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Stereoselective One-Step Construction of Vicinal Quaternary and Tertiary Stereocenters of the 5,10b-Ethanophenanthridine Skeleton: Total Synthesis of (±)-Maritidine

Ganesh Pandey,* Nishant R. Gupta, and Tukaram M. Pimpalpalle

Division of Organic Chemistry, National Chemical Laboratory, Dr. Homi Bhabha Road, Pune-411 008, India

gp.pandey@ncl.res.in

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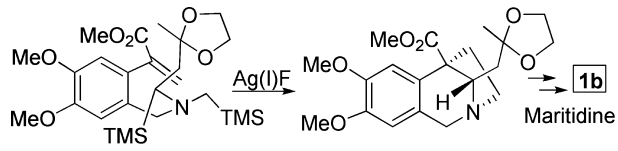
ABSTRACT



The challenging vicinal quaternary and tertiary stereocenters of the 5,10b-ethanophenanthridine skeleton are created in a single step utilizing intramolecular [3 + 2]-cycloaddition of nonstabilized azomethine ylide as the key step. The application of the chemistry is demonstrated by synthesizing (±)-maritidine.

The Amaryllidaceae alkaloids[1] have long been the source of structurally intriguing target molecules due to their architectural diversity, limited supply, and promising biological activities. Crinine alkaloids[2] which belong to the biggest and truly representative class of this family comprises more than 50 members possessing immunostimulant, antitumor, and antiviral activities.[3] Maritidine (**1b**), isolated from *Pancratium maritimum*, *Pancratium tortuosum*, and *Zephyranthes* genera,[4] is the first alkaloid with a 5,10b-ethanophenanthridine nucleus containing dimethoxy rather than methylenedioxy substituents at C-8 and C-9 positions of the crinine skeleton (Figure 1). These alkaloids display adjacent quaternary and tertiary carbon stereocenters with a fused pyrrolidine ring whose stereochemical incorporation is the critical element in the synthesis of these types of alkaloids. Alkaloid **1b** is of particular interest due to its cytotoxic properties[5] and limited supplies from natural sources.[6] A literature survey has revealed that assembling of the core 5,10b-ethanophenanthridine skeleton of **1b** has utilized

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(2) For recent synthesis of Crinine-type alkaloids, see: (a) Tam, N. T.; Chang, J.; Jung, E.-J.; Cho, C.-G. *J. Org. Chem.* **2008**, *73*, 6258. (b) Bohno, M.; Sugie, K.; Imase, H.; Yusof, Y. B.; Oishi, T.; Chida, N. *Tetrahedron* **2007**, *63*, 6977, and references therein.

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(5) (a) Alarcon, M.; Cea, G.; Weigert, G. *Environ. Contam. Toxicol.* **1986**, *37*, 508. (b) Pacheco, P.; Silva, M.; Steglich, W.; Watson, W. H. *Rev. Latinoam. Quim.* **1978**, *9*, 28. (c) Elgorashi, E. E.; Stafford, G. I.; Jager, A. K.; van Staden, J. *Planta Med.* **2006**, *72*, 470 (inhibition of [3*H*]citalopram binding to the rat brain serotonin transporter). (d) Cea, G.; Alarcon, M.; Weigart, G. *Med. Sci.* **1986**, *14*, 90 (clastogenic effect/mutagenic).

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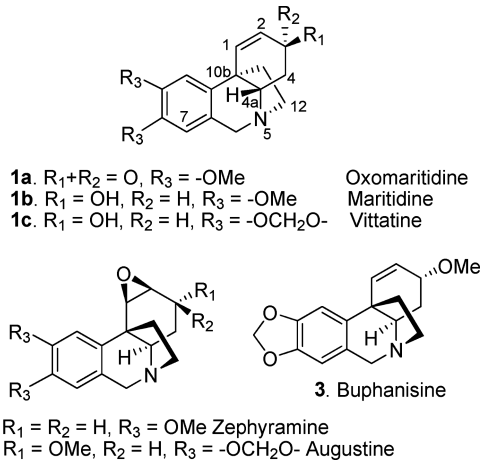
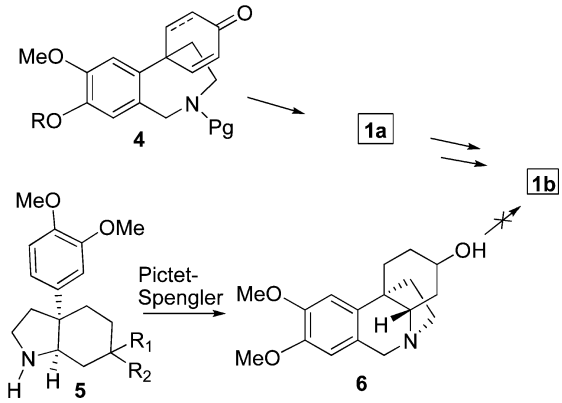


Figure 1. Representative structures of 5,10b-ethanophenanthridine alkaloids.

essentially two approaches. While the majority of approaches used spiro-fused dienone **4** to elaborate to **1b**, few strategies have also employed the Pictet−Spengler cyclization of 3-aryl-substituted hydroindole derivatives **5** into dihydromaritidine **6**. Spiro-fused **4** has been synthesized employing phenolic oxidative para−para coupling[7−10,14] and photochemical cyclization[11] of norbelladine derivatives. Other routes to **4** involve intramolecular Heck coupling[12] or the cyclization of an intermediate iron carbonyl complex.[13] The synthesis of **5** involved key reactions such as regioselective reduction of 1-methyl-3,3-disubstituted pyrrolidine-2,5-dione,[15a] intramolecular ene cyclization of an appropriately constructed acylnitroso olefin,[15b] or condensation of 3-arylated Δ^1-pyrrolinium salts with the *tert*-butyl 3-oxopent-4-enoate[15c] (Scheme 1).

Scheme 1. Various Approaches Towards Maritidine



From the preceding discussion, it is apparent that these strategies employed stepwise generation of vicinal quaternary and tertiary stereocenters along with the use of a cyclic precursor for C-ring formation. Moreover, the Pictet−Spengler cyclization route has produced only the dihydromaritidine whose oxidative conversion to **1b** has remained unsuccessful to date.

Our continuing interest in exploring the application of nonstabilized azomethine ylides generated by sequential double desilylation of α,α′-bis(trimethylsilylmethyl)alkylamines[16] in the total synthesis of alkaloids[17] with complex architectures and the need to develop a concise and versatile strategy to synthesize these types of alkaloids led us to envisage the synthesis of **1** through an intramolecular 1,3-dipolar cycloaddition of a nonstabilized azomethine ylide (AMY) as shown retrosynthetically in Scheme 2. This proposed strategy originated from our recently accomplished formal synthesis of the fused polycyclic 5,11-methanomorphanthridine skeleton of (±)-pancracine.[18]

Regio- as well as stereochemical issues, the two important aspects of this cycloaddition strategy, were evaluated at the planning stage of the synthesis itself. The origin of the 5,10b-ethanophenanthridine regiochemistry during cycloaddition, in contrast to the 5,11-methanophenanthridine skeleton,[18] was speculated based on the change in the LUMO energy of the dipolarophile due to its conjugation with the aromatic ring and ester moiety present on the same carbon. Cycloaddition reaction of **8** was visualized to generate the vicinal quaternary

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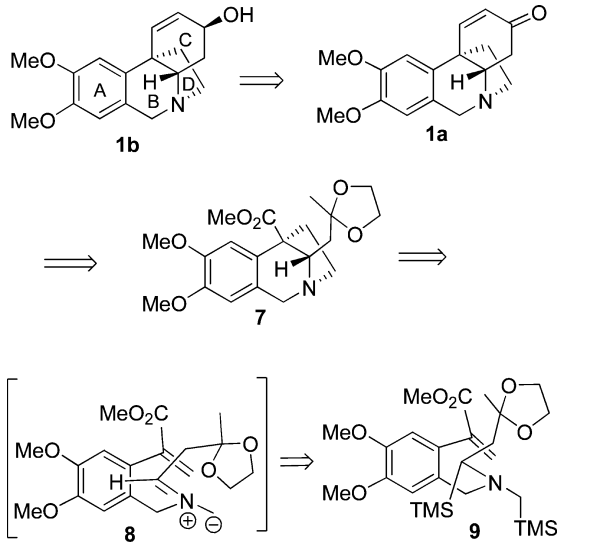
Scheme 2. Retrosynthetic Analysis



and tertiary stereocenters in one step with the orientation of substituents in the dipole deciding the stereochemical outcome at the C_{4a} position. For illustration, it was hypothesized that the alkyl ketal moiety of the dipole in AMY may experience severe stereoelectronic conjestion with the tethered aromatic ring flanked between the dipole and the dipolarophile as shown in TS-I (Figure 2) resulting in

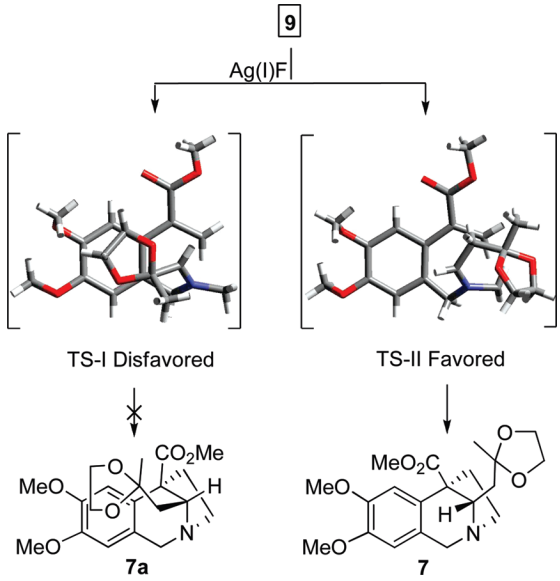
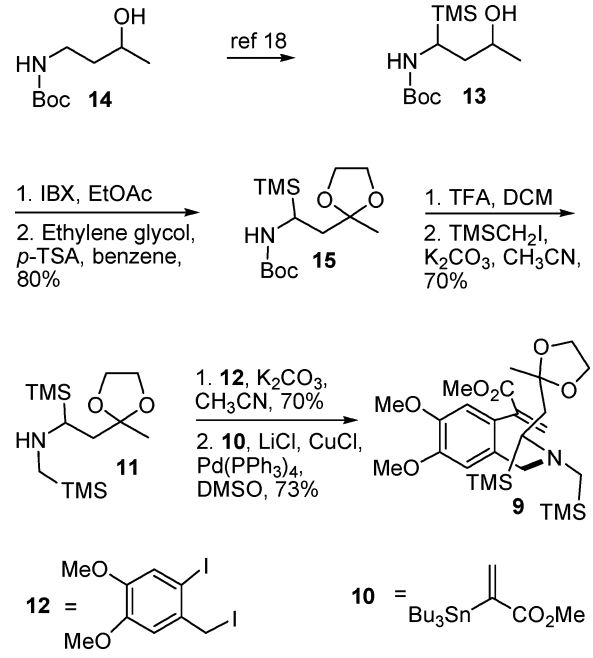


Figure 2. Proposed transition state model of the [3 + 2] cycloaddition step.

epimeric C_{4a} stereochemistry in cycloadduct **7a**. On the other hand, TS-II, in which the alkyl ketal side chain and the aromatic ring are distantly away from each other, may generate the desired C_{4a} stereochemistry (**7**). Thus, we anticipated that the substrate-controlled stereoelectronic favor during the cycloaddition of **8** would reinforce the stereochemical outcome in the tricyclic skeleton with suitable stereochemical disposition of substituents required for assembling the C-ring of the target alkaloid.

