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Studies on the Synthesis of the Alkaloid (−)-Gilbertine via Indolidene Chemistry

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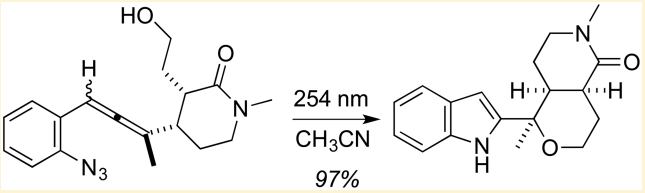
Supporting Information

ABSTRACT: A synthesis route to the pentacyclic alkaloid (−)-gilbertine, which features a cyclization cascade passing through a transient indolidene intermediate, was pursued. A key stereochemical relationship was set via a Nicholas-type enolate alkylation. Ultimately, undesired C−N cyclization thwarted the final projected C−C bond forming ring closure, and gilbertine could not be prepared by this route.



INTRODUCTION

(−)-Gilbertine (**1**), which was isolated in 1982 from the Brazilian tree *Aspidosperma gilbertii*, is a member of the uleine family of natural products (Figure 1).[1] Compared to the rest of the family, (−)-gilbertine has an extra ring (E) and stereogenic center at C(16), making it a more complex synthetic target.

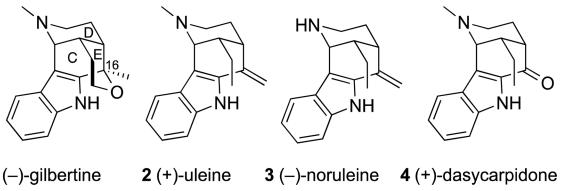
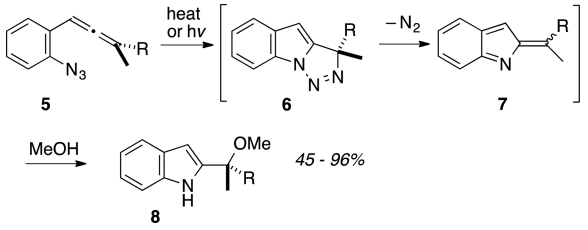


Figure 1. Uleine alkaloids.

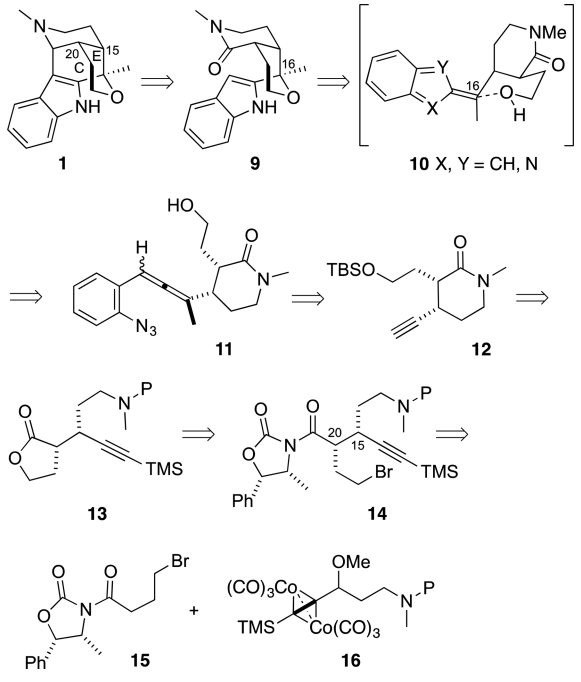
Blechert completed the only reported synthesis of (−)-gilbertine in 2004 through a route that utilized a cationic cyclization to set the C(16) stereocenter.[2] Herein, we describe a different approach toward gilbertine using allenyl azide cyclization chemistry[3] to close the E-ring and set the stereochemistry at C(16) simultaneously. This allenyl azide-based cyclization strategy involves a cascade of reactions initiating with intramolecular [3 + 2] cycloaddition of an allene and azide, as in **5**, which provides triazoline intermediate **6** (Scheme 1).[3] Concerted loss of nitrogen gas[4] from **6** results in an electrophilic indolidene intermediate **7**, which, upon nucleophilic addition of an alcohol (exemplified by methanol in Scheme 1), generates the product indole **8**.

Scheme 1. Generation of an Indolidene Intermediate from an Allenyl Azide Precursor; Trapping with Methanol



In the proposed synthesis of gilbertine, an allenyl azide cyclization of allene **11** should generate indolidene intermediate **10**, which could undergo an intramolecular cyclization with the pendant alcohol to provide the indole ring and set the stereocenter at C(16) (Scheme 2). The stereochemistry at C(16) within **9** was anticipated to conform to gilbertine's relative stereochemistry based on the expectation that

Scheme 2. Retrosynthesis of (−)-Gilbertine



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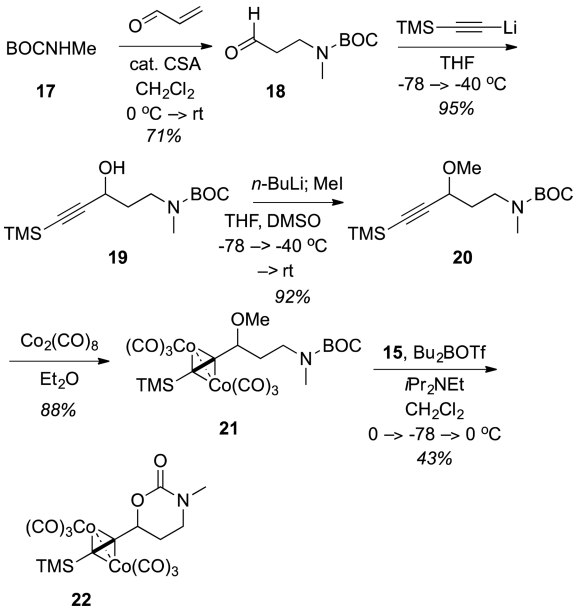
cyclization will proceed through an energetically favorable chair transition state with the indolidene unit in a pseudoequatorial position, as shown in **10**. Lactam **9** could then be converted to gilbertine through a reduction of the amide and subsequent cationic cyclization of C(3) of the indole nucleus into the derived iminium ion. Allene **11** could be formed from alkyne **12** through chemistry described earlier.[3] Deprotection of the nitrogen in lactone **13** and subsequent cyclization of the liberated amine into the proximate lactone carbonyl should provide lactam **12**. Cleavage of the chiral auxiliary in **14** would generate lactone **13** based on previous work by Jacobi and co-workers.[5] The two stereogenic centers labeled C(15) and C(20) in gilbertine would be set through a key Nicholas reaction[6] of cobalt complex **16** and oxazolidinone **15**.

RESULTS

Work on this route to gilbertine commenced with the synthesis of cobalt complex **16** from *tert*-butyl carbonate (BOC) protected methylamine **17**, as shown in Scheme 3. The

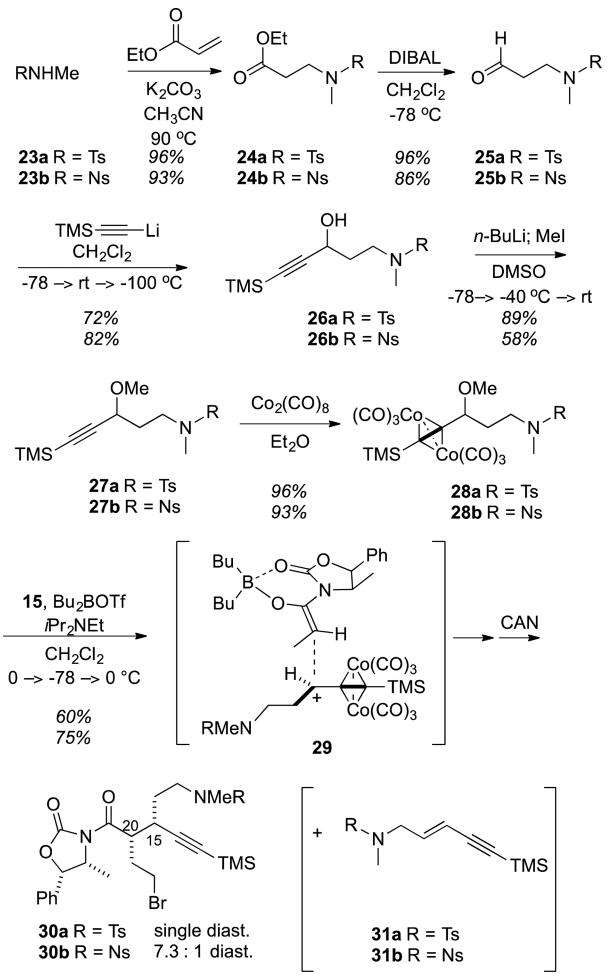
Scheme 3. Synthesis of a BOC-Protected Electrophile; Failure of the Nicholas Reaction



Nicholas reaction of cobalt complex **16** with oxazolidinone **15** resulted in the formation of carbamate **22**, instead of the expected Nicholas adduct **14**. Carbamate **22** presumably arose through an intramolecular cyclization of the carbamate's oxygen into the transiently formed carbocation derived by Bu_2BOTf-mediated ionization of the methyl ether moiety in **21**. To avoid this undesirable cyclization, a new protecting group for the nitrogen in **21**, *p*-toluene sulfonyl, was explored.

