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Approach to the Homoerythrina Alkaloids Using a Tandem N-Alkylation/Azomethine Ylide Cycloaddition

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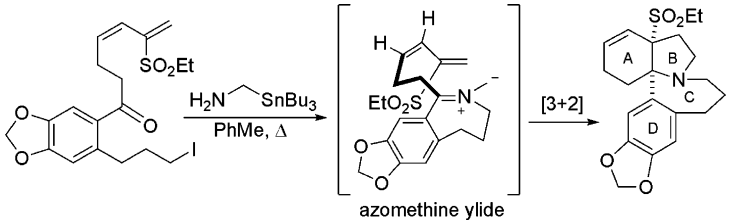

Synthetic efforts toward the homoerythrina alkaloids **1**−**3** are described. Two separate model systems guided the pivotal [3 + 2] azomethine ylide cycloaddition cascade to form the A−C rings of these alkaloids. The cycloaddition precursors **63** and **68**, prepared in nine and ten steps, respectively, from alkyne **47**, each contain an enolizable ketone, a tethered electrophile, and an electron-poor dipolarophile. Heating **63** and **68** with the stannyl amine **17** generated demethoxyschelhammeridine **65** and demethoxyschelhammericine **70**, the products of intramolecular azomethine ylide cycloadditions. Subsequent attempts to install the C-3 methoxy group of **1**−**3** are also described.

Introduction

The homoerythrina alkaloids are comprised of over 70 natural products that are widely distributed in the plant kingdom and have been isolated from six plant genera (*Athrotaxis*, *Cephalotaxus*, *Dysoxylum*, *Lagarostrobos*,[1] *Phelline*, and *Schelhammera*).[2] The alkaloids possess an intriguing azatetracyclic framework and are grouped structurally into aromatic or nonaromatic D-ring categories. The former category is predominant and includes homoerythratine (**1**), 3-*epi*-schelhammeridine (**2**),[3] and 3-*epi*-schelhammericine (**3**).[4] The homoerythrina alkaloids are structurally similar and biosynthetically related to the *Erythrina* alkaloids[2a] as the *Erythrina* alkaloids (**4a**) contain an azacyclohexene C-ring rather than the azacycloheptene C-ring found in the homoerythrina alkaloids (**4b**). Many of the *Erythrina* alkaloids (though few homoerythrina alkaloids) have demonstrated biological activity including curare and hypnotic effects.[2a] There are no reports on pharmacological effects of either homoerythratine (**1**) or 3-*epi*-schelhammeridine (**2**), although in two separate studies isolated alkaloids that were extracted from leaves of the genus *Dysoxylum lenticellare*, which includes 3-*epi*-schelhammericine (**3**), are shown to have both cardiac effects in rats[5] and molluscicidal activity.[6]

Numerous synthetic strategies have led to the successful construction of the erythrinan ring system.[2a] Specifically, we note that Livinghouse and co-workers[7] used an intramolecular [3 + 2] azomethine ylide cycloaddition[8] to generate the erythrinan framework (Scheme 1). Alkylation of dihydroiso-

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(1) Has also been classified as the genus *Manoao*: (a) Bloor, S. J.; Benner, J. P.; Irwin, D.; Boother, P. *Phytochemistry* **1996**, *41*, 801−802. (b) Molloy, B. P. J. *N. Z. J. Bot.* **1995**, *33*, 183−201.

(2) (a) Tsuda, Y.; Sano, T. Erythrina and Related Alkaloids. In *The Alkaloids*; Cordell, G. A., Ed.; Academic Press: New York, 1996; Vol. 48, pp 249−337. (b) Bick, I. R. C.; Panichanun, S. Homoerythrina and Related Alkaloids. In *Alkaloids: Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Springer-Verlag: New York, 1991; Vol. 7, pp 1−41.

(3) For total synthesis, see: (a) Tsuda, Y.; Murata, M.; Hosoi, S.; Ikeda, M.; Sano, T. *Chem. Pharm. Bull.* **1996**, *44*, 515−524. (b) Tsuda, Y.; Hosoi, S.; Murata, M. *Heterocycles* **1990**, *30*, 311−316.

(4) For total synthesis, see: (a) Tsuda, Y.; Ohshima, T.; Hosoi, S.; Kaneuchi, S.; Kiuchi, F.; Toda, J.; Sano, T. *Chem. Pharm. Bull.* **1996**, *44*, 500−508. (b) Tsuda, Y.; Hosoi, S.; Ohshima, T.; Kaneuchi, S.; Murata, M.; Kiuchi, F.; Toda, J.; Sano, T. *Chem. Pharm. Bull.* **1985**, *33*, 3574−3577.

(5) Aladesanmi, A. J.; Ilesanmi, O. R. *J. Nat. Prod.* **1987**, *50*, 1041−1044.

(6) Aladesanmi, A. J.; Adewunmi, C. O.; Kelley, C. J.; Leary, J. D.; Bischoff, T. A.; Zhang, X.; Snyder, J. K. *Phytochemistry* **1988**, *27*, 3789−3792.

(7) Westling, M.; Smith, R.; Livinghouse, T. *J. Org. Chem.* **1986**, *51*, 1159−1165.

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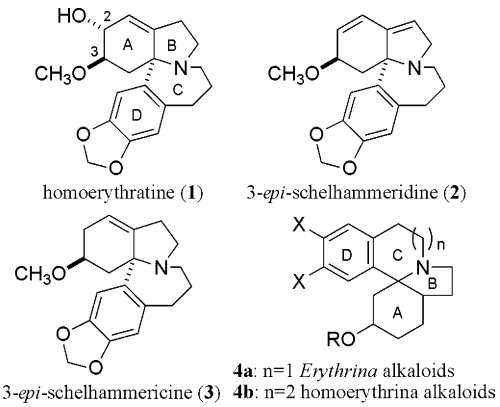
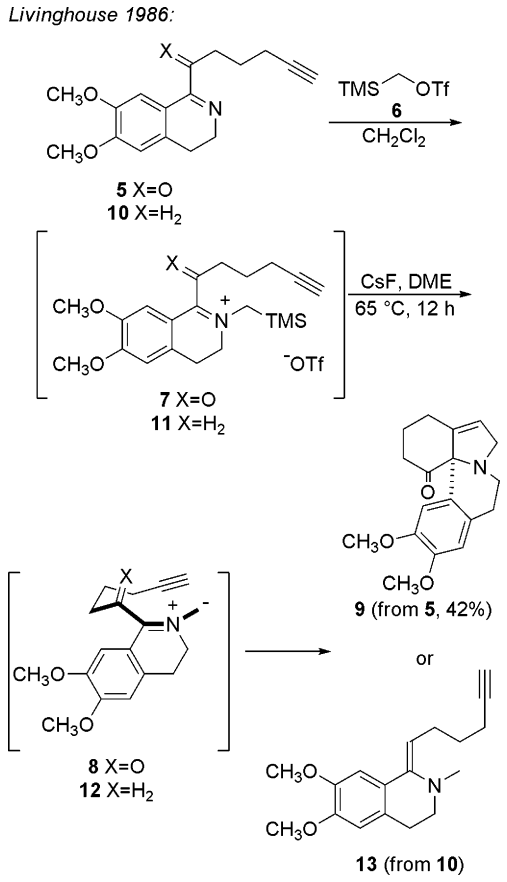


quinoline **5** with trimethylsilylmethyl triflate (**6**) gave the iminium ion **7**, which was then desilylated with cesium fluoride to form the azomethine ylide **8**. An intramolecular cycloaddition between the ylide and the terminal acetylenic dipolarophile of **8** resulted in the azatetracycle **9**. A similar sequence was also attempted by using dihydroisoquinoline **10**, which bears enolizable hydrogens.[9] However, heating iminium **11** in the presence of cesium fluoride resulted only in deprotonation to form enamine **13**. This result is not an isolated case, as a number of literature reports demonstrate that generating an azomethine ylide by desilylating an *N*-(trimethylsilyl)methyl iminium salt is often not compatible with enolizable hydrogens.[10]

In comparison to the erythrinans, far fewer synthetic reports have appeared on the synthesis of the homoerythrinans.[2a,3,4,11] The only reported total syntheses of homoerythrina alkaloids have been accomplished by the Tsuda group, who have constructed six natural products with the framework of **4b**, including 3-*epi*-schelhammeridine (**2**) and 3-*epi*-schelhammericine (**3**).[3,4,11f] Although these syntheses are lengthy (22−26 steps), they use a synthetic strategy similar to that employed in the synthesis of an *Erythrina* alkaloid.[12] Despite the slight structural difference between **4a** and **4b**, the utilization of a common synthetic strategy to access both natural product families has proven to be difficult.[2a,13] In addition to the work

SCHEME 1



of the Tsuda group, only the recent literature examples described by the Tu and Padwa groups have overcome this difficulty.[11a,b,d] Despite these recent examples, the synthesis of the intriguing polycyclic architecture of the homoerythrina alkaloids remains challenging and relatively unexplored. Herein, we describe a full account of our synthetic studies on these alkaloids, culminating in efficient syntheses of demethoxyschelhammeridine **65** and demethoxyschelhammericine **70**.

Retrosynthetic Plan

Our approach to the alkaloids **1**−**3** is retrosynthetically outlined in Scheme 2. We envisioned that manipulating the sulfoxide group of the advanced intermediate **14** would generate **1** and **2**. Thus, a sulfoxide−sulfenate (Mislow−Evans) rearrangement[14] or a sulfoxide elimination of **14** would give the alkaloids **1** and **2**, respectively. Both of these compounds have been independently converted to **3**.[15,16] The cornerstone of our approach involved a one-pot sequence that would efficiently assemble the A−C rings of the azatetracycle **14** (cf. **4b**). An intramolecular [π4s + π2s] cycloaddition between the semistabilized azomethine ylide and the terminal vinyl sulfide of **15** would complete the homoerythrina core by providing the perhydroindole A and B rings. Ylide **15** may be generated in

(8) For reviews, see: (a) Coldham, I.; Hufton, R. *Chem. Rev.* **2005**, *105*, 2765−2810. (b) Harwood, L. M.; Vickers, R. J. Azomethine Ylides. In *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*; Padwa, A., Pearson, W. H., Eds.; John Wiley & Sons: New York, 2002; pp 169−252. (c) Padwa, A. Intermolecular 1,3-Dipolar Cycloadditions. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, UK, 1991; Vol. 4, pp 1069−1109. (d) Wade, P. A. Intramolecular 1,3-Dipolar Cycloadditions. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, UK, 1991; Vol. 4, pp 1111−1168.

(9) Smith, R.; Livinghouse, T. *Tetrahedron* **1985**, *41*, 3559−3568.

(10) (a) Pearson, W. H.; Stoy, P.; Mi, Y. *J. Org. Chem.* **2004**, *69*, 1919−1939. (b) Fishwick, C. W. G.; Jones, A. D.; Mitchell, M. B. *Tetrahedron Lett.* **1989**, *30*, 4447−4448. (c) Tsuge, O.; Kanemasa, S.; Yamada, T.; Matsuda, K. *J. Org. Chem.* **1987**, *52*, 2523−2530. (d) Smith, R.; Livinghouse, T. *J. Org. Chem.* **1983**, *48*, 1554−1555.

(11) (a) Gao, S.; Tu, Y. Q.; Hu, X.; Wang, S.; Hua, R.; Jiang, Y.; Zhao, Y.; Fan, X.; Zhang, S. *Org. Lett.* **2006**, *8*, 2373−2376. (b) Cassidy, M.; Özdemir, A. D.; Padwa, A. *Org. Lett.* **2005**, *7*, 1339−1342. (c) Hart, J. B.; Mason, J. M.; Gerard, P. J. *Tetrahedron* **2001**, *57*, 10033−10038. (d) Toda, J.; Niimura, Y.; Sano, T.; Tsuda, Y. *Heterocycles* **1998**, *48*, 1599−1607. (e) Le Dréau, M. A.; Desmaële, D.; Dumas, F.; d'Angelo, J. *J. Org. Chem.* **1993**, *58*, 2933−2935. (f) Tsuda, Y.; Murata, M. *Tetrahedron Lett.* **1986**, *27*, 3385−3386.

(12) Sano, T.; Toda, J.; Ohshima, T.; Tsuda, Y. *Chem. Pharm. Bull.* **1992**, *40*, 873.

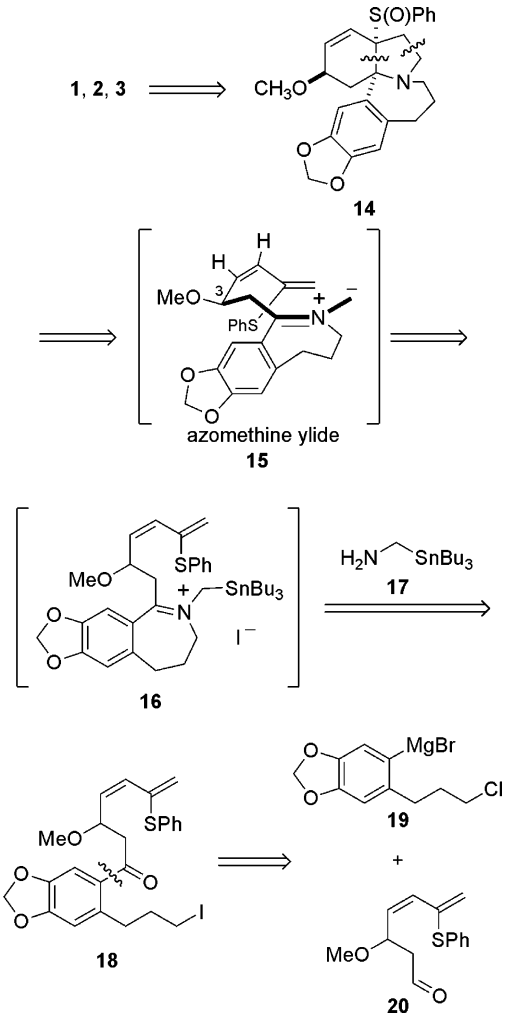
(13) (a) Chikaoka, S.; Toyao, A.; Ogasawara, M.; Tamura, O.; Ishibashi, H. *J. Org. Chem.* **2003**, *68*, 312−318. (b) Toda, J.; Niimura, Y.; Takeda, K.; Sano, T.; Tsuda, Y. *Chem. Pharm. Bull.* **1998**, *46*, 906−912.