With the above premises, we began our synthetic endeavor by synthesizing key precursor **9** (73% yield) by modified Stille coupling between appropriately substituted aryl iodide and vinyl stannane **10** by following Corey's protocol.[19] The Stille precursor was obtained in 70% yield by N-alkylation of **11** with **12** in the presence of anhydrous K_2CO_3 in CH_3CN. Secondary amine **11** was synthesized from **13** as shown in Scheme 3. Compound **13** was readily obtained by following

Scheme 3. Synthesis of Cycloaddition Precursor



our earlier protocol[18] from **14**. Compound **14** in turn was obtained in 70% yield by aza-Michael reaction between $BocNH_2$ and methyl vinyl ketone followed by $NaBH_4$ reduction. Compound **13** on IBX oxidation followed by ketalization gave ketal **15** in 80% yield. N-Boc deprotection of **15** followed by N-alkylation with iodomethyltrimethylsilane gave bis-silylated compound **11** in 70% yield.

The key cycloaddition reaction was performed by dropwise addition of **9** dissolved in DCM to a stirring mixture of flame-dried Ag(I)F in dry DCM. To our delight, the reaction conferred desired cycloadduct **7** in 56% isolated yield along with other minor unidentifiable impurities. The cycloadduct was completely characterized by ^1H and ^{13}C NMR experiments. The stereochemical assignment of cycloadduct was based on extensive COSY, NOESY, and HETCOR NMR studies.[20]

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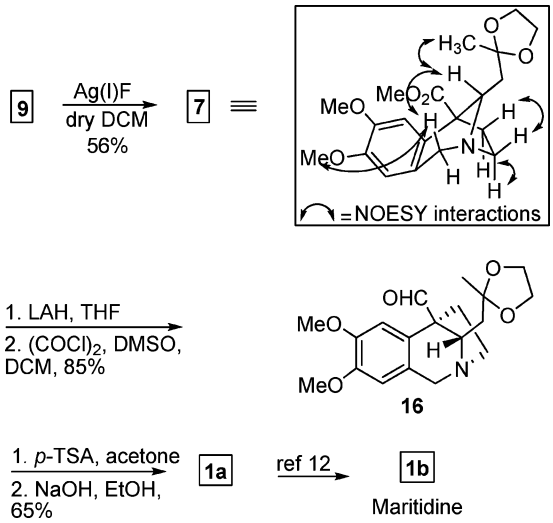
Scheme 4. Synthesis of Maritidine



To proceed further along the proposed synthesis, cycloadduct **7** was subjected to DIBAL reduction. However, this reaction led to the reduction of ester functionality along with ketal deprotection presumably via coordination of alkoxy aluminum with ketal oxygen followed by deprotection of the ketal group to give a stable hemi ketal. Thus, we were compelled to adopt a two-step protocol to obtain **16**. LAH reduction of the ester moiety of **7** followed by Swern oxidation produced aldehyde-ketal **16** in 85% yield. In an attempt to perform one-pot ketal deprotection and aldol condensation, **16** was stirred overnight with 80% acetic acid. However, this reaction produced only a ketal-deprotected compound in poor yield along with traces of **1a**. Therefore, **16** was subjected to *trans*-ketalization using *p*-TSA and acetone to obtain the corresponding δ-keto-aldehyde which was immediately treated with NaOH/EtOH to obtain **1a** in 65% yield. The spectral data of **1a** are in excellent agreement with the reported one.[12] Compound **1a** on subjecting to Luche reduction[21] and mesylation followed by substitution using CsOAc and saponification of the resultant acetate gave **1b** in 45% yield[12] (Scheme 4). The spectral data of **1b** are in good agreement with those of the reported one.[12]

In conclusion, we have successfully developed a conceptually new and versatile protocol for the construction of 5,10b-ethanophenanthridine alkaloids. The significance of the approach is demonstrated by synthesizing (±)-maritidine. The versatility of this strategy is being elaborated to the asymmetric synthesis of this class of alkaloids and will be shortly revealed in a full paper.

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Supporting Information Available: Experimental procedures and full spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(20) For details, see Supporting Information.

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Construction of the 5,10b-Phenanthridine Skeleton Using [3+2]-Cycloaddition of a Non-Stabilized Azomethine Ylide: Total Synthesis of (±)-Maritidine and (±)-Crinine Alkaloids

Ganesh Pandey,*[a] Nishant R. Gupta,[a] and Smita R. Gadre[a]

Keywords: Natural products / Alkaloids / Cycloaddition / Azomethine ylides / Ylides

Vicinal quaternary and tertiary stereocenters of the 5,10b-phenanthridine skeleton **1** are constructed simultaneously in one step by the [3+2]-cycloaddition of non-stabilized azomethine ylide **9**, generated by sequential double desilylation of **10** utilizing silver(I) fluoride as a one-electron oxidant. The regio- as well as stereochemical origin of this cycloaddition reaction is explained through a favorable transition state **9′′**. The strategy is successfully applied for the total synthesis of the biologically active alkaloids (±)-maritidine (**1a**), (±)-crinine (**1b**), and their analogues (**1d**, **1e**, and **1f**).

Introduction

Alkaloids **1**–**4**, isolated from plants of the *Amaryllidaceae*[1–4] family have long been a source of structurally intriguing target molecules that continue to challenge the capabilities of contemporary organic synthesis. The family has produced over 500 structurally diverse alkaloids with a wide range of interesting physiological effects, including antitumor, antiviral, acetylcholinesterase inhibitory, immunostimulatory and antimalarial activities.[5,6] Maritidine (**1a**) and its structural analogues, isolated from *Pancratium maritimum*, *Pancratium tortuosum*, and *Zephyranthes* genera,[7–11] is the first alkaloid with the 5,10b-ethanophenanthridine nucleus containing dimethoxy rather than methylenedioxy substituents at the C-8 and C-9 positions of the crinine skeleton (Figure 1). These alkaloids possess fused tetracyclic skeletons displaying adjacent quaternary and tertiary carbon stereocenters with fused pyrrolidine ring systems for which stereochemical incorporation is the

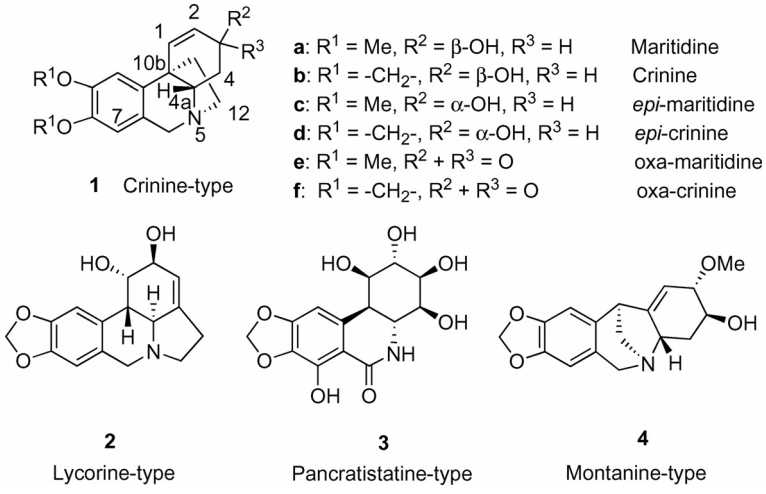

Figure 1. Representative members of *Amaryllidaceae* alkaloids.

critical element in their synthesis. Alkaloid **1a** is of particular interest due to its cytotoxic properties[12–15] and limited supplies from natural sources.[16–23]

A number of synthetic efforts have been employed to solve the challenging problem of incorporating these steri-

[a] Division of Organic Chemistry, National Chemical Laboratory, Dr. Homi Bhabha Road, Pune 411008, India
Fax: +91-20-2590-2628
E-mail: gp.pandey@ncl.res.in

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cally congested stereocenters into the 5,10b-ethanophenanthridine structural framework. In this context, intramolecular oxidative *para–para* phenolic coupling[24–28] and Pictet–Spengler cyclization[19–38] of 3-aryl hydroindole derivatives have emerged as the two main strategies. In the former approach, spiro-fused dienone precursor **7** is obtained by the *para–para* coupling of substituted norbelladine derivatives employing various oxidizing agents,[24,25,27] photochemical cyclization,[26] intramolecular Heck reaction,[39] and cyclization of an intermediate iron carbonyl complex.[27,28] Substituted 3a-arylhydroindoles **6**, which are used for the Pictet–Spengler reaction, are synthesized through key reactions such as regioselective reduction of 1-methyl-3,3-disubstituted pyrrolidine-2,5-dione,[30] intramolecular ene cyclization[31] of an appropriately constructed acylnitroso olefin, or condensation of 3-arylated Δ^1-pyrrolinium salts with *tert*-butyl 3-oxopent-4-enoate.[32] A few other approaches reported for the synthesis of **1** have involved intramolecular cycloamination reactions from an appropriate spiro precursor for the carbon–nitrogen bond formation in the construction of the substituted angular phenanthridine skeleton (Figure 2).[40]

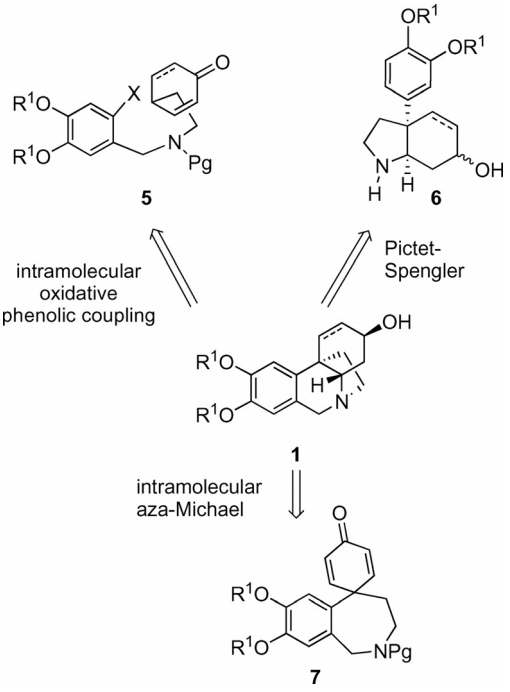


Figure 2. Summary of the strategies reported for the synthesis of **1**.

From the above introductory remarks, it is apparent that these approaches employ sequential generation of vicinal quaternary and tertiary stereocenters along with the use of cyclic precursors for C-ring formation. Moreover, the Pictet–Spengler cyclization route has produced only the dihydromaritidine, whose oxidative transformation into maritidine has so far been unsuccessful. Therefore, we surmised that a strategy that could deliver all the stereocenters in one step would significantly advance the syntheses of these classes of alkaloids.

