Total Syntheses of (−)-Lycoricidine, (+)-Lycoricidine, and (+)-Narciclasine via 6-*exo* Cyclizations of Substituted Vinyl Radicals with Oxime Ethers†

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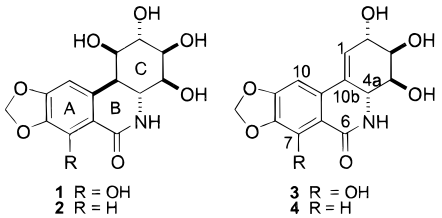
Abstract: The development of an approach to the total synthesis of the title alkaloids is described. The approach utilizes as the key strategic element a stereoselective 6-*exo* radical cyclization of a vinyl radical to an *O*-benzyloxime radical acceptor group. The vinyl radical was itself generated by regioselective addition of phenylthiyl radical to a disubstituted alkyne. The regiochemical issues of such additions, which result in different outcomes with tri-*n*-butylstannyl radicals and phenylthiyl radicals, are discussed. The first such synthesis described, that of (−)-lycoricidine, proceeded in 14 steps and 11% overall yield from **10** and served to develop the radical chemistry required. A second-generation synthesis, this time of the natural (+) enantiomer, was developed using insights gleaned from the first study and proved much more efficient, providing the target alkaloid in nine steps and 44% overall yield. This approach was then employed in the more demanding case of (+)-narciclasine. Several problems arising due to the more electron rich aromatic moiety present in this structure are described. The synthesis developed to deal with these aspects afforded (+)-narciclasine in 12 steps and 26% overall yield.

Introduction

Pancratistatin (**1**) and structurally related naturally occurring materials such as 7-deoxypancratistatin (**2**), narciclasine (**3**), and lycoricidine (**4**) have attracted considerable synthetic attention because of interest in the biological activity of these compounds and their novel structural aspects.[1] In particular, five recent total syntheses of **1** have been recorded,[2] as have six total syntheses of **2**,[3] five total syntheses of **4**,[4] and one synthesis of **3**.[5] Our own efforts in this area have led to two reported syntheses of **2** via radical cyclization based strategies.[3e,f] We now report the development of a rather different radical-based approach to **4**. Specifically, we provide herein a full account of our synthesis of *ent*-**4**, as well as the development of a considerably more efficient route in the context of a total synthesis of the naturally occurring (+)-**4**, and finally the application of the methodology so developed to the synthesis of (+)-**3**.



Synthetic Analysis

The strategy chosen for experimental scrutiny was based on establishing the $C_{4a}-C_{10b}$ bond late in the synthesis, via radical cyclization using an *O*-benzyloxime as the radical acceptor.[6] For generation of the requisite vinyl radical, the addition of some radical X• to an appropriate disubstituted alkyne was viewed as an attractive possibility. Since the group X would need to be removed later, ideally without introducing additional steps,

† The syntheses of (+)-lycoricidine and (+)-narciclasine described herein have been previously disclosed: Keck, G. E.; Wager, T. T; Rodriquez, J. F. D. *Abstracts of Papers*; 216th National Meeting of the American Chemical Society, Boston, MA, August 1998; American Chemical Society: Washington, DC, 1998; ORG #547.

(1) For a review on the Amaryllidaceae alkaloids, see: (a) Martin, S. F. In *The Alkaloids*; Brossi, A. R., Ed.; Academic Press: New York, 1987; Vol. 30, pp 251−376. For a review of other synthetic work on the *Amaryllidaceae* alkaloids, see: (b) Polt, R. L. Amaryllidaceae Alkaloids with Antitumor Activity. *Organic Synthesis: Theory and Application*; Hudlicky, T., Ed.; JAI Press: Greenwich, CT, 1996; Vol. 3, pp 109−148.

(2) For syntheses of pancratistatin, see: (a) Danishefsky, S.; Lee, J. Y. *J. Am. Chem. Soc.* **1989**, *111*, 4829. (b) Hudlicky, T.; Tian, X.; Königsberger, K.; Maurya, R.; Rouden, J.; Fan, B. *J. Am. Chem. Soc.* **1996**, *118*, 10752. (c) Trost, B. M.; Pulley, S. R. *J. Am. Chem. Soc.* **1995**, *117*, 10143. (d) Doyle, T. J.; Hendrix, M.; VanDerveer, D.; Javanmard, S.; Haseltine, J. *Tetrahedron*, **1997**, *53*, 11153. (e) Magnus, P.; Sebhat, I. K. *J. Am. Chem. Soc.* **1998**, *120*, 5341.

(3) For syntheses of 7-deoxypancratistatin, see: (a) Ohta, S.; Kimoto, S. *Chem. Pharm. Bull.* **1976**, *24*, 2977. (b) Paulsen, H.; Stubbe, M. *Liebigs Ann. Chem.* **1983**, 535. (c) Tian, X.; Maurya, R.; Königsberger, K.; Hudlicky, T. *Synlett* **1995**, 1125. (d) Chida, N.; Iitsuoka, M.; Yamamoto, Y.; Ohtsuka, M.; Ogawa, S. *Heterocycles* **1996**, *43*, 1385. (e) Keck, G. E.; McHardy, S. F.; Murry, J. A. *J. Am. Chem. Soc.* **1995**, *117*, 7289. (f) Keck, G. E.; Wager, T. T.; McHardy, S. F. *J. Org. Chem.* **1998**, *63*, 9164.

(4) For syntheses of lycoricidine, see: (a) Ohta, S.; Kimoto, S. *Tetrahedron Lett.* **1975**, 2270. (b) Ohta, S.; Kimoto, S. *Chem. Pharm. Bull.* **1976**, *24*, 2969. (c) Ohta, S.; Kimoto, S. *Chem. Pharm. Bull.* **1976**, *24*, 2977. (d) Paulsen, H.; Stubbe, M *Tetrahedron Lett.* **1982**, *23*, 3171. (e) Paulsen, H.; Stubbe, M. *Liebigs Ann. Chem.* **1983**, 535. (f) Ogawa, S.; Ohtsuka, M.; Chida, N. *Tetrahedron Lett.* **1991**, *32*, 4525. (g) Hudlicky, T.; Olivo, H. R. *J. Am. Chem. Soc.* **1992**, *114*, 9694. (h) Martin, S. F.; Tso, H.-H. *Heterocycles* **1993**, *35*, 85. (i) Ogawa, S.; Ohtsuka, M.; Chida, N. *J. Org. Chem.* **1993**, *58*, 4441. (j) Hudlicky, T.; Olivo, H. F.; McKibben, B. *J. Am. Chem. Soc.* **1994**, *116*, 5108. For the isolation of lycoricidine and narciclasine, see: (k) Okamoto, T.; Torii, Y.; Isogai, Y. *Chem. Pharm. Bull.* **1968**, *16*, 1860.

(5) (a) Rigby, J. H.; Mateo, M. E. *J. Am. Chem. Soc.* **1997**, *119*, 12655. (b) For the isolation of narciclasine, see: Piozzi, F.; Modelli, R.; Fuganti, C.; Ceriotti, G. *Tetrahedron* **1968**, *24*, 1119. (c) For the isolation of narciclasine 4-*O*-*β*-glucoside, see: Abou-Donia, A. H.; De Giulio, A.; Evidente, A.; Gaber, M.; Habib, A.-A.; Lanzetta, R.; Seif El Din, A. A. *Phytochemistry* **1991**, *30*, 3445.

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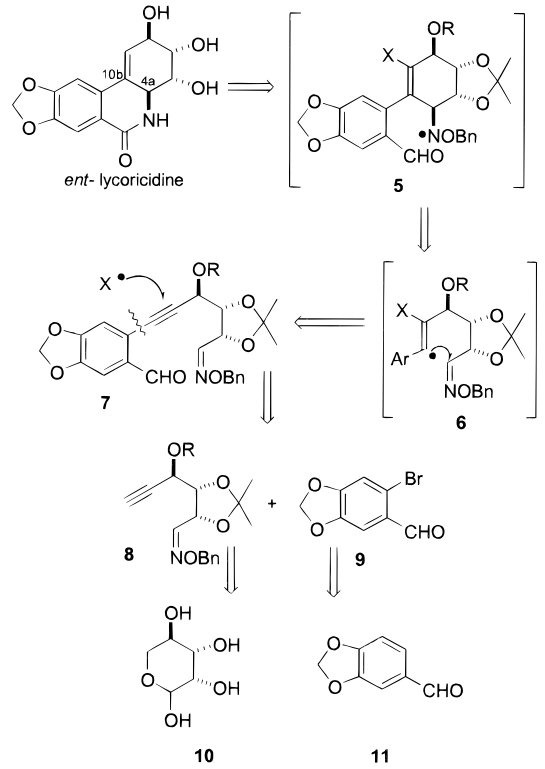
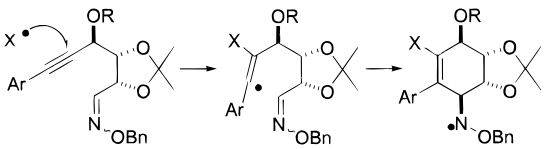
the most promising candidates for this group were deemed to be either a stannyl group, a thio group such as phenylthio, or a selenyl group, such as phenylselenenyl. The stannyl group would be expected to undergo protiodestannylation during acid-catalyzed hydrolysis of an acetonide moiety employed to protect the C_3 and C_4 oxygen substituents, while the sulfur or selenium substituents could in principle be removed reductively. A reductive step would be required at some point to cleave the N−O bond in the *O*-benzylhydroxylamine product of such a radical sequence, and we knew from previous work that the projected means of accomplishing this step, by reaction using SmI_2, could be employed to reduce vinyl sulfones as well.[7]

Such an approach to generating the vinyl radical raises concerns about the regiochemistry of the addition reaction. We anticipated that the preferred regiochemistry in this case would be controlled primarily by benzylic stabilization of the desired vinyl radical. This is not clear-cut, however, since steric effects would presumably favor addition in the undesired sense. Assuming for the moment that the radical addition did occur with the desired regiochemistry, then the use of an alkyne such as **7** can be seen to considerably simplify the overall approach to these materials, since a highly convergent assembly of the two main subunits of the aryl alkyne would be possible via a palladium-mediated coupling reaction. For the synthesis of the terminal alkyne subunit, a carbohydrate-based approach was chosen to obtain the correct absolute and relative configurations at C_2−C_4.

***ent*-Lycoricidine. Construction of Radical Substrates.** The synthesis of potential substrates for the radical cyclization reaction is outlined below (Scheme 1). The route began with D-lyxose (**10**), which was converted to the *O*-benzyl-3,4-isopropylidenelyxopyranoside via known[8] procedures; silyation of the remaining hydroxyl afforded **12**. Reduction of **12** with lithium in liquid ammonia, followed by reaction of the crude lactol with *O*-benzylhydroxylamine hydrochloride in pyridine gave an 89% isolated yield of the *O*-benzyloxime **13** as a 2.5:1 mixture of *E/Z* oxime isomers.[9] This material was then processed to afford the terminal alkyne **15**. This conversion commenced by oxidation of **13** to the corresponding aldehyde using the general procedure of Ley[10] followed by application of the Corey−Fuchs protocol.[11] Thus, reaction with CBr_4 and triphenylphosphine in the presence of NEt_3 gave the one carbon homologated dibromoalkene **14**, but in only 55% yield from **13**. However, treatment of the dibromoalkene with ^{n}BuLi proceeded uneventfully to give alkyne **15** in 91% yield. Coupling with the aromatic subunit was achieved in excellent yield by reaction of the terminal alkyne **15** with bromopiperonal[12] using the palladium-catalyzed process developed by Sonogashira and co-workers,[13] affording the alkyne−aldehyde **16**. This material was also processed to afford two additional radical cyclization substrates: removal of the TBS group afforded hydroxyaldehyde **17**, which was converted (81% isolated yield) to the hydroxy ester **18** using the Corey−Gilman−Ganem oxidation.[14]



Investigation of the Radical Cyclization Reaction. With potential substrates **16**−**18** in hand, we were positioned to study the critical reaction envisioned for establishing the functionalized cyclohexene moiety present in **4**, namely, the addition of a radical X• to the alkyne moiety, followed by cyclization of the resulting vinyl radical onto the pendant oxime moiety. Although the relative amounts of the potential products of this reaction are a function of a fairly complex kinetic scheme, clearly regiochemistry in the addition of X• to the alkyne is an issue here. We anticipated that the regiochemical issue should be dominated by benzylic stabilization[15] of the vinyl radical intermediate, thus leading to the vinyl radical desired for our purposes. It has been previously suggested[15b] that aryl-substituted vinyl radicals are linear, presumably as a consequence of such interactions. As candidates for X•, we focused our attention on tri-*n*-butylstannyl and phenylthiyl radicals.



Initial experiments with **16** and Bu_3SnH provided an unexpected result: *addition of stannyl radical and trapping by Bu_3SnH occurred without radical cyclization and exclusively*

(6) For additional earlier examples see ref 3e and references therein. (a) Marco-Contelles, J.; Destabel, C.; Chiara, J. L.; Bernabe, M.*Tetrahedron Asymmetry* **1995**, *6*, 1547. (b) Naitio, T.; Ninomiya, I.; Tajiri, K.; Kiguchi, T. *Tetrahedron Lett.* **1995**, *36*, 253. (c) Marco-Contelles, J.; Chiara, J. L.; Khiar, N.; Gallego, P.; Destabel, C.; Bernabe, M. *J. Org. Chem.* **1995**, *60*, 6010. (d) Parker, K. A.; Fokas, D. *J. Org. Chem.* **1994**, *59*, 3927. (e) Booth, S. E.; Jenkins, P. R.; Swain, C. J.; Sweeney, J. B. *J. Chem. Soc., Perkin Trans. 1* **1994**, 3499. (f) Parker, K. A.; Fokas, D. *J. Org. Chem.* **1994**, *59*, 3933. (g) Grissom, J. W.; Klingberg, D. *J. Org. Chem.* **1993**, *58*, 6559. (h) Pattenden, G.; Schulz, D. J. *Tetrahedron Lett.* **1993**, *34*, 6787. (i) Enholm, E. J.; Burroff, J. A.; Jaramillo, L. M. *Tetrahedron Lett.* **1990**, *31* 3727.

(7) Keck, G. E.; Savin, K. A.; Weglarz, M. A. *J. Am. Chem. Soc.* **1995**, *60*, 3194.

(8) Keck, G. E.; Kachensky, D. F.; Enholm, E. J. *J. Org. Chem.* **1985**, *50*, 0, 4317.

(9) For purposes of characterization, the major oxime isomer of all synthetic intermediates enroute to *ent*-**4** was isolated and characterized; for preparative purposes, the mixture of oxime isomers was carried through the sequence.

(10) Ley, S. V.; Norman, J.; Griffith, W. P.; Marsden, S. P. *Synthesis* **1994**, 639.

(11) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769.

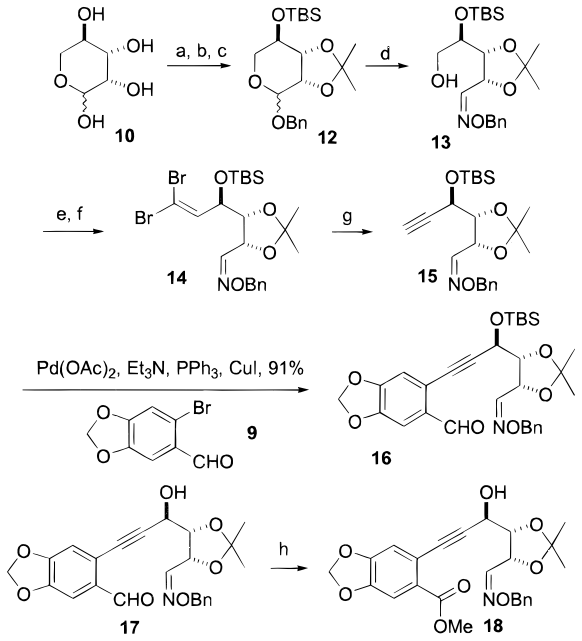
(12) Dallacker, F. *Liebigs Ann. Chem.* **1960**, 14.

(13) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467.

(14) Corey, E. J.; Gilman, N.W.; Ganem, B. E. *J. Am. Chem. Soc.* **1968**, *90*, 5618.

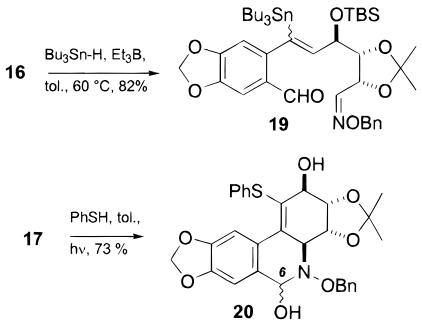
(15) (a) Dolbier, W. R., Jr.; Bartberger, M. D. *J. Org. Chem.* **1995**, *60*, 4984. (b) Bennett, J. E.; Howard, J. A. *Chem. Phys. Lett.* **1971**, *9*, 460.

Scheme 1[a]



[a] Reagents: (a) BnOH, *p*-TsOH, 81%. (b) DMP, acetone, *p*-TsOH, 90%. (c) TBS−Cl, imidazole, 95%. (d) i. Li, NH_3. ii. $BnONH_2$·HCl, pyridine, 89% over two steps. (e) i. TPAP, NMO, 4 Å MS. ii. CBr_4, PPh_3, NEt_3, 55% over two steps. (f) ^{n}BuLi, 91%. (g) HF·pyridine, 88%. (h) MnO_2, NaCN, HOAc, MeOH, 81%.

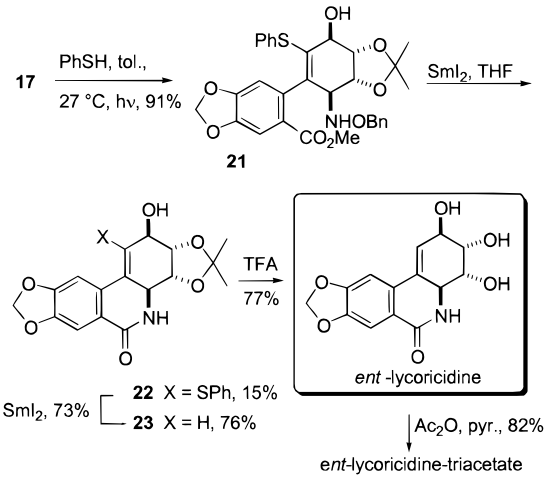
with the "wrong" regiochemistry,[16] *yielding vinyl stannane* ***19****.* Since the observed regiochemistry could have resulted from the influence of steric factors on the initial addition of stannyl radicals to alkyne **16**, the reaction was also investigated with hydroxyaldehyde **17**, but with essentially the same outcome. Much better results were achieved with thiyl radicals. Reaction of hydroxyaldehyde **17** with thiophenol in toluene solution, under irradiation from a sunlamp, afforded cyclized product **20** (73% isolated yield, not optimized) as a 4:1 mixture of isomers at the hemiaminal carbon C_6. Thus, the entire framework necessary for lycoricidine was constructed in a single operation by sequential one-electron and two-electron cyclization processes.