(14) (a) Evans, D. A.; Andrews, G. C. *Acc. Chem. Res.* **1974**, *7*, 147−155. (b) Tang, R.; Mislow, K. *J. Am. Chem. Soc.* **1970**, *92*, 2100−2104.

(15) For conversion of homoerythratine **1** to 3-*epi*-schelhammericine **3**, see: Panichanun, S.; Bick, I. R. C. *Tetrahedron* **1984**, *40*, 2677−2684.

(16) For conversion of 3-*epi*-schelhammeridine **2** to 3-*epi*-schelhammericine **3**, see: Johns, S. R.; Lamberton, J. A.; Sioumis, A. A. *Aust. J. Chem.* **1969**, *22*, 2219−2256.

SCHEME 2



situ by destannylation of the *N*-(tributylstannyl)methyl iminium ion **16**[17] which, based on our earlier work, was expected to tolerate the enolizable hydrogens, unlike work in the silicon area (cf. Scheme 1). Formation of the azaheptene C ring along with the iminium salt in **16** would be accomplished by heating the ketone **18** together with (tributylstannyl)methylamine (**17**).[10a] The expected cis-fused ring junction shown in **14** would be consistent with previous work from our laboratories in which [3 + 2] intramolecular cycloadditions of 2-azaallyllithiums[18] gave solely cis-fused perhydroindoles.[19] The C-3 methoxy substituent was anticipated to prefer the equatorial conformation in **15**, which would lead to the desired relative configuration at the methoxy group and the ring-junction stereocenters. The cycloaddition precursor, iodoketone **18**, should be available from the addition of Grignard reagent **19** to the aldehyde **20**.

Results and Discussion

We began our approach to the homoerythrina alkaloids by attempting to synthesize aldehyde **20**. The known (*Z*)-vinyl iodide **26**, a key intermediate, may be readily obtained using minor modifications of a route previously developed in our laboratories (Scheme 3).[19b] Hence, commercially available 1,3-propanediol was monoprotected to give alcohol **21**,[20] which was then oxidized to aldehyde **22**[21] using a Swern oxidation. The union of ethynylmagnesium bromide with aldehyde **22** gave the propargylic alcohol **23**. Following the formation of methyl ether **24**, iodination of the alkyne terminus provided **25**. Diimide reduction of alkyne **25** selectively furnished (*Z*)-vinyl iodide **26** in excellent yield.

Next, we attempted a Negishi cross-coupling reaction[22] to access the phenylsulfanyl-functionalized diene **27**. The phenylsulfanyl substituent of **27** was sought because we have successfully employed phenyl vinyl sulfide in an intermolecular fashion as both an anionophile and a dipolarophile in [3 + 2] cycloadditions with 2-azaallyl anions[17d,19a,23] and azomethine ylides,[10a] respectively. However, work by Negishi and Luo[24] describes the stereoselective formation of (*E*)-dienes by the Pd-catalyzed cross-coupling of (*E*)-vinyl iodides solely with *alkyl* vinyl sulfides. We sought to apply this selective sequence by coupling (*Z*)-vinyl iodide **26** with the 1-(phenylsulfanyl)vinyl zinc reagent, produced in situ by treating phenyl vinyl sulfide with *sec*-butyllithium followed by zinc chloride. Unfortunately, all efforts to form the cross-coupling product **27** failed presumably due to the reported difficulty in cleanly forming the required organolithium. A nearly 50-year-old literature report demonstrates that the major product from the treatment of phenyl vinyl sulfide with a variety of organolithiums is β-addition to the double bond.[25] Subsequent examples have appeared describing conditions that improve the direct α-lithiation of phenyl vinyl sulfide;[26] however, in our hands these conditions either gave unacceptable ratios of direct lithiation vs alkyllithium addition[27] or were incompatible with the Negishi reaction conditions. In sharp contrast, *ethyl* vinyl sulfide is cleanly lithiated with *sec*-butyllithium,[28] and thus coupling the corresponding vinyl zinc of **26** afforded the ethylsulfanyl-functionalized diene **28** in quantitative yield. Carrying on, aldehyde **30** was formed from **28** by deprotection and Swern oxidation. It is worth noting that aldehyde **30** was not stable to chromatography and decomposed within days even when stored frozen in benzene; therefore, it was made fresh and used immediately without purification.

(17) For generation of azomethine ylides by destannylation of *N*-(tri-*n*-butylstannyl)methyl iminiums, see: ref 10a; (a) Pearson, W. H.; Dietz, A.; Stoy, P. *Org. Lett.* **2004**, *6*, 1005−1008. (b) Clark, R. B.; Pearson, W. H. *Org. Lett.* **1999**, *1*, 349−351. (c) Pearson, W. H.; Clark, R. B. *Tetrahedron Lett.* **1999**, *40*, 4467−4471. (d) Pearson, W. H.; Mi, Y. *Tetrahedron Lett.* **1997**, *38*, 5441−5444.

(18) For a recent review, see: Pearson, W. H.; Stoy, P. *Synlett* **2003**, 903−921.

(19) (a) Pearson, W. H.; Lovering, F. E. *J. Org. Chem.* **1998**, *63*, 3607−3617. (b) Pearson, W. H.; Postich, M. J. *J. Org. Chem.* **1994**, *59*, 5662−5671. (c) Pearson, W. H.; Walters, M. A.; Oswell, K. D. *J. Am. Chem. Soc.* **1986**, *108*, 2769−2771.

(20) McDougal, P. G.; Rico, J. G.; Oh, Y. I.; Condon, B. D. *J. Org. Chem.* **1986**, *51*, 3388−3390.

(21) Pirrung, M. C.; Webster, N. J. G. *J. Org. Chem.* **1987**, *52*, 3603−3613.

(22) (a) Negishi, E. -I.; Liu, F. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH Verlag GmbH: Weinheim, Germany, 1998; pp 0−47. (b) Erdik, E. *Tetrahedron* **1992**, *48*, 9577−9648.

(23) (a) Pearson, W. H.; Lee, I. Y.; Mi, Y.; Stoy, P. *J. Org. Chem.* **2004**, *69*, 9109−9122. (b) Pearson, W. H.; Ren, Y. *J. Org. Chem.* **1999**, *64*, 688−689.

(24) Negishi, E. -I.; Luo, F. -T. *J. Org. Chem.* **1983**, *48*, 1560−1562.

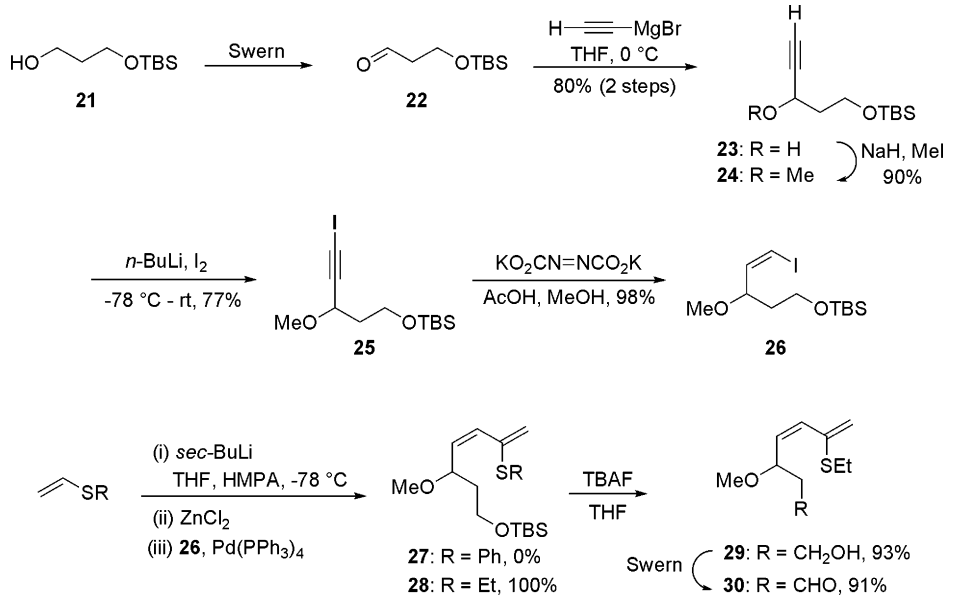
(25) Parham, W. E.; Motter, R. F. *J. Am. Chem. Soc.* **1959**, *81*, 2146−2148.

(26) (a) Trost, B. M.; Lavole, A. C. *J. Am. Chem. Soc.* **1983**, *105*, 5075−5090. (b) Ager, D. J. *Tetrahedron Lett.* **1981**, *22*, 587−590. (c) Cookson, R. C.; Parsons, P. J. *J. Chem. Soc., Chem. Commun.* **1978**, 821−822. (d) Harirchian, B.; Magnus, P. *J. Chem. Soc., Chem. Commun.* **1977**, 522−523.

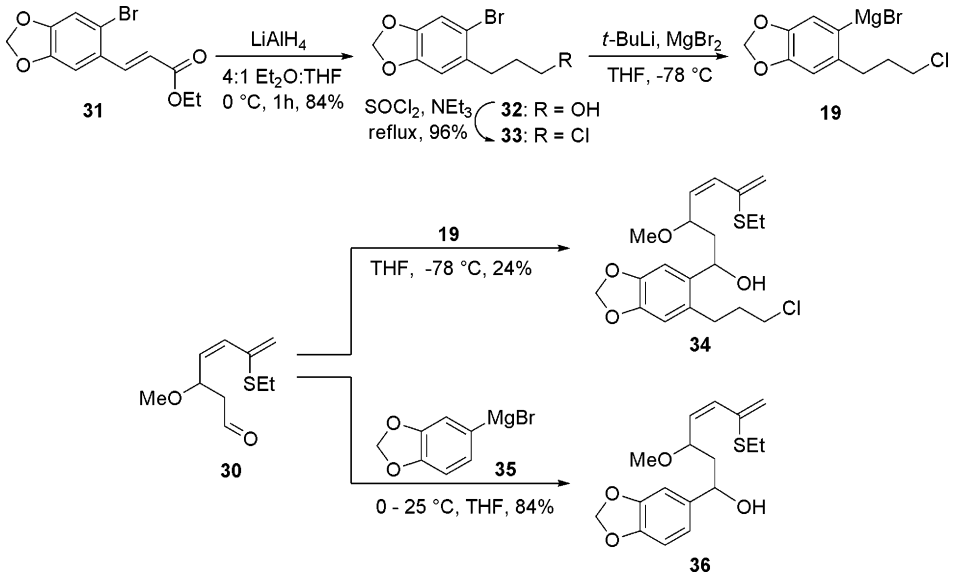
(27) Determined by incorporating deuterium upon quenching with D_2O; see Table 1 in the Supporting Information.

(28) Oshima, K.; Shimoji, K.; Takahashi, H.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1973**, *95*, 2694−2695.

SCHEME 3



SCHEME 4



Grignard reagent **19**, a coupling partner for aldehyde **30**, was accessible starting with a lithium aluminum hydride reduction of **31**[29] to give the known alcohol **32**,[30] which was then treated with thionyl chloride to provide **33** (Scheme 4). Our initial efforts to couple **19** with **30** drew upon similar work reported by Parham and co-workers.[31] Unfortunately, halogen−metal exchange of aryl bromide **33** followed by addition of aldehyde **30** did not yield the desired product. We then found that in situ Grignard formation from the corresponding organolithium via magnesium bromide at −78 °C did provide the desired alcohol **34** as a mixture of diastereomers, although in low yield. The low temperature of the reaction was required to prevent cyclization. However, when the structurally simpler and commercially available model Grignard reagent 3,4-(methylenedioxy)phenylmagnesium bromide **35** was added to **30**, alcohol **36** was formed in a much improved 84% yield.

At this stage, we elected to continue with the model alcohol **36** to test the key cycloaddition step (Scheme 5). Thus, following oxidation of the alcohol **36** to the ketone **37**, the cyclization cascade began by using an earlier method from our laboratory for the formation of ketone-derived (2-azaallyl)stannanes.[23,32] Condensing ketone **37** and (tributylstannyl)methylamine (**17**)[10a] in the presence of trimethylaluminum formed the (2-azaallyl)-stannane **38** in situ as a mixture of (*E*)- and (*Z*)-isomers. Heating **38** with benzyl bromide triggered alkylation, destannylation, azomethine ylide formation, and [3 + 2] cycloaddition. The resulting cycloadduct **39** was isolated as a single diastereomer in 28% yield. The structure of **39** was firmly established by

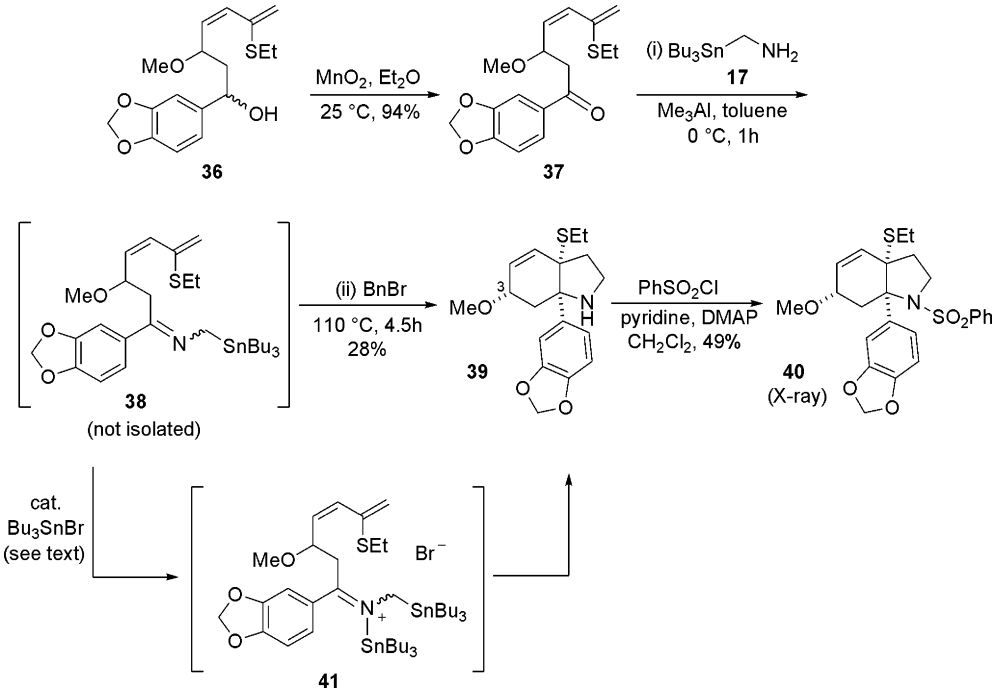
(29) Ester **31** is readily available from a Wittig reaction of 6-bromopiperonal. For a similar example, see: Arya, P.; Durieux, P.; Chen, Z. X.; Joseph, R.; Leek, D. M. *J. Comb. Chem.* **2004**, *6*, 54−64.