Our continuing interest in exploring the application of non-stabilized azomethine ylides, generated by the sequential double desilylation of α,α′-bis(trimethylsilylmethyl)alkylamines[41–42] in the total synthesis of alkaloids[43–45] with complex architecture, and the need to develop a concise and versatile strategy to synthesize these types of alkaloids, led us to envisage the synthesis of **1a** through an intramolecular 1,3-dipolar cycloaddition of a non-stabilized azomethine ylide (AMY). This strategy emerged from our success in the construction of examples of the fused polycyclic 5,11-methanomorphanthridine class of alkaloids through the use of non-stabilized azomethine cycloaddition reactions.[45] We report herein full details[46] of the intramolecular [3+2]-cycloaddition of a non-stabilized azomethine ylide as a route for the stereoselective synthesis of (±)-maritidine (**1a**) and (±)-crinine (**1b**).

Results and Discussion

Retrosynthetic Plan

While designing a route to 5,10b-ethanophenanthridine alkaloids such as maritidine and crinine via oxomaritidine **1e** and oxocrinine **1f**, respectively, we speculated on the formation of the C^1–C^2 double bond by cycloaldolization/condensation of the corresponding δ-keto aldehyde from **8**, which possesses vicinal quaternary and tertiary stereocenters at the ring fusion center (Figure 3). A detailed evaluation of the structural framework of **8** revealed the presence of a fused pyrrolidine ring (BD rings) with adjacent vicinal quaternary and tertiary stereocenters.

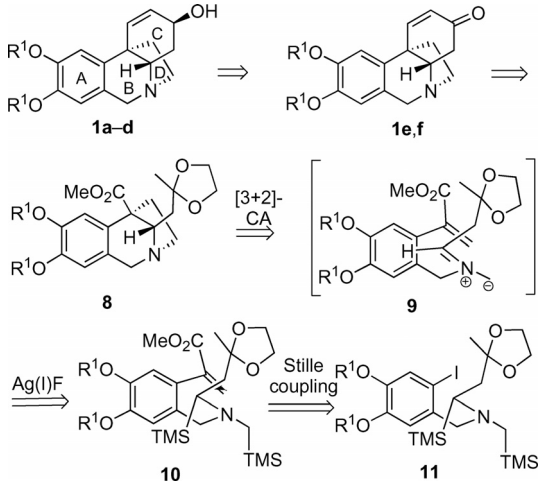


Figure 3. Retrosynthetic analysis for maritidine and crinine types of *Amaryllidaceae* alkaloids.

Therefore, we envisioned that an intramolecular [3+2]-cycloaddition reaction of non-stabilized azomethine ylide **9** with a tethered geminally disubstituted dipolarophile would result in the construction of both C^{4a}–C^{10b} and C^{11}–C^{12} bonds in one step with the required stereochemistry of **8**.

The corresponding azomethine ylide intermediate could be easily generated in situ from the corresponding α,α′-bis(trimethylsilylmethyl)alkylamine **10** using silver(I) fluoride as a one-electron oxidant, using a protocol developed in our group.[41–42]

Regio- as well as stereochemical issues, the two important aspects of this cycloaddition strategy, were evaluated at the planning stage of the synthesis itself. The origin of the 5,10b-ethanophenanthridine regiochemistry during cycloaddition, in contrast to that of the 5,11-methanophenanthridine skeleton,[45] was considered to arise from the change in the LUMO energy of the dipolarophile due to its conjugation with the aromatic ring and the ester moiety present on the same carbon. The cycloaddition reaction of **10** was envisaged to generate the vicinal quaternary and tertiary carbon stereocenters in one step, with the orientation of substituents in the dipole directing the stereochemical outcome at the C-4a position. For example, it was hypothesized that the alkyl ketal moiety of the dipole in AMY **9′** may experience severe stereoelectronic congestion with the tethered aromatic ring flanked between the dipole and the dipolarophile as shown in **TS-I** (Figure 4), resulting in the epimeric C-4a stereochemistry of cycloadduct **8**. On the other hand **TS-II**, in which the alkyl ketal side chain of AMY **9′′** and the aromatic ring are distant from each other, may generate the desired C-4a stereochemistry in **8**. Thus, we anticipated that suitable substrate controlled stereoelectronic factors operating during cycloaddition of **9′′** would reinforce the stereochemical outcome of the formation of the tricyclic skeleton and lead to a suitable stereochemical disposition of substituents required for assembling the C-ring of the target alkaloid.

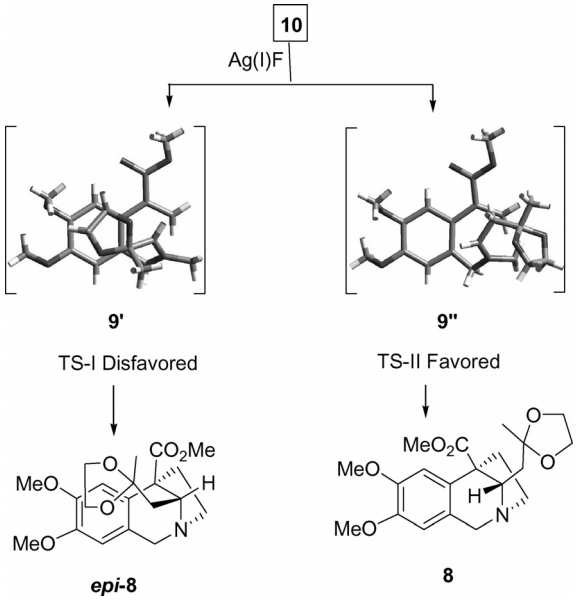
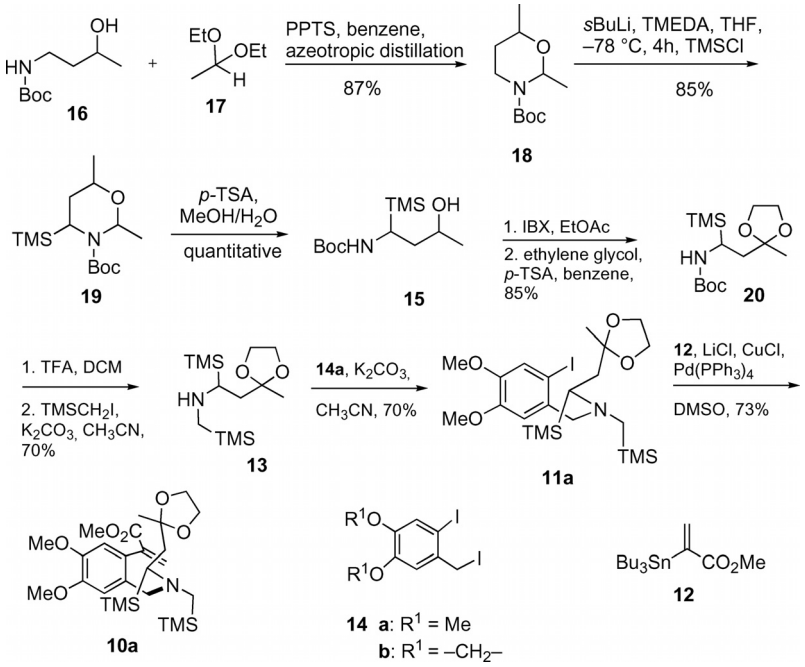


Figure 4. Proposed transition state model for the [3+2]-cycloaddition step.

The requisite key precursor **10** for the transformation was envisaged to be obtained from modified Stille coupling[47] of the corresponding aryl iodide **11** and a suitable vinylstannane **12**.[48] The aryl iodide **11** could, in turn, be synthesized by alkylation of the bis-silylated (alkylamino)-alkyl-substituted ketal **13** with the diiodo component **14**. These components may be obtained from commercially available aryl methyl alcohol and methyl vinyl ketone (MVK).

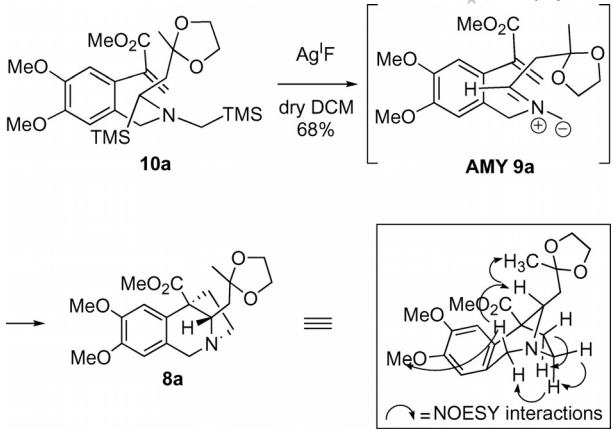


Scheme 1. Synthesis of the precursor for cycloaddition.

Synthesis of (±)-Maritidine (1a): With the above design in mind, we began by synthesizing the key precursor **10a** (73% yield) by a modified Stille coupling between appropriately substituted aryl iodide **11a** and vinyl stannane **12** by following Corey's protocol.[47] The Stille precursor was obtained in 70% yield by *N*-alkylation of **13** with the corresponding di-iodo component **14a**, in the presence of anhydrous K_2CO_3 in CH_3CN. Secondary amine **13** was synthesized from **15** as shown in Scheme 1. Compound **15** was readily obtained from **16** by following a sequence of reactions similar to those previously reported.[45] Compound **16** was obtained in 70% yield by an aza-Michael reaction between $BocNH_2$ and methyl vinyl ketone, followed by $NaBH_4$-mediated reduction. Compound **15**, on oxidation with 2-iodoxybenzoic acid (IBX) followed by ketalization, gave ketal **20** in 85% yield. *N*-Boc deprotection of **20**, followed by *N*-alkylation with iodomethyltrimethylsilane, gave bis-silylated compound **13** in 70% yield.

With key precursor **10a** in hand, we performed the crucial cycloaddition reaction by dropwise addition of its solution (2.87 mmol) dissolved in dichloromethane (15 mL) to a stirring mixture of flame-dried silver(I) fluoride in anhydrous dichloromethane. To our delight, the reaction gave the desired cycloadduct **8a** in 56% isolated yield along with some other minor unidentifiable impurities. The yield of **8a** was optimized up to 68% by manipulating the rate of the addition of **10a** to the stirring suspension of properly dried silver(I) fluoride. The cycloadduct was fully characterized by ^1H and ^{13}C NMR experiments. The stereochemical assignment was established based on extensive COSY, NOESY and HETCOR NMR spectroscopic studies (Scheme 2).[49]

After the successful synthesis and complete characterization of the fused tricyclic intermediate **8a** with the ABD ring, the next task towards completing the synthesis of the natural product was to construct ring C. In order to proceed further, cycloadduct **8a** was subjected to diisobutylaluminum hydride (DIBAL-H) mediated reduction. However, this reaction led to the reduction of ester functionality along with ketal deprotection, presumably through coordination of the alkoxy aluminum with the ketal oxygen atom

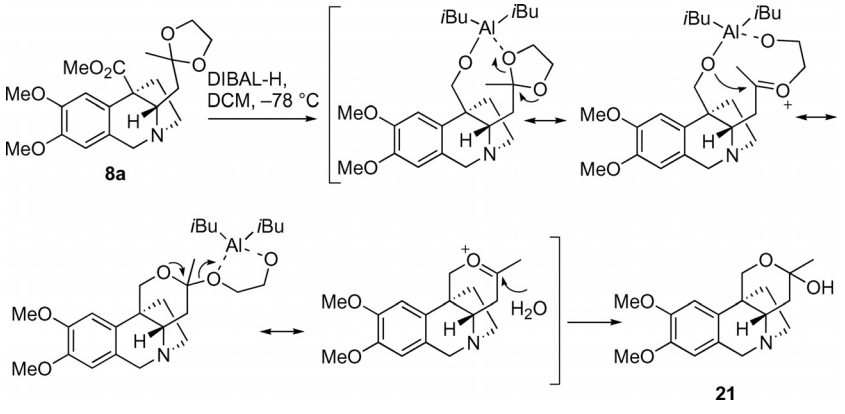


Scheme 2. Synthesis of tricyclic core of maritidine.