Further progress in the synthesis required oxidation at C_6 to provide the lactam carbonyl present in **4**. Selective protection of the C_2 hydroxyl group was achieved by reaction with Ac_2O/pyr followed by aqueous workup. Although we have no hard evidence bearing on the apparent regioselectivity observed in this operation, we presume that both hydroxyls present are acetylated in this process and that the labile C_6 acetate solvolyzes upon workup. However, no satisfactory means for accomplishing the requisite oxidation at C_6 could be identified, despite a survey of essentially all of the common oxidants which might be expected to effect this transformation. The highest yields (ca. 30%) were obtained using TPAP/CH_3CN, but this was clearly an unacceptable solution. To circumvent this problem, we examined the use of the substrate **18**, in which the C_6 carbon was brought into the radical cyclization at the proper oxidation state.

Reaction of hydroxy ester **18** with thiophenol under optimized conditions (toluene solution, 27 °C, sunlamp, 2 h) afforded the amino ester **21** in 91% isolated yield;[17] none of the other possible diastereomer was detected. In contrast to the aldehyde substrate, **21** showed no tendency to cyclize spontaneously (no reaction upon heating in toluene at reflux).

Completion of the Route to *ent*-Lycoricidine. Subjection of **21** to the SmI_2 procedure[18] developed during the course of our work on 7-deoxypancratistatin effected three operations: reductive cleavage of the N−O bond, cyclization of the resulting amino ester, and removal of the thiophenyl group, affording **23** in 76% isolated yield. Also isolated from this reaction was 15%



of **22**, which still contained the thiophenyl moiety; thus, the yield of tricyclic material is actually 91%. Intermediate **22** could be resubjected to the SmI_2 reduction to give **23** in 73% isolated yield.[19] Completion of the synthesis required only the known removal of the acetonide moiety to give (−)-lycoricidine (mp 221−224 °C (dec); lit.[4e] mp 224−226 °C (dec)), which gave ^{1}H and ^{13}C NMR data indistinguishable from those previously reported for the (+) enantiomer. Further characterization was achieved by conversion to the known triacetate whose spectral data were also in excellent agreement with those previously reported. The overall route as described thus affords lycoricidine in optically pure form and 11% overall yield in 14 steps from lyxose.[20]

Synthesis of (+)-Lycoricidine: A Greatly Improved Route. At the time we began these studies, no synthesis of narciclasine

(16) This result is in contrast to the finding of Marco-Contelles and co-workers,[6a] who observed very high yielding 5-*exo* cyclization upon stannyl radical additions to closely related terminal alkynes; undoubtedly, steric effects slow the rate of 5-*exo* cyclization in the present system.

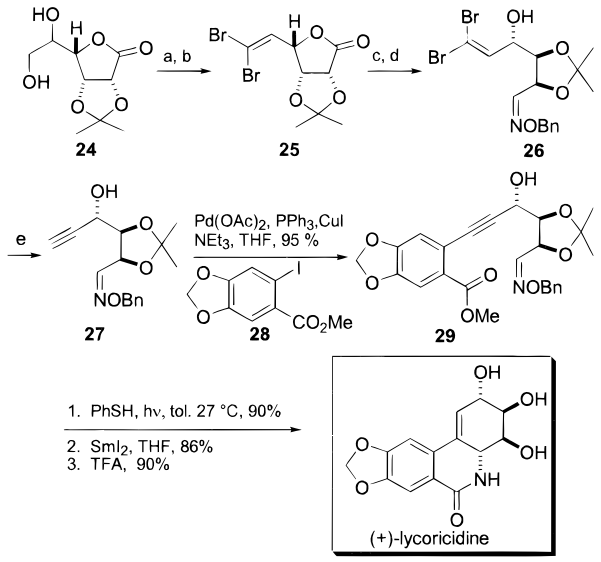
(17) This reaction has been extensively optimized and was found qualitatively to proceed better (faster reaction, higher isolated yields) at lower temperature rather than at elevated temperatures, a result that clearly seems related to the reversibility of the initial thiyl radical addition. For example, conducting the same reaction thermally (65 °C) gave a 76% yield after 48 h.

(18) Keck, G. E.; McHardy, S. F.; Wager, T. T. *Tetrahedron Lett.* **1995**, *36*, 7419.

(19) This is not an isolated result. Small amounts of **22** were always detected in the reduction of **21**, even with excess SmI_2 and long reaction times. Curiously, however, isolation and resubjection of **22** to these conditions affords **23**.

(20) Keck, G. E.; Wager, T. T. *J. Org. Chem.* **1996**, *24*, 8366.

Scheme 2.[a] A Greatly Improved Route



[a] Key: (a) $NaIO_4$, CH_2Cl_2. (b) CBr_4, PPh_3, NEt_3, 80% over two steps. (c) L-Selectride, Et_2O, −78 °C. (d) $HCl{\cdot}H_2NOBn$, pyridine, 90% over two steps. (e) ^{n}BuLi, Et_2O, −90 °C, 93%.

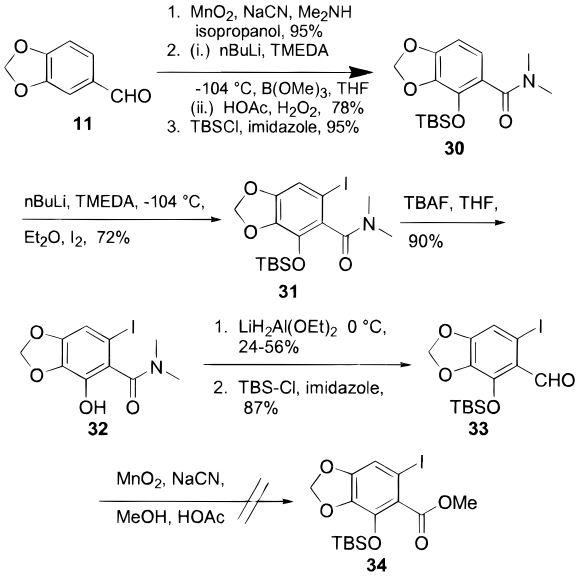
had as yet been reported. It seemed plausible that a sequence similar to that described above could be used to construct the more highly functionalized narciclasine structure (**3**), provided that the critical radical cyclization and palladium coupling steps were successful with the more electron rich aromatic ring present in **3** and that an efficient route to the construction of this ring could be devised. Since it was clear from the outset that the more complex aromatic segment would necessitate a longer overall synthesis, our first objective was to streamline the route as much as possible. To this end, the synthesis of (+)-lycoricidine was used essentially as an advanced model system for optimizing the synthesis of the C_1-C_6 segment.

Examination of the existing synthesis of the *ent* structure revealed two main deficiencies where improvements might be achievable. Thus, the key radical cyclization and subsequent transformations were very efficient: only two steps were required after the radical cyclization, and yields were high for this segment of the approach. However, eight steps were required for the carbohydrate manipulations to reach this point, and most of the inefficiency in terms of yield occurred in this portion of the route, particularly in the Corey−Fuchs step. Therefore a new approach was devised that moved this step earlier in the synthesis, such that it was carried out *prior* to introduction of the *O*-benzyloxime moiety. The synthesis of (+)-lycoricidine which resulted proved extraordinarily efficient, providing **4** in nine linear steps from **24** in 44% overall yield, as shown in Scheme 2.

The synthesis began with the 2,3-*O*-isopropylidene derivative of D-gulonolactone (**24**), available in two steps from D-gulonolactone using the procedure of Fleet.[21] Oxidative cleavage of the diol and Corey−Fuchs reaction on the resulting aldehyde cleanly afforded the dibromoalkene **25** in 80% yield. Reduction of the lactone to the corresponding lactol was accomplished using L-Selectride, and this was directly converted to the *O*-benzyl oxime **26**. Rearrangement to the desired alkyne was accomplished at this stage by treatment with ^{n}BuLi to give **27** in 93% yield.

Palladium-mediated coupling with iodo ester **28**[22] then directly gave the substrate previously identified as optimal for the radical cyclization event, the hydroxy ester **29**. The radical cyclization step proceeded as before in 90% isolated yield. Reduction with SmI_2 effected N−O bond cleavage, cyclization to the lactam, and reductive removal of sulfide (86%). Finally, optimization of the acetonide removal using trifluoroacetic acid furnished (+)-lycoricidine in 91% isolated yield.

Synthesis of (+)-Narciclasine. To apply this approach to narciclasine, it was first necessary to construct a suitable aryl iodide for use in the palladium-mediated coupling with alkyne **27**. We chose to approach this segment, as have others,[23] using a directed metalation sequence. Conversion of piperonal to the corresponding *N*,*N*-dimethylamide was accomplished in 95% yield using the procedure of Gilman.[24] Metalation (^{n}BuLi) and reaction with trimethyl borate gave (after oxidation with hydrogen peroxide) the desired phenol,[25] which was silylated to afford **30**. A second metalation (^{n}BuLi) and quenching with iodine then gave the aryl iodide **31** in 72% yield. It remained to convert the dimethylamide to the corresponding methyl ester, which we had hoped to do by reduction to the aldehyde (following a previous report by Hudlicky and co-workers[23f]) and subsequent Corey−Gilman−Ganem oxidation to the methyl ester. However, reduction to the aldehyde could only be accomplished in low yield[26] and the requisite oxidation failed completely.



A new process was developed to overcome these problems.[27] Treatment of **31** with trimethyloxonium tetrafluoroborate in CH_3-

(21) Fleet, G. W. J.; Ramsden, N. G.; Witty, D. R. *Tetrahedron* **1989**, *45*, 319.

(22) This material was prepared by oxidation of iodopiperonal, which in turn is available in three steps from bromopiperonal using the method of Charlton: Bogucki, D. E.; Charlton, J. L. *J. Org. Chem.* **1995**, *60*, 588.

(23) (a) Danishefsky, S.; Lee, J. Y. *J. Am. Chem. Soc.* **1989**, *111*, 4829. (b) Heathcock, C. H.; Lopes, C. C.; Lopes, R. S. C. *Tetrahedron Lett.* **1992**, *33*, 6775. (c) Chapleur, Y.; Chrétien, F.; Khaldi, M. *Tetrahedron Lett.* **1995**, *36*, 3003. (d) Xinrong, T.; Hudlicky, T.; Königsberger, K. *J. Am. Chem. Soc.* **1995**, *117*, 3643. (e) Haseltine, J.; VanDerveer D.; Doyle, T. J. *Tetrahedron Lett.* **1995**, *36*, 6197. (f) Hudlicky, T.; Xinrong, T.; Königsberger, K.; Maurya, R.; Rouden, J.; Fan, B. *J. Am. Chem. Soc.* **1996**, *118*, 10752. (g) Haseltine, J. Javanmard, S.; VanDerveer, D.; Hendrix, M,; Doyle, T. J. *Tetrahedron* **1997**, *53*, 11153.

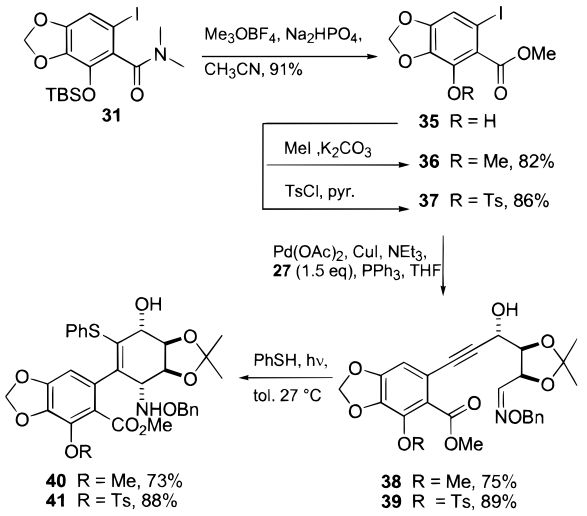
(24) Gilman N. W. *Chem. Commun.* **1971**, 733.

(25) Snieckus, V.; Reed, J. N.; Iwao, M. *J. Am. Chem. Soc.* **1982**, *104*, 5531. For a review of ortho lithiation, see: Snieckus, V. *Chem. Rev.* **1990**, *90*, 879.

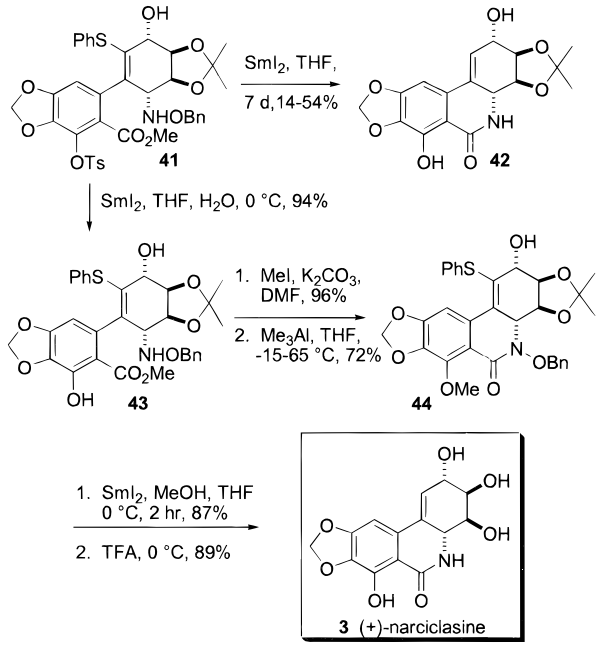
(26) Using the conditions of Hudlicky on **32** we were unable to obtain any of the desired aldehyde. Although we were able to reduce the dimethyl amide of the free phenol with $LiH_2Al(OEt)_2$, the yields were low (24−56%) and the product was accompanied by unwanted side products arising from reduction of the aryl iodide.

CN buffered with solid Na_2HPO_4, followed by quenching with saturated aqueous $NaHCO_3$ solution, afforded phenol **35** in 91% yield (reproducibly on 10 g scale). Methylation of **35** (K_2CO_3, MeI, acetone, 82% yield) then gave **36**, which was coupled with the alkyne **27** to give **38** in 75% yield. Radical cyclization as in the lycoricidine route afforded 73% of the desired **40**. As feared, both yields were ca. 20% lower than in the lycoricidine synthesis, undoubtedly as a consequence of the more electron rich aromatic system present in these substrates.

We were thus led to consider use of an electron-withdrawing protecting group, ideally one that could potentially be removed reductively in the SmI_2 step. We reasoned that one-electron reduction of an aryl tosylate, Ar−OTs, should result in scission of the radical anion to ArO• plus $^-SO_2Ar$ or ArO^- plus $ArSO_2$•. Thus, the same sequence was probed using the tosylate derivative of **37**, formed in 86% yield by reaction of **35** with TsCl/pyridine. In this instance, the palladium coupling and radical cyclization were considerably improved, to 89% and 88% yields, respectively. However, reduction of **41** with SmI_2 was now problematic, affording **42** in low and variable yields only after extended reaction times.



Upon further investigation, the reason for this result became readily apparent: the tosylate group suffered reductive cleavage much faster than did the N−O bond, leading to a very electron rich phenoxide structure in which the ester carbonyl was reluctant to undergo nucleophilic addition. However, this finding could be used to advantage. Selective reductive removal of the tosylate (SmI_2, THF, H_2O, 10 min, 94% yield) followed by methylation (MeI, K_2CO_3, DMF, 96% yield) gave **40**. We had hoped that conducting the SmI_2 reduction on this substrate would solve the problem encountered with the tosylate; however, the same behavior was observed.[28] It was subsequently determined that the methyl group was adventitiously and rapidly cleaved in this reductive step as well, presumably by a reaction sequence involving complexation with Sm^{3+} and nucleophilic attack by a species such as iodide. The unusual lability of various protecting groups in a closely related system had been previously noted by Hudlicky and co-workers during their pancratistatin synthesis; in their case, a benzyl ether was cleaved by reaction with sodium benzoate in water.[2b] Thus the critical cyclization reaction had to be accomplished in such a way that the phenolic oxygen protecting group could not be cleaved under the reaction conditions, which meant in the total absence of potentially nucleophilic species. Cyclization of the methyl ether substrate **40** was achieved using Me_3Al[29] to give **44** in 72% yield. After this result was obtained, the same cyclization conditions were also examined using the tosylate **41** as the substrate. Although a successful cyclization to the lactam without loss of the tosyl group was realized, the isolated yield in this instance (50%) was considerably lower than that obtained using the methyl ether. The optimal sequence thus proved to be one in which the electron-withdrawing tosylate was employed in both the palladium-mediated coupling and radical cyclization steps and was then selectively removed and replaced by methyl for the subsequent cyclization and reductive cleavage steps. This *O*-Me cyclized material (**44**) underwent SmI_2 reduction to give narciclasine acetonide in 87% isolated yield. (Notice that the methyl group is again lost in this step.) Finally, removal of the acetonide gave narciclasine in 89% isolated yield.



Discussion

Radical Cyclization Results. Several aspects of the radical cyclization methodology utilized herein merit a somewhat more detailed discussion than that provided above in a purely synthetic context. The results obtained in reactions using PhSH and Bu_3SnH are curious in that the observed products with these two reactants result from reversed regiochemistry for the addition of Bu_3Sn• and PhS• to the same alkynyl substrate. Moreover, no products of 5-*exo* cyclization are observed in either case, despite a preponderance of literature that would seem to suggest that this pathway should be considerably preferred, in terms of

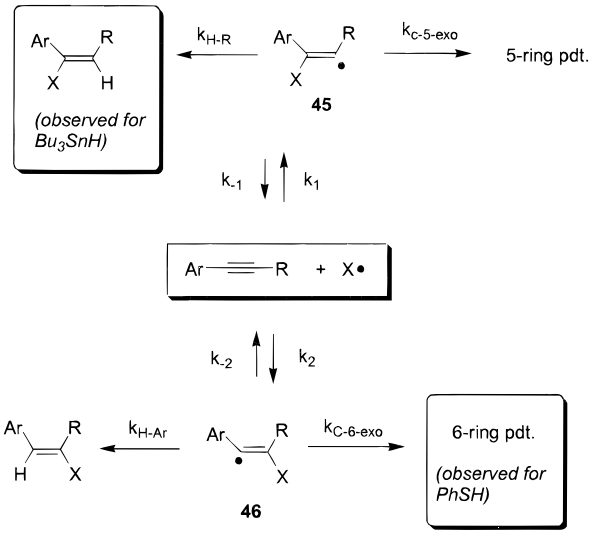
(27) (a) This transformation is known for secondary amides, proceeding via isolable imidates which are subsequently hydrolyzed under acidic conditions: Hanessian, S. *Tetrahedron Lett.* **1968**, 1549. However, extensive literature searching revealed no examples of such an amide to ester conversion with tertiary amides. (b) After this work was completed, we did locate by serendipity one previous example of this reaction: Hegedus, L. S.; Stille, J. K.; Kalivretenos, A. *J. Org. Chem.* **1991**, *56*, 2883. (c) Further studies on the scope and generality of this process will be reported separately.

(28) Problems similar to those encountered initially with tosylate **41** were also encountered in the OCH_3 series; thus, the methyl group in **40** was adventitiously cleaved during the SmI_2 reduction step, precluding formation of the B ring. It should also be noted that the vinyl sulfide is not removed in satisfactory yield unless the B-ring is closed.