As shown in Scheme 4, tosyl protected amine **28a** was synthesized using similar chemistry to the BOC protection series of Scheme 3. One minor point of distinction between the two routes can be found at the beginning; whereas acrolein was a suitable partner for BOCNHMe conjugate addition, attempts to add TsNHMe to acrolein resulted in only trace (~2%) yields of the *β*-tosylamido aldehyde. Fortunately, switching electrophiles to ethyl acrylate solved the conjugate addition problem, and *β*-tosylamido ester **24a** could be formed in excellent yield. Using THF at −78 °C, as in the BOC route, for acetylide

Scheme 4. Synthesis of a Tosyl- and Nosyl-Protected Electrophile; Successful Nicholas Reactions



addition into aldehyde **25a** resulted in a 45% yield. Surprisingly, using either a mixture of CH_2Cl_2 and toluene or neat CH_2Cl_2 as the solvent resulted in a significantly higher yield (72%) of alcohol **26a**. Upon submitting cobalt complex **28a** to the Nicholas reaction, the desired adduct **30a** was isolated as essentially a single diastereomer (^{1}H NMR detection limit < 5%). The relative stereochemistry of this adduct was tentatively assigned by comparison to the results of a similar Nicholas reaction reported by Schreiber[6] and later confirmed by NOE measurements on a downstream intermediate (vide infra). The mechanistic picture proposed by Schreiber[6] is encapsulated in the transition state structure **29**. In this depiction, the stereochemistry in **30a** is controlled through the chirality present in oxazolidinone **15**; the methyl and phenyl substituents of the oxazolidinone block addition of the Nicholas carbocation to the "top" face of the boron enolate, thereby setting the C(20) stereocenter. The C(15) stereochemistry is presumably controlled through reaction via an orientation featuring an energetically less penalizing steric interaction between the Lewis acid's butyl group and the proton on the carbocation species rather than a more energetically costly interaction with the methyl group if the carbocation component's orientation is flipped by 180°. The Nicholas adduct **30a** was obtained in moderate yield, but if the temperature of the reaction solution was allowed to warm above 0 °C, the carbocation was diverted down a different path

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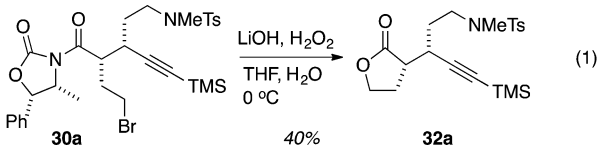
and the major product isolated was alkene **31a** (90%). This species presumably originated through simple deprotonation from the carbocationic Nicholas intermediate.

The chiral auxiliary in **30a** was cleaved with lithium hydroperoxide, and the resulting acid cyclized by displacing the primary bromide to provide lactone **32a** in modest yield (eq 11). Removal of the tosyl protecting group in **32a** was expected to provide lactam **12** through cyclization of the free amine into the lactone. However, all efforts to cleave the tosyl protecting group from the nitrogen (Mg/MeOH, Na(Hg), Na/naphthalene) resulted in either cleavage of the TMS group or no observed reaction. Thus, it became apparent that, whereas introduction of the tosyl protecting group solved the Nicholas reaction problem, it eventually led to a dead end at the deprotection step. Therefore, a new protecting group was required, and in this vein, the tosyl group was replaced with the *p*-nitrotoluenesulfonyl (nosyl) protecting group.



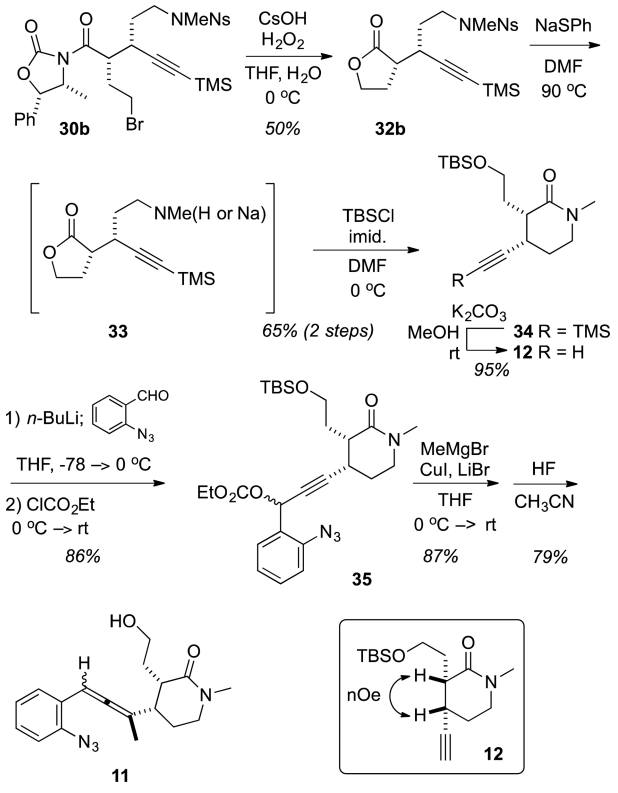
(1)

The synthesis of nosyl cobalt complex **28b** was achieved by the same procedure as detailed earlier with the tosyl route, with one improvement. In this newer route (Scheme 5), aldehyde **25b** was converted directly to methyl ether **27b**, in 94% yield without isolation of alcohol intermediate **26b** (Scheme 4). The Nicholas reaction of nosyl cobalt complex **28b** and oxazolidinone **15** resulted in a 7:1 mixture of product diastereomers, **30b** and **30c**. The Nicholas adduct **30b**, with the desired *syn* stereochemistry, was converted to the lactone **32b** through cleavage of the chiral auxiliary (Scheme 5). Initially, the chiral auxiliary was cleaved with lithium hydroxide monohydrate and hydrogen peroxide, which resulted in a 30–45% yield of the lactone. Other bases were then explored in an effort to improve the yield. Sodium hydroxide also generated inconsistent yields (30–50%), while potassium hydroxide resulted in a materially lower yield (28%). Cesium hydroxide was discovered to afford a moderate, but consistent, yield of lactone **32b**. Removal of the nosyl protecting group in **32b** was achieved with sodium thiophenolate, and the nascent amine did in fact cyclize into the lactone as desired to provide lactam **34** upon TBS protection of the first-formed alcohol. Cleavage of the alkyne's TMS group then provided alkyne **12**; at this point, NOESY NMR analysis confirmed the initial mechanism-based assignment of relative stereochemistry, as illustrated in Scheme 5. Addition of the lithiated alkyne derived from deprotonation of **12** into azidobenzaldehyde, followed by condensation of the first-formed alkoxide with ethyl chloroformate, provided carbonate **35**. Methylcuprate addition into the propargyl carbonate unit of **35** generated allene **36** which, upon removal of the TBS group with hydrofluoric acid, afforded the key cyclization cascade precursor, azido allene **11**. Allene **11** was isolated as an inconsequential mixture (~1:1) of diastereomers.

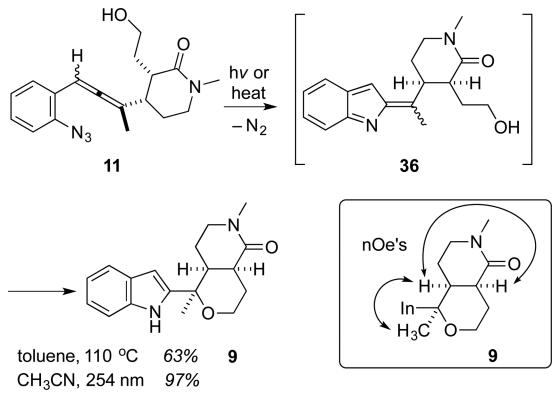
Attempts at the key allenyl azide cyclization cascade of alcohol **11** resulted in formation of a single diastereomer **9** in moderate yield under thermal conditions and in almost quantitative yield under photochemical conditions (Scheme 6). As discussed earlier, the allenyl azide cyclization of **11** generates indolidene intermediate **36**, which, upon cyclization of the pendant alcohol, closes the E-ring of the target molecule and sets the C(16) stereochemistry. NOESY correlations within **9** (see Scheme 6) suggested that the desired stereochemical outcome at C(16) necessary for the synthesis of gilbertine was obtained.

Reduction of the lactam in **9** was expected to form the iminium ion intermediate **37**, which, upon C(3) cyclization of the indole, would generate gilbertine (**1**) (Scheme 7). However, when lactam **9** was reduced with lithium aluminum hydride, a mixture of over-reduced product **38** and enamine **39** was isolated. These products likely stem from the desired iminium ion. Apparently, both a second hydride addition to the putative iminium ion intermediate (→ **38**) and deprotonation of the iminium ion (→ **39**) were faster than the desired cyclization. Other reducing agents were explored in an effort to avoid the second hydride addition and hopefully generate gilbertine. Sodium borohydride and Red-Al did not reduce the

Scheme 5. Use of the Nosyl-Protected Nicholas Product in Lactam Formation



Scheme 6. Allenyl Azide–Indolidene Cascade Cyclization



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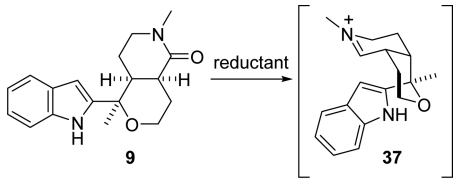
Scheme 7. Attempts at Reductive Cyclization of 9



$LiAlH_4$	31%[a]	21%[a]
$NaBH_4$	no reaction	
Red-Al	no reaction	
DIBAL	19%[a]	38%[a]
Cp_2ZrHCl	0%[a]	65%[a]

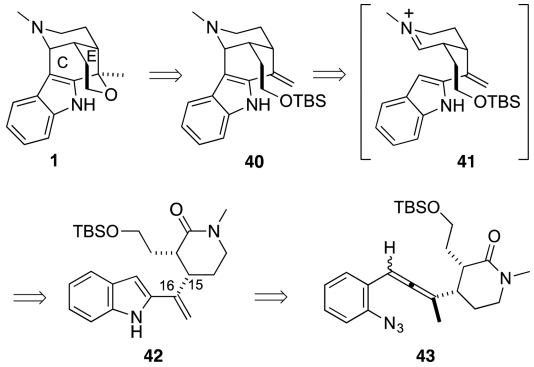
[a]Yields determined by integrating key signals in the ^1H NMR spectrum of the mixture

[a]Yields determined by integrating key signals in the ^1H NMR spectrum of the mixture

lactam, whereas DIBAL-mediated reduction of **9** resulted in a mixture of the over-reduced product **38** and enamine **39**. Solely, the enamine product **39** was generated upon reducing the amide **9** with the Schwartz reagent (Cp_2ZrHCl). Attempts to cyclize enamine **39** ($HOAc/H_2O$) did not lead to gilbertine.