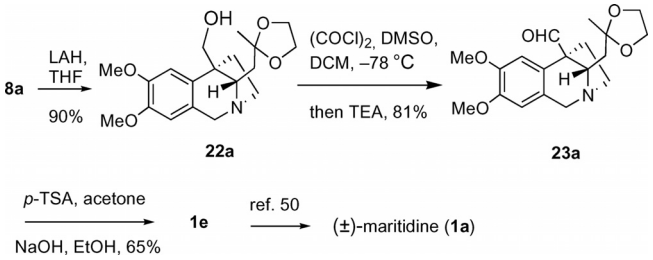
followed by deprotection of the ketal group to give the stable hemiketal **21** as shown in Scheme 3.

Thus, we were compelled to adopt a two-step protocol to obtain **23**. Lithium aluminum hydride (LAH) mediated reduction of the ester moiety of **8a**, followed by Swern oxidation, produced the aldehyde-ketal **23a** in 81% yield. In an attempt to perform one-pot ketal deprotection and aldol condensation, **23a** was initially stirred overnight with 80% acetic acid. However, these conditions produced only the ketal deprotected compound in poor yield along with traces of **1e**. Therefore, **23a** was subjected to *trans*-ketalization using *p*-toluenesulfonic acid (*p*-TsA) and acetone to obtain the corresponding δ-keto aldehyde, which was immediately treated with NaOH/EtOH to obtain **1e** in 65% yield. The spectroscopic data of **1e** was also found to be in excellent agreement with the reported data.[39]

Although the synthesis of **1e** concludes the formal total synthesis of **1c** and **1a**, we proceeded further to complete the total synthesis of **1a** by subjecting **1e** to Luche reduction,[50] which produced **1c**. Mesylation, followed by substitution using CsOAc and saponification of the resultant acetate, gave **1a** in 45% yield (Scheme 4). The spectroscopic data of **1a** were found to be in excellent agreement with those of the reported compound.[39a]



Scheme 3. DIBAL-H reduction of **8a**.



Scheme 4. Synthesis of maritidine.

Synthesis of (±)-Crinine (1b): After accomplishing the total synthesis of **1a**, we turned our attention towards the total synthesis of (±)-crinine (**1b**). The crinine alkaloids elicit continued interest in the synthetic community due in part to their intriguing physiological activities,[51,52] as exemplified by a recent study that unveiled the highly selective apoptosis induction properties against tumor cells at micromolar concentrations. Crinine alkaloids have also been shown to possess immuno-stimulant, antitumor, and antiviral activities.[53]

The synthesis of **1b** was accomplished through the cycloaddition of **10b** by following identical synthetic steps to those described above for **1a** (Scheme 5).

The stereochemistry of the cycloadduct was confirmed by submitting **22b** to detailed COSY, NOESY, and HETCOR NMR spectroscopic studies. The spectroscopic data of **1b** was found to be in good agreement with those of the reported compound.[39b]

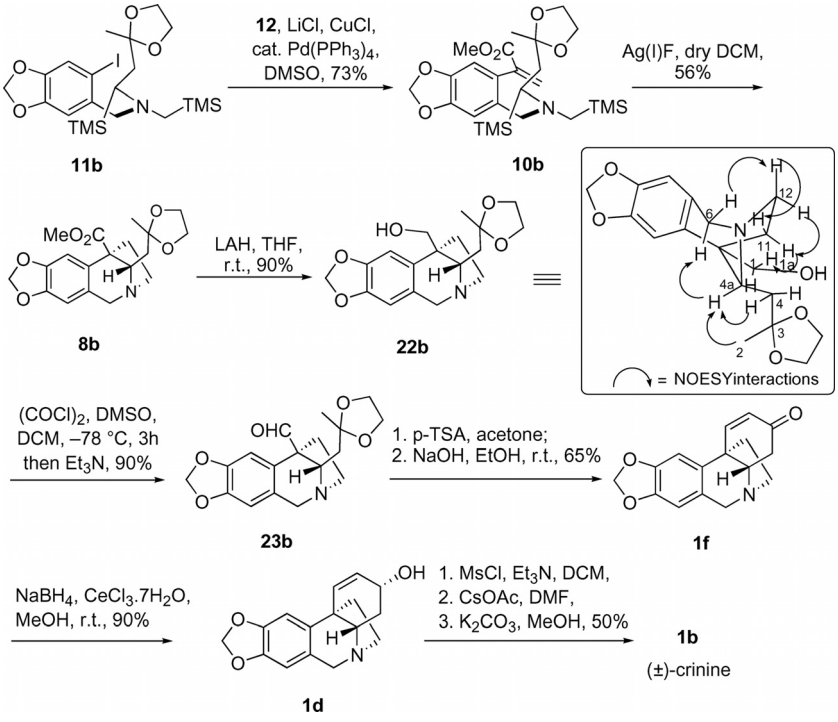
Conclusions

We have successfully developed a conceptually new and versatile protocol for the construction of 5,10b-ethanophenanthridine alkaloids. The significance of the approach has been demonstrated by synthesizing (±)-maritidine, (±)-crinine, and some of their analogues (**1d**, **1e**, and **1f**).

Experimental Section

General: All reactions requiring anhydrous conditions were performed under a positive pressure of argon using oven-dried glassware (110 °C), which were cooled under argon. Solvents for anhydrous reactions were dried according to Perrin and Armarego.[54] Benzene, CH_2Cl_2, and triethylamine were both distilled from CaH_2 and stored over molecular sieves and KOH, respectively. THF and diethyl ether were distilled from sodium benzophenone ketyl. Solvents used for chromatography were distilled at their respective boiling points using known procedures. Petroleum ether (PE) used in the experiments was of 60–80 °C boiling range.

All commercial reagents were obtained from Sigma–Aldrich or Lancaster Chemical Co. (UK). *s*-Butyllithium was titrated using diphenylacetic acid as an indicator. Trimethylsilyl chloride (TMSCl) and methanesulfonyl chloride (MsCl) were distilled before use. Progress of the reactions was monitored by TLC, which was performed on plates pre-coated with silica gel 60 (Merck, 230–400 mesh). Compounds were visualized by heating after dipping in alkaline solution of either $KMnO_4$ or $(NH_4)_6Mo_7O_{24}$ (6.25 g) in aqueous H_2SO_4 (250 mL). Column chromatography was performed



Scheme 5. Synthesis of crinine.

with silica gel 60–120/100–200/230–400 mesh. Standard syringe and cannula techniques were used to transfer air- and moisture-sensitive reagents.

IR spectra were recorded with a Perkin–Elmer infrared spectrometer model 599-B and model 1620 FTIR. ^{1}H NMR spectra were recorded with Bruker ACF 200, Bruker AV 400, or Bruker DRX 500 instruments using deuterated solvent. Chemical shifts are reported in ppm. Proton coupling constants (*J*) are reported as absolute values in Hz; multiplicity is reported as follows: broad (br.), singlet (s), doublet (d), triplet (t), doublet of triplet (dt), doublet of doublet of doublet (ddd), multiplet (m). ^{13}C NMR spectra were recorded with Bruker ACF 200, AV 400, or Bruker DRX 500 instruments operating at 50 MHz, 100 MHz, and 125 MHz, respectively. ^{13}C NMR chemical shifts are reported in ppm relative to the central line of $CDCl_3$ (δ = 77.0 ppm). Mass spectra were recorded with a PE SCIEX API QSTAR pulsar (LC-MS) and high resolution mass spectra (HRMS) were recorded with an MSI (U.K.) Autoconcept instrument operating in the electron impact mode of ionization (70 eV) at the National Chemical Laboratory, Pune, India.

***tert*-Butyl 2,6-Dimethyl-1,3-oxazinane-3-carboxylate (18):** To a stirring solution of the *N*-Boc derivative of the aminobutanol **16** (14 g, 73.99 mmol) in benzene (220 mL) and pyridinium *p*-toluenesulfonate (PPTS; 0.93 g, 3.7 mmol) in a 500 mL round-bottomed flask, acetaldehyde diethyl acetal (11.6 mL, 81.38 mmol) was added at r.t. slowly. The reaction mixture was subjected to azeotropic distillation for a period of 16–18 h using a long distillation head. The vapor temperature was maintained between 67–71 °C. After completion of the reaction, the brown reaction mixture was allowed to cool and washed with saturated $NaHCO_3$ (100 mL), water (2 × 100 mL), brine (2 × 50 mL), dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by vacuum distillation (b.p. 75–78 °C/1 Torr) to obtain **18** (13.86 g, 87%) as a colorless oil. R_f = 0.3 (PE/EtOAc, 85:15). IR (neat): $\tilde{\nu}_{max}$ = 2977, 2934, 1698, 1410, 1366, 1337, 1161, 1092, 945, 861 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 5.74 (br. q, *J* = 6.35, 10.56 Hz, 1 H; CH), 3.92 (m, 2 H; H of CH and H of CH_2), 3.06 (m, 1 H; CH_2), 1.45 (m, 2 H; CH_2), 1.40 [s, 9 H; $(CH_3)_3$], 1.38 (d, *J* = 6.32 Hz, 3 H; CH_3), 1.11 (d, *J* = 6.06 Hz, 3 H; CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 153.4, 79.8, 78.3, 64, 36.2, 32.7, 28.3, 21.7, 15.6 ppm. MS: *m*/*z* = 238.27 [M + Na]$^+$. $C_{11}H_{21}NO_3$ (215.29): calcd. C 61.37, H 9.83, N 6.51; found C 61.19, H 9.65, N 6.32.

***tert*-Butyl 2,6-Dimethyl-4-(trimethylsilyl)-1,3-oxazinane-3-carboxylate (19):** A solution of **18** (10 g, 46.46 mmol) in anhydrous THF (92 mL) was charged into a 250 mL two-necked round-bottomed flask equipped with magnetic stirring bar and an argon gas balloon, and was cooled to –78 °C. TMEDA (9 mL, 92.91 mmol) followed by *s*BuLi (1.5 M in cyclohexane, 62 mL, 92.91 mmol) were introduced to the stirring mixture dropwise over a period of 30 min. The mixture was further stirred for 4 h at –78 °C. TMSCl (13.6 mL, 106.84 mmol) was added dropwise to the reaction mixture at –78 °C, which was then warmed to r.t. slowly and further stirred for 2 h. The reaction was quenched by addition of saturated aqueous NH_4Cl (40 mL). The mixture was extracted with ethyl acetate (3 × 120 mL) and the combined organic layer was washed with brine (2 × 75 mL), dried with Na_2SO_4 and concentrated under vacuum. The yellowish mixture was purified by column chromatography (ethyl acetate/PE, 3:97) to obtain **19** (11.35 g, 85%) as a colorless oil. R_f = 0.3 (PE/EtOAc, 95:5). IR (neat): $\tilde{\nu}_{max}$ = 2977, 2934, 1698, 1416, 1365, 1318, 1289, 1248, 1168, 1096, 843 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 5.78 (q, *J* = 6.44 Hz, 1 H; CH), 3.97 (m, 1 H, CH), 2.69 (dd, *J* = 2.91 Hz, 1 H, 12.38; CH), 1.47 (d, *J* = 6.57 Hz, 3 H; CH_3), 1.42 [s, 9 H; $(CH_3)_3$], 1.35 (d, *J* = 5.69 Hz, 1 H; CH_2), 1.21 (d, *J* = 6.32 Hz, 1 H; CH_2), 1.12 (d, *J* = 6.07 Hz, 3 H; CH_3), 0.05 [s, 9 H; $(CH_3)_3$] ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 154.6, 83.7, 79.4, 65.8, 40.3, 34.5, 28.2, 21.9, 16.1, 0.4 ppm. MS: *m*/*z* = 310 [M + Na]$^+$. $C_{14}H_{29}NO_3Si$ (287.47): calcd. C 58.49, H 10.17, N 4.87; found C 58.30, H 10.01, N 4.65.