(29) The application of Me_3Al in this closure of the B-ring is an intramolecular variant of the better known intermolecular Weinreb amide reaction: Weinreb, S. M.; Lipton, M.; Basha, A. *Tetrahedron Lett.* **1977**, *48*, 4171.

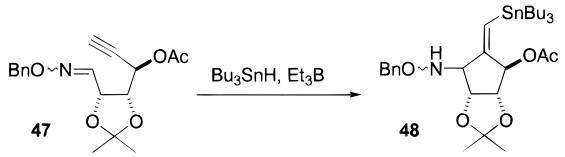
kinetics, over the observed 6-*exo* one. Also curious is the observation that products resulting from H-abstraction after the initial addition are observed only for the Bu_3SnH reaction and not for the reaction using PhSH. Thiophenol is normally considered to be a better H atom donor than is Bu_3SnH, and kinetic data for the few cases that are available with both reagents support this contention.[30] Although the observed results were not entirely predictable at the time we began these investigations, they are in retrospect largely understandable.

It is important to note that the products obtained from the overall process are the result of a rather complex kinetic scheme (outlined below using a simplified structure for the aryl−alkyne reactant) which may or may not reflect the intrinsic regiochemical preferences in the initial alkyne addition. Thus, either radical may add initially to either carbon (abbreviated here as Ar−C and R−C) of the alkyne, to generate radicals **45** and **46**. Both of these additions are in principle reversible, as β-scission is extremely well-known for reactions that generate $Bu_3Sn^{\bullet}$ and $PhS^{\bullet}$. Either radical formed in the initial addition (**45** or **46**) can in principle also abstract hydrogen (k_H) or undergo a cyclization reaction (k_C) onto the pendant oxime moiety. (There will of course be two such rate constants k_H: one for the case of Bu_3SnH, and one for the case of PhSH. All rate constants in this scheme will have two values at any given temperature corresponding to the two reactants used.) This would lead to a 5-ring product via 5-*exo* cyclization from **45** or to 6-ring products via a 6-*exo* pathway from **46**.



It is instructive to first examine what the observed results demand. First of all, it is clear that stannyl radicals add to the alkynyl substrate at Ar−C to generate radical **45**, since products derived from this mode of addition are observed. The observed product from this mode of addition is the reduction product. Thus the alternative 5-*exo* cyclization pathway which could originate from **45** must be considerably slower than hydrogen transfer in this case, as no 5-ring products are observed. This result stands in marked contrast to a closely related example previously reported by Marco-Contelles and co-workers, who found that addition of stannyl radicals to the terminal alkyne **47** led to 5-*exo* cyclization in high yield.[6a]

(30) For the cases of benzyl radical, cyclopropyl radical, and phenyl radical, H-abstraction from thiophenol is ca. 10−50 times faster than from Bu_3SnH. See: (a) Franz, J. A.; Suleman, N. K.; Alnajar, M. S. *J. Org. Chem.* **1986**, *51*, 19. (b) Johnston, L. J.; Sciano, J. C.; Ingold, K. U. *J. Am. Chem. Soc.* **1984**, *106*, 4877. (c) Johnston, L. J.; Lusztyk, J.; Wayner, D. D. M.; Abeywickreyma, A. N.; Beckwith, A. L. J.; Sciano, J. C.; Ingold, K. U. *J. Am. Chem. Soc.* **1985**, *107*, 4594.

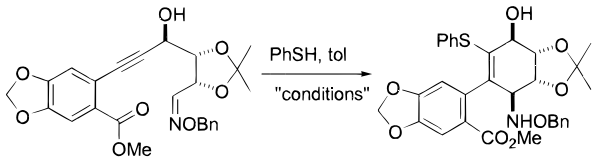


The slower cyclization in the present case is not surprising when one considers the trajectory required for approach of the *O*-benzyloxime to the radical center in **45**. Since the p-type orbital lies in the same plane as the aryl and stannyl substituents in **45** (with X = Bu_3Sn), approach of the *O*-benzyloxime to this center would generate significant steric interactions. Thus, cyclization in this case is slow for exactly the same reason that the case studied by Marco-Contelles (**47** to **48**) exhibits exceptionally high levels of stereoselectivity for the generation of the *Z* isomer.

Second, the observed results demand that phenylthiyl radicals add to R−C, since products derived from **46** (the 6-ring cyclization product) are formed in high yield. This is again not surprising and is in accord with our initial expectations regarding the regioselectivity of radical addition to **17**, since this generates the vinyl radical which can benefit from benzylic stabilization. Products derived from reduction of **46** by PhSH are not observed. This then strongly suggests that stannyl radicals never add with this regioselectivity, i.e. to R−C to generate the benzylic radical **46**. If they did, it would be very difficult to understand why cyclization should not ensue as in the case of $PhS^{\bullet}$ addition, since reduction and β-scission should both be slower with the tin system than with sulfur. We are forced to conclude that, contrary to what one might initially have expected, the regioselectivity for addition of stannyl radicals to **16** is governed solely by steric considerations.

In contrast, we do not believe that the addition of $PhS^{\bullet}$ to the alkyne occurs with complete regioselectivity, although products derived from only one mode of addition are observed. Instead, we believe that addition to Ar−C does occur to generate radical **45** as observed with stannyl radicals, but that the back-reaction (β-scission) is simply faster than the sterically encumbered 5-*exo* cyclization or reduction by PhSH.

Evidence to support this hypothesis is available from the somewhat unusual temperature profile associated with this reaction. It was found during the course of optimizing this reaction for synthetic purposes that the reaction apparently ran faster at lower temperatures than at elevated temperatures, as measured simply by conversion over time. The following results summarize some of these data:



Entry	Initiator	Temperature	Time (h)	Yield (%)
a	none	rt	44	86
b	heat	65 °C	48	76
c	sunlamp	rt to reflux	8	83
*d	sunlamp	27 °C	2	91

Thus, by lowering the reaction temperature from 65 to 27 °C, complete consumption of starting material was achieved in only 2 h, as opposed to 48 h. This result would be consistent with a very significant back-reaction rate at the more elevated

temperatures, such that β-scission was sufficiently fast that only a very small fraction of the radicals generated underwent cyclization. It is also reasonable that β-scission should be a more important component of the reaction starting from the unstabilized radical **45** than from the stabilized benzylic radical **46**. In summary, then, we believe that a more highly reversible process is observed with thiyl radicals than with stannyl radicals and that this reversibility is largely responsible for obtention of the desired outcome in this case. This hypothesis has clear implications for further synthetic applications of this type of chemistry which we are presently exploring.

Summary and Conclusions

In conclusion, total syntheses of both (+)-lycoricidine and (+)-narciclasine have been accomplished. The approach to lycoricidine and narciclasine is both concise and synthetically appealing, giving the title alkaloids in nine linear steps (44% overall yield) and 12 linear steps (26% overall yield), respectively. During the course of this work, several interesting transformations surfaced, including reversed regiochemistry for the addition of stannyl and phenylthiyl radicals to the same disubstituted alkyne, direct conversion of a hindered benzamide to a methyl ester, use of a tosylate as an electron-withdrawing protecting group for a phenolic hydroxyl, deblocking of a phenolic tosyl group using SmI_2, and closure of the B-ring using an intramolecular Weinreb reaction.

Experimental Section

General Procedure. Solvents were purified according to the guidelines in *Purification of Common Laboratory Chemicals* (Perrin, Armarego, and Perrin, Pergamon: Oxford, U.K., 1966). Reagent-grade dimethoxypropane, pyridine, methanol, and acetone were purchased and used without further purification. Triethylamine was distilled from CaH_2 and stored over oven-dried 4 Å molecular sieves, benzyl alcohol was fraction distilled under reduced pressure prior to use, and thiophenol was distilled from calcium sulfate. The titer of ^{n}BuLi was determined by the method of Eastham and Watson.[31] Samarium diiodide was freshly prepared by a modification of the Imamoto and Ono method.[32] Manganese dioxide was prepared by the method of Giovanoli[33] and dried at 110 °C for 2 days. All other reagents were used without further purification. Yields were calculated for material judged homogeneous by thin-layer chromatography and NMR. Thin-layer chromatography was performed on Merck Kieselgel 60 F_{254} plates, eluting with the solvents indicated, visualized by a 254 nm UV lamp, and stained with a ethanolic solution of either 12-molybdophosphoric acid, *p*-anisaldehyde, or cerium sulfate. Flash column chromatography was performed with Davisil 62 silica gel, slurry packed with 4% EtOAc/hexanes in glass columns, and flushed with hexanes prior to use or slurry packed with 1% MeOH/$CHCl_3$ in glass columns, and flushed with chloroform. Preparative chromatography was also carried out using a Chromatotron using glass plates coated with silica gel (P. F. 254 60) of 2 and 4 mm thicknesses (RPLC). Nuclear magnetic resonance spectra were acquired at 500 MHz for ^{1}H and 125 MHz for ^{13}C. The abbreviations s, d, t, q, br s, br t, and ABq stand for the resonance multiplicities singlet, doublet, triplet, quartet, broad singlet, broad triplet, and AB quartet, respectively. Optical rotations were obtained (Na D line) using a microcell with a 1 dm path length. Concentrations are reported in g/100 mL. Melting points were obtained on an Electro thermal melting point apparatus and are uncorrected. Analytical C & H combustion analyses were performed by Atlantic Microlab, Inc., Norcross, GA. Glassware for all reactions was oven dried at 125 °C and cooled in a desiccator prior to use. Liquid reagents and solvents were introduced by oven dried syringes through septa-sealed flasks under a nitrogen atmosphere. In the reactions involving oxime ethers or lactols, a mixture of oxime isomers or anomers was used. However, for characterization purposes, the major oxime isomer or anomer was separated and fully characterized utilizing the separation method described in the Experimental Section for that compound.

Preparation of (5*S*,3*R*,4*R*)-2-(Phenylmethoxy)perhydro-2*H*-pyran-3,4,5-triol (10a). To a stirring suspension of D-lyxose (5.50 g, 36.6 mmol) in 18.3 mL of benzyl alcohol was added *p*-toluenesulfonic acid monohydrate (34.9 mg, 0.200 mmol), and this suspension was heated at 60 °C. After 48 h the clear colorless solution was cooled to room temperature (rt) to give a semisolid white mass, which was suspended in 2:1 hexanes/CH_2Cl_2 and filtered. The white solid was washed with Et_2O, and the filtrate was concentrated under reduced pressure. Benzyl alcohol (ca 10 mL) was removed from the filtrate by high vacuum distillation (65 °C, 0.025 mmHg), and upon being cooled to rt, a semisolid white mass formed which was subjected to the same treatment as above to yield a total of 7.2 g (81% yield) of colorless crystals as a mixture of anomers: R_f 0.49, 0.56 (20% MeOH/$CHCl_3$) for the major and minor anomers, respectively. For analytical purposes a sample of 0.5 g of this material was purified by flash column chromatography on a 2 × 16 cm column, eluting with 200 mL of 10% MeOH/$CHCl_3$, collecting 8 mL fractions. The product-containing fractions (12−14) were collected and concentrated under reduced pressure to yield **10a** as a single anomer and as colorless needles (major anomer): mp 144 °C; $[\alpha]^{22}_D = +83.0$ (*c* 3.10, MeOH); 500 MHz ^{1}H NMR (CD_3OD) δ 7.38−7.26 (m, 5H), 4.76 (d, J = 2.5 Hz, 1H), 4.72 (d, J = 11.8 Hz, 1H), 4.50 (d, J = 11.8 Hz, 1H), 3.85−3.80 (m, 2H), 3.71 (dd, J = 8.8, 3.3 Hz, 1H), 3.67 (dd, J = 10.7, 3.3 Hz, 1H), 3.51 (dd, J = 10.7, 9.3 Hz, 1H); 125 MHz ^{13}C NMR (CD_3OD) δ 139.1, 129.5, 129.2, 128.9. 101.2, 71.9, 70.3, 68.4, 64.4.

Preparation of (1*S*,6*S*,2*R*)-8,8-Dimethyl-4,7,9-trioxa-5-(phenylmethoxy)bicyclo[4.3.0]nonan-2-ol (10b). To a stirring suspension of **10a** (7.00 g, 29.0 mmol) in 98 mL of acetone were added dimethoxypropane (10.7 g, 102 mmol) and *p*-toluenesulfonic acid monohydrate (0.110 g, 0.600 mmol). After 24 h at rt 200 mL of a 1:1 mixture of hexanes/Et_2O was added, and the solution was washed with a saturated solution of $NaHCO_3$ (3 × 50 mL). The organic layer was dried over $MgSO_4$, filtered through a pad of Celite (1 × 3 cm), and concentrated under reduced pressure. Purification of this clear colorless oil was accomplished by flash column chromatography on a 5 × 26 cm column, eluting with a gradient of 300 mL each of hexanes, 5%, 10%, and 15% EtOAc/hexanes, collecting 20 mL fractions. The product-containing fractions (41−69) were collected and concentrated to give the acetonide **10b** (7.30 g, 90% yield) as colorless needles and a mixture of anomers: R_f 0.31, 0.36 (40% EtOAc/hexanes) for the major and minor anomers, respectively; (major anomer) mp 62 °C; $[\alpha]^{22}_D = +86.2$ (*c* 3.10, CH_2Cl_2); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.38−7.27 (m, 5H), 4.85 (d, J = 2.4 Hz, 1H), 4.82 (d, J = 11.7 Hz, 1H), 4.58 (d, J = 11.7 Hz, 1H) 4.24−2.22 (m, 1H), 4.19 (dd, J = 5.8, 2.4 Hz, 1H), 3.86−3.79 (m, 2H), 3.74 (dd, J = 6.4, 5.4 Hz, 1H), 3.39 (d, J = 7.3 Hz, 1H), 1.44 (s, 3H), 1.32 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 136.9, 128.6, 128.3, 128.1, 109.6, 97.5, 76.8, 74.7, 69.8, 67.5, 63.0, 27.7, 25.8.

Preparation of 1-[(6*S*,1*R*,2*R*)-8,8-Dimethyl-4,7,9-trioxa-5-(phenylmethoxy)bicyclo[4.3.0]non-2-yloxy]-1,1,2,2-tetramethyl-1-silapropane (12). To a stirring solution of alcohol **10b** (6.30 g, 22.5 mmol) as a mixture of anomers, in 18.7 mL of DMF was added imidazole (3.20 g, 45.0 mmol) followed by *tert*-butyldimethylsilyl chloride (5.30 g, 33.7 mmol) in one portion. After 2 h at rt the reaction was diluted with 150 mL of Et_2O and washed with a solution of saturated $NaHCO_3$ (3 × 50 mL) and once with 50 mL of water. The organic layer was dried over $MgSO_4$, filtered through a pad of Celite (1 × 6 cm), and concentrated under reduced pressure. Purification of this material was accomplished by flash column chromatography on a 5 × 25 cm column, eluting with 300 mL each of hexanes through 5%, 10%, 15%, and 20% EtOAc/hexanes, collecting 20 mL fractions. The product-containing fractions (21−37) were collected and concentrated to give **12** (8.80 g, 95% yield) as a colorless solid and a mixture of anomers: R_f 0.56, 0.63 (20% EtOAc/hexanes) for the major and minor anomers, respectively; (major anomer) mp 45 °C; $[\alpha]^{22}_D = +41.2$ (*c* 3.40, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.39−7.30 (m, 5H), 4.98 (d, J = 1.5

(31) Eastham, J. F.; Watson, S. C. *J. Organomet. Chem.* **1967**, *9*, 165.
(32) Imamoto, T.; Ono, M. *Chem. Lett.* **1987**, 501.
(33) (a) Giovanoli, R.; Stahi, E.; Feitknecht, W. *Helv. Chim. Acta* **1970**, *53*, 453. (b) Fatiadi, A. J. *Synthesis* **1976**, 65.

Hz, 1H), 4.76 (d, $J = 11.7$ Hz, 1H), 4.52 (d, $J = 11.7$ Hz, 1H), 4.15 (dd, $J = 5.4$, 1.5 Hz, 1H), 4.07 (t, $J = 6.1$ Hz, 1H), 3.81 (ddd, $J = 9.8$, 6.4, 5.4 Hz, 1H), 3.59−3.49 (m, 2H), 1.51 (s, 3H), 1.36 (s, 3H), 0.91 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 137.3, 128.7, 128.4, 128.1, 109.2, 96.9, 78.9, 75.8, 69.8, 69.3, 61.6, 28.3, 26.6, 26.0, 18.2, −4.3, −4.6; IR ($CHCl_3$) 1462, 1381 cm^{-1}. Anal. Calcd for $C_{21}H_{34}O_5Si$: C, 63.92; H, 8.68. Found: C, 63.88; H, 8.67.

Preparation of (1*S*,5*R*,6*R*)-8,8-Dimethyl-3,7,9-trioxa-5-(1,1,2,2-tetramethyl-1-silapropoxy)bicyclo[4.3.0]nonan-2-ol (12i). To a stirring solution of benzyl pyranoside **12** (8.12 g, 21.8 mmol) as a mixture of anomers in 218 mL of THF was added 218 mL of condensed ammonia followed by freshly cleaned lithium metal (excess). After 25 min the reaction was quenched cold with solid NH_4Cl (ca. 10 g). After the reaction turned from a blue to a cloudy colorless solution, it was allowed to warm to rt and stir 2 h before being diluted with 150 mL of Et_2O. This solution was washed once with 100 mL of a saturated solution of $NaHCO_3$, then dried over $MgSO_4$, filtered through a pad of Celite (1 × 6 cm), and concentrated under reduced pressure to give **12(d)i** (6.64 g, quantitative yield) of a colorless solid as a mixture of anomers: R_f 0.26 (20% EtOAc/hexanes) major anomer.

An analytical pure sample of the major anomer was obtained by chromatography of a sample of this intermediate by RPLC (4 mm), eluting with a gradient of 100 mL each of hexanes, 5%, 10%, 15%, 20%, 30%, and 40% EtOAc/hexanes, collecting 8 mL fractions. The product-containing fractions (60−70) were collected to yield **12(d)i** as a colorless solid: (major anomer) mp 92−94 °C; $[\alpha]^{22}_D = -13.5$ (*c* 1.35, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 5.08 (dd, $J = 6.3$, 2.0 Hz, 1H), 4.50 (d, $J = 6.4$ Hz, 1H), 4.10−4.06 (m, 2H), 3.76 (ddd, $J = 11.2$, 6.8, 4.4 Hz, 1H), 3.61 (dd, $J = 11.7$, 6.8 Hz, 1H), 3.59 (dd, $J = 11.7$, 4.4 Hz, 1H), 1.45 (s, 3H), 1.30 (s, 3H), 0.84 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 109.3, 92.6, 76.9, 75.9, 68.9, 62.5, 27.7, 25.9, 25.8, 18.1, −4.7, −4.8; IR ($CHCl_3$) 3406, 1471 cm^{-1}. Anal. Calcd for $C_{14}H_{28}O_5Si$: C, 55.23; H, 9.27. Found: C, 55.30; H, 9.26.

