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# Synthetic Studies in the Intramolecular Carbocyclization of *N*-Acyloxyiminium Ions. Stereoelectronic and Steric Implications of Nucleophilic Alkene, Alkyne, and Allene Tethers

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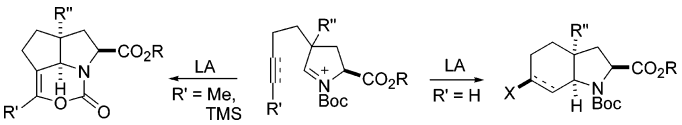


*N*-Acyloxyiminium ions generated from 4-substituted L-pyroglutamic esters with 4-(3-butenyl), 4-(3-butynyl), 4-(3-cinnamylmethyl), and 4-allenic tethers undergo rapid Lewis acid mediated carbocyclization to give stereodefined azacyclic compounds depending on the nature of the nucleophilic tether. In general, reactions of alkenes and alkynes with terminal alkyl or aryl substituents, as well as allenes, proceed through transient vinylic carbocations that are attacked internally by the *N*-Boc group to give tricyclic dihydrooxazinones. Diastereotopic bis-4-(3-butenyl) and 4-(3-butynyl) tethers undergo stereochemically controlled attack favoring an antiperiplanar rather than synclinal approach to give enantiopure 6-halo octahydroindole-2-carboxylic acids and 6-halo hexahydroindole-2-carboxylic acids as their methyl esters, respectively. The aza bicyclic and tricyclic compounds are excellent scaffolds for diversification.

## Introduction

Cyclization reactions involving *N*-acyloxyiminium ions harboring *N*- or *C*-functionalized tethers have been the cornerstone of many strategies for the synthesis of azacyclic ring systems.[1] Among these are ubiquitous natural products belonging to indolizidine and quinolizidine classes, for example.[2] Traditionally, alkenyl and alkynyl tethers attached to the nitrogen atom as part of the *N*-acyliminium group have been cyclized in the presence of protic or Lewis acids. Such *endo* cyclizations from alkenes can incorporate an external nucleophile such as formate or halide, arising from the capture of carbocationic intermediates by formic acid or Lewis acid, respectively.[3,4] In the case of *N*-tethered alkenes and alkynes, cyclization requires that the precursors be derived from the corresponding imides, which are partially reduced to the carbinollactams, then transformed

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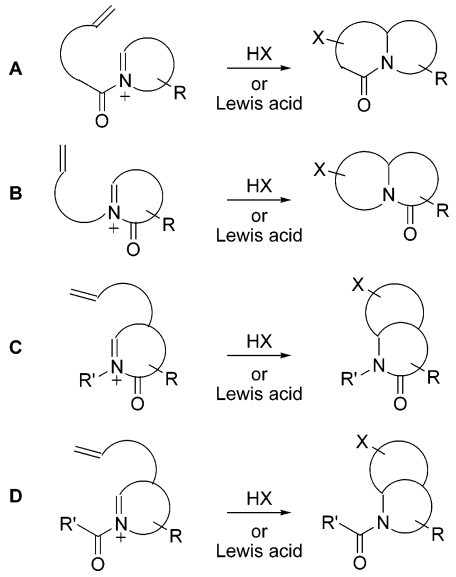
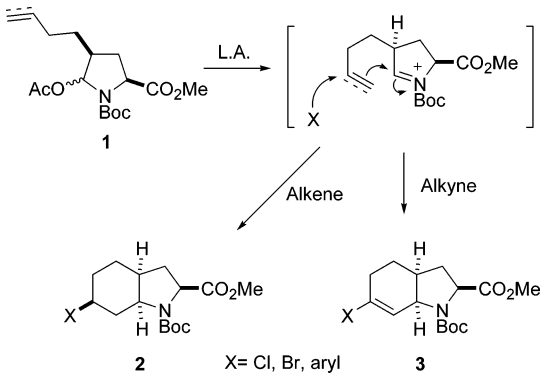



**FIGURE 1.** Intramolecular carbocyclization of *N*-tethered (A, B), and *C*-tethered (C, D) *N*-acyliminium ions.

to reactive iminium ions.[5] In the above cases, carbocyclizations lead to azabicyclics with nitrogen at the junction of the two rings, as shown in Figure 1, A and B. In contrast, there are fewer examples of carbocyclizations in which the alkenyl and alkynyl tether is attached to a distal carbon in the *N*-acyliminium ion motif.[6] Such cyclizations would lead to azabicyclics in which the nitrogen is part of one of the two rings (Figure 1, C and D). In the case of C, the products are *N*-alkyl lactams,[1] whereas D represents a novel class related to *N*-acyl hydroindoles and hydroquinolines.[7] In a different context, *N*-tethered alkenes have also been involved in azonia-

**SCHEME 1**




Cope cyclizations[8] via suitably activated iminium ions leading to azacyclic products.

In a previous publication connected with the total synthesis and structural confirmation of the antithrombotic marine metabolite oscillarin, we reported on a highly stereoselective aza(azonia)-Prins-type halocarbocyclization leading to 6-halo octahydroindole-2-carboxylic acids.[7] Thus, a stereodefined 4-butenyl tether, as in the readily available precursor **1**, could be easily transformed into the 6-halo bicyclic adduct **2** (X = Br, Cl) in the presence of the appropriate tin tetrahalide at −78 °C within a few minutes (Scheme 1). Subsequent studies[9] were extended to 4-butynyl tethers which led to the endocyclic vinyl halide **3** (X = Br, Cl). The utility of these facile carbocyclizations of unactivated terminal alkenes and alkynes was further manifested by a tandem Friedel−Crafts-type capture of $sp^2$ and $sp^3$ hybridized carbocations in aromatic hydrocarbons as solvents to give 6-aryl octahydro- and hexahydro-2-carboxylic acid derivatives (**2** and **3**, X = aryl).[9]

The stereochemical outcome of these cyclizations can be rationalized based on a favorable antiperiplanar attack[3e,7,10] of the nucleophilic unsaturated terminus as in the chairlike[11] *N*-acyloxyiminium ion conformer A, which would allow good orbital overlap (Figure 2).[12] A synclinal attack as depicted in B would be less favored, especially because $A^{1,2}$ strain[13] dictates the pseudoaxial orientation of the ester group, resulting in a steric clash

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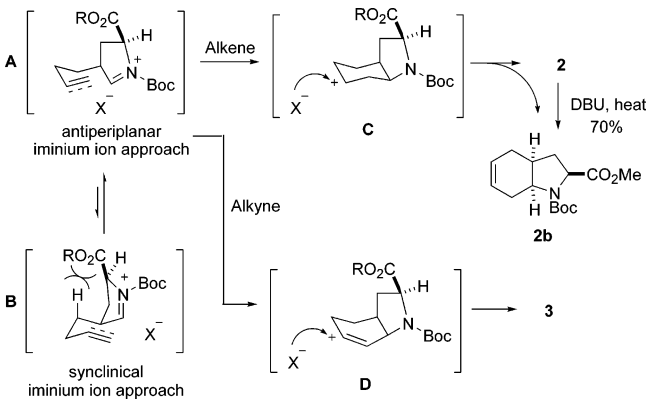



**FIGURE 2.** Proposed reactive intermediates in the *N*-acyloxyiminium ion azonia-Prins halocarbocyclization to octahydroindoles and hexahydroindoles.

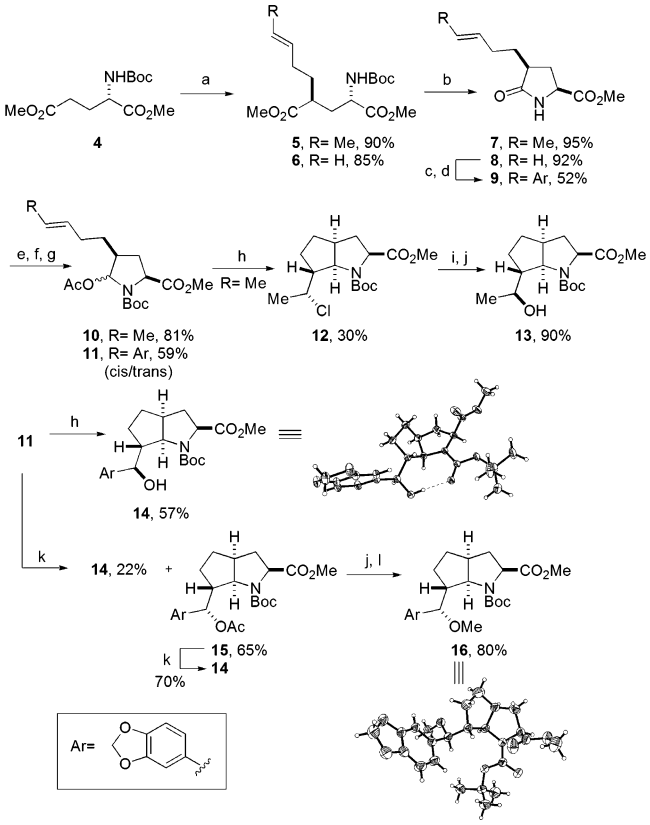
with the tether. It is difficult to propose an exact mechanistic pathway for the stereocontrolled incorporation of a halogen (or other nucleophile).[9] The carbocyclization reaction may in fact be asynchronous with the formation of a secondary carbocation C, which may be attacked by a nucleophile in an equatorial mode to give the observed product (Scheme 1, **2**: X = Cl, Br, aryl). Indirect evidence for this hypothesis comes from the fact that in the case of less nucleophilic aryls, such as halobenzenes, substantial amounts of 5,6-alkene **2b** could be identified.[9] The latter, an important intermediate for the synthesis of the marine natural product dysinosin A,[14] could also be prepared by treatment of **2** (X = Br) in neat DBU. The conversion of 4-butynyl analogues to the corresponding 6-halo hexahydroindoles[9] can occur through the intermediacy of cyclic vinyl cation D for which there are many examples in the case of solvolytic reactions.[15]

We report herein the extension of such carbocyclizations of *C*-tethered *N*-acyloxyiminium ions with substituted alkene, alkyne, and allene tethers to give novel azacyclic ring systems. The combination of stereoelectronic, steric, and A[1,2] strain effects will be the underlying mechanistic principles of these carbocyclization reactions.

## Results

Since the olefinic 4-(3-butenyl) or 4-(3-butynyl) tethers act as internal nucleophiles, it was of interest to study the effect of a terminal substituent on the course of carbocyclization. The readily available protected glutamate derivative **4**[16,17] was transformed into the corresponding

**SCHEME 2**[a]




[a] Reagents and conditions: (a) LiHMDS, THF, −78 °C, then $RCHCHCH_2CH_2OTf$; (b) TFA, $CH_2Cl_2$, then toluene reflux; (c) $OsCl_3$, $NaIO_4$, $THF/H_2O$; (d) LiHMDS, $ArCH_2PPh_3Br$, THF, −78 °C, then **8**; (e) $Boc_2O$, $Et_3N$, DMAP, $CH_2Cl_2$; (f) $LiBHEt_3$, THF, −78 °C; (g) $Ac_2O$, $Et_3N$, DMAP, $CH_2Cl_2$; (h) $SnCl_4$, $CH_2Cl_2$, −78 °C; (i) $Bu_4NOAc$, toluene; (j) NaOMe, MeOH; (k) $BF_3OEt_2$, $CH_2Cl_2$, −78 °C; (l) NaH, MeI, THF.

dianion, and the latter was alkylated with *trans*-3-pentenyl-1-ol triflate to give the anti-product **5** in high yield (Scheme 2).[7,18] An identical sequence led to the 4-(3-butenyl) analogue **6**. Application of the same protocol in the case of the (3,4-methylenedioxy)benzyl variant was unsuccessful because of the instability of the corresponding triflate. Therefore, a two-step procedure was used (Scheme 2). Cleavage of the *N*-Boc group in **5** and **6**,

