Approach to 6a-Epipretazettine and 6a-Epiprecriwelline via an Intramolecular 2-Azaallyl Anion Cycloaddition Reaction

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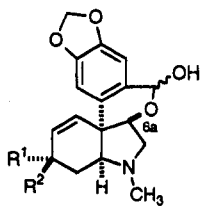
An intramolecular 2-azaallyl anion cycloaddition with a diene produced the 2,3,4,6,7,7a-hexahydroindole **33** with complete control of relative stereochemistry, thus providing the first example of the use of such a cycloaddition in an approach to a relatively complex target molecule. The 2-azaallyl anion was generated by tin–lithium exchange of the (2-azaallyl)stannane **32**. The stannane was prepared by a convergent route using a Stille coupling of the vinyl bromide **14** with the vinylstannane **28**, providing the diene **29**. An unexpected isomerization occurred in the Stille coupling. Transformation of the cycloadduct **33** to the allylic methyl ethers **36** and **37** produced potential precursors of 6a-epiprecriwelline (**4**) and 6a-epipretazettine (**3**), respectively. The inability to carry out an oxidative desilylation thwarted the completion of the syntheses of these alkaloids.

Introduction

Pretazettine (**1**), a member of the *Amaryllidaceae* family of alkaloids, has been isolated from a wide variety of plants including the "sacred lily" *Narcissus tazetta* L.[1,2] It shows a wide spectrum of biological activity[2,3] including reverse transcriptase inhibition in various oncogenic RNA viruses[4,5] and activity against various leukemias,[6–8] Ehrlich ascites carcinoma,[9] and Lewis lung carcinoma.[10] Pretazettine was found to be an inhibitor of protein synthesis in KB, P388, HeLa, and Krebs II cells by a mechanism which does not affect DNA or RNA synthesis.[6] The hemiacetal ring was found to be crucial for biological activity.[11] The stereochemistry of the allylic methoxy group did not reduce the activity against Rauscher leukemia virus, as evidenced by the equal potency of the related alkaloid precriwelline (**2**).[11]

Considerable synthetic effort has been focused on pretazettine and related compounds.[3] Wildman showed that pretazettine could be prepared in good yield from the related alkaloid haemanthidine.[12] Syntheses of haemanthidine and/or pretazettine have been reported by



1 R^1=OCH_3, R^2=H : pretazettine
2 R^1=H, R^2=OCH_3 : precriwelline

3 R^1=OCH_3, R^2=H : 6a-epipretazettine
4 R^1=H, R^2=OCH_3 : 6a-epiprecriwelline

Hendrickson,[13] Tsuda,[14] and Martin.[15] A challenging problem has been the generation of the C-6a hydroxyl group with the correct stereochemistry, resulting in the synthesis of 6a-epipretazettine (**3**) by several groups.[16–19] Syntheses of tazettine[14,16,19] also represent formal syntheses of pretazettine, since tazettine can be converted to pretazettine.[20] Tazettine has been made from 6a-epipretazettine.[16] Formal syntheses and partial syntheses of pretazettine and related compounds have also been reported.[3,16,21]

Reports from our laboratories have demonstrated that monocyclic and fused-bicyclic pyrrolidines may be synthesized by inter- and intramolecular [π4s + π2s] cycloadditions of nonstabilized 2-azaallyl anions with elec-

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(20) (a) Kobayashi, S.; Kihara, M. *Heterocycles* **1979**, *12*, 1547–1550. (b) Kobayashi, S.; Kihara, M.; Shingu, T.; Shingu, K. *Chem. Pharm. Bull.* **1980**, *28*, 2924–2932.
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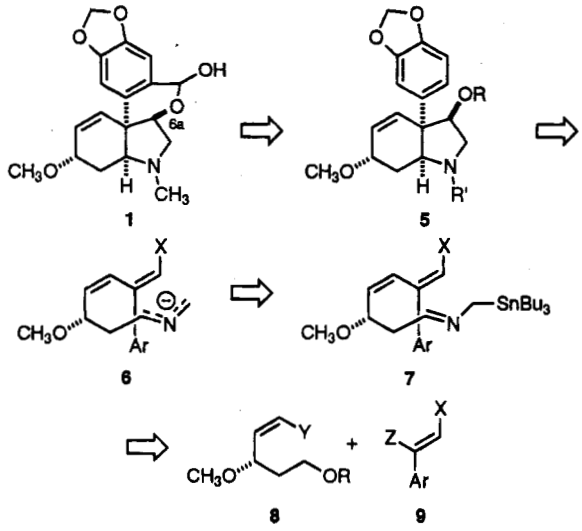
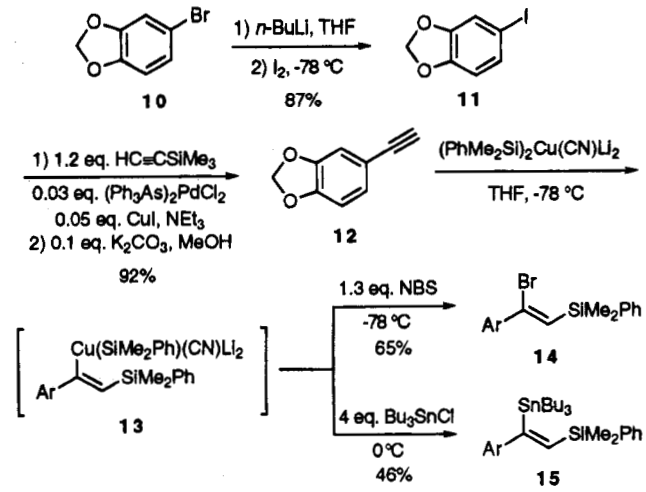
Scheme 1. Retrosynthetic Analysis of Pretazettine Using a 2-Azaallyl Anion Cycloaddition



tron-rich alkenes.[22-27] The anions were generated by tin–lithium exchange of (2-azaallyl)stannanes. The 2-azaallyl anion method is complementary to azomethine ylide cycloaddition chemistry, since the latter species generally require electron-poor dipolarophiles except in certain intramolecular cases.[26,28,29] As an extension of our work on 2-azaallyl anion cycloadditions, we planned to use this method as the key step in a total synthesis of pretazettine.

Our synthetic plan (Scheme 1) centered around an intramolecular cycloaddition of a 2-azaallyl anion with a diene (i.e., **6** → **5**). Martin has converted **5** (R = CO-*t*-Bu, R′ = CHO or CH_3) to pretazettine through the intermediacy of haemanthidine. Workup of the 2-azaallyl anion cyclization with iodomethane or a formylating agent would place the proper group on the pyrrolidine nitrogen. Regarding the choice of the group X, we had previously found that while enol ethers are unsuitable for 2-azaallyl anion cycloadditions, vinylsilanes are useful surrogates for oxygen functionality.[18,22,30] We chose X = $SiMe_2Ph$, since we had been able to convert this group into a hydroxyl group in a closely related model system.[22]

Scheme 2. Synthesis of the β-Silylstyrene Portion of the Diene



Since 2-azaallyl anion cycloadditions proceed by a stereospecific *cis*-addition to the anionophile,[22,27,31] the geometry of the alkene should govern the relative stereochemistry at the 3- and 4-positions of the newly formed pyrrolidine ring. Previous experience with intramolecular 2-azaallyl anion cycloadditions showed that the *cis*-ring juncture is most often observed.[22,31] Hence, three of the four stereocenters in **5** should be controlled in a relative sense in the cycloaddition reaction. The relationship of these three centers to the stereocenter at the allylic methoxy group was less certain, since we had no experience with cycloadditions using chiral cyclization precursors such as **6**. Molecular models indicated that the diastereoselectivity of the cyclization of **6** might proceed to give the precriwelline rather than pretazettine stereochemistry. However, since methods are available to invert this center,[15] we felt that the stereochemistry could be adjusted after the cycloaddition if necessary. The 2-azaallyl anion would be generated from the (2-azaallyl)-stannane **7**, which would be prepared by condensation of (aminomethyl)tri-*n*-butylstannane with an aldehyde. A transition metal-catalyzed cross-coupling reaction of **8** and **9** was envisioned for the construction of the diene segment. These methods are known to proceed with good stereocontrol, which is important for ultimately obtaining the correct stereoisomer at C-6a relative to the bridgehead positions in the cycloadduct **5**.

Results and Discussion

The transition metal-catalyzed cross-coupling approach[32] to the diene fragment required a vinyl halide (or equivalent group) and a vinylmetal species (**8** and **9** in Scheme 1). While several vinylmetal species were examined, the Stille coupling between a vinyl halide and a vinylstannane in the presence of a palladium catalyst proved most fruitful.[32-34] We examined both permutations of stannane/halide for the coupling of **8** with **9**. Scheme 2 shows the synthesis of the stannane and halide

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(29) Recent examples of intramolecular dipolar cycloadditions of azomethine ylides with unactivated alkenes: (a) Henke, B. R.; Kouklis, A. J.; Heathcock, C. H. *J. Org. Chem* **1992**, *57*, 7056–7066. (b) Harwood, L. M.; Lilley, I. A. *Tetrahedron Lett.* **1993**, *34*, 537–540. (c) Harwood, L. M.; Kitchen, L. C. *Tetrahedron Lett.* **1993**, *34*, 6603–6606.
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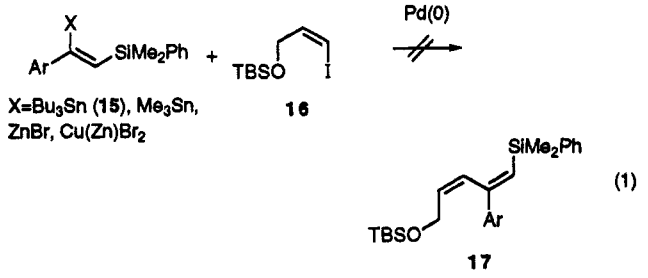
(34) Mitchell, T. N. *Synthesis* **1992**, 803–815.

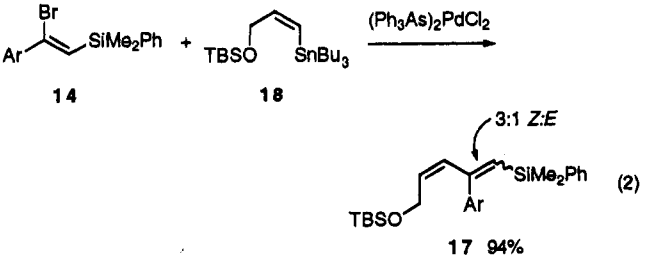
versions of the β-silylstyrene **9**. The key step was the silylcupration of the alkyne **12** using Fleming's method.[35] Quenching of the vinyl cuprate intermediate **13** with either NBS or tri-*n*-butylstannyl chloride gave the vinyl bromide **14** or the vinylstannane **15**, respectively.[36] In our hands, the alkyne **12**[37,38] was best prepared by a palladium-catalyzed coupling of the iodide **11** with ethynyltrimethylsilane[39] followed by desilylation.[40] Attempts to use the bromide **10** in the coupling reaction failed; thus, it was necessary to convert it first into the iodide **11**.

Before attempting the preparation of the allylic ether-containing portion of the diene (i.e., **8**), we studied the coupling of **14** and **15** with simpler models for **8**. All attempts to couple the vinylstannane **15** with the model iodide **16** under a wide variety of palladium-catalyzed conditions failed to produce the diene **17** (eq 1).[41] Other



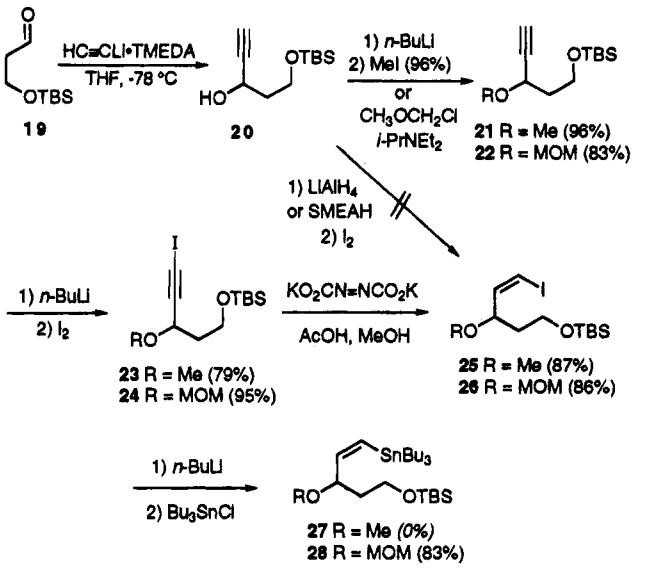
vinyl metal species such as organocopper and organozinc reagents were also unsuccessful. A variety of other cross-coupling partners failed to react with **15**.[42] We suspect that the highly hindered nature of **15** makes it a poor vinyl donor.