(30) Tietze, L. F.; Schirok, H.; Wöhrmann, M.; Schrader, K. *Eur. J. Org. Chem.* **2000**, *13*, 2433−2444.

(31) Parham, W. E.; Jones, L. D.; Sayed, Y. A. *J. Org. Chem.* **1976**, *41*, 1184−1186.

(32) Pearson, W. H.; Barta, N. S.; Kampf, J. W. *Tetrahedron Lett.* **1997**, *38*, 3369−3372.

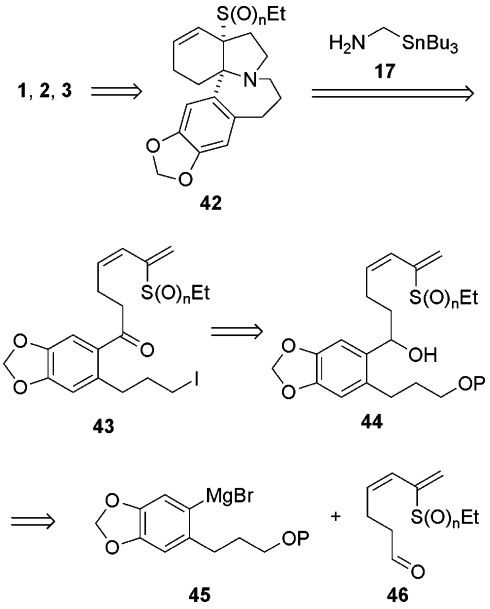
SCHEME 5



performing an $^1H-^1H$ COSY experiment as well as a series of NOE experiments. Ultimately, the relative configuration of **39** was unambiguously established by X-ray cyrstallography of the *N*-benzenesulfonyl derivative **40**. Several features of this cycloaddition reaction are noteworthy. First, one of the few correctly anticipated features of **39** was the cis-fused ring junction of the perhydroindole. In addition to being consistent with previous reports in our laboratory,[19] inspection of molecular models predicts that either the (*E*)- or the (*Z*)-(2-azaallyl)-stannanes (**38**) can lead to this cis-fused ring junction. In contrast, we are unable to provide a compelling explanation for the unexpected relative configuration of the C-3 methoxy substituent and the ring-junction stereocenters. Fortunately, not only is the epimerization of this stereocenter possible[33] but also the homoerythrina alkaloids include numerous examples of both C-3 methoxy epimers. Last, the isolation of the unconventional N-unsubstituted rather than the *N*-benzyl cycloadduct **39** may be rationalized via a mechanism proposed in a related example by Imai and Achiwa,[34] where a catalytic amount of tributylstannyl bromide is formed in situ and acts as the electrophile to form the iminium **41**. The bromide counterion of **41** subsequently destannylates the iminium ion to regenerate tributylstannyl bromide and *N*-stannylazomethine ylide, producing **39**. Control experiments confirming this type of mechanism have been reported by our group.[10a]

Revised Strategy. Because of the suboptimal [3 + 2] cycloaddition described above, we shifted to the modified strategy outlined in Scheme 6. As compared with our initial strategy, two structural variations to the cycloaddition precursor were planned to increase the efficiency of the key cyclization step. First, because azomethine ylide cycloadditions typically favor electron-poor dipolarophiles, an oxidized sulfur moiety

SCHEME 6



(n = 1 or 2) should decrease the electron density of diene **43** and narrow the $HOMO_{(dipole)}-LUMO_{(dipolarophile)}$ gap. Second, we felt that **43** may be more likely to withstand the cycloaddition conditions by installing the sensitive C-3 methoxy group after cycloaddition via allylic oxidation of **42**. Such an allylic oxidation seemed well-precedented; however, this presumption would later prove problematic (vide infra). An additional change included combining **45**, which bears a protected hydroxypropyl chain rather than the chloropropyl chain of **19** (cf. Scheme 4), with aldehyde **46** to afford **44**.

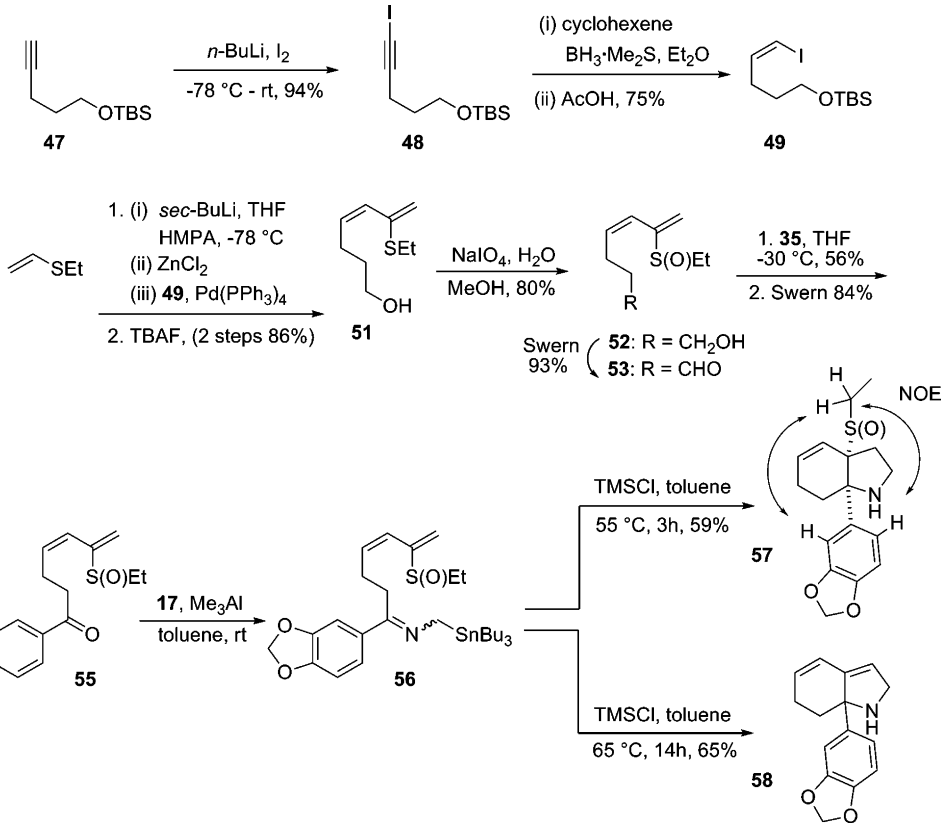
The revised approach started by treating alkyne **47**[35] with butyllithium and I_2 to give iodoalkyne **48** (Scheme 7). Diimide

(33) (a) Martin, S. F.; Davidsen, S. K. *J. Am. Chem. Soc.* **1984**, *106*, 6431−6433. (b) White, J. D.; Chong, W. K. M.; Thirring, K. *J. Org. Chem.* **1983**, *48*, 2300−2302. (c) Danishefsky, S.; Morris, J.; Mullen, G.; Gammill, R. *J. Am. Chem. Soc.* **1980**, *102*, 2838−2840.

(34) Imai, N.; Achiwa, K. *Chem. Pharm. Bull.* **1987**, *35*, 593−601.

(35) Guo, H.; O'Doherty, G. A. *Org. Lett.* **2005**, *7*, 3921−3924.

SCHEME 7



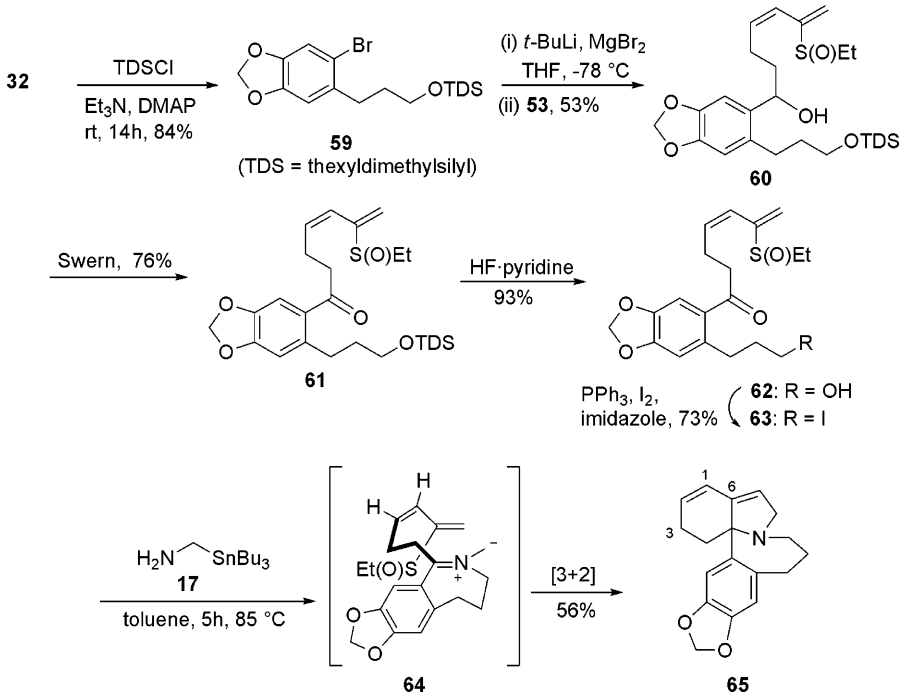
reduction of **48**, similar to that used to reduce iodoalkyne **25** (cf. Scheme 3), resulted in **49** along with significant amounts of starting material as well as trace amounts of the corresponding overreduced alkane. However, reduction of **48** was cleanly accomplished by hydroboration followed by acid hydrolysis of the corresponding vinylborane[36] to afford the *cis*-vinyl iodide **49**. The Negishi cross-coupling reaction previously described (vide supra) once again used ethyl vinyl sulfide to provide diene **50** (not shown). Deprotection of **50** furnished **51** in 86% yield over two steps. It is noteworthy that intermediates **49**−**51** were surprisingly prone to isomerization to a mixture of the *trans*- and *cis*-dienes upon purification via silica gel chromatography unless 1−3% triethylamine was included in the mobile phase. The ethylsulfanyl group of **51** was oxidized with sodium periodate to the sulfoxide **52**, and Swern oxidation gave aldehyde **53**. As in the previous sequence (cf. Scheme 4), we opted to test the forthcoming cycloaddition step by combining model compound **35** with the aldehyde **53**. The resulting benzyl alcohol **54** (not shown) was then oxidized to give ketone **55**.

With ketone **55** in hand, we reexamined the azomethine ylide cycloaddition cascade. Thus, ketone **55** and (tributylstannyl)-methylamine **17** were condensed to provide the (2-azaallyl)-stannane **56** as a mixture of (*E*)- and (*Z*)-isomers. We were able to follow the progress of this condensation using neutral alumina TLC. Once the reaction appeared complete (about 90 min), **56** was subjected to an aqueous workup and combined without further purification with an electrophile to initiate ylide formation. Although the choice of the electrophile was quite flexible (BnBr, HF·pyr, $Sc(OTf)_3$, Bu_3SnCl), the best results were achieved when TMSCl and **56** were combined and heated at 55 °C for 3 h to provide sulfoxide **57** in 59% yield. The structure and configuration of **57** were confidently established using ^{1}H NMR decoupling experiments and focused ^{1}H NOE enhancements, including those between the methylene protons of the sulfoxide moiety and the two indicated phenyl ring protons. Furthermore, the ^{13}C NMR spectrum closely correlated with the similar **39**, whose structure was confirmed by X-ray. The expected cis configuration of the hydroindole ring junction of **57** matched three separate hydroindole forming [3 + 2] cycloaddition reactions reported by our group.[19] If the same reaction was heated at 65 °C for 14 h, a thermal elimination of the sulfoxide group gave diene **58** without any detectable amount of **57**. A simple adjustment in the reaction length allowed us to generate either of the alkene variants found in the A and B rings of **1**−**3**.

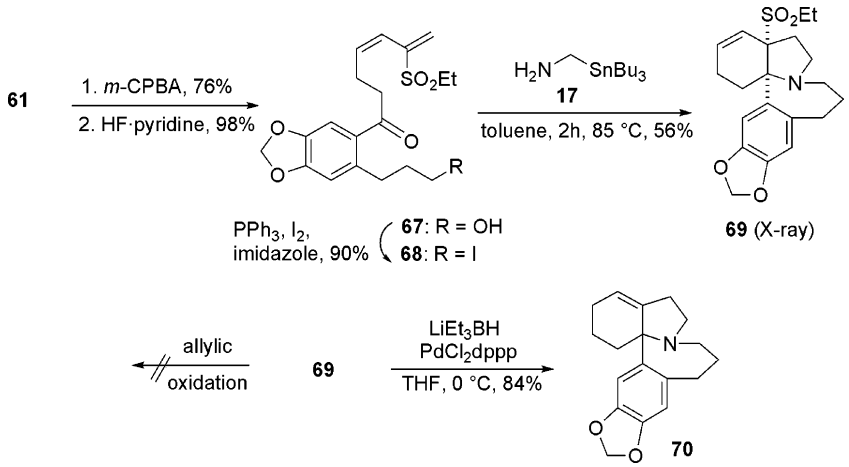
Synthesis of Demethoxyschelhammeridine 65 and Demethoxyschelhammericine 70. On the basis of the success of our revised model system, we sought to generate the fully elaborated homoerythrina architecture and, we hoped, **1**−**3**. Toward this end (Scheme 8), protection of alcohol **32** gave the thexyldimethylsilyl (TDS) ether **59**. The corresponding organomagnesium was generated in situ and then combined with aldehyde **53** to provide the benzyl alcohol **60**. A Swern oxidization of **60** to the ketone **61** was followed by desilylation and iodination to furnish the cycloaddition precursor **63**. Heating **63** with the amine **17** caused the key tandem N-alkylation/azomethine ylide cycloaddition, presumably via the semistabilized ylide **64**, to give demethoxyschelhammeridine **65** in 56% yield. The formation of the entire homoerythrina core by this single-pot sequence extends the scope of [4πs + 2πs] azomethine ylide cycloadditions as the first example in which an intramolecular electrophile and dipolarophile converged to form

(36) Corey, E. J.; Cashman, J. R.; Eckrich, T. M.; Corey, D. R. *J. Am. Chem. Soc.* **1985**, *107*, 713−715.