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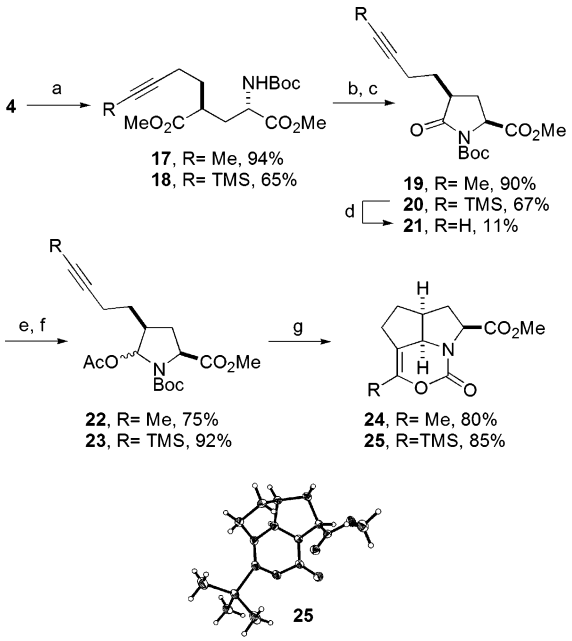
**SCHEME 3**[a]

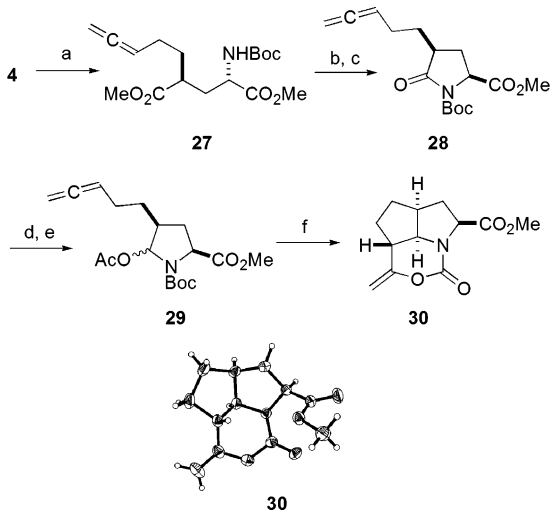



[a] Reagents and conditions: (a) LiHMDS, THF, −78 °C, then $RCCCH_2CH_2OTf$; (b) TFA, $CH_2Cl_2$, then toluene reflux; (c) $Boc_2O$, $Et_3N$, DMAP, $CH_2Cl_2$; (d) TBAF, THF, quant.; (e) $LiBHEt_3$, THF, −78 °C; (f) $Ac_2O$, $Et_3N$, DMAP, $CH_2Cl_2$; (g) $SnCl_4$, $CH_2Cl_2$, −78 °C.

followed by lactam formation afforded **7** and **8**, respectively. Osmium trichloride/$NaIO_4$ oxidative cleavage of the terminal olefin **8**, followed by Wittig olefination gave the 3,4-methylenedioxy analogue **9** in 52% overall yield as a cis/trans mixture. Since the stereochemistry of the olefin in **9** had no effect on the course of the final cyclization, the mixture was used as such. Protection of the nitrogen in lactams **7** and **9** with Boc anhydride, followed by reduction of the carbonyl moiety with Superhydride and acetylation gave **10** and **11**, respectively. Treatment of **10** with $SnCl_4$ in $CH_2Cl_2$ at −78 °C led to the chloro 1-aza-[3.3.0]bicyclooctane-2-carboxylic acid analogue **12** in a modest yield of 30%, accompanied by a significant amount of ene-carbamate elimination product (not shown). Displacement of the chlorine with tetrabutylammonium acetate, followed by sodium methoxide treatment gave the alcohol **13**. The stereochemistry of the latter was confirmed by detailed nOe studies. The same reaction of **11** with $SnCl_4$ in $CH_2Cl_2$ at −78 °C led to the crystalline hydroxy analogue **14** in 57% yield. Its structure and absolute configuration were ascertained from a single-crystal X-ray analysis (Scheme 2). Surprisingly, in the presence of $BF_3OEt_2$ as Lewis acid, the products were the acetate **15** (65%) along with the alcohol **14** (22%). Treatment of **15** with $BF_3OEt_2$ and quenching with aqueous $NH_4Cl$ or $NaHCO_3$, as in the case of **11**, gave **14** in high yield. The absolute configuration of **15** was confirmed by a single-crystal X-ray analysis of **16**, easily obtained from **15** by deacetylation with sodium methoxide, followed by methylation with MeI.

Alkylation of the dianion of protected glutamate derivative **4** with pent-3-yn-1-ol triflate and 4-(trimethylsilyl)but-3-yn-1-ol triflate gave **17** and **18**, respectively (Scheme 3). Cleavage of the *N*-Boc group in **17** with TFA, followed by lactamization and *N*-protection of the lactam led to **19** in excellent overall yield. Application of the same protocol to **18** resulted in the formation of the protected lactam **20** and a minor amount of **21**, obtained due to the partial cleavage of the TMS on the terminal position during the acidic treatment. The lactam **21** can be obtained in a quantitative yield when **20** is treated with TBAF. Partial reduction of the lactam function in **19** and **20**, followed by acetylation resulted in the formation of the carbinolamines **22** and **23**, respectively. Application of the same cyclization protocol in the presence of $SnCl_4$ led to the corresponding tricyclic dihydrooxazinone derivatives **24** and **25** (X-ray) in excellent yields (Scheme 3).

**SCHEME 4**[a]




[a] Reagents and conditions: (a) LiHMDS, THF, −78 °C, then $CH_2CCHCH_2CH_2OTf$, 77%; (b) TFA, $CH_2Cl_2$, then toluene reflux; (c) $Boc_2O$, $Et_3N$, DMAP, $CH_2Cl_2$, 84% (2 steps); (d) $LiBHEt_3$, THF, −78 °C; (e) $Ac_2O$, $Et_3N$, DMAP, $CH_2Cl_2$, 81% (2 steps); (f) $SnCl_4$, $CH_2Cl_2$, −78 °C, 45%.

A similar reactivity was observed when we studied the cyclization of a 4-(3-allenyl) analogue. Alkylation of the dianion of **4** with the triflate of penta-3,4-dien-1-ol, readily available from the corresponding alkyne by using the Crabbé homologation,[19] afforded **27** in high yield (Scheme 4). Lactamization, followed by reduction of the carbonyl and acetylation gave the hemiaminal acetate derivative **29**. Treatment of the latter with $SnCl_4$ afforded the tricyclic tetrahydrooxazinone **30**, whose structure and stereochemistry were confirmed from a single-crystal X-ray analysis. Thus, the nature of the olefinic tether had a profound influence on the stereochemical and structural outcome of the carbocyclizations from essentially the same *N*-acyloxyiminium ion precursor.

We next studied the cyclization of 4,4′-bis(3-alkenyl and alkynyl) tethers, with the expectation that selective carbocyclization would occur from one of the two diastereotopically deployed precursors. Bis-alkylation of **31** and **32** with 3-buten-1-ol triflate afforded compounds **33** and **34**, respectively, in reasonable yields (Scheme 5). Similarly, alkylation of **31** and **32** with 4-(trimethylsilyl)-

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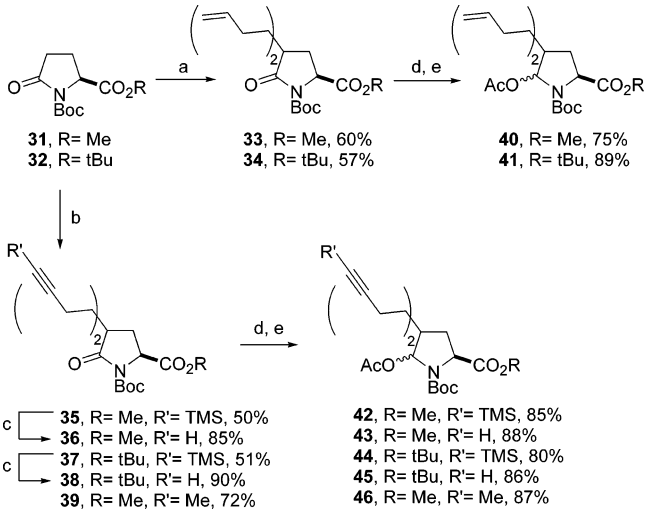
**SCHEME 5**[a]



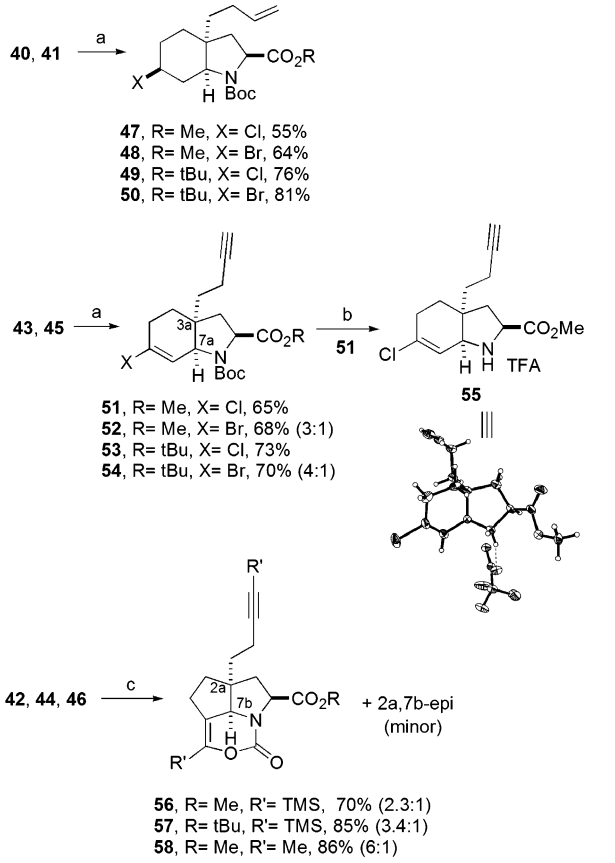

[a] Reagents and conditions: (a) LiHMDS, THF, −78 °C, then 3-butenol-OTf (two times); (b) LiHMDS, THF, −78 °C, then $R'CCCH_2CH_2OTf$ (two times); (c) TBAF, THF; (d) $LiBHEt_3$, THF, −78 °C; (e) $Ac_2O$, $Et_3N$, DMAP, $CH_2Cl_2$.

but-3-yn-1-ol triflate afforded the lactams **35** and **37**, respectively, which were transformed into **36** and **38** by treatment with TBAF. The lactam **39** could also be prepared by using the same double alkylation protocol from **31** in a good yield with 3-pentynyl-1-ol triflate. Finally, pro-diastereomeric bis-alkylated lactams **33**−**39** were partially reduced with Super-hydride, and acetylated to give the *O*-acyl hemiaminal derivatives **40**−**46** in very good yields.

Treatment of the bis-alkenyl hemiaminal **40** with $SnX_4$ (X = Cl, Br), resulted in a rapid halocarbocyclization to give **47** and **48**, respectively, as major isomers in which a new quaternary stereogenic center was formed (Scheme 6). In comparaison, the *tert*-butyl ester analogue **41** afforded the 6-halooctahydroindoles **49** and **50** in improved yields as single isomers. The results were somewhat different when the cyclization was tried with the bis-alkynyl derivatives **43** and **45**. Treatment of these with $SnCl_4$ afforded **51** and **53** respectively as single diastereoisomers. Cleavage of the *N*-Boc group from **51** gave X-ray quality crystals of the trifluoroacetate salt **55**. On the other hand, treatment of **41** and **45** with $SnBr_4$ afforded inseparable diastereoisomeric mixtures of **52** and **54** in 68% and 70% yield and ratios of 3:1 and 4:1 (minor isomer is the corresponding 3a,7a-epi), respectively. Finally, treatment of the hemiaminals **42**, **44**, and **46** with $SnCl_4$ afforded inseparable diastereomeric mixtures of their respective dihydrooxazinones **56**−**58**. The diastereoisomeric ratio was slightly better with the *tert*-butyl ester **57** (6:1 by NMR).