***N*-(2-Iodo-4,5-dimethoxybenzyl)-2-(2-methyl-1,3-dioxolan-2-yl)-1-(trimethylsilyl)-*N*-[(trimethylsilyl)methyl]ethanamine (11a):** To a stirring solution of **14a** (7 g, 17.39 mmol) in anhydrous CH_3CN (51 mL), K_2CO_3 (12 g, 86.95 mmol) and bis-silylated (alkylamino)-alkyl-substituted ketal **13** (5 g, 17.39 mmol) were added at r.t. The resulting suspension was heated to reflux for 8 h. On completion of the reaction, the mixture was cooled, filtered, and the solvent was evaporated under vacuum. The resultant pasty mass was taken in EtOAc and washed with H_2O (2 × 50 mL), brine (2 × 40 mL), dried with Na_2SO_4, and concentrated under vacuum to obtain a red-brown mass, which was purified by column chromatography (PE/ethyl acetate, 95:5) to obtain **11a** as a pale-yellow oil (6.88 g, 70%). R_f = 0.4 (PE/EtOAc, 90:10). IR (neat): $\tilde{\nu}_{max}$ = 2953, 2843, 1682, 1595, 1501, 1464, 1437, 1376, 1250, 1207, 1152, 1048, 838 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.24 (s, 1 H; CH), 7.18 (s, 1 H; CH), 3.86 [s, 6 H; $(CH_3)_2$], 3.87–3.74 [m, 4 H; $(CH_2)_2$], 3.62 (d, *J* = 15.31 Hz, 1 H; CH_2), 3.40 (d, *J* = 15.31 Hz, 1 H; CH_2), 2.36 (dd, *J* = 4.02, 7.28 Hz, 1 H; CH), 2.24 (d, *J* = 14.56 Hz, 1 H; CH_2), 2.15 (four-lines pattern, *J* = 4.27, 14.81, 4.01, 14.55 Hz, 1 H; CH_2), 1.92 (d, *J* = 14.55 Hz, 1 H; CH_2), 1.82 (four-lines pattern, *J* = 7.53, 14.81, 7.28, 14.56 Hz, 1 H; CH_2), 1.30 (s, 3 H; CH_3), 0.12 [s, 9 H; $(CH_3)_3$], 0.02 [s, 9 H; $(CH_3)_3$] ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 149.2, 148, 134.8, 121.1, 112.7, 109.9, 87, 64.3, 64.2, 63.7, 56, 55.8, 49.6, 44.4, 34, 24.3, –0.2, –0.9 ppm. MS: *m*/*z* = 566.55[M + H]$^+$. $C_{22}H_{40}INO_4Si_2$ (565.63): calcd. C 46.72, H 7.13, N 2.48; found C 46.61, H 7.01, N 2.40.

Methyl 2-[4,5-Dimethoxy-2-({[2-(2-methyl-1,3-dioxolan-2-yl)-1-(trimethylsilyl)ethyl][(trimethylsilyl)methyl]amino}methyl)phenyl]-acrylate (10a): A 100 mL two-necked round-bottomed flask was charged with LiCl (0.9 g, 21.22 mmol) and flame-dried under high vacuum. Upon cooling, $[Pd(PPh_3)_4]$ (0.061 g, 0.53 mmol) and CuCl (1.75 g, 17.68 mmol) were added, and the mixture was degassed (3–4 times) under high vacuum with an argon purge. Anhydrous DMSO (25 mL) was introduced with concomitant stirring, followed by the sequential addition of **11a** (2 g, 3.53 mmol) and vinyl stannane compound **12** (1.59 g, 4.24 mmol), both diluted with DMSO (1 mL). The resulting mixture was rigorously degassed (4 times) by the freeze-thaw cycles (–78 to 25 °C, Ar). The reaction mixture was stirred at r.t. for 1 h followed by heating at 60 °C for 2 h. Following completion of the coupling as monitored by TLC, the reaction mixture was cooled, diluted with Et_2O (70 mL), and washed with a mixture of brine (2 × 40 mL) and 5% aqueous NH_4OH (100 mL). The aqueous layer was further extracted with ethyl acetate (2 × 100 mL), and the combined organic layers were washed with water (2 × 100 mL), brine (2 × 50 mL), dried with Na_2SO_4 and concentrated under reduced pressure. The reddish-brown residue was purified by column chromatography (PE/ethyl acetate, 90:10) to yield **10a** (1.35 g, 73%) as a yellow viscous liquid. R_f = 0.3 (PE/EtOAc, 80:20). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3018, 2956, 2873, 2852, 1720, 1600, 1509, 1465, 1440, 1376, 1249, 1216, 1136, 1048, 838, 756 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.31 (s, 1 H; CH), 6.60 (s, 1 H; CH), 6.47 (br. d, *J* = 1.26 Hz, 1 H; CH), 5.64 (br. d, *J* = 1.25 Hz, 1 H; CH), 3.88 (s, 3 H; CH_3), 3.87–3.80 [m, 4 H; $(CH_2)_2$], 3.84 (s, 3 H; CH_3), 3.72 (s, 3 H; CH_3), 3.37 (q, *J* = 14.56, 16.81, Hz, 2 H; CH_2), 2.37 (dd, *J* = 4.27, 7.53 Hz, 1 H; CH), 2.11 (d, *J* = 14.56 Hz, 1 H; CH_2), 2.01 (dd, *J* = 4.26, 14.56 Hz, 1 H; CH_2), 1.86 (d, *J* = 14.56 Hz, 1 H; CH_2), 1.71 (dd, *J* = 7.53, 14.56 Hz, 1 H; CH_2), 1.24 (s, 3 H; CH_3), 0.06 [s, 9 H; $(CH_3)_3$], 0.01

[s, 9 H; $(CH_3)_3$] ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 167.1, 148.7, 146.7, 140.8, 129, 128.6, 128.3, 112.5, 111.3, 109.9, 64.2, 64, 56.1, 55.8, 55.7, 52.1, 49.4, 44, 33.7, 24.1, –0.3, –0.9 ppm. MS: *m*/*z* = 524.3 $[M + H]^+$. $C_{26}H_{45}NO_6Si_2$ (523.81): calcd. C 59.62, H 8.66, N 2.67; found C 59.48, H 8.50, N 2.50.

Synthesis of 8a from 10a: A solution of **10a** (1.5 g, 2.87 mmol) in anhydrous CH_2Cl_2 (15 mL) was introduced dropwise over a period of 1 h into an argon-flushed 500 mL two-neck flask containing flame-dried AgF (1.82 g, 14.33 mmol) in anhydrous CH_2Cl_2 (200 mLCH_2Cl_2). The color of the reaction mixture gradually turned to dark-brown with concomitant deposition of silver on the inner surface of the flask in the form of a mirror. The progress of reaction was monitored periodically by TLC. After completion, the reaction mixture was filtered through a small plug of basic alumina (eluent MeOH) and the solvent was evaporated to obtain a crude brown residue, which was purified by silica gel chromatography (PE/acetone, 75:25) to obtain **8a** (0.73 g, 68%) as yellow gummy liquid. R_f = 0.4 (PE/Acetone, 60:40). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3018, 2956, 1730, 1611, 1518, 1466, 1260, 1215, 1130, 854, 754 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 6.49 (s, 1 H; CH), 6.27 (s, 1 H; CH), 4.39 (d, *J* = 16.81 Hz, 1 H; CH_2), 3.94 [m, 4 H; $(CH_2)_2$], 3.80 (br. s, 4 H; CH_3, CH_2), 3.77 [s, 6 H; $(CH_3)_2$], 3.56 (br. d, *J* = Hz, 1 H 7.78; CH), 3.36 (m, 1 H; CH_2), 2.76 (m, 1 H; CH_2), 2.48 (m, 1 H; CH_2), 2.12 (m, 1 H; CH_2), 1.67 (dd, *J* = 9.54, 14.56 Hz, 1 H; CH_2), 1.56 (dd, *J* = 2.51, 14.56 Hz, 1 H; CH_2), 1.42 (s, 3 H; CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.3, 148.3, 147.4, 134.2, 123.5, 109.5, 109.1, 108.1, 66.3, 64.6, 64.2, 61.4, 57.3, 55.9, 55.8, 51.8, 50.8, 38.3, 37.9, 23.8 ppm. MS: *m*/*z* = 378.27$[M + H]^+$. $C_{20}H_{27}NO_6$ (377.43): calcd. C 63.64, H 7.21, N 3.71; found C 63.50, H 7.15, N 3.65.

Reduction of 8a to 22a: To a suspension of LAH (0.12 g, 3.18 mmol) and anhydrous THF (8 mL) in a 25 mL two-necked round-bottomed flask equipped with magnetic stirring bar and an argon balloon system at 0 °C, was added dropwise by using a cannula, a solution of **8a** (0.6 g, 1.59 mmol) dissolved in anhydrous THF (1 mL) over a period of 2 min. The reaction mixture was warmed to r.t. and stirred for 24 h. After completion of reaction, the suspension was cooled to 0 °C and quenched by dropwise addition of 1 N NaOH. The mixture was then stirred at r.t. for 2 h. The whole mass was taken up into CH_2Cl_2 (25 mL) and washed with water. The aqueous layer was then partitioned with CH_2Cl_2 (2 × 10 mL), and the combined organic layer was shaken with brine and dried with Na_2SO_4. The solvent was removed in vacuo to obtain a gummy mass, which, on column chromatography (CH_2Cl_2/MeOH, 85:15), afforded **22a** as a yellow gummy liquid (0.528 g, 90%). R_f = 0.3 (CH_2Cl_2/MeOH, 80:20). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3449, 3018, 2959, 2937, 2854, 2343, 2359, 1610, 1516, 1466, 1260, 1215, 1045, 854, 754 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 6.92 (s, 1 H; CH), 6.54 (s, 1 H; CH), 4.64 (d, *J* = 16.23 Hz, 1 H; CH_2), 4.36 (d, *J* = 13.20 Hz, 1 H; CH_2), 4.11 (d, *J* = 16.50 Hz, 1 H; CH_2), 4.04–3.99 [m, 4 H; $(CH_2)_2$], 3.90 (d, *J* = 13.20 Hz, 1 H; CH_2), 3.89 (s, 3 H; CH_3), 3.82 (s, 3 H; CH_3), 3.67 (br. t, *J* = 4.95, 15.13, 10.18 Hz, 1 H; CH), 3.61 (t, *J* = 4.24 Hz, 1 H; CH_2), 3.06 (five-lines pattern, *J* = 7.98, 14. 85 Hz, 1 H; CH_2), 2.18 (m, 2 H; CH_2), 1.91 (m, 1 H; CH_2), 1.85 (m, 1 H; CH_2), 1.43 (s, 3 H; CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 148.4, 147.4, 133.8, 121.7, 109.5, 109.4, 107.4, 64.8, 64.5, 64.4, 60.7, 60.3, 56.1, 56, 51.6, 51.2, 37, 36.6, 24 ppm. MS: *m*/*z* = 350.3$[M + H]^+$. $C_{19}H_{27}NO_5$ (349.42): calcd. C 65.31, H 7.79, N 4.01; found C 65.20, H 7.60, N 3.90.

