 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.84 and 7.50 (2 br s, 1 H, H1), 7.79–7.74 (m, 4 H, aromatic), 7.48–7.37 (m, 8 H, aromatic), 7.31–7.18 (m, 5 H, aromatic), 5.68 and 5.62 (2 br s, 1 H, H6), 4.99 and 4.68 (2 br s, 1 H, H10), 4.56 and 4.55 (2 s, 2 H, C≡CH_2O), 2.54–2.43 (m, 1 H, H7), 2.32–2.19 (m, 1 H, H7), 2.22 (br s, 1 H, C≡CH), 2.08–1.87 (m, 3 H), 1.78–1.62 (m, 1 H), 1.11 (s, 9 H, ^{t}Bu), 1.06 and 0.95 (2 t, J = 7.9 Hz, 9 H, Si(CH$_2$CH_3)$_3$), 0.78 and 0.67 (2 q, J = 7.9 Hz, 6 H, Si(CH_2CH$_3$)$_3$); ^{13}C NMR (125 MHz, CDCl$_3$) δ 150.8, 135.4, 133.1, 130.0, 129.7, 129.5, 129.4, 129.1, 127.8, 127.7, 127.5, 127.1, 126.3, 125.8, 121.6, 121.5, 120.9, 87.1, 84.6 and 84.5, 79.7 and 79.5, 72.0 and 71.9, 64.8 and 64.6, 53.2 and 53.1, 48.7 and 48.1, 32.7 and 31.9, 28.2 and 27.8, 26.7, 19.2, 18.2, 7.1 and 6.9, 5.6 and 5.3; MS (FAB$^+$) m/e (relative intensity) 884 (M + Cs, 68), 694 (70), 620 (36), 197 (100); HRMS for C$_{47}$H$_{53}$NO$_4$Si$_2$Cs (M + Cs) calcd 884.2567, found 884.2567.

***N*-[(Phenyloxy)carbonyl]-2-[3-[(*tert*-butyldiphenylsilyl)oxy]propynyl]-6a,10a-epoxy-6-ethynyl-10-[(triethylsilyl)oxy]-5,6,6a,7,8,9,10,10a-octahydrophenanthridine (86).** Prepared in 87% yield in a similar manner as that described for **58**. **86**, **major isomer**: R_f = 0.41 (silica, 10% ethyl acetate in petroleum ether); IR (film) ν_{max} 3282, 2954, 2226, 2122, 1727, 1590, 1494, 1372, 1315, 1202 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.99 (br s, 1 H, H1), 7.79–7.74 (m, 4 H, aromatic), 7.48–7.39 (m, 7 H, aromatic), 7.38–7.31 (m, 3 H, aromatic), 7.22 (br t, J = 7.0 Hz, 1 H, aromatic), 7.18–7.11 (m, 2 H, aromatic), 5.58 (d, J = 1.9 Hz, 1 H, H6), 4.78 (dd, J = 9.8, 5.6 Hz, 1 H, H10), 4.55 (s, 2 H, C≡CCH_2O), 2.34 (br dd, J = 14.7, 5.5 Hz, 1 H, CH_2), 2.12 (br s, 1 H, C≡CH), 1.97–1.88 (m, 2 H, CH_2), 1.79–1.72 (m, 1 H, CH_2), 1.68 (br d, J = 10.7 Hz, 1 H, CH_2), 1.43–1.31 (m, 1 H, CH_2), 1.10 (s, 9 H, t-Bu), 1.01 (t, J = 7.9 Hz, 9 H, Si(CH$_2$CH_3)$_3$), 0.73 (q, J = 7.9 Hz, 6 H, Si(CH_2CH$_3$)$_3$); ^{13}C NMR (125 MHz, CDCl$_3$) δ 150.9, 135.6, 135.3, 133.1, 132.5, 131.2, 129.8, 129.3, 127.7, 125.7, 121.5, 87.7, 84.2, 78.3, 73.6, 72.9, 69.6, 60.2, 53.1, 47.7, 29.3, 26.6, 23.8, 20.3, 19.2, 7.0, 5.7; MS (FAB$^+$) m/e (relative intensity) 900 (M + Cs, 100), 710 (15), 197 (48); HRMS for C$_{47}$H$_{53}$NO$_5$Si$_2$Cs (M + Cs) calcd 900.2517, found 900.2526. **86**, **minor isomer**: R_f = 0.48 (silica, 10% ethyl acetate in petroleum ether); IR (film) ν_{max} 3307, 2955, 2222, 2124, 1726, 1590, 1494, 1371, 1317, 1202 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.79 (br s, 1 H, H1), 7.78–7.74 (m, 4 H, aromatic), 7.48–7.33 (m, 10 H, aromatic), 7.21 (br t, J = 7.0 Hz, 1 H, aromatic), 7.18–7.08 (m, 2 H, aromatic), 5.54 (d, J = 2.2 Hz, 1 H, H6), 4.94 (br s, 1 H, H10), 4.55 (s, 3 H, C≡CCH_2O), 2.42 (br dd, J = 14.2, 6.1 Hz, 1 H, CH_2), 2.16 (br s, 1 H, C≡CH), 2.06–1.97 (m, 2 H, CH_2), 1.97–1.86 (m, 2 H, CH_2), 1.72–1.66 (m, 1 H, CH_2), 1.50–1.42 (m, 1 H, CH_2), 1.10 (s, 9 H, ^{t}Bu), 0.98 (t, J = 8.0 Hz, 9 H, Si(CH$_2$CH_3)$_3$), 0.72 (q, J = 8.0 Hz, 6 H, Si(CH_2CH$_3$)$_3$); ^{13}C NMR (125 MHz, CDCl$_3$) δ 150.9, 135.6, 134.8, 133.1, 131.6, 131.0, 129.8, 129.3, 127.7, 125.7, 121.5, 87.7, 84.1, 78.2, 73.0, 70.5, 65.3, 58.6, 53.1, 47.7, 29.7, 26.7, 25.6, 22.7, 19.2, 6.9, 5.4; MS (FAB$^+$) m/e (relative intensity) 900 (M + Cs, 74), 710 (24), 197 (100); HRMS for C$_{47}$H$_{53}$NO$_5$Si$_2$Cs (M + Cs) calcd 900.2517, found 900.2526.