Preparation of 2-{5-[(1*E*)-2-Aza-2-(phenylmethoxy)vinyl](4*R*,5*R*)-2,2-dimethyl(1,3-dioxolan-4-yl)}(2*R*)-2-(1,1,2,2-tetramethyl-1-silapropoxy)ethan-1-ol (13). To a stirring solution of the crude lactol **12(d)i** prepared above (6.64 g, 21.8 mmol) in 142 mL of pyridine at rt was added *O*-benzylhyroxylamine·HCl (4.53 g, 28.4 mmol) in one portion. After 13 h the solution was concentrated under reduced pressure to near dryness, then diluted with 200 mL of EtOAc and washed with 100 mL each of water, saturated copper sulfate, water, and brine. The organic layer was dried over $MgSO_4$, filtered through a pad of Celite (1 × 6 cm), and concentrated under reduced pressure. Purification of this material was accomplished by flash column chromatography on a 4.5 × 37 cm column, eluting with a solvent gradient of 500 mL each of 5%, 10%, 15%, and 20% EtOAc/hexanes, collecting 12 mL fractions. The product-containing fractions (50−100) were collected and concentrated to give the alcohol **13** (8.94 g, 89% yield over two steps) as a clear colorless oil and a 2.4:1 mixture of oxime isomers: (major oxime isomer) R_f 0.60 (50% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.38 (d, $J = 8.8$ Hz, 1H), 7.37−7.31 (m, 5H), 5.09 (s, 2H), 4.61 (dd, $J = 8.3$, 5.9 Hz, 1H), 4.27 (dd, $J = 8.3$, 5.9 Hz, 1H), 3.71 (ddd, $J = 8.3$, 7.8, 3.9 Hz, 1H), 3.51 (ddd, $J = 11.7$, 5.4, 3.9 Hz, 1H), 3.44 (ddd, $J = 11.7$, 7.3, 3.9 Hz, 1H), 2.0 (dd, $J = 7.3$, 5.4 Hz, 1H), 1.49 (s, 3H), 1.37, (s, 3H), 0.90 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 147.9, 137.5, 128.7, 128.6, 128.3, 109.7, 79.4, 76.5, 74.7, 71.6, 63.5, 28.2, 26.1, 25.7, 18.5, −4.1, −4.5; IR (neat) 3493, 1462 cm^{-1}; HRMS *m/z* (EI) calcd $C_{21}H_{35}NO_5Si$ 409.2285, obsd 409.2285. Anal. Calcd for $C_{21}H_{35}NO_5Si$: C, 61.58; H, 8.61; N, 3.42. Found: C, 61.48; H, 8.69: N, 3.38.

Preparation of (2*E*)-1-{5-[(1*E*)-2-Aza-2-(phenylmethoxy)vinyl]-(4*R*,5*R*)-2,2-dimethyl(1,3-dioxolan-4-yl)}(1*R*)-3,3-dibromo-1-(1,1,2,2-tetramethyl-1-silapropoxy)prop-2-ene (14). To a stirring solution of alcohol **13** (4.80 g, 11.6 mmol) as a 2.2:1 mixture of oxime isomers in 78 mL of CH_2Cl_2 at rt was added 4.80 g of oven-dried 4 Å molecular sieves, *N*-methylmorpholine *N*-oxide (2.70 g, 23.3 mmol), and tetrapropylammonium perruthenate (0.290 g, 0.820 mmol). The reaction temperature was kept below 40 °C by means of a water bath. After 20 min, the solution was filtered through a pad of Celite (1 × 6 cm) and silica (1 × 6 cm). The filter pad was washed with 500 mL of EtOAc, and the solution was concentrated under reduced pressure to give the aldehyde **13(e)i** (4.80 g) as a clear yellow oil: R_f 0.45, 0.54 (10% acetone/hexanes) for the major and minor oxime isomers, respectively.

Crude aldehyde **13(e)i** was immediately used in the next step. To a stirring solution of carbon tetrabromide (8.90 g, 26.8 mmol) in 58 mL of CH_2Cl_2 at 0 °C (ice/water bath) was added triphenylphosphine (14.4 g, 54.8 mmol). After 15 min, triethylamine (1.53 g, 15.2 mmol) was added to this golden yellow solution and the mixture was stirred for 5 min before cooling to −78 °C (2-propanol−dry ice). To this − 78 °C solution was added a solution of crude aldehyde **13(e)i** in 29 mL of CH_2Cl_2 down the side of the flask rapidly (wash with CH_2Cl_2, 2 × 3 mL). After 10 min this solution was poured rapidly into 400 mL of a cold 1:1 mixture of hexanes and a saturated solution of $NaHCO_3$ (aq) and was allowed to stir for 2 h. The layers were separated, and the aqueous layer was washed with Et_2O (3 × 100 mL). The combined organic layers were dried over Na_2SO_4, filtered through a pad of Celite (1 × 6 cm), and concentrated under reduced pressure. Purification was accomplished by flash column chromatography using a 5 × 25 cm column, loading the material in a minimal amount of CH_2Cl_2, and eluting with a gradient of 500 mL each of hexanes, 2%, 4%, and 6% EtOAc/hexanes, collecting 20 mL fractions. The product-containing fractions (20−60) were collected and concentrated under reduced pressure to give the dibromide **14** (3.57 g, 55% over two steps) as a 2.7:1 mixture of oxime isomers and a clear light yellow oil: R_f 0.42, 0.46 (10% EtOAc/hexanes) for the major and minor oxime isomers, respectively; (major oxime isomer) $[\alpha]^{25}_D = -10.7$ (*c* 1.56, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 8.59 (d, $J = 7.8$ Hz, 1H), 7.39−7.30 (m, 5H), 6.50 (d, $J = 8.8$ Hz, 1H), 5.12 (s, 2H), 4.75 (dd, $J = 7.3$, 7.3 Hz, 1H), 4.40 (dd, $J = 8.8$, 4.4 Hz, 1H), 4.21 (dd, $J = 7.3$, 4.4 Hz, 1H), 1.53 (s, 3H), 1.38 (s, 3H), 0.92 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 147.7, 137.9, 137.5, 128.6, 128.5, 128.1, 110.2, 92.1, 80.7, 76.4, 74.9, 72.8, 27.1, 26.0, 25.4, 18.3, −3.9, −4.6; IR (neat) 3306, 1618 cm^{-1}. Anal. Calcd for $C_{22}H_{33}Br_2NO_4Si$: C, 46.90; H, 5.90; N, 2.49. Found: C, 47.02; H, 5.86; N, 2.41.

Preparation of 1-(1-{5-[(1*E*)-2-Aza-2-(phenylmethoxy)vinyl]-(4*R*,5*R*)-2,2-dimethyl(1,3-dioxolan-4-yl)}(1*R*)prop-2-ynyloxy)-1,1,2,2-tetramethyl-1-silapropane (15). To a stirring solution of dibromide **14** (3.0 g, 5.3 mmol) as a 1.4:1 mixture of oxime isomers in 53 mL of Et_2O at −78 °C (2-propanol/CO_2 bath) was added a solution of ^{n}BuLi (5.4 mL, 2.1 M in hexanes) slowly down the side of the flask. After 20 min the reaction was quenched cold by addition of 12 mL of a saturated NH_4Cl solution and was then allowed to warm to rt and stirred for 1 h. The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic layers were dried over $MgSO_4$, filtered through a pad of Celite (1 × 4 cm), and concentrated under reduced pressure to give a golden yellow oil. Purification of this material was accomplished by flash column chromatography on a 3 × 23 cm column, eluting with a gradient of 200 mL each of hexanes, 2%, 4%, 6%, and 8% EtOAc/hexanes, collecting 20 mL fractions. The product fractions (28−35) were collected and concentrated to give alkyne **15** (2.0 g, 91% yield) as a 1.1:1 mixture of oxime isomers and a clear colorless oil: R_f 0.37, 0.46 (5% acetone/hexanes) for the major and minor oxime isomers, respectively; (major oxime isomer) $[\alpha]^{25}_D = -15.3$ (*c* 4.88, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.73 (d, $J = 8.2$ Hz, 1H), 7.35−7.27 (m, 5H), 5.08 (s, 2H), 4.77 (dd, $J = 7.8$, 7.0 Hz, 1H), 4.43 (dd, $J = 5.8$, 2.2 Hz, 1H), 4.25 (dd, $J = 6.2$, 6.2 Hz, 1H), 2.39 (dd, $J = 2.2$, 0.6 Hz, 1H), 1.52 (s, 3H), 1.36 (s, 3H), 0.88 (s, 9H), 0.13 (s, 3H), 0.09 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 147.4, 137.6, 128.6, 128.5, 128.1, 110.5, 82.5, 80.5, 76.3, 75.4, 75.1, 62.7, 27.3, 25.9, 25.4, 18.3, −4.3, −4.9; IR (neat) 3308, 1628, 1471 cm^{-1}. Anal. Calcd for $C_{22}H_{33}NO_4Si$; C, 65.47; H, 8.24; N, 3.47. Found: C, 65.54; H, 8.29; N, 3.53.

Preparation of 6-((3*R*)-3-{(4*R*,5*R*)-5-[(1*Z*)-2-Aza-2-(phenylmethoxy)vinyl]-2,2-dimethyl(1,3-dioxolan-4-yl)}-3-(1,1,2,2-tetramethyl-1-silapropoxy)prop-1-ynyl)-2*H*-benzo[*d*]1,3-dioxolene-5-carbaldehyde (16). To a stirring solution of terminal alkyne **15** (0.91 g, 2.3 mmol) as a 12:1 mixture of oxime isomers in 14 mL of THF were added NEt_3 (0.63 g, 6.2 mmol), PPh_3 (0.059 g, 0.22 mmol), CuI (0.051 g, 0.26 mmol), $Pd(OAc)_2$ (0.023 g, 0.10 mmol), and bromopiperonal **9**[12] (0.47 g, 2.0 mmol). After 9 h the reaction was diluted with 100 mL of Et_2O and washed with a saturated solution of NH_4Cl (3 × 20 mL).

The organic layer was dried over $MgSO_4$, filtered through a pad of Celite (1 × 3 cm), and concentrated under reduced pressure. The brown oil was purified by flash column chromatography using a 3 × 20 cm column, eluting with a gradient of 100 mL each, hexanes through 3%, 6%, 9%, 12%, 15%, 18%, and 21% EtOAc/hexanes, collecting 20 mL fractions. The product containing fractions (24−34) were collected to give alkyne **16** (1.0 g, 91% yield) as a 12:1 mixture of oxime isomers and a yellow foam: R_f 0.36, 0.40 (20% EtOAc/hexanes) for the major and minor oximer isomers, respectively; (major oxime isomer) $[\alpha]^{25}_D = -30.1$ (*c* 8.76, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 10.33 (s, 1H), 7.72 (d, J = 8.0, 1H) 7.32−7.23 (m, 6H), 6.90 (s, 1H), 6.03 (s, 2H), 5.04 (s, 2H), 4.82 (dd, J = 8.0, 6.7 Hz, 1H), 4.68 (d, J = 6.0 Hz, 1H), 4.34 (dd, J = 6.4, 6.4 Hz, 1H), 1.51 (s, 3H), 1.37 (s, 3H), 0.90 (s, 9H), 0.16 (s, 3H), 0.13 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 190.0, 152.5, 149.1, 146.9, 137.3, 132.9, 128.5, 128.4, 128.1, 122.8, 112.5, 110.5, 106.1, 102.6, 93.7, 82.5, 80.5, 76.4, 75.1, 63.4, 27.4, 25.9, 25.4, 18.4, −4.3, −4.7; IR (neat) 3018, 2401, 1683 cm^{-1}. Anal. Calcd for $C_{30}H_{37}NO_7Si$: C, 65.31; H, 6.76; N, 2.54. Found: C, 65.15; H, 6.83; N, 2.69.

Preparation of 6-((3*R*)-3-{(4*S*,5*R*)-5-[(1*Z*)-2-Aza-2-(phenylmethoxy)-vinyl]-2,2-dimethyl(1,3-dioxolan-4-yl)}-3-hydroxyprop-1-ynyl)-2*H*-benzo[*d*]1,3-dioxolene-5-carbaldehyde (17). To a solution of alkyne **16** (1.72 g, 3.12 mmol) in 62 mL of THF in a plastic reaction vessel was added at 0 °C (ice/water bath) a premade solution consisting of HF−pyridine (15.5 g), pyridine (21.0 mL), and 62.0 mL of THF. The solution was allowed to stand at rt for 10 h, at which time it was diluted with 200 mL of Et_2O and slowly quenched with a saturated solution of $NaHCO_3$. The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 100 mL). The combined organic layers were dried over Na_2SO_4, filtered through a pad of Celite (1 × 6 cm), and concentrated under reduced pressure. Purification was accomplished by flash column chromatography on a 3 × 21 cm column, eluting with a gradient of 200 mL each of hexanes, 10%, 20%, 30%, 40%, and 50% EtOAc/hexanes, collecting 25 mL fractions. The product-containing fractions (36−48) were collected and concentrated to give alcohol **17** (1.21 g, 88% yield) as a 2.3:1 mixture of oxime isomers and as a light yellow foam: R_f 0.37, 0.44 (50% EtOAc/hexane) for the major and minor oxime isomers, respectively; (major oxime isomer) $[\alpha]^{25}_D = +57.7$ (*c* 1.39, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 10.30 (s, 1H), 7.58 (d, J = 7.7 Hz, 1H), 7.32−7.26 (m, 6H), 6.93 (s, 1H), 6.07 (s, 2H), 5.06 (ABq, $\Delta\nu$ = 9.1 Hz, J = 12.1 Hz, 2H), 4.86 (dd, J = 7.3, 7.3 Hz, 1H), 4.59 (dd, J = 6.1, 6.1 Hz, 1H), 4.43 (dd, J = 6.3, 6.3 Hz, 1H), 2.69 (d, J = 6.3 Hz, 1H), 1.56 (s, 3H), 1.42 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 190.0, 152.4, 149.2, 147.4, 137.2, 132.8, 128.6, 128.4, 128.2, 122.3, 112.6, 110.8, 106.3, 102.7, 92.1, 82.6, 80.8, 76.5, 75.0, 62.0, 27.5, 25.2; IR ($CHCl_3$) 3406, 1681, 1608 cm^{-1}. Anal. Calcd for $C_{24}H_{23}NO_7$: C, 65.90; H, 5.30; N, 3.20. Found: C, 66.03; H, 5.40; N, 3.25.

Preparation of Methyl 6-((3*R*)-3-{(4*S*,5*R*)-5-[(1*Z*)-2-Aza-2-(phenylmethoxy)vinyl]-2,2-dimethyl(1,3-dioxolan-4-yl)}-3-hydroxyprop-1-ynyl)-2*H*-benzo[*d*]1,3-dioxolene-5-carboxylate (18). To a stirring solution of acetic acid (0.338 g, 5.62 mmol) in 12 mL of MeOH were added sodium cyanide (0.538 g, 11.1 mmol), a solution of aldehyde **17** (0.971 g, 2.22 mmol in 5 mL of MeOH) as a 2.7:1 mixture of oxime isomers via cannula (wash, 2 × 3 mL), and precipitated activated manganese dioxide (3.85 g, 44.4 mmol). The reaction mixture was allowed to stir at rt for 16 h, at which time it was concentrated to near dryness under reduced pressure, then diluted with 100 mL of Et_2O and washed with 50 mL of water. The layers were separated, and the aqueous layer was back-extracted with Et_2O (3 × 100 mL). The combined organic layers were dried over Na_2SO_4, filtered through a pad of Celite (1 × 6 cm), and concentrated under reduced pressure. Purification was accomplished by flash column chromatography using a 3 × 21 cm column, eluting with a gradient of 200 mL each of 20%, 30%, 40%, and 50% EtOAc/hexanes, collecting 25 mL fractions. The product-containing fractions (22−35) were collected and concentrated to give the ester **18** (0.836 g, 81% yield) as a 1.5:1 mixture of oxime isomers and as a light yellow foam: R_f 0.34, 0.38 (50% EtOAc/hexane) for the major and minor oxime isomers, respectively; (major oxime isomer) $[\alpha]^{25}_D = +65.5$ (*c* 4.58, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.64 (d, J = 7.8 Hz, 1H), 7.39 (s, 1H), 7.31−7.28 (m, 5H), 6.94 (s, 1H), 6.04 (s, 2H), 5.06 (ABq, $\Delta\nu$ = 8.9 Hz, J = 12.2 Hz, 2H), 4.87 (dd, J = 7.8, 6.8 Hz, 1H), 4.62 (dd, J = 5.9, 5.9 Hz, 1H), 4.47 (dd, J = 6.4, 6.4 Hz, 1H), 3.86 (s, 3H), 2.82 (d, J = 6.4 Hz, 1H), 1.56 (s, 3H), 1.43 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 165.7, 150.6, 148.1, 147.5, 137.4, 128.5, 128.3, 128.1, 126.9, 118.2, 113.6, 110.6, 110.3, 102.5, 90.2, 85.8, 80.9, 76.4, 75.0, 62.1, 52.3, 27.6, 25.3; IR ($CHCl_3$) 3497, 1720, 1610 cm^{-1}. Anal. Calcd for $C_{25}H_{25}NO$: C, 64.23; H, 5.39; N, 3.00. Found: C, 64.23; H, 5.46; N, 2.98.

Preparation of Methyl 6-{(4*S*,7*S*,7a*S*,3a*R*)-7-Hydroxy-2,2-dimethyl-4-[(phenylmethoxy)amino]-6-phenylthio-2,3,4,7,3a,7a-hexahydro-1,3-dioxainden-5-yl}-2*H*-benzo[*d*]1,3-dioxolane-5-carboxylate (21). To a stirring solution of alkyne **18** (0.35 g, 0.99 mmol) as a 1.5:1 mixture of oxime isomers in 15 mL of toluene was added thiophenol (0.11 g, 0.11 mL, 1.4 mmol) via syringe. This reaction mixture at 21−27 °C (circulating water bath) was then subjected to photolysis conditions utilizing a sun lamp (200 W, 120 V, GE Crystal Clear Light bulb) placed approximately 5 cm from the Pyrex reaction vessel. The reaction vessel was kept below 27 °C (circulating water bath) for 2 h before being concentrating under reduced pressure to give a yellow oil. Purification was accomplished by flash column chromatography on a 2 × 16 cm column, eluting with a gradient of 100 mL each of 10%, 20%, 30%, and 40% EtOAc/hexanes, collecting 8 mL fractions. The product-containing fractions (27−38) were collected and concentrated to give hydroxylamine **21** (0.39 g, 91% yield) as a single diastereomer and a light yellow foam: $[\alpha]^{25}_D = -61.0$ (*c* 14.3, $CHCl_3$); R_f 0.35 (35% EtOAc/hexane); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.36−7.30 (m, 8H), 7.22−7.15 (m, 3H), 6.93 (d, J = 2.5 Hz, 1H), 6.74 (s, 1H), 6.00 (d, J = 1.1 Hz, 1H), 5.97 (d, J = 1.1 Hz, 1H), 5.00 (d, J = 12.4 Hz, 1H), 4.73 (s, 2H), 4.66 (dd, J = 7.1, 1.6 Hz, 1H), 4.42 (dd, J = 7.1, 1.6 Hz, 1H), 4.02−3.72 (m, 2H), 3.71 (s, 3H), 1.51 (s, 3H), 1.31 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 167.2, 151.2, 147.2, 139.1, 137.2, 137.0, 134.3, 132.4, 129.0, 128.7, 128.7, 128.4, 127.5, 124.4, 109.5, 109.2, 108.2, 102.2, 78.9, 77.2, 74.2, 68.2, 65.5, 52.5, 26.3, 23.9; IR ($CHCl_3$) 3252, 1712 cm^{-1}; HRMS *m*/*z* (EI) calcd for $C_{31}H_{31}NO_8S$ 577.1770, obsd 577.1744. Anal. Calcd for $C_{31}H_{31}NO_8S$: C, 64.46; H, 5.41; N, 2.42; S, 5.55. Found: C, 64.26; H, 5.48; N, 2.37; S, 5.43.