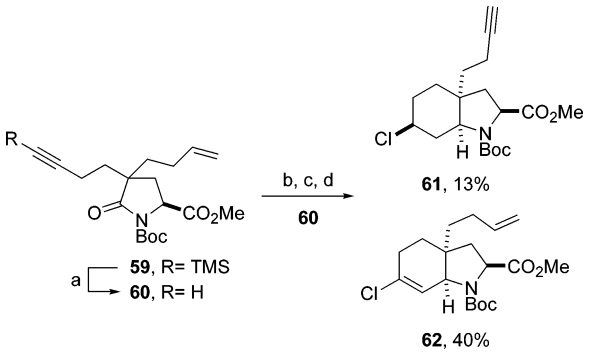
Next, we challenged the system with variations on the nature (and the nucleophilicity) of the tethered subunits. Thus treatment of the diastereomeric 1:1 mixture of 4-(3-butenyl) and 4-(3-butynyl) lactams **60**, readily obtained from **59**, with $SnCl_4$ in $CH_2Cl_2$ at −78 °C afforded **61** (17%) resulting from a chloro azonia-Prins reaction of the alkene,[7] and 50% of the vinylic chloride **62** resulting from the attack of the alkyne onto the *N*-acyloxyiminium (Scheme 7). Thus, cyclization of the 4-(3-butynyl) side

**SCHEME 6**[a]




[a] Reagents and conditions: (a) $SnX_4$, $CH_2Cl_2$, −78 °C; (b) TFA, $CH_2Cl_2$, quant.; (c) $SnCl_4$, $CH_2Cl_2$, −78 °C.

**SCHEME 7**[a]

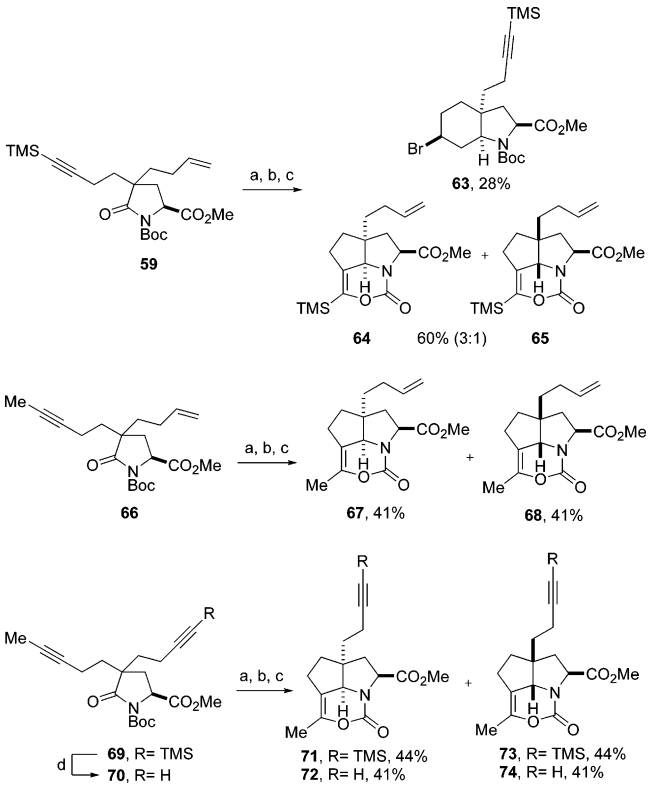



[a] Reagents and conditions: (a) TBAF, THF, 90%; (b) $LiBHEt_3$, THF, −78 °C; (c) $Ac_2O$, $Et_3N$, DMAP, $CH_2Cl_2$; (d) $SnCl_4$, $CH_2Cl_2$, −78 °C.

chain had occurred in preference to the 4-(3-butenyl) counterpart by a ratio of ∼3:1.

Engaging the 4-(3-butenyl) and 4-(4-trimethylsilyl-3-butynyl) tethers in the carbocyclization of **59** (1:1 diastereomeric mixture) resulted in the formation of the bromo azonia-Prins product **63** (28%), accompanied by a 3:1 mixture of the trimethylsilyl dihydrooxazinone analogues **64** and **65**, respectively (Scheme 8). This result was similar to that of **60** inasmuch as there was a competing cyclization in the azonia-Prins mode (compare **61** and **63**). However, the tricyclic dihydrooxazinones were still preferred over the octahydroindole.

**SCHEME 8**[a]



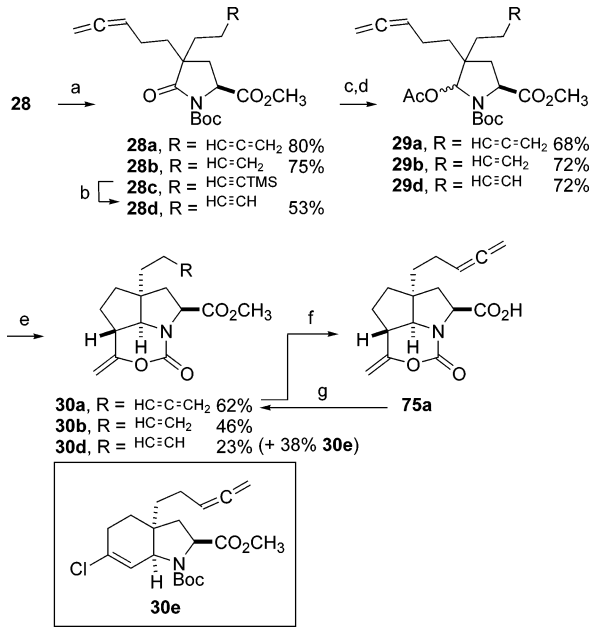

[a] Reagents and conditions: (a) $LiBEt_3H$, THF, −78 °C; (b) $Ac_2O$, $Et_3N$, DMAP, $CH_2Cl_2$ (2 steps, from **59** 87%, from **66** 80%, from **69** 90%, from **70** 90%); (c) $SnBr_4$, $CH_2Cl_2$, −78 °C ($SnCl_4$ from **66**); (d) TBAF, THF, 95%.

This preference was even more pronounced in the case of the 4-(3-pentynyl)/4-(3-butenyl) combination **66**, obtained as a 1:1 mixture of diastereomers (Scheme 8). Treatment with $SnCl_4$ in $CH_2Cl_2$ at −78 °C gave a 1:1 mixture of chromatographically separable tricyclic dihydrooxazinones **67** and **68** in a combined yield of 82%.

Since it was evident that the substituted alkyne tethers led preferentially to dihydrooxazinones rather than to the cyclic vinyl halides, we studied the case of diastereomeric tethers represented in the precursors **69** and **70** (Scheme 8). It was of particular interest to compare the nucleophilicities of 4-(3-butynyl), 4-(3-pentynyl), and 4-(4-trimethylsilyl-3-butynyl) tethers in cyclization reactions. Thus, treatment of acetates derived from **69** and **70**, respectively, led in each case to equimolar amounts of products (**71**−**74**) resulting from cyclization of the 4-(3-pentynyl) side chain exclusively.

Finally, various combinations of allenic and alkene/alkyne tethers led to the diastereomerically enriched hydrooxazinones corresponding to **30a**, **30b**, and **30d** (Scheme 9). In the case of the mixed allene/alkyne tethers **28d**, a 3:1 diastereomeric mixture of the hexahydroindole **30e** was also formed. The allene tether appears to preferentially compete with alkene or alkyne tethers in these carbocyclizations. Treatment of **30a** with aqueous LiOH afforded the corresponding carboxylic acid leaving the cyclic urethane intact. Esterification with trimethylsilyl diazomethane gave the starting ester **30a** in 95% yield.

**SCHEME 9**[a]




[a] Reagents and conditions: (a) LiHMDS, THF, −78 °C, then $RCH_2CH_2OTf$; (b) TBAF, AcOH, THF, (c) $LiBHEt_3$, THF, −78 °C; (d) $Ac_2O$, $Et_3N$, DMAP, $CH_2Cl_2$; (e) $SnCl_4$, $CH_2Cl_2$, −78 °C; (f) 4 equiv of LiOH, $H_2O$/MeOH, 0 °C, 97%; (g) $TMSCHN_2$, $CH_3OH$, PhH, 95%.

## Discussion

As previously mentioned, the novel halocarbocyclization reaction of *C*-tethered *N*-acyloxyiminium ions offered a highly stereocontrolled route to the octahydroindole-2-carboxylic acid core[20−23] of members of the aeruginosin family of marine metabolites.[24] The reaction was also successfully applicable to diastereomeric analogues of **1** (Scheme 1) in which the olefinic tether had a trans relationship to the ester group.[7] The same type of halocarbocyclization of *N*-acyloxyiminium ions derived from 6-oxo-2-pipecolic acid derivatives afforded the corresponding perhydroquinolines in enantiopure form.[7]

We have proposed plausible mechanistic pathways for the stereocontrolled carbocyclization of 4-(3-alkenyl) and 4-(3-alkynyl) *N*-acyloxyiminium ions, relying on stereoelectronic arguments (Figure 2). In the case of 4-(3-

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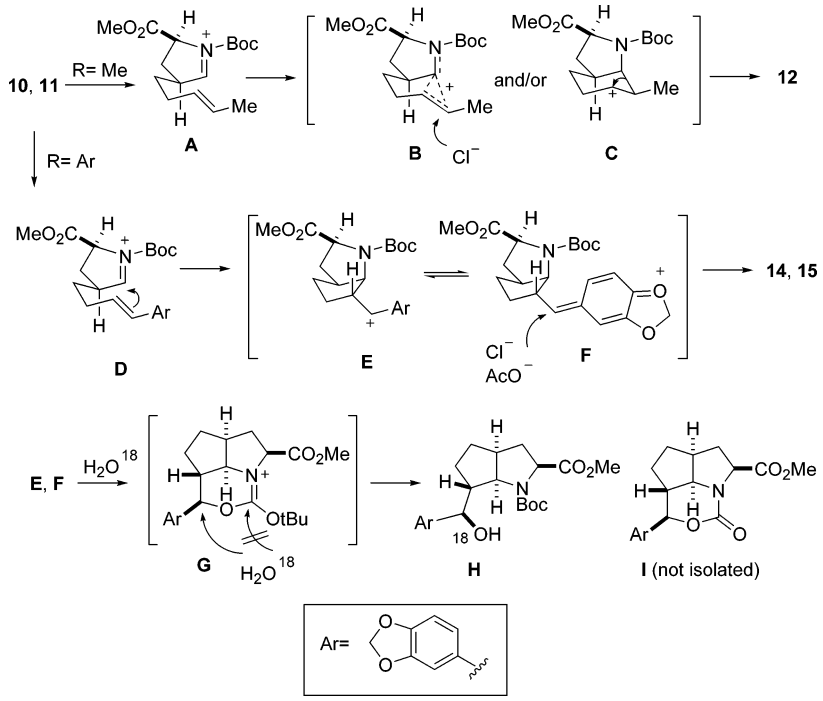