***N*-[(Phenyloxy)carbonyl]-2-[3-[(*tert*-butyldiphenylsilyl)oxy]propynyl]-6a,10a-epoxy-6-ethynyl-10-hydroxy-5,6,6a,7,8,9,10,10a-octahydrophenanthridine (87).** Prepared in 92% yield in a similar manner as that described for **59**. **87**: R_f = 0.23 (major isomer) and 0.25 (minor isomer) (silica, 40% ethyl ether in petroleum ether); IR (film) ν_{max} 3483, 3289, 2931, 2222, 1723, 1590, 1494, 1372, 1319, 1202, 1111 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.98 and 7.89 (d, J = 1.5 Hz, and br s, 1 H, H1), 7.80–7.76 (m, 4 H, aromatic), 7.48–7.40 (m, 7 H, aromatic), 7.40–7.32 (m, 3 H, aromatic), 7.22 (br t, J = 7.3 Hz, 1 H, aromatic), 7.18–7.10 (m, 2 H, aromatic), 5.63 and 5.59 (2 d, J = 2.4 and 2.2 Hz, 1 H, H6), 4.84 and 4.67 (2 br s, 1 H, H10), 4.57 and 4.56 (2 s, 2 H, C≡CCH_2O), 2.45 and 2.36 (dd and ddd, J = 15.2, 7.6 Hz and J = 14.7, 5.0, 5.0 Hz, 1 H, CH_2), 2.23 and 2.17 (2 br s, 1 H, C≡CH), 2.14 (br s, 1 H, OH), 2.08–1.88 (m, 2 H, CH_2), 1.78–1.68 (m, 1 H, CH_2), 1.64–1.51 (m, 1 H, CH_2), 1.45–1.35 (m, 1 H, CH_2), 1.11 (s, 9 H, t-Bu); ^{13}C NMR (125 MHz, CDCl$_3$) δ 150.8, 135.6, 135.3, 133.1 and 133.0, 132.0, 131.7, 129.7, 129.3, 127.7, 125.8, 121.4, 88.1 and 87.9, 84.4 and 84.3, 78.3 and 78.0, 74.6, 73.4 and 70.6, 66.3 and 64.1, 60.5 and 58.0, 53.1, 47.6, 29.9 and 29.6, 26.7, 24.1, 22.7 and 19.1, 18.8; MS (FAB$^+$) m/e (relative intensity) 786 (M + Cs, 100), 596 (14), 566 (16), 199 (49); HRMS for C$_{41}$H$_{39}$NO$_5$SiCs (M + Cs) calcd 786.1652, found 786.1691.

***N*-[(Phenyloxy)carbonyl]-2-[3-[(*tert*-butyldiphenylsilyl)oxy]propynyl]-6a,10a-epoxy-6-ethynyl-10-oxo-5,6,6a,7,8,9,10,10a-octahydrophenanthridine (88).** Prepared in 90% yield in a similar manner as that described for **60**. **88**: R_f = 0.54 (silica, 50% ethyl ether in petroleum ether); IR (film) ν_{max} 3289, 2930, 2238, 2090, 1725, 1590, 1494, 1372, 1317, 1203, 1112 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.43 (br s, 1 H, H1), 7.79–7.73 (m, 4 H, aromatic), 7.47–7.39 (m, 7 H, aromatic), 7.39–7.32 (m, 3 H, aromatic), 7.23 (br t, J = 6.9 Hz, 1 H, aromatic), 7.16–7.08 (m, 2 H, aromatic), 5.73 (d, J = 1.2 Hz, 1 H, H6), 4.54 (s, 2 H, C≡CCH_2O), 2.76 (ddd, J = 15.5, 4.8, 4.8 Hz, 1 H, H9), 2.60 (ddd, J = 15.5, 10.0, 6.1 Hz, 1 H, H9), 2.38–2.28 (m, 2 H, CH_2), 2.24 (br s, 1 H, C≡CH), 2.06–1.89 (m, 2 H, CH_2), 1.10 (s, 9 H, ^{t}Bu); ^{13}C NMR (125 MHz, CDCl$_3$) δ 200.5, 150.8, 135.6, 135.4, 133.3, 133.1, 132.1, 129.8, 129.4, 127.7, 125.9, 121.4, 88.2, 84.2, 77.3, 74.9, 74.6, 57.0, 53.1, 47.3, 38.7, 26.7, 23.7, 19.2, 18.3; MS (FAB$^+$) m/e (relative intensity) 784 (M + Cs, 100), 564 (50), 197 (46); HRMS for C$_{41}$H$_{37}$NO$_5$SiCs (M + Cs) calcd 784.1495, found 784.1495.