Preparation of ((2a*S*,5b*S*,2*R*,5a*R*)-2-Hydroxy-4,4-dimethyl-2,6,-2a,5a,5b-pentahydro-10*H*-1,3-dioxolano[4,5-*j*]1,3-dioxolano[4,5-c]-phenanthridin-7-one (23) and (2a*S*,2*R*,5a*R*,5b*R*)-2-Hydroxy-4,4-dimethyl-1-phenylthio-2,6,2a,5a,5b-pentahydro-10*H*-1,3-dioxolano[4,5-*j*]1,3-dioxolano[4,5-c]phenanthridin-7-one (22). To a stirring solution of hydroxylamine **21** (0.40 g, 0.69 mmol) in 14.0 mL of THF was added a freshly prepared solution of SmI_2 (14.5 mL, 1.45 mmol, 0.10 M in THF), prepared by heating Sm (0.66 g, 4.4 mmol) and iodine (0.80 g, 3.1 mmol) in 31.5 mL of THF at 65 °C for 4 h. After 45 min an additional amount of SmI_2 (14.5 mL, 1.45 mmol, 0.10 M in THF) was added to this yellow solution. After 44 h at rt the blue solution was diluted with 100 mL of THF and quenched with 40 mL of a 1% aqueous HCl solution. This solution was diluted further with 100 mL of EtOAc, and the layers were separated. The organic layer was washed with 60 mL of brine, then dried over $MgSO_4$, filtered through a pad of Celite (1 × 6 cm), and concentrated under reduced pressure. Purification of this material was accomplished by flash column chromatography on a 2 × 12 cm column, eluting with a gradient of 100 mL each of 1%, 2%, and 3% MeOH/$CHCl_3$, collecting 8 mL fractions. The product-containing fractions [vinyl sulfide **22** (13−18) and desired lactam **23** (19−30)] were collected in separate flasks and concentrated under reduced pressure to give vinyl sulfide **22** (50 mg, 15% yield) and the desired lactam **23** (174 mg, 76% yield) as a viscous yellow oil and a colorless crystalline solid, respectively: (vinyl sulfide **22**) $[\alpha]^{25}_D = -99.2$ (*c* 1.44, $CHCl_3$); R_f 0.34 (5% MeOH/$CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 8.53 (s, 1H), 7.69 (s, 1H), 7.31−7.27 (m, 2H), 7.24−7.20 (m, 3H), 6.51 (bs, 1H), 6.02 (ABq, $\Delta\nu$ = 2.2 Hz, J = 1.0 Hz, 2H), 4.38 (d, J = 6.3 Hz, 1H), 4.35 (ddd, J = 7.8, 1.5, 1.5 Hz, 1H), 4.16 (dd, J = 7.8, 7.8 Hz, 1H), 4.10 (dd, J = 7.81, 6.3 Hz, 1H), 3.31 (bs, 1H), 1.54 (s, 3H), 1.38 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 162.4, 151.0, 149.2, 135.1, 134.4, 129.9, 128.2, 127.6, 127.1, 124.1, 112.0, 108.2, 107.1, 102.3, 78.8, 77.7, 73.6, 57.5, 27.4, 25.2; IR ($CHCl_3$) 3542−3143, 1667 cm^{-1}; HRMS *m*/*z* (EI) calcd for $C_{23}H_{21}NO_6S$ 439.1089, obsd 439.1103. Lactam **23**: mp 231 °C; $[\alpha]^{25}_D = +34.2$ (*c* 0.72, MeOH); R_f 0.28 (5% MeOH/$CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$)

δ 7.57 (s, 1H), 7.00 (s, 1H), 6.26−6.25 (m, 2H), 6.01 (ABq, $\Delta\nu = 3.1$ Hz, $J = 1.1$ Hz, 2H), 4.37−4.36 (m, 1H), 4.12−4.11 (m, 3H), 2.96 (bs, 1H), 1.54 (s, 3H), 1.36 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 162.7, 152.1, 148.9, 128.6, 127.8, 124.3, 121.1, 111.7, 107.9, 102.2, 101.7, 79.8, 79.2, 73.1, 56.2, 27.3, 25.0; IR ($CHCl_3$) 3462, 3329, 1668 cm^{-1}; HRMS *m*/*z* (EI) calcd for $C_{17}H_{17}NO_6$ 331.1056, obsd 331.1059.

Preparation of (2a*S*,5b*S*,2*R*,5a*R*)-2-Hydroxy-4,4-dimethyl-2,6,-2a,5a,5b-pentahydro-10*H*-1,3-dioxolano[4,5-*j*]1,3-dioxolano[4,5-*c*]-phenanthridin-7-one (23). To a stirring solution of vinyl sulfide **22** (16 mg, 0.037 mmol) in 0.74 mL of THF was added a freshly made solution of SmI_2 (0.78 mL, 0.078 mmol, 0.10 M in THF), prepared as described above. After 1 h an additional amount of SmI_2 (0.40 mL, 0.04 mmol, 0.10 M in THF) was added to this yellow solution. After a total of 8 h at rt this yellow solution was diluted with 5 mL of THF and quenched with 2 mL of a 1% aqueous HCl solution. This mixture was further diluted with 10 mL of EtOAc, and the layers were separated. The organic layer was washed with a saturated $Na_2S_2O_3$ solution (3 × 2 mL) and once with 5 mL of brine. The organic layers were dried over $MgSO_4$, filtered through a pad of Celite, and concentrated under reduced pressure. Purification of this material was accomplished by flash column chromatography on a 1 × 6 cm column, eluting with a gradient of 50 mL each, 1%, 2%, and 3% (MeOH/$CHCl_3$), collecting 3 mL fractions. The product-containing fractions were collected and concentrated under reduced pressure to give lactam **23** (9.0 mg, 73% yield), as a colorless crystalline solid, whose physical properties were identical to those described in the previous experimental above.

Preparation of (3*S*,4a*S*,2*R*,4*R*)-2,3,4-Trihydroxy-2,3,4,5,4a-pentahydro-9*H*-1,3-dioxolano[4,5-*j*]phenanthridin-6-one, [(−)-Lycoricidine]. To lactam **23** (9.8 mg, 0.029 mmol) in a ice-cooled bath was added trifluoroacetic acid (0.59 mL) down the side of the flask. After 1 h at 0 °C the reaction was diluted with 2 mL of dioxane. The TFA and dioxane was removed under reduced pressure to give a light yellow solid. Purification of this material was accomplished by column flash chromatography on a pipet colunm (0.5 × 6 cm), eluting with a gradient of 10 mL of each, 10% and 20% (MeOH/$CHCl_3$), collecting 0.6 mL fractions. The product-containing fractions (10−20) were collected and concentrated to give (−)-lycoricidine (6.6 mg, 77% yield) as a colorless crystalline solid: mp 221−224 °C (dec), [lit.[4e] mp 224−226 °C (dec), lit.[4i] 214.5−215.5 °C (dec), lit.[4k] mp 217−221 °C (dec)]; $[\alpha]^{25}_D = -164$ (*c* 0.45, pyridine), [lit.[4e] $[\alpha]^{25}_D = +180$ (*c* 0.45, pyridine), lit.[4i] $[\alpha]^{23}_D = +199$ (pyridine)]; R_f 0.36 (20% MeOH/$CHCl_3$); 500 MHz ^{1}H NMR (CD_3OD) δ 7.39 (s, 1H), 7.15 (s, 1H), 6.17 (ddd, $J = 3.9, 2.9, 1.0$ Hz, 1H), 6.07 (d, $J = 1.0$ Hz, 1H), 6.05 (d, $J = 1.0$ Hz, 1H), 4.39 (ddd, $J = 8.3, 2.4, 1.5$ Hz, 1H), 4.25 (ddd, $J = 3.9, 1.5, 1.5$ Hz, 1H), 3.94−3.91 (m, 2H); 125 MHz ^{13}C NMR (CD_3OD) δ 166.8, 153.6, 150.3, 133.6, 132.8, 123.5, 122.9, 107.8, 104.6, 103.7, 74.5, 71.1, 71.0, 54.0; IR (KBr) 3567, 3419, 3359, 1654 cm^{-1}.

Preparation of (3*S*,4a*S*,2*R*,4*R*)-2,3-Diacetyloxy-6-oxo-2,3,4,5,4a-pentahydro-9*H*-1,3-dioxolano[4,5-j]phenanthridin-4-yl Acetate [(−)-Lycoricidine Triacetate]. To a stirring solution of (−)-lycoricidine (0.029 g, 0.10 mmol) in 1 mL of pyridine was added 1 mL of acetic anhydride. After 18 h at rt the reaction mixture was concentrated under reduced pressure, then azeotroped with 5 mL of toluene to give a colorless crystalline residue. Purification of this material was accomplished by flash column chromatography on a 1 × 13 cm column, eluting with 100 mL of 1% MeOH/$CHCl_3$, collecting 3 mL fractions. The product-containing fractions (13−20) were collected and concentrated to give the triacetate (0.034 g, 82% yield) of a colorless crystalline residue: mp 205−210 °C (from $CHCl_3$/pentane) [lit.[4e] mp 236−237 °C, lit.[4i] mp 233−235 °C, natural product[4e] mp 238−239 °C]; $[\alpha]^{23}_D = -205$ (*c* 0.40, $CHCl_3$) [lit.[4e] $[\alpha]^{24}_D = +214$ (*c* 0.45, $CHCl_3$), lit.[4i] $[\alpha]^{23}_D = +238$ (*c* 0.1, $CHCl_3$), natural product[4e] $[\alpha]^{20}_D = +201$ (*c* 0.38, $CHCl_3$); R_f 0.31 (50% EtOAc/toluene); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.53 (s, 1H), 7.00 (s, 1H), 6.87 (bs, 1H), 6.12 (ddd, $J = 4.7, 2.7, 1.1$ Hz, 1H), 6.06 (ABq, $\Delta\nu = 10.3$ Hz, $J = 1.4$ Hz, 2H), 5.47 (ddd, $J = 2.5, 2.5, 0.8$ Hz, 1H), 5.35 (ddd, $J = 4.1, 2.5, 0.8$ Hz, 1H), 5.26 (dd, $J = 9.5, 2.5$ Hz, 1H), 4.67 (ddd, $J = 9.3, 2.2, 0.8$ Hz, 1H), 2.16 (s, 3H), 2.12 (s, 3H), 2.10 (s, 3H); 500 MHz ^{1}H NMR (acetone-d_6) δ 7.42 (s, 1H), 7.25 (s, 1H), 6.28 (m, 1H), 6,15 (d, $J = 1.1$ Hz, 1H) 6.13 (d, $J = 1.1$, 1H), 5.44 (ddd, $J = 2.7, 2.7, 1.1$, 1H), 5.36 (ddd, $J = 4.9, 2.7, 1.4$ Hz, 1H), 5.18 (dd, $J = 9.3, 2.5$ Hz, 1H), 4.70 (ddd, $J = 9.3, 2.5, 1.1$ Hz, 1H), 2.09 (s, 3H), 2.09 (s, 3H), 2.07 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 170.5, 170.0, 169.7, 164.4, 152.0, 149.4, 134.2, 130.5, 122.6, 117.4, 107.8, 103.6, 102.3, 71.5, 68.7, 68.4, 50.4, 21.2, 21.1, 20.9; IR ($CDCl_3$) 3402, 1749, 1667 cm^{-1}.

Preparation of 4-((1*E*)-2,2-Dibromovinyl)(4*S*,5*S*,1*R*)-7,7-dimethyl-3,6,8-trioxabicyclo[3.3.0]octan-2-one (25). To a stirring solution of 2,3-*O*-isopropylidene-D-gulonolactone[21] **24** (1.25 g, 5.73 mmol) in 38 mL of a 2:1 mixture of THF/H_2O was added $NaIO_4$ (1.81 g, 8.60 mmol) in one portion. After 2.1 h at rt the reaction was filtered through a fritted funnel and diluted with 100 mL of EtOAc. The layers were separated, and the aqueous layer was back extracted with EtOAc (3 × 50 mL). The combined organic layers were dried over $MgSO_4$, filtered through a pad of $MgSO_4$ (0.5 × 3 cm), and concentrated under reduced pressure. This colorless foam (R_f 0.5, EtOAc) was used without any further purification.

To a stirring solution of carbon tetrabromide (3.81 g, 11.5 mmol) in 60 mL of CH_2Cl_2 at 0 °C (ice/water bath) was added triphenylphosphine (6.01 g, 22.9 mmol) in one portion. After 10 min triethylamine (0.798 mL, 22.9 mmol) was added to this yellow-orange colored solution. Upon complete addition of triethylamine, the resulting solution was cooled to −78 °C (acetone/CO_2 bath). This solution was added via cannula to a precooled solution (−78 °C, acetone/CO_2 bath) of the crude aldehyde prepared above (inverse addition) over a 3 min period. The reaction mixture was allowed to stir for an additional 10 min before being poured into a rapidly stirring solution of saturated $NaHCO_3$ (300 mL) and then diluted with 100 mL of CH_2Cl_2. After 20 min of stirring, the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 75 mL). The combined organic layers were dried over $MgSO_4$, filtered through a pad of Celite (0.5 × 6 cm) and $MgSO_4$ (0.5 × 6 cm), and concentrated under reduced pressure. Purification was accomplished by flash chromatography (dry pack) on a 3.5 × 20 cm column, eluting with 200 mL each of hexanes, 10%, 20%, and 30% EtOAc/hexanes, collecting 20 mL fractions. The product-containing fractions (13−30) were collected and concentrated to give **25** (1.56 g, 80% yield over two steps) as a crystalline solid: mp 106−108 °C; R_f 0.32 (30% EtOAc/hexanes); $[\alpha]^{23}_D = -24.6$ (*c* 5.9, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 6.68 (d, $J = 8.2$ Hz, 1H), 5.13 (dd, $J = 8.2, 3.6$ Hz, 1H); 4.87 (dd, $J = 5.2, 3.3$ Hz, 1H), 4.84 (d, $J = 5.2$, 1H), 1.46 (s, 3H), 1.38 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 173.4, 131.0, 114.6, 97.0, 78.5, 76.6, 75.9. 26.9, 25.9; IR ($CDCl_3$) 3019, 1793, 1635 cm^{-1}. Anal. Calcd for $C_9H_{10}Br_2O_4$: C, 31.61; H, 2.95. Found: C, 31.56; H, 2.97.

Preparation of (2*E*)-1-{5-[(1*E*)-2-Aza-2-(phenylmethoxy)vinyl]-(5*S*,4*R*)-2,2-dimethyl(1,3-dioxolan-4-yl)}(1*S*)-3,3-dibromoprop-2-en-1-ol (26). To a stirring solution of **25** (4.53 g, 13.2 mmol) in 66 mL of THF at −78 °C (acetone/CO_2 bath) was added L-Selectride (26.5 mL, 26.5 mmol, 1.00 M in THF) down the side of the flask. After 3 h the reaction was quenched cold by the slow addition of 50 mL of H_2O and then allowed to warm to rt. The reaction mixture was diluted with 300 mL of EtOAc, and the layers were separated. The aqueous layer was back-extracted with EtOAc (3 × 75 mL), then the combined organic layers were dried over $MgSO_4$, filtered through a pad of $MgSO_4$ (0.5 × 6 cm), and concentrated to yield a colorless oil having R_f 0.58 (50% EtOAc/hexanes) which was used without further purification.

To a stirring solution of crude lactol prepared above (as an 8:1 mixture of anomers) in 66 mL of pyridine was added *O*-benzylhydroxylamine·HCl (31.8 g, 19.9 mmol) in one portion. After 21 h at rt the reaction mixture was concentrated to a colorless paste, which was diluted with 300 mL of EtOAc and washed with 60 mL each of H_2O, 2% aqueous HCl, saturated aqueous $CuSO_4$ solution, H_2O-saturated aqueous $CuSO_4$ solution, and one more portion of H_2O. The organic layer was dried over $MgSO_4$, filtered as before, and concentrated under reduced pressure to give a golden yellow oil. Purification was accomplished by flash chromatography on a 3.5 × 20 cm column, eluting with a gradient of 200 mL each of hexanes, 10%, 20%, and 30% EtOAc/hexanes, collecting 20 mL fractions. The product-containing fractions (18−32) were collected and concentrated to give the olefin dibromide **26** (5.34 g, 90%) as a 1.0:1.7 inseparable mixture of oxime isomers and a clear colorless oil: (major and minor isomers); R_f 0.26 (20% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.57 (d, $J = 7.7$ Hz, 1H) (minor), 7.37−7.31 (m, 10H) (major and minor), 7.05 (d, $J = 4.1$ Hz, 1H) (major), 6.49 (d, $J = 8.5$ Hz, 1H) (minor), 6.47 (d, $J =$

8.2 Hz, 1H) (major), 5.23 (dd, $J = 7.4$, 4.1 Hz, 1H) (major), 5.12 (d, $J = 3.6$ Hz, 2H) (major), 5.10 (s, 2H) (minor), 4.75 (dd, $J = 7.1$, 3.3 Hz, 1H) (minor), 4.37, (dd, $J = 7.4$, 1.9 Hz, 1H) (major), 4.25 (dd, $J = 8.5$, 3.3 Hz, 1H) (minor), 4.23 (dd, $J = 7.1$, 3.3 Hz, 1H) (minor), 4.19 (dd, $J = 8.5$, 1.9 Hz, 1H) (major), 2.39 (bs, 1H) (major), 2.23 (bs, 1H) (major), 1.53 (s, 3H) (major), 1.52, (s, 3H) (minor), 1.37(s, 3H) (minor), 1.35 (s, 3H) (major); 125 MHz ^{13}C NMR ($CDCl_3$) (one set) δ 148.1, 137.4, 137.0, 128.4, 128.3, 128.2, 110.3, 93.5, 79.6, 76.5, 75.0, 70.8, 27.0, 24.7; (one set) 150.5, 137.9, 137.2, 128.8, 128.7, 128.6, 109.7, 92.1, 79.1, 77.1, 72.7, 71.3, 26.6, 24.5; IR (neat) 3470(br), 1623 cm^{-1}. Anal. Calcd for $C_{16}H_{19}Br_2NO_4$: C, 42.79; H, 4.26; N, 3.12. Found: C, 42.93; H, 4.36; N, 3.17.