Since closure of the C-ring of the gilbertine structure from intermediate **9** (or derived iminium ion **37**) was problematic, an alternative end-game strategy was explored. In this alternative approach, the E-ring of gilbertine would be closed last (Scheme 8). The hope here was that burgeoning strain

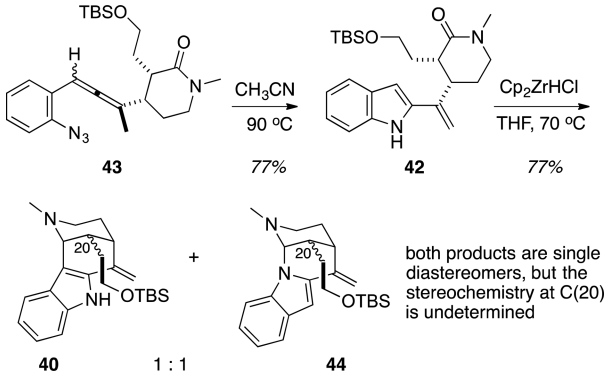
Scheme 8. An Alternative Approach − C-Ring Closure Prior to E-Ring Closure



upon C-ring closure from **37** was the issue, and therefore, by attempting C-ring closure from a more "open" and presumably less constrained substrate **41**, this problem with the initial route can be avoided. In this new approach, gilbertine (**1**) would be formed through a deprotection/cycloetherification of **40**. A Schwartz reagent-mediated reduction of the lactam in **42** should provide iminium ion intermediate **41**, and the precursor indole **42** could be generated from an allenyl azide cyclization of the TBS protected allene **43**, which was already in hand.

Indole **42** was formed in good yield from allene **43** upon simple heating in acetonitrile (Scheme 9). Photochemically

Scheme 9. Synthesis and Reductive Cyclization of the Alkene Cyclization Precursor



mediated reaction of allenyl azide **43** was explored as well, but upon irradiation in DMF, **43** led to an inseparable mixture of the disubstituted alkene **42** and an undesired product with the alkene between C(15) and C(16) (35−53%). Schwartz reagent-mediated reduction of indole **42** resulted in a mixture of *C*- and *N*-cyclized products **40** and **44**, respectively. This result is consistent with the notion that accrued ring strain thwarted C-ring forming cyclization within **37**. Whereas both **40** and **44** are isolated as single diastereomers (<5% impurity, ^1H NMR detection limit), the relative stereochemistry at C(20) could not be determined through NOESY NMR. Efforts to convert the *C*-cyclized species **40** into gilbertine (**1**) through a deprotection and O → C cyclization at C(16) promoted by trifluoroacetic acid resulted in a mixture of products which could not be separated. The ^1H NMR spectrum of the crude mixture showed alkene protons, suggesting that no O → C cyclization had occurred. Treating **40** with acetic acid at room temperature did not lead to any chemical reaction, whereas refluxing the reaction mixture indole **40** decomposed the indole. According to the ^1H NMR spectrum of the reaction mixture, the TBS group was cleaved from **40** using hydrofluoric acid or tetra-butylammonium fluoride. The presumed primary alcohol resulting from this deprotection could not be purified through column chromatography, and so, the crude alcohol was submitted to trifluoroacetic acid in dichloromethane in an attempt to effect cyclization at C(16). Unfortunately, gilbertine was not identifiable in the crude reaction mixture's ^1H NMR spectrum, suggesting that O → C cyclization did not occur. This result was unexpected since Blechert has shown that gilbertine can be synthesized in quantitative yield from the deprotected alcohol of **40** upon treatment with trifluoroacetic acid.[2] It is possible that C(20) epimerization had occurred during the C-ring closure, and therefore, the E-ring could not be closed from this incorrect C(20) stereochemistry.

Efforts to convert the *N*-cyclized product **44** to gilbertine (**1**) also were explored. When submitted to acetic acid at reflux for 5 h, *N*-cyclized species **44** generated a mixture of five products. On the basis of the ^1H NMR spectrum of the crude reaction mixture, the five products were all *C*-cyclized species, suggesting that acetic acid can successfully convert the *N*-cyclized species **44** to *C*-cyclized products. Once again, no gilbertine was detected by examination of the ^1H NMR spectrum of this reaction mixture. In an effort to avoid this mixture of products, intermediate **40** was submitted to deprotection conditions first. Either hydrofluoric acid or tetra-butylammonium fluoride successfully cleaved the TBS group

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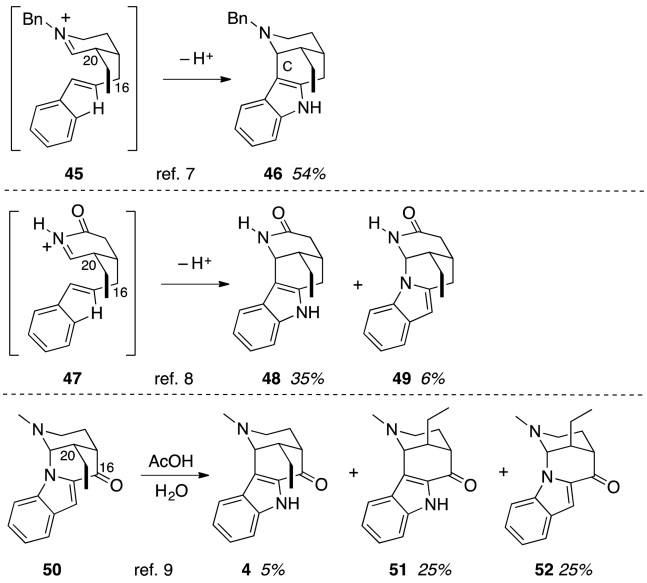
based on the ^{1}H NMR spectrum of the reaction mixture, whereas the use of cesium fluoride resulted in no reaction. Attempts to convert this *N*-cyclized alcohol into gilbertine through treatment with either acetic acid or trifluoroacetic acid once again failed.

DISCUSSION

The issue of cyclization efficiency and cyclization selectivity (*N* vs *C*) for the closure of the C-ring of members of the uleine family has been an ongoing challenge. Complicating the cyclization chemistry is the observation that the C(20) position can epimerize under acidic reaction conditions, Scheme 10. On

Scheme 10. Prior Art for C-Ring Closure of the Uleine Alkaloids



the positive side, Ogasawara's synthesis of uleine proceeded through iminium ion **45**, and the desired C(3) cyclized product **46** was formed with only trace amounts of the C(20) epimer and no C−N bond formation.[7] However, both Bosch[8] and Joule[9] observed *N*-cyclization in their syntheses of dasycarpidone. Bosch obtained only trace amounts of the *N*-cyclized product **49** from iminium ion **47**. In Joule's synthesis of dasycarpidone, reaction through an iminium ion derived from opening the C-ring of **50** resulted in both *N*-recyclization/C(20) epimerization (→ **52**) and *C*-cyclization with and without C(20) epimerization (→ **51**, **4**) and thus only provided trace amounts of dasycarpidone (**4**).

Our initial approach to gilbertine through iminium ion **37** would have skirted the C(20) epimerization problem, since presumably any C(20) epimer formed could equilibrate with **37** via the iminium ion, and only **37** could cyclize to close the C-ring. However, since no cyclization of iminium ion **37** was detected, it is not possible to analyze this premise further. In the final route toward gilbertine, cyclization of the iminium ion did occur, but we were unable to ascertain the relative stereochemistry at C(20) of the two cyclization products **40** and **44**. Whereas complete C(20) epimerization within these species could explain why neither product could be converted to gilbertine (**1**), none of the previous approaches toward the uleine family have reported complete C(20) epimerization during C-ring closure.

Although gilbertine could not be formed through this allenyl azide approach, the results obtained did provide some insight into the scope of the allenyl azide cyclization cascade process. The allenyl azide cyclization cascade of **11** was able to generate the single product diastereomer **9** in high yield in a reaction that formed one new C−N bond and one new C−O bond. Attempts to generate gilbertine (**1**) through a reduction of the amide in **9** with traditional hydride sources resulted in a mixture of over-reduced product **38** and enamine **39**, suggesting that the desired ring closure in this multi-ring system was too slow to compete. Incipient ring strain may be the culprit, as a Schwartz reagent-mediated reduction/cyclization of a presumably less strained system **42** resulted in a mixture of the *C*- and *N*-cyclized products **40** and **44**. These results suggest that the C-ring of gilbertine **1** should be formed before the E-ring. For reasons that are unclear, efforts to convert the *N*- and *C*-cyclized products **40** and **44** into gilbertine were unsuccessful.

EXPERIMENTAL SECTION

General Procedure 1. Sulfonyl Protection of Methylamine. A solution of sulfonyl chloride in CH_2Cl_2 (2 M) was cooled to 0 °C, and methylamine (40 wt % in water, 2.2 equiv) was added slowly. Upon consumption of the sulfonyl chloride (determined by TLC), the mixture was diluted with an equal volume of brine. The layers were separated, and the organic layer was washed with water and then brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by recrystallization in 95% ethanol to give pure sulfonamide.

General Procedure 2. Sulfonamide Addition into Ethyl Acrylate. To the sulfonamide substrate in MeCN (0.35 M) were added K_2CO_3 (1.5 equiv) and ethyl acrylate (1.2 equiv). The solution was brought to 90 °C and held there for the indicated time. At that time, the solution was cooled to room temperature, diluted with Et_2O, and run through a plug of Celite. The filtrate was concentrated under reduced pressure, and the residue was purified by flash column chromatography on SiO_2 with the indicated eluent.

General Procedure 3. DIBAH Reduction. The ester in the indicated solvent (0.3 M) was cooled to −78 °C, and 1.0 M DIBAH in hexanes (1.1 equiv) was added slowly. After 2 h at −78 °C, EtOH (0.5 equiv) was added, and the solution was warmed to room temperature. After 30 min, an equal volume of saturated Rochelle's salt solution was added, and the mixture was stirred vigorously for 2 h. The layers were separated, and the aqueous layer was extracted with EtOAc (3×). The organic layers were combined and washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by SiO_2 flash column chromatography with the indicated eluent.

General Procedure 4. Trimethylsilylacetylene Addition into an Aldehyde. To a solution of trimethylsilylacetylene in the indicated solvent (0.3 M) was added 2.5 M *n*-BuLi in hexanes (1.1 equiv) at −78 °C. After the addition, the solution was warmed to room temperature and held there for 15 min, and then cooled to −100 °C (Et_2O/CO_2 bath). The aldehyde in the indicated solvent (0.9 M) was added at −100 °C. Upon consumption of the aldehyde (determined by TLC), the solution was diluted with an equal volume of saturated NH_4Cl solution and extracted with CH_2Cl_2 (3×). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by SiO_2 flash column chromatography with the indicated eluent.