SCHEME 8



SCHEME 9



three rings.[37] Both the ^{1}H and ^{13}C NMR spectra of **65** are consistent with those of diene **58** as well as 3-*epi*-schelhammeridine (**2**). Interestingly, under these conditions, sulfoxide elimination occurred rapidly without any measurable quantities of the putative parent sulfoxide cycloadduct (not shown) that would be analogous to the sulfoxide **57**. Although efforts to install a C-3 methoxy group by allylic oxidation of **65** were unsuccessful, a more thorough investigation of this transformation focused on a subsequent analogue (vide infra).

The spontaneous elimination of the sulfoxide moiety in the cycloaddition of **63** furnished the adduct **65** bearing the 1,6-diene arrangement of the A and B rings of 3-*epi*-schelhammeridine (**2**). To access the A ring olefin arrangement found in homoerythratine (**1**) and 3-*epi*-schelhammericine (**3**), we used the thermally more stable sulfone derivative which would not be expected to eliminate under the reaction conditions because sulfones are generally more endothermic than sulfoxides (Scheme 9). Thus, sulfoxide **61** was oxidized to the sulfone **66** (not shown) with *m*-chloroperbenzoic acid. The cycloaddition precursor **68** was then prepared following desilylation and iodination of **67**. Once again, the tandem N-alkylation/azomethine ylide cycloaddition proceeded smoothly upon heating **68** with the amine **17** in toluene for 2 h to provide the cycloadduct **69** in 56% yield. The cis configuration of the A and B rings, which has been consistent throughout, was unequivocally established by X-ray crystallography of the corresponding picrate of **69**.

The previously described cycloadditions of the model ketones **37** and **55** (cf. Schemes 5 and 7) began with a dehydrative

(37) For examples of an intramolecular N-alkylation and an *intermolecular* azomethine ylide cycloaddition via a three-component single-pot sequence, see refs 10a and 17d. For examples of an intramolecular N-alkylation followed by an azomethine ylide generation and afterwards an *intramolecular* cycloaddition, see: Hassner, A.; Fischer, B. *J. Org. Chem.* **1992**, *57*, 3070−3075. Vedejs, E.; Naidu, B. N.; Klapars, N. A.; Warner, D. L.; Li, V.; Na, Y.; Kohn, H. *J. Am. Chem. Soc.* **2003**, *125*, 15796−15806.

condensation step that required trimethylaluminum to promote the otherwise sluggish formation of the corresponding imines, whereas the cycloadditions of **63** and **68** proceed smoothly without trimethylaluminum. We believe this provides strong evidence that the sequence of events in the cycloaddition cascades of **63** and **68** is intermolecular N-alkylation of **17** with the tethered electrophile followed by intramolecular dehydrative condensation. Thus, using an intramolecular condensation of ketones **63** and **68** has the advantage of milder reaction conditions over the intermolecular condensation of ketones **37** and **55** by not requiring a strong Lewis acid despite all of the ketones being similarly hindered and electron rich.

We then focused on installing a methoxy group at the C-3 of **69** via an allylic oxidation followed by methylation of the corresponding alcohol. Papers by the Muxfeldt[38] and Mori groups[39] reported successful allylic oxidations of a closely related tetrahydroindole with SeO_2. Unfortunately, these conditions resulted in recovered starting material when applied to **69**. Allylic oxidations of five- and six-membered ring alkenes are generally difficult,[40] and we suspected that the basic nitrogen of **69** might be a further interfering factor.[41] Therefore, we also explored the reaction under acidic conditions[38,42] as well as on the corresponding HCl salt of **69**. We investigated alternative allylic oxidants including the use of 2,2′-dipyridyldiselenide and iodoxybenzene to generate 2-pyridineseleninic anhydride in situ (Crich[43]), SeO_2 with *t*-butyl hydroperoxide (Sharpless[44]), and palladium-catalyzed oxidation with *t*-butyl hydroperoxide (Corey[45]). Ultimately, despite considerable effort, we were not able to oxidize the C-3 position of **69**.

Despite the fact that the allylic oxidation precluded us from functionalizing the C-3 position of **69**, we were able to successfully achieve desulfonylation of **69** by a palladium-catalyzed $LiBHEt_3$ reduction[46] to generate demethoxyschelhammericine **70** in 84% yield. This compound has previously been isolated as a minor component of the platinum oxide catalyzed hydrogenolysis of natural schelhammeridine.[16] The ^{1}H NMR spectrum of **70** compares and, not surprisingly, improves upon the quality of that shown in ref 16 from 1969. In addition, the ^{13}C NMR olefin resonances in the A ring of **70** (142.6 and 118.4 ppm) compare with those of **1** (145 and 121 ppm).

Summary

Synthetic efforts directed at the total synthesis of the homoerythrina alkaloids **1**−**3**, including the synthesis of demethoxyschelhammeridine (**65**) and demethoxyschelhammericine (**70**), are presented. A key feature of the syntheses involves the successful formation of the A−C rings of the alkaloids using a tandem N-alkylation/azomethine ylide [3 + 2] cycloaddition. This key step features both an intramolecular N-alkylation of a tethered electrophile and an intramolecular cycloaddition of a tethered dipolarophile. Two separate model systems guided our approach by demonstrating improved yields of the key cascade sequence with the incorporation of an electron-poor vinyl sulfoxide dipolarophile and removal of an allylic methoxy group. Unfortunately, subsequent efforts to install the methoxy group via an allylic oxidation of the advanced intermediate **69** were unsuccessful. The synthesis of **65** and **70** nicely complements the construction of the *Erythrina* ring system by Livinghouse and co-workers by demonstrating that an azomethine ylide [3 + 2] cycloaddition can generate the core ring system of both the homoerythrina and *Erythrina* alkaloids. This adaptability represents an accomplishment that has proven to be challenging in previous approaches.[2a,11c,d] In addition, our method of generating azomethine ylides from 2-(azaallyl)stannanes was tolerant to the presence of enolizable hydrogens with no detectable enamine formation and thereby addresses a shortcoming of prior work in the organosilane area.

Experimental Section

For general experimental procedures, see the Supporting Information.

3-[(*t*-Butyldimethylsilyl)oxy]-propan-1-ol (21). Prepared by a modification of the published procedure.[20] Sodium hydride (6.0 g, 150 mmol) was washed with hexanes and combined with THF (200 mL) at room temperature. A solution of distilled 1,3-propanediol (11.9 mL, 165 mmol) in THF (40 mL) was added in a dropwise fashion, and the resultant mixture was stirred for 1 h. The mixture was cooled to 0 °C, and a solution of *t*-butyldimethylsilylchloride (22.6 g, 150 mmol) in THF (50 mL) was added in a dropwise manner. After stirring overnight at room temperature, 10% (w/w) aqueous K_2CO_3 was added and the mixture was concentrated in vacuo. Et_2O was added, and the organic layer was separated, washed with 10% K_2CO_3 and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (gradient, 100% hexane−20% EtOAc/hexane) to afford 25.4 g (89%) of the title compound as an oil. The ^{1}H NMR spectrum was consistent with the reported data.[20]

5-[(*t*-Butyldimethylsilyl)oxy]-1-pentyn-3-ol (23). Prepared by a modification of the published procedure.[19b,21] Dimethyl sulfoxide (4.7 mL, 66 mmol) in CH_2Cl_2 (20 mL) was added in a dropwise fashion to a solution of oxalyl chloride (2.0 M in CH_2Cl_2, 16.5 mL, 33 mmol) in CH_2Cl_2 (100 mL) at −78 °C. After stirring for 15 min, alcohol **21** (5.7 g, 30 mmol) in CH_2Cl_2 (20 mL) was then added in a dropwise fashion. After stirring for another 15 min, triethylamine (21 mL, 150 mmol) was added in a dropwise manner, and the resulting mixture was then stirred for 15 min. The reaction was allowed to warm to 15 °C and then was washed successively with water, ice-cold 0.1 M aqueous HCl, water, saturated aqueous $NaHCO_3$, and water. The organic layer was dried (Na_2SO_4) and concentrated in vacuo. The resultant oil was diluted with Et_2O, filtered through a pad of Celite to remove NEt_3·HCl salts, and concentrated in vacuo to provide aldehyde **22**[21] which was used immediately without further purification. Aldehyde **22** (4.7 g, 25 mmol) in THF (23 mL) was added in a dropwise fashion to a solution of ethynylmagnesium bromide (0.5 M in THF, 50 mL, 25 mmol) in THF (250 mL) at 0 °C. After complete addition, saturated aqueous NH_4Cl was added and the mixture was concentrated in vacuo. Et_2O was added, and the layers were separated. The aqueous layer was extracted with Et_2O (3×), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue

(38) Muxfeldt, H.; Schneider, R. S.; Mooberry, J. B. *J. Am. Chem. Soc.* **1966**, *88*, 3670−3671.
(39) Nichimata, T.; Mori, M. *J. Org. Chem.* **1998**, *63*, 7586−7587.
(40) (a) Warpehoski, M. A.; Chadaud, B.; Sharpless, K. B. *J. Org. Chem.* **1982**, *47*, 2897−2900. (b) Sharpless, K. B.; Verhoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63−74.
(41) For allylic oxidations performed on six-membered ring substrates that also contain basic amines, see: ref 38. Campos, O.; Cook, J. M. *Tetrahedron Lett.* **1979**, *19*, 1025−1028. Cain, M.; Comapos, O.; Guzman, F.; Cook, J. M. *J. Am. Chem. Soc.* **1983**, *105*, 907.
(42) (a) Snider, B. B.; Shi, B. *Tetrahedron* **1999**, *55*, 14823−14828. (b) Shibuya, K. *Synth. Commun.* **1994**, *24*, 2923−2941.
(43) Barton, D. H. R.; Crich, D. *Tetrahedron* **1985**, *41*, 4359−4364. Crich, D.; Zou, Y. *Org. Lett.* **2004**, *6*, 775−777.
(44) Umbreit, M. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 5526−5528.
(45) Yu, J. Q.; Corey, E. J. *Org. Lett.* **2002**, *4*, 2727−2730.
(46) Orita, A.; Watanabe, A.; Tsuchiya, H.; Otera, J. *Tetrahedron* **1999**, *55*, 2889−2898.

was chromatographed (gradient, 100% hexanes−10% EtOAc/hexanes) to afford 4.5 g (80% from **23**) of the title compound. The ^{1}H NMR spectrum was consistent with the reported data.[19b]

3-Methoxy-5-[(*t*-butyldimethylsilyl)oxy]-1-pentyne (24). Prepared by a modification of the published procedure.[19b] Sodium hydride (0.92 g, 23.0 mmol) was washed with hexanes, suspended in 80 mL of THF, and cooled to 0 °C. Alcohol **23** (4.48 g, 20.9 mmol) in THF (20 mL) was added in a dropwise fashion, and after complete addition, the ice bath was removed. Methyl iodide (2 mL, 31.4 mmol) was added, and the reaction was stirred overnight. Saturated aqueous NH_4Cl was added, and the mixture was concentrated in vacuo. After diluting with Et_2O, the mixture was extracted with Et_2O (3×). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (gradient, 100% hexanes−5% EtOAc/hexanes) to afford 4.3 g (90%) of the title compound. The ^{1}H NMR spectrum was consistent with the reported data.[19b]

(*Z*)-5-Methoxy-7-[(*t*-butyldimethylsilyl)oxy]-2-ethylsulfanyl-1,3-heptadiene (28). *sec*-Butyllithium (1.3 M in cyclohexane, 2.7 mL, 3.5 mmol)[47] was added in a dropwise fashion to a solution of ethyl vinyl sulfide (0.39 mL, 3.8 mmol) in THF−HMPA (9:1, 16.0 mL) at −78 °C. After stirring for 1 h, a solution of anhydrous $ZnCl_2$ (0.87 M in THF, 4.1 mL, 3.6 mmol) was added in a dropwise fashion, and the resultant mixture was then warmed to 0 °C. A solution of vinyl iodide **26** (1.14 g, 3.2 mmol) and $Pd(PPh_3)_4$ (185 mg, 0.16 mmol) in THF (8 mL) was added in a dropwise fashion, and the resultant mixture was then warmed to room temperature. After stirring for 18 h in the dark, the reaction was treated with saturated aqueous NH_4Cl and diluted with Et_2O. The organic layer was washed with saturated aqueous NH_4Cl, water, and saturated aqueous $NaHCO_3$. The combined aqueous layers were then extracted with Et_2O until the aqueous layer was clear and colorless. The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (gradient, 100% hexanes−3% EtOAc/hexanes) to afford 1.0 g (100%) of the title compound as a yellow oil: R_f = 0.36 (5% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.07 (dt, J = 11.7, 1.1 Hz, 1 H), 5.44 (dd, J = 11.7, 9.5 Hz, 1 H), 5.11 (d, J = 1.1 Hz, 1 H), 5.04 (s, 1 H), 4.40 (td, J = 9.5, 4.4 Hz, 1 H), 3.77−3.62 (m, 2 H), 3.23 (s, 3 H), 2.70 (q, J = 7.3 Hz, 2 H), 1.78−1.62 (m, 2 H), 1.27 (t, J = 7.3 Hz, 3 H), 0.87 (s, 9 H), 0.03 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 135.3, 130.6, 111.5, 73.1, 59.1, 56.3, 38.9, 25.9, 25.8, 18.2, 13.6, −5.4, −5.5; ^{13}C NMR (100 MHz, C_6D_6) δ 140.8, 136.3, 130.8, 111.2, 73.4, 59.5, 56.3, 39.5, 26.1, 26.0, 18.4, 13.7, −5.2, −5.3; IR (neat) 1588, 1471 cm^{-1}; MS (CI, NH_3) *m*/*z* (rel intensity) 317.1 [(M + H)$^+$, 13], 287.1 [(M − CH_2CH_3)$^+$, 14], 203.1 [(M − $C_6H_{13}Si$)$^+$, 30], 110.0 [($C_7H_{10}O$)$^+$, 100]; HRMS (CI, NH_3) calcd for $C_{16}H_{33}O_2SSi$ [(M + H)$^+$] 317.1971, found 317.1959.