***N*-[(Phenyloxy)carbonyl]-2-[3-[(*tert*-butyldiphenylsilyl)oxy]propynyl]-6-[6-(trimethylsilyl)-3(*Z*)-hexene-1,5-diynyl]-6a,10a-epoxy-10-oxo-5,6,6a,7,8,9,10,10a-octahydrophenanthridine (89).** Prepared in 67% yield in a similar manner as that described for **62**. **89**: R_f = 0.71 (silica, 50% ethyl ether in petroleum ether); IR (film) ν_{max} 2927, 2143, 1725, 1593, 1493, 1374, 1314, 1252, 1202, 1111, 884 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.42 (d, J = 1.5 Hz, 1 H, H1), 7.79–7.73 (m, 4 H, aromatic), 7.48–7.38 (m, 7 H, aromatic), 7.36 (br t, J = 7.6 Hz, 2 H, aromatic), 7.34 (dd, J = 8.5, 1.5 Hz, 1 H, H3), 7.22 (br t, J = 7.6 Hz, 1 H, aromatic), 7.16–7.08 (m, 2 H, aromatic), 5.97 (d, J = 1.6 Hz, 1 H, H6), 5.84 (d, J = 10.8 Hz, 1 H, olefinic), 5.68 (d, J = 10.8 Hz, 1 H, olefinic), 4.54 (s, 2 H, C≡CCH_2O), 2.76 (ddd, J = 15.0, 5.1, 5.1 Hz, 1 H, H9), 2.71 (ddd, J = 15.0, 10.1, 6.1 Hz, 1 H, H9), 2.40–2.29 (m, 2 H, CH_2), 2.06–1.88 (m, 2 H, CH_2), 1.11 (s, 9 H, t-Bu), 0.23 (s, 9 H, Si(CH_3)$_3$); ^{13}C NMR (125 MHz, CDCl$_3$) δ 200.5, 150.9, 135.7, 135.6, 133.4, 133.1, 132.1, 129.8, 129.4, 127.7, 125.9, 121.4, 121.0, 118.7, 103.8, 101.5, 90.1, 88.2, 84.3, 83.2, 74.0, 57.2, 53.1, 48.2, 38.8, 26.7, 23.9, 19.2, 18.2, –0.1; MS (FAB$^+$) m/e (relative intensity) 906 (M + Cs, 100), 197 (72); HRMS for C$_{48}$H$_{47}$NO$_5$Si$_2$Cs (M + Cs) calcd 906.2047, found 906.2049.

***N*-[(Phenyloxy)carbonyl]-2-[3-[(*tert*-butyldiphenylsilyl)oxy]propynyl]-6-[3(*Z*)-hexene-1,5-diynyl]-6a,10a-epoxy-10-oxo-5,6,6a,7,8,9,10,10a-octahydrophenanthridine (90).** Prepared in 90% yield in a similar manner as that described for **63**. **90**: R_f = 0.44 (silica, 50% ethyl ether in petroleum ether); IR (film) ν_{max} 3290, 2930, 2228, 2094, 1723, 1590, 1493, 1371, 1316, 1201, 1112 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.44 (d, J = 1.5 Hz, 1 H, H1), 7.82–7.55 (m, 4 H, aromatic), 7.48–7.41 (m, 7 H, aromatic), 7.38 (br t, J = 7.6 Hz, 2 H, aromatic), 7.34 (dd, J = 8.4, 1.5 Hz, 1 H, H3), 7.23 (br t, J = 7.6 Hz, 1 H, aromatic), 7.18–7.10 (m, 2 H, aromatic), 5.93 (d, J = 1.8 Hz, 1 H, H6), 5.81 (dd, J = 11.1, 1.7 Hz, 1 H, olefinic), 5.78 (br d, J = 11.1 Hz, 1 H, olefinic), 4.55 (s, 2 H, C≡CCH_2O), 3.17 (d, J = 1.7 Hz, 1 H, C≡CH), 2.77 (ddd, J = 15.4, 4.9, 4.9 Hz, 1 H, H9), 2.70 (ddd, J = 15.4, 10.1, 6.0 Hz, 1 H, H9), 2.41–2.38 (m, 2 H, CH_2), 2.06–1.99 (m, 2 H, CH_2), 1.11 (s, 9 H, ^{t}Bu); ^{13}C NMR (125 MHz, CDCl$_3$) δ 200.7, 150.8, 135.6, 133.3, 133.0, 131.9, 129.7, 129.3, 127.7, 125.8, 121.4, 120.7, 90.1, 88.1, 85.3, 84.3, 82.9, 80.1, 75.1, 57.1, 53.1, 48.2, 38.7, 26.7, 23.8, 19.1, 18.3; MS (FAB$^+$) m/e (relative intensity) 834 (M + Cs, 100), 197 (83); HRMS for C$_{45}$H$_{39}$NO$_5$SiCs (M + Cs) calcd 834.1652, found 834.1652.