General Procedure 5. Methylation of an Alcohol. The alcohol substrate in THF (0.2 M) was cooled to −78 °C, and 2.5 M *n*-BuLi in hexanes (1 equiv) was added. After 10 min, iodomethane (8 equiv) was added to the mixture and the solution was warmed to −40 °C (MeCN/CO_2 bath). DMSO (2 equiv) was added at −40 °C, and the reaction mixture was allowed to warm to room temperature overnight. After 14 h, the solution was diluted with an equal volume of saturated NH_4Cl solution and extracted with CH_2Cl_2 (3×). The layers were separated, and the combined organic layers were dried over Na_2SO_4,

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filtered, concentrated under reduced pressure, and purified by SiO_2 flash column chromatography with the indicated eluent.

General Procedure 6. Cobalt Complex Formation. To a solution of octacarbonyl dicobalt (1 equiv) in Et_2O (0.6 M) was added slowly the alkyne in Et_2O (0.6 M). Once no evolution of gas was visible, the mixture was concentrated under reduced pressure and purified by the indicated method.

General Procedure 7. Nicholas Reaction. The oxazolidinone substrate (2 equiv) in the indicated solvent (0.3 M) was cooled to 0 °C. 1.0 M Bu_2BOTf in CH_2Cl_2 (4 equiv) was added, followed by freshly distilled iPr_2NEt (2 equiv). After 15 min at 0 °C, the mixture was cooled to −78 °C and the cobalt complex in the indicated solvent (0.5 M) was added slowly. The solution was warmed to the indicated temperature after the specified time. Upon consumption of the cobalt complex (determined by TLC), the reaction mixture was diluted with an equal volume of pH 7 buffer and extracted with CH_2Cl_2 (3×). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure.

General Procedure 8. Removal of $Co_2(CO)_6$. The Nicholas adduct was dissolved in acetone (0.05 M), and cerium ammonium nitrate was added in portions until no bubbles formed. The mixture was diluted with an equal volume of H_2O and extracted with EtOAc (3×). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by SiO_2 flash column chromatography with the indicated eluent.

General Procedure 9. Cleavage of the Chiral Auxiliary. The bromide substrate in 3:1 THF:H_2O (0.3 M) was cooled to 0 °C. 30% H_2O_2 (8 equiv) was added, followed by the indicated base (3.3 equiv) in H_2O (1 M). After the designated time at the specified temperature, Na_2SO_3 (8.8 equiv) in H_2O (1.2 M) was added. The mixture then was acidified to pH 1 with the indicated acid and extracted with CH_2Cl_2 (3×). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by SiO_2 flash column chromatography with the indicated eluent.

General Procedure 10. Thermal Allenyl Azide Cyclization. The allenyl azide substrate in the indicated solvent (0.005 M) was heated to the indicated temperature for the specified time. At that time, the solution was cooled to room temperature and concentrated under reduced pressure, and the residue was purified by flash column chromatography with the indicated support and eluent.

*tert-Butyl Methylcarbamate (**17**).* Di-*tert*-butyl dicarbonate (10.91 g, 49.99 mmol) and 2.0 M methylamine in THF (25 mL, 50 mmol) were added to Amberlyst-15 catalyst (0.23 g, 15% w/w) at room temperature. More 2.0 M methylamine in THF was added in portions until all of the di-*tert*-butyldicarbonate was consumed (determined by TLC). The mixture was concentrated under reduced pressure and purified by SiO_2 flash column chromatography (10% EtOAc in hexanes) to give carbamate **17** (6.07 g, 93%) as a clear oil. The derived spectral data matched those reported by Kumar.[10]

*tert-Butyl Methyl(2-oxopropyl)carbamate (**18**).* Carbamate **17** (11.00 g, 83.86 mmol) in CH_2Cl_2 (100 mL) was added to camphor sulfonic acid (3.90 g, 16.8 mmol). The mixture was cooled to 0 °C, and acrolein (56 mL, 840 mmol) was added. After 15 min at 0 °C, the reaction mixture was warmed to room temperature. Upon complete consumption of **17** (determined by TLC), the solution was diluted with saturated $NaHCO_3$ (50 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. The resulting oil was diluted in Et_2O (65 mL) and washed with H_2O (25 mL) and then brine (25 mL). The layers were separated, and the organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by SiO_2 flash column chromatography (10% EtOAc in hexanes) gave aldehyde **18** (11.10 g, 71%) as a yellow oil. The spectral data matched those reported by Xiao.[11]

*tert-Butyl (3-Hydroxy-5-(trimethylsilyl)pent-4-yn-1-yl)(methyl)-carbamate (**19**).* Following General Procedure 4, aldehyde **18** (0.37 g, 2.0 mmol) in THF was converted to alcohol **19**. The residue was purified by SiO_2 flash column chromatography (10% EtOAc in hexanes) to give alcohol **19** (0.54 g, 95%) as a clear oil. IR (thin film) 3400, 2171, 1670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.42−4.35 (m, 2H), 3.60−3.17 (m, 2H), 2.82 (s, 3H), 1.89−1.86 (m, 2H), 1.44 (s, 9H), 0.14 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3, 106.6, 88.2, 80.4, 59.1, 44.4, 35.4, 34.4, 28.5, 0.0; LRMS (ESI-TOF) m/z (relative intensity) 286.2 (16%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{14}H_{28}NO_3Si$ 286.1838, found 286.1838.

*tert-Butyl (3-Methoxy-5-(trimethylsilyl)pent-4-yn-1-yl)(methyl)-carbamate (**20**).* Following General Procedure 5, alcohol **19** (0.12 g, 0.40 mmol) was converted to methyl ether **20**. The residue was purified by SiO_2 flash column chromatography (10% EtOAc in hexanes) to give methyl ether **20** (0.11 g, 92%) as a clear oil. IR (thin film) 2169, 1695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.94 (t, J = 6.4 Hz, 1H), 3.39−3.32 (m, 5H), 2.85 (s, 3H), 1.91 (q, J = 8.2 Hz, 2H), 1.46 (s, 9H), 0.18 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.8, 103.9, 91.1, 79.4, 69.4, 56.4, 45.5, 34.6, 34.1, 28.6, 0.0; LRMS (ESI-TOF) m/z (relative intensity) 300.2 (100%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{15}H_{30}NO_3Si$ 300.1995, found 300.1980.

*tert-Butyl (3-Methoxy-5-(trimethylsilyl)pent-4-yn-1-yl)(methyl)-carbamate Dicobalt Hexacarbonyl Complex (**21**).* Following General Procedure 6, alkyne **20** (0.35 g, 1.2 mmol) was converted to cobalt complex **21**. The residue was purified by SiO_2 flash column chromatography (10% Et_2O in hexanes) to give cobalt complex **21** (0.60 g, 88%) as a red oil. IR (thin film) 2087, 2009, 1696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.29 (s, 1H), 3.54 (s, 3H), 3.50−3.21 (bs, 2H), 2.88 (s, 3H), 2.05−1.78 (m, 2H), 1.46 (s, 9H), 0.32 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.4, 156.0, 80.1, 79.7, 78.9, 58.8, 46.1, 45.9, 37.8, 34.6, 28.6, 1.1; LRMS (ESI-TOF) m/z (relative intensity) 608.0 (26%, M + Na^+); HRMS (ESI-TOF) m/z: [M + Na^+]; calcd for $C_{21}H_{29}Co_2NO_9SiNa$ 608.0173, found 608.0200.

*(4R,5S)-3-(4-Bromobutanoyl)-4-methyl-5-phenyloxazolidin-2-one (**15**).* To a solution of chiral auxiliary (4*R*,5*S*)-(+)-4-methyl-5-phenyl-2-oxazolidinone (0.18 g, 1.0 mmol) in THF (3.16 mL) was added 2.5 M *n*-BuLi in hexanes (0.4 mL, 1 mmol) at −78 °C. After 15 min, 4-bromobutyryl chloride (0.14 mL, 1.2 mmol) was added at −78 °C. The mixture was warmed to 0 °C after 15 min. Upon consumption of the chiral auxiliary (determined by TLC), the solution was diluted with H_2O (10 mL) and extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by SiO_2 flash column chromatography (30% EtOAc in hexanes) gave oxazolidinone **15** (0.11 g, 92%) as a white solid. $[\alpha]_D^{20}$ = +29.7 (c = 0.14, $CHCl_3$); mp 46−49 °C; IR (thin film) 1777, 1699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37−7.45 (m, 3H), 7.30 (d, J = 6.3 Hz, 2H), 5.68 (d, J = 7.3 Hz, 1H), 4.76 (apparent pentet, J = 6.7 Hz, 1H), 3.52 (t, J = 6.5 Hz, 2H), 3.13 (q, J = 7.0 Hz, 2H), 2.23 (p, J = 6.7 Hz, 2H), 0.90 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 153.2, 133.3, 129.0, 128.9, 125.8, 79.3, 54.9, 34.2, 32.8, 27.2, 14.7; LRMS (ESI-TOF) m/z (relative intensity) 326.0 (25%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{14}H_{17}NO_3Br$ 326.0392, found 326.0382.

*3-Methyl-6-((trimethylsilyl)ethynyl)-1,3-oxazinan-2-one Dicobalt Hexacarbonyl Complex (**22**).* Following General Procedure 7, oxazolidinone **15** (0.03 g, 0.1 mmol) in CH_2Cl_2 and cobalt complex **21** (0.03 g, 0.05 mmol) in CH_2Cl_2 were stirred at −78 °C for 10 min before warming to 0 °C. The residue was purified by SiO_2 flash column chromatography (20% Et_2O in hexanes) to give carbamate **22** (11 mg, 43%) as a red oil. IR (thin film) 2090, 2002, 1690 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 5.38 (dd, J = 10.8, 2.5 Hz, 1H), 3.55 (td, J = 11.7, 5.2 Hz, 1H), 3.31 (ddd, J = 11.7, 6.1, 2.1 Hz, 1H), 3.03 (s, 3H). 2.35−2.25 (m, 1H), 2.12−2.20 (m, 1H), 0.28 (s, 9H); ^{13}C NMR (125 MHz, C_6D_6) δ 200.3, 152.1, 108.5, 80.2, 76.9, 46.1, 36.5, 31.1, 0.9; LRMS (ESI-TOF) m/z (relative intensity) 497.9 (100%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{16}H_{18}Co_2NO_8Si$ 497.9466, found 497.9445.