**FIGURE 3.**

pentenyl) tethers (Scheme 2), carbocyclization can proceed via an exocyclic ($\pi$-cation) or endocyclic carbenium ion (Figure 3, B and C, respectively). Evidently, when the terminal substituent can stabilize the carbenium ion by an electron donating group such as an alkyl or an aryl (Scheme 2, **10** and **11**), the products are the corresponding 1-aza-[3.3.0]bicyclooctane-2-carboxylic acid esters **12**, **14** (and **15**), respectively.[11a,25] The isolation of a stereodefined chloro compound **12**, even in a modest yield, implies a preferred mode of attack on a $\pi$-cationic complex such as B or the cyclic carbenium ion C, which can also rearrange back to B. The effect of terminal substituents in related cyclizations of *N*-tethered acyliminium has been discussed by Moeller and co-workers.[3k,l,m] The diversely substituted products in the case of **11** were of interest, since $SnCl_4$ and $BF_3OEt_2$ led to the same bicyclic core motif except for the nature and configuration of the newly created stereogenic center at the benzylic position. The isolation of the configurationally defined (*R*)-alcohol **14** is most likely the result of a rapid, but stereocontrolled solvolysis of an intermediate nonisolable chloride with an opposite configuration (Figure 3). Since a cis/trans olefinic mixture of **11** was used, the mechanistic pathway must necessarily proceed via an intermediate benzylic carbenium ion such as E (or the resonance stabilized counterpart F), which is attacked by the external nucleophile. An alternative pathway could conceivably involve intramolecular attack by the *N*-Boc carbonyl group on the chloride or the carbenium/oxocarbenium ions E and F, to give a transient tetrahydro alkoxyoxazinium ion G, which could lose isobutylene to give the corresponding tetrahydrooxazinone I. Considering that the attack of water during the workup would be a faster process than the elimination of isobutylene, addition of water onto G could restore the *N*-Boc group resulting in the "transfer" of an oxygen atom from the carbonyl group to the benzylic position. To explore this possibility, we conducted the reaction with $SnCl_4$ as usual, and performed the quenching process with 95% $O^{18}$ enriched water. The resulting alcohol was identical with **14** and contained all of the label on the hydroxyl group rather than on the Boc carbonyl (Figure 3, H). Thus, the hydroxyl group at the benzylic carbon probably originates from a stereocontrolled attack on an intermediate (*S*)-chloride with inversion, or by site-selective opening of the benzylic carbon in G. The formation of the (*S*)-acetoxy analogue **15** (Scheme 2) is in line with the notion that attack at the benzylic carbon atom occurs from the same "open" *Si* face of a resonance stabilized quinonoid form of the aryl appendage as in the case of $SnCl_4$. Note that the reaction is also accompanied by the formation of the same (*R*)-alcohol **14**, presumably as a result of an incomplete solvolysis during the workup. In fact, when the (*S*)-acetate **15** was treated with $BF_3OEt_2$, then quenched with aqueous $NH_4Cl$ or $NaHCO_3$, the (*R*)-alcohol **14** was obtained in high yield. Two further observations are worthy of note with regard to the abovementioned carbocyclizations. First, they generate three contiguous stereogenic centers of defined configuration. Second, the formation of the acetate **15** results from an internal return of the acetate released from the precursor, which may be present as a $BF_3$-associated counteranion to the *N*-acyloxyiminium ion. No fluorides could be isolated as in the case of analogous cyclizations of steroidal imines.[26]

The drastic change in the nature of the carbocyclized products in the case of substituted 4-(3-butynyl) tethers (Scheme 3) also can be rationalized based on a reaction

(25) For example, see: Chamberlin, A. R.; Nguyen, D. H.; Chung, J. Y. L. *J. Org. Chem.* **1984**, *49*, 1682.

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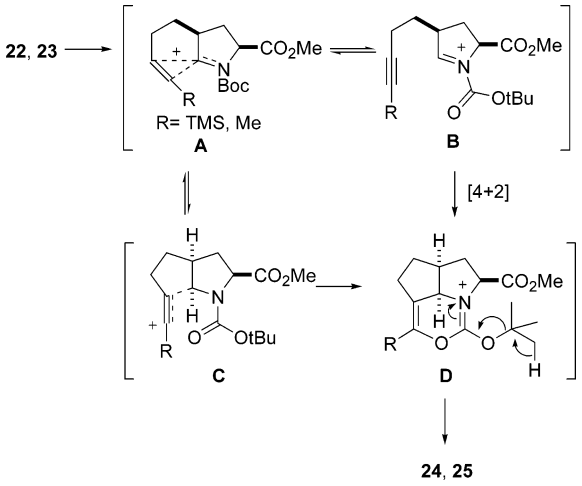


**FIGURE 4.**

pathway that involves stabilized linear carbocations.[15,11a] Rather than be subject to halide capture, they undergo intramolecular attack by the *N*-Boc group giving rise to dihydrooxazinones[27,28] with concomitant loss of isobutylene. This reaction was in fact reported by Overman and Fisher[28] for similar *C*-tethered *N*-acyloxyiminium ions, although the 1-aza-[3.3.0]bicyclooctane systems reported here appear to be unprecedented. There are a number of mechanistic proposals for the formation of the observed products, especially when R = Me (Figure 4). As previously commented,[28] the iminium ion can undergo an asynchronous [4+2] cycloaddition, either directly as in D, or via a $\pi$-cationic species A,[28,29] or a linear propenyl cation C.[15] The successful cyclization with R = $Me_3Si$ raises issues with some of the mechanistic scenarios, since α-silyl carbocations (C, R = $Me_3Si$) are not viable intermediates.[30] A $\pi$-complex A with a higher positive coefficient on the $\beta$-carbon, or a [4+2] cycloaddition may be plausible alternatives. That the nature of the *N*-carbamoyl group plays a role was gleaned from the cyclization of the *N*-Cbz analogue of **22**, which afforded the dihydrooxazinone **24** (52%), with a minor quantity (11%) of the corresponding *N*-Cbz methyl ketone (not shown). Evidently, the loss of isobutylene is more favored compared to that of benzyl chloride in this case. The likelihood of participation by the *N*-Cbz carbonyl via a linear propenyl cation of type C (Figure 4) cannot be excluded.

Perhaps the more intriguing result was the stereodifferention of two diastereotopic, 4-(3-butenyl) tethers in the cyclization of **41** to afford an 81% yield of **50** with

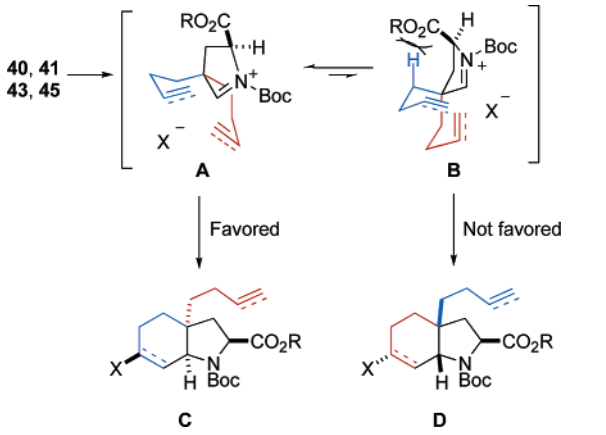


**FIGURE 5.** Proposed mechanism for the diastereoselective azonia-Prins cyclization of bis alkene and alkyne tethers.

three new stereogenic carbons including a quaternary center (Scheme 6). Based on our original rationale[7,9] for the preference of an antiperiplanar approach and better orbital alignment in such carbocyclizations, we had anticipated that of two conformations involving antiperiplanar trajectories, the one corresponding to conformer A (blue butenyl tether) would prevail (Figure 5). Because of the minimization of A[1,2] strain in conformer B (red butenyl tether), a steric clash between the ester group and the side chain would probably favor conformer A. In agreement with this assumption, cyclization of the corresponding methyl ester **40** in the presence of $SnCl_4$ and $SnBr_4$ led to **47** and **48** in 55% and 64% yields, respectively, accompanied by the formation of minor amounts of the other diastereoisomers. The corresponding cyclization with the *tert*-butyl esters **41** gave **49** and **50** in 76% and 81% yields, respectively. The same rationale can be invoked in the cyclization of the bis-4-(3-butynyl) tethers, where conformer A (Figure 5, blue butynyl tether) prevails over B (red butynyl tether) especially in the case of a *tert*-butyl ester (compare **51** and **54**, Scheme 6). No products resulting from 1,2-migration were isolated.[31]

Competition between 4-(3-butenyl) and 4-(3-butynyl tethers (Scheme 7) shows a preference in favor of the alkyne to afford **61** and **62** in a ratio of 3:1, respectively. Excluding a synclinal attack, the antiperiplanar arrangement of the respective tethers (Figure 6, conformers A and C) can account for the stereochemical outcome. The 4-(3-butenyl) tether does manifest its nucleophilicity vis-à-vis a 4-(trimethylsilyl-3-butynyl) tether in the reaction of **59** (Scheme 8). A relatively significant amount of the azonia-Prins product **63** is formed, presumably via a favored antiperiplanar approach (Figure 6, C). However, the diastereoisomeric dihydrooxazinones **64** and **65** prevail in this cyclization as a result of an early participation of the Boc group in stabilizing the developing charge. The minor amount of **65** was formed at the expense of **63** by a competing pathway from the same diastereomer. In accord with the results of 4-(3-pentynyl) tethers and unlike the other cases, no nucleophilic participation of the 4-(3-butenyl) tether was observed in the formation of **67** and **68** in high yield from the cyclization of **66**

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(29) For an early example involving *N*-acyliminium ions, see: (a) Dijkink, J.; Schoemaker, H. E.; Speckamp W. N. *Tetrahedron Lett.* **1975**, *16*, 4043. See also: (b) Ent, H.; de Koning, H.; Speckamp, W. N. *J. Org. Chem.* **1986**, *51*, 1687.

(30) For examples of intramolecular silicon directed *N*-acyliminium ion cyclizations, see ref 1a−f.

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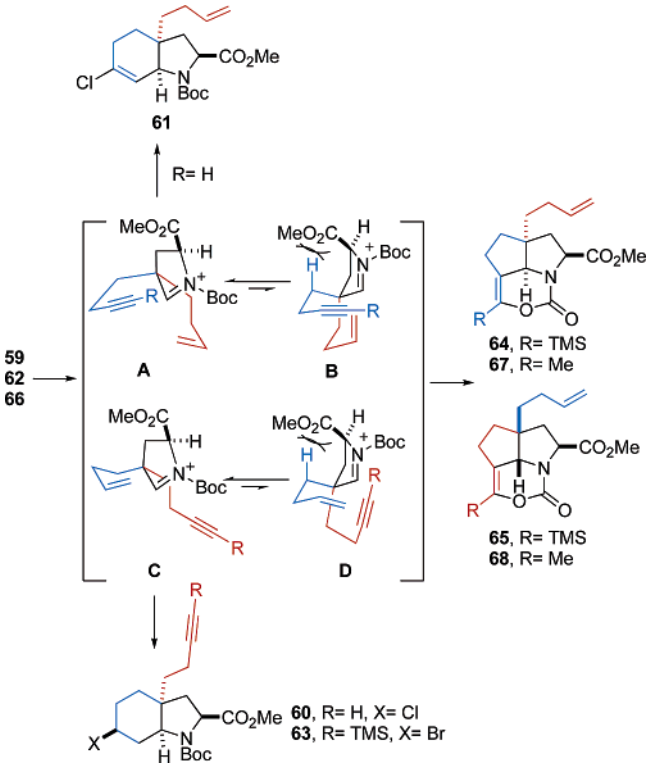


**FIGURE 6.**

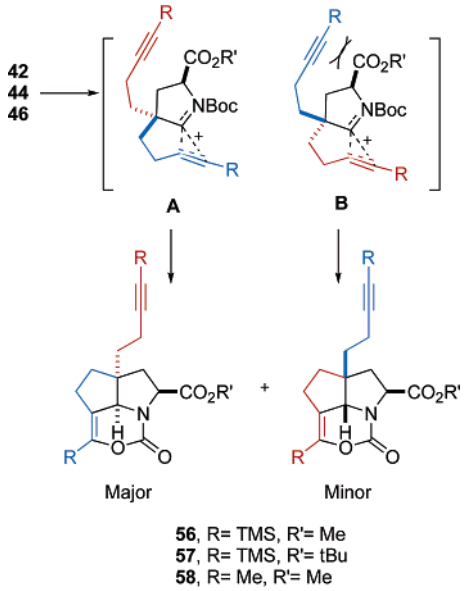


**FIGURE 7.**

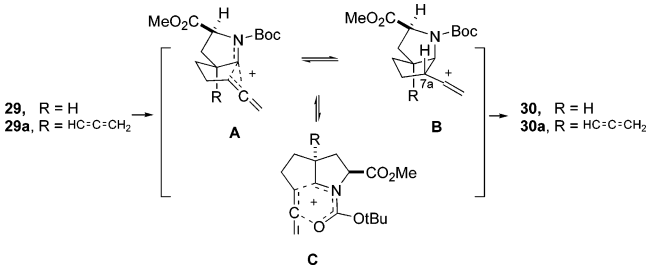


**FIGURE 8.**

(Scheme 8). In contrast to the case of an unsubstituted 4-(3-butynyl) tether, equal amounts of the diastereomeric dihydrooxazinones were found, demonstrating a higher chemoselectivity for the substituted alkyne tethers (Figure 6, A, C, R = Me). It is not surprising that the 4-(3-pentynyl) tether wins over the 4-(4-trimethylsilyl-3-butynyl) or 4-(3-butenyl) counterpart in the cyclization of **69** and **70**, respectively (Scheme 8). None of the trimethylsilyl dihydrooxazinones related to **64** and **65**, or hexahydroindoles related to **61** are formed, the 4-(3-pentynyl) tether being the dominant nucleophile. Obviously, this is a reflection of the effect of a terminal methyl versus trimethylsilyl in stabilizing a transient vinyl carbenium ion or a $\pi$-complex that is trapped by the participating Boc group.