The use of the bromide **14** in the coupling reaction was more fruitful (eq 2). Coupling with the model stannane



18 was accomplished under mild conditions with bis(triphenylarsine)palladium(II) chloride,[43] producing **17** in excellent yield. To our surprise, isomerization of the vinyl silane had occurred, producing a 1:3 mixture of the desired (*E,Z*)-diene and the undesired (*Z,Z*)-diene. The (*Z*)-vinylsilane would lead to a synthesis of 6a-epipretazettine rather than pretazettine. Although 6a-epipretazettine has been converted into tazettine and pretazettine, the ability to proceed directly to pretazettine would have been preferable. With the hope that we might be able to avoid this isomerization by modifying the coupling conditions, we proceeded with assembly of the actual diene required for pretazettine.

Scheme 3. Synthesis of the Allylic Ether Portion of the Diene



The synthesis of the allylic ether fragment corresponding to the synthon **8** is shown in Scheme 3. Addition of lithium acetylide to the known aldehyde **19**[44] produced the propargyl alcohol **20**. The direct conversion of **20** to the (*Z*)-iodoalkene (**25**, R = H) using aluminum hydride reagents followed by an iodine quench failed.[45] An alternate strategy involving partial reduction of a 1-iodoalkyne was successful. Hence, conversion of **20** to its methyl ether **21** followed by metalation and iodination afforded the 1-iodoalkyne **23**. Diimide reduction[46,47] cleanly produced the desired (*Z*)-iodoalkene **25**. Unfortunately, this vinyl iodide also failed in palladium-catalyzed cross-coupling reactions with the vinylstannane **15** (cf. eq 1). On the basis of the success of the coupling shown in eq 2, we required instead the vinylstannane **27**. However, all attempts to transmetalate **25** and quench the resultant vinyllithium with a chlorostannane failed. We suspected that the failed conversion of **23** to **25** in some way involved the methoxy group, since we had prepared **18** (eq 2) by a similar reaction. We also examined partial reduction of an alkynylstannane as a route to **27** (not shown). While we were able to prepare the necessary alkynylstannane, semihydrogenation with borane reagents, Lindlar conditions, and diimide all returned starting material. We then turned our attention to a methoxymethyl protecting group for the allylic alcohol. Given our uncertainty regarding the diastereoselectivity of the intramolecular 2-azaallyl anion cycloaddition (**6** → **5** in Scheme 1), we felt that it would be prudent to use an allylic ether that could be converted

(35) (a) Fleming, I.; Roessler, F. *J. Chem. Soc., Chem. Commun.* **1980**, 276–277. (b) Fleming, I.; Newton, T. W.; Roessler, F. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2527–2532. (c) Fleming, I.; Newton, T. W. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1805–1808.

(36) An alternative route to **15** has been reported. See ref 18.

(37) Overman, L. E.; Shim, J. *J. Org. Chem.* **1993**, *58*, 4662–4672.

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(41) Catalysts used: $Pd(Ph_3)_4$, $PdCl_2(PPh_3)_2$, $PdCl_2$(dppe), $PdCl_2(PhCN)_2$, $PdCl_2(MeCN)_2$, $PdCl_2(AsPh_3)_2$, $Pd(TFP)_4$. Solvents used: NEt_3, THF, DME, DMF, Et_2O, toluene.

(42) Phenylacetylene, (dimethylphenyl)silylacetylene, (*E*)-1-iodo-1-hexene, and bis[(*Z*)-1-hexenyl]$CuZnI_2$ all failed to couple with **15**.

(43) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585–9595.

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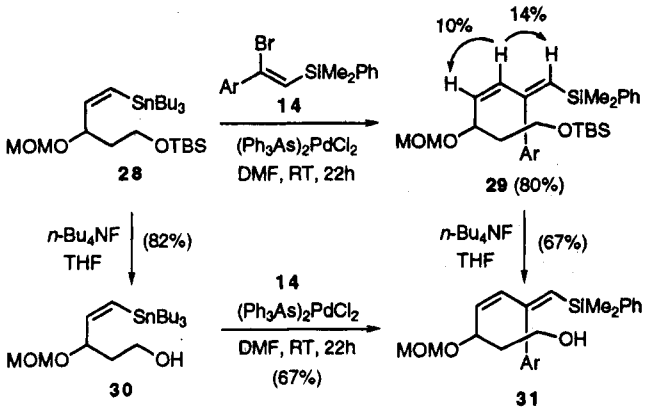
(47) Berson, J. A.; Gajewski, J. J.; Donald, D. S. *J. Am. Chem. Soc.* **1969**, *91*, 5550–5566.

Scheme 4. Diene Synthesis by Palladium-Catalyzed Cross-Coupling

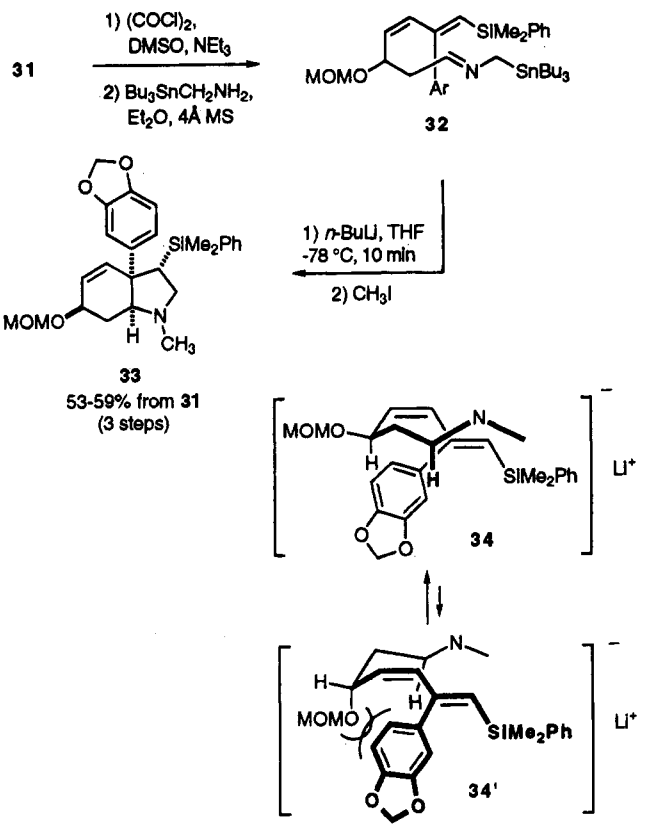


to an allylic alcohol in case a stereochemical adjustment was necessary. This would later prove to be a fortuitous strategy. Conversion of **20** to the MOM-protected propargyl alcohol **22** proceeded smoothly. Metalation, iodination, and diimide reduction gave **26** via **24**. Metal–iodine exchange and subsequent stannylation was now uneventful, affording the vinylstannane **28** in good yield.

The coupling of the two halves of the diene is shown in Scheme 4. Combination of the vinylstannane **28** and the vinyl bromide **14** in the presence of bis(triphenylarsine)palladium(II) chloride[43] produced the diene **29** in good yield as a single geometrical isomer. Unfortunately, difference NOE experiments (enhancements shown) proved that complete isomerization of the vinylsilane double bond had occurred, producing only (*Z,Z*)-**29**. All attempts to obtain (*E,Z*)-**29** by modifying the coupling conditions failed to produce even a trace of the desired isomer. Alkene isomerization in the Stille coupling is very rare.[33c] We believe the silicon substitutent facilitates isomerization of the intermediate vinyl palladium species prior to coupling. Related (2-silyl-1-arylvinyl)-lithium reagents are known to be configurationally mobile, resulting in a preference for a *trans* relationship of the lithium and the β-silicon.[18,48,49] A similar *trans* preference for palladium and silicon may explain the formation of **29**. Our plan for a synthesis of pretazettine was now diverted toward an approach to 6a-epipretazettine. Desilylation of **29** gave the alcohol **31**. Alternatively, desilylation of **28** to **30** followed by the Stille coupling also produced **31**. Since the dienes were found to be slightly sensitive to silica gel, the second route (which requires one chromatographic operation rather than two) was preferred.

Swern oxidation[50] of the alcohol **31** afforded a quantitative yield of a sensitive aldehyde which was directly condensed with (aminomethyl)tri-*n*-butylstannane[23] to provide the (2-azaallyl)stannane **32** (Scheme 5). Without purification, **32** was added to *n*-butyllithium in THF at −78 °C. After 10 min, iodomethane was added, producing the cycloadduct **33** as a single diastereomer in 53–59% overall isolated yield from the alcohol **31**. This exceptionally facile cycloaddition process illustrates that 2-azaallyl anions show considerable potential for the assembly of relatively complex systems. Spectroscopic

Scheme 5. 2-Azaallyl Anion Generation and Cycloaddition



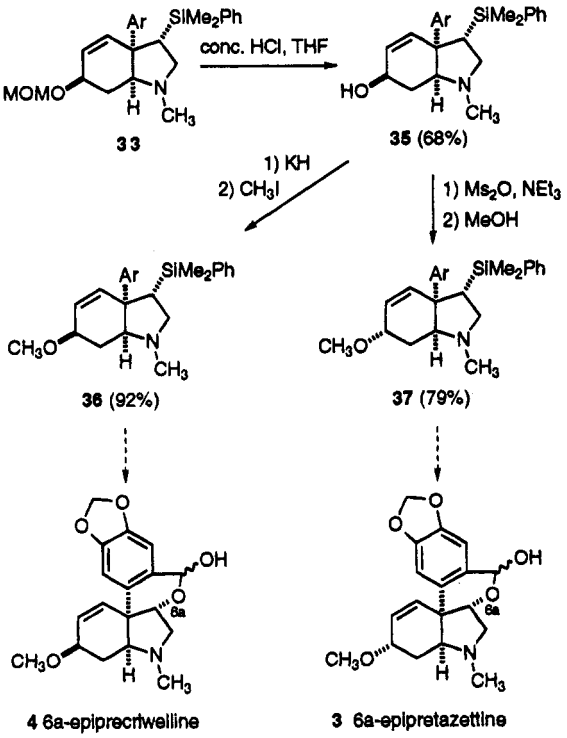
studies (vide infra) showed that **33** had the 6a-epiprecriwelline rather than 6a-epipretazettine stereochemistry at the allylic ether stereocenter. The (*Z*)-disubstituted double bond of the diene clearly exerts a strong influence on the reactive conformation of the 2-azaallyl anion, depicted as **34**. In conformation **34'**, which would lead directly to the pretazettine stereochemistry, a serious steric interaction between the allylic methoxymethoxy group and the aromatic ring is evident from examination of molecular models. A rationale for the predominance of the *cis* ring juncture over the *trans* is not readily apparent from the examination of models, but is consistent with our previous work.

Transformation of the allylic methoxymethyl ether to the methyl ether required for both 6a-epiprecriwelline and 6a-epipretazettine is shown in Scheme 6. Hydrolysis of the methoxymethyl group of **33** with HCl gave the alcohol **35**. The stereochemistry of **35** was assigned unambiguously at this stage by NOE experiments. Methylation of the alcohol **35** gave the methyl ether **36** required for a synthesis of 6a-epiprecriwelline (**4**). Mesylation of **35** and solvolysis in methanol[15] provided the appropriate allylic ether **37** for 6a-epipretazettine (**3**). All that remained was the oxidative desilylation of **36** and **37** to install the requisite hydroxyl groups.