(*Z*)-6-Ethylsulfanyl-3-methoxy-4,6-heptadien-1-ol (29). Tetrabutylammonium fluoride (1.0 M in THF, 3.5 mL) was added to a solution of silyl ether **28** (1.0 g, 3.2 mmol) in THF (16 mL) at room temperature. After stirring for 2.5 h in the dark, the mixture was treated with water and concentrated in vacuo. The mixture was diluted with EtOAc, and the organic layer was separated and washed with water and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (gradient, 100% hexanes−30% EtOAc/hexanes) to afford 600 mg (93%) of the title compound as an oil: R_f = 0.23 (30% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.13 (d, J = 11.7 Hz, 1 H), 5.47 (dd, J = 11.7, 9.2 Hz, 1 H), 5.04 (d, J = 1.5 Hz, 1 H), 5.01 (s, 1 H), 4.46 (td, J = 9.2, 4.4 Hz, 1 H), 3.75 (app q, J = 5.5 Hz, 2 H), 3.26 (s, 3 H), 2.72 (qd, J = 7.3, 1.5 Hz, 2 H), 2.62 (t, J = 5.7 Hz, 1 H), 1.92−1.80 (m, 1 H), 1.75−1.65 (m, 1 H), 1.28 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (100 MHz, C_6D_6) δ 140.7, 135.4, 131.1, 111.0, 76.0, 60.1, 56.2, 38.8, 25.9, 13.6; IR (neat) 3402 (br), 1589, 1449 cm^{-1}; MS (CI, NH_3) *m*/*z* (rel intensity) 203.1 [(M + H)$^+$, 60], 186.2 (100), 171.1 [(M − OCH_3)$^+$, 89], 141.1 [(M − SCH_2CH_3)$^+$, 61]; HRMS (CI, NH_3) calcd for $C_{10}H_{19}O_2S$ [(M + H)$^+$] 203.1106, found 203.1095. Anal. Calcd for $C_{10}H_{18}O_2S$: C, 59.37; H, 8.97. Found: C, 59.39; H, 8.89.

(*Z*)-6-Ethylsulfanyl-3-methoxy-4,6-heptadienal (30). Dimethyl sulfoxide (0.46 mL, 6.5 mmol) in CH_2Cl_2 (0.5 mL) was added in a dropwise fashion to a solution of oxalyl chloride (2.0 M in CH_2Cl_2, 1.6 mL, 3.3 mmol) in CH_2Cl_2 (15 mL) at −78 °C. After stirring for 15 min, alcohol **29** (600 mg, 2.96 mmol) in CH_2Cl_2 (1.0 mL) was added in a dropwise fashion. Upon stirring for another 15 min, triethylamine (2.1 mL, 14.8 mmol) was added over the course of 5 min. The reaction was warmed to room temperature and washed successively with water, ice-cold 0.1 M aqueous HCl, water, saturated aqueous $NaHCO_3$, and water. The organic layer was dried (Na_2SO_4) and concentrated in vacuo. The resultant oil was diluted with Et_2O, filtered through a pad of Celite to remove NEt_3·HCl salts, and concentrated in vacuo to provide 540 mg (91%) of the title compound. Aldehyde **30** was used immediately without further purification: R_f = 0.38 (20% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.78 (dd, J = 3.0, 1.9 Hz, 1 H), 6.19 (d, J = 11.5 Hz, 1 H), 5.50 (dd, J = 11.5, 9.3 Hz, 1 H), 5.08 (d, J = 1.4 Hz, 1 H), 5.05 (s, 1 H), 4.83−4.77 (m, 1 H), 3.29 (s, 3 H), 2.74 (q, J = 7.4 Hz, 2 H), 2.68 (ddd, J = 16.2, 8.8, 3.0 Hz, 1 H), 2.51 (ddd, J = 16.2, 4.0, 1.9 Hz, 1 H), 1.32 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (100 MHz, C_6D_6) δ 199.0, 140.6, 133.9, 131.6, 111.0, 72.4, 56.2, 49.5, 25.9, 13.5; IR (neat) 1726 (s), 1588, 1450 cm^{-1}.

3-[6-Bromo-3,4-(methylenedioxy)phenyl]-1-propanol (32). Prepared by a modification of the published procedure.[30] Lithium aluminum hydride (1.6 g, 42.1 mmol) in Et_2O (40 mL) was added to a solution of ester **31**[29] (5.3 g, 17.6 mmol) in Et_2O/THF (2:1, 75 mL) at 0 °C. After stirring for 1 h at 0 °C, water (1.6 mL), aqueous NaOH (2 M, 1.6 mL), and water (4.8 mL) were each carefully added to the mixture. The resulting slurry was filtered through a pad of Celite and concentrated in vacuo. The residue was chromatographed (40% EtOAc/hexanes) to afford 4.1 g (90%) yield of the title compound. The ^{1}H NMR spectrum was consistent with the reported data.[30]

(*Z*)-1-[3,4-(Methylenedioxy)phenyl]-3-methoxy-6-ethylsulfanyl-4,6-heptadien-1-ol (36). Aldehyde **30** (400 mg, 2.0 mmol) was diluted with THF (3 mL) and added in a dropwise fashion to a solution of 3,4-(methylenedioxy)phenylmagnesium bromide (**35**, 1.0 M in 50:50 THF/toluene, 2.1 mL, 2.1 mmol) in THF (7 mL) at 0 °C. The reaction was stirred for 30 min at 0 °C and then stirred for 1 h at room temperature. The mixture was treated with half-saturated aqueous NH_4Cl and diluted with Et_2O. The organic layer was separated and washed with half-saturated aqueous NH_4Cl and brine. The aqueous layer was re-extracted with Et_2O (3×), and the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed (gradient, 100% hexanes−20% EtOAc/hexanes) to afford 540 mg (84%) of two diastereomers (1:1 by ^{1}H NMR) of the title compound as a viscous, yellow oil. The diastereomers were separated only for characterization purposes, and the relative configuration was not determined. Less polar diastereomer: R_f = 0.26 (20% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (d, J = 1.5 Hz, 1 H), 6.81−6.73 (m, 2 H), 6.11 (d, J = 11.7 Hz, 1 H), 5.92 (s, 2 H), 5.55 (dd, J = 11.7, 9.4 Hz, 1 H), 4.95−4.90 (m, 3 H), 4.52−4.45 (m, 1 H), 3.52 (d, J = 4.8 Hz, 1 H), 3.25 (s, 3 H), 2.67 (qd, J = 7.3, 1.5 Hz, 2 H), 2.02−1.86 (m, 2 H), 1.24 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 146.5, 139.9, 138.7, 134.0, 131.2, 118.7, 111.1, 108.0, 106.3, 100.9, 74.9, 71.2, 56.4, 44.0, 25.9, 13.5; IR (neat) 3437 (br), 1588, 1502, 1487, 1442, 1245 cm^{-1}; MS (CI, NH_3) *m*/*z* (rel intensity) 323.1 [(M + H)$^+$, 12], 305.1 [(M − OH)$^+$, 43], 273.1 [(M − CH_5O_2)$^+$, 100], 261.1 [(M − SCH_2CH_3)$^+$, 22]; HRMS (CI, NH_3) calcd for $C_{17}H_{23}O_4S$ ([M + H]$^+$) 323.1317, found 323.1308. More polar diastereomer: R_f = 0.20 (20% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (d, J = 1.8 Hz, 1 H), 6.81−6.72 (m, 2 H), 6.12 (d, J = 11.4 Hz, 1 H), 5.91 (s, 2 H), 5.42 (dd, J =

(47) Titrated with diphenylacetic acid: Kofron, W. G.; Baclawshi, L. M. *J. Org. Chem.* **1976**, *41*, 1879−1880.

11.7, 9.2 Hz, 1 H), 4.99 (app s, 2 H), 4.82 (dd, J = 9.5, 1.8 Hz, 1 H), 4.51 (td, J = 9.7, 3.3 Hz, 1 H), 3.84 (d, J = 1.1 Hz, 1 H), 3.29 (s, 3 H), 2.71 (qd, J = 7.3, 1.3 Hz, 2 H), 1.99 (dt, J = 14.7, 9.7 Hz, 1 H), 1.71 (dt, J = 14.7, 3.3 Hz, 1 H), 1.28 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 146.6, 140.0, 138.5, 134.0, 131.2, 119.0, 110.8, 107.9, 106.4, 100.8, 77.2, 73.2, 56.3, 45.0, 25.9, 13.5; IR (neat) 3435 (br), 1653, 1488, 1443, 1245 cm^{-1}; MS (CI, NH_3) m/z (rel intensity) 323.1 [$(M + H)^+$, 31], 296.2 (72), 261.1 [$(M - SCH_2CH_3)^+$, 32], 247.1 [$(M - C_3H_7S)^+$, 100]; HRMS (CI, NH_3) calcd for $C_{17}H_{23}O_4S$ [$(M + H)^+$] 323.1317, found 323.1304.

(*Z*)-1-[3,4-(Methylenedioxy)phenyl]-3-methoxy-6-ethylsulfanyl-4,6-heptadienone (37). Manganese(IV) oxide (3.9 g) was added to a solution of diastereomeric alcohols **36** (161 mg, 0.5 mmol) in Et_2O (50 mL). The reaction was performed in a 1-neck round-bottom flask fitted with a ground-glass stopper. After stirring for 15 h in the dark, the mixture was filtered through a pad of Celite and rinsed with several portions of Et_2O. The filtrate was dried (Na_2SO_4) and concentrated in vacuo to afford 150 mg (94%) of the title compound as a yellow oil, which was used immediately without further purification. A small portion was purified by chromatography (gradient, 100% hexanes−5% EtOAc/hexanes) to provide an analytical sample for characterization purposes: R_f = 0.18 (10% EtOAc/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, J = 8.3, 1.7 Hz, 1 H), 7.44 (d, J = 1.7 Hz, 1 H), 6.82 (d, J = 1.7 Hz, 1 H), 6.82 (d, J = 8.3 Hz, 1 H), 6.14 (d, J = 11.6 Hz, 1 H), 6.02 (s, 2 H), 5.53 (dd, J = 11.6, 9.5 Hz, 1 H), 5.10 (d, J = 1.5 Hz, 1 H), 5.04 (s, 1 H), 4.88 (td, J = 9.5, 3.7 Hz, 1 H), 3.31−3.26 (m, 1 H), 3.24 (s, 3 H), 2.86 (dd, J = 15.6, 3.7 Hz, 1 H), 2.72 (q, J = 7.3 Hz, 2 H), 1.28 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.4, 151.7, 148.1, 139.8, 133.9, 132.1, 131.3, 124.7, 111.1, 108.0, 107.7, 101.8, 73.3, 56.6, 44.3, 25.9, 13.5; IR (neat) 1677 (s), 1603, 1504, 1488, 1443, 1355, 1248 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{20}NaO_4S$ [$(M + Na)^+$] 343.0980, found 343.0977.

(3aα,6α,7aα)-2,3,3a,6,7,7a-Hexahydro-3a-ethylsulfanyl-6-methoxy-7a-[3,4-(methylenedioxy)phenyl]indole (39). A solution of amine **17**[10a] (42 mg, 0.13 mmol) in toluene (0.3 mL) was cooled to 0 °C. Trimethylaluminum (2.0 M in heptane, 66 μL, 0.13 mmol) was added in a dropwise fashion, followed by the dropwise addition of ketone **37** (28 mg, 0.09 mmol) in toluene (0.6 mL). After stirring for 2 h, benzyl bromide (31 μL, 0.26 mmol) was added, and the mixture was placed in an oil bath preheated to 110 °C and heated to reflux for 4.5 h. Upon cooling to room temperature, EtOAc and saturated aqueous NH_4Cl were added and the layers were separated. The organic layer was washed with water, saturated aqueous $NaHCO_3$, water, and brine. The aqueous layers were back-extracted with EtOAc (3×). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed (gradient, 100% hexanes−50% EtOAc/hexanes) to afford 8 mg (28%) of the title compound as a single diastereomer: R_f = 0.32 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.00 (d, J = 2.0 Hz, 1 H), 6.94 (dd, J = 8.3, 2.0 Hz, 1 H), 6.77 (d, J = 8.3 Hz, 1 H), 5.96 (s, 2 H), 5.93 (dd, J = 10.0, 2.0 Hz, 1 H), 5.60 (dd, J = 10.3, 2.0 Hz, 1 H), 4.15 (tt, J = 8.1, 2.0 Hz, 1 H), 3.41 (s, 3 H), 3.26 (t, J = 9.0 Hz, 1 H), 3.06 (dt, J = 10.5, 6.8 Hz, 1 H), 2.37 (dq, J = 11.5, 7.3 Hz, 1 H), 2.20 (d, J = 8.1 Hz, 2 H), 2.12−2.01 (m, 2 H), 1.76 (dd, J = 12.7, 6.6 Hz, 1 H), 1.56 (br s, 1 H), 1.06 (t, J = 7.6 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.0, 146.2, 141.8, 133.5, 128.4, 120.1, 108.1, 107.0, 101.0, 74.2, 68.3, 56.7, 56.1, 43.8, 36.1, 35.8, 23.5, 14.4; IR (neat) 3382 (br), 1607 cm^{-1}; MS (EI, 70 eV) m/z (rel intensity) 272.2 [$(M - SCH_2CH_3)^+$, 100], 240.2 [$(M - C_3H_9O)^+$, 18], 147.1 (44); HRMS (ESI) calcd for $C_{18}H_{24}NO_3S$ [$(M + H)^+$] 334.1477, found 334.1477.