Preparation of 1-{5-[(1*E*)-2-Aza-2-(phenylmethoxy)vinyl](5*S*,4*R*)-2,2-dimethyl(1,3-dioxolan-4-yl)}(1*S*)-prop-2-yn-1-ol (27). To a stirring solution of the dibromo-olefin **26** (3.00 g, 6.68 mmol) as a 1:1.5 mixture of oxime isomers in 70 mL of Et_2O at −90 °C (Et_2O/CO_2 bath) was added a solution of ^{n}BuLi (10.2 mL, 20.0 mmol, 1.96 M in hexanes) over a 15 min period down the side of the flask. After complete addition the reaction was allowed to stir an additional 15 min before it was quenched cold by addition of 20 mL of a saturated solution of NH_4Cl. After warming to rt, 200 mL of Et_2O was added and the layers were separated. The aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a golden yellow oil. Purification was accomplished by flash chromatography on a 3.5 × 20 cm column, eluting with a gradient of 200 mL each of 10%, 20%, 30%, and 40% EtOAc/hexanes, collecting 20 mL fractions. The product-containing fractions (17−27) were collected to give alkyne **27** (1.80 g, 93% yield) as a 1.3:1 mixture of oxime isomers and as a clear colorless oil: R_f 0.33, 0.29 (30% EtOAc/hexanes) for the major and minor oxime isomers, respectively; (minor oxime isomer)[34] $[\alpha]^{22}_D$ +20.8 (*c* 2.9, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.53 (d, $J = 7.7$ Hz, 1H), 7.34−7.28 (m, 5H), 5.09 (s, 2H), 4.79, (dd, $J = 7.4$, 6.9 Hz, 1H), 4.34 (dd, $J = 6.9$, 4.9 Hz, 1H), 4.29, (ddd, $J = 6.9$, 4.9, 2.2 Hz, 1H), 2.54, (bd, $J = 6.9$ Hz, 1H), 2.42 (d, $J = 2.2$ Hz, 1H), 1.52 (s, 3H), 1.39 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 147.7, 137.5, 128.6, 128.4, 128.2, 110.7, 81.4, 80.7, 76.5, 75.0, 74.9, 61.1, 27.3, 25.0; IR (neat) 3445 (br), 2874, 1713 cm^{-1}. Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.52: H, 6.63; N, 4.84.

Preparation Methyl 6-Iodo-2*H*-benzo[*d*]1,3-dioxolene-5-carboxylate (28). To a stirring solution of acetic acid (0.33 g, 5.4 mmol) in 20 mL of MeOH was added sodium cyanide (0.89 g, 18 mmol) followed by iodopiperonal[22] (1.0 g, 3.6 mmol) in 16 mL of MeOH and then MnO_2 (6.3 g, 72 mmol) in one portion. After 27 h the reaction was filtered through a pad of Celite (1 × 6 cm) and concentrated under reduced pressure to near dryness to give a colorless paste. This material was diluted with 200 mL of Et_2O and washed with 100 mL of a saturated solution of $NaHCO_3$. The organic layer was than dried over $MgSO_4$, filtered through a pad of Celite and $MgSO_4$, and concentrated under reduced pressure. Purification of this material was accomplished by flash chromatography using a 3 × 18 cm column, eluting with 100 mL each of hexanes, 10%, and 15% EtOAc/hexanes, collecting 20 mL fractions. The product-containing fractions (12−20) were collected and concentrated to give ester **28** (1.1 g, 98% yield) as a colorless crystalline solid: mp 70−72 °C; R_f 0.43 (30% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.39 (s, 1H), 7.35 (s, 1H), 6.02 (s, 2H), 3.87 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 166.1, 151.3, 148.3, 127.7, 121.1, 111.2, 102.6, 85.1,52.6; IR ($CHCl_3$) 3019, 1726, 1614 cm^{-1}. Anal. Calcd for $C_9H_7IO_4$: C, 35.32; H, 2.31. Found: C, 35.31; H, 2.40.

Preparation of Methyl 6-((3*S*)-3-{(5*S*,4*R*)-5-[(1*Z*)-2-Aza-2-(phenylmethoxy)vinyl]-2,2-dimethyl(1,3-dioxolan-4-yl)}-3-hydroxyprop-1-ynyl)-2*H*-benzo[*d*]1,3-dioxolene-5-carboxylate (29). To a stirring solution of terminal alkyne **27** (1.13 g, 3.91 mmol) as a 1:1.7 mixture of oxime isomers in 20 mL of THF were added Et_3N (1.27 mL, 0.920 g, 9.02 mmol), triphenylphosphine (86.6 mg, 0.331 mmol), and aryl iodide **28** (0.920 g 3.01 mmol). To this reaction mixture were added, in the absence of light (reaction flask covered with Al foil), CuI (74.3 mg, 0.391 mmol) and $Pd(OAc)_2$ (33.7 mg, 0.150 mmol). After 23 h the reaction was quenched with 50 mL of a saturated solution of NH_4Cl and then diluted with 250 mL of Et_2O. The layers were separated, and the organic layer was washed with a saturated solution of NH_4Cl (3 × 20 mL), dried over $MgSO_4$, then filtered and concentrated under reduced pressure. Purification was accomplished by flash chromatography using a 3.5 × 20 cm column, eluting with a gradient of 300 mL each of 20%, 30%, 40%, and 50% EtOAc/hexanes, collecting 20 mL fractions. The product-containing fractions (26−37) were collected and concentrated under reduced pressure to give alkyne **29** (1.34 g, 95% yield) as a 1:1.7 mixture of oxime isomers and as a yellow foam: R_f 0.18, 0.14 (30% EtOAc/hexanes) for the major and minor oxime isomers, respectively; (minor) $[\alpha]^{21}_D = -51.8$ (*c* 7.1, $CHCl_3$) (lit.[20] $[\alpha]^{21}_D = +65.5$ (*c* 4.6, $CHCl_3$) (minor oxime isomer); 500 MHz ^{1}H NMR, 125 MHz ^{13}C NMR, and IR were in excellent agreement with the results obtained previously.[20]

Preparation of Methyl 6-{(3a*S*,4*R*,7*R*,7a*R*)-7-Hydroxy-2,2-dimethyl-4-[(phenylmethoxy)amino]-6-phenylthio-2,3,4,7,3a,7a-hexahydro-1,3-dioxainden-5-yl}-2*H*-benzo[*d*]1,3-dioxolane-5-carboxylate (29.1). To a stirring solution of alkyne 29 (277 mg, 0.592 mmol) as a 1.7:1 mixture of oxime isomers in 8 mL of toluene was added thiophenol (85.3 uL, 81.2 mg, 0.829 mmol) via syringe. This reaction mixture at 21−27 °C (circulating water bath) was then subjected to photolysis conditions by utilizing a sun lamp (200 W, 120 V, GE Crystal Clear Light bulb) placed approximately 5 cm distance from the Pyrex reaction vessel. The reaction vessel was kept below 27 °C (circulating water bath) for 5 h before concentrating under reduced pressure, to give a yellow oil. Purification of this material was accomplished by flash column chromatography on a 2 × 16 cm column, eluting with a gradient of 100 mL each of 10%, 20%, 30%, and 40% EtOAc/hexanes, collecting 8 mL fractions. The product-containing fractions (20−30) were collected and concentrated to give the hydroxylamine 29.1 (309 mg, 90% yield) as a single diastereomer and a light yellow foam: $[\alpha]^{21}_D = +69.0$ (*c* 1.2, $CHCl_3$) (lit.[20] $[\alpha]^{25}_D = -61.0$ (*c* 14.3, $CHCl_3$)); R_f 0.35 (35% EtOAc/hexane); 500 MHz ^{1}H NMR, 125 MHz ^{13}C NMR, and IR were in excellent agreement with results obtained previously.[20]

Preparation of (2*S*,5a*S*,2a*R*,5b*R*)-2-Hydroxy-4,4-dimethyl-2,6,-2a,5a,5b-pentahydro-10*H*-1,3-dioxolano[4,5-*j*]1,3-dioxolano[4,5-*c*]-phenanthridin-7-one (29.2) and the Intermediate (5a*S*,2*R*,2a*R*,5b*R*)-2-Hydroxy-4,4-dimethyl-1-phenylthio-2,6,2a,5a,5b-pentahydro-10*H*-1,3-dioxolano[4,5-*j*]1,3-dioxolano[4,5-*c*]phenanthridin-7-one (29.2a). To a stirring solution of hydroxylamine **29.1** (231 mg, 0.40 mmol) in 8 mL of THF was added a freshly prepared solution of samarium diiodide (8.4 mL, 0.84 mmol, 0.10 M in THF), prepared by heating samarium metal (661 mg, 4.4 mmol) and iodine (800 mg, 3.2 mmol) in 31.5 mL of THF at 65 °C for 4 h. After 1 h an additional amount of samarium diiodide (8.4 mL, 0.84 mmol, 0.10 M in THF) was added to this yellow solution. After a total of 42 h at rt this blue solution was diluted with 75 mL of THF and quenched with 20 mL of a 1% aqueous HCl solution. This solution was diluted further with 75 mL of EtOAc, and the layers were separated. The organic layer was washed with a saturated solution of $Na_2S_2O_3$ (3 × 30 mL) and finally brine (30 mL). The organic layer was dried over $MgSO_4$, filtered through a pad of Celite (1 × 6 cm), and concentrated under reduced pressure. Purification was accomplished by RPLC, using a 2 mm plate, eluting with a gradient of 1%, 2%, 3%, 4%, and 5% MeOH/$CHCl_3$, collecting 8 mL fractions. The fractions containing vinyl sulfide **29.2a** and the desired lactam **29.2** (26−35) were collected in separate flasks and concentrated under reduced pressure to give vinyl sulfide **29.2a** (26 mg, 13% yield) and the desired lactam **29.2** (114 mg, 86% yield), as a viscous yellow oil and a colorless crystalline solid, respectively: lactam **29.2** $[\alpha]^{22}_D = -34.3$ (*c* 0.76, MeOH) (lit.[20] $[\alpha]^{25}_D = +34.3$ (*c* 0.72, MeOH); R_f 0.35 (35% EtOAc/hexane); 500 MHz ^{1}H NMR, 125 MHz ^{13}C NMR, and IR were in excellent agreement with results obtained previously.[20]

Preparation of (2*S*,4*S*,3*R*,4a*R*)-2,3,4-Trihydroxy-2,3,4,5,4a-pentahydro-9*H*-1,3-dioxoleno[4,5-*j*]phenanthridin-6-one [(+)-Lycoricidine] (4). To lactam **29.2** (20.3 g, 0.0613 mmol) in an ice-cooled bath was added cold (−20 °C) TFA (1.2 mL) down the side of the flask. After 45 min, the reaction was diluted with cold dioxanes, and the TFA was removed under high vacuum (0.05 Torr) while the flask was cooled to 0 °C. After 1 h, the reaction was warmed to rt and the

(34) The minor oxime isomer was characterized in this instance because a similar compound prepared by us (TBS ether version, *ent*-lycoricidine case) was isolated as the major oxime isomer and was fully characterized.

dioxane was removed (12 h) to give a light yellow solid. Purification of this material was accomplished by flash column chromatography on a 1 × 10 cm column, eluting with a gradient of 20 mL each of 10%, 20%, and 30% (MeOH/CHCl), collecting 2 mL fractions. The product-containing fractions (13−23) were collected and concentrated to give lycoricidine (16.2 mg, 91% yield) as a colorless crystalline solid: 500 MHz ^{1}H NMR and 125 MHz ^{13}C NMR were in excellent agreement with results obtained previously.[20]

Preparation of [6-Iodo-4-(1,1,2,2-tetramethyl-1-silapropoxy)(2H-benzo[*d*]1,3-dioxolen-5-yl)]-*N*,*N*-dimethylcarboxamide (31). To a stirring solution of TMEDA (3.09 mL, 2.38 g, 20.5 mmol) in 137 mL of Et_2O at −78 °C (acetone/CO_2 bath) was added a solution of ^{n}BuLi (12.9 mL, 5.26 mmol, 2.45 M in hexanes) over 2 min. After 15 min, the mixture was cooled to −104 °C (cyclohexene/N_2 bath) and a solution of amide **30**[23f,25] (5.09 g, 15.7 mmol, in 32 mL of Et_2O) precooled to −78 °C was added via cannula slowly down the side of the flask over 30 min (wash with 5 mL of Et_2O). The resulting solution was stirred at −104 °C for 1 h, and then a solution of iodine (8.00 g, 31.5 mmol, in 62 mL of Et_2O) precooled to −78 °C was added over 15 min down the side of the flask. After complete addition, the −104 °C bath was replaced with a −78 °C bath and the reaction was allowed to warm to rt overnight (10 h), then quenched by addition of 100 mL of a saturated aqueous solution of $Na_2S_2O_3$ and diluted with 200 mL of EtOAc. The layers were separated, and the organic layer was washed with a saturated solution of $Na_2S_2O_3$ (2 × 100 mL) and 100 mL of brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a yellow solid. Purification of this material was accomplished by gravity chromatography on a 4.5 × 30 cm column, eluting with a gradient of 10%, 20%, and 30% EtOAc/hexanes, collecting 20 mL fractions. The product-containing fractions were collected and concentrated to give **31** (5.10 g, 72% yield) as a colorless crystalline solid: mp 108−109 °C; R_f 0.37 (35% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 6.86 (s, 1H), 5.89 (d, J = 9.9 Hz, 2H), 3.02 (s, 3H), 2.80 (s, 3H), 0.88 (s, 9H), 0.17 (s, 3H), 0.14 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 168.2, 149.6, 137.5, 135.9, 130.4, 112.5, 101.6, 81.7, 37.8, 34.7, 25.5, 18.2, −4.2, −4.5; IR ($CHCl_3$) 1639 cm^{-1}. Anal. Calcd for $C_{16}H_{24}INO_4Si$: C, 42.77; H, 5.38; N,3.12. Found: C, 42.95; H, 5.47; N, 3.00.

Preparation of (4-Hydroxy-6-iodo(2H-benzo[*d*]1,3-dioxolen-5-yl))-*N*,*N*-dimethylcarboxamide (32). To a stirring solution of silyl ether **31** (3.54 g, 7.88 mmol) in 79 mL of THF was added a solution of TBAF (15.8 mL, 15.8 mmol, 1M in THF) dropwise over 5 min. After 4 h the reaction was quenched with 100 mL of a saturated solution of NH_4Cl, then diluted with 400 mL of EtOAc, and the layers were separated. The organic layer was washed with a saturated solution of NH_4Cl (2 × 100 mL) and brine (100 mL), then dried over $MgSO_4$ and concentrated under reduced pressure. Purification was accomplished by flash chromatography on a 2.5 × 24 cm column, eluting with a gradient of 200 mL each of 50%, 60%, 70%, and 80% acetone/pentane, collecting 25 mL fractions. The product-containing fractions (11−30) were collected and concentrated to give the phenol **32** (2.38 g, 90% yield) as a colorless crystalline solid: mp 218−220 °C; R_f 0.21 (EtOAc); 500 MHz ^{1}H NMR ($CDCl_3$) δ 9.51 (s, 1H), 6.74 (s, 1H), 5.95 (bs, 1H), 5.89 (bs, 1H), 3.14 (bs, 3H), 2.91 (bs, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 170.7, 149.7, 138.3, 137.3, 126.9, 111.1, 102.5, 80.9, 38.6, 35.3; IR ($CHCl_3$) 3096, 1620 cm^{-1}. Anal. Calcd for $C_{10}H_{10}INO_4$: C, 35.84; H, 3.01; N, 4.18. Found: C, 35.80; H, 3.05; N, 4.12.

Preparation of 4-Hydroxy-6-iodo-2*H*-benzo[*d*]1,3-dioxolene-5-carbaldehyde (32.1). A suspension of amide **32** (998 mg, 2.98 mmol) in 60 mL of Et_2O was stirred for 1 h prior to cooling to 0 °C (ice/water bath) (solubility reasons). To the stirring slurry of amide **32** at 0 °C was added a premade solution of $LiH_2Al(OEt)_2$[35] (6.0 mL, 2.98 mmol, 0.5 M in Et_2O) dropwise slowly over 1.5 h via syringe pump. After complete addition the mixture was stirred for 50 min before an additional amount of $LiH_2Al(OEt)_2$ (6.0 mL, 2.98 mmol) was added over a 3 h period. After an additional 4.5 h the mixture was quenched cold by addition of 12 mL of 1 M H_2SO_4. The reaction mixture was then warmed to rt and diluted with 300 mL of Et_2O. The layers were separated, and the organic layer was washed with a saturated solution of NH_4Cl (2 × 20 mL) and 20 mL of brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of this material was accomplished by flash column chromatography on a 1.5 × 20 cm column, eluting with a gradient of 100 mL each of 20% and 30% EtOAc/hexanes, collecting 8 mL fractions. The product-containing fractions (7−18) were collected and concentrated to give **32.1** (440 mg, 50% yield)[36a] as a yellow crystalline solid: R_f 0.59 (35% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 12.08, (s, 1H), 9.90 (s, 1H), 7.10(s, 1H), 6.12 (s, 2H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 201.5, 155.2, 147.7, 135.6, 116.0, 114.0, 103.5, 94.7.

Preparation of 6-Iodo-4-(1,1,2,2-tetramethyl-1-silapropoxy)-2*H*-benzo[*d*]1,3-dioxolene-5-carbaldehyde (33). To a stirring solution of the phenol **32.1** (156 mg, 0.53 mmol) in 1 mL of CH_2Cl_2 was added imidazole (73 mg, 1.1 mmol) followed by TBS−Cl (120 mg, 0.80 mmol). After 4 h the reaction was diluted with 10 mL of CH_2Cl_2 and quenched with a saturated solution of $NaHCO_3$ (1 mL). The layers were separated, and the organic layer was washed with a saturated solution of $NaHCO_3$ (2 mL) and 1 mL of brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of this material was accomplished by flash column chromatography, using a 1 × 8 cm column, eluting with 50 mL of 5% EtOAc/hexanes, collecting 4 mL fractions. The product-containing fractions (8−12) were collected and concentrated to give the TBS ether **33** (187 mg, 87% yield) as a colorless oil: R_f 0.54 (15% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 10.0 (s, 1H), 7.12 (s, 1H), 5.99 (s, 2H), 0.95 (s, 9H), 0.19 (s, 6H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 190.4, 153.4, 142.4, 138.7, 122.9, 115.9, 102.4, 87.6, 25.8, 18.7, −4.2.