*N-4-Dimethyl-benzenesulfonamide (**23a**).* Following General Procedure 1, tosyl chloride (15.3 g, 80.0 mmol) was converted to sulfonamide **23a**, recovered as white crystals (13.8 g, 93%). The spectral data matched those reported by Xu.[12]

*N-Methyl-4-nitrobenzenesulfonamide (**23b**).* Following General Procedure 1, 4-nitrobenzenesulfonyl chloride (11 g, 50 mmol) was

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converted to sulfonamide **23b**, recovered as white crystals (9.77 g, 90%). The spectral data matched those reported by Maclean.[13]

*Ethyl 3-((N,4-Dimethylphenyl)sulfonamide)propanoate (**24a**).* Following General Procedure 2, tosylamide **23a** (5.22 g, 28.2 mmol) was converted to ester **24a** after stirring at 90 °C for 16 h. The residue was purified by column chromatography on SiO_2 (30% ethyl acetate in hexanes) to give ester **24a** as a colorless oil (7.67 g, 96%). IR (thin film) 1730 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 4.13 (q, J = 7.1 Hz, 2H), 3.31 (t, J = 7.2 Hz, 2H), 3.76 (s, 3H). 2.61 (t, J = 7.2 Hz, 2H). 2.43 (s, 3H), 1.26 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 143.3, 130.0, 129.8, 127.4, 60.8, 46.0, 35.7, 34.1, 21.6, 14.3; LRMS (ESI-TOF) m/z (relative intensity) 286.1 (100%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{13}H_{20}NO_4S$ 286.1113, found 286.1109.

*Ethyl 3-(N-Methyl-4-nitrophenyl)sulfonamide)propanoate (**24b**).* Following General Procedure 2, nosylamide **23b** (1.85 g, 8.56 mmol) and ethyl acrylate were heated to 90 °C and held there for 3 h. The residue was purified by flash column chromatography on SiO_2 (30% EtOAc in hexanes) to give **24b** as a light yellow solid (2.52 g, 93%). mp 95−97 °C; IR (thin film) 1734, 1527 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.37 (d, J = 8.8 Hz, 2H), 7.97 (d, J = 8.8 Hz, 2H), 4.13 (q, J = 7.1 Hz, 2H), 3.37 (t, J = 7.1 Hz, 2H), 2.84 (s, 3H), 2.63 (t, J = 7.1 Hz, 2H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 150.2, 143.7, 128.6, 124.6, 61.1, 46.3, 35.7, 33.9, 14.3; LRMS (ESI-TOF) m/z (relative intensity) 317.1 (50%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{12}H_{17}N_2O_6S$ 317.0807, found 317.0820.

*N-4-Dimethyl-N-(3-oxopropyl)benzenesulfonamide (**25a**).* Following General Procedure 3, ester **24a** (0.97 g, 3.4 mmol) in toluene was converted to aldehyde **25a**. The residue was purified by SiO_2 flash column chromatography (20% EtOAc in hexanes) to give aldehyde **25a** (0.79 g, 96%) as a colorless oil. IR (thin film) 1721 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 9.80 (t, J = 1.1 Hz 1H), 7.67 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 3.30 (t, J = 6.8 Hz, 2H), 2.78 (td, J = 6.8, 1.1 Hz, 2H), 2.75 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 134.3, 129.9 (2), 127.6, 46.2, 35.9, 21.7; LRMS (ESI-TOF) m/z (relative intensity) 242.1 (100%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{11}H_{16}NO_3S$ 242.0851, found 242.0843.

*N-Methyl-4-nitro-N-(3-oxopropyl)benzenesulfonamide (**25b**).* Following General Procedure 3, ester **24b** (3.68 g, 11.6 mmol) in CH_2Cl_2 was converted to aldehyde **25b**. Purification of the residue by SiO_2 flash column chromatography (20% EtOAc in hexanes) gave aldehyde **25b** (2.72 g, 86%) as an orange solid. mp 72−74 °C; IR (thin film) 1718, 1523 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.98 (s, 1H), 8.37 (d, J = 8.7 Hz, 2H), 7.97 (d, J = 8.7 Hz, 2H), 3.38 (t, J = 6.7 Hz, 2H), 2.85−2.82 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.6, 150.2, 143.2, 128.6, 124.6, 43.9, 42.9, 35.8; LRMS (ESI-TOF) m/z (relative intensity) 290.1 (19%, M + NH_4^+); HRMS (ESI-TOF) m/z: [M + NH_4^+]; calcd for $C_{10}H_{16}N_3O_5S$ 290.0811, found 290.0829.

*N-(3-Hydroxy-5-(trimethylsilyl)pent-4-yn-1-yl)-N,4-dimethylbenzenesulfonamide (**26a**).* Following General Procedure 4, aldehyde **25a** (0.20 g, 0.85 mmol) in CH_2Cl_2 was converted to alcohol **26a**. Purification of the residue by SiO_2 flash column chromatography (30% EtOAc in hexanes) gave alcohol **26a** (0.21 g, 72%) as a colorless oil. IR (thin film) 3497, 2171, 1737 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.67 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 4.61−4.56 (m, 1H), 3.36−3.32 (m, 1H), 2.96−2.89 (m, 1H), 2.76 (s, 3H), 2.50 (d, J = 5.4 Hz, 1H), 2.43 (s, 3H), 1.97−1.88 (m, 2H), 0.18 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.6, 134.2, 129.8, 127.4, 105.9, 89.7, 59.7, 46.5, 35.7, 35.4, 21.6, −0.1; LRMS (ESI-TOF) m/z (relative intensity) 340.1 (100%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{16}H_{26}NO_3SSi$ 340.1403, found 340.1402.

*N-(3-Hydroxy-5-(trimethylsilyl)pent-4-yn-1-yl)-N-methyl-4-nitrobenzenesulfonamide (**26b**).* Following General Procedure 4, aldehyde **25b** (15.7 g, 57.9 mmol) in CH_2Cl_2 was converted to alcohol **26b**. Purification of the residue by SiO_2 flash column chromatography (30% EtOAc in hexanes) gave alcohol **26b** (17.5 g, 82%) as an orange solid. mp 98−100 °C; IR (thin film) 3514, 3112, 2171, 1528 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.38 (d, J = 8.7 Hz, 2H), 7.98 (d, J = 8.7 Hz, 2H), 4.73−4.69 (m, 1H), 3.42−3.33 (m, 1H), 3.14−3.06 (m, 1H), 2.83 (s, 3H), 2.38 (d, J = 5.0 Hz, 1H), 1.97 (p, J = 6.7 Hz, 2H), 0.17 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.2, 143.6, 128.6, 124.6, 150.4, 90.4, 59.7, 46.6, 35.6, 35.3, −0.1 ; LRMS (ESI-TOF) m/z (relative intensity) 371.1 (100%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{15}H_{23}N_2O_5SSi$ 371.1079, found 371.1097.

*N-(3-Methoxy-5-(trimethylsilyl)pent-4-yn-1-yl)-N,4-dimethylbenzenesulfonamide (**27a**).* Following General Procedure 5, alcohol **26a** (0.41 g, 1.2 mmol) was converted to ether **27a**. The residue was purified by SiO_2 flash column chromatography (10% EtOAc in hexanes) to give methyl ether **27a** (0.35 g, 89%) as a colorless oil. IR (thin film) 2169, 1740 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.67 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 4.04 (t, J = 6.3 Hz, 1H), 3.39 (s, 3H), 3.38−3.17 (m, 1H), 3.05−3.00 (m, 1H), 2.73 (s, 3H), 2.43 (s, 3H), 1.93 (q, J = 6.6 Hz, 2H) 0.18 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.4, 134.5, 129.8, 127.6, 103.7, 91.3, 68.8, 56.7, 46.8, 35.5, 34.2, 21.6, 0.0; LRMS (ESI-TOF) m/z (relative intensity) 354.2 (100%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{17}H_{28}NO_3SSi$ 354.1559, found 354.1561.

*N-(3-Methoxy-5-(trimethylsilyl)pent-4-yn-1-yl)-N-methyl-4-nitrobenzenesulfonamide (**27b**).* **Method A**. Trimethylsilyl acetylene (6.4 mL, 46 mmol) in THF (23 mL) was cooled to −78 °C. 2.5 M *n*-BuLi in hexanes (19.9 mL, 49.7 mmol) was added, and the reaction mixture was warmed to room temperature for 15 min. The solution was cooled to −100 °C (Et_2O/CO_2 bath), and aldehyde **25b** (12.30 g, 45.19 mmol) in THF (226 mL) was added. Iodomethane (22.5 mL, 362 mmol) was added after 45 min, and the reaction solution was warmed to −40 °C (MeCN/CO_2 bath). DMSO (6.4 mL, 90. mmol) was added, and the reaction mixture was allowed to warm to room temperature overnight. A 150 mL portion of saturated NH_4Cl solution was added, the layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 100 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give an oily red residue. The residue was purified by SiO_2 flash column chromatography (10% EtOAc in hexanes) to give alkyne **27b** (12.60 g, 73%) as a light yellow solid. **Method B**. Following General Procedure 5, alcohol **26b** (2.50 g, 7.45 mmol) was converted to ether **27b**. The residue was purified by SiO_2 flash column chromatography (20% EtOAc in hexanes) to give ether **27b** (1.50 g, 58%) as a light yellow solid. mp 103−104 °C; IR (thin film) 2170, 1527 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.35 (d, J = 8.7 Hz, 2H), 7.96 (d, J = 8.7 Hz, 2H), 4.01 (t, J = 6.0 Hz, 1H), 3.36 (s, 3H), 3.29−3.24 (m, 1H), 3.17−3.03 (m, 1H), 2.79 (s, 3H), 1.94 (q, J = 6.4 Hz, 2H), 0.16 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.1, 143.7, 128.6, 124.5, 103.2, 91.6, 68.6, 56.7, 46.8, 35.3, 34.0, −0.1; LRMS (ESI-TOF) m/z (relative intensity) 402.1 (100%, M + NH_4^+); HRMS (ESI-TOF) m/z: [M + NH_4^+]; calcd for $C_{16}H_{28}N_3O_5SSi$ 402.1519, found 402.1504.