(3aα,6α,7aα)-2,3,3a,6,7,7a-Hexahydro-1-benzenesulfonyl-3a-ethylsulfanyl-6-methoxy-7a-[3,4-(methylenedioxy)phenyl]-indole (40). Benzenesulfonyl chloride (50 μL, 0.4 mmol) and 4-dimethylaminopyridine (1 mg, 0.01 mmol) were added to a solution of amine **39** (10 mg, 0.03 mmol) in pyridine (0.10 mL) at room temperature. After stirring overnight, water was added and the mixture was extracted with EtOAc (3×). The combined organic layers were washed with 1 M aqueous HCl, water, saturated aqueous $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (30% EtOAc/hexanes) to afford 7 mg (49%) of the title compound as a white solid: mp = 161−162 °C; R_f = 0.28 (30% EtOAc/hexane); ^{1}H NMR (500 MHz, C_6D_6) δ 7.58−7.54 (m, 2 H, SO_2Ph), 6.96−6.92 (m, 1 H, SO_2Ph), 6.88−6.84 (m, 2 H, SO_2Ph), 6.48 (br s, 1 H, Ar-*H*), 6.43 (d, J = 8.3 Hz, 1 H, Ar-*H*), 6.37 (br d, J = 7.6 Hz, 1 H, Ar-*H*), 5.97 (dt, J = 10.0, 1.7 Hz, 1 H, CH=C*H*, H-5), 5.25 (AB_q, J = 1.5 Hz, $\Delta\nu_{AB}$ = 10.0 Hz, 2H, OCH_2O), 5.19 (dd, J = 10.0, 2.1 Hz, 1 H, CH=C*H*, H-4), 4.53 (ddt, J = 10.0, 5.1, 1.7 Hz, 1 H, H-6β), 3.57 (ddd, J = 12.7, 5.1, 1.2 Hz, 1 H, H-7β), 3.40−3.34 (m, 1 H, H-2), 3.36 (s, 3 H, OCH_3), 3.22 (t, J = 9.0 Hz, 1 H, H-2), 2.37 (dd, J = 12.7, 10.0 Hz, 1 H, H-7α), 2.02 (dq, J = 11.2, 7.3 Hz, 1 H, SCH_2), 1.86−1.75 (m, 2 H, SCH_2, H-3), 1.27 (dd, J = 12.7, 6.6 Hz, 1 H, H-3), 0.76 (t, J = 7.6 Hz, 3 H, SCH_2CH_3); ^{13}C NMR (100 MHz, C_6D_6) δ 147.0, 146.7, 139.9, 136.5, 132.3, 131.0, 128.5, 127.5, 121.1, 108.6, 106.9, 101.1, 74.4, 73.9, 59.3, 56.5, 47.0, 34.8, 33.5, 23.2, 14.3; IR (CH_2Cl_2) 1335, 1157 cm^{-1}; MS (EI, 70 eV) m/z (rel intensity) 473.4 [$(M)^+$, 6], 412.4 [$(M - SCH_2CH_3)^+$, 100]; HRMS (ESI) calcd for $C_{24}H_{27}NNaO_5S_2$ [$(M + Na)^+$] 496.1228, found 496.1220. All ^{1}H assignments were made from a two-dimensional COSY experiment.

1-[(*t*-Butyldimethylsilyl)oxy]-5-iodo-4-pentyne (48). *n*-Butyllithium (2.0 M in hexanes, 38 mL, 77.4 mmol)[47] was added to a solution of alkyne **47**[35] (12.8 g, 64.5 mmol) in THF (230 mL) at −78 °C. After stirring for 1 h at −78 °C, a solution of I_2 (19.7 g, 77.4 mmol) in THF (100 mL) was added via cannula and the resulting mixture was then warmed to room temperature. After stirring for 1 h, the reaction was treated with water and concentrated in vacuo. The mixture was extracted with Et_2O (3×). The combined organic layers were washed with saturated aqueous $Na_2S_2O_3$ (2×) and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed (gradient, 100% hexanes−3% EtOAc/hexanes) to afford 19.7 g (94%) of the title compound as a colorless oil: R_f = 0.26 (2% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.68 (t, J = 6.1 Hz, 2 H), 2.46 (t, J = 7.1 Hz, 2 H), 1.72 (ddd, J = 13.2, 6.8, 6.8 Hz, 2 H), 0.90 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 94.2, 61.3, 31.4, 25.9, 18.2, 17.2, −5.4, −7.1; IR (neat) 2361 (w) cm^{-1}; MS (CI, NH_3) m/z (rel intensity) 325.1 [$(M + H)^+$, 4], 267.0 [$(M - C(CH_3)_3)^+$, 100]; HRMS (CI, NH_3) calcd for $C_{11}H_{22}IOSi$ 325.0485, found 325.0481. Anal. Calcd for $C_{11}H_{21}IOSi$: C, 40.74; H, 6.63. Found: C, 40.60; H, 6.58.

(*Z*)-1-[(*t*-Butyldimethylsilyl)oxy]-5-iodo-4-pentene (49). BH_3·Me_2S (2.0 M in THF, 21 mL, 42.8 mmol) was added to a solution of cyclohexane (8.6 mL, 85.1 mmol) in Et_2O (280 mL) at 0 °C. After stirring for 1 h at 0 °C, alkyne **48** in Et_2O (50 mL) was added via cannula and the resulting mixture was allowed to warm to room temperature. After stirring for 90 min, acetic acid (35 mL, 604 mmol) was added to the mixture. Upon stirring for another 30 min, the mixture was carefully poured into saturated aqueous $NaHCO_3$ (200 mL) cooled to 0 °C. The mixture was extracted with Et_2O (3×). The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed (gradient, 100% hexanes−2% EtOAc/hexanes) to afford 6.7 g (75%) of the title compound. The ^{1}H NMR spectrum was consistent with the reported data.[48]

(*Z*)-6-Ethylsulfanyl-4,6-heptadien-1-ol (51). *sec*-Butyllithium (1.1 M in cyclohexane, 20.1 mL, 22.6 mmol)[47] was added to a solution of ethyl vinyl sulfide (2.5 mL, 24.6 mmol) in THF−HMPA (9:1, 103 mL) at −78 °C. After stirring for 1 h, a solution of anhydrous $ZnCl_2$ (0.9 M in THF, 25.7 mL, 23.1 mmol) was added and the resultant mixture was then warmed to 0 °C. A solution of vinyl iodide **49** (6.70 g, 20.5 mmol) and $Pd(PPh_3)_4$ (1.2 g, 1.0 mmol)

(48) Mukai, C.; Sugimoto, Y.; Ikeda, Y.; Hanaoka, M. *Tetrahedron* **1998**, *54*, 823−850.

in THF (51 mL) was added via cannula. After stirring for 18 h in the dark at room temperature, the reaction was treated with saturated aqueous NH_4Cl and concentrated in vacuo. The mixture was extracted with Et_2O (3×). The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated in vacuo. The crude residue was then diluted with THF (100 mL), and tetrabutylammonium fluoride (1.0 M in THF, 35 mL, 34.9) was added at room temperature. After stirring for 90 min, the mixture was treated with water and extracted with Et_2O (3×). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (17% EtOAc, 3% Et_3N, 80% hexanes) to afford 3.0 g (86%) of the title compound as a colorless oil: $R_f = 0.17$ (20% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 (dd, $J = 11.2$, 1.5 Hz, 1 H), 5.54 (dt, $J = 11.2$, 7.3 Hz, 1 H), 5.06 (d, 1.5 Hz, 1 H), 5.03 (s, 1 H), 3.58 (t, $J = 6.3$ Hz, 2 H), 2.66 (ddd, $J = 7.3$, 7.3, 7.3 Hz, 2 H), 2.32 (dt, $J = 7.6$, 1.7 Hz, 2 H), 2.27 (br s, 1 H), 1.61 (ddd, $J = 14.2$, 6.6, 6.6 Hz, 2 H), 1.23 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.1, 133.9, 128.1, 110.8, 61.9, 32.5, 25.7, 24.7, 13.7; IR (neat) 3340 (br), 1633 (w); MS (EI, 70 eV) *m*/*z* (rel intensity) 172.1 [$(M)^+$, 9], 143.0 [$(M - CH_2CH_3)^+$, 39], 125.0 [$(M - CH_2CH_3 - H_2O)^+$, 100]; HRMS (EI, 70 eV) calcd for $C_9H_{16}OS$ (M^+) 172.0922, found 172.0924.

(*Z*)-6-Ethylsulfanyl-4,6-heptadien-1-ol (52). Sodium periodate (5.3 g, 24.6 mmol) followed by water (20 mL) was added to a solution of vinyl sulfide **51** (3.0 g, 17.6 mmol) in MeOH (150 mL) at room temperature. After stirring for 1 h, the reaction was concentrated in vacuo. The mixture was diluted with CH_2Cl_2 and saturated aqueous $NaHCO_3$ and extracted (3×). The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (1% Et_3N/EtOAc) to afford 2.7 g (80%) of the title compound as a colorless oil: $R_f = 0.13$ (100% EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.86 (s, 1 H), 5.80 (dt, $J = 11.5$, 7.3 Hz, 1 H), 5.73 (dd, $J = 11.7$, 1.2 Hz, 1 H), 5.67 (s, 1 H), 3.52 (t, $J = 6.4$ Hz, 2 H), 3.23 (br s, 1 H), 2.74 (dq, $J = 14.9$, 7.6 Hz, 1 H), 2.48 (dq, $J = 14.7$, 7.3 Hz, 1 H), 2.29−2.16 (m, 2 H), 1.61−152 (m, 2 H), 1.11 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.0, 138.7, 119.3, 118.9, 61.3, 44.2, 32.1, 25.5, 5.2; IR (neat) 3410 (br), 1630, 1059 (s) cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel intensity) 189.1 [$(M + H)^+$, 4], 171.1 [$(M - H_2O)^+$, 28], 111.1 [$(M - S(O)CH_2CH_3)^+$, 37], 77.0 (100); HRMS (EI, 70 eV) calcd for $C_9H_{17}O_2S$ [$(M + H)^+$] 189.0949, found 189.0953.

(*Z*)-6-Ethylsulfanyl-4,6-heptadien-1-al (53). Dimethyl sulfoxide (0.39 mL, 5.6 mmol) in CH_2Cl_2 (1.0 mL) was added in a dropwise fashion to a solution of oxalyl chloride (2.0 M in CH_2Cl_2, 1.4 mL, 2.8 mmol) in CH_2Cl_2 (9 mL) via cannula at −78 °C. After stirring for 10 min, alcohol **52** (476 mg, 2.5 mmol) in CH_2Cl_2 (2.6 mL) was then added in a dropwise fashion via cannula. After stirring for 30 min, triethylamine (1.8 mL, 12.6 mmol) was added. The reaction was warmed to room temperature, treated with water, and extracted with CH_2Cl_2 (3×). The combined organic layers were washed successively with water, saturated aqueous $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated in vacuo. The resultant oil was diluted with Et_2O, filtered through a pad of Celite to remove triethylamine salts, and concentrated in vacuo to afford 140 mg (93%) of the title compound as a colorless oil. Aldehyde **53** was used immediately without further purification: $R_f = 0.33$ (100% EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.79 (d, $J = 1.0$ Hz, 1 H), 6.02 (d, $J = 1.0$ Hz, 1 H), 5.88 (d, $J = 11.5$ Hz, 1 H), 5.80 (dt, $J = 11.5$, 7.1 Hz, 1 H), 5.76 (s, 1 H), 2.84 (dddd, $J = 14.9$, 7.6, 7.6, 7.6 Hz, 1 H), 2.62−2.51 (m, 5 H), 1.22 (dt, $J = 7.6$, 1.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.6, 147.4, 136.2, 120.7, 118.9, 44.4, 43.1, 21.6, 5.2; IR (neat) 2828, 2727, 1721 (s), 1634, 1059 (s) cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel intensity) 186.1 [$(M)^+$, 2], 157.1 [$(M - CH_2CH_3)^+$, 9], 109.1 [$(M - S(O)CH_2CH_3)^+$, 79], 81.1 [$(M - S(O)CH_2CH_3 - CHO)^+$, 100]; HRMS (EI, 70 eV) calcd for $C_9H_{14}O_2S$ (M^+) 186.0714, found 186.0708.

(*Z*)-1-[3,4-(Methylenedioxy)phenyl]-6-ethanesulfinyl-4,6-heptadien-1-ol (54). 3,4-(Methylenedioxy)phenylmagnesium bromide (**35**, 1.0 M in 50:50 THF/toluene, 0.6 mL, 0.46 mmol) was added to a solution of aldehyde **53** (78 mg, 0.42 mmol) in THF (2 mL) at −30 °C. After stirring for 30 min, the mixture was treated with half-saturated aqueous NH_4Cl. After warming to room temperature, the mixture was extracted with Et_2O (3×). The combined organic layers were washed with half-saturated aqueous NH_4Cl and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (100% EtOAc) to afford 73 mg (56%) of the title compound as a colorless oil that contained two inseparable diastereomers (1:1 by NMR): $R_f = 0.10$ (33% EtOAc/CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 (s, 1 H), 6.72−6.68 (m, 2 H), 5.88 (app d, $J = 1.7$ Hz, 2 H), 5.85 (d, $J = 3.4$ Hz, 1 H), 5.83−5.71 (m, 2 H), 5.64 (d, $J = 3.4$ Hz, 1 H), 4.54−4.49 (m, 1 H), 3.25 (d, $J = 2.7$ Hz, 0.5 H), 3.16 (d, $J = 2.5$ Hz, 0.5 H), 2.76−2.67 (m, 1 H), 2.51−2.40 (m, 1 H), 2.30−2.13 (m, 2 H), 1.82−1.75 (m, 1 H), 1.72−1.62 (m, 1 H), 1.11 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.6, 147.5, 147.1, 146.7, 146.6, 138.7, 138.6, 138.4, 138.2, 131.9, 131.8, 128.4, 128.3, 119.5, 119.1, 119.0, 118.7, 107.84, 107.82, 106.16, 106.15, 100.79, 100.77, 73.2, 72.9, 44.32, 44.28, 38.6, 25.69, 25.57, 5.3, 5.2; IR (neat) 3378 (br), 1609, 1040 (s) cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{20}NaO_4S$ 331.0980, found 331.0977.

(*Z*)-1-[3,4-(Methylenedioxy)phenyl]-6-ethanesulfinyl-4,6-heptadien-1-one (55). Dimethyl sulfoxide (3.5 M in CH_2Cl_2, 150 μL, 0.52 mmol) was added in a dropwise fashion to a solution of oxalyl chloride (2.0 M in CH_2Cl_2, 130 μL, 0.26 mmol) in CH_2Cl_2 (0.8 mL) at −78 °C. Stirring for 10 min, alcohol **54** (73 mg, 0.24 mmol) in CH_2Cl_2 (0.4 mL) was then added in a dropwise fashion via cannula. After stirring for 30 min, triethylamine (0.17 mL, 1.2 mmol) was added. The reaction was warmed to room temperature, treated with water, and extracted with CH_2Cl_2 (3×). The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (75% EtOAc/hexanes) to afford 61 mg (84%) of the title compound as a colorless oil: $R_f = 0.31$ (75% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (dd, $J = 8.1$, 1.7 Hz, 1 H), 7.42 (d, $J = 1.7$ Hz, 1 H), 6.85 (d, $J = 8.3$ Hz, 1 H), 6.04 (s, 2 H), 6.00 (s, 1 H), 5.91−5.84 (m, 2 H), 5.78 (s, 1 H), 3.02 (t, $J = 7.1$ Hz, 2 H), 2.82 (dddd, $J = 14.7$, 7.3, 7.3, 7.3 Hz, 1 H), 2.68−2.62 (m, 2H), 2.56 (dddd, $J = 14.7$, 7.3, 7.3, 7.3 Hz, 1 H), 1.22 (t, $J = 7.6$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.6, 151.8, 148.2, 147.5, 137.2, 131.4, 124.2, 120.4, 118.9, 107.8, 107.7, 101.8, 44.6, 37.7, 23.9, 5.4; IR (neat) 1675 (s), 1604, 1037 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{18}NaO_4S$ [$(M + Na)^+$] 329.0824, found 329.0822.