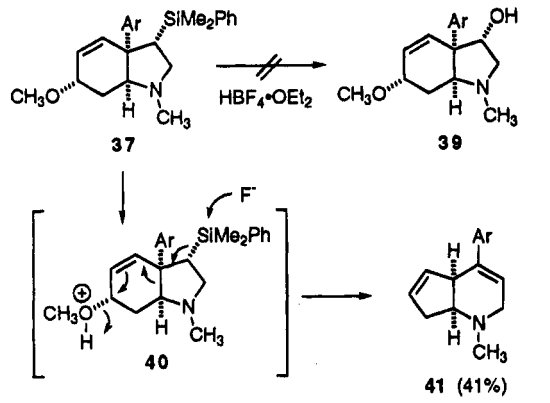
Attempted oxidative desilylation[30] of **37** under conditions which had been successful in related 3-(dimethylphenylsilyl)pyrrolidines[18,22] is shown in Scheme 7. Rather than the desired alcohol **39**, we isolated the tetrahydropyrindene **41**, apparently the result of an acid-catalyzed rearrangement as depicted for **40**. Attempts to find alternative methods for the oxidative desilylation

(48) Chenard, B. L.; Van Zyl, C. M. *J. Org. Chem.* **1986**, *51*, 3561–3566.
(49) Mitchell, T. N.; Wickenkamp, R.; Amamria, A.; Dicke, R.; Schneider, U. *J. Org. Chem.* **1987**, *52*, 4868–4874.
(50) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480–2482.

Scheme 6



Scheme 7



were not unsuccessful.[51] Oxidation of **35** to the enone followed by oxidative desilylation also failed. A successful route to pretazettine or 6a-epipretazettine will require an alternate method for incorporating an oxygen functional group at C-6a.

While we were ultimately thwarted at the last stages by an uncooperative oxidative desilylation, there is no question that the 2-azaallyl anion cycloaddition method has shown its potential for the synthesis of significant pyrrolidine-containing materials. In one operation, three stereocenters (including a quaternary center) and two rings were formed. The efficiency and stereoselectivity of the process are reminiscent of the powerful Diels–Alder reaction. Application of this method to the synthesis of other alkaloids is currently being explored.

(51) Among the other methods examined: mercuric oxide in the presence of peracetic acid (Rehders, F.; Hoppe, D. *Synthesis* **1992**, 865–870); KBr/peracetic acid/NaOAc; and Birch reduction of the phenylsilyl group to a vinyl silane or allyl silane followed by peracid oxidation. The latter method was successful for the conversion of 1-phenyl-2-(dimethylphenylsilyl)ethane to 2-phenylethanol. Attempted oxidation to an iminium ion at N-1/C-2 of the pyrrolidine followed by desilylation was also unsuccessful using mercuric acetate or platinum black in oxygen, resulting only in N-demethylation.

Experimental Section

General Methods. All commercial reagents (if liquid) were distilled prior to use. All other solid reagents were used as obtained. Iodine-containing compounds were distilled from copper powder into a receiver containing copper shot and protected from light prior to use. Cuprous iodide was recrystallized from aqueous potassium iodide according to the procedure of Kauffman.[52] Diethyl ether, 1,4-dioxane, and tetrahydrofuran were distilled from sodium/benzophenone ketyl. Benzene, dichloromethane, diethylamine, diisopropylamine, dimethyl sulfoxide, hexane, and triethylamine were distilled from calcium hydride. Dimethylformamide was distilled from barium oxide at reduced pressure. Methanol and ethanol were distilled from calcium oxide. Analytical thin layer chromatography (TLC) was conducted on precoated silica gel plates (Kieselgel 60 F_{254}, 0.25-mm thickness, manufactured by E. Merck & Co., Germany). For visualization, TLC plates were either placed under ultraviolet light or stained with iodine vapor, acidic vanillin solution, acidic anisaldehyde solution, phosphomolybdic acid solution, or ninhydrin solution. Most reactions were followed by TLC or GC by monitoring the disapperance of starting materials. GC analyses were carried out on a Hewlett-Packard 5890 gas chromatograph equipped with a five- and 15- 100% fused methyl polysiloxane (3-μm film thickness) capillary column, using He carrier gas and a flame ionization detector (FID). The temperature program used was 100 °C for 2 min and then a 100–200 °C ramp at a rate of 40 °C per min. Elemental analyses were performed by Spang Microanalytical Laboratory (Eagle Harbor, MI) or by the University of Michigan Department of Chemistry CHN/AA Services Branch. For ^{1}H NMR spectra of compounds which exhibited satellite peaks due to coupling with ^{117}Sn and ^{119}Sn, the average of the two couplings is reported when measurable. Assignments in the ^{1}H NMR spectra were made on the basis of homonuclear decoupling experiments or two-dimensional correlated off-resonance spectroscopy (COSY) experiments. Relative stereochemical assignments were made on the basis of differential nuclear Overhauser effect (dNOE) experiments or nuclear Overhauser enhancement and exchange spectroscopy (NOESY) experiments, performed at ambient temperature on thoroughly degassed samples (vacuum freeze/thaw cycles). Flash column chromatography was performed according to the general procedure described by Still[53] using flash grade Merck silica gel 60 (230–400 mesh). Radial chromatography was performed on a Harrison Research Chromatotron, using glass plates coated with Merck silica gel 60. Solvent was delivered by an FMI Lab Pump solvent metering system.

5-Iodo-1,3-benzodioxole (11). Prepared by a modification of the published procedure,[54] 5-bromo-1,3-benzodioxole (**10**) (9.14 g, 45.5 mmol) was added to *n*-butyllithium (20.0 mL of a 2.5 M solution in hexanes, 50.0 mmol) in hexane (16 mL) and THF (35 mL) at −90 °C. The resulting white suspension was warmed to -50 °C for 15 min and then was recooled to −78 °C. A solution of iodine (12.7 g, 50.0 mmol) in THF (25 mL) was added. The mixture was warmed to room temperature, diluted with Et_2O (25 mL), and then washed with H_2O (1 × 20 mL), saturated $Na_2S_2O_3$ (1 × 20 mL), and saturated brine (1 × 25 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Distillation from copper powder afforded 9.77 g (87%) of the title compound as a clear, colorless, light sensitive oil, bp 79–82 °C at 0.40 mmHg, R_f = 0.22 (100% hexane): IR (neat) 2892 (s), 1422 (s), 1229 (s), 1040 (s), 935 (s), 797 (s) cm^{-1}; ^{1}H NMR (360 MHz) δ 7.15–7.12 (m, 2 H), 6.59 (d, 1 H, J = 8.0 Hz), 5.95 (s, 2 H); ^{13}C NMR (90 MHz) δ 148.5, 147.6, 130.4, 117.5, 110.3, 101.3, 82.2; MS m/z (rel int) 248 (100, M$^+$), 247 (39), 127 (6), 121 (15), 65 (19), 63 (27), 62 (15), 61 (7), 50 (5), 39 (6); HRMS calcd for $C_7H_5IO_2$ 247.9334, found 247.9328. Anal. Calcd for $C_7H_5IO_2$: C, 33.90; H, 2.03. Found: C, 34.25; H, 2.19.

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5-[2-(Trimethylsilyl)ethynyl]-1,3-benzodioxole. According to the method of Lu,[55] copper(I) iodide (0.25 g, 1.30 mmol) and bis(triphenylarsine)palladium(II) chloride (0.36 g, 0.40 mmol) were added to aryl iodide **11** (6.57 g, 26.5 mmol) in triethylamine (40 mL) at room temperature. The yellow suspension was cooled to 0 °C, and (trimethylsilyl)acetylene (3.13 g, 31.9 mmol) was added in a dropwise fashion. The dark brown mixture was allowed to stir at room temperature for 1.5 h and then was diluted with Et_2O (50 mL) and filtered through Celite. The filtrate was washed with saturated NH_4Cl (5 × 50 mL) and saturated brine (1 × 50 mL) and then dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford 5.77 g (100%) of the title compound as golden plates which were used without further purification, mp 51.5–52.5 °C, R_f = 0.40 (10% EtOAc/hexane): IR (neat) 2957 (w), 2153 (m), 1484 (m), 1246 (s), 846 (s) cm^{-1}; ^1H NMR (300 MHz) δ 6.99 (dd, 1 H, J = 8.0, 1.6 Hz), 6.90 (d, 1 H, J = 1.6 Hz), 6.72 (d, 1 H, J = 8.0 Hz), 5.96 (s, 2 H), 0.23 (s, 9 H); ^{13}C NMR (50 MHz) δ 148.0, 147.3, 126.7, 116.5, 111.8, 108.3, 105.0, 101.2, 92.2, 0.0; MS m/z (rel int) 218 (36, M^+), 205 (6), 204 (19), 203 (100, $M^+ - CH_3$), 173 (6), 117 (4), 101 (17), 87 (2), 53 (3), 43 (3); HRMS calcd for $C_{12}H_{14}O_2Si$, 218.0763, found 218.0765.

5-Ethynyl-1,3-benzodioxole (12). Anhydrous potassium carbonate (0.34 g, 2.50 mmol) was added to 5-(2-(trimethylsilyl)ethynyl)-1,3-benzodioxole (5.40 g, 24.8 mmol) in anhydrous methanol (48 mL) at room temperature. After 2 h, the mixture was concentrated *in vacuo* to remove most of the methanol and then diluted with Et_2O (50 mL) and washed with H_2O (3 × 25 mL) and saturated brine (1 × 25 mL). The organic phase was then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Kugelrohr distillation afforded 3.35 g (92%) of the title compound as a white solid, 82–85 °C air bath at 0.80 mmHg, mp = 29.5–31.0 °C (lit.[37] mp 33 °C), R_f = 0.39 (10% EtOAc/hexane): IR (neat) 3287 (m), 2892 (w), 2103 (w), 1482 (s), 1246 (s), 1036 (s) cm^{-1}; ^1H NMR (360 MHz) δ 7.00 (dd, 1 H, J = 7.9, 1.6 Hz), 6.92 (d, 1 H, J = 1.6 Hz), 6.73 (d, 1 H, J = 7.9 Hz), 5.97 (s, 2 H), 3.00 (s, 1 H); ^{13}C NMR (90 MHz) δ 148.2, 147.3, 126.8, 115.2, 11.9, 108.3, 101.3, 83.5, 75.6; MS m/z (rel int) 146 (100, M^+), 145 (85), 89 (28), 88 (40), 87 (29), 73 (24), 63 (20), 62 (80), 61 (19), 38 (21); HRMS calcd for $C_9H_6O_2$, 146.0368, found 146.0370.

(*Z*)-5-[1-Bromo-2-(dimethylphenylsilyl)ethenyl]-1,3-benzodioxole (14). (Dimethylphenylsilyl)lithium[56] (3.80 mL of a 0.36 M solution in THF, 1.37 mmol) was added to copper(I) cyanide (0.06 g, 0.68 mmol) at 0 °C. After 15 min, the silyl cuprate reagent was cooled to −50 °C and alkyne **12** (0.10 g, 0.68 mmol) in THF (1 mL) was added dropwise. After 30 min, a solution of *N*-bromosuccinimide (0.13 g, 0.75 mmol) in THF (4 mL) was added and the mixture was allowed to warm to room temperature. After 2 h, the mixture was diluted with Et_2O (15 mL) and then washed with saturated NH_4Cl (2 × 20 mL) and saturated brine (1 × 20 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Chromatography (2% EtOAc/hexane) afforded 0.16 g (66%) of the title compound as a pale yellow oil, R_f = 0.46 (10% EtOAc/hexane): IR (neat) 2956 (m), 2895 (m), 1574 (s), 1485 (s), 1245 (s), 1040 (s), 820 (s) cm^{-1}; ^1H NMR (300 MHz) δ 7.62–7.59 (m, 2 H), 7.38–7.35 (m, 3 H), 7.12 (dd, 1 H, J = 8.1, 1.9 Hz), 7.08 (d, 1 H, J = 1.9 Hz), 6.71 (d, 1 H, J = 8.1 Hz), 6.61 (s, 1 H), 5.93 (s, 2 H), 0.54 (s, 6 H); ^{13}C NMR (90 MHz) δ 148.2, 147.4, 139.4, 138.0, 135.5, 133.8, 129.0, 128.4, 127.8, 121.7, 107.8, 107.5, 101.3, −2.0; MS m/z (rel int) 360 (7, M^+), 281 (28, $M^+ - Br$), 265 (13), 179 (17), 136 (14), 135 (100), 107 (10), 105 (12), 91 (51), 43 (14); HRMS calcd for $C_{17}H_{17}{}^{79}BrO_2Si$, 360.0181, found 360.0170.