*N-(3-Methoxy-5-(trimethylsilyl)pent-4-yn-1-yl)-N-4-dimethylbenzenesulfonamide Dicobalt Hexacarbonyl Complex (**28a**).* Following General Procedure 6, alkyne **27a** (0.18 g, 0.51 mmol) was converted to cobalt complex **28a**. The residue was purified by SiO_2 flash column chromatography (10% Et_2O in hexanes) to give cobalt complex **28a** (0.31 g, 96%) as a red solid. mp 38−40 °C; IR (thin film) 2959, 2087, 2008, 1738 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, J = 8.1 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 4.48 (dd, J = 10.0, 2.2 Hz, 1H), 3.68−3.48 (m, 4H), 2.83−2.81−2.67 (m, 4H), 2.44 (s, 3H), 1.98−1.95 (m, 1H), 1.86−1.81 (m, 1H), 0.32 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.4, 143.6, 134.1, 129.9, 127.7, 111.2, 79.1(2), 59.1, 47.3, 37.3, 35.1, 21.6, 1.1; LRMS (ESI-TOF) m/z (relative intensity) 608.0 (100%, M − OMe^-); HRMS (ESI-TOF) m/z: [M − OMe^-]; calcd for $C_{22}H_{24}Co_2NO_8SSi$ 607.9656, found 607.9659.

*N-(3-Methoxy-5-(trimethylsilyl)pent-4-yn-1-yl)-N-methyl-4-nitrobenzenesulfonamide Dicobalt Hexacarbonyl Complex (**28b**).* Following General Procedure 6, alkyne **27b** (7.44 g, 19.4 mmol) was converted to cobalt complex **28b**. The residue was purified through trituration with hexanes to give cobalt complex **28b** (12.01 g, 93%) as a red solid. mp 95−97 °C; IR (thin film) 2086, 1990, 1524 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.38 (d, J = 8.6 Hz, 2H), 7.99

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(d, J = 8.6 Hz, 2H), 4.45 (ad, J = 10.0 Hz, 1H), 3.83−3.64 (m, 1H), 3.53 (s, 3H), 2.99−2.88 (m, 1H), 2.82 (s, 3H), 2.04−1.97 (m, 1H), 1.87−1.82 (m, 1H), 0.32 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.3, 150.2, 143.3, 128.7, 124.6, 110.5, 79.1, 78.9, 59.0, 47.3, 37.1, 35.0, 1.1; LRMS (ESI-TOF) m/z (relative intensity) 692.9 (38%, M + Na^+); HRMS (ESI-TOF) m/z: [M + Na^+]; calcd for $C_{22}H_{24}Co_2N_2O_{11}SSiNa$ 692.9432, found 692.9409.

*N-((3S,4S)-6-Bromo-4-(4R,5S)-4-methyl-2-oxo-5-phenyloxazolidine-3-carbonyl)-3-((trimethylsilyl)ethynyl)hexyl)-N,4-dimethylbenzenesulfonamide (**30a**).* Following General Procedure 7, oxazolidinone **15** (1.54 g, 4.73 mmol) in toluene and cobalt complex **28a** (1.51 g, 2.37 mmol) in toluene were stirred at −78 °C for 10 min before warming the solution to 0 °C. The resulting crude oil was converted to Nicholas product **30a** following General Procedure 8. Purification of the resulting yellow residue by SiO_2 flash column chromatography (100% hexanes to 10% Et_2O in hexanes) gave Nicholas adduct **30a** (0.91 g, 60%) as a white solid. $[\alpha]_D^{20}$ = −2.8 (c = 0.05, $CHCl_3$); mp 65−69 °C; IR (thin film) 2168, 1778, 1694 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, J = 8.2 Hz, 2H), 7.44−7.35 (m, 3H), 7.33−7.30 (m, 4H), 5.68 (d, J = 7.3 Hz, 1H), 4.81 (p, J = 6.8 Hz, 1H), 4.23 (d, J = 7.2 Hz, 2H), 3.45−3.42 (m, 1H), 3.38−3.34 (m, 1H), 3.15 (t, J = 7.2 Hz, 2H), 2.74 (s, 3H), 2.42−2.34 (m, 4H), 2.28−2.21 (m, 1H), 1.85−1.81 (m, 1H), 1.65−1.60 (m, 1H), 0.93 (d, J = 5.4 Hz, 3H), 0.11 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 152.8, 143.3, 134.5, 133.2, 129.7, 128.9, 128.8, 127.6, 125.8, 104.5, 89.9, 79.1, 55.1, 48.3, 45.1, 35.4, 32.9, 32.5, 31.2, 31.1, 21.6, 14.7, 0.1; LRMS (ESI-TOF) m/z (relative intensity) 647.1 (38%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{30}H_{40}N_2O_5SSiBr$ 647.1611, found 647.1639.

*N,4-Dimethyl-N-(5-(trimethylsilyl)pent-2-en-4-yn-1-yl)benzenesulfonamide (**31a**).* Following General Procedure 7, oxazolidinone **15** (0.05 g, 0.2 mmol) in toluene and cobalt complex **28a** (0.05 g, 0.08 mmol) in toluene were stirred at −78 °C for 10 min before warming to room temperature. The resulting crude oil was converted to the enyne **31a** following General Procedure 8. Purification of the resulting residue by SiO_2 flash column chromatography (100% hexanes to 10% Et_2O in hexanes) gave enyne **31a** (0.04 g, 90%) as a yellow oil. IR (thin film) cm^{-1} 2135, 1597; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.2 Hz, 2H), 6.02 (dt, J = 15.9, 6.3 Hz, 1H), 5.63 (d, J = 15.9 Hz, 1H), 3.63 (d, J = 6.3 Hz, 2H), 2.64 (s, 3H), 2.41 (s, 3H), 0.28 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 138.3, 134.2, 129.8, 127.5, 113.8, 102.3, 95.9, 52.0, 34.6, 21.6, −0.1; LRMS (ESI-TOF) m/z (relative intensity) 322.0 (59%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{16}H_{24}NO_2SSi$ 322.1297, found 322.1308.

*N-4-Dimethyl-N-((S)-3-((S)-2-oxotetrahydrofuran-3-yl)-5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide (**32a**).* Following General Procedure 9, alkyne **30a** (0.05 g, 0.08 mmol), $LiOH·H_2O$, and 30% H_2O_2 were kept at 0 °C for 2 h before the addition of Na_2SO_3. Purification of the residue by SiO_2 flash column chromatography (20% EtOAc in hexanes) gave lactone **32a** (12 mg, 40%) as a white solid, and some starting material **30a** was recovered (6.8 mg, 6%). $[\alpha]_D^{20}$ = −35.4 (c = 0.05, $CHCl_3$); mp 61−63 °C; IR (thin film) 2166, 1761 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 4.40 (td, J = 8.7, 4.3 Hz, 1H), 4.23 (q, J = 8.0 Hz, 1H), 3.28−3.23 (m, 1H), 3.02−2.84 (m, 3H), 2.71 (s, 3H), 2.46−2.42 (m, 1H), 2.43 (s, 3H), 2.31−2.25 (m, 1H), 2.95 (q, J = 6.8 Hz, 2H), 0.14 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.0, 143.6, 134.1, 129.8, 127.6, 105.3, 88.2, 66.9, 48.3, 41.8, 35.3, 30.9, 29.5, 26.6, 21.6, 0.1; LRMS (ESI-TOF) m/z (relative intensity) 408.1 (88%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{20}H_{30}NO_4SSi$ 408.1665, found 408.1668.

*N-((3S,4S)-6-Bromo-4-((4R,5S)-4-methyl-2-oxo-5-phenyloxazolidinine-3-carbonyl)-3-((trimethylsilyl)ethynyl)hexyl)-N-methyl-4-nitrobenzenesulfonamide (**30b**) and N-((3R,4S)-6-Bromo-4-((4R,5S)-4-methyl-2-oxo-5-phenyloxazolidinine-3-carbonyl)-3-((trimethylsilyl)ethynyl)hexyl)-N-methyl-4-nitrobenzenesulfonamide (**30c**).* Following General Procedure 7, oxazolidinone **15** (5.85 g, 17.9 mmol) in toluene and cobalt complex **28b** (6.00 g, 8.96 mmol) in toluene were stirred at −78 °C for 10 min before warming to 0 °C. The resulting crude oil was converted to Nicholas adducts **30b** and **30c** following General Procedure 8. Purification of the residue by SiO_2 flash column chromatography (10% Et_2O in hexanes) gave Nicholas adduct **30b** (3.94 g, 64%) as a yellow foam and Nicholas adduct **30c** (0.56 g, 9%) as a yellow foam.

30b: $[\alpha]_D^{20}$ = +5.9 (c = 0.01, CH_3Cl); mp 59−60 °C; IR (thin film) 2168, 1778, 1693, 1530 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 8.8 Hz, 2H), 7.98 (d, J = 8.7 Hz, 2H), 7.45−7.36 (m, 3H), 7.30 (d, J = 7.0 Hz, 2H), 5.69 (d, J = 7.2 Hz, 1H), 4.82 (p, J = 6.8 Hz, 1H), 4.28−4.23 (m, 1H), 3.47−3.43 (m, 1H), 3.38−3.33 (m, 1H), 3.24 (t, J = 7.2 Hz, 2H), 2.89−2.82 (m, 4H), 2.40−2.35 (m, 1H), 2.22−2.17 (m, 1H), 1.92−1.87 (m, 1H), 1.68−1.59 (m, 1H), 0.88 (d, J = 6.5 Hz, 3H), 0.12 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 152.5, 150.0, 143.4, 133.1, 128.8, 128.7, 128.5, 125.6, 124.4, 104.8, 89.1, 78.8, 55.0, 48.5, 44.6, 35.7, 32.4, 32.1, 30.7, 29.9, 14.6, 13.9, −0.05; LRMS (ESI-TOF) m/z (relative intensity) 695.2 (95%, M + NH_4^+); HRMS (ESI-TOF) m/z: [M + NH_4^+] calcd for $C_{29}H_{40}N_4O_7BrSSi$ 695.1570, found 695.1572.