(3aα,7aα)-2,3,3a,6,7,7a-Hexahydro-3a-ethylsulfinyl-7a-[3,4-(methylenedioxy)phenyl]-1*H*-indole (57). Trimethylaluminum (2.0 M, in heptane 0.22 mL, 0.45 mmol) was added to a solution of amine **17**[10a] (143 mg, 0.45 mmol) in toluene (1.4 mL) at room temperature. After stirring for 5 min, a solution of ketone **55** (62 mg, 0.20 mmol) in toluene (0.6 mL) was added via cannula. After stirring for an additional 90 min, the reaction was treated with saturated aqueous $NaHCO_3$ and extracted with Et_2O (3×). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. Without further purification, the crude residue ($R_f = 0.38$ (50% EtOAc/hexanes using neutral Alumina plates)) was dissolved in toluene (10 mL) at room temperature. Chlorotrimethylsilane (26 μL, 0.20 mmol) was added, and the reaction was heated to 55 °C. After stirring for 3 h, the mixture was cooled to room temperature and concentrated in vacuo. The residue was chromatographed on neutral alumina (gradient, 2%−10% MeOH/EtOAc) to afford 38 mg (59%) of the title compound as a yellow oil containing two inseparable diastereomers: $R_f = 0.55$ (5% MeOH/EtOAc, neutral alumina plate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 (d, $J = 2.0$ Hz, 1 H), 6.98 (dd, $J = 8.3$, 2.0 Hz, 1 H), 6.77 (d, $J = 8.3$ Hz, 1 H), 6.14 (dt, $J = 10.3$, 3.9 Hz, 1 H), 5.96 (AB_q, $J = 1.5$ Hz, $\Delta\nu = 8.6$ Hz, 2 H), 5.75 (dt, $J = 10.3$,

2.0 Hz, 1 H), 3.29 (ddd, J = 11.5, 9.8, 2.7 Hz, 1 H), 3.18 (dt, J = 11.2, 8.3 Hz, 1 H), 2.82 (dt, J = 13.4, 9.0 Hz, 1 H), 2.67−2.52 (m, 2 H), 2.35−2.18 (m, 2 H), 2.02−1.91 (m, 2 H), 1.81 (dt, J = 13.4, 5.9 Hz, 1 H), 1.27 (t, J = 7.6 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.4, 146.5, 137.3, 132.7, 125.3, 120.2, 108.1, 107.5, 101.0, 70.0, 67.8, 44.0, 41.3, 34.2, 31.7, 22.5, 7.8; IR (neat) 3343 (br), 1673, 1609, 1039 (s) cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{20}NO_3S$ [(M + H)$^+$] 320.1320, found 320.1315.

2,6,7,7a-Tetrahydro-7a-[3,4-(methylenedioxy)phenyl]-1*H*-indole (58). Trimethylaluminum (2.0 M, in heptane, 75 μL, 0.15 mmol) was added to a solution of amine **17**[10a] (48 mg, 0.15 mmol) in 0.4 mL of toluene at room temperature. After stirring for 5 min, a solution of ketone **55** (21 mg, 0.07 mmol) in 0.3 mL of toluene was added via cannula. After stirring an additional 90 min, the reaction was treated with saturated aqueous $NaHCO_3$ and extracted with Et_2O (3×). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. Without further purification, the crude residue (R_f = 0.38 (50% EtOAc/hexanes using neutral Alumina plates)) was dissolved in toluene (1.7 mL) and placed in a sealed tube at room temperature. Chlorotrimethylsilane (8.7 μL, 0.07 mmol) was added, and the reaction was heated to 65 °C. After stirring for 14 h, the mixture was cooled to room temperature and concentrated in vacuo. The residue was chromatographed (3% Et_3N, 2% MeOH/EtOAc) to afford 8.0 mg (48%) of the title compound as a yellow oil: R_f = 0.42 (15% MeOH/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.88 (d, J = 1.7 Hz, 1 H), 6.84 (dd, J = 8.1, 1.7 Hz, 1 H), 6.74 (d, J = 8.1 Hz, 1 H), 6.41 (dd, J = 9.8, 2.7 Hz, 1 H), 5.93 (AB_q, J = 1.5 Hz, $\Delta\nu_{AB}$ = 1.9 Hz, 2 H), 5.81−5.75 (m, 2 H), 3.63 (dd, J = 21.5, 15.4 Hz, 2 H), 2.95−2.62 (m, 2 H), 2.47 (dd, J = 12.5, 4.9 Hz, 1 H), 2.14 (dt, J = 18.8, 5.1 Hz, 1 H), 1.94 (dt, J = 12.2, 4.9 Hz, 1 H), 1.81−1.72 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.6, 146.4, 141.8, 131.6, 122.5, 122.3, 119.3, 108.0, 106.9, 100.9, 77.2, 69.6, 50.7, 36.1, 24.7; IR (neat) 3299, 1676, 1607 cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel intensity) 241.1 [(M)$^+$, 100]; HRMS (ESI) calcd for $C_{15}H_{16}NO_2$ [(M + H)$^+$] 242.1181, found 242.1185.

3-[6-Bromo-3,4-(methylenedioxy)phenyl]-1-[dimethyl-1,1,2-(trimethylpropyl)silyloxy]propane (59). Triethylamine (0.63 mL, 4.6 mmol), dimethylthexylsilyl chloride (0.86 mL, 4.1 mmol) and 4-dimethylaminopyridine (15 mg, 0.12 mmol) were each added to a solution of alcohol **32** (1.1 g, 4.1 mmol) in CH_2Cl_2 (8.3 mL) at room temperature. After stirring for 14 h, the mixture was filtered through a pad of Celite and concentrated in vacuo. The residue was chromatographed (2% EtOAc/hexanes) to afford 1.6 g (95%) of the title compound as a colorless oil: R_f = 0.29 (2% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98 (s, 1 H), 6.72 (s, 1 H), 5.94 (s, 2 H), 3.62 (t, J = 6.2 Hz, 2 H), 2.73−2.67 (m, 2 H), 1.80−1.71 (m, 2 H), 1.64 (septet, J = 7.0 Hz, 1 H), 0.90 (d, J = 7.0 Hz, 6 H), 0.86 (s, 6 H), 0.95 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2, 146.5, 134.7, 114.3, 112.6, 110.0, 101.5, 61.9, 34.2, 33.0, 32.6, 25.1, 20.4, 18.6, −3.4; IR (neat) 1503, 1477, 830 cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel intensity) 316.9 [(M + 2 − $C(CH_3)_2$-$CH(CH_3)_2$)$^+$, 100], 314.9 [(M − $C(CH_3)_2CH(CH_3)_2$)$^+$, 100], 236.0 [(M − Br − $C(CH_3)_2CH(CH_3)_2$, 37]; HRMS (ESI) calcd for $^{79}BrC_{18}H_{29}NaO_3Si$ [(M + Na)$^+$] 423.0967, found 423.0958.

(*Z*)-1-(6-{3-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]propyl}-3,4-(methylenedioxy)phenyl)-6-ethanesulfinyl-4,6-heptadien-1-ol (60). *tert*-Butyllithium (1.73 M in pentane, 2.8 mL, 4.9 mmol) was added to a solution of bromide **59** (930 mg, 2.3 mmol) in THF (10 mL) at −78 °C. After stirring for 10 min, $MgBr_2$[49] (0.2 M in THF, 16 mL, 3.2 mmol) was added to the mixture, and after an additional 15 min, a solution of aldehyde **53** (430 mg, 2.3 mmol) in THF (2 mL) was added via cannula. Following another 15 min, the mixture was treated with half-saturated aqueous NH_4Cl. After warming to room temperature, the mixture was extracted with Et_2O (3×). The combined organic layers were washed with half-saturated aqueous NH_4Cl and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (60% EtOAc/hexanes) to afford 620 mg (53%) of the title compound as a colorless oil that contained two inseparable diastereomers (ratio not determined): R_f = 0.50 (50% EtOAc/CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.95 (d, J = 0.7 Hz, 1 H), 6.61 (d, J = 1.7 Hz, 1H), 5.96 (d, J = 1.5 Hz, 1 H), 5.92 (d, J = 2.2 Hz, 2 H), 5.90−5.79 (m, 2 H), 5.74 (d, J = 4.9 Hz, 1 H), 4.92 (dddd, J = 7.8, 7.8, 4.2, 4.2 Hz, 1 H), 3.65−3.55 (m, 2 H), 2.81 (dddd, J = 14.7, 7.3, 7.3, 7.3 Hz, 1 H), 2.67 (dddd, J = 15.1, 8.6, 8.6, 8.6 Hz, 1 H), 2.61−2.49 (m, 2 H), 2.45−2.25 (m, 2 H), 1.91−1.82 (m, 1 H), 1.78−1.64 (m, 3 H), 1.63 (dddd, J = 13.2, 6.8, 6.8, 6.8 Hz, 1 H), 1.19 (t, J = 7.6 Hz, 3 H), 0.90 (d, J = 6.8 Hz, 6 H), 0.85 (s, 6 H), 0.09 (d, J = 4.4 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.4, 146.7, 146.6, 146.10, 146.07, 138.3, 138.2, 135.5, 135.4, 132.4, 132.3, 119.83, 119.78, 119.2, 118.8, 109.3, 109.2, 105.77, 105.75, 100.80, 100.78, 69.0, 68.7, 61.81, 61.77, 69.0, 68.7, 61.81, 61.77, 44.44, 44.42, 38.03, 38.02, 34.8, 34.7, 34.1, 28.4, 26.2, 26.0, 25.1, 20.3, 18.5, 5.4, 5.3, −3.37, −3.41; IR (neat) 3389 (s), 1623, 1041 (s) cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{44}NaO_5SSi$ [(M + Na)$^+$] 531.2576, found 531.2578.

(*Z*)-1-(6-{3-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]propyl}-3,4-(methylenedioxy)phenyl)-6-ethanesulfinyl-4,6-heptadien-1-one (61). Dimethyl sulfoxide (0.48 mL, 6.8 mmol) was added in a dropwise fashion to a solution of oxalyl chloride (0.30 mL, 3.4 mmol) in CH_2Cl_2 (12 mL) at −78 °C. After stirring for 10 min, alcohol **60** (1.6 g, 3.1 mmol) in CH_2Cl_2 (4 mL) was then added via cannula. After stirring for an additional 30 min, triethylamine (2.1 mL, 15 mmol) was added. The reaction was warmed to room temperature, treated with water, and extracted with CH_2Cl_2 (3×). The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (gradient, 33−50% EtOAc/hexanes) to afford 1.2 g (76%) of the title compound as a colorless oil: R_f = 0.29 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (s, 1 H), 6.72 (s, 1 H), 5.99 (s, 1 H), 5.98 (s, 2 H), 5.86−5.83 (m, 2 H), 5.76 (s, 1 H), 3.59 (t, J = 6.4 Hz, 2 H), 2.92 (t, J = 7.3 Hz, 2 H), 2.87−2.76 (m, 3 H), 2.63−2.58 (m, 2 H), 2.57−2.50 (m, 1 H), 1.76−1.69 (m, 2 H), 1.61 (dddd, J = 13.7, 13.7, 6.8, 6.8 Hz, 1 H), 1.20 (t, J = 7.3 Hz, 3 H), 0.87 (d, J = 6.8 Hz, 6 H), 0.83 (s, 6 H), 0.07 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.2, 149.9, 147.5, 145.5, 139.3, 137.1, 130.4, 120.4, 118.9, 111.3, 108.5, 101.6, 62.2, 44.6, 40.7, 34.7, 34.1, 30.7, 25.0, 24.1, 20.3, 18.5, 5.3, −3.4; IR (neat) 1682 (s), 1610, 1061 (s) cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{42}NaO_5SSi$ [(M + Na)$^+$] 529.2420, found 529.2419.

(*Z*)-1-[6-(3-Hydroxypropyl)-3,4-(methylenedioxy)phenyl]-6-ethanesulfinyl-4,6-heptadien-1-one (62). Hydrogen fluoride-pyridine (0.1 mL) was added to a solution of silyl ether **61** (90 mg, 0.18 mmol) in CH_3CN (1.4 mL) at room temperature. After stirring for 3 h, the mixture was carefully neutralized with solid $NaHCO_3$, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (gradient, 100% EtOAc−3% MeOH/EtOAc) to afford 60 mg (93%) of the title compound as colorless oil: R_f = 0.25 (100% EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (s, 1 H), 6.73 (s, 1 H), 5.99 (s, 2 H), 5.98 (s, 1 H), 5.87−5.83 (m, 2 H), 5.76 (s, 1 H), 3.56 (t, J = 5.9 Hz, 2 H), 2.94 (t, J = 7.0 Hz, 2 H), 2.87−2.78 (m, 3 H), 2.63−2.51 (m, 4 H), 1.82 (dddd, J = 5.9, 5.9, 5.9, 5.9 Hz, 2 H), 1.20 (t, J = 7.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.4, 150.3, 147.4, 145.7, 138.7, 137.1, 130.6, 120.5, 119.1, 111.1, 108.5, 101.7, 61.2, 44.6, 40.8, 34.5, 29.6, 24.1, 5.4; IR (neat) 3400 (s), 1683 (s), 1609, 1038 cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel intensity) 347.1 [(M − H_2O)$^+$, 5], 287.1 [(M − S(O)-CH_2CH_3)$^+$, 42], 207.0 [(M − $C_8H_{13}OS$), 100]; HRMS (ESI) calcd for $C_{19}H_{24}NaO_5S$ [(M + Na)$^+$] 387.1242, found 387.1237.