Compound 91. Prepared in 90% yield in a similar manner as that described for **64**. **91**: R_f = 0.36 (silica, 50% ethyl ether in petroleum ether); IR (film) ν_{max} 3450, 2930, 2230, 1723, 1590, 1494, 1381, 1320, 1120, 1111, 703 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.73 (d, J = 1.7 Hz, 1 H, aromatic), 7.80–7.74 (m, 4 H, aromatic), 7.47–7.38 (m, 7 H, aromatic), 7.36 (br t, J = 7.8 Hz, 2 H, aromatic), 7.28 (dd, J = 8.4, 1.7 Hz, 1 H, aromatic), 7.22 (br t, J = 7.8 Hz, 1 H, aromatic), 7.18–7.12 (m, 2 H, aromatic), 5.87 (d, J = 10.0 Hz, 1 H, olefinic), 5.68 (dd, J = 10.0, 1.6 Hz, 1 H, olefinic), 5.64 (d, J = 1.1 Hz, 1 H, NCHC≡C), 4.53 (s, 2 H, C≡CCH_2O), 2.70 (br s, 1 H, OH), 2.31 (dd, J = 15.0, 8.2 Hz, 1 H, CH_2), 2.24–2.11 (m, 2 H, CH_2), 2.06–1.87 (m, 2 H, CH_2), 1.78–1.68 (m, 1 H, CH_2), 1.10 (s, 9 H, t-Bu); ^{13}C NMR (125 MHz, CDCl$_3$) δ 150.8, 135.6, 134.8, 133.1, 131.2, 129.7, 129.3, 127.9, 127.7, 125.8, 124.4, 122.0, 121.5, 119.9, 100.5, 94.2, 93.5, 88.8, 87.3, 85.0, 73.9, 73.0, 64.1, 53.2, 50.2, 35.1, 29.6, 26.7, 23.1, 19.1; MS (FAB$^+$) m/e (relative intensity) 834 (M + Cs, 87), 197 (100); HRMS for C$_{45}$H$_{39}$NO$_5$SiCs (M + Cs) calcd 834.1652, found 834.1660.

Compound 92. Prepared in 76% yield in a similar manner as that described for **65**. **92**: R_f = 0.27 (silica, 50% ethyl ether in petroleum ether); IR (film) ν_{max} 2930, 2233, 1727, 1590, 1493, 1385, 1319, 1283, 1197, 1106, 703 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.38 (s, 1 H, imidazole), 7.73 (d, J = 1.5 Hz, 1 H, aromatic), 7.72–7.67 (m, 4 H, aromatic), 7.59 (s, 1 H, imidazole), 7.51–7.36 (m, 9 H, aromatic), 7.32 (dd, J = 8.4, 1.5 Hz, 1 H, aromatic), 7.25 (br t, J = 7.5 Hz, 1 H, aromatic), 7.18 (br d, J = 7.5 Hz, 2 H, aromatic), 6.98 (s, 1 H, imidazole), 5.99 (d, J = 10.0 Hz, 1 H, olefinic), 5.78 (dd, J = 10.0, 1.7 Hz, 1 H, olefinic), 5.60 (d, J = 1.5 Hz, 1 H, NCHC≡C), 4.42 (s, 2 H, C≡CCH_2O), 3.20–3.11 (m, 1 H, CH_2), 2.43 (dd, J = 15.2, 8.0 Hz, 1 H, CH_2), 2.37–2.18 (m, 2 H, CH_2), 2.17–2.05 (m, 1 H, CH_2), 1.90–1.80 (m, 1 H, CH_2), 1.05 (s, 9 H, t-Bu); ^{13}C NMR (125 MHz, CDCl$_3$) δ 179.3, 150.8, 137.3, 135.9, 135.6, 133.1, 133.0, 132.8, 131.7, 131.1, 129.8, 129.5, 128.3, 127.7, 126.7, 126.0, 124.3, 123.4, 121.5, 120.4, 117.5, 100.6, 94.4, 93.7, 89.2, 88.1, 85.4, 84.0, 74.9, 63.6, 53.1, 50.3, 28.5, 26.7, 22.7, 19.2, 18.5; MS (FAB$^+$) m/e (relative intensity) 944 (M + Cs, 95), 684

(38), 476 (46), 197 (100); HRMS for $C_{49}H_{41}N_3O_5SSiCs$ (M + Cs) calcd 944.1591, found 944.1272.

Compound 93. Prepared in 77% yield in a similar manner as that described for **66**. **93**: R_f = 0.70 (silica, 50% ethyl ether in petroleum ether); IR (film) ν_{max} 2930, 2226, 2184, 1726, 1591, 1493, 1371, 1317, 1201, 1112, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82–7.76 (m, 4 H, aromatic), 7.59 (d, J = 1.3 Hz, 1 H, H1), 7.49–7.35 (m, 7 H, aromatic), 7.29 (dd, J = 8.4, 1.3 Hz, 1 H, H3), 7.23 (br t, J = 7.4 Hz, 1 H, aromatic), 7.18–7.12 (m, 2 H, aromatic), 5.83 (dd, J = 9.8, 1.2 Hz, 1 H, olefinic), 5.70 (dd, J = 9.8, 1.5 Hz, 1 H, olefinic), 5.54 (s, 1 H, H6), 4.57 (s, 2 H, C≡CCH_2O), 3.74 (br s, 1 H, H10), 2.42 (dd, J = 15.5, 8.3 Hz, 1 H, CH_2), 2.26 (ddd, J = 15.3, 9.5, 9.5 Hz, 1 H, CH_2), 2.09–1.90 (m, 2 H, CH_2), 1.89–1.80 (m, 1 H, CH_2), 1.68–1.58 (m, 1 H, CH_2), 1.11 (s, 9 H, t-Bu); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.8, 135.7, 135.3, 133.1, 131.3, 130.6, 129.7, 129.3, 128.7, 127.7, 125.8, 125.2, 121.9, 121.5, 119.9, 101.5, 93.5, 91.5, 89.0, 87.7, 84.6, 70.2, 60.7, 53.2, 49.8, 29.4, 26.7, 23.2, 22.5, 19.2, 15.6; MS (FAB$^+$) m/e (relative intensity) 818 (M + Cs, 100), 598 (48), 430 (22), 197 (51); HRMS for $C_{45}H_{39}NO_4SiCs$ (M + Cs) calcd 818.1703, found 818.1703.