DIBAL-H Mediated Reduction of 8a to 21: The cycloadduct **8a** (0.050 g, 0.132 mmol) was taken in a 10 mL two-necked round-bottomed flask charged with argon. Anhydrous CH_2Cl_2 (0.4 mL) was added to the reaction flask and the solution was cooled to –78 °C. To the solution of cycloadduct in anhydrous CH_2Cl_2 was added DIBAL-H (1.2 M in toluene, 0.278 mmol) at –78 °C and the mixture was stirred at the same temperature for 30 min. The reaction was quenched by addition of a few drops of a saturated aq. sodium potassium tartrate solution. Solid sodium sulfate was added to the reaction flask and the mixture was further stirred at r.t. for 1 h and then filtered through a sintered funnel. Concentration of the reaction mixture followed by column chromatography (EtOAc/hexane, 70%) afforded **21** as a gummy liquid in 70% yield. R_f = 0.2 (hexane/EtOAc, 10:90). ^1H NMR ($CDCl_3$, 400 MHz): δ = 6.51 (s, 1 H; CH), 6.42 (s, 1 H; CH), 4.40 (d, *J* = 16.82 Hz, 1 H; CH_2), 4.28 (d, *J* = 11.04 Hz, 1 H; CH_2), 4.21 (d, *J* = 11.04 Hz, 1 H; CH_2), 3.88 (d, *J* = 16.82 Hz, 1 H; CH_2), 3.83 (s, 3 H; CH_3), 3.81 (s, 3 H; CH_3), 3.38–3.33 (m, 2 H; H of CH and H of CH_2), 2.87–2.80 (m, 1 H; CH_2), 2.42–2.35 (m, 2 H; CH_2), 1.94–1.86 (m, 2 H; CH_2), 1.48 (s, 3 H; CH_3) ppm. MS: *m*/*z* = 306.36 $[M + H]^+$.

Oxidation of 22a to 23a: To a mixture of DMSO (0.15 mL, 2.15 mmol) in CH_2Cl_2 (3 mL), oxalyl chloride (0.19 mL, 2.15 mmol) was added dropwise at –78 °C, and the resulting mixture was stirred for 15 min. A solution of alcohol **20a** (0.5 g, 1.43 mmol) in CH_2Cl_2 (1 mL) was added dropwise to the reaction flask at –78 °C. The mixture was stirred for 1 h, then triethylamine (1 mL, 7.15 mmol) was added dropwise and the resultant mixture was gradually warmed to r.t.. over 1 h by removing the cooling bath and stirred for a further 1 h. The reaction mixture was quenched with water (5 mL) and extracted with CH_2Cl_2 (2 × 25 mL). The combined organic layer was washed with brine, dried with Na_2SO_4, filtered and concentrated under vacuum. Purification of the residue by silica gel column chromatography (CH_2Cl_2/MeOH, 92:8) afforded aldehyde **23a** (0.447 g, 90%) as a gummy liquid. R_f = 0.3 (CH_2Cl_2/MeOH, 85:15). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3018, 2930, 2854, 1713, 1609, 1516, 1464, 1362, 1260, 1217, 1119, 1032, 856, 756 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 9.93 (s, 1 H; CH), 6.60 (s, 1 H; CH), 6.27 (s, 1 H; CH), 4.48 (d, *J* = 16.81 Hz, 1 H; CH_2), 3.90 [m, 4 H; $(CH_2)_2$], 3.83 (br. s, 4 H; CH_3 and CH), 3.80 (s, 3 H, CH_3), 3.60 (t, *J* = 4.95 Hz, 1 H; CH), 3.35 (dt, *J* = 3.26, 10.42, 13.30 Hz, 1 H; CH_2), 2.81 (five-lines pattern, *J* = 8.03, 8.28, 5.27, 6.52, Hz, 1 H; CH_2), 2.53 (ddd, *J* = 6.53, 10.79, 17.07 Hz, 1 H; CH_2), 1.88 (m, 1 H; CH_2), 1.67 (dd, *J* = 6.53, 14.56 Hz, 1 H; CH_2), 1.61 (dd, *J* = 3.51, 14.55 Hz, 1 H; CH_2), 1.37 (s, 3 H; CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 202.2, 148.6, 147.6, 132.2, 124, 109.7, 109.4, 108.2, 64.7, 64.5, 64.4, 61.5, 61.4, 56, 55.9, 51.3, 39.4, 34.76, 24 ppm. MS: *m*/*z* = 348.4 $[M + H]^+$. $C_{19}H_{25}NO_5$ (347.41): calcd. C 65.69, H 7.25, N 4.03; found C 65.50, H 7.10, N 3.91.

Oxomaritidine (1e) from 23a: To a solution of **23a** (0.020 g, 0.06 mmol) in acetone (0.18 mL), *p*TSA (0.011 g, 0.06 mmol) was added at r.t., and the reaction mixture was stirred for 3 h. Progress of the reaction was monitored by TLC. On completion of the reaction, the solvent was evaporated under vacuum and the residue was dissolved in CH_2Cl_2 (25 mL) and washed with saturated $NaHCO_3$ (2 × 10 mL), brine (2 × 5 mL), dried with Na_2SO_4 and concentrated under vacuum to obtain a crude mass, which was used in the next step without any purification. To a stirred solution of the crude reaction mixture of δ-keto aldehyde (0.014 g, 0.05 mmol) in EtOH (2 mL) at r.t. was added solid NaOH (0.011 g, 0.28 mmol) and the resulting mixture was stirred for 20 h. The reaction mixture was concentrated and the residue was dissolved in CH_2Cl_2 (20 mL), washed with water (5 mL), brine (2 × 5 mL), dried with anhydrous Na_2SO_4, filtered and concentrated. Purification of the residue by flash column chromatography (CH_2Cl_2/MeOH, 95:5) afforded **1e** as a white powder (0.011 g, 65% over two steps). R_f = 0.4 (CH_2Cl_2/

MeOH, 90:10). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2961, 2925, 1682, 1609, 1515, 1261, 1220, 1134, 1038 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 7.70 (d, J = 10.17 Hz, 1 H; CH), 6.90 (s, 1 H; CH), 6.55 (s, 1 H; CH), 6.12 (d, J = 10.18 Hz, 1 H; CH), 4.43 (d, J = 16.78 Hz, 1 H; CH_2), 3.90 (s, 3 H; CH_3), 3.86 (d, J = 16.90 Hz, 1 H; CH_2), 3.83 (s, 3 H; CH_3), 3.67 (dd, J = 5.77, 12.93 Hz, 1 H; CH), 3.58 (ddd, J = 3.85, 10.73, 13.76 Hz, 1 H; CH_2), 3.03 (ddd, J = 6.5, 9.0, 13.14 Hz, 1 H; CH_2), 2.71 (dd, J = 5.50, 16.78 Hz, 1 H; CH_2), 2.49 (dd, J = 13.21, 16.78 Hz, 1 H; CH_2), 2.40 (ddd, J = 3.85, 9.08, 12.65 Hz, 1 H; CH_2), 2.17 (ddd, J = 6.43, 10.58, 12.24 Hz, 1 H; CH_2) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 197.4, 148.8, 148.2, 147.9, 134.2, 129, 124.1, 110.1, 105.4, 68.7, 61.1, 56.2, 55.9, 53.8, 44.5, 44.3, 39.6 ppm. MS: m/z = 286.5 $[M + H]^+$, 308.6 $[M + Na]^+$, 324.6 $[M + K]^+$.

Maritidine (1a) from Oxomaritidine (1e):[39a] To a solution of **1e** (0.066 g; 0.02 mmol) in anhydrous MeOH (0.7 mL) was added $NaBH_4$ (0.016 g, 0.05 mmol) and $CeCl_3{\cdot}7H_2O$ (0.172 g, 0.05 mmol) at r.t. After stirring for 45 min at the same temperature, the reaction mixture was filtered through Celite (elution with MeOH) and the solvents evaporated. The residue was extracted with $CHCl_3$ (2 × 5 mL) and the combined organic layers were washed with aqueous saturated $NaHCO_3$, dried with Na_2SO_4, evaporated and used directly for the further synthesis of maritidine. To a solution of the crude reaction mixture of *epi*-maritidine **1c** (0.066 g, 0.02 mmol) in anhydrous CH_2Cl_2 (0.5 mL), was added MsCl (12 μL, 0.11 mmol) and Et_3N (15 μL, 0.11 mmol) at r.t. After stirring the reaction mixture for 1 h at r.t., the solvent was removed under reduced pressure and the residue was dissolved in DMF (0.5 mL) and transferred by using a syringe to a flask containing CsOAc (0.063 g, 0.33 mmol). The resulting greenish suspension was stirred at r.t. for 40 h then filtered (elution with EtOAc). The combined filtrates were dissolved in 1 N HCl and the aqueous solution was washed with Et_2O (2 × 5 mL). The aqueous phase was basified with saturated K_2CO_3 to pH 12 and then extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were washed with water (2 × 5 mL), brine (5 mL), and dried using Na_2SO_4. Filtration, followed by solvent evaporation under reduced pressure gave the crude allylic acetate, which was immediately dissolved in anhydrous MeOH (0.5 mL) containing powdered K_2CO_3 (0.026 g, 0.19 mmol). After stirring the reaction mixture for 2 h at r.t., the solvent was removed in vacuo. The residue was dissolved in CH_2Cl_2 (20 mL) and washed with saturated $NaHCO_3$ (5 mL). The combined organic layers were washed with water, brine, dried with anhydrous Na_2SO_4 and concentrated. Preparative thin layer chromatography of the reaction mixture (CH_2Cl_2/MeOH/Et_3N, 9:1:1) yielded **1a** (0.03 g, 45% over 4 steps) as a white powder. R_f = 0.4 (CH_2Cl_2/MeOH/Et_3N, 90:10:10). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3406, 3019, 2956, 2925, 2853, 1610, 1514, 1464, 1311, 1262, 1133, 1092, 1039 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 6.85 (s, 1 H; CH), 6.65 (d, J = 9.9 Hz, 1 H; CH), 6.52 (s, 1 H; CH), 5.99 (dd, J = 9.8, 5 Hz, 1 H; CH), 4.46 (d, J = 16.3 Hz, 1 H; CH_2), 4.36 (m, 1 H; CH), 3.88 (s, 3 H; CH_3), 3.83 (d, J = 16.5 Hz, 1 H; CH_2), 3.82 (s, 3 H; CH_3), 3.5–3.40 (m, 2 H; H of CH and H of CH_2), 2.93 (m, 1 H; CH_2), 2.21 (m, 1 H; CH_2), 2.06 (m, 1 H; CH_2), 1.96 (m, 1 H; CH_2), 1.77 (m, 1 H) ppm. MS: m/z = 288 $[M + H]^+$.