(*Z*)-1-[6-(3-Iodopropyl)-3,4-(methylenedioxy)phenyl]-6-ethanesulfinyl-4,6-heptadien-1-one (63). Triphenylphosphine (150 mg, 0.58), imidazole (63 mg, 0.92 mmol), and I_2 (105 mg, 0.42 mmol) were sequentially added to a solution of alcohol **62** (84 mg, 0.23 mmol) in CH_2Cl_2 (3.9 mL) in the dark at 0 °C. After stirring for

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15 min, the mixture was warmed to room temperature. Upon stirring for an additional 30 min, the mixture was treated with 5% (w/w) aqueous $Na_2S_2O_4$ and extracted with CH_2Cl_2 (3×). The combined organic layers were washed with 5% aqueous $Na_2S_2O_4$ and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (gradient, 33%−66% EtOAc/hexanes) to afford 80 mg (73%) as a colorless oil: R_f = 0.31 (66% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 (s, 1 H), 6.76 (s, 1 H), 6.02 (s, 2 H), 6.01 (s, 1 H), 5.90−5.83 (m, 2 H), 5.78 (s, 1 H), 3.21 (t, J = 6.8 Hz, 2 H), 2.95 (t, J = 7.1 Hz, 2 H), 2.89−2.81 (m, 3 H), 2.66−2.53 (m, 3 H), 2.09 (q, J = 7.1 Hz, 2 H), 1.23 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.0, 150.2, 147.6, 145.9, 137.8, 137.0, 130.2, 120.6, 119.0, 111.4, 108.9, 101.8, 44.7, 40.6, 35.4, 35.2, 24.2, 6.6, 5.5; IR (neat) 1679 (s), 1609, 1038 cm^{-1}; MS (EI, 70 eV) 397.0 [(M − S(O)CH_2CH_3)$^+$, 86], 317.0 [(M − $C_8H_{13}OS$)$^+$, 100]; HRMS (ESI) calcd for $C_{19}H_{23}INaO_4S$ [(M + Na)$^+$] 497.0260, found 497.0266.

Demethoxyschelhammeridine (65). Iodide **63** (11 mg, 0.02 mmol) in toluene (0.4 mL) was added to a solution of amine **17**[10a] (18 mg, 0.06 mmol) in toluene (0.4 mL) at 85 °C. After stirring for 5 h, the reaction was treated with EtOH, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (5% MeOH/EtOAc) to afford 4 mg (56%) of the title compound as a yellow oil: R_f = 0.23 (5% MeOH/EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.61 (s, 1 H), 6.53 (s, 1 H), 6.40 (dd, J = 9.8, 2.6 Hz, 1 H), 5.89 (AB_q, J = 1.5 Hz, $\Delta\nu_{AB}$ = 8.3 Hz, 2 H), 5.80−5.74 (m, 2 H), 3.66 (dd, J = 14.4, 2.2 Hz, 1 H), 3.27 (ddd, J = 15.6, 95, 5.4 Hz, 1 H), 3.13 (d, J = 14.4 Hz, 1 H), 3.04 (ddd, J = 12.5, 6.4, 2.0 Hz, 1 H), 2.81−2.73 (m, 2 H), 2.43 (t, J = 11.2 Hz, 1 H), 2.12−1.91 (m, 3 H), 1.81 (dt, J = 12.5, 4.4 Hz, 1 H), 1.67−1.57 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.9, 145.4, 143.7, 132.3, 131.1, 123.5, 121.5, 111.5, 109.9, 100.7, 77.2, 70.9, 59.2, 49.4, 34.2, 32.8, 24.5, 23.3; IR (neat) 1683, 1618, 1484, 1241, 1038 cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel intensity) 281.1 [(M)$^+$, 100]; HRMS (ESI) calcd for $C_{18}H_{20}NO_2$ [(M + H)$^+$] 282.1494, found 282.1494.

(*Z*)-1-(6-{3-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]propyl}-3,4-(methylenedioxy)phenyl)-6-ethanesulfonyl-4,6-heptadien-1-one (66). *m*-Chloroperbenzoic acid (77%, w/w water, 177 mg, 0.69 mmol) was added to a solution of sulfoxide **61** (232 mg, 0.46 mmol) in CH_2Cl_2 (20 mL) at room temperature. After stirring for 15 min, the mixture was treated with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2 (3×). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (gradient, 20%−25% EtOAc/hexanes) to afford 182 mg (76%) of the title compound as a colorless oil: R_f = 0.49 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (s, 1 H), 6.74 (s, 1 H), 6.43 (s, 1 H), 6.17 (dddd, J = 11.5, 1.7, 1.7, 1.7 Hz, 1 H), 6.00 (s, 2 H), 5.97−5.91 (m, 2 H), 3.60 (t, J = 6.4 Hz, 2 H), 3.00 (q, J = 7.3 Hz, 2 H), 2.97 (t, J = 6.8 Hz, 2 H), 2.82−2.77 (m, 2 H), 2.62 (ddd, J = 7.1, 7.1, 2.0 Hz, 2 H), 1.78−1.70 (m, 2 H), 1.62 (septet, J = 6.8 Hz, 1 H), 1.30 (t, J = 7.3 Hz, 3 H), 0.89 (d, J = 6.8 Hz, 6 H), 0.85 (s, 6 H), 0.08 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.0, 149.9, 145.5, 143.7, 139.2, 138.4, 130.3, 126.9, 120.7, 111.3, 108.5, 101.6, 62.1, 46.6, 40.4, 34.7, 34.1, 30.7, 25.0, 23.4, 20.3, 18.4, 6.8, −3.5; IR (neat) 1681 (s), 1610, 1113 (s) cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel intensity) 437.1 [(M − $C(CH_3)_2CH(CH_3)_2$)$^+$, 33], 343.1 [(M − $C_8H_{18}O_2S$), 22], 161.0 (100); HRMS (ES) calcd for $C_{27}H_{42}NaO_6SSi$ [(M + Na)$^+$] 545.2370, found 545.2369.

(*Z*)-1-[6-(3-Hydroxypropyl)-3,4-(methylenedioxy)phenyl]-6-ethanesulfonyl-4,6-heptadien-1-one (67). Hydrogen fluoride-pyridine (0.12 mL) was added to a solution of silyl ether **66** (131 mg, 0.25 mmol) in CH_3CN (2 mL) at room temperature. After stirring for 3 h, the mixture was carefully neutralized with solid $NaHCO_3$, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (60% EtOAc/hexanes) to afford 93 mg (98%) of the title compound as a colorless oil: R_f = 0.13 (50% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (s, 1 H), 6.74 (s, 1 H), 6.42 (s, 1 H), 6.15 (dddd, J = 11.5, 1.7, 1.7, 1.7 Hz, 1 H), 6.00 (s, 2 H), 5.96−5.90 (m, 2 H), 3.56 (t, J = 5.9 Hz, 2 H), 3.01−2.96 (m, 4 H), 2.83 (t, J = 7.3 Hz, 2 H), 2.69 (br s, 1 H), 2.61 (dddd, J = 7.1, 7.1, 7.1, 2.0 Hz, 2 H), 1.82 (dddd, J = 7.3, 7.3, 6.1, 6.1 Hz, 2 H), 1.29 (t, J = 7.6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.2, 150.4, 145.7, 143.7, 138.7, 138.3, 130.5, 127.1, 120.9, 111.2, 108.5, 101.7, 61.1, 46.7, 40.5, 34.4, 29.6, 23.4, 6.8; IR (neat) 3524 (br), 1679 (s), 1609, 1112 cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel intensity) 380.2 [(M)$^+$, 16], 362.2 [(M − H_2O)$^+$, 9], 287.2 [(M − $SO_2CH_2CH_3$)$^+$, 100], 269.2 [(M − $C_2H_7O_3S$)$^+$, 26]; HRMS (ESI) calcd for $C_{19}H_{24}O_6S$ [(M)$^+$] 380.1294, found 380.1290.

(*Z*)-1-[6-(3-Iodopropyl)-3,4-(methylenedioxy)phenyl]-6-ethanesulfinyl-4,6-heptadien-1-one (68). Triphenylphosphine (123 mg, 0.47), imidazole (35 mg, 0.52 mmol), and I_2 (142 mg, 0.56 mmol) were sequentially added to a solution of alcohol **67** (89 mg, 0.23 mmol) in Et_2O and CH_3CN (1:1, 4 mL) in the dark at 0 °C. After stirring for 15 min, the mixture was warmed to room temperature. Upon stirring for an additional 30 min, the mixture was treated with 5% (w/w) aqueous $Na_2S_2O_4$ and extracted with EtOAc (3×). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (gradient, 25%−33% EtOAc/hexanes) to afford 103 mg (90%) as a colorless oil: R_f = 0.25 (33% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (s, 1 H), 6.75 (s, 1 H), 6.43 (s, 1 H), 6.17 (dddd, J = 11.5, 1.7, 1.7, 1.7 Hz, 1 H), 6.02 (s, 2 H), 5.97−5.92 (m, 2 H), 3.20 (t, J = 7.1 Hz, 2 H), 3.00 (q, J = 7.3 Hz, 2 H), 2.98 (t, J = 7.1 Hz, 2 H), 2.85 (app t, J = 7.6 Hz, 2 H), 2.62 (dddd, J = 7.1, 7.1, 7.1, 1.7 Hz, 2 H), 2.11−2.03 (m, 2 H), 1.30 (t, J = 7.6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.7, 150.3, 145.9, 143.7, 138.4, 137.8, 130.1, 127.1, 120.9, 111.4, 108.9, 101.8, 46.7, 40.3, 35.3, 35.2, 23.4, 6.9, 6.5; IR (neat) 1681 (s), 1610, 1112 cm^{-1}; MS (EI, 70 eV) 490.1 [(M)$^+$, 11], 397.1 [(M − $SO_2CH_2CH_3$)$^+$, 100], 362.2 [(M − I)$^+$, 10], 317.0 [(M − $C_8H_{13}O_2S$)$^+$, 45]; HRMS (EI, 70 eV) calcd for $C_{19}H_{23}IO_5S$ [(M)$^+$] 490.0311, found 490.0316.

6α-Ethanesulfonyldemethoxycomosine (69). Iodide **68** (8.5 mg, 0.02 mmol) in toluene (0.5 mL) was added to a solution of amine **17**[10a] (11 mg, 0.04 mmol) in toluene (0.3 mL) at 85 °C. After stirring for 2 h, the reaction was treated with EtOH, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed with basic alumina (gradient, 5%−10% Et_2O/toluene) to afford 4 mg (63%) of the title compound as a white solid: mp = 142−144 °C; R_f = 0.33 (33% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (s, 1 H), 6.55 (s, 1 H), 6.22 (dddd, J = 8.3, 2.9, 2.9, 2.9 Hz, 1 H), 5.95 (dt, J = 10.3, 2.2 Hz, 1 H), 5.91 (AB_q, J = 1.5 Hz, $\Delta\nu_{AB}$ = 10.5 Hz, 2 H), 3.13 (dt, J = 9.0, 2.0 Hz, 1 H), 3.05−2.95 (m, 2 H), 2.87 (ddd, J = 14.4, 8.3, 3.9 Hz, 1 H), 2.81−2.69 (m, 2 H), 2.61 (dt, J = 12.7, 9.0 Hz, 1 H), 2.44−2.36 (m, 2 H), 2.27−2.09 (m, 4 H), 1.93 (ddd, J = 12.7, 7.1, 1.0 Hz, 1 H), 1.81 (dt, J = 13.4, 5.1 Hz, 1 H), 1.70−1.60 (m, 1 H), 1.15 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.4, 145.8, 135.8, 133.9, 133.7, 124.2, 112.0, 110.9, 101.1, 77.4, 70.1, 46.6, 44.6, 41.5, 33.4, 33.0, 30.5, 26.2, 23.0, 5.4; IR (CH_2Cl_2) 1622, 1129 cm^{-1}; MS (EI, 70 eV) *m*/*z* (rel intensity) 375.2 [(M)$^+$, 2]; 282.2 [(M − $SO_2CH_2CH_3$)$^+$, 100]; HRMS (ESI) calcd for $C_{20}H_{26}NO_4S$ [(M + H)$^+$] 376.1583, found 376.1581. The relative configuration was determined by an X-ray crystal structure of the corresponding picrate salt. See Supporting Information for details.

Demethoxyschelhammericine (70). Lithium triethylborohydride (1 M in THF, 46 μL, 0.05 mmol) was slowly added over a period of 15 min to a mixture of $PdCl_2$dppp (1.3 mg, 0.002 mmol) and sulfone **69** (8 mg, 0.2 mmol) in THF (0.4 mL) at 0 °C. After stirring for an additional 30 min, the mixture was treated with 10% (w/w) aqueous KCN and extracted with Et_2O (3×). The combined organic layers were washed with water and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed (3% Et_3N/2% EtOAc/hexanes) to afford 5 mg (84%) of the title compound as a white solid. Although this compound has been previously reported,[16] it has not been fully characterized: mp = 119−120 °C; R_f = 0.30 (3% Et_3N/5% EtOAc/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83 (s, 1 H), 6.62 (s, 1 H), 5.89 (AB_q, J = 1.5 Hz, $\Delta\nu_{AB}$

= 7.6 Hz, 2 H), 5.57 (s, 1 H), 3.54 (ddd, J = 14.9, 12.7, 2.2 Hz, 1 H), 3.26 (dddd, J = 14.9, 2.9, 2.9, 2.9 Hz, 1 H), 3.12 (ddd, J = 14.9, 12.9, 1.5 Hz, 1 H), 2.76−2.67 (m, 3 H), 2.53−2.44 (m, 2 H), 2.32−2.24 (m, 1 H), 2.13−2.07 (m, 2 H), 1.88 (qdd, J = 12.7, 2.7, 1.5 Hz, 1 H), 1.67−1.45 (m, 3 H), 1.33−1.20 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.4, 144.7, 142.6, 135.7, 135.4, 118.4, 112.4, 111.3, 100.8, 67.1, 50.1, 45.7, 37.6, 32.4, 28.0, 25.3, 23.2, 18.1; IR (CH_2Cl_2) 1618, 1484, 1235, 1039 cm^{-1}; MS (EI, 70 eV) m/z (rel intensity) 283.2 [$(M + H)^+$, 30]; 254.1 (100), 148.1 (84); HRMS (EI, 70 eV) calcd for $C_{18}H_{21}NO_2$ [$(M + H)^+$] 283.1572, found 283.1574.

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Supporting Information Available: Table surveying deprotonation of phenyl vinyl sulfide. General experimental methods. Copies of ^{1}H and/or ^{13}C spectra of compounds without elemental analysis. ORTEP plots and cif files for **40** and **69**. This material is available free of charge via the Internet at http://pubs.acs.org.

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