(*Z*)-5-[1-(Tri-*n*-butylstannyl)-2-(dimethylphenylsilyl)ethenyl]-1,3-benzodioxole (15).[36] (Dimethylphenylsilyl)lithium[56] (5.82 mL of a 0.31 M solution in THF, 2.00 mmol) was added to copper(I) cyanide (0.09 g, 1.00 mmol) at 0 °C. After 20 min, alkyne **12** (0.15 g, 1.00 mmol) in THF (1 mL) was added dropwise. After another 20 min, tri-*n*-butyltin chloride (1.30 g, 4.00 mmol) in THF (2.5 mL) was added, and the mixture was allowed to warm to room temperature. After 40 min, the mixture was diluted with petroleum ether (10 mL), washed with saturated NH_4Cl (2 × 10 mL) and saturated brine (1 × 10 mL), and then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Chromatography (100% hexane) afforded 0.26 g (46 %) of the title compound as a clear, colorless oil, R_f = 0.43 (5% EtOAc/hexane): IR (neat) 2955 (s), 2921 (s), 1480 (s), 1427 (s), 1237 (s), 1112 (m), 1041 (m), 813 (s), 761 (s), 700 (s) cm^{-1}; ^1H NMR (360 MHz) δ 7.58–7.55 (m, 2 H), 7.36–7.32 (m, 3 H), 6.73 (d, 1 H, J = 8.0 Hz), 6.70 (s, 1 H), 6.57 (d, 1 H, J = 1.7 Hz), 6.49 (dd, 1 H, J = 8.0, 1.7 Hz), 5.92 (s, 2 H), 1.36–1.26 (m, 6 H), 1.23–1.13 (m, 6 H), 0.83–0.74 (m, 15 H), 0.41 (s, 6 H); ^{13}C NMR (90 MHz) δ 147.2, 146.4, 145.6, 145.4, 139.5, 134.1, 133.7, 129.0, 127.8, 119.2, 107.8, 106.7, 100.8, 29.0, 27.3, 13.6, 11.9, −0.6; MS m/z (rel int) 515 (63, M^+), 514 (31), 513 (49), 512 (23), 511 (27), 281 (52), 179 (18), 136 (17), 135 (100), 91 (24); HRMS calcd for $C_{25}H_{35}O_2Si^{120}Sn$, 515.1428, found 515.1411.

(*Z*)-1-Iodo-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-propene (16). Diisopropylethylamine (1.55 g, 12.0 mmol) was added in a dropwise fashion to (*Z*)-3-iodo-2-propen-1-ol[45] (2.00 g, 10.9 mmol) and *tert*-butyldimethylsilyl chloride (1.81 g, 12.0 mmol) in CH_2Cl_2 (35 mL) at room temperature with protection from light. After 12 h the reaction mixture was washed with H_2O (2 × 30 mL) and saturated brine (1 × 30 mL). The resultant organic phase was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Chromatography (100% hexane) afforded 3.14 g (96%) of the title compound as a clear, colorless, light sensitive oil, R_f = 0.69 (100% hexane): IR (neat) 2954 (s), 2928 (s), 2856 (s), 1610 (w), 1471 (s), 1256 (s), 1099 (s), 838 (s) cm^{-1}; ^1H NMR (360 MHz) δ 6.41 (dt, 1 H, J = 7.6, 5.4 Hz), 6.23 (dt, 1 H, J = 7.6, 2.0 Hz), 4.24 (dd, 2 H, J = 5.4, 2.0 Hz), 0.93 (s, 9 H), 0.12 (s, 6 H); ^{13}C NMR (75 MHz) δ 41.5, 79.8, 66.9, 25.9, 18.3, −5.1; MS m/z (rel int) 241 (100, $M^+ - C_4H_9$), 185 (72), 167 (15), 113 (18), 99 (26), 85 (92), 75 (26), 73 (46), 59 (27), 45 (50). Anal. Calcd for $C_9H_{19}ISiO$: C, 36.24; H, 6.42. Found: C, 36.29; H, 6.45.

(*Z*)-1-(Tri-*n*-butylstannyl)-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-propene (18). Prepared by a modification of the published procedure.[57] *n*-Butyllithium (0.48 mL of a 2.10 M solution in hexanes, 1.76 mmol) was added in a dropwise fashion to iodoolefin **16** (0.50 g, 1.68 mmol) in Et_2O (10 mL) at −78 °C. After 5 min, tri-*n*-butyltin chloride (0.57 g, 1.76 mmol) was added. The mixture was warmed to room temperature, washed with H_2O (2 × 10 mL) and saturated brine (1 × 10 mL), and then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Chromatography (100% hexane) afforded 0.55 g (71%) of the title compound as a clear, colorless oil, R_f = 0.75 (10% EtOAc/hexane): IR (neat) 2944 (s), 1600 (w), 1462 (m), 1374 (m), 1251 (m), 1082 (s), 836 (s), 774 (m), 656 (m) cm^{-1}; ^1H NMR (300 MHz) δ 6.61 (dt, 1 H, J = 12.8, 6.0 Hz), 5.96 [dt, 1 H, J = 12.8, 1.2 Hz, $^2J(^{117/119}Sn-^1H)$ = 64.1 Hz], 4.11 (dd, 2 H, J = 4.7, 1.2 Hz), 1.55–1.44 (m, 6 H), 1.37–1.25 (m, 6 H), 0.94–0.87 (m, 24 H), 0.08 (s, 6 H); ^{13}C NMR (75 MHz) δ 148.1, 129.3, 67.0, 29.2, 27.3, 26.0, 18.4, 13.7, 10.4, −5.0; MS (CI/NH_3) m/z (rel int) 405 (12, $M^+ - C_4H_9$), 312 (24), 310 (20), 309 (19), 308 (100), 307 (45), 306 (95), 305 (37), 304 (55), 291 (10); HRMS (CI, NH_3) calcd for $C_{17}H_{37}OSiSn$ ($M^+ - C_4H_9$) 405.1636, found 405.1641. Anal. Calcd for $C_{21}H_{46}OSiSn$: C, 54.67; H, 10.05. Found: C, 54.43; H, 9.91.

(1*Z*,3*Z*)- and (1*E*,3*Z*)-5-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-(dimethylphenylsilyl)-2-[3,4-(methylenedioxy)phenyl]-1,3-pentadiene (17). Bis(triphenylarsine)-palladium(II) chloride[58] (5.00 mg, 0.006 mmol) was added to the vinylstannane **18** (100 mg, 0.22 mmol) and the bromoalkene **15** (78.0 mg, 0.22 mmol) in DMF (2 mL) at room temperature. After 1.5 h, the reaction mixture was diluted with Et_2O (10 mL), washed with H_2O (5 × 10 mL) and saturated brine (1 × 10 mL), and then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. ^1H NMR of the crude reaction mixture indicated the presence of two diastereomers in a ratio

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(58) Uson, R.; Fornies, J.; Martinez, F. *J. Organomet. Chem.* **1977**, *132*, 429–437.

of 3.1:1 based upon integration of the allylic methylene signals. Chromatography (gradient, 100% hexane to 2% EtOAc/hexane) afforded 92.4 mg (94%) of the title compounds as a pale yellow oil in an unchanged ratio. Radial chromatography of this mixture (2 mm silica gel plate, 2% EtOAc/hexane, 6 mL/min flow rate) allowed the isolation of a small quantity of pure **(1Z,3Z)-17** (major isomer) for characterization, $R_f = 0.45$ (10% EtOAc/hexane): IR (neat) 2953 (s), 2855 (s), 1485 (s), 1435 (s), 1237 (s), 1086 (s), 840 (s), 774 (s) cm^{-1}; ^1H NMR (300 MHz) δ 7.47–7.44 (m, 2 H, $SiMe_2Ph$), 7.35–7.32 (m, 3 H, $SiMe_2Ph$), 6.68 (d, 1 H, $J = 7.6$ Hz, Ar-*H*), 6.58 (dd, 1 H, $J = 7.6$, 1.7 Hz, Ar-*H*), 6.57 (d, 1 H, $J = 1.7$ Hz, Ar-*H*), 6.12 (dt, 1 H, $J = 11.7$, 2.0 Hz, H-3), 5.94 (s, 2 H, OCH_2O), 5.78 (s, 1 H, H-1), 5.63 (dt, 1 H, $J = 11.7$, 5.7 Hz, H-4), 3.99 (dd, 2 H, $J = 5.7$, 2.0 Hz, $tBuMe_2SiOCH_2$), 0.87 (s, 9 H, $OSiMe_2tBu$), 0.15 (s, 6 H, $SiMe_2$-Ph), 0.01 (s, 6 H, $OSiMe_2tBu$); dNOE: irradiation at 6.12 ppm (H-3) produced a 3.8% enhancement of the signal at 5.78 ppm (H-1) and a 12.1% enhancement of the signal at 5.63 ppm (H-4); irradiation at 5.63 ppm (H-4) produced an 11.0% enhancement of the signal at 6.12 ppm (H-3); irradiation of the signal at 5.78 ppm (H-1) produced a 5.4% enhancement of the signal at 6.12 ppm (H-3); ^{13}C NMR (90 MHz) δ 154.6, 147.1, 147.0, 136.2, 133.8, 133.6, 132.9, 131.9, 128.6, 127.6, 123.3, 122.0, 109.1, 107.8, 100.9, 60.4, 25.9, 18.3, −1.4, −5.3; MS *m/z* (rel int) 452 (100, M^+), 317 (8), 209 (23), 186 (9), 147 (11), 136 (16), 135 (77), 91 (19), 75 (14), 73 (43); HRMS calcd for $C_{26}H_{36}O_3Si_2$, 452.2203, found 452.2185. No pure fractions of **(1E,3Z)-17** were isolated. However, ^1H NMR assignments for **(1E,3Z)-17** were possible from analysis of column fractions which contained a mixture of **(1E,3Z)-17** and **(1Z,3Z)-17**. Data for **(1E,3Z)-17**: $R_f = 0.46$ (10% EtOAc/hexane); ^1H NMR (300 MHz) δ 7.40–7.33 (m, 5 H, $SiMe_2Ph$), 6.68 (d, 1 H, $J = 7.6$ Hz, Ar-*H*), 6.65 (d, 1 H, $J = 1.6$ Hz, Ar-*H*), 6.59 (dd, 1 H, $J = 7.6$, 1.6 Hz, Ar-*H*), 6.50 (dt, 1 H, $J = 12.1$, 1.8 Hz, H-3), 5.99 (s, 1 H, H-1), 5.92 (s, 2 H, OCH_2O), 5.82 (dt, 1 H, $J = 12.1$, 6.1 Hz, H-4), 4.47 (dd, 2 H, $J = 6.1$, 1.8 Hz, $tBuMe_2SiOCH_2$), 0.90 (s, 9 H, $OSiMe_2tBu$), 0.08 (s, 6 H, $SiMe_2Ph$), 0.01 (s, 6 H, $OSiMe_2tBu$).