Preparation of Methyl 4-Hydroxy-6-iodo-2*H*-benzo[*d*]1,3-dioxolene-5-carboxylate (35). To a stirring solution of benzamide **31** (10.8 g, 24.0 mmol) in 120 mL of CH_3CN was added Na_2HPO_4 (5.26 g, 36.0 mmol) followed by trimethyloxonium tetrafluoroborate (10.7 g, 72.1 mmol). After 5 h TLC analysis indicated complete consumption of the starting material. The reaction was quenched slowly with 150 mL of a saturated solution of $NaHCO_3$ and further neutralized with solid $NaHCO_3$ (10 g). The resulting mixture was vigorously stirred for 7 h then diluted with 200 mL of EtOAc and 50 mL of water. The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 100 mL). The combined organic layers were dried over $MgSO_4$, filtered through a pad of Celite (1 × 6 cm), and concentrated under reduced pressure. Purification of this material was accomplished by first shaking the yellow solid with pentane (2 × 100 mL), and the resulting solid was further purified by gravity column chromatography on a 4.5 × 40 cm column, eluting with a gradient of 500 mL each of 50%, 60%, and 70% acetone/hexanes, collecting 25 mL fractions. The product-containing fractions (26−70) were collected and concentrated to give the methyl ester **35** (7.6 g, 91% yield) as a colorless crystalline solid: mp 154−155 °C; R_f 0.58 (50% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 11.0 (s, 1H), 7.20 (s, 1H), 6.08 (s, 2H), 3.97 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 168.9, 152.9, 147.0, 135.8, 115.7, 112.7, 103.1, 84.9, 52.1; IR ($CHCl_3$) 3152 (br), 3064, 1666 cm^{-1}. Anal. Calcd for $C_9H_7IO_5$: C, 33.56; H, 2.19. Found: C, 33.80; H, 2.27.

Preparation of Methyl 6-Iodo-4-(phenylmethoxy)-2H-benzo-[*d*]1,3-dioxolene-5-carboxylate. To a stirring solution of phenol **35** (200 mg, 0.620 mmol) in 6.2 mL of DMF was added K_2CO_3 (146 mg, 1.06 mmol) followed by benzyl bromide (221 μL, 319 mg, 1.86 mmol). After 5 h the reaction was quenched with 5 mL of a saturated solution of $Na_2S_2O_3$, then diluted with 50 mL of EtOAc. The layers were separated, and the organic layer was washed with a saturated solution of $Na_2S_2O_3$ (3 × 10 mL) and 10 mL of brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification was accomplished by RPLC on a 2 mm plate eluting with a gradient of 100 mL each of 5% and 10% EtOAc/hexanes, collecting 8 mL fractions. The product containing fractions (23−37) were collected and concentrated to give the benzyl ether (237 mg, 92% yield) as a colorless crystalline solid: mp 84−85 °C; R_f 0.46 (35% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.37−7.30 (m, 5H), 6.95 (s, 1H), 5.95 (s, 2H), 5.23 (s, 2H), 3.86 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 167.5, 150.9, 140.1, 137.5, 136.6, 128.5, 128.4, 128.0, 127.9, 113.5, 102.1, 81.2, 74.4, 52.9; IR ($CHCl_3$) 3066, 1730 cm^{-1}. Anal. Calcd for $C_{16}H_{13}IO_5$: C, 46.62; H, 3.18. Found: C, 46.71; H, 3.22.

(35) Brown, H. C.; Tsukamoto, A. *J. Am. Chem. Soc.* **1964**, *88*, 1089.

(36) (a) Yields for this reaction range from 20 to 50%. (b) Yields for this reaction ranged from 14 to 56%.

Preparation of Methyl 6-Iodo-4-methoxy-2*H*-benzo[*d*]1,3-dioxolene-5-carboxylate (36). To a stirring solution of phenol **35** (2.11 g, 6.55 mmol) in 110 mL of acetone was added K_2CO_3 (1.81 g, 13.1 mmol) followed by methyl iodide (4.07 mL, 9.30 g, 65.5 mmol). The reaction mixture was then heated at 50 °C for 4 h, at which time TLC analysis indicated complete consumption of starting material. The reaction was cooled to rt, quenched with 40 mL of H_2O, and diluted with 300 mL of Et_2O. The layers were separated, and the organic layer was washed with 40 mL of brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of this material was accomplished by RPLC using a 4 mm plate, eluting with a gradient of 100 mL each of 20%, 30%, and 40% acetone/hexanes, collecting 8 mL fractions. The product-containing fractions (15−29) were collected and concentrated to give **36** (1.80 g, 82% yield) as a colorless crystalline solid: mp 55−57 °C; R_f 0.60 (50% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 6.93 (s, 1H), 5.96 (s, 2H), 3.97 (s, 3H), 3.90 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 167.6, 151.0, 141.3, 137.1, 127.4, 113.2, 102.0, 81.2, 60.5, 52.9; IR ($CHCl_3$) 1728 cm^{-1}. Anal. Calcd for $C_{10}H_9IO_5$: C, 35.74; H, 2.70. Found: C, 35.99; H, 2.75.

Preparation of Methyl 6-Iodo-4-[(4-methylphenyl)sulfonyloxy]-2*H*-benzo[*d*]1,3-dioxolene-5-carboxylate (37). To a stirring solution of phenol **35** (2.0 g, 6.2 mmol) in 12.4 mL of pyridine was added *p*-toluenesulfonyl chloride (1.3 g, 6.8 mmol). After 2 h this orange reaction mixture was slowly quenched with a saturated solution of $NaHCO_3$ (50 mL) and then diluted with 300 mL of EtOAc. The layers were separated, and the organic layer was washed with a saturated solution of $CuSO_4$ (3 × 100 mL) and 100 mL of brine. The organic layer was then dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of this material was accomplished by flash chromatography on a 2.5 × 20 cm column, eluting with a gradient of 100 mL each of 5%, 10%, 15%, 20%, 30%, 40%, and 50% acetone/hexanes, collecting 8 mL fractions. The product-containing fractions (46−66) were collected and concentrated to give **37** (2.5 g, 86% yield) as a colorless crystalline solid: mp 112−114 °C; R_f 0.29 (35% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.81 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 7.17 (s, 1H), 5.94 (s, 2H), 3.71, (s, 3H), 2.45 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 165.5, 151.2, 146.0, 141.5, 132.9, 129.9, 129.8, 128.7, 128.6, 118.0, 103.4, 82.1, 52.9, 21.9; IR ($CHCl_3$) 1731, 1621 cm^{-1}. Anal. Calcd for $C_{16}H_{13}IO_7S$: C, 40.35; H, 2.75; S, 6.73. Found: C, 40.61; H, 2.87; S, 6.67.

Preparation of Methyl 6-((3*S*)-3-{(5*S*,4*R*)-5-[(1*Z*)-2-Aza-2-(phenylmethoxy)vinyl]-2,2-dimethyl(1,3-dioxolan-4-yl)}-3-hydroxyprop-1-ynyl)-4-methoxy-2*H*-benzo[*d*]1,3-dioxolene-5-carboxylate (38). To a stirring solution of alkyne **27** (1.30 g, 4.49 mmol) in 20 mL of THF were added NEt_3 (1.26 mL, 0.917 g, 8.99 mmol), iodide **36** (1.01 g, 2.99 mmol), PPh_3 (86.0 mg, 0.328 mmol), and in the absence of light (reaction vessel covered with Al foil) CuI (74.0 mg, 0.389 mmol) and $Pd(OAc)_2$ (36.3 g, 0.150 mmol). After 84 h the reaction was quenched with 10 mL of a saturated solution of NH_4Cl and diluted with 200 mL of Et_2O. The layers were separated, and the organic layers was washed with a saturated solution of NH_4Cl (3 × 10 mL) and 10 mL of brine, then dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of this material was accomplished by RPLC using a 4 mm plate, eluting with a gradient of 200 mL each of 50%, 60%, and 70% EtOAc/hexanes, collecting 8 mL fractions. The product-containing fractions (21−38) were collected and concentrated to give **38** (1.13 g, 75% yield) as a yellow foam and a mixture of oxime isomers (1:2.5): R_f 0.25, 0.27 (50% EtOAc/hexanes) for the major and minor oxime isomers, respectively; (major oxime isomer) $[\alpha]^{20}_D$ = −22.9 (*c* 0.51, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.58 (d, J = 7.7 Hz, 1H), 7.32−7.26 (m, 5H), 6.62 (s, 1H), 5.98 (s, 2H), 5.08 (s, 2H), 4.81 (dd, J = 7.4, 7.1 Hz, 1H), 4.50 (dd, J = 6.5, 5.5 Hz, 1H), 4.37 (dd, J = 6.9, 5.2 Hz, 1H), 3.98 (s, 3H), 3.89 (s, 3H), 2.70 (bd, J = 6.9 Hz, 1H), 1.54 (s, 3H), 1.40 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 166.7, 150.2, 147.6, 140.9, 137.8, 128.6, 128.3, 128.1, 124.6, 114.8, 110.6, 107.1, 102.1, 88.8, 83.7, 80.8, 76.4, 75.0, 61.7, 60.5, 52.7, 27.4, 25.2; IR ($CHCl_3$) 3323 (b), 1732, 1608 cm^{-1}. Anal. Calcd for $C_{26}H_{27}NO_9$: C, 62.77; H, 5.47; N, 2.82. Found: C, 62.73; H, 5.65; N, 2.71.

Preparation of Methyl 6-((3*S*)-3-{(5*S*,4*R*)-5-[(1*Z*)-2-Aza-2-(phenylmethoxy)vinyl]-2,2-dimethyl(1,3-dioxolan-4-yl)}-3-hydroxyprop-1-ynyl)-4-[(4-methylphenyl)sulfonyloxy]-2*H*-benzo[*d*]1,3-dioxolene-5-carboxylate (39). To a stirring solution of alkyne **27** (1.39 g, 4.80 mmol) in 21.4 mL of THF were added NEt_3 (1.35 mL, 0.981 g, 9.61 mmol), iodide **37** (1.53 g, 3.20 mmol), PPh_3 (0.094 g, 0.353 mmol), and in the absence of light (reaction vessel covered with Al foil) CuI (0.0792 g, 0.417 mmol) and $Pd(OAc)_2$ (0.0388 g, 0.160 mmol). After 48 h the reaction was quenched with 50 mL of a saturated solution of NH_4Cl, diluted with 300 mL of Et_2O, and the layers were separated. The organic layers was washed with a saturated solution of NH_4Cl (3 × 40 mL), 40 mL of brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of this material was accomplished by flash column chromatography using a 3 × 24 cm column, eluting with a gradient of 200 mL each of 30%, 40%, 50%, 60%, and 70% EtOAc/hexanes, collecting 8 mL fractions. The product-containing fractions (52−83) were collected and concentrated to give **39** (2.14 g, 89% yield) as a pale yellow foam and a mixture of oxime isomers (1:1.6): R_f 0.25, 0.29 (50% EtOAc/hexanes) for the major and minor oxime isomers, respectively; (major oxime isomer) $[\alpha]^{20}_D$ = +105.5 (*c* 1.2, $CHCl_3$) (major); 500 MHz ^{1}H NMR ($CDCl_3$) (major) δ 7.77 (d, J = 8.3 Hz, 2H), 7.33−7.28 (m, 7H), 7.05 (d, J = 4.17 Hz, 1H), 6.80 (s, 1H), 5.87 (S, 2H), 5.25 (dd, J = 7.42, 4.4 Hz, 1H), 5.09 (ABq, $\Delta\nu$ = 7.1 Hz, J = 12.4 Hz, 2H), 4.50 (dd, 7.4, 2.2 Hz, 1H), 4.34 (bd, J = 7.4 Hz, 1H). 3.67 (s, 3H), 2.63 (bd, J = 9.3 Hz, 1H), 2.42 (s, 3H), 1.53 (s, 3H), 1.35 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 164.4, 150.5, 150.4, 145.8, 141.4, 137.1, 132.6, 129.8, 129.6, 128.7, 128.6, 128.3, 128.2, 125.8, 116.5, 112.2, 109.7, 103.2, 91.1, 81.9, 80.1, 76.7, 72.2, 61.7, 52.5, 26.6, 24.3, 21.8; IR ($CHCl_3$) 3629, 1730, 1601 cm^{-1}. Anal. Calcd for $C_{32}H_{31}NO_{11}S$: C, 60.27; H, 4.90; N, 2.20; S, 5.03. Found: C, 60.33; H, 4.96; N, 2.25; S, 4.99.

Preparation of Methyl 6-{(3a*S*,4*R*,7*R*,7a*R*)-7-Hydroxy-2,2-dimethyl-4-[(phenylmethoxy)amino]-6-phenylthio(2,3,4,7,3a,7a-hexahydro-1,3-dioxainden-5-yl)}-4-methoxy-2*H*-benzo[*d*]1,3-dioxolene-5-carboxylate (40). To a stirring solution of alkyne **38** (1.00 g, 2.01 mmol) in 40 mL of toluene (deoxygenated with N_2 for 15 min) was added thiophenol (0.310 mL, 0.332 g, 3.01 mmol) via syringe. The reaction mixture was then subjected to photolysis conditions utilizing a sun lamp (200 W, 120 V, GE Crystal Clear Light bulb), placed approximately 5 cm distance from the Pyrex reaction vessel. The reaction was maintained at 25−30 °C (circulating water bath) for 84 h before the reaction mixture was concentrated under reduced pressure to give a yellow oil. Purification of this material was accomplished by RPLC using a 4 mm plate, eluding with 40% Et_2O/pentane, collecting 8 mL fractions. The product containing fractions were collected and concentrated to give **40** (0.876 g, 73% yield) as a pale yellow foam: R_f 0.52 (50% EtOAc/hexanes); $[\alpha]^{20}_D$ = +12.1 (*c* 1.2, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.37−7.30 (m, 7H), 7.24−7.18 (m, 3H), 6.90 (bs, 1H), 6.45 (s, 1H), 5.98 (d, J = 1.4 Hz, 1H), 5.93 (d, J = 1.4 Hz, 1H), 5.09 (bs, 1H), 4.73 (ABq, $\Delta\nu$ = 7.5 Hz, J = 11.8 Hz, 2H), 4.65 (dd, J = 6.9, 1.6 Hz, 1H), 4.39 (dd, J = 6.9, 1.9 Hz, 1H), 3.98 (s, 3H), 3.97 (s, 1H), 3.90 (s, 1H), 3.70 (s, 3H), 1.48 (s, 3H), 1.28 (S, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 167.6, 151.2, 141.2, 141.2, 137.0, 136.5, 134.9, 132.7, 132.5, 132.3, 128.9, 128.7, 128.6, 128.4, 127.6, 120.4, 108.2, 103.3, 101.9, 78.9, 77.1, 74.0, 68.2, 65.4, 60.4, 52.6, 26.3, 23.9; IR ($CHCl_3$) 3532(b), 1708 cm^{-1}. Anal. Calcd for $C_{32}H_{33}NO_9S$: C, 63.25; H, 5.47; N, 2.30; S, 5.28. Found: C, 63.41; H, 5.55; N, 2.31; S, 5.28.

Preparation of Methyl 6-{(3a*S*,4*R*,7*R*,7a*R*)-7-Hydroxy-2,2-dimethyl-4-[(phenylmethoxy)amino]-6-phenylthio(2,3,4,7,3a,7a-hexahydro-1,3-dioxainden-5-yl)}-4-[(4-methylphenyl)sulfonyloxy]-2*H*-benzo[*d*]1,3-dioxolene-5-carboxylate (41). To a stirring solution of alkyne **39** (2.00 g, 3.14 mmol) as a 1:1.6 mixture of oxime isomers in 63 mL of toluene, (deoxygenated with N_2 for 15 min) was added thiophenol (0.484 mL, 0.520 g, 4.70 mmol) via syringe. The reaction mixture was then subjected to photolysis conditions utilizing a sun lamp (200 W, 120 V, GE Crystal Clear Light bulb), placed approximately 5 cm distance from the Pyrex reaction vessel. The reaction was maintained at 25−30 °C (circulating water bath) for 43 h before the reaction mixture was concentrated under reduce pressure to give a yellow oil. Purification of this material was accomplished by flash column chromatography using a 3 × 24 cm column, eluding with a gradient of 200 mL each of

30%, 40%, and 50% EtOAc/hexanes, collecting 8 mL fractions. The product-containing fractions (33−53) were collected and concentrated to give **41** (2.06 g, 88% yield) as a colorless foam and a single isomer: R_f 0.45 (50% EtOAc/hexanes); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.80 (d, J = 8.2 Hz, 2H), 7.39−7.19 (m, 12 H), 7.04 (d, J = 1.9 Hz,1H), 6.65 (s, 1H), 5.91 (d, J = 1.4 Hz, 1H), 5.80 (d, J = 1.4 Hz,1H), 5.04 (bd, J = 11.0 Hz, 1H), 4.75 (ABq, $\Delta\nu$ = 19.4 Hz, J = 11.5 Hz, 2H), 4.62 (dd, J = 6.9, 1.9 Hz, 1H), 4.35 (dd, J = 6.9, 2.2 Hz, 1H), 3.97−3.95 (m, 2H), 3.65 (s, 3H), 2.45 (s, 3H), 1.46 (s, 3H), 1.28 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 165.7, 151.5, 145.8, 141.1, 140.4, 137.0, 136.5, 132.9, 132.6, 132.5, 132.1, 129.8, 129.6, 129.2, 128.9, 128.8, 128.7, 128.5, 127.8, 122.2, 108.3, 107.9, 103.1, 79.1, 77.4, 74.3, 74.1, 68.5, 65.3, 52.9, 26.3, 24.0, 21.9; IR ($CHCl_3$) 3650 (b), 3173 (b), 1715 cm^{-1}. Anal. Calcd for $C_{38}H_{37}NO_{11}S_2$: C, 61.03; H, 4.99; N, 1.87; S, 8.58. Found: C, 61.17; H, 5.07; N, 1.85; S, 8.54.

Preparation of (2*S*,5a*S*,2a*R*,5b*R*)-2,8-Dihydroxy-4,4-dimethyl-2,6,2a,5a,5b-pentahydro-10*H*-1,3-dioxolano[4,5-*c*]1,3-dioxoleno[4,5-*j*]phenanthridin-7-one (42). To a stirring solution of the hydroxylamine **41** (70 mg, 0.094 mmol) in THF (1.9 mL) was added a premade solution of SmI_2 (1.9 mL, 0.19 mmol, 0.1 M in THF). After the indicated time an additional amount of SmI_2 (1.9 mL, 0.19 mmol) was added: 36 min, 27 h, and 42 h (8 equiv of SmI_2 total). After a total of 6 days the reaction was diluted with 15 mL of THF and quenched with 20 mL of a 1% aqueous solution of HCl. The reaction was further diluted with 30 mL of EtOAc, and the layers were separated. The aqueous layer was back extracted with EtOAc (3 × 10 mL), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of this material was accomplished by flash chromatography on a 1 × 8 cm column, eluting with a gradient of 20 mL each of 40%, 50%, 60%, and 70% EtOAc/hexanes, collecting 4 mL fractions. The product-containing fractions (18−25) were collected and concentrated to give the acetonide **42** (15 mg, 46% yield)[36b] as a tan crystalline solid: mp 270−271 °C (dec) [lit.[37] 275−276 °C (dec), lit.[5a] 274 °C]; $[\alpha]^{20}_D$ = −24.0 (*c* 0.35, THF) (lit.[37] $[\alpha]^{20}_D$ = −33 (*c* 0.35, THF); R_f 0.16 (35% EtOAc/hexanes); 500 MHz ^{1}H NMR (DMSO-d_6) δ 13.75 (s, 1H), 8.82 (s, 1H), 7.01 (s, 1H), 6.48 (bs, 1H), 6.06 (d, 3.3 Hz, 2H), 5.82 (d, J = 5.5 Hz, 1H), 4.16−4.09 (m, 2H), 4.07 (dd, J = 7.7, 7.7, 1H), 3.97 (dd, J = 7.7, 6.3 Hz, 1H), 1.46 (s, 3H), 1.32 (s, 3H); 125 MHz ^{13}C NMR (DMSO-d_6) δ 167.6, 152.6, 145.2, 133.3, 128.9, 128.3, 125.9, 109.8, 104.3, 102.1, 94.3, 79.0, 78.5, 71.0, 54.6; IR ($CHCl_3$) 3640, 1675 cm^{-1}; HRMS *m*/*z* (EI) calcd for $C_{17}H_{17}NO_6$ 347.1005, obsd 347.0991.