***N*-{(6-Iodobenzo[*d*][1,3]dioxol-5-yl)methyl}-2-(2-methyl-1,3-dioxolan-2-yl)-1-(trimethylsilyl)-*N*-[(trimethylsilyl)methyl]ethanamine (11b):** To a stirring solution of **14b** (7 g, 18.048 mmol) in anhydrous CH_3CN (54 mL), K_2CO_3 (12.47 g, 90.24 mmol) and the bissilylated (alkylamino)alkyl-substituted ketal **13** (5.189 g, 18.048 mmol) were added at r.t. The resultant suspension was heated to reflux for 8 h. On completion of the reaction, the mixture was cooled, filtered, and the solvent was evaporated under vacuum. The resultant pasty mass was taken in EtOAc (150 mL) and washed with H_2O (2 × 50 mL), brine (2 × 40 mL), dried with Na_2SO_4, and concentrated under vacuum to obtain a red-brown mass, which was purified by column chromatography (PE/ethyl acetate, 97:3) to obtain **11b** as a pale-yellow oil (6.44 g, 65%). R_f = 0.5 (PE/EtOAc, 90:10). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3015, 2953, 1683, 1503, 1474, 1247, 1040, 935, 837, 757, 667 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ = 7.25 [s, 2 H; $(CH)_2$], 6.01 (ABq, J = 1.39, 5.06 Hz, 2 H; CH_2), 3.96–3.88 [m, 3 H; $(CH_2)_2$], 3.83 [dd, J = 3.66, 9.34 Hz, 1 H; $(CH_2)_2$], 3.59 (d, J = 15.66 Hz, 1 H; CH_2), 3.42 (d, J = 15.66 Hz, 1 H; CH_2), 2.41 (dd, J = 3.80, 7.20 Hz, 1 H; CH), 2.24 (d, J = 14.66 Hz, 1 H; CH_2), 2.23 (dd, J = 3.90, 14.78 Hz, 1 H; CH_2), 1.96 (d, J = 14.65 Hz, 1 H; CH_2), 1.89 (dd, J = 7.20, 14.78 Hz, 1 H; CH_2), 1.36 (s, 3 H; CH_3), 0.16 [s, 9 H; $(CH_3)_3$], 0.09 [s, 9 H; $(CH_3)_3$] ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 148.3, 146.8, 135.9, 118, 110.1, 109.8, 101.3, 86.5, 64.3, 64.2, 64.1, 49.4, 44.3, 33.9, 24.3, –0.41, –0.95 ppm. MS: m/z = 550.23 $[M + H]^+$.

Methyl 2-[6-({[2-(2-Methyl-1,3-dioxolan-2-yl)-1-(trimethylsilyl)-ethyl]-[(trimethylsilyl)methyl]amino}methyl)benzo[*d*][1,3]dioxol-5-yl]acrylate (10b): A 100 mL two-necked round-bottomed flask was charged with LiCl (0.93 g, 21.85 mmol) and flame-dried under high vacuum. Upon cooling, $[Pd(PPh_3)_4]$ (0.42 g, 0.36 mmol) and CuCl (1.80 g, 18.21 mmol) were added and the mixture was degassed (3–4 times) under high vacuum with an argon purge. Anhydrous DMSO (26 mL) was introduced with concomitant stirring, followed by sequential addition of **11b** (2 g, 3.64 mmol) and vinyl stannane compound **12** (1.639 g, 4.37 mmol), both diluted with DMSO (1 mL). The resulting mixture was rigorously degassed (4 times) by freeze–thaw cycles (–78 to 25 °C, Ar). The reaction mixture was stirred at r.t. for 1 h then heated at 60 °C for 2 h. Following completion of the coupling (reaction monitored by TLC), the reaction mixture was cooled, diluted with Et_2O (70 mL), and washed with a mixture of brine (2 × 40 mL) and 5% aqueous NH_4OH (100 mL). The aqueous layer was further extracted with ethyl acetate (2 × 100 mL), and the combined organic layers were washed with water (2 × 100 mL), brine (2 × 50 mL), dried with Na_2SO_4, and concentrated under reduced pressure. The reddish-brown residue was purified by column chromatography (PE/ethyl acetate, 90:10) to yield **10b** (1.44 g, 73%) as a yellow viscous liquid. R_f = 0.3 (PE/EtOAc, 80:20). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2951, 1723, 1679, 1622, 1503, 1480, 1375, 1247, 1105, 1041, 938, 837, 752, 667 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.25 (s, 1 H; CH), 6.59 (s, 1 H; CH), 6.47 (d, J = 1.50 Hz, 1 H; CH), 5.96 (ABq, J = 10.54 Hz, 2 H; CH_2), 5.64 (d, J = 1.75 Hz, 1 H; CH), 3.92–3.84 [m, 4 H; $(CH_2)_2$], 3.73 (s, 3 H; CH_3), 3.34 (d, J = 14.80 Hz, 1 H; CH_2), 3.30 (d, J = 14.80 Hz, 1 H; CH_2), 2.37 (dd, J = 4.02, 7.53 Hz, 1 H; CH), 2.11 (d, J = 14.81 Hz, 1 H; CH_2), 2.03 (dd, J = 4.02, 14.56 Hz, 1 H; CH_2), 1.84 (d, J = 14.56 Hz, 1 H; CH_2), 1.72 (dd, J = 7.52, 14.56 Hz, 1 H; CH_2), 1.26 (s, 3 H; CH_3), 0.08 [s, 9 H; $(CH_3)_3$], 0.03 [s, 9 H; $(CH_3)_3$] ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 167, 147.6, 145.4, 140.9, 133, 129.2, 128.7, 110, 109.6, 108.6, 100.9, 64.2, 64, 56.2, 52.2, 49.1, 43.8, 33.7, 24.1, –0.3, –0.9 ppm. HRMS (EI): calcd. for $C_{25}H_{41}NO_6Si_2$: 507.2472; found 507.2466.

Synthesis of 8b from 10b: A solution of **10b** (1.5 g, 2.957 mmol) in anhydrous CH_2Cl_2 (20 mL) was introduced dropwise over a period of 1 h into an argon-flushed 500 mL two-necked flask containing flame-dried AgF (1.876 g, 14.78 mmol) in anhydrous CH_2Cl_2 (200 mL). The color of the reaction mixture gradually turned to dark-brown with concomitant deposition of silver on the inner surface of the flask in the form of a mirror. The progress of the reaction was monitored periodically by TLC. After completion, the reaction mixture was filtered through a small plug of basic alumina

(eluent MeOH) and the solvent was evaporated to obtain a crude brown residue, which was purified by silica gel chromatography (PE/ethyl acetate, 45:55) to obtain **8b** (0.587 g, 56%) as yellow gummy liquid. R_f = 0.3 (PE/EtOAc, 10:90). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2956, 1730, 1671, 1504, 1483, 1437, 1246, 1119, 1039, 935, 753, 722 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 6.46 (s, 1 H; CH), 6.29 (s, 1 H; CH), 5.87 (ABq, J = 6.12 Hz, 2 H; CH_2), 4.36 (d, J = 16.87 Hz, 1 H; CH_2), 3.97–3.91 [m, 4 H; $(CH_2)_2$], 3.89–3.85 (m, 1 H; CH_2), 3.77 (s, 3 H; CH_3), 3.54 (br. d, J = 8.80 Hz, 1 H; CH), 3.35 (m, 1 H; CH_2), 2.76 (m, 1 H; CH_2), 2.48 (m, 1 H; CH_2), 2.11 (m, 1 H; CH_2), 1.66 (dd, J = 9.78, 14.43 Hz, 1 H; CH_2), 1.55 (dd, J = 2.20, 14.42 Hz, 1 H; CH_2), 1.42 (s, 3 H; CH_3) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 174.1, 146.7, 146.1, 135.2, 124.8, 109.5, 106.3, 105.1, 100.9, 66.2, 64.6, 64.3, 61.6, 57.8, 52.0, 50.8, 38.2, 38.0, 23.8 ppm. HRMS (EI): calcd. for $C_{19}H_{23}NO_6$: 361.1525; found 361.1552.

Reduction of 8b to 22b: To a suspension of LAH (0.126 g, 3.322 mmol) and anhydrous THF (9 mL) in a 25 mL two-necked round-bottomed flask equipped with magnetic stirring bar and an argon balloon system at 0 °C, was added dropwise by using a cannula, a solution of **8b** (0.6 g, 1.661 mmol) dissolved in anhydrous THF (1 mL) over a period of 2 min. The reaction mixture was warmed to r.t. and stirred for 24 h. After completion of the reaction, the suspension was cooled to 0 °C and quenched by dropwise addition of 1 N NaOH, then stirred at r.t. for 2 h. The whole mass was dissolved in CH_2Cl_2 (25 mL) and washed with water. The aqueous layer was then partitioned with CH_2Cl_2 (2 × 25 mL), and the combined organic layer was shaken with brine and dried with Na_2SO_4. The solvent was removed in vacuo to obtain a gummy mass, which was purified by column chromatography (CH_2Cl_2/MeOH, 85:15) to afford **22b** as a yellow gummy liquid (0.5 g, 90%). R_f = 0.3 (CH_2Cl_2/MeOH, 80:20). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3455 (br), 3016, 2957, 1622, 1505, 1480, 1378, 1238, 1143, 1041, 939, 857, 667 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 6.90 (s, 1 H; CH), 6.45 (s, 1 H; CH), 5.88 (ABq, J = 0.91, 15.56 Hz, 2 H; CH_2), 4.43 (d, J = 16.78 Hz, 1 H; CH_2), 4.30 (d, J = 13.13 Hz, 1 H; CH_2), 3.97 [s, 4 H; $(CH_2)_2$], 3.86 (d, J = 13.13 Hz, 1 H; CH_2), 3.81 (d, J = 16.78 Hz, 1 H; CH_2), 3.34 (t, J = 4.27 Hz, 1 H; CH), 3.28 (br. d, J = 3.97, 10.98, 16.48 Hz, 1 H; CH_2), 2.88 (br. d, J = 6.72, 8.55, 14.35 Hz, 1 H; CH_2), 2.07 (dd, J = 4.89, 14.96 Hz, 1 H; CH_2), 1.86 (dd, J = 3.97, 14.96 Hz, 1 H; CH_2), 1.79 (ddd, J = 3.97, 8.85, 12.51 Hz, 1 H; CH_2), 1.67 (ddd, J = 6.24, 10.65, 12.32 Hz, 1 H; CH_2), 1.39 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 146.5, 146.1, 136.5, 126.1, 109.9, 106.4, 104.1, 100.7, 64.4, 64.3, 63.5, 61.46, 61.44, 51.4, 50.7, 38.4, 37.9, 23.4 ppm. HRMS (EI): calcd. for $C_{18}H_{23}NO_5$: 333.1576; found 333.1556.