Compound 94. Prepared in 92% yield in a similar manner as that described for **28**. **94**: R_f = 0.52 (silica, 40% ethyl ether in petroleum ether); IR (film) ν_{max} 2931, 2246, 2193, 1713, 1587, 1496, 1391, 1318, 1269, 1111 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81–7.76 (m, 4 H, aromatic), 7.54 (d, J = 1.1 Hz, 1 H, aromatic), 7.48–7.38 (m, 8 H, aromatic), 7.38–7.32 (br, 1 H, aromatic), 7.31 (t, J = 7.5 Hz, 2 H, aromatic), 7.26 (dd, J = 7.5, 1.1 Hz, 1 H, aromatic), 7.22 (t, J = 7.5 Hz, 1 H, aromatic), 5.80 (dd, J = 9.8, 1.1 Hz, 1 H, olefinic), 5.67 (dd, J = 9.8, 1.4 Hz, 1 H, olefinic), 5.41 (br s, 1 H, NCHC≡C), 4.57 (s, 2 H, C≡CCH_2O), 4.38 (dt, J = 11.1, 7.1 Hz, 1 H, $PhSCH_2CH_2O$), 4.32–4.21 (br s, 1 H, $PhSCH_2CH_2O$), 3.69 (br s, 1 H, C≡CCHC), 3.23–3.09 (m, 2 H, $PhSCH_2CH_2O$), 2.37 (dd, J = 15.3, 8.4 Hz, 1 H, CH_2), 2.20 (ddd, J = 15.3, 9.6, 9.6 Hz, 1 H, CH_2), 2.04–1.87 (m, 2 H, CH_2), 1.84–1.78 (m, 1 H, CH_2), 1.63–1.56 (m, 1 H, CH_2), 1.11 (s, 9 H, t-Bu); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.9, 135.6, 135.4, 134.8, 133.1, 131.2, 130.4, 130.0, 129.7, 129.1, 128.3, 127.6, 126.6, 125.1, 121.9, 119.4, 101.5, 93.7, 91.4, 88.7, 87.5, 84.7, 70.4, 64.8, 60.6, 53.2, 49.3, 32.4, 29.3, 26.7, 23.1, 22.5, 19.2, 15.6; MS (FAB$^+$) m/e (relative intensity) 878 (M + Cs, 100), 197 (30); HRMS for $C_{47}H_{43}NO_4SSiCs$ (M + Cs) calcd 878.1736, found 878.1701.

Compound 95. To a solution of **94** (29 mg, 0.039 mmol) in THF (1 mL) was added tetra-n-butylammonium fluoride (58 μL, 1.0 M solution in THF, 0.058 mmol) at 0 °C. After being stirred for 15 min, the mixture was concentrated in vacuo, and the residue was purified by flash column chromatography (silica, 70% ethyl ether in petroleum ether) to afford 16 mg (81%) of **95**: R_f = 0.68 (silica, 80% ethyl ether in petroleum ether); IR (film) ν_{max} 3398, 2933, 2226, 2194, 1713, 1609, 1583, 1496, 1391, 1319, 1237 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (s, 1 H, aromatic), 7.42–7.32 (m, 4 H, aromatic), 7.29 (t, J = 7.6 Hz, 2 H, aromatic), 7.20 (t, J = 7.6 Hz, 1 H, aromatic), 5.77 (dd, J = 9.8, 1.4 Hz, 1 H, olefinic), 5.67 (dd, J = 9.8, 1.6 Hz, 1 H, olefinic), 5.39 (br s, 1 H, NCHC≡C), 4.48 (s, 2 H, C≡CCH_2O), 4.36 (dt, J = 11.1, 6.9 Hz, 1 H, $PhSCH_2CH_2O$), 4.30–4.19 (m, 1 H, $PhSCH_2CH_2O$), 3.70 (br s, 1 H, C≡CCHC), 3.22–3.08 (m, 2 H, $PhSCH_2CH_2O$), 2.34 (dd, J = 15.1, 8.3 Hz, 1 H, CH_2), 2.18 (ddd, J = 15.1, 9.6, 9.6 Hz, 1 H, CH_2), 2.04 (br s, 1 H, OH), 2.01–1.83 (m, 2 H, CH_2), 1.81–1.74 (m, 1 H, CH_2), 1.61–1.53 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.9, 135.6, 134.7, 131.2, 130.6, 129.9, 129.1, 128.5, 126.6, 125.1, 121.9, 119.0, 101.4, 93.6, 91.5, 88.7, 87.2, 85.2, 70.4, 64.8, 60.6, 51.5, 49.3, 32.4, 29.3, 23.1, 22.5, 15.5; MS (FAB$^+$) m/e (relative intensity) 640 (M + Cs, 96), 186 (100); HRMS for $C_{31}H_{25}NO_4SCs$ (M + Cs) calcd 640.0559, found 640.0572.