5-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-pentyn-3-ol (20). TMEDA (7.10 g, 61.2 mmol) was added dropwise to *n*-butyllithium (24.3 mL of a 2.10 M solution in hexanes, 51.0 mmol) at room temperature. The yellow solution was then cooled to −65 °C and diluted with THF (42 mL). Acetylene gas (passed through, in series, a −78 °C cold trap, a H_2SO_4 wash bottle, and a K_2CO_3 drying tube) was introduced into the alkyllithium solution over a 40-min period via a pasteur pipet. A solution of 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-propanal[44] (8.00 g, 42.5 mmol) in THF (10 mL) was added. The mixture was warmed to room temperature, washed with H_2O (2 × 75 mL) and saturated brine (1 × 75 mL), and then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Chromatography (gradient 5–15% EtOAc/hexane) afforded 6.90 g (76%) of the title compound as a clear, colorless oil, $R_f = 0.45$ (30% EtOAc/hexane): IR (neat) 3404 (br, s), 3312 (s), 2953 (s), 2861 (s), 1471 (m), 1256 (s), 1092 (s), 835 (s) cm^{-1}; ^1H NMR (300 MHz) δ 4.63 (dddd, 1 H, $J = 6.4$, 6.1, 4.1, 2.1 Hz), 4.06 (ddd, 1 H, $J = 10.3$, 8.0, 3.8 Hz), 3.84 (ddd, 1 H, $J = 10.3$, 5.8, 4.4 Hz), 3.58 (d, 1 H, $J = 6.1$ Hz), 2.46 (d, 1 H, $J = 2.1$ Hz), 2.01 (dddd, 1 H, $J = 14.4$, 8.0, 4.4, 4.1 Hz), 1.87 (dddd, 1 H, $J = 14.4$, 6.4, 5.8, 3.8 Hz), 0.89 (s, 9 H), 0.08 (s, 6 H); ^{13}C NMR (75 MHz) δ 84.5, 72.8, 61.5, 60.9, 38.6, 25.8, 18.1, −5.6; MS *m/z* (rel int) 157 (6, $M^+ - C_4H_9$), 106 (18), 105 (99), 91 (13), 76 (18), 75 (100), 73 (33), 59 (15), 57 (18), 45 (24). Anal. Calcd for $C_{11}H_{22}O_2Si$: C, 61.63; H, 10.34. Found: C, 61.46; H, 10.23.

3-Methoxy-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-pentyne (21). The propargyl alcohol **20** (1.00 g, 4.66 mmol) in THF (4 mL) was added to *n*-butyllithium (3.30 mL of a 1.4 M solution in hexanes, 4.60 mmol) in THF (3 mL) at -25 °C. Dimethyl sulfoxide (1.60 mL) was added, and after 5 min, iodomethane (1.00 g, 7.00 mmol) was introduced. The mixture was warmed to room temperature and then heated to 40 °C. After 2 h, the mixture was cooled to room temperature, diluted with petroleum ether (15 mL), washed with H_2O (5 × 25 mL) and saturated brine (1 × 25 mL), and then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Chromatography (gradient, 100% hexane to 6% EtOAc/hexane) afforded 1.02 g (96%) of the title compound as a clear, colorless oil, $R_f = 0.52$ (10% EtOAc/hexane): IR (neat) 3313 (m), 2933 (s), 2862 (s), 1472 (m), 1256 (m), 1113 (s), 836 (s) cm^{-1}; ^1H NMR (300 MHz) δ 4.12 (ddd, 1 H, $J = 7.6$, 6.0, 2.1 Hz), 3.77–3.72 (m, 2 H), 3.40 (s, 3 H), 2.43 (d, 1 H, $J = 2.1$ Hz), 2.01–1.81 (m, 2 H), 0.89 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (90 MHz) δ 82.6, 73.7, 67.8, 58.8, 56.5, 38.7, 25.9, 18.3, −5.4; MS *m/z* (rel int) 171 (3, $M^+ - C_4H_9$), 141 (3), 131 (4), 119 (94), 113 (13), 105 (12), 89 (100), 83 (22), 73 (39), 69 (28), 59 (45). Anal. Calcd for $C_{12}H_{24}O_2Si$: C, 63.10; H, 10.59. Found: C, 63.09; H, 10.45.

3-(Methoxymethoxy)-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-pentyne (22). Chloromethyl methyl ether (4.14 g, 51.5 mmol) was added to propargyl alcohol **20** (8.48 g, 39.6 mmol) in CH_2Cl_2 (50 mL) at 0 °C. Diisopropylethylamine (6.60 g, 51.5 mmol) was then added dropwise, and the mixture was heated to 40 °C. After 18 h, the mixture was cooled to room temperature and washed with H_2O (1 × 50 mL), saturated NH_4Cl (4 × 50 mL), and saturated brine (1 × 50 mL), and then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Kugelrohr distillation afforded 8.88 g (87%) of the title compound as a clear, colorless oil, bp 70–75 °C (air bath) at 0.17 mmHg, $R_f = 0.39$ (10% EtOAc/hexane): IR (neat) 3312 (m), 2958 (s), 2929 (s), 2889 (s), 2860 (s), 1472 (m), 1255 (m), 1098 (s), 1034 (s), 838 (s) cm^{-1}; ^1H NMR (300 MHz) δ 4.92 (d, 1 H, $J = 6.7$ Hz), 4.61 (d, 1 H, $J = 6.7$ Hz), 4.52 (app dt, 1 H, J *app* = 6.8, 2.0 Hz), 3.79–3.74 (m, 2 H), 3.38 (s, 3 H), 2.41 (d, 1 H, $J = 2.0$ Hz), 2.00–1.87 (m, 2 H), 0.88 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (75 MHz) δ 94.5, 82.8, 73.4, 62.9, 59.0, 55.6, 39.1, 25.9, 18.3, −5.4; MS (CI, NH_3) *m/z* (rel int) 259 (39, $M^+ + H$), 228 (20), 227 (100, $MH^+ - OCH_3$), 215 (6), 171 (22), 169 (31), 155 (5), 145 (7), 119 (8), 106 (14); HRMS (CI, NH_3) calcd for $C_{13}H_{27}O_3Si$ ($M^+ + H$), 259.1729, found 259.1732. Anal. Calcd for $C_{13}H_{26}O_3Si$: C, 60.42; H, 10.14. Found: C, 60.70; H, 10.00.

1-Iodo-3-methoxy-5-[[(1,1-dimethylethyl)dimethylsilyl]-ox]y-1-pentyne (23). *n*-Butyllithium (1.46 mL of a 2.1 M solution in hexanes, 3.06 mmol) was added in a dropwise fashion to a solution of propargyl ether **21** (0.70 g, 3.06 mmol) in Et_2O (10 mL) at −78 °C. After 15 min, iodine (0.86 g, 3.37 mmol) in THF (5 mL) was added dropwise via cannula. The mixture was warmed to room temperature, washed with H_2O (1 × 10 mL), saturated $Na_2S_2O_3$ (1 × 10 mL), and saturated brine (1 × 10 mL), and then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Chromatography (gradient, 2–5% EtOAc/hexane) afforded 0.86 g (79%) of the title compound as a pale yellow, light sensitive oil, $R_f = 0.48$ (10% EtOAc/hexane): IR (neat) 2933 (m), 2862 (m), 1467 (w), 1256 (w), 1103 (s), 836 (s) cm^{-1}; ^1H NMR (300 MHz) δ 4.26 (dd, 1 H, $J = 7.4$, 6.3 Hz), 3.75–3.71 (m, 2 H), 3.40 (s, 3 H), 1.95–1.84 (m, 2 H), 0.89 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (75 MHz) δ 94.1, 69.7, 59.0, 56.5, 38.9, 26.0, 18.3, 1.1, −5.3; MS (CI, NH_3) *m/z* (rel int) 355 (23, $M^+ + H$), 345 (2), 344 (4), 343 (13), 136 (100), 229 (70), 106 (2), 100 (1), 94 (2), 77 (3); HRMS (CI, NH_3) calcd for $C_{12}H_{24}IO_2Si$ ($M^+ + H$) 355.0590, found 355.0603.

1-Iodo-3-(methoxymethoxy)-5-[[(1,1-dimethylethyl)-dimethylsilyl]ox]y-1-pentyne (24). *n*-Butyllithium (16.4 mL of a 2.08 M solution in hexanes, 34.1 mmol) was added in a dropwise fashion to a solution of propargyl ether **22** (8.00 g, 31.0 mmol) in Et_2O (100 mL) at −78 °C. After 15 min, iodine (8.64 g, 34.1 mmol) in THF (70 mL) was added dropwise via cannula. The mixture was warmed to room temperature, washed with H_2O (2 × 75 mL), saturated $Na_2S_2O_3$ (1 × 75 mL), and saturated brine (1 × 75 mL), and then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Kugelrohr distillation afforded 11.4 g (95%) of the title compound as a pale yellow, light sensitive oil, bp 120–125 °C (air bath) at 0.20 mmHg, $R_f = 0.34$ (10% EtOAc/hexane): IR (neat) 2948 (s), 2929 (s), 2889 (s), 2860 (s), 2182 (w), 1471 (m), 1255 (m), 1098 (s), 1029 (s), 838 (s) cm^{-1}; ^1H NMR (360 MHz) δ 4.90 (d, 1 H, $J = 6.8$ Hz), 4.64 (t, 1 H, $J = 6.6$ Hz), 4.59 (d, 1 H, $J = 6.8$ Hz), 3.76–3.72 (m, 2 H), 3.36 (s, 3 H), 2.01–1.84 (m, 2 H), 0.88 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR (75 MHz) δ 93.6, 92.8, 63.6, 58.0, 54.6, 38.1, 24.9, 17.2, 0.0, −6.4; MS (CI, NH_3) *m/z* (rel int) 385 (27, $M^+ + H$), 353 (36), 341 (20), 324 (14), 323 (76), 188 (3), 136 (100), 133 (10), 132 (80), 272 (20); HRMS (CI, NH_3) calcd for $C_{13}H_{26}IO_3Si$ ($M^+ + H$) 385.0696, found 385.0698. Anal. Calcd for $C_{13}H_{25}IO_3Si$: C, 40.63; H, 6.56. Found: C, 41.00, H, 6.46.

(Z)-1-Iodo-3-methoxy-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-pentene (25). Glacial acetic acid (0.48 g, 8.02 mmol) in anhydrous methanol (5 mL) was added via a syringe pump over a 4-h period to a suspension of iodoalkyne **23** (1.14 g, 3.21 mmol) and dipotassium azodicarboxylate[47] (1.31 g, 6.74 mmol) in anhydrous methanol (17 mL) at room temperature. After 19 h, the resulting white suspension was concentrated *in vacuo* to remove most of the methanol. The residue was diluted with Et_2O (30 mL), washed with H_2O (2 × 10 mL), saturated $NaHCO_3$ (1 × 10 mL), and saturated brine (1 × 10 mL), and then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Chromatography (gradient, 100% hexane to 3% EtOAc/hexane) afforded 0.99 g (87%) of the title compound as a pale yellow, light sensitive oil, R_f = 0.46 (10% EtOAc/hexane): IR (neat) 2927 (s), 1608 (m), 1471 (s), 1255 (s), 1108 (s), 838 (s), 759 (s) cm^{-1}; ^1H NMR (360 MHz) δ 6.46 (dd, 1 H, J = 7.6, 1.0 Hz), 6.12 (app t, 1 H, J_{app} = 7.9 Hz), 4.15 (app dt, 1 H, J_{app} = 4.9, 8.1 Hz), 3.78–3.65 (m, 2 H), 3.31 (s, 3 H), 1.85–1.69 (m, 2 H), 0.92 (s, 9 H), 0.08 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (90 MHz) δ 141.7, 83.8, 79.7, 58.8, 56.6, 37.5, 26.0, 18.3, −5.3, −5.4; MS (CI, NH_3) m/z (rel int) 357 (100, M^+ + H), 325 (14), 193 (7), 159 (5), 132 (8), 119 (5), 107 (6), 106 (58), 91 (7), 89 (6); HRMS (CI, NH_3) calcd for $C_{12}H_{26}IO_2Si$ (M^+ + H) 357.0747, found 357.0753.