Swern Oxidation of 22b to 23b: To a mixture of DMSO (0.21 mL, 3 mmol) in CH_2Cl_2 (3 mL), oxalyl chloride (0.25 mL, 3 mmol) was added dropwise at –78 °C, and the resulting mixture was stirred for 15 min. A solution of alcohol **22b** (0.5 g, 1.5 mmol) in CH_2Cl_2 (1.5 mL) was added dropwise to the reaction flask at –78 °C. The mixture was stirred for 1 h, triethylamine (1.04 mL, 7.5 mmol) was added dropwise, and the resultant mixture was gradually warmed to r.t. over 1 h by removing the cooling bath and the mixture was stirred for another 1 h. The reaction mixture was quenched with water (5 mL) and extracted with CH_2Cl_2 (2 × 25 mL), and the combined organic layer was washed with brine, dried with Na_2SO_4, filtered, and concentrated under vacuum. Purification of the residue by silica gel column chromatography (CH_2Cl_2/MeOH, 94:6) afforded the aldehyde **23b** (0.447 g, 90%) as a gummy liquid. R_f = 0.4 (CH_2Cl_2/MeOH, 90:10). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2927, 1713, 1672, 1504, 1484, 1379, 1239, 1091, 1039, 936, 857, 755 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 9.86 (s, 1 H; CH), 6.56 (s, 1 H; CH), 6.30 (s, 1 H; CH), 5.91 (s, 2 H; CH_2), 4.46 (d, J = 17.06 Hz, 1 H; CH_2), 3.95–3.87 [m, 4 H; $(CH_2)_2$], 3.83 (d, J = 16.81 Hz, 1 H; CH_2), 3.59 (br. t, J = 5.27 Hz, 1 H; CH), 3.38 (ddd, J = 3.52, 10.80, 13.56 Hz, 1 H; CH_2), 2.83 (five-lines pattern, J = 8.04, 14.81 Hz, 1 H; CH_2), 2.54 (ddd, J = 6.52, 10.54, 12.29 Hz, 1 H; CH_2), 1.87 (seven-lines pattern, J = 3.27, 8.79, 12.30 Hz, 1 H; CH_2), 1.74 (dd, J = 6.53, 14.81 Hz, 1 H; CH_2), 1.62 (dd, J = 4.02, 14.81 Hz, 1 H; CH_2), 1.37 (s, 3 H; CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 201.4, 147.1, 146.4, 133, 125, 109.2, 107.1, 105.4, 101, 64.59, 64.56, 64.4, 61.7, 61.5, 51.3, 39.1, 34.7, 24 ppm. HRMS (EI): calcd. for $C_{18}H_{21}NO_5$: 331.1420; found 331.1403.

Synthesis of Oxo-crinine (1f) from 23b: To a solution of **19b** (0.020 g, 0.06 mmol) in acetone (0.18 mL), *p*TSA (0.023 g, 0.12 mmol) was added at r.t., and the reaction mixture was stirred for 3 h. Progress of the reaction was monitored by TLC. On completion of reaction, the solvent was evaporated under vacuum and the residue was dissolved in CH_2Cl_2 (25 mL) and washed with saturated $NaHCO_3$ (2 × 10 mL), brine (2 × 5 mL), dried with Na_2SO_4, and concentrated under vacuum to obtain a crude mass, which was used in the next step without any purification. To a stirred solution of the crude reaction mixture of δ keto aldehyde (0.014 g, 0.05 mmol) in EtOH (2.1 mL) at r.t. was added solid NaOH (0.012 g, 0.292 mmol) and the resulting mixture was stirred for 20 h. The reaction mixture was concentrated and the residue was dissolved in CH_2Cl_2 (20 mL), washed with water (5 mL), brine (2 × 5 mL), dried with anhydrous Na_2SO_4, filtered, and concentrated. Purification of the residue by flash column chromatography (CH_2Cl_2/MeOH, 95:5) afforded **1f** as a white powder (0.011 g, 65% over two steps). R_f = 0.5 (CH_2Cl_2/MeOH, 85:15). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3014, 2926, 1708, 1681, 1504, 1483, 1398, 1315, 1247, 1159, 1109, 1039, 1001, 935, 854, 754, 667 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 7.61 (d, J = 10.37 Hz, 1 H; CH), 6.90 (s, 1 H; CH), 6.51 (s, 1 H; CH), 6.09 (d, J = 10.4 Hz, 1 H; CH), 5.92 (ABq, 2 H; CH_2), 4.41 (d, J = 16.79 Hz, 1 H; CH_2), 3.81 (d, J = 16.79 Hz, 1 H; CH_2), 3.64 (dd, J = 5.8, 13.12 Hz, 1 H; CH), 3.54 (ddd, J = 3.97, 10.38, 13.74 Hz, 1 H; CH_2), 3.00 (ddd, J = 6.10, 8.85, 14.65 Hz, 1 H; CH_2), 2.70 (dd, J = 5.80, 16.79 Hz, 1 H; CH_2), 2.47 (dd, J = 13.13, 16.79 Hz, 1 H; CH_2), 2.37 (ddd, J = 3.97, 8.8, 12.82 Hz, 1 H; CH_2), 2.17 (ddd, J = 6.10, 10.38, 12.20 Hz, 1 H; CH_2) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 198, 149.4, 146.5, 146.3, 135.9, 128.8, 126.2, 107.2, 102.5, 101, 68.8, 61.7, 54, 44.76, 44.7, 40 ppm. HRMS (EI): calcd. for $C_{16}H_{15}NO_3$: 269.1052; found 269.1073.

Synthesis of *epi*-Crinine (1d) from 1f: To a solution of **1f** (0.010 g, 0.037 mmol) in anhydrous MeOH (1 mL) was added $NaBH_4$ (0.026 g, 0.074 mmol) and $CeCl_3{\cdot}7H_2O$ (0.028 g, 0.074 mmol) at r.t. After stirring for 45 min at same temperature, the reaction mixture was filtered through Celite (elution with MeOH) and the solvents evaporated. The residue was extracted with $CHCl_3$ (2 × 25 mL) and the combined organic layers were washed with aqueous saturated $NaHCO_3$, dried with Na_2SO_4 and the solvents evaporated in vacuo to obtain a gummy mass, which was purified by column chromatography (CH_2Cl_2/MeOH, 85:15) to afford **1d** as a yellow gummy liquid (9 mg, 90%). R_f = 0.3 (CH_2Cl_2/MeOH, 80:20). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3142 (br), 3018, 2926, 1506, 1483, 1365, 1317, 1232, 1091, 1039, 1001, 935, 862, 754, 667 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 6.80 (s, 1 H; CH), 6.48 (s, 1 H; CH), 6.39 (dd, J = 2.13, 10.37 Hz, 1 H; CH), 5.89 (ABq, 2 H; CH_2), 5.79 (d, J = 10.37 Hz, 1 H; CH), 4.45 (d, J = 16.48 Hz, 1 H; CH_2), 4.4 (m, 1 H; CH), 3.83 (d, J = 16.78 Hz, 1 H; CH_2), 3.50 (ddd, J = 4.23, 10.30, 13.62 Hz, 1 H: CH_2), 3.29 (dd, J = 3.66, 13.42 Hz, 1 H; CH_2), 2.95 (ddd, J = 6.10, 9.15, 15.45 Hz, 1 H; CH_2), 2.25–2.08 (m, 3 H; CH_2 and H of CH), 1.64 (four-lines pattern, J = 11.90 Hz, 1 H; CH_2) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 146.3, 145.9,

138.2, 131.5, 128.5, 125.2, 106.9, 102.8, 100.8, 67.5, 66.7, 61.8, 53.1, 44.7, 44.4, 34.6 ppm. MS: *m*/*z* = 272.2 [M + H]$^+$.

Synthesis of Crinine (1b) from *epi*-Crinine (1d): To a solution of *epi*-crinine **1d** (0.090 g, 0.033 mmol) in anhydrous CH_2Cl_2 (0.75 mL) was added MsCl (20 μL, 0.172 mmol) and Et_3N (23 μL, 0.172 mmol) at r.t. After stirring the reaction mixture for 1 h at r.t., the solvent was removed under reduced pressure and the residue was dissolved in DMF (0.75 mL) and transferred by using a syringe to a flask containing CsOAc (0.100 g, 0.518 mmol). The resulting greenish suspension was stirred at r.t. for 40 h then filtered (elution with EtOAc). The combined filtrates were dissolved in 1 N HCl (5 mL) and the aqueous solution was washed with Et_2O (2 × 5 mL). The aqueous phase was basified with saturated aqueous K_2CO_3 to pH 12 and then extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were washed with water (2 × 5 mL), brine (5 mL), and dried using Na_2SO_4. Filtration, followed by solvent evaporation under reduced pressure gave the crude allylic acetate, which was immediately dissolved in anhydrous MeOH (0.75 mL) containing powdered K_2CO_3 (0.041 g, 0.297 mmol). After stirring the reaction mixture for 2 h at r.t., the solvent was removed in vacuo. The residue was dissolved in CH_2Cl_2 (20 mL) and washed with saturated $NaHCO_3$ (5 mL). The combined organic layers were washed with water, brine, dried with anhydrous Na_2SO_4, and concentrated. Preparative thin layer chromatography of the reaction mixture (CH_2Cl_2/MeOH/Et_3N, 9:1:1) yielded **1b** (4.5 mg, 50% over 3 steps) as a white powder. R_f = 0.4 (CH_2Cl_2/MeOH/Et_3N, 90:10:10). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 3325 (br), 2926, 1504, 1484, 1317, 1234, 1039, 757 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 6.78 (s, 1 H; CH), 6.55 (d, *J* = 10.07 Hz, 1 H; CH), 6.47 (s, 1 H; CH), 5.98 (dd, *J* = 4.88, 10.07 Hz, 1 H; CH), 5.89 (ABq, 2 H; CH_2), 4.49 (d, *J* = 16.48 Hz, 1 H; CH_2), 4.36 (m, 1 H; CH), 3.83 (d, *J* = 16.48 Hz, 1 H; CH_2), 3.47–3.44 (m, 2 H; H of CH and H of CH_2), 2.91 (ddd, *J* = 6.41, 8.85, 13.43 Hz, 1 H; CH_2), 2.18 (ddd, *J* = 3.96, 8.85, 12.82 Hz, 1 H; CH_2), 1.97–1.94 (m, 2 H; H of CH_2 and H of CH_2), 1.75 (ddd, *J* = 3.97, 13.74 Hz, 1 H; CH_2) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 146.3, 145.9, 138.2, 132.1, 131.4, 128.6, 127.6, 107, 102.9, 100.8, 63.7, 63, 61.8, 53.1, 44.48, 44.42, 32.1 ppm. MS: *m*/*z* = 272.2 [M + H]$^+$.

Supporting Information (see also the footnote on the first page of this article): Copies of the ^{1}H and ^{13}C NMR spectra for compounds **11a**, **10a**, **8a**, **22a**, **21**, **23a**, **1e**, **1a**, **11b**, **10b**, **8b**, **22b**, **23b**, **1f**, **1d**, **1b** and a Table for comparison of NMR spectroscopic data for compounds **1a** and **1b** with the literature.

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