Compound 19. Prepared in 82% yield in a similar manner as that described for **12**. **19**: R_f = 0.37 (silica, ethyl ether); IR (film) ν_{max} 3498, 2932, 2226, 2196, 1713, 1498, 1396, 1321, 1144, 734 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (br s, 2 H, aromatic), 7.62 (br s, 2 H, aromatic), 7.51 (br s, 2 H, aromatic), 7.27 (t, J = 6.8 Hz, 1 H, aromatic), 7.18 (br s, 1 H, aromatic), 5.76 (d, J = 9.8 Hz, 1 H, olefinic), 5.63 (d, J = 9.8 Hz, 1 H, olefinic), 5.28 (br s, 1 H, NCHC≡C), 4.62–4.32 (m, 2 H, $SO_2CH_2CH_2O$), 4.47 (m, 2 H, C≡CCH_2O), 3.67 (br s, 1 H, C≡CCHC), 3.55–3.39 (m, 2 H, $SO_2CH_2CH_2O$), 2.31 (dd, J = 15.1, 7.8 Hz, 1 H, CH_2), 2.22 (br s, 1 H, OH), 2.16 (ddd, J = 15.1, 9.5, 9.5 Hz, 1 H, CH_2), 1.99–1.73 (m, 3 H, CH_2), 1.62–1.52 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.5, 138.7, 135.2, 134.0, 131.3, 130.6, 129.4, 128.6, 127.9, 125.1, 121.8, 119.3, 101.3, 93.2, 91.5, 88.8, 87.4, 84.9, 70.2, 60.5, 59.5, 55.0, 51.4, 49.4, 29.2, 23.1, 22.4, 15.5; MS (FAB$^+$) m/e (relative intensity) 672 (M + Cs, 100); HRMS for $C_{11}H_{25}NO_6SCs$ (M + Cs) calcd 672.0457, found 672.0457.

Compound 96. A solution of **81** (54 mg, 0.109 mmol) in benzene (1.5 mL) and freshly distilled 1,4-cyclohexadiene (0.5 mL) was treated with p-toluenesulfonic acid (36 mg, 0.189 mmol) and water (36 μL, 2.0 mmol) followed by heating at 80 °C for 30 min. The reaction mixture was diluted with ethyl ether (5 mL), filtered through a 1 × 1 cm plug of silica, and evaporated in vacuo. The residue was purified by preparative TLC (silica, 12% ethyl ether in dichloromethane) to give 43 mg (80%) of **96**: white foam; R_f = 0.14 (silica, 30% ethyl ether in petroleum ether); IR ($CDCl_3$) ν_{max} 3480, 2933, 2872, 1750, 1718, 1490, 1378, 1314, 1288, 1205, 1161, 1121 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47–7.38 (m, 5 H, aromatic), 7.23–7.13 (m, 5 H, aromatic), 6.89 (d, J = 7.3 Hz, 1 H, aromatic), 6.79 (dd, J = 9.0, 2.7 Hz, 1 H, aromatic), 5.79 (s, 1 H, NCHAr), 3.32 (s, 1 H, CH_2CHAr), 3.14 (s, 1 H, OH), 2.55 (s, 1 H, OH), 2.28 (m, 1 H, CH_2), 2.05 (m, 1 H, CH_2), 1.75 (m, 1 H, CH_2), 1.42–1.30 (m, 2 H, CH_2), 1.32 (s, 9 H, $C(O)C(CH_3)_3$), 0.84 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.1, 151.1, 147.8, 138.9, 135.3, 131.9, 129.4, 128.7, 128.4, 127.5, 126.9, 125.7, 124.2, 121.7, 120.7, 119.2, 72.9, 69.3, 51.4, 39.0, 32.6, 27.1, 26.6, 18.3; MS (FAB$^+$) m/e (relative intensity) 646 (M + Cs, 100), 584 (34); HRMS for $C_{31}H_{31}NO_6Cs$ (M + Cs) calcd 646.1206, found 646.1219.

Compound 97. A solution of **81** (123 mg, 0.25 mmol) and cesium carbonate (33 mg, 1.00 mmol) in dry methanol (5 mL) was stirred at 40 °C for 1 h. Dry ice (1 g) was added and stirring was continued for 10 min. The solution was evaporated in vacuo, and the residue was dissolved in dichloromethane (10 mL) and ethyl ether (2 mL). The solution was filtered through a 1 × 1 cm plug of silica and evaporated to give 95 mg (93%) of **97**: white foam; R_f = 0.34 (silica, 50% ethyl ether in petroleum ether); IR ($CDCl_3$) ν_{max} 3394, 3055, 2941, 1707, 1593, 1499, 1382, 1314, 1289, 1199, 1024, 909 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.06 (m, 7 H, aromatic), 6.73 (m, 1 H, aromatic), 5.79 (dd, J = 9.9, 1.7 Hz, 1 H, olefinic), 5.67 (dd, J = 9.9, 1.7 Hz, 1 H, olefinic), 5.47 (d, J = 1.7 Hz, NCHC≡C), 5.42 (br s, 1 H, ArOH), 3.67 (s, 1 H, CHC≡C), 2.39 (dd, J = 15.7, 8.4 Hz, 1 H, CH_2), 2.22 (m, 1 H, CH_2), 2.04–1.89 (m, 2 H, CH_2), 1.79 (m, 1 H, CH_2), 1.59 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.1, 129.9, 129.3, 128.5, 127.6, 125.7, 125.0, 121.9, 121.5, 115.3, 114.2, 112.2, 104.1, 101.6, 94.0, 91.4, 88.9, 70.0, 61.0, 50.0, 29.5, 23.2, 22.5, 15.6; HRMS (FAB$^+$) for $C_{26}H_139NO_4Cs$ (M + Cs) calcd 542.0368, found 542.0379.