(Z)-1-Iodo-3-(methoxymethoxy)-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-pentene (26). Glacial acetic acid (6.68 g, 111 mmol) in anhydrous methanol (22 mL) was added via a syringe pump over a 6-h period to a suspension of iodoalkyne **24** (10.2 g, 26.5 mmol) and dipotassium azodicarboxylate[47] (10.8 g, 55.6 mmol) in anhydrous methanol (150 mL) at room temperature. After 20 h, the resulting white suspension was concentrated *in vacuo* to remove most of the methanol. The residue was diluted with Et_2O (100 mL), washed with H_2O (2 × 50 mL), saturated $NaHCO_3$ (1 × 50 mL), and saturated brine (1 × 50 mL), and then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Kugelrohr distillation from copper powder afforded 9.68 g (95%) of the title compound as a pale yellow, light sensitive oil, bp 110–115 °C (air bath) at 0.12 mmHg, R_f = 0.32 (10% EtOAc/hexane): IR (neat) 2948 (s), 2929 (s), 2889 (m), 2860 (m), 1472 (w), 1255 (m), 1152 (m), 1098 (s), 1029 (s), 838 (s) cm^{-1}; ^1H NMR (300 MHz) δ 6.40 (dd, 1 H, J = 7.7, 0.9 Hz), 6.19 (app t, 1 H, J_{app} = 7.9 Hz), 4.60 (ABq, 2 H, $\Delta\nu_{AB}$ = 27.6 Hz, J_{AB} = 6.6 Hz), 4.57–4.50 (m, 1 H), 3.79–3.67 (m, 2 H), 3.37 (s, 3 H), 1.85–1.68 (m, 2 H), 0.91 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (50 MHz) δ 141.8, 94.9, 82.7, 75.8, 58.9, 55.6, 37.6, 25.9, 18.2, −5.3; MS (CI, NH_3) m/z (rel int) 404 (2, M^+ + NH_4), 387 (14, M + H), 357 (4), 355 (6), 343 (4), 342 (11), 325 (6), 214 (6), 137 (7), 136 (100); HRMS (CI, NH_3) calcd for $C_{13}H_{28}IO_3Si$ (M^+ + H) 387.0853, found 387.0854. Anal. Calcd for $C_{13}H_{27}IO_3Si$: C, 40.42; H, 7.04. Found: C, 40.97; H, 6.97.

(Z)-1-(Tri-*n*-butylstannyl)-3-(methoxymethoxy)-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-pentene (28). *n*-Butyllithium (5.48 mL of a 2.08 M solution in hexanes, 11.4 mmol) was added in a dropwise fashion to a solution of iodoalkene **26** (4.00 g, 10.4 mmol) in Et_2O (50 mL) at −78 °C. After 15 min, tri-*n*-butyltin chloride (3.71 g, 11.4 mmol) was added, and the mixture was allowed to warm to room temperature. After 4 h, the mixture was washed with H_2O (3 × 25 mL) and saturated brine (1 × 25 mL) and then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Chromatography (gradient, 100% hexane to 5% EtOAc/hexane) afforded 4.96 g (87%) of the title compound as a clear, colorless oil, R_f = 0.52 (10% EtOAc/hexane): IR (neat) 2958 (s), 2929 (s), 2860 (m), 1599 (w), 1462 (m), 1255 (m), 1152 (m), 1098 (s), 1034 (s), 838 (s) cm^{-1}; ^1H NMR (300 MHz) δ 6.36 (dd, 1 H, J = 13.0, 8.6 Hz), 6.04 [d, 1 H, J = 13.0 Hz, ^2J ($^{117/119}Sn-^1H$) = 60.0 Hz), 4.60 (ABq, 2 H, $\Delta\nu_{AB}$ = 53.0 Hz, J_{AB} = 6.5 Hz), 3.98 (ddd, 1 H, J = 8.6, 8.5, 4.3 Hz), 3.77–3.70 (m, 2 H), 3.34 (s, 3 H), 1.87–1.67 (m, 2 H), 1.54–1.44 (m, 6 H), 1.37–1.25 (m, 6 H), 0.98–0.88 (m, 24 H), 0.06 (s, 6 H); ^{13}C NMR (75 MHz) δ 148.8, 131.7, 94.0, 59.7, 55.2, 39.4, 29.2, 27.3, 26.9, 26.0, 18.3, 13.5, 10.5, −5.3; MS (CI, NH_3) m/z (rel int) 551 (10, M^+ + H), 493 (46), 491 (37), 489 (44), 433 (56), 431 (44), 308 (100), 307 (45), 306 (80), 304 (54); HRMS (CI, NH_3) calcd for $C_{25}H_{55}O_3SiSn$ (M^+ + H) 551.2942, found 551.2962. Anal. Calcd for $C_{25}H_{54}O_3SiSn$: C, 54.65; H, 9.91. Found: C, 54.95; H, 10.25.

(1Z,3Z)-5-(Methoxymethoxy)-7-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-(dimethylphenylsilyl)-2-[3,4-(methylenedioxy)phenyl]-1,3-heptadiene (29). Bis(triphenylarsine)palladium(II) chloride[58] (0.08 g, 0.11 mmol) was added to vinyl stannane **28** (1.92 g, 3.50 mmol) and bromoalkene **14** (2.00 g, 3.50 mmol) in DMF (9 mL) at room temperature. After 26 h, the reaction mixture was diluted with Et_2O (75 mL), washed with H_2O (5 × 50 mL) and saturated brine (1 × 50 mL), and then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. ^1H NMR analysis of the crude reaction mixture indicated the presence of a single diastereomer. Chromatography (CH_2Cl_2) afforded 1.51 g (80%) of the title compound as a yellow oil. Although only a single diastereomer was obtained, 100% isomerization of the terminal double bond occurred, as evidenced by dNOE experiments, R_f = 0.26 (CH_2Cl_2): IR (neat) 3068 (w), 2953 (s), 2929 (s), 2885 (s), 1579 (w), 1503 (m), 1486 (s), 1437 (m), 1248 (s), 1235 (s), 1153 (m), 1096 (s), 1038 (s) cm^{-1}; ^1H NMR (360 MHz, C_6D_6) δ 7.50–7.48 (m, 2 H), 7.23–7.17 (m, 3 H), 6.77 (d, 1 H, J = 1.6 Hz), 6.65 (dd, 1 H, J = 7.8, 1.6 Hz), 6.51 (d, 1 H, J = 7.8 Hz), 6.22 (d, 1 H, J = 11.7 Hz), 6.03 (s, 1 H), 5.36 (dd, 1 H, J = 11.7, 9.6 Hz), 5.29 (dd, 2 H, J = 6.8, 1.4 Hz), 4.66 (d, 1 H, J = 6.6 Hz), 4.60–4.53 (m, 1 H), 4.39 (d, 1 H, J = 6.6 Hz), 3.84–3.77 (m, 1 H), 3.74–3.66 (m, 1 H), 3.14 (s, 3 H), 2.00–1.91 (m, 1 H), 1.86–1.76 (m, 1 H), 0.96 (s, 9 H), 0.20 (s, 3 H), 0.18 (s, 3 H), 0.06 (s, 6 H), dNOE; irradiation at 6.03 ppm (H-1) produced a 5.7% enhancement of the signal at 6.22 ppm (H-3), and a 3.2% enhancement of the signal at 5.36 ppm (H-4); irradiation at 6.22 ppm (H-3) produced a 13.5% enhancement of the signal at 6.03 ppm (H-1) and a 10.4% enhancement of the signal at 5.36 ppm (H-4); rrradiation at 5.36 ppm (H-4) produced a 22.3% enhancement of the signal at 6.22 ppm (H-3) and a 7.9% enhancement of the signal at 6.03 ppm (H-1); ^{13}C NMR (90 MHz, C_6D_6) δ 155.7, 148.5, 148.3, 143.9, 140.7, 137.1, 137.0, 134.7, 133.9, 132.7, 129.7, 123.1, 110.3, 108.8, 101.6, 94.7, 69.3, 61.0, 60.2, 55.6, 40.4, 26.9, 19.2, −0.4, −4.5; MS m/z (rel int) 540 (14, M^+), 495 (27), 337 (31), 313 (25), 269 (100), 267 (80), 265 (56), 135 (56), 89 (50), 45 (47); HRMS calcd for $C_{30}H_{44}O_5Si_2$ 540.2727, found 540.2723. Anal. Calcd for $C_{30}H_{44}O_5Si_2$: C, 66.62; H, 8.20. Found: C, 66.70; H, 8.30.

(Z)-5-(Tri-*n*-butylstannyl)-3-(methoxymethoxy)-4-penten-1-ol (30). Tetrabutylammonium fluoride (6.32 mL of a 1 M solution in THF, 6.32 mmol) was added to silyl ether **28** (3.16 g, 5.74 mmol) in THF (20 mL) at room temperature. After 2 h, the mixture was washed with H_2O (3 × 20 mL) and saturated brine (1 × 20 mL) and then dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Chromatography (gradient, 10 to 20% EtOAc/hexane) afforded 2.06 g (82%) of the title compound as a clear, colorless oil, R_f = 0.40 (30% EtOAc/hexane): IR (neat) 3422 (br, s), 2916 (s), 1460 (m), 1032 (s) cm^{-1}; ^1H NMR (300 MHz) δ 6.40 (dd, 1 H, J = 12.9, 8.6 Hz), 6.10 (d, 1 H, J = 12.9 Hz), 4.61 (ABq, 2 H, $\Delta\nu_{AB}$ = 58.3 Hz, J_{AB} = 6.6 Hz), 4.07 (app dt, 1 H, J_{app} = 8.6, 4.1 Hz), 3.82–3.77 (m, 2 H), 3.37 (s, 1 H), 2.48 (bs, 1 H), 1.94–1.71 (m, 2 H), 1.55–1.44 (m, 6 H), 1.37–1.25 (m, 6 H), 0.97–0.87 (m, 15 H); ^{13}C NMR (75 MHz) δ 148.0, 132.9, 93.9, 78.9, 60.4, 55.4, 38.7, 29.2, 27.3, 13.5, 10.6; MS (CI, NH_3) m/z (rel int) 437 (20, M^+ + H), 379 (100, M − C_4H_9), 377 (81), 375 (99), 373 (52), 319 (67), 317 (58), 308 (55), 291 (63), 115 (28); HRMS (CI, NH_3) calcd for $C_{19}H_{41}O_3{}^{120}Sn$ (M^+ + H) 437.2078, found 437.2051. Anal. Calcd for $C_{19}H_{40}O_3Sn$: C, 52.44; H, 9.26. Found: C, 52.54; H, 9.21.

(4Z,6Z)-3-(Methoxymethoxy)-7-(dimethylphenylsilyl)-6-[(3,4-methylenedioxy)phenyl]-4,6-heptadien-1-ol (31). Method A. Bis(triphenylarsine)palladium(II) chloride[58] (0.28 g, 0.36 mmol) was added to vinylstannane **30** (3.18 g, 7.02 mmol) and bromoalkene **14** (2.54 g, 7.02 mmol) in DMF at room temperature. After 18 h, the reaction mixture was diluted with Et_2O (60 mL), washed with H_2O (4 × 50 mL) and saturated brine (1 × 50 mL), and then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Chromatography (gradient, 10–30% EtOAc/hexane) affforded 2.01 g (67%) of the title compound as a yellow oil. Although only a single diastereomer was obtained, 100% isomerization of the terminal double bond occurred, as evidenced by spectral comparison to the compound obtained by method B.