30c: $[\alpha]_D^{20}$ = +34.2 (c = 0.02, CH_3Cl); mp 50−52 °C; IR (thin film) 1777, 1699, 1530 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.38 (d, J = 8.6 Hz, 2H), 8.00 (d, J = 8.6 Hz, 2H), 7.37−7.44 (m, 3H), 7.31 (d, J = 6.8 Hz, 2H), 5.71 (d, J = 7.3 Hz, 1H), 4.82 (p, J = 6.8 Hz, 1H), 4.09−4.03 (m, 1H), 3.54−3.51 (m, 1H), 3.41 (q, J = 6.8 Hz, 1H), 3.36−3.18 (m, 2H), 2.98 (q, J = 6.7 Hz, 1H), 2.81 (s, 3H), 2.52−2.47 (m, 1H). 2.28−2.22 (m, 1H), 1.93−1.73 (m, 2H), 0.91 (d, J = 6.5 Hz, 3H), 0.13 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) 172.8, 153.0, 150.1, 143.8, 133.1, 129.0, 128.9, 128.7, 125.8, 124.5, 104.1, 90.2, 79.2, 55.3, 48.3, 45.0, 35.3, 32.8, 32.6, 31.2, 31.1,14.6, 0.1; LRMS (ESI-TOF) m/z (relative intensity) 695.1 (95%, M + NH_4^+); HRMS (ESI-TOF) m/z: [M + NH_4^+] calcd for $C_{29}H_{40}N_4O_7BrSSi$ 695.1570, found 695.1572.

*N-Methyl-4-nitro-N-((S)-3-((S)-2-oxotetrahydrofuran-3-yl)-5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide (**32b**).* Following General Procedure 9, CsOH and H_2O_2 were added to alkyne **30b** (0.16 g, 0.24 mmol) at −5 °C. After 30 min at −5 °C, the solution was warmed to room temperature. After 30 min at room temperature, Na_2SO_3 was added. The mixture was acidified to pH 1 with 1 N phosphoric acid and extracted with EtOAc. Purification of the residue by SiO_2 flash column chromatography (20% EtOAc in hexanes) gave lactone **32b** (52 mg, 50%) as a light yellow solid. $[\alpha]_D^{20}$ = −35.9 (c = 0.04, CH_3Cl); mp 105−107 °C; IR (thin film) 2170, 1748, 1530 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.37 (d, J = 8.6 Hz, 2H), 7.97 (d, J = 8.6 Hz, 2H), 4.39 (td, J = 8.8, 4.0 Hz, 1H), 4.23 (q, J = 8.2 Hz, 1H), 3.29−3.26 (m, 1H), 3.17−3.13 (m, 1H), 2.93−2.78 (m, 5H), 2.47−2.43 (m, 1H), 2.29−2.25 (m, 1H), 1.99−1.88 (m, 2H), 0.14 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.7, 150.1, 143.4, 128.6, 124.5, 104.8, 88.6, 66.8, 48.4, 42.2, 35.1, 30.7, 29.4, 26.3, 0.0; LRMS (ESI-TOF) m/z (relative intensity) 439.2 (10%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{19}H_{27}N_2O_6SSi$ 439.1359, found 439.1351.

*(3S,4S)-3-(2-((tert-Butyldimethylsilyl)oxy)ethyl)-1-methyl-4-((trimethylsilyl)ethynyl)piperidin-2-one (**34**).* A solution of lactone **32b** (0.15 g, 0.34 mmol) and NaSPh (0.09 g, 0.7 mmol) in 3.4 mL of DMF was heated to 90 °C. After 1 h at 90 °C, the solution was cooled to room temperature, diluted with H_2O (10 mL), and extracted with EtOAc (3 × 5 mL). The organic layers were combined and washed with H_2O (2 × 5 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude alcohol product (labeled **S3** in the Supporting Information). Imidazole (0.05 g, 0.7 mmol) was added to this crude alcohol in DMF (3.4 mL) at 0 °C. After 10 min, TBSCl (0.06 g, 0.4 mmol) was added at 0 °C. After 5 min, the reaction mixture was warmed to room temperature and stirred for 1 h. The solution was diluted with H_2O (10 mL) and extracted with EtOAc (3 × 5 mL). The organic layers were combined and washed with H_2O (2 × 5 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by SiO_2 flash column chromatography (10−20% EtOAc in hexanes) gave lactam **34** (0.08 g, 65%) as a yellow oil. $[\alpha]_D^{20}$ = +57.8 (c = 0.05, MeOH); IR (thin film) 2167, 1646 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.76−3.70 (m, 2H), 3.59 (td, J = 11.4, 5.5 Hz, 1H), 3.25−3.15 (m, 1H), 3.03 (q, J = 5.1 Hz, 1H), 2.88 (s, 3H), 2.51−2.44 (m, 1H), 2.35−2.25 (m, 1H), 1.98−1.90 (m, 2H), 1.75−1.67 (m, 1H), 0.85 (s, 9H), 0.09 (s, 9H), 0.01 (s, 6H); ^{13}C NMR

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(75 MHz, $CDCl_3$) δ 171.1, 104.8, 88.5, 61.0, 46.8, 41.5, 34.8, 31.7, 29.6, 27.4, 26.0, 18.3, 0.1, −5.2, −5.3; LRMS (ESI-OF) m/z (relative intensity) 368.2 (100%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{19}H_{38}NO_2Si_2$ 368.2441, found 368.2464.

*(3S,4S)-3-(2-((tert-Butyldimethylsilyl)oxy)ethyl)-4-ethynyl-1-methylpiperidin-2-one (**12**).* To lactam **34** (0.14 g, 0.38 mmol) in MeOH (4 mL) was added K_2CO_3 (0.16 g, 1.1 mmol). After stirring for 1 h, the mixture was diluted with H_2O (5 mL) and extracted with EtOAc (3 × 5 mL). The organic layers were combined, dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by SiO_2 flash column chromatography with the indicated eluent. Purification of the residue by SiO_2 flash column chromatography (30% EtOAc in hexanes) gave **12** (0.11 g, 95%) as a yellow oil. $[\alpha]_D^{20}$ = +45.8 (c = 0.08, MeOH); IR (thin film) 3230, 1716, 1643; cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.74−3.63 (m, 2H), 3.60 (td, J = 11.6, 5.5 Hz, 1H), 3.22−3.10 (m, 1H), 3.09−2.98 (m, 1H), 2.86 (s, 3H), 2.60−2.49 (m, 1H), 2.44−2.34 (m, 1H), 2.05 (d, J = 2.4 Hz, 1H), 1.98−1.90 (m, 2H), 1.66 (m, 1H), 0.81 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 82.2, 72.0, 60.8, 46.6, 41.1, 34.8, 31.5, 28.4, 27.2, 25.9, 18.2, −5.3, −5.4; LRMS (ESI-TOF) m/z (relative intensity) 296.2 (100%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{16}H_{30}NO_2Si$ 296.2046, found 296.2062.

*1-(2-Azidophenyl)-3-((3S,4S)-3-((tert-butyldimethylsilyl)oxy)-ethyl)-1-methyl-2-oxopiperidin-4-yl)prop-2-yn-1-yl Ethyl Carbonate (**35**).* 2.5 M n-BuLi in hexanes (0.13 mL, 0.32 mmol) was added to alkyne **12** (0.10 g, 0.32 mmol) in THF (4.6 mL) at −78 °C. After 1 h, 2-azidobenzaldehyde (52 mg, 0.35 mmol) in THF (1.2 mL) was added dropwise, and the solution was warmed to 0 °C. Ethyl chloroformate (33 μL, 0.35 mmol) was added 2.5 h later, and the reaction mixture was allowed to warm to room temperature. Upon consumption of the intermediate alcohol (determined by TLC), the reaction was diluted with saturated NH_4Cl solution (15 mL) and extracted with Et_2O (3 × 10 mL). The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by SiO_2 flash column chromatography (20% EtOAc in hexanes) gave azide **35** (0.14 g, 86%) as a yellow oil. $[\alpha]_D^{20}$ = +34.0 (c = 0.13, $CHCl_3$); IR (thin film) 2126, 1749, 1644 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, J = 7.9 Hz, 1H), 7.36 (t, J = 7.6 Hz, 1H), 7.15−7.11 (m, 2H), 6.45 (s, 1H), 4.19 (q, J = 7.0 Hz, 2H) 3.76−3.68 (m, 2H), 3.65−3.53 (m, 1H), 3.21−3.13 (m, 2H), 2.88−2.86 (m, 3H), 2.68−2.50 (m, 1H), 2.42−2.31 (m, 1H), 2.04−1.93 (m, 2H), 1.78−1.62 (m, 1H), 1.28 (t, J = 7.1 Hz, 3H), 0,84 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 154.0, 137.9, 130.6, 129.4, 129.2, 127.5, 125.0, 118.3, 87.0, 79.5, 64.5, 60.9, 46.7, 41.4, 34.8, 31.7, 28.9, 27.2, 25.9, 18.2, 14.3, −5.2, −5.3; LRMS (ESI-TOF) m/z (relative intensity) 515.2 (100%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{26}H_{39}N_4O_5Si$ 515.2690, found 515.2667.

*(3S,4S)-4-(4-(2-Azidophenyl)-3λ^5-buta-2,3-dien-2-yl)-3-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1-1-methylpiperidin-2-one (**43**).* 3 M methylmagnesium bromide in Et_2O (0.20 mL, 0.60 mmol) was added to copper iodide (0.12 g, 0.60 mmol) and lithium bromide (52 mg, 0.60 mmol) in THF (7 mL) at 0 °C. After stirring for 30 min at room temperature, alkyne **35** (0.03 g, 0.06 mmol) in THF (0.6 mL) was added to the mixture. After 30 min at room temperature, the solution was washed with saturated NH_4Cl solution (3 × 10 mL) and H_2O (3 × 10 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by SiO_2 flash column chromatography (20−30% EtOAc in hexanes) to give azide **43** (23 mg, 87%) as a yellow oil (2:1 mixture of diastereomers). $[\alpha]_D^{20}$ = +39.8 (c = 0.09, CH_3Cl); IR (thin film) 2123, 1716, 1643 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32−7.26 (m, 1H), 7.24−7.19 (m, 1H), 7.12−7.03 (m, 2H), 6.42−6.40 (m, 1H), 3.83−3.76 (m, 2H), 3.29−3.21 (m, 2H), 2.87 (s, 3H, minor isomer), 2.72 (s, 3H, major isomer), 2.98−2.59 (m, 2H), 1.93−1.70 (m, 7H), 0.90−0.79 (m, 9H), 0.08−0.04 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.1, 203.9, 172.4, 172.3, 136.3, 136.2, 128.2, 128.0, 127.9, 126.7, 126.6, 124.9, 124.7, 118.6, 118.5, 103.5, 103.2, 90.3, 89.9, 61.8, 61.7, 48.5, 48.3, 40.7, 40.6, 39.9, 39.4, 34.5, 34.4, 31.7, 31.2, 26.1, 26.0, 24.1, 23.9, 18.4, 18.3, 17.7, 17.5, −5.2(3); LRMS (ESI-TOF) m/z (relative intensity) 441.2 (100%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{24}H_{37}N_4O_2Si$ 441.2686, found 441.2684.