Compound 98. Cesium carbonate (203 mg, 0.623 mmol) was flame dried under vacuum for 10 min and allowed to cool to ambient temperature. To the cesium carbonate were added **97** (85 mg, 0.208 mmol), 18-crown-6 (27 mg, 0.104 mmol), $^tBuMe_2SiOCH_2CH_2OTs$ (152 mg, 0.415 mmol), and dry acetonitrile (10 mL). After stirring for 6 h at 25 °C, the reaction mixture was filtered through a cotton plug and evaporated in vacuo. The residue was diluted with ethyl ether (20 mL), filtered from the precipitated 18-crown-6·CH_3CN complex, and evaporated in vacuo. The residue was purified by preparative TLC (silica, 9:1:1 petroleum ether/ethyl ether/dichloromethane) to give 78 mg (66%) of **98**: white foam; R_f = 0.42 (silica, 20% ethyl ether in petroleum ether); IR ($CDCl_3$) ν_{max} 3054, 2951, 2929, 2881, 2855, 1723, 1504, 1494, 1378, 1273, 1200, 1131, 960 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.33 (m, 3 H, aromatic), 7.21–7.10 (m, 3 H, aromatic), 7.14 (d, J = 2.8 Hz, 1 H, aromatic), 6.86 (dd, J = 8.9, 2.8 Hz, 1 H, aromatic), 5.78 (dd, J = 9.9, 1.3 Hz, 1 H, olefinic), 5.67 (dd, J = 9.9, 1.3 Hz, 1 H, olefinic), 5.48 (d, J = 1.3 Hz, 1 H, NCHC≡C), 4.05 (t, J = 5.2 Hz, 2 H, $ArOCH_2CH_2OTBS$), 3.97 (t, J = 5.2 Hz, 2 H, $ArOCH_2CH_2OTBS$), 3.73 (br s, 1 H, CHC≡C), 2.40 (dd, J = 15.2, 8.0 Hz, 1 H, CH_2), 2.23 (dt, J = 15.2, 9.5 Hz, 1 H, CH_2), 2.06–1.90 (m, 2 H, CH_2), 1.81 (m, 1 H, CH_2), 1.61 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.3, 153.7, 151.2, 129.8, 129.3, 128.7, 127.4, 125.6, 125.0, 121.9, 121.5, 113.9, 113.8, 101.6, 94.1, 91.4, 88.9, 70.0, 69.6, 61.9, 61.0, 50.0, 29.5, 25.9, 23.3, 22.5, 18.4, 15.6, –5.2; MS (FAB$^+$) m/e (relative intensity) 700 (M + Cs, 100), 568 (50), 510 (11); HRMS for $C_{34}H_{37}NO_5SiCs$ (M + Cs) calcd 700.1495, found 700.1488.

Compound 99. A solution of **98** (62 mg, 0.109 mmol) in benzene (1.5 mL) and freshly distilled 1,4-cyclohexadiene (0.5 mL) was treated with p-toluenesulfonic acid (39 mg, 0.189 mmol) and water (36 μL, 2.0 mmol) followed by heating at 50 °C for 2 h. The reaction mixture was diluted with ethyl acetate (5 mL), filtered through a 1 × 1 cm plug of sodium bicarbonate, and evaporated in vacuo. The residue was purified by preparative TLC (silica, ethyl acetate) to give 35 mg (71%) of **99**: white foam; R_f = 0.54 (silica, ethyl acetate); IR ($CDCl_3$) ν_{max} 3453, 3065, 2932, 2872, 1703, 1611, 1493, 1456, 1381, 1301, 1203, 1062, 907 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43–7.05 (m, 10 H, aromatic), 6.84 (d, J = 7.4 Hz, 1 H, aromatic), 6.61 (dd, J = 9.1, 3.0 Hz, 1 H, aromatic), 5.74 (s, 1 H, NCHAr), 3.94 (dt, J = 5.2, 4.3 Hz, 2 H, $ArOCH_2CH_2OH$), 3.83 (t, J = 4.3 Hz, 2 H, $ArOCH_2CH_2OH$), 3.28 (s, 1 H, CH_2CHAr), 3.27 (br s, 1 H, OH), 2.90 (br s, 1 H, OH), 2.26 (tt, J = 13.0, 3.6 Hz, 1 H, CH_2), 2.08 (td, J = 13.5, 6.2 Hz, 1 H, CH_2), 1.91 (br s, 1 H, OH), 1.75 (dd, J = 13.5, 4.7 Hz, 1 H, CH_2), 1.40–1.33 (m, 2 H, CH_2), 0.83 (m, 1 H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.6, 151.1, 139.0, 136.5, 135.5, 129.4, 128.5, 128.3, 127.8, 127.3, 126.8, 125.6, 123.9, 121.8, 114.3, 111.6, 72.9, 69.5, 69.3, 64.1, 61.2, 51.5, 32.7, 26.6, 18.3; HRMS (FAB$^+$)

for $C_{28}H_{27}NO_6Cs$ (M + Cs) calcd 606.0893, found 606.0899.