Method B. Tetrabutylammonium fluoride (2.98 mL of a 1 M solution in THF, 2.98 mmol) was added in a dropwise fashion to silyl ether **29** (1.47 g, 2.71 mmol) in THF (3 mL) at room temperature. After 4 h, the mixture was diluted with Et_2O (30 mL), washed with H_2O (1 × 15 mL), saturated $NaHCO_3$ (1 × 15 mL), and saturated brine (1 × 15 mL), and then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Chromatography (gradient, 10–30% EtOAc/hexane) afforded 0.77 g (67%) of the title compound as a yellow oil, R_f = 0.15 (30% EtOAc/hexane): IR (neat) 3428 (br, w), 3069 (w), 2951 (m), 2888 (m), 1604 (w), 1503 (m), 1489 (s), 1440 (m), 1248 (s), 1151 (m), 1115 (s), 1039 (s) cm^{-1}; ^1H NMR (360 MHz) δ 7.44–7.41 (m, 2 H), 7.32–7.29 (m, 3 H), 6.68 (dd, 1 H, J = 6.7, 1.7 Hz), 6.57 (dd, 1 H, J = 6.7, 1.6 Hz), 6.56 (s, 1 H), 6.28 (d, 1 H, J = 11.8 Hz), 5.93 (s, 2 H), 5.87 (s, 1 H), 5.37 (dd, 1 H, J = 11.8, 9.5 Hz), 4.59 (d, 1 H, J = 6.5 Hz), 4.43 (d, 1 H, J = 6.5 Hz), 4.31 (dt, 1 H, J = 3.3, 9.5 Hz), 3.67–3.60 (m, 1 H), 3.57–3.51 (m, 1 H), 3.28 (s, 3 H), 1.80–1.70 (m, 1 H), 1.64–1.54 (m, 1 H), 0.14 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (90 MHz) δ 154.3, 147.4, 147.2, 139.6, 136.2, 135.9, 133.6, 132.9, 132.1, 128.7, 127.6, 122.1, 109.2, 107.8, 100.9, 94.1, 70.6, 60.2, 55.1, 38.1, −1.5; MS m/z (rel int) 426 (12, M^+), 381 (11), 303 (15), 229 (17), 199 (14), 136 (17), 135 (100), 91 (33), 75 (16), 45 (43); HRMS calcd for $C_{24}H_{30}O_5Si$ 426.1863, found 426.1871. Anal. Calcd for $C_{24}H_{30}O_5Si$: C, 67.57; H, 7.09. Found: C, 67.66; H, 6.91.

(4*Z*,6*Z*)-3-(Methoxymethoxy)-7-(dimethylphenylsilyl)-6-[3,4-(methylenedioxy)phenyl]-4,6-heptadienal. Dimethyl sulfoxide (0.59 g, 7.60 mmol) in CH_2Cl_2 (4 mL) was added to freshly distilled oxalyl chloride (0.48 g, 3.80 mmol) in CH_2Cl_2 (8 mL) at −70 °C. After 5 min, alcohol **31** (1.35 g, 3.16 mmol) in CH_2Cl_2 (4 mL) was added. After another 5 min, triethylamine (1.61 g, 15.9 mmol) in CH_2Cl_2 (4 mL) was added, and the reaction mixture was allowed to warm to room temperature. The mixture was washed with saturated NH_4Cl (5 × 50 mL) and saturated brine (1 × 50 mL) and then dried ($MgSO_4$), filtered, and concentrated *in vacuo*, which afforded 1.33 g (99%) of the title compound as a thick orange oil. The aldehyde was not purified, since it was analytically pure as obtained and exposure to silica gel or alumina caused elimination of the methoxymethoxy group, R_f = 0.39 (30% EtOAc/hexane): IR (neat) 3068 (w), 2952 (m), 2892 (m), 1728 (s), 1563 (w), 1502 (m), 1486 (s), 1438 (m), 1235 (s), 1151 (m), 1101 (s), 1038 (s) cm^{-1}; ^1H NMR (300 MHz) δ 9.50 (dd, 1 H, J = 3.2, 1.5 Hz), 7.44–7.40 (m, 2 H), 7.34–7.30 (m, 3 H), 6.69 (dd, 1 H, J = 7.4, 1.0 Hz), 6.60–6.57 (m, 2 H), 6.32 (d, 1 H, J = 11.8 Hz), 5.94 (s, 2 H), 5.91 (s, 1 H), 5.37 (dd, 1 H, J = 11.8, 9.5 Hz), 4.64–4.56 (m, 2 H), 4.41 (d, 1 H, J = 6.7 Hz), 2.55 (ddd, 1 H, J = 16.1, 9.2, 3.2 Hz), 2.31 (ddd, 1 H, J = 16.1, 3.5, 1.5 Hz), 0.16 (s, 3 H), 0.13 (s, 3 H); ^{13}C NMR (75 MHz) δ 199.8, 154.0, 147.4, 139.4, 136.9, 136.6, 133.8, 133.6, 130.0, 128.3, 127.7, 122.1, 109.2, 107.9, 101.0, 94.2, 67.0, 55.3, 49.2, −1.5; MS m/z (rel int) 424 (1, M^+), 364 (1, $M^+ - C_2H_5O_2$), 229 (9), 201 (42), 185 (17), 136 (14), 135 (100), 121 (14), 105 (9), 91 (39), 89 (15), 45 (78); HRMS calcd for $C_{24}H_{28}O_5Si$ 424.1706, found 424.1704. Anal. Calcd for $C_{24}H_{28}O_5Si$: C, 67.90; H, 6.65. Found: C, 67.61; H, 6.73.

(4*Z*,6*Z*)-*N*-[(Tri-*n*-butylstannyl)methyl]-3-(methoxymethoxy)-7-(dimethylphenylsilyl)-6-[3,4-(methylenedioxy)phenyl]-4,6-heptadienimine (32). Hydrazine monohydrate (1.22 g, 24.4 mmol) was added to *N*-[(tri-*n*-butylstannyl)methyl]phthalimide[23] (0.22 g, 0.49 mmol) in absolute ethanol (2 mL), and the mixture was heated at reflux (80 °C) for 10 min. The resulting clear, yellow solution was cooled to room temperature and concentrated *in vacuo* to remove most of the ethanol. The residue was diluted with Et_2O (10 mL), washed with H_2O (4 × 10 mL) and saturated brine (1 × 10 mL), and then dried (Na_2SO_4), filtered through Celite, and concentrated *in vacuo*. The crude amine (≤0.49 mmol) was diluted with Et_2O (0.5 mL) and added dropwise to a suspension of aldehyde prepared above (0.20 g, 0.47 mmol) and 4-Å molecular sieves (0.15 g) in Et_2O (0.5 mL). After 6 h at room temperature, the mixture was filtered through Celite and concentrated *in vacuo*, which afforded 0.33 g (97%) of a thick orange oil which was used without further purification: IR (neat) 2922 (s), 1650 (m), 1485 (s), 1235 (s), 1099 (s), 1040 (s), 848 (s) cm^{-1}; ^1H NMR (300 MHz) δ 7.44–7.28 (m, 5 H), 6.66 (d, 1 H, J = 8.3 Hz), 6.59–6.56 (m, 2 H), 6.29 (d, 1 H, J = 11.8 Hz), 5.92 (s, 2 H), 5.87 (s, 1 H), 5.39 (dd, 1 H, J = 11.8, 9.6 Hz), 4.59 (d, 1 H, J = 6.6 Hz), 4.44 (d, 1 H, J = 6.6 Hz), 4.41–4.36 (m, 1 H), 3.54 [s, 2 H, ^2J ($^{117/119}Sn-^1H$) = 43.8 Hz], 3.26 (s, 3 H), 2.44–2.30 (m, 2 H), 1.55–1.44 (m, 6 H), 1.37–1.24 (m, 6 H), 0.95–0.86 (m, 15 H), 0.14 (s, 3 H), 0.12 (s, 3 H); ^{13}C NMR (75 MHz) δ 155.6, 154.2, 147.2, 147.1, 139.5, 136.1, 135.8, 133.5, 132.3, 132.0, 128.5, 127.5, 122.0, 109.1, 107.6, 100.7, 93.9, 69.4, 54.8, 47.2, 41.9, 28.9, 27.1, 26.8, 13.4, 9.2, −1.5; MS m/z (rel int) 727 (4, M^+), 291 (41), 289 (34), 235 (48), 233 (37), 179 (62), 177 (60), 175 (42), 135 (100), 45 (41); HRMS calcd for $C_{37}H_{57}O_4NSi^{120}Sn$ 727.3079, found 727.3087.

(3α,3aα,6β,7aα)-2,3,4,6,7,7a-Hexahydro-6-(methoxymethoxy)-1-methyl-3-(dimethylphenylsilyl)-3a-[3,4-(methylenedioxy)phenyl]indole (33). Imine **32** (0.32 g, 0.44 mmol) in THF (2 mL) was added dropwise over a 15-min period to *n*-butyllithium (0.40 mL of a 1.76 M solution in hexanes, 0.44 mmol) in THF (58 mL) at −78 °C. After 10 min, the deep burgundy-colored solution was warmed to -40 °C, and methyl iodide (0.11 g, 0.75 mmol) was added. The mixture was warmed to room temperature and concentrated *in vacuo* to a volume of approximately 10 mL. The residue was diluted with Et_2O (30 mL), washed with H_2O (2 × 30 mL), saturated $NaHCO_3$ (1 × 30 mL), and saturated brine (1 × 30 mL), and then dried ($MgSO_4$), filtered, and concentrated *in vacuo*. ^1H NMR analysis of the crude reaction mixture indicated the presence of a single diastereomer. Chromatography (gradient, 100% $CHCl_3$ to 20% MeOH/$CHCl_3$) afforded 0.11 g (53%) of the title compound (overall from the alcohol **31**) as a golden oil, R_f = 0.33 (10% MeOH/$CHCl_3$): IR (neat) 2947 (m), 2887 (m), 1482 (s), 1427 (m), 1233 (s), 1039 (s), 730 (m) cm^{-1}; ^1H NMR (300 MHz) δ 7.31–7.23 (m, 5 H, $SiMe_2Ph$), 6.66 (s, 1 H, Ar-*H*), 6.62–6.61 (m, 2 H, Ar-*H*), 5.91 (ABq, 2 H, $\Delta\nu_{AB}$ = 3.2 Hz, J_{AB} = 1.4 Hz, OCH_2O), 5.87 (d, 1 H, J = 10.2 Hz, CH=C*H*), 5.75 (dd, 1 H, J = 10.2, 3.8 Hz, CH=C*H*), 4.68 (ABq, 2 H, $\Delta\nu_{AB}$ = 16.1 Hz, J_{AB} = 6.9 Hz, OCH_2OCH_3), 3.97 (ddd, 1 H, J = 4.8, 4.1, 3.8 Hz, H-6α), 3.37 (s, 1 H, OCH_2OCH_3), 3.30 (dd, 1 H, J = 9.0, 7.4 Hz, H-3β), 2.56 (dd, 1 H, J = 4.6, 4.1 Hz, H-7aα), 2.52 (dd, 1 H, J = 12.4, 9.0 Hz, H-2β), 2.38 (s, 3 H, N-CH_3), 1.97 (dd, 1 H, J = 12.4, 7.4 Hz, H-2α), 1.91 (dt, 1 H, J = 14.8, 4.1 Hz, H-7α), 1.67 (dt, 1 H, J = 14.8, 4.6 Hz, H-7β), 0.07 (s, 3 H, SiMe_2Ph), 0.02 (s, 3 H, SiMe_2Ph); Note: The relative stereochemistry of this compound was inferred from dNOE experiments carried out on the free allylic alcohol (see compound **35** below); ^{13}C NMR (75 MHz) δ 147.3, 146.0, 141.0, 138.9, 137.1, 133.9, 128.8, 127.6, 124.3, 121.1, 109.3, 107.4, 100.9, 95.2, 72.5, 68.3, 59.4, 55.3, 52.3, 40.9, 39.4, 28.2, −2.7, −2.8; MS (CI, NH_3) m/z (rel int) 452 (100, $M^+ + H$), 451 (6, M^+), 450 (9), 438 (4), 406 (4), 392 (5), 391 (11), 390 (9), 152 (3), 135 (8); HRMS (CI, NH_3) calcd for $C_{26}H_{34}NO_4Si$ ($M^+ + H$) 452.2257, found 452.2232.