The stereodifferentiation between two identical 4-(3-butenyl) tethers with terminal methyl or trimethylsilyl substituents in **42**, **44**, and **46** (Scheme 6) in the preferential formation of the dihydrooxazinone **56**−**58** might result from an unfavorable steric interaction of the pseudoaxial ester moiety with the side chain as shown in Figure 7 A,B.

The cyclization of the allenic precursor **29** (Scheme 4) leads to a highly strained crystalline hydrooxazinone **30** possibly via a $\pi$-complex A or a vinyl cation B,[15] which undergoes intramolecular attack by the *N*-Boc group to the dihydrooxazinium ion C (Figure 8).[32] It is very interesting that in the process, a new stereogenic center is created at C7a. Unfortunately, the precise nature of intervening cationic species cannot be delineated at this time. Despite the modest yield, the formation of **30** is another example of the involvement of vinylic cations in the sequential intramolecular nucleophilic attack of unsaturated tethers onto *N*-acyloxyiminium ions, followed by *N*-Boc participation.

Finally, with diastereotopic bis-allenic tethers, the major cyclization product **30a** is obtained in 62% yield favoring an antiperiplanar trajectory (Figure 8). It is also of interest that carbocyclization of mixed allene/alkene/alkyne tethers favors reaction of the allene, leading to the preferential formation of relatively strained hydrooxazinones rather than the corresponding hydroindoles (Scheme 9).

## Conclusion

We described methods for the stereocontrolled Lewis acid carbocyclization of cyclic *N*-acyloxyiminium ions harboring nucleophilic and acetylenic tethers. 4-(3-Butenyl) and 4-(3-butynyl) tethers undergo face selective cyclization controlled by a favored antiperiplanar approach. Depending on the presence or absence of a terminal electron-donating substituent on the 4-(3-butenyl) tether, the products are substituted 1-aza-[3.3.0]-bicyclooctanes and hexahydro- or octahydroindoles. In the latter two cases, a halogen atom is introduced in a regio- and stereoselective manner. 4-(3-Pentynyl) and 4-(4-trimethylsilyl-3-butynyl) tethers lead to 1-aza-[3.3.0]-bicyclooctanes with incorporation of a dihydrooxazinone motif. When the unsubstituted alkene and alkyne tethers

(32) For examples of allenes as $\pi$-nucleophiles, see: Nossin, P. M. M.; Speckamp, W. N. *Tetrahedron Lett.* **1981**, *22*, 3289. See also refs 6j,k.

are identical, the major products of carbocyclization from the 1:1 mixture of diastereomers result from a face-selective antiperiplanar approach, leading to 6-halo octahydroindoles and 6-halo hexahydroindoles, respectively. A preference for alkyne vs alkene cyclization is observed and rationalized on the basis of faster reaction of $sp^2$ cyclic vinyl cations vis-à-vis their saturated counterparts. 3-Pentynyl tethers dominate the cyclization mode when in competition with 4-trimethylsilyl, or 4-(3-butenyl) tethers, affording 1-aza-[3.3.0]bicyclooctanes cores with an appended dihydrooxazinone. 4-(3-Allenyl) tethers are also preferred nucleophilic partners in carbocyclizations onto *N*-acyloxyiminium ions leading to tricyclic hydrooxazinones.

The potential utility of the various functionalized azacyclic systems reported in this paper can be considered in a number of practical applications such as natural product synthesis and versatile scaffolds for pharmaceutically oriented research.[33]

## Experimental Section

**(2*S*,4*S*)-2-*tert*-Butoxycarbonylamino-4-pent-3-enylpentanedioic Acid Dimethyl Ester (5).** To a solution of *N*-Boc-glutamic acid dimethyl ester **4** (2.00 g, 7.26 mmol) in THF (42 mL) at −78 °C was added LiHMDS (15.2 mL, 1.0 N in THF) with stirring for 45 min, then a solution of *trans*-3-pentenol-*O*-Tf (2.06 g, 9.44 mmol), easily prepared from the corresponding commercially available methyl ester, in THF (14 mL) at −78 °C was added dropwise via cannula. After being stirred for 20 min, the solution was quenched with $NH_4Cl$ (2 N), warmed to RT, and concentrated under vacuum. The resulting aqueous solution was extracted with $CH_2Cl_2$, and the combined organic extracts were washed with brine and dried over $Na_2SO_4$. The solvent was removed under vacuum and the resulting oil was purified by flash chromatography (EtOAc/hexanes 10:90 to 15:85) to give **5** (2.24 g, 90%) as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.42−5.23 (m, 2H), 4.93−4.85 (m, 1H), 4.35−4.22 (m, 1H), 3.75 (s, 3H), 3.68 (s, 3H), 2.50−2.40 (m, 1H), 2.05−1.86 (m, 4H), 1.73−1.50 (m, 5H), 1.42 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 176.5, 173.2, 155.7, 130.2, 126.4, 80.3, 52.7, 52.0, 41.9, 34.8, 32.6, 30.3, 28.7, 18.2; $[\alpha]_D$ +8.3 (*c* 1.0, $CHCl_3$); HRMS for $C_{17}H_{30}NO_6$ calculated ($M + H^+$) 344.207313, found 344.204910.

**(2*S*,4*S*)-2-But-3-enyl-4-(*tert*-butoxycarbonylamino)pentanedioic Acid Dimethyl Ester (6).** By using the same procedure for **5**, compound **4** (5.00 g, 18.2 mmol) was converted into **6** (5.08 g, 85%) with 3-buten-1-ol-*O*-Tf as the alkylating agent. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.80−5.65 (m, 1H), 5.00−4.92 (m, 2H), 4.20−4.15 (m, 1H), 3.71 (s, 3H), 3.66 (s, 3H), 2.55−2.45 (m, 1H), 2.10−1.95 (m, 4H), 1.78−1.70 (m, 1H), 1.65−1.58 (m, 1H), 1.43 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 176.5, 173.4, 155.7, 137.7, 115.9, 80.4, 52.9, 52.8, 52.2, 41.9, 34.8, 31.9, 31.5, 28.7; $[\alpha]_D$ +12.9 (*c* 1.18, $CHCl_3$); HRMS for $C_{16}H_{28}NO_6$ calculated ($M + H^+$) 330.19165, found 330.19050.

**(2*S*,4*S*)-4-But-3-enyl-5-oxo-pyrrolidine-2-carboxylic Acid Methyl Ester (8).** To a solution of compound **6** (4.80 g, 14.6 mmol) in $CH_2Cl_2$ (38 mL) was added TFA (9.5 mL) and the solution was stirred at RT until no trace of starting material remained (approximately 1 h). After the solution was concentrated under vacuum, the resulting oil was dissolved in toluene (180 mL) and heated at reflux for 1.5 h. The solution was concentrated under vacuum to give the corresponding lactam **8** (2.30 g, 80%) as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 6.65−6.60 (br s, 1H), 5.80−5.70 (m, 1H), 5.00−4.90 (m, 2H), 4.08 (t, 1H, $J$ = 9.2 Hz), 3.78 (s, 3H), 2.70−2.58 (m, 1H), 2.45−2.38 (m, 1H), 2.20−1.82 (m, 3H), 1.82−1.75 (m, 1H), 1.42−1.35 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 179.5, 172.7, 138.0, 115.8, 54.1, 53.0, 40.8, 31.8, 31.7, 30.4; $[\alpha]_D$ +16.1 (*c* 1.50, $CHCl_3$); HRMS for $C_{10}H_{15}NO_3$ calculated 197.105194, found 197.104977.

**(2*S*,4*S*,6*R*,7*R*)-6-(1-Chloroethyl)hexahydrocyclopenta[*b*]-pyrrole-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (12).** To a solution of compound **5** (1.00 g, 2.91 mmol) in $CH_2Cl_2$ (8 mL) was added TFA (1.9 mL) with stirring at RT until no trace of starting material remained (approximately 1 h). After the solution was concentrated under vacuum, the resulting oil was dissolved in toluene (36 mL) and heated at reflux for 1.5 h and the solution was concentrated under vacuum. To a solution of the resulting lactam **(7)** in $CH_2Cl_2$ (14 mL),was added successively $Et_3N$ (1.22 mL, 8.73 mmol), $Boc_2O$ (0.953 g, 4.37 mmol), and DMAP (cat.). After the solution was stirred overnight, $NH_4Cl$ (2 N) was added, the solution was extracted with $CH_2Cl_2$, and the combined organic extracts were washed with brine and dried over $Na_2SO_4$. The solvent was removed under vacuum and the resulting oil was purified by flash chromatography (EtOAc/hexanes 20:80) to give the corresponding *N*-Boc lactam (0.810 g, 90%) as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.45−5.22 (m, 2H), 4.50−4.38 (m, 1H), 3.74 (s, 3H), 2.53−2.40 (m, 2H), 2.12−1.87 (m, 3H), 1.63 (d, 3H, $J$ = 6.2 Hz), 1.50−1.35 (m, 11H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 175.4, 172.4, 149.8, 130.1, 126.6, 83.9, 57.7, 52.8, 42.2, 31.2, 30.3, 28.6, 28.2, 28.1, 18.2; $[\alpha]_D$ −9.2 (*c* 0.94, $CHCl_3$); HRMS for $C_{16}H_{26}NO_5$ calculated ($M + H^+$) 312.181098, found 312.181440. To a solution of the *N*-Boc lactam (0.800 g, 2.57 mmol) in THF (17 mL) at −78 °C was added a solution of $LiHBEt_3$ (2.83 mL, 1.0 N in THF), then the mixture was stirred for 1 h and quenched with $NaHCO_3$ (sat.), 2 drops of $H_2O_2$ (30% in $H_2O$) were added, and the solution was concentrated under vacuum. The aqueous layer was extracted with $CH_2Cl_2$, the combined organic extracts were washed with brine, dried over $Na_2SO_4$, and concentrated under vacuum. The resulting oil was dissolved in $CH_2Cl_2$ (6 mL) and $Et_3N$ (1.07 mL, 7.70 mmol), $Ac_2O$ (0.722 mL, 7.70 mmol), and DMAP (cat.) were added successively. After being stirred overnight, the solution was quenched with $NaHCO_3$ (sat.), the aqueous layer was extracted with $CH_2Cl_2$, and the combined organic extracts were washed with brine, dried over $Na_2SO_4$, and concentrated under vacuum. The crude oil obtained was purified by flash chromatography (EtOAc/hexanes 15:85) to give the corresponding hemiaminal derivative **10** (0.821 g, 90%) as a mixture of diastereoisomers. To a solution of the hemiaminal **10** (0.500 g, 1.41 mmol) in $CH_2Cl_2$ (9 mL) at −78 °C was added a solution of $SnCl_4$ (1.83 mL, 1.0 M in $CH_2Cl_2$) dropwise. After being stirred for 5 min, the solution was quenched with $NaHCO_3$ (sat.), warmed to RT, and filtered on a small Celite pad, then the filtrate was washed with brine, dried over $Na_2SO_4$, and concentrated under vacuum. The crude oil obtained was purified by flash chromatography (EtOAc/hexanes 10:90 to 15:85) to give **12** (0.140 g, 30%) as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (rotamers) 5.02−4.90 (m, 0.5H), 4.80−4.70 (m, 0.5H), 4.50−4.40 (m, 0.5H), 4.35−4.25 (m, 0.5H), 4.22−4.10 (m, 1H), 3.75 (s, 3H), 2.74−2.60 (m, 1H), 2.50−2.40 (m, 1H), 2.39−2.25 (m, 1H), 1.90−1.70 (m, 4H), 1.60−1.30 (m, 13H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (rotamers) 174.6, 174.4, 154.8, 154.5, 81.0, 80.3, 68.4, 67.9, 63.0, 62.2, 61.0, 60.8, 54.0, 52.5, 52.3, 44.6, 43.7, 34.6, 34.1, 30.9, 30.6, 30.1, 29.0, 28.7, 25.9, 25.5, 24.8, 18.3; $[\alpha]_D$ −44 (*c* 0.63, $CHCl_3$); HRMS for $C_{16}H_{26}NO_4Cl$ calculated ($M^+$) 331.155036, found 331.156502.