Preparation of (2*S*,5a*S*,2a*R*,5b*R*)-2,8-Dihydroxy-4,4-dimethyl-2,6,2a,5a,5b-pentahydro-10*H*-1,3-dioxolano[4,5-*c*]1,3-dioxoleno[4,5-*j*]phenanthridin-7-one (42) and (5a*S*,2*R*,2a*R*,5b*R*)-2,8-Dihydroxy-4,4-dimethyl-1-phenylthio-2,6,2a,5a,5b-pentahydro-10*H*-1,3-dioxolano[4,5-*c*]1,3-dioxoleno[4,5-*j*]phenanthridin-7-one (42s). To a stirring solution of **38** (76 mg, 0.12 mmol) in 2.5 mL of THF was added a solution of SmI_2 (2.8 mL, 0.28 mmol, 0.1 M in THF). After 2 h an additional portion of SmI_2 (2.8 mL, 0.28 mmol) was added. The reaction was allowed to stir for 42 h, then quenched with a 1% aqueous HCl solution (20 mL) and diluted with 15 mL of THF and 30 mL of EtOAc. The layers were separated, and the aqueous layer was back-extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of this material was accomplished by flash column chromatography on a 1 × 8 cm column, eluting with a gradient of 25 mL each of 40%, 50%, 60%, and 70% EtOAc/hexanes, collecting 4 mL fractions. The product-containing fractions [12−15 (vinyl sulfide **42s**) and 16−25 (narciclasine-3,4-acetonide **42**)] were collected and concentrated to give vinyl sulfide **42s** (7.5 mg, 13% yield) as a crystalline pale yellow solid and narciclasine-3,4-acetonide **42** (16.5 mg, 38% yield) as a tan crystalline solid: R_f 0.14, 0.16 (50% EtOAc/hexanes) for **42s** and **42**, respectively; $[\alpha]^{20}_D$ = +295 (*c* 0.54, THF) (vinyl sulfide **42s**); 500 MHz ^{1}H NMR ($CDCl_3$) (vinyl sulfide **42s**) δ 13.14 (s, 1H), 8.23 (s, 1H), 7.31−7.20 (m, 5H), 6.95 (bs, 1H), 6.04 (s, 2H), 4.37 (d, J = 5.2, 5.2 Hz, 1H), 4.32 (d, J = 7.9, Hz, 1H), 4.13 (dd, J = 7.9, 7.9 Hz, 1H), 4.07 (dd, J = 7.9, 6.1 Hz, 1H), 3.16 (d, J = 4.3 Hz, 1H), 1.55 (s, 3H), 1.39 (3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 167.6, 152.3, 146.6, 135.8, 134.4, 134.1, 129.9, 129.4, 127.9, 127.6, 127.2, 112.3, 106.7, 102.8, 100.7, 78.6, 77.6, 74.0, 57.2, 27.3, 25.2; IR ($CHCl_3$) 1671, 1548 cm^{-1}; HRMS *m*/*z* (EI) calcd for $C_{23}H_{21}NO_7S$ 455.1039, found 455.1046.

Preparation of Methyl 6-{(3a*S*,4*R*,7*R*,7a*R*)-7-Hydroxy-2,2-dimethyl-4-[(phenylmethoxy)amino]-6-phenylthio(2,3,4,7,3a,7a-hexahydro-1,3-dioxainden-5-yl)}-4-hydroxy-2*H*-benzo[*d*]1,3-dioxolene-5-carboxylate (43). To a stirring solution of **41** (303 mg, 0.405 mmol) in 8.1 mL of THF at 0 °C (ice/water bath) was added H_2O (145 uL, 145 mg, 8.1 mmol) followed by a solution of SmI_2 (10 mL, 1.0 mmol, 0.1 M in THF). After 10 min the reaction was quenched with 10 mL of a 2% aqueous HCl solution and diluted with 75 mL of EtOAc. The layers were separated, and the organic layer was washed with 25 mL of a saturated solution of $Na_2S_2O_3$, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of this material was accomplished by RPLC using a 4 mm plate eluting with a gradient of 100 mL each of 40, 50, and 60% EtOAc/hexanes, collecting 8 mL fractions. The product-containing fractions (15−21) were collected and concentrated to give the phenol **43** (212 mg, 94% yield) as a colorless foam: R_f 0.61 (50% EtOAc/hexanes); $[\alpha]^{20}_D$ = +108.5 (*c* 1.2, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 10.6 (s, 1H) (exchangeable with D_2O), 7.38−7.20 (m, 10H), 6.42 (s, 1H), 6.04 (ABq, $\Delta\nu$ = 7.6 Hz, J = 4.4 Hz, 2H), 5.93 (bs, 1H) (exchangeable with D_2O), 4.83−4.80 (m, 3H), 4.64 (d, J = 12.4 Hz, 1H), 4.55 (dd, J = 6.9, 2.2 Hz, 1H), 4.04 (bs, 1H), 3.98 (bs, 1H), 3.48 (s, 3H), 1.52 (s, 3H), 1.36 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 169.7, 152.8, 145.3, 139.5, 137.5, 136.9, 134.4, 133.0, 132.8, 131.7, 129.0, 128.9, 128.9, 128.6, 127.9, 109.5, 108.5, 102.8, 102.4, 78.4, 77.1, 73.8, 67.6, 65.9, 52.2, 26.3, 24.1; IR ($CHCl_3$) 3371, 1676 cm^{-1}. Anal. Calcd for $C_{31}H_{31}NO_9S$: C, 62.72; H, 5.26; N, 2.36; S, 5.40. Found: C, 62.82; H, 5.33; N, 2.30; S, 5.34.

Preparation of Methyl 6-{(3a*S*,4*R*,7*R*,7a*R*)-7-Hydroxy-2,2-dimethyl-4-[(phenylmethoxy)amino]-6-phenylthio(2,3,4,7,3a,7a-hexahydro-1,3-dioxainden-5-yl)}-4-methoxy-2H-benzo[*d*]1,3-dioxolene-5-carboxylate (40). To a stirring solution of phenol **43** (352 mg, 0.593 mmol) in 6 mL of DMF was added K_2CO_3 (164 mg, 1.18 mmol) followed by MeI (369 μL, 842 mg, 5.93 mmol) via syringe. After 22 h the reaction was quenched with 25 mL of H_2O and diluted with 100 mL of EtOAc. The layers were separated, and the organic layer was washed with 25 mL of a saturated solution of $Na_2S_2O_3$, saturated aqueous $CuSO_4$ solution (2 × 25 mL), H_2O (25 mL), and 25 mL of brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of this material was accomplished by RPLC using a 4 mm plate eluting with a gradient of 100 mL each of 20%, 30%, and 40% EtOAc/hexanes, collecting 8 mL fractions. The product-containing fractions (18−27) were collected and concentrated to give **40** (347 mg, 96% yield) as a colorless foam: R_f 0.39 (35% acetone/hexanes); $[\alpha]^{20}_D$ = +12.1 (*c* 1.2, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.37−7.30 (M, 7H), 7.24−7.18 (m, 3H), 6.90 (bs, 1H), 6.45 (s, 1H), 5.98 (d, J = 1.4 Hz, 1H), 5.93 (d, J = 1.4 Hz, 1H), 5.09 (bs, 1H), 4.73 (ABq, $\Delta\nu$ = 7.5 Hz, J = 11.8 Hz, 2H), 4.65 (dd, J = 6.9, 1.6 Hz, 1H) 4.39 (dd, J = 6.9, 1.9 Hz, 1H), 3.98 (s, 3H), 3.97 (s, 3H), 3.90 (s, 1H), 3.70 (s, 3H), 1.48 (s, 3H), 1.28 (s, 3H),; 125 MHz ^{13}C NMR ($CDCl_3$) δ 167.6, 151.2, 141.2, 141.2, 137.0, 136.5, 134.9, 132.7, 132.5, 132.3, 128.9, 128.7, 128,6, 128.4, 127.6, 120.4, 108.2, 103.3, 101.9, 78.9, 77.1, 74.0, 68.2, 65.4, 60.4, 52.6, 26.3, 23.9; IR ($CHCl_3$) 3532 (b), 3221, 1708 cm^{-1}. Anal. Calcd for $C_{32}H_{33}NO_9S$: C, 63.25; H, 5.47; N, 2.30; S, 5.28. Found: C, 63.41; H, 5.55; N, 2.31; S, 5.28.

Preparation of (2*S*,5a*S*,2a*R*,5b*R*)-2-Hydroxy-8-methoxy-4,4-dimethyl-6-(phenylmethoxy)-1-phenylthio-2,6,2a,5a,5b-pentahydro-10*H*-1,3-dioxolano[4,5-*c*]1,3-dioxoleno[4,5-*j*]phenanthridin-7-one (44). To a stirring solution of hydroxylamine **40** (102 mg, 0.168 mmol) in 3.4 mL of THF was added Me_3Al (92.6 μL, 0.185 mmol, 2.0 M in hexanes) dropwise. The reaction was then slowly warmed to 60−65 °C and allowed to stir for 12 h, then cooled to rt and quenched with 6 mL of a saturated solution of Na and K tartrates. After 30 min of stirring, the reaction mixture was diluted with 20 mL of EtOAc and the layers were separated. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of this material was accomplished by flash chromatography using a 1 × 8 cm column, eluting with a gradient of 50 mL each of 20%, 30%, and 40%

(37) Mondon, A.; Krohn, K. *Chem. Ber.* **1975**, *108*, 445.

acetone/hexanes, collecting 8 mL fractions. The product-containing fractions (25−33) were collected and concentrated to give **44** (69.5 mg, 72% yield) as a pale yellow foam: $[\alpha]^{20}_D = +239$ (*c* 1.0, $CHCl_3$); R_f 0.13 (70% Et_2O/pentane); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.57−7.55 (m, 2H), 7.39−7.34 (m, 4H), 7.28−7.26 (m, 4H), 7.23−7.21 (m, 1H), 6.00 (ABq, $\Delta\nu = 2.4$ Hz, $J = 1.4$ Hz, 2H), 5.16 (ABq, $\Delta\nu = 41.0$ Hz, $J = 9.1$ Hz, 2H), 4.73 (dd, $J = 6.6$, 4.4 Hz, 1H), 4.49 (d, $J = 4.4$ Hz, 1H), 4.38 (d, $J = 4.7$ Hz, 1H), 4.29 (dd, $J = 6.6$, 4.7 Hz, 1*H*), 4.07 (s, 3H), 2.60 (bs, 1H), 1.48 (s, 3H), 1.38 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 164.4, 151.5, 144.4, 139.5, 135.3, 133.7, 133.6, 131.8, 131.2, 129.9, 129.7, 129.2, 128.8, 128.6, 127.3, 116.2, 110.3, 102.7, 102.3, 78.0 77.5, 73.1, 70.2, 65.1, 61.4, 27.6, 25.6; IR ($CHCl_3$) 3503, 3208, 1669 cm^{-1}. Anal. Calcd for $C_{31}H_{29}NO_8S$: C, 64.68; H, 5.08; N, 2.43; S, 5.57. Found: C, 64.73; H, 5.08; N, 2.31; S, 5.29.

Preparation of (5a*S*,2*R*,2a*R*,5b*R*)-2-Hydroxy-4,4-dimethyl-7-oxo-6-(phenylmethoxy)-1-phenylthio-2,6,2a,5a,5b-pentahydro-10*H*-1,3-dioxolano[4,5-*c*]1,3-dioxoleno[4,5-*j*]phenanthridin-8-yl 4-Methylbenzenesulfonate (44a). To a stirring solution of hydroxylamine **41** (75 mg, 0.10 mmol) in 2 mL of THF at −15 °C (ethylene glycol/CO_2 bath) was added a solution of Me_3Al (100 μL, 0.20 mmol, 2 M in hexanes). After 15 min, the cold bath was removed and the reaction was slowly heated to 65 °C. The reaction was stirred 48 h before being cooled to rt and quenched with a saturated solution of Na and K tartrates (5 mL). After 30 min, the mixture was diluted with 20 mL of EtOAc and the layers were separated. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of this material was accomplished by RPLC using a 1 mm plate eluting with a gradient of 40 mL each of 20%, 30%, and 40% EtOAc/hexanes, collecting 2 mL fractions. The product-containing fractions (27−32) were collected and concentrated to give **44Ts** (36 mg, 50% yield) as a pale yellow foam: R_f 0.43 (50% EtOAc/hexanes); $[\alpha]^{20}_D = +191.5$ (*c* 0.78, $CHCl_3$); 500 MHz ^{1}H NMR ($CDCl_3$) δ 7.96 (d, $J = 8.5$ Hz, 2H), 7.59 (s, 1H), 7.55 (dd, $J = 7.7$, 1.7 Hz, 2H), 7.38−7.33 (m, 5H), 7.28−7.21 (m, 5H), 5.94 (ABq, $\Delta\nu = 3.4$ Hz, $J = 1.1$ Hz, 2H), 5.04 (ABq, $\Delta\nu = 23.8$, $J = 9.3$ Hz, 2H), 4.73 (dd, $J = 6.6$, 4.4 Hz, 1H), 4.45 (d, $J = 4.4$ Hz, 1H), 4.39 (db, $J = 4.1$ Hz, 1H), 4.28 (dd, $J = 6.6$, 4.7 Hz, 1H). 2.62 (bs, 1H), 2.42 (s, 3H), 1.49 (s, 3H), 1.39 (s, 3H); 125 MHz ^{13}C NMR ($CDCl_3$) δ 162.0, 151.5, 145.7, 142.5, 135.4, 133.3, 133.2, 132.3, 132.3, 131.1, 130.4, 130.0, 129.8, 129.7, 129.2, 129.2, 128.8, 128.6, 127.5, 118.8, 110.5, 106.1, 103.3, 77.7, 73.1, 70.3, 65.0, 27.7, 25.7, 21.9; IR ($CHCl_3$) 2988, 1683 cm^{-1}; HRMS *m*/*z* (E/I) calcd for $C_{37}H_{33}NO_{10}S_2$ 715.1546, found 715.1554.

Preparation of (2*S*,5a*S*,2a*R*,5b*R*)-2,8-Dihydroxy-4,4-dimethyl-2,6,2a,5a,5b-pentahydro-10*H*-1,3-dioxolano[4,5-*c*]1,3-dioxoleno[4,5-*j*]phenanthridin-7-one (42). To a stirring solution of hydroxamic acid **44** (96.4 mg, 0.168 mmol) in 3.3 mL of THF at 0 °C (ice/water bath) was added MeOH (67.6 μL, 53.5 mg, 1.68 mmol) followed by a solution of SmI_2 (7.00 mL, 0.700 mmol, 0.1 M in THF). The mixture was then allowed to warm to rt. After 2 h the reaction was yellow in color and TLC analysis indicated complete consumption of starting material. The reaction was quenched with 10 mL of a 5% aqueous solution of HCl, then diluted with 100 mL of EtOAc. The layers were separated, and the organic layer was washed with a saturated solution of $Na_2S_2O_3$ (10 mL), then dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of this material was accomplished by trituration using 25% Et_2O/pentane followed by filtration. The mother liquor was concentrated and resubjected to trituration to give **42** (50.2 mg, 87% yield) as a tan crystalline solid: R_f 0.79 (20% MeOH/$CHCl_3$). All analytical data were in excellent agreement with those previously obtained by us (data above) as well as those reported by Mondon and Krohn.[37]

Preparation of (2*S*,4*S*,3*R*,4a*R*)-2,3,4,7-Tetrahydroxy-2,3,4,5,4a-pentahydro-9*H*-1,3-dioxoleno[4,5-*j*]phenanthridin-6-one, [Narciclasine] (2). To acetonide **42** (50.2 mg, 0.144 mmol) at 0 °C (ice/water bath) was added 2.9 mL of TFAA (precooled to −20 °C) down the side of the flask. After 10 min TLC analysis indicated complete consumption of starting material, at which time the reaction was concentrated cold via high vacuum (0.09 Torr). After approximately 4 min all of the TFA was removed to give a tan solid that was kept under vacuum for an additional 2 h. Purification of this material was accomplished by flash column chromatography using a 1 × 8 cm column, eluting with a gradient of 30 mL each of 10%, 20%, and 30% MeOH/$CHCl_3$, collecting 4 mL fractions. The product-containing fractions (11−20) were collected and concentrated to give narciclasine (39.7 mg, 89% yield) as a tan crystalline solid: mp, has no sharp mp, begins to color at 190 °C and slowly decomposes above 215 °C (lit.[4k] mp begins to color at 200 °C and slowly decomposes above 216 °C, lit.[5b] mp 250−251 (dec) (Me_2CO/MeOH), lit.[5a] 232−234 °C (dec) (AcOH)); $[\alpha]^{20}_D = +112$ (*c* 0.57, MeOH) (lit.[4k] $[\alpha]^{25}_D = +142.8$ (*c* 0.7, MeOH), lit.[5b] $[\alpha]^{temp}_D = +145$ (*c* 1.5, EtOH)); R_f 0.33 (20% MeOH/$CHCl_3$), strong yellow green fluorescence; 500 MHz ^{1}H NMR (DMSO-d_6) δ 13.3 (s, 1H), 7.91 (s, 1H), 6.86 (s, 1H), 6.15 (s, 1H), 6.08 (d, $J = 1.6$ Hz, 1H), 5.21−5.19 (m, 2H), 5.04 (s, 1H), 4.20 (d, $J = 8.3$ Hz, 1H), 4.01(s, 1H), 3.79 (d, 8.3 Hz, 1H), 3.70 (s, 1H); 500 MHz ^{1}H NMR (CD_3OD) δ 6.70 (s 1H), 6.11−6.10 (m, 1H), 5.96 (d, $J = 2.4$ Hz, 1H), 4.29−4.27 (m, 1H), 4.16 (dd, 5.9, 3.1 Hz, 1H), 3.84−3.82 (m, 2H); 125 MHz ^{13}C NMR (DMSO-d_6) δ 168.9 (C), 152.4 (C), 144.8 (C), 133.4 (C), 132.1 (C), 129.3 (C), 124.8 (CH), 105.6 (C), 102.1 (CH_2), 95.9 (CH), 72.4 (CH), 69.2 (CH), 68.8 (CH), 52.9 (CH); IR (KBr) 3400 (b), 3204, 1673 cm^{-1}.

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