(3α,3aα,6β,7aα)-2,3,4,6,7,7a-Hexahydro-6-hydroxy-1-methyl-3-(dimethylphenylsilyl)-3a-[3,4-(methylenedioxy)phenyl]indole (35). Concentrated HCl (2 drops) was added to allylic ether **33** (12.9 mg, 0.03 mmol) in THF (2 mL) at room temperature. After 7 h, the mixture was diluted with EtOAc (10 mL), washed with 10% NaOH (2 × 10 mL), H_2O (1 × 10 mL), and saturated brine (1 × 10 mL), and then dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Chromatography (gradient, 5 to 20% MeOH/$CHCl_3$) afforded 8.30 mg (68%) of the title compound as a golden oil, R_f = 0.63 (20% MeOH/$CHCl_3$): IR (neat) 3348 (w), 2928 (m), 2854 (m), 1485 (s), 1433 (m), 1233 (s), 1043 (s), 807 (m), 733 (m) cm^{-1}; ^1H NMR (360 MHz) δ 7.32–7.21 (m, 5 H, $SiMe_2Ph$), 6.60–6.59 (m, 3 H, Ar-*H*), 5.98 (dd, 1 H, J = 10.2, 5.3 Hz, CH=C*H*), 5.93 (ABq, 2 H, $\Delta\nu_{AB}$ = 5.7 Hz, J_{AB} = 1.4 Hz, OCH_2O), 5.85 (d, 1 H, J = 10.2 Hz, CH=C*H*), 3.97 (ddd, 1 H, J = 5.3, 3.3, 2.8 Hz, H-6α), 3.33 (dd, 1 H, J = 9.4, 7.0 Hz, H-3α), 2.68 (dd, 1 H, J = 3.3, 2.8 Hz, H-7aα), 2.49 (dd, 1 H, J = 13.3, 9.4 Hz, H-2β), 2.42 (s, 3 H, N-CH_3), 2.13 (dt, 1 H, J = 14.9, 2.8 Hz, H-7α), 1.96 (dd, 1 H, J = 13.3, 7.0 Hz, H-2α), 1.50 (dt, 1 H, J = 14.9, 3.3 Hz, H-7β), 0.14 (s, 3 H), 0.07 (s, 3 H); all ^1H assignments were made from a two dimentional COSY experiment; dNOE: irradiation at 2.49 ppm (H-2β) produced a 20.8% enhancement of the signal at 3.33 ppm (H-3β); irradiation at 3.33 ppm (H-3β) produced

an 18.2% enhancement of the signal at 2.49 ppm (H-2β); irradiation at 6.60 ppm (Ar-H) produced a 9.2% enhancement of the signal at 2.68 ppm (H-7aα); irradiation at 3.97 ppm (H-6α) produced a 2.0% enhancement of the signal at 2.13 ppm (H-7α); irradiation at 2.13 ppm (H-7α) produced a 2.7% enhancement of the signal at 3.97 ppm (H-6α) and a 3.8% enhancement of the signal at 2.68 ppm (H-7aα); irradiation at 2.68 ppm (H-7aα) produced a 13.7% enhancement of the multiplet at 6.60–6.59 ppm (Ar-H); the observed NOE enhancements involving the allylic proton (H-6α) were quite small; further evidence for the relative stereochemistry of this center was inferred from the synthesis and comparison of allylic ethers **36** and **37** (see below); ^{13}C NMR (50 MHz) δ 147.1, 145.9, 140.2, 138.4, 135.8, 133.6, 128.7, 127.5, 125.1, 121.0, 109.0, 107.3, 100.8, 74.9, 63.0, 60.9, 52.3, 42.4, 40.3, 27.1, −2.4, −3.0; MS *m*/*z* (rel int) 407 (24, M$^+$), 406 (8), 350 (10), 337 (11), 272 (13), 135 (35), 91 (8), 71 (9), 70 (100), 42 (13); HRMS calcd for $C_{24}H_{29}NO_3Si$ 407.1918, found 407.1923.

(3α,3aα,6β,7aα)-2,3,4,6,7,7a-Hexahydro-6-methoxy-1-methyl-3-(dimethylphenylsilyl)-3a-[3,4-(methylenedioxy)phenyl]indole (36). Allylic alcohol **35** (17.0 mg, 0.04 mmol) in THF (1 mL) was added to a suspension of potassium hydride (washed free of mineral oil with hexane, 18.9 mg, 0.47 mmol) in THF (1 mL) at 0 °C. After 1.5 h at room temperature, the mixture was recooled to 0 °C, and methyl iodide (0.02 g, 0.11 mmol) was added. The mixture was warmed to room temperature, diluted with Et_2O (15 mL), washed with H_2O (2 × 10 mL) and saturated brine (1 × 10 mL), and then dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Chromatography (10% Et_3N/hexane) afforded 26.8 mg (92%) of the title compound as a golden oil, R_f = 0.32 (8:1:1 hexane:EtOAc:Et_3N): IR (neat) 2924 (s), 1486 (s), 1235 (s), 1109 (m), 1039 (s), 803 (m) cm^{-1}; ^{1}H NMR (300 MHz) δ 7.31–7.22 (m, 5 H, SiMe$_2$*Ph*), 6.67–6.59 (m, 3 H, Ar-*H*), 5.92 (ABq, 2 H, $\Delta\nu_{AB}$ = 0.1 Hz, J_{AB} = 3.9 Hz, OC*H*$_2$O), 5.89–5.84 (m, 2 H, C*H*=C*H*), 3.55 (ddd, 1 H, *J* = 4.6, 4.5, 2.3 Hz, H-6α), 3.37 (s, 3 H, NCH$_3$), 3.30 (bt, 1 H, *J* = 8.2 Hz, H-3β), 2.62–2.53 (m, 2 H, H-2β, H-7aα), 2.41 (s, 3 H, OC*H*$_3$), 1.99 (dd, 1 H, *J* = 12.2, 7.5 Hz, H-2α), 1.91 (dt, 1 H, *J* = 14.6, 4.5 Hz, H-7α), 1.68 (dt, 1 H, *J* = 14.6, 4.6 Hz, H-7β), 0.07 (s, 3 H, Si*Me*$_2$Ph), 0.03 (s, 3 H, Si*Me*$_2$Ph); ^{13}C NMR (75 MHz) δ 147.2, 145.9, 141.0, 138.7, 136.5, 133.8, 128.7, 127.4, 124.3, 121.0, 109.2, 107.3, 100.8, 72.9, 72.5, 59.2, 56.5, 52.6, 40.9, 39.3, 27.8, −2.6, −2.7; MS *m*/*z* (rel int) 421 (11, M$^+$), 230 (16), 135 (26), 71 (19), 70 (100), 69 (15), 57 (22), 55 (15), 43 (17), 41 (14); HRMS calcd for $C_{25}H_{31}NO_3Si$ 421.2073, found 421.2052.

(3α,3aα,6α,7aα)-2,3,4,6,7,7a-Hexahydro-6-methoxy-1-methyl-3-(dimethylphenylsilyl)-3a-[3,4-(methylenedioxy)phenyl]indole (37). Triethylamine (0.23 g, 2.22 mmol) and methanesulfonic anhydride (0.39 g, 2.22 mmol) in THF (1 mL) were added to allylic alcohol **35** (0.13 g, 0.32 mmol) in THF (6.4 mL) at 0 °C. After 40 min, anhydrous methanol (4.0 mL, 99 mmol) was added, and the mixture was allowed to warm to room temperature. After 24 h, the reation mixture was diluted with EtOAc (10 mL), washed with 10% NaOH (2 × 10 mL), H_2O (1 × 10 mL), and saturated brine (1 × 10 mL), and then dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Chromatography (10% Et_3N/hexane) afforded 0.11 g (79%) of the title compound as a yellow oil, R_f = 0.33 (8:1:1 hexane:EtOAc:Et_3N): IR (neat) 2949 (s), 2777 (m), 1726 (w), 1487 (s), 1235 (s), 1095 (s), 1041 (s), 734 (s) cm^{-1}; ^{1}H NMR (360 MHz) δ 7.32–7.22 (m, 5 H, SiMe$_2$*Ph*), 6.65–6.58 (m, 3 H, Ar-*H*), 5.90 (app d, 2 H, J_{app} = 4.9 Hz, C*H*=C*H*), 5.81 (ABq, 2 H, $\Delta\nu_{AB}$ = 4.6 Hz, J_{AB} = 10.4 Hz, OC*H*$_2$O), 3.87 (dd, 1 H, *J* = 10.9, 5.2 Hz, H-6β), 3.36 (s, 3 H, OC*H*$_3$), 3.25 (dd, 1 H, *J* = 9.1, 6.9 Hz, H-3α), 2.46 (br s, 1 H, H-7aα), 2.44 (dd, 1 H, *J* = 13.1, 9.1 Hz, H-2β), 2.38 (s, 3 H, NC*H*$_3$), 2.09 (ddd, 1 H, *J* = 13.5, 5.2, 4.3 Hz, H-7β), 1.80 (dd, 1 H, *J* = 13.1, 6.9 Hz, H-2α), 1.28 (ddd, 1 H, *J* = 13.5, 10.9, 3.0 Hz, H-7α), 0.13 (s, 3 H, Si*Me*$_2$Ph), 0.05 (s, 3 H, Si*Me*$_2$Ph); ^{13}C NMR (90 MHz) δ 146.8, 145.6, 140.4, 138.4, 136.0, 133.7, 128.7, 127.4, 123.8, 121.2, 109.2, 107.1, 100.8, 75.2, 72.1, 60.0, 55.6, 51.9, 42.8, 40.2, 26.3, −2.3, −3.1; MS *m*/*z* (rel int) 421 (17, M$^+$), 406 (9, M-CH$_3$), 338 (17), 337 (45), 202 (20), 201 (14), 135 (33), 71 (9), 70 (100), 42 (12); HRMS calcd for $C_{25}H_{31}NO_3Si$ 421.2073, found 421.2076.

(4aα,7aα)-1-Methyl-4-[3,4-(methylenedioxy)phenyl]-1,2,7,7a-tetrahydro-4a*H*-1-pyrindine (41). Tetrafluoroboric acid–diethyl ether complex (160 mg of an 85% solution in Et_2O, 0.86 mmol) was added to silane **37** (24.1 mg, 0.06 mmol) in CH_2Cl_2 (1.7 mL) at 0 °C, and the mixture was allowed to warm to room temperature. After 2 h, the mixture was recooled to 0 °C, and the excess tetrafluoroboric acid was quenched by the dropwise addition of saturated $NaHCO_3$ (2 mL). The biphasic mixture was diluted with Et_2O (10 mL), warmed to room temperature, and washed with saturated $NaHCO_3$ (1 × 10 mL), H_2O (1 × 10 mL) and saturated brine (1 × 10 mL), and then dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Chromatography (8:1:1 hexane:EtOAc:Et_3N) afforded 5.90 mg (41%) of the title compound as a pale yellow oil, R_f = 0.23 (8:1:1 hexane:EtOAc:Et_3N): IR (neat) 2892 (m), 2771 (m), 1501 (m), 1486 (s), 1439 (m), 1245 (s), 1040 (s) cm^{-1}; ^{1}H NMR (300 MHz) δ 6.75–6.68 (m, 3 H, Ar-*H*), 5.92 (s, 2 H, OC*H*$_2$O), 5.87 (ddt, 1 H, *J* = 9.9, 5.8, 2.2 Hz, C*H*=CH), 5.69 (dddd, 1 H, *J* = 9.9, 3.1, 1.1, 0.9 Hz, C*H*=CH), 5.54 (br s, 1 H, ArC=C*H*), 4.14 (br s, 1 H), 3.79 (ddd, 1 H, *J* = 13.2, 4.6, 2.2 Hz), 3.38–3.31 (m, 1 H), 3.19 (ddt, 1 H, *J* = 13.2, 5.2, 1.6 Hz), 2.64 (dt, 1 H, *J* = 16.7, 5.8 Hz), 2.47 (s, 3 H, N-C*H*$_3$), 2.12–2.00 (m, 1 H); due to extensive long-range ^{1}H–^{1}H coupling, a two-dimensional COSY experiment did not allow unambiguous ^{1}H assignments to be made; ^{13}C NMR (90 MHz) δ 147.6, 142.9, 138.3, 128.4, 127.5, 125.7, 120.2, 119.4, 108.1, 107.9, 100.9, 65.2, 61.3, 43.3, 40.7, 33.1; MS *m*/*z* (rel int) 255 (100, M$^+$), 254 (23), 253 (29), 212 (21), 174 (25), 144 (22), 116 (46), 115 (30), 94 (24), 42 (23); HRMS calcd for $C_{16}H_{17}NO_2$ 255.1259, found 255.1259.

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Supplementary Material Available: ^{1}H NMR spectra of compounds without elemental analysis (11 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.