**(2*S*,3a*S*,6*R*,6a*R*)-6-(Benzo[1,3]dioxol-5-ylhydroxymethyl)hexahydrocyclopenta[*b*]pyrrole-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (14).** To a solution of the alkene **8** (1.97 g, 10.0 mmol) in THF/$H_2O$ (40 mL, 9:1) at 0 °C was added $NaIO_4$ (6.42 g, 30.0 mmol) and a catalytic amount of $OsCl_3$. After being stirred for 4 h, the solution was extracted

(33) (a) Ohkawa, T.; Imamura, K.; Kurosaki, T.; Kobayashi, M.; Shimizu, S. PCT Int. Appl. 2004, WO2004111041; CAN 142, 56169. (b) Barvian, N. C.; Connolly, C. J. C.; Guzzo, P. R.; Hamby, J. M.; Hicks, J. L.; Johnson, M. R.; Le, V.-D.; Mitchell, L. H.; Roark, W. H. PCT Int. Appl. 2004, WO 2004092132; CAN 141, 380130.

with $Et_2O$, the organic extracts were dried over $Na_2SO_4$ and concentrated under vacuum, and the resulting residue was purified by flash chromatography (EtOAc/hexanes 50:50 to 100:0) to give the corresponding aldehyde (1.77 g, 92%) as a colorless oil. $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 9.80 (s, 1H), 6.95 (s, 1H), 4.15 (t, 1H, $J$ = 8.7 Hz), 3.85 (s, 3H), 2.80−2.60 (m, 3H), 2.60−2.40 (m, 1H), 2.20−2.00 (m, 1H), 1.90−1.70 (m, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 202.0, 179.1, 172.5, 54.1, 53.0, 41.5, 40.3, 31.7, 23.6; $[\alpha]_D$ −17.0 (*c* 1.00, $CHCl_3$); FAB/MS for $C_9H_{14}NO_4$ calculated (M + $H^+$) 200.1, found 200.0. To a solution of benzo[1,3]dioxol-5-ylphosphonium bromide (1.91 g, 4.00 mmol) in THF (35 mL) at −10 °C was added a solution of LiHMDS (4.2 mL, 1.0 M in THF). After the mixture was stirred for 10 min, a solution of the aldehyde prepared (0.398 g, 2.00 mmol) in THF (2 mL) was added and stirring was continued for 1 h. The solution was neutralized with $NH_4Cl$ (2 N) and concentrated under vacuum, the aqueous solution was extracted with $CH_2Cl_2$, and the combined organic extracts were concentrated under vacuum to give the lactam **9**. To a solution of the lactam obtained in $CH_2Cl_2$ (10 mL) was added successively $Et_3N$ (0.6 mL, 4.00 mmol), $Boc_2O$ (0.872 g, 4.00 mmol), and DMAP (cat.). After the solution was stirred overnight, $NH_4Cl$ (2 N) was added, the solution was extracted with $CH_2Cl_2$, and the combined organic extracts were washed with brine and dried over $Na_2SO_4$. The solvent was removed under vacuum and the resulting oil was purified by flash chromatography (EtOAc/hexanes 20:80 to 25:75) to give the corresponding *N*-Boc lactam (0.484 g, 58%) as a colorless oil. $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (mixture of cis/trans stereoisomers) 6.86 (s, 1H), 6.73 (s, 2H), 6.30 (d, 1H, $J$ = 15.8 Hz), 5.97−5.90 (m, 3H), 4.50−4.45 (m, 1H), 3.76 (s, 3H), 2.60−2.50 (m, 2H), 2.40−2.10 (m, 2H), 2.08−2.00 (m, 1H), 1.70−1.45 (m, 11H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (mixture of stereoisomers) 175.3, 172.4, 149.8, 148.4, 147.2, 132.3, 131.1, 127.6, 120.8, 108.6, 105.8, 101.4, 84.0, 57.8, 52.9, 42.2, 31.1, 30.6, 28.3; $[\alpha]_D$ + 2.3 (*c* 1.0, $CHCl_3$); FAB/MS for $C_{22}H_{28}NO_7$ calculated (M + $H^+$) 418.2, found 418.2. To a solution of the *N*-Boc lactam derivative of **9** (0.240 g, 0.575 mmol) in THF (4 mL) at −78 °C was added a solution of $LiHBEt_3$ (0.64 mL, 1.0 N in THF), then the mixture was stirred for 1 h and quenched with $NaHCO_3$ (sat.), then 1 drop of $H_2O_2$ (30% in $H_2O$) was added and the solution was concentrated under vacuum. The aqueous layer was extracted with $CH_2Cl_2$, and the combined organic extracts were washed with brine, dried over $Na_2SO_4$, and concentrated under vacuum. The resulting oil was dissolved in $CH_2Cl_2$ (3 mL) and $Et_3N$ (0.24 mL, 1.72 mmol), $Ac_2O$ (0.16 mL, 1.72 mmol), and DMAP (cat.) were added successively. After being stirred overnight, the solution was quenched with $NaHCO_3$ (sat.), the aqueous layer was extracted with $CH_2Cl_2$, and the combined organic extracts were washed with brine, dried over $Na_2SO_4$, and concentrated under vacuum. The crude oil obtained was purified by flash chromatography (EtOAc/hexanes 15:85) to give the corresponding hemiaminal derivative **11** (0.173 g, 65%) as a mixture of diastereoisomers. To a solution of the hemiaminal **11** (0.173 g, 0.375 mmol) in $CH_2Cl_2$ (4 mL) at −78 °C was added a solution of $SnCl_4$ (0.49 mL, 1.0 M in $CH_2Cl_2$) dropwise. After being stirred for 5 min, the solution was quenched with $NaHCO_3$ (sat.), warmed to RT, and filtered on a small Celite pad. The filtrate was washed with brine, dried over $Na_2SO_4$, and concentrated under vacuum. The crude oil obtained was purified by flash chromatography (EtOAc/hexanes 10:90 to 15:85) to give **14** (0.090 g, 57%) as a crystalline white solid. $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.23−7.20 (d, 1H $J$ = 2.4 Hz), 6.94−6.88 (dd, 1H, $J$ = 7.7 Hz, $J$ = 2.4 Hz), 6.80−6.65 (d, 1H, $J$ = 7.7 Hz), 6.62−6.60 (d, 1H, $J$ = 3.1 Hz), 5.42−5.38 (d, 2H, $J$ = 3.4 Hz), 4.42−4.38 (dd, 1H, $J$ = 9.3 Hz, $J$ = 6.2 Hz), 4.32−4.25 (dd, 1H, $J$ = 9.3 Hz, $J$ = 6.0 Hz), 4.25−4.18 (dd, 1H, $J$ = 7.7 Hz, $J$ = 3.1 Hz), 3.42 (s, 3H), 2.80−2.70 (m, 1H), 2.30−2.18 (m, 1H), 1.90−1.80 (m, 1H), 1.65−1.55 (m, 1H), 1.55−1.47 (m, 2H), 1.45 (s, 9H), 1.43−1.35 (m, 1H), 1.30−1.10 (m, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 173.3, 155.6, 148.3, 147.3, 121.1, 108.3, 107.9, 100.9, 81.2, 78.3, 68.6, 61.0, 55.9, 51.7, 44.2, 34.2, 30.1, 28.4; $[\alpha]_D$ +101 (*c* 1.00, $C_6H_6$); mp 114−116 °C; FAB/MS for $C_{22}H_{30}NO_7$ calculated (M + $H^+$) 420.2, found 420.2.

The above-described sequence was repeated and the quench was done with $H_2O^{18}$ to give **14** in which the label was located on the benzylic hydroxyl group (determined by mass spectrometry after removal of the *N*-Boc group).

**(2*S*,3a*S*,6*R*,6a*R*)-6-(Acetoxybenzo[1,3]dioxol-5-ylmethyl)hexahydrocyclopenta[*b*]pyrrole-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (15).** To a solution of the *N*-Boc lactam derivative of **9** (0.240 g, 0.575 mmol) in THF (4 mL) at −78 °C was added a solution of $LiHBEt_3$ (0.64 mL, 1.0 N in THF), then the mixture was stirred for 1 h and quenched with $NaHCO_3$ (sat.), and 1 drop of $H_2O_2$ (30% in $H_2O$) was added and the solution was concentrated under vacuum. The aqueous layer was extracted with $CH_2Cl_2$, the combined organic extracts were washed with brine, dried over $Na_2SO_4$, and concentrated under vacuum. The resulting oil was dissolved in $CH_2Cl_2$ (3 mL) and $Et_3N$ (0.24 mL, 1.72 mmol), $Ac_2O$ (0.16 mL, 1.72 mmol), and DMAP (cat.) were added successively. After being stirred overnight, the solution was quenched with $NaHCO_3$ (sat.), the aqueous layer was extracted with $CH_2Cl_2$, and the combined organic extracts were washed with brine, dried over $Na_2SO_4$, and concentrated under vacuum. The crude oil obtained was purified by flash chromatography (EtOAc/hexanes 15:85) to give the corresponding hemiaminal derivative **11** (0.173 g, 65%) as a mixture of diastereomers. To a solution of the hemiaminal **11** (0.173 g, 0.375 mmol) in $CH_2Cl_2$ (4 mL) at −78 °C was added a solution of $BF_3OEt_2$ (46 $\mu$L, 0.487 mmol) dropwise. After being stirred for 5 min, the solution was quenched with aqueous $NaHCO_3$ (sat.) and warmed to RT. The filtrate was washed with brine, dried over $Na_2SO_4$, and concentrated under vacuum. The crude oil obtained was purified by flash chromatography (EtOAc/hexanes 10:90 to 15:85) to give **15** (0.112 g, 65%) as a colorless oil. $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (rotamers) 6.90−6.60 (m, 3H), 6.30 (s, 0.5H), 6.20 (s, 0.5H), 5.90 (s, 2H), 4.50−4.40 (m, 0.5H), 4.40−4.30 (m, 0.5H), 4.20−4.10 (m, 0.5H), 4.10−3.80 (m, 0.5H), 3.70 (s, 3H), 2.80−2.58 (m, 2H), 2.42−2.30 (m, 1H), 2.22−2.10 (m, 3H), 2.00−1.70 (m, 3H), 1.60 (s, 4.5H), 1.50 (s, 4.5H), 1.60−1.30 (m, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (rotamers) 174.4, 174.1, 170.5, 154.8, 148.0, 147.0, 131.3, 128.7, 119.4, 118.8, 108.5, 108.3, 106.8, 106.3, 101.4, 81.4, 80.2, 67.1, 67.0, 60.9, 60.8, 53.1, 52.6, 52.5, 44.7, 43.3, 35.0, 33.9, 29.3, 28.6, 25.6, 25.4, 21.6; $[\alpha]_D$ −5.5 (*c* 4.5, $CHCl_3$); FAB/MS for $C_{24}H_{32}NO_8$ calculated (M + $H^+$) 462.2, found 462.2.