*(3S,4S)-4-(4-(2-Azidophenyl)-3λ^5-buta-2,3-dien-2-yl)-3-(2-hydroxylethyl)-1-methylpiperidin-2-one (**11**).* In a plastic vial, azide **43** (0.03 g, 0.08 mmol) was dissolved in MeCN (1 mL). HF (8 μL, 0.4 mmol) was added, and the mixture was stirred for 1 h at room temperature. The reaction mixture was diluted with H_2O (5 mL) and extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residue by SiO_2 flash column chromatography (20−80% EtOAc in hexanes) gave alcohol **11** (0.02 g, 79%) as a yellow oil (1:1 mixture of diastereomers). $[\alpha]_D^{20}$ = +29.7 (c = 0.04, CH_3Cl); IR (thin film) 3398, 2121, 1620 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40−7.20 (m, 1H), 7.19−7.00 (m, 1H), 7.14−7.04 (m, 2H), 6.42 (q, J = 3.2 Hz, 1H), 4.55 (dd, J = 6.9, 4.8 Hz, 1H), 4.43 (t, J = 6.0 Hz, 1H), 3.79−3.69 (m, 2H), 3.35−3.25 (m, 2H), 2.96−2.93 (m, 2H), 2.85−2.70 (m, 2H), 2.62−2.54 (m, 1H), 2.01−1.62 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.1, 204.0, 173.6, 136.5, 136.4, 128.3, 128.2, 128.1, 128.0, 126.5, 126.4, 125.0, 124.8, 118.7, 103.1, 103.0, 90.7, 90.4, 62.6, 62.4, 49.0, 48.7, 43.2, 42.3, 41.7, 41.3, 34.9, 34.8, 31.1, 30.9, 24.0, 23.7, 17.8, 17.6; LRMS (ESI-TOF) m/z (relative intensity) 327.1 (100%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{18}H_{23}N_4O_2$ 327.1821, found 327.1796.

*(1R,4aS,8aS)-1-(1H-Indol-2-yl)-1,6-dimethylhexahydro-1H-pyrano[4,3-c]pyridine-5(3H)-one (**9**).* **Method A**: Following General Procedure 10, azide **11** (10 mg, 0.031 mmol) in MeCN was brought to 90 °C and held there for 24 h. The residue was purified by SiO_2 flash column chromatography (50−80% EtOAc in hexanes) to give indole **9** (5.7 mg, 63%) as a yellow oil. **Method B**: The allenyl azide **11** (0.10 g, 0.31 mmol) in MeCN (62 mL) was irradiated at 254 nm for 2 h. The residue was concentrated under reduced pressure and purified by SiO_2 flash column chromatography (50−80% EtOAc in hexanes) to give indole **9** (0.09 g, 99%) as a yellow oil. $[\alpha]_D^{20}$ = +22.8 (c = 0.04, CH_3Cl); IR (thin film) 3275, 1626 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.53 (d, J = 7.6 Hz, 1H), 7.35 (d, J = 7.6 Hz, 1H), 7.17 (t, J = 7.1 Hz, 1H), 7.08 (t, J = 6.9 Hz, 1H), 6.37 (s, 1H), 3.85−3.70 (m, 1H), 3.46−3.40 (m, 3H), 3.12−3.00 (m, 1H), 2.97 (s, 3H), 2.57 (d, J = 12.5 Hz, 1H), 2.31−2.10 (m, 1H), 2.09−1.95 (m, 1H), 1.85−1.71 (m, 3H), 1.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 141.0, 136.1, 128.3, 122.1, 120.5, 119.8, 110.8, 100.5, 74.5, 63.2, 49.2, 38.7, 37.1, 34.6, 29.0, 25.2, 18.8; LRMS (ESI-TOF) m/z (relative intensity) 299.2 (100%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{18}H_{23}N_2O_2$ 299.1760, found 299.1747.

*(3S,4S)-4-(1H-Indol-2-yl)vinyl)3-(2-((tert-butyldimethylsilyl)oxy)-ethyl)-1-methylpiperidin-2-one (**42**).* Following General Procedure 10, azide **43** (0.21 g, 0.46 mmol) in MeCN was heated to 90 °C and held there for 30 h. The residue was purified by alumina flash column chromatography (100% hexanes to 30% EtOAc in hexanes) to give indole **42** (0.15 mg, 77%) as a light yellow foam. $[\alpha]_D^{20}$ = −21.6 (c = 0.05, CH_3Cl); mp 46−50 °C; IR (thin film) 3280, 1622 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.55 (d, J = 7.8 Hz, 1H), 7.32 (d, J = 8.1 Hz, 1H), 7.18 (t, J = 7.6 Hz, 1H), 7.08 (t, J = 7.4 Hz, 1H), 6.55 (s, 1H), 5.53 (s, 1H), 4.97 (s, 1H), 3.69−3.56 (m, 2H), 3.39−3.33 (m, 3H), 2.94 (s, 3H), 2.90−2.80 (m, 1H), 2.07−2.04 (m, 2H), 2.03−1.90 (m, 1H), 1.80−1.62 (m, 1H), 0.79 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9, 138.7, 137.3, 136.6, 128.7, 122.8, 120.8, 120.0, 110.8, 110.4, 101.0, 61.9, 48.1, 40.8, 39.1, 34.8, 31.1, 26.0, 25.0, 18.3, −5.3; LRMS (ESI-TOF) m/z (relative intensity) 413.1 (100%, M + H^+); HRMS (ESI-TOF) m/z: [M + H^+]; calcd for $C_{24}H_{37}N_2O_2Si$ 413.2624, found 413.2641.

*(1S,5S,13S)-13-(2-((tert-Butyldimethylsilyl)oxy)ethyl)-2-methyl-6-methylene-1,2,3,4,5,6-hexahydro-1,5-methano[1,3]diazocino[1,8-a]indole (**40**) and (1S,5S,12S)-12-(2-((tert-Butyldimethylsilyl)oxy)-ethyl)-2-methyl-6-methylene-2,3,4,5,6,7-hexahydro-1H-1,5-methanodiazocino[4,3-b]indole (**44**).* Lactam **42** (0.09 g, 0.2 mmol) in THF (2 mL) was added to the Schwartz reagent (0.11 g, 0.44 mmol). Once the mixture became clear, it was heated to 70 °C for 14 h. Purification of the residue by alumina flash chromatography (10% EtOAc in hexanes to 100% EtOAc) of the residue gave *N*-cyclized

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product **44** (34 mg, 39%) and *C*-cyclized produce **40** (33 mg, 38%) as yellow oils.

44: $[\alpha]_D^{20}$ = −53.6 (*c* = 0.01, $CHCl_3$); IR (thin film) cm^{-1} 3274, 1768; ^1H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.8 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.19−7.00 (m, 2H), 6.72 (s, 1H), 5.85 (s, 1H), 5.18 (s, 1H), 5.05 (s, 1H), 3.56 (t, *J* = 6.1 Hz, 1H), 2.77 (m, 1H), 2.54−2.47 (m, 2H), 2.34 (s, 3H), 2.22−2.12 (m, 3H), 1.85−1.75 (m, 1H), 1.25−1.17 (m, 2H), 0.87 (s, 9H), 0.0 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 128.1, 121.6, 120.4, 199.9, 111.3, 110.1, 95.7, 70.9, 61.7, 46.0, 44.3, 39.2, 38.6, 34.9, 33.6, 26.1, 18.4, 1.13, −5.3; LRMS (ESI-TOF) *m*/*z* (relative intensity) 397.1 (100%, M + H^+); HRMS (ESI-TOF) *m*/*z*: [M + H^+]; calcd for $C_{24}H_{37}N_2OSi$ 397.2675, found 397.2667.

40: $[\alpha]_D^{20}$ = +45.5 (*c* = 0.01, $CHCl_3$); IR (thin film) cm^{-1} 3227, 1611; ^1H NMR (300 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.15 (td, *J* = 7.5, 1.1 Hz, 1H), 7.10 (td, *J* = 6.9, 1.0 Hz, 1H), 5.17 (s, 1H), 4.93 (s, 1H), 3.97 (s, 1H), 3.77 (t, *J* = 6.2 Hz, 1H), 2.69−2.59 (m, 1H), 2.50−2.45 (m, 1H), 2.29−2.16 (m, 7H), 2.11−1.88 (m, 2H), 1.40 (d, *J* = 13.0 Hz, 1H), 0.87 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.2, 136.6, 135.9, 128.7, 122.8, 120.0, 119.8, 110.9, 104.6, 62.0, 55.8, 46.5, 45.0, 39.7, 38.9, 34.0, 28.9, 26.1, 25.9, 18.5, −5.2; LRMS (ESI-TOF) *m*/*z* (relative intensity) 397.2 (100%, M + H^+); HRMS (ESI-TOF) *m*/*z*: [M + H^+]; calcd for $C_{24}H_{37}N_2OSi$ 397.2675, found 397.2656.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00348.

General methods; copies of ^1H spectra for **17** and **18**; ^1H NMR and ^{13}C NMR spectra for **9**, **11**, **12**, **15**, **19**−**22**, **23a**/**b**−**28a**/**b**, **30a**/**b**−**32a**/**b**, **30c**, **34**, **35**, **40**, **42**−**44**; and HMBC, HSQC, COSY, NOESY of **9** and **12** (PDF)

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Notes

The authors declare no competing financial interest.

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