X-ray Crystallographic Analyses. Compounds 13 and 35. A single platelike crystal of **13** or an irregularly shaped crystal of **35** was mounted on a glass fiber along the largest dimension on a Nicolet R3m/V diffractometer equipped with a Mo ($K\alpha$ radiation) sealed tube anode generator. The data were collected at 23 °C with a variable scan speed of 2.5–5.0 deg/min in ω. The intensities of three monitor reflections measured after every 200 reflections did not change significantly during the data collection process. Cell parameters and an orientation matrix were obtained from a least-squares refinement using setting angles of 20 reflections in the range $15 < 2\theta < 30°$. Diffraction data were corrected for Lorentz and polarization effects but not for absorption.

For the structure **13**, the space group $P2_12_12_1$ ($h00$, $h = 2n + 1$; $0k0$, $k = 2n + 1$; $00l$, $l = 2n + 1$), and for **35**, space group $P4_2/n$ ($hk0$, $h + k = 2n + 1$; $00l$, $l = 2n + 1$) were determined from the systematic absences. Both of the structures were solved by SHELXTL-plus on a microvax II using a VMS operating system. The non-hydrogen atoms in the case of **35** were refined with anisotropic thermal parameters, while for **13**, only S, N, and O atoms were refined anisotropically and carbon atoms isotropically. Hydrogen atoms were fixed in the idealized positions ($U = 0.08$ Å^2). In the case of **35**, there was evidence of disorder on the methoxy carbon (C20). The two positions refined for this atom have occupancy factors of 0.6 and 0.4. In the final cycles of calculations a weighting scheme of the form $w = [1/\sigma^2(F) + gF^2]$ was employed with final g values of 0.0021 (for **13**) and 0.0019 (for **35**). The refinement converged to R factors of 0.0951 (for **13**) and 0.0492 (for **35**). The final difference map had no significant features.

Compounds 41 and 82. A brown, platelike crystal of **41** or a colorless platelike crystal of **82** was mounted along with the largest dimension, and data were collected with a Rigaku AFC6R diffractometer equipped with a copper rotating anode and a highly oriented graphite monochromator. A constant scan speed of 16 deg/min in ω was used, and the weak reflections [$I < 5\sigma(I)$] were rescanned to a maximum of four times and the counts accumulated to assure good counting statistics. The intensities of three monitor reflections measured after every 200 reflections did not change significantly during data collection. The data collection for **82** was carried out at −100 °C while for **41** at 23 °C. Unit cell dimensions and standard deviations were obtained by least-squares fit to 15 reflections ($30 < 2\theta < 50°$). The data were corrected for Lorentz and polarization effects but not for absorption because of the low value of μ. See the supplementary material for cell parameters and other relevant data.

The systematic absences ($h0l$, $h + l = 2n + 1$ and $0k0$, $k = 2n + 1$) for **41** indicated the space group $P2_1/n$. For compound **82** there were no systematic absences in the data. Therefore, space group $P\bar{1}$ was assumed and later confirmed by successful refinement of the structure. Both of the structures were solved by direct methods using SHELXS. In each case, carbon atoms were refined isotropically while other non-hydrogen atoms were refined anisotropically. The structure of **41** was refined by the block diagonal least-squares matrix method as follows: Co1–Co4 every cycle; P1–P4, O1–O8, and C1–C4 in alternate cycles with C25–C77. The structure **82** was refined by full-matrix least-squares methods. In the case of **82**, the *tert*-butyl substituent was found to be disordered in two different positions with fractional occupancy factors of 0.5 for its carbon atoms. The function minimized was $\sum w(|F_o| - |F_c|)^2$. Hydrogen atoms were refined in the ideal positions with fixed isotropic U values of 0.08 Å^2. A weighing scheme of the form $w = 1/[\sigma^2(F) + gF^2]$ with $g = 0.001$ was used. There was no evidence of secondary extinction; therefore, it was not applied. The refinement converged to the R values 0.1149 and 0.1005, respectively, for **41** and **82**. The high R factors were primarily the results of poor quality crystals which gave weak data sets. However, the crystals used were the best available. The final difference map was devoid of significant features.

All calculations were done on an IBM-compatible PC using programs TEXSAN[18] (data reduction), SHELXS[19] (structure solution), SHELX86[19] (refinement), and ORTEP[20] (plotting).

Final atomic coordinates, bond lengths, bond angles, temperature factors, and other relevant data for all four compounds **13**, **35**, **41**, and **82** are listed in the supplementary material.

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Supplementary Material Available: Tables of X-ray crystallographic data for compounds **13**, **35**, **41**, and **82** (42 pages); tables of observed and calculated structure factors (34 pages). Ordering information is given on any current masthead page.

(18) TEXSAN/TEXRAY structure analysis package: Molecular Structure Corporation, 3200 Research Forest Drive, The Woodlands, TX 77381-4238, 1985.

(19) SHELXS and SHELX86: G. M. Sheldrick, Instiüt für Anorganische Chemie der Universität Göttingen, Göttingen, Germany, 1986.

(20) ORTEPII: C. K. Johnson, Report ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, TN, 1976.