**(2*S*,3a*S*,6*R*,6a*R*)-6-(Benzo[1,3]dioxol-5-ylmethoxymethyl)hexahydrocyclopenta[*b*]pyrrole-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (16).** To a solution of the acetate **15** (0.030 g, 0.065 mmol) in MeOH (1 mL) was added a catalytic amount of NaOMe. After being stirred at RT for 2 h, the solution was neutralized with $NH_4Cl$ (2 N) and concentrated under vacuum, the aqueous solution was extracted with $CH_2Cl_2$, and the combined organic extracts were washed with brine and dried over $Na_2SO_4$. To a solution of the residue (dried with toluene codistillation) in THF (1 mL) at 0 °C was added MeI (8 $\mu$L, 0.13 mmol) followed by NaH (0.005 g, 60% in oil, 0.13 mmol). The solution was progressively warmed to RT over a period of 1 h. After being stirred for an additional 3 h, the solution was concentrated under vacuum, and the residue was purified by flash chromatography (EtOAc/hexanes 15:85) to give **16** (0.022 g, 80%) as a crystalline white solid. $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ (rotamers) 6.90−6.60 (m, 3H), 5.90 (s, 2H), 5.00−4.85 (m, 0.5H), 4.75−4.65 (m, 0.5H), 4.65−4.55 (m, 0.5H), 4.50−4.00 (m, 0.5H), 4.20−4.10 (m, 2H), 3.75 (s, 1.5H), 3.35 (s, 1.5H), 3.30 (s, 1.5H), 3.18 (s, 1.5H), 2.80−2.60 (m, 1H), 2.40−2.15 (m, 1H), 2.15−1.85 (m, 1H), 1.85−1.65 (m, 1H), 1.65−1.50 (m, 1H), 1.45 (s, 9H), 1.40−1.10 (m, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ (rotamers) 174.4, 174.1, 154.8, 148.0, 147.0, 138.0, 137.5, 120.4, 119.7, 108.3, 107.6, 107.2, 101.1, 83.7, 81.0, 80.3, 67.5, 66.4, 63.9, 61.1, 57.8, 56.9, 54.7, 52.2, 52.0, 50.5, 43.7, 43.2, 35.5, 34.9, 31.0, 29.3, 28.9, 25.6, 24.7;

$[\alpha]_D$ +12.9 (*c* 1.18, $CHCl_3$); mp 138−140 °C; FAB/MS for $C_{23}H_{32}NO_7$ calculated (M + $H^+$) 434.2, found 434.2.

**(2*S*,4*S*)-2-*tert*-Butoxycarbonylamino-4-pent-3-ynylpentanedioic Acid Dimethyl Ester (17).** With use of the same procedure as for **5**, compound **4** (2.00 g, 7.26 mmol) was converted into **17** (2.32 g, 94%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.98 (d, 1H, $J$ = 8.6 Hz), 4.38−4.25 (m, 1H), 3.71 (s, 3H), 3.66 (s, 3H), 2.67−2.50 (m, 1H), 2.18−2.08 (m, 2H), 2.05−1.90 (m, 2H), 1.85−1.60 (m, 5H), 1.42 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 176.2, 173.2, 155.7, 80.4, 52.8, 52.6, 52.3, 41.6, 34.4, 31.9, 28.7, 17.0, 3.9; $[\alpha]_D$ +4.08 (*c* 1.25, $CHCl_3$); HRMS for $C_{17}H_{28}NO_6$ calculated (M + $H^+$) 342.191663, found 3342.191200.

**(2*S*,4*S*)-2-*tert*-Butoxycarbonylamino-4-(4-(trimethylsilyl)but-3-ynyl)pentanedioic Acid Dimethyl Ester (18).** With use of the same procedure as for **5**, compound **4** (2.00 g, 7.26 mmol) was converted into **18** (1.89 g, 65%), using 3-(4-trimethylsilyl)butyn-1-ol-*O*-Tf as the alkylating agent. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.00−4.88 (m, 1H), 4.30−4.20 (m, 1H), 3.68 (s, 3H), 3.63 (s, 3H), 2.58−2.47 (m, 1H), 2.16 (t, 2H, $J$ = 7.3 Hz), 2.00−1.85 (m, 2H), 1.83−1.75 (m, 1H), 1.75−1.61 (m, 1H), 1.39 (s, 9H), 0.09 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 175.8, 173.1, 155.7, 106.0, 85.7, 80.4, 52.8, 52.5, 52.2, 41.6, 34.4, 31.5, 28.6, 18.1, 0.4; $[\alpha]_D$ +3.2 (*c* 1.5, $CHCl_3$); FAB/MS for $C_{19}H_{34}NO_6Si$ calculated (M + $H^+$) 400.2, found 400.2.

**(2*S*,4*S*)-5-Oxo-4-(pent-3-ynyl)pyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (19).** To a solution of compound **17** (2.30 g, 6.74 mmol) in $CH_2Cl_2$ (20 mL) was added TFA (5.0 mL). After being stirred at RT until no trace of starting material remained, the solution was concentrated under vacuum, the resulting oil was dissolved in toluene (78 mL) and heated at reflux for 1.5 h, and the solution was concentrated under vacuum. To a solution of the lactam obtained in $CH_2Cl_2$ (20 mL) was added successively $Et_3N$ (2.82 mL, 20.2 mmol), $Boc_2O$ (4.41 g, 20.2 mmol) followed by DMAP (cat.). After being stirred overnight, the solution was quenched with $NH_4Cl$ (2 N), the aqueous layer was extracted with $CH_2Cl_2$, and the combined organic extracts were washed with brine, dried over $Na_2SO_4$, and concentrated under vacuum. The crude oil obtained was purified by flash chromatography (EtOAc/hexanes 15:85 to 30:70) to give compound **19** (1.87 g, 90%) as a white solid. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.48 (t, 1H, $J$ = 7.7 Hz), 3.75 (s, 3H), 2.75−2.70 (m, 1H), 2.60−2.50 (m, 1H), 2.33−2.26 (m, 1H), 2.20−2.01 (m, 2H), 1.75−1.40 (m, 14H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 175.2, 172.3, 149.7, 84.0, 57.8, 52.9, 41.9, 30.5, 28.7, 28.2, 28.1, 17.0, 3.8; $[\alpha]_D$ −0.60 (*c* 1.1, $CHCl_3$); HRMS for $C_{16}H_{24}NO_5$ calculated (M + $H^+$) 310.165448, found 310.165333.

**(2*S*,4*S*)-5-Oxo-4-(4-(trimethylsilyl)but-3-ynyl)pyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (20).** To a solution of compound **18** (5.17 g, 12.9 mmol) in $CH_2Cl_2$ (40 mL) was added TFA (9.5 mL). After being stirred at RT until no trace of starting material remained, the solution was concentrated under vacuum, the resulting oil was dissolved in toluene (150 mL) and heated at reflux for 1.5 h, and the solution was concentrated under vacuum. To a solution of the lactams obtained in $CH_2Cl_2$ (40 mL) was added successively $Et_3N$ (5.41 mL, 38.8 mmol), $Boc_2O$ (4.24 g, 19.4 mmol) followed by DMAP (cat.). After being stirred overnight, the solution was quenched with $NH_4Cl$ (2 N), the aqueous layer was extracted with $CH_2Cl_2$, and the combined organic extracts were washed with brine, dried over $Na_2SO_4$, and concentrated under vacuum. The crude oil obtained was purified by flash chromatography (EtOAc/hexanes 15:85 to 30:70) to give compound **20** (1.68 g, 67%) and **21** (0.280 g, 11%) as colorless oils. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.49 (t, 1H, $J$ = 8.2 Hz), 3.76 (s, 3H), 2.75−2.63 (m, 1H), 2.61−2.50 (m, 1H), 2.45−2.34 (m, 1H), 2.33−2.22 (m, 1H), 2.17−2.07 (m, 1H), 1.70−1.62 (m, 1H), 1.61−1.50 (m, 1H), 1.47 (s, 9H), 0.11 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 175.1, 172.3, 149.7, 105.8, 86.3, 84.1, 57.8, 52.9, 42.0, 30.1, 28.2, 18.2, 0.4; $[\alpha]_D$ +1.0 (*c* 1.0, $CHCl_3$); HRMS for $C_{18}H_{30}NO_5Si$ calculated (M + $H^+$) 368.189327, found 368.187631.

**(2*S*,4*S*)-4-But-3-ynyl-5-oxo-pyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (21).** To a solution of **20** (0.552 g, 1.50 mmol) and AcOH (0.13 mL, 2.25 mmol) in THF (6.5 mL) was added a solution of TBAF (2.25 mL, 1.0 M in THF). After being stirred for 1 h, the solution was concentrated and the residue was purified by flash chromatography (EtOAc/hexanes 25:75) to give compound **21** (0.438 g, quant.) as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.47 (t, 1H, $J$ = 8.2 Hz), 3.74 (s, 3H), 2.75−2.65 (m, 1H), 2.60−2.50 (m, 1H), 2.42−2.31 (m, 1H), 2.28−2.18 (m, 1H), 2.13−2.04 (m, 1H), 1.94 (t, 1H, $J$ = 2.6 Hz), 1.70−1.50 (m, 2H), 1.45 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 175.0, 172.3, 149.6, 84.1, 83.2, 69.9, 57.7, 52.9, 41.8, 30.1, 28.2, 16.7; $[\alpha]_D$ −10.7 (*c* 1.00, $CHCl_3$); HRMS for $C_{15}H_{22}NO_5$ calculated (M + $H^+$) 296.149798, found 296.151085.

**General Procedure for Reduction, Acetylation, and Azonia-Prins Cyclizations with $SnBr_4$ or $SnCl_4$.** To a solution of the appropriate *N*-Boc lactam (1 equiv) in THF (3 mL) at −78 °C was added a solution of $LiHBEt_3$ (1.1 equiv, 1.0 N in THF). After the mixture was stirred for 1 h at −78 °C the reaction was quenched with $NaHCO_3$ (sat.) and 2 drops of $H_2O_2$ (30% in $H_2O$), and concentrated under vacuum. The aqueous layer was extracted with $CH_2Cl_2$ and the combined organic extracts were washed with brine, dried over $Na_2SO_4$, and concentrated under vacuum. The resulting oil, dissolved in $CH_2Cl_2$ (5 mL), was then treated with $Et_3N$ (2 equiv), $Ac_2O$ (3 equiv), and DMAP (cat.) at RT. After being stirred overnight, the solution was quenched with $NaHCO_3$ (sat.), the aqueous layer was extracted with $CH_2Cl_2$, and the combined organic extracts were washed with brine, dried over $Na_2SO_4$, and concentrated under vacuum. The crude diastereomeric mixture of *O*-acyl hemiaminals was purified by passage through a silica plug eluting with 85:15 EtOAc:hexane. Finally, to a solution of the resulting diastereomeric mixture in $CH_2Cl_2$ (9 mL) at −78 °C was added $SnX_4$ (X = Cl or Br) (1.2 equiv, 1.0 M in $CH_2Cl_2$) dropwise. After being stirred for 5 min, the solution was quenched with $NaHCO_3$ (sat.), warmed to RT, and filtered on a small Celite pad. The filtrate was washed with brine, dried over $Na_2SO_4$, and concentrated under vacuum. Purification by flash chromatography gave the corresponding pure cyclized product(s).

**(2a*S*,4*S*,7b*R*)-7-Methyl-5-oxo-1,2,2a,3,4,7b-hexahydro-6-oxa-4a-aza-cyclopenta[*cd*]indene-4-carboxylic Acid Methyl Ester (24).** With use of the general procedure described above with $SnCl_4$, compound **19** (0.200 g, 0.646 mmol) was converted (via **22**) into **24** (0.153 g, 60%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.49 (dd, 1H, $J$ = 3.3 Hz, $J$ = 10.1 Hz), 4.32 (d, 1H, $J$ = 8.5 Hz), 3.71 (s, 3H), 2.83−2.68 (m, 1H), 2.61−2.51 (m, 1H), 2.50−2.40 (m, 1H), 2.37−2.22 (m, 1H), 2.08−1.97 (m, 1H), 1.96−1.83 (m, 4H), 1.55−1.38 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 172.3, 153.3, 144.7, 119.5, 64.9, 61.9, 53.0, 41.8, 34.7, 34.0, 30.5, 16.6; $[\alpha]_D$ +4.1 (*c* 1.4, $CHCl_3$); mp 89−91 °C; HRMS for $C_{12}H_{15}NO_4$ calculated ($M^+$) 237.100108, found 237.099239.

**(2a*S*,4*S*,7b*R*)-5-Oxo-7-trimethylsilanyl-1,2,2a,3,4,7b-hexahydro-6-oxa-4a-aza-cyclopenta[*cd*]indene-4-carboxylic Acid Methyl Ester (25).** By using the general procedure described above with $SnCl_4$, compound **20** (0.200 g, 0.544 mmol) was converted (via **23**) into **25** (0.125 g, 78%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.53 (dd, 1H, $J$ = 2.8 Hz, $J$ = 10.4 Hz), 4.34 (d, 1H, $J$ = 8.5 Hz), 3.69 (s, 3H), 2.82−2.70 (m, 1H), 2.62−2.50 (m, 2H), 2.40−2.29 (m, 1H), 2.10−2.00 (m, 1H), 1.92 (dd, 1H, $J$ = 1.9 Hz, $J$ = 14.1 Hz), 1.57−1.40 (m, 1H), 0.24 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 172.2, 154.0, 137.1, 65.5, 61.5, 52.8, 41.2, 34.3, 30.7, −1.5; $[\alpha]_D$ +23.9 (*c* 1.10, $CHCl_3$); HRMS for $C_{14}H_{20}NO_4Si$ calculated (M − $H^-$) 294.116162, found 294.114951.

**(2*S*,4*S*)-2-*tert*-Butoxycarbonylamino-4-penta-3,4-dienylpentanedioic Acid Dimethyl Ester (27).** By using the same procedure as for **5**, compound **4** (2.00 g, 7.26 mmol) was

converted into **27** (1.91 g, 77%) with 3,4-pentadien-1-ol-*O*-Tf as the alkylating agent. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.05−5.00 (m, 1H), 5.00−4.90 (m, 1H), 4.63−4.60 (m, 2H), 4.37−4.25 (m, 1H), 3.70 (s, 3H), 3.65 (s, 3H), 2.58−2.45 (m, 1H), 2.02−1.87 (m, 4H), 1.78−1.57 (m, 2H), 1.42 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 208.9, 176.4, 173.2, 155.7, 89.3, 80.4, 75.7, 52.7, 52.6, 52.1, 41.9, 34.8, 32.0, 28.7, 26.0; $[\alpha]_D$ +14 (*c* 1.5, $CHCl_3$); HRMS for $C_{17}H_{28}NO_6$ calculated ($M + H^+$) 342.191663, found 342.193100.

**(2*S*,4*S*)-5-Oxo-4-(penta-3,4-dienyl)pyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (28).** With use of the same procedure as for **19**, compound **27** (0.500 g, 1.46 mmol) was converted into **28** (0.381 g, 84%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.10−5.01 (m, 1H), 4.70−4.62 (m, 2H), 4.49 (t, 1H, $J$ = 7.8 Hz), 3.77 (s, 3H), 2.62−2.45 (m, 2H), 2.20−1.98 (m, 3H), 1.70−1.60 (m, 1H), 1.59−1.40 (m, 10H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 209.0, 175.2, 172.4, 149.8, 89.2, 84.0, 75.8, 57.8, 52.9, 42.2, 30.6, 28.3, 28.2, 26.0; $[\alpha]_D$ −9.2 (*c* 1.5, $CHCl_3$); HRMS for $C_{16}H_{23}NO_5$ calculated ($M^+$) 309.157623, found 309.158038.

**(2a*S*,4*S*,7a*R*,7b*R*)-7-Methylene-5-oxo-octahydro-6-oxa-4a-aza-cyclopenta[*cd*]indene-4-carboxylic Acid Methyl Ester (30).** With use of the general procedure described above with $SnCl_4$, compound **28** (0.380 g, 1.23 mmol) was converted (via **29**) into **30** (0.105 g, 36%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.57 (t, 1H, $J$ = 1.9 Hz), 4.45 (dd, 1H, $J$ = 6.9 Hz, $J$ = 9.9 Hz), 4.06 (t, 1H, $J$ = 2.0 Hz), 3.77 (s, 3H), 3.73 (t, 1H, $J$ = 15.8 Hz), 2.88−2.78 (m, 1H), 2.60−2.43 (m, 2H), 2.35−2.23 (m, 1H), 2.20−2.10 (m, 1H), 2.00−1.88 (m, 1H), 1.82−1.60 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.2, 157.6, 151.4, 88.2, 69.5, 66.2, 53.2, 44.7, 39.0, 38.2, 33.2, 28.2; $[\alpha]_D$ +22.4 (*c* 1.12, $CHCl_3$); mp 129−131 °C; HRMS for $C_{12}H_{15}NO_4$ calculated ($M^+$) 237.100108, found 237.099752.

**(2*S*)-4,4-Dibut-3-enyl-5-oxo-pyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (33).** To a solution of the lactam **31** (0.500 g, 2.06 mmol) in THF (13 mL) at −78 °C was added LiHMDS (2.47 mL, 1.0 N in THF). After the mixture was stirred for 30 min, a solution of 3-butenol-*O*-Tf (0.588 g, 2.88 mmol) in THF (6 mL) at −78 °C was added dropwise via cannula. After the solution was slowly warmed to −35 °C over a period of 3 h, the mixture was quenched with $NH_4Cl$ (2 N), warmed to RT, and concentrated under vacuum. The resulting aqueous solution was extracted with $CH_2Cl_2$, and the combined organic extracts were washed with brine and dried over $Na_2SO_4$. The solvent was removed under vacuum and the resulting oil was purified by flash chromatography (EtOAc/hexanes 10:90 to 15:85). The same procedure was repeated a second time with the same conditions to give **33** (0.433 g, 60%) as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.80−5.69 (m, 2H), 5.05−4.91 (m, 4H), 4.50−4.45 (m, 1H), 3.76 (s, 3H), 2.27−2.20 (m, 1H), 2.10−1.85 (m, 5H), 1.67−1.58 (m, 4H), 1.47 (s, 9H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 177.1, 172.5, 149.7, 138.1, 137.9, 115.9, 115.6, 115.4, 84.1, 56.5, 52.9, 48.8, 36.4, 35.7, 32.0, 28.7, 28.5, 28.3; $[\alpha]_D$ −20.7 (*c* 1.17, $CHCl_3$); FAB/MS for $C_{19}H_{30}NO_5$ calculated ($M + H^+$) 352.2, found 352.2.

**(2*S*)-4,4-Dibut-3-enyl-5-oxo-pyrrolidine-1,2-dicarboxylic Acid Di-*tert*-butyl Ester (34).** With use of the same procedure as for **33**, compound **32** (0.500 g, 1.75 mmol) was converted into **34** (0.393 g, 57%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.80−5.65 (m, 2H), 5.05−4.90 (m, 4H), 4.36 (dd, 1H, $J$ = 5.1 Hz, $J$ = 10.1 Hz), 2.24 (dd, 1H, $J$ = 10.2 Hz, $J$ = 13.8 Hz), 2.10−1.93 (m, 4H), 1.85 (dd, 1H, $J$ = 8.7 Hz, $J$ = 13.8 Hz), 1.70−1.55 (m, 4H), 1.49 (s, 9H), 1.46 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 177.3, 171.0, 149.8, 138.1, 138.0, 115.5, 115.3, 83.7, 82.6, 57.1, 48.7, 36.4, 35.9, 31.8, 28.7, 28.6, 28.3; $[\alpha]_D$ +12 (*c* 1.0, $CHCl_3$); FAB/MS for $C_{22}H_{36}NO_5$ calculated ($M + H^+$) 394.2, found 394.2.

**(2*S*)-5-Oxo-4,4-bis(4-(trimethylsilanyl)but-3-ynyl)pyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (35).** With use of the same procedure as for **33**, compound **31** (0.500 g, 2.06 mmol) was converted into **35** (0.505 g, 50%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.53 (dd, 1H, $J$ = 6.2 Hz, $J$ = 9.5 Hz), 3.78 (s, 3H), 2.41 (dd, 1H, $J$ = 9.6 Hz, $J$ = 13.8 Hz), 2.30−2.20 (m, 4H), 2.02 (dd, 1H, $J$ = 6.1 Hz, $J$ = 13.7 Hz), 1.90−1.78 (m, 4H), 1.50 (s, 9H), 0.13 (s, 18H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 176.0, 172.3, 149.6, 106.5, 106.1, 86.0, 85.8, 84.3, 56.4, 52.9, 48.7, 35.0, 34.7, 32.2, 28.3, 15.5, 15.4, 0.4, 0.2; $[\alpha]_D$ −18.9 (*c* 1.00, $CHCl_3$); HRMS for $C_{25}H_{41}NO_5Si_2$ calculated ($M^+$) 514.242100, found 514.240900.

**(2*S*)-4,4-Dibut-3-ynyl-5-oxo-pyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (36).** To a solution of **35** (0.400 g, 0.814 mmol) and AcOH (0.10 mL, 1.79 mmol) in THF (6 mL) was added a solution of TBAF (1.79 mL, 1.0 N in THF). After being stirred for 1.5 h, the solution was concentrated and the residue was purified by flash chromatography (EtOAc/hexanes 20:80) to give compound **36** (0.240 g, 85%) as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.52 (dd, 1H, $J$ = 5.9 Hz, $J$ = 9.7 Hz), 3.77 (s, 3H), 2.39 (dd, 1H, $J$ = 9.7 Hz, $J$ = 13.9 Hz), 2.30−2.17 (m, 4H), 2.02−1.90 (m, 3H), 1.88−1.80 (m, 4H), 1.48 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 175.9, 172.3, 149.5, 84.3, 83.7, 83.3, 69.7, 69.5, 56.4, 53.0, 48.5, 35.0, 34.8, 32.0, 28.2, 14.1; $[\alpha]_D$ −15.0 (*c* 1.13, $CHCl_3$); FAB/MS for $C_{19}H_{26}NO_5$ calculated ($M + H^+$) 348.2, found 348.1.

**(2*S*)-5-Oxo-4,4-bis(4-(trimethylsilanyl)but-3-ynyl)pyrrolidine-1,2-dicarboxylic Acid Di-*tert*-butyl Ester (37).** With use of the same procedure as for **33**, compound **32** (0.500 g, 1.75 mmol) was converted into **37** (0.476 g, 51%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.39 (dd, 1H, $J$ = 5.0 Hz, $J$ = 9.9 Hz), 2.39 (dd, 1H, $J$ = 9.9 Hz, $J$ = 13.9 Hz), 2.30−2.21 (m, 4H), 1.93 (dd, 1H, $J$ = 5.0 Hz, $J$ = 13.9 Hz), 1.86−1.75 (m, 4H), 1.50 (s, 9H), 1.48 (s, 9H), 0.12 (s, 9H), 0.10 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 176.2, 170.8, 149.7, 106.5, 106.2, 85.9, 85.6, 83.9, 82.8, 57.1, 48.5, 34.9, 34.7, 32.5, 28.7, 28.3, 15.5, 15.3, 0.7, 0.4; $[\alpha]_D$ −15.2 (*c* 1.25, $CHCl_3$); FAB/MS for $C_{28}H_{48}NO_5Si_2$ calculated ($M + H^+$) 534.3, found 534.3.

**(2*S*)-4,4-Dibut-3-ynyl-5-oxo-pyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (38).** With use of the same procedure as for **36**, compound **37** (0.200 g, 0.375 mmol) was converted into **38** (0.131 g, 90%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.35 (dd, 1H, $J$ = 4.9 Hz, $J$ = 10.0 Hz), 2.32 (dd, 1H, $J$ = 10.0 Hz, $J$ = 14.0 Hz), 2.25−2.10 (m, 4H), 1.97−1.85 (m, 3H), 1.84−1.70 (m, 4H), 1.46 (s, 9H), 1.44 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 175.5, 170.2, 149.1, 83.4, 83.1, 82.8, 82.3, 69.1, 68.8, 56.4, 47.8, 34.4, 34.3, 31.3, 28.1, 27.7, 13.5, 13.4; $[\alpha]_D$ −15.1 (*c* 1.00, $CHCl_3$); FAB/MS for $C_{22}H_{32}NO_5$ calculated ($M + H^+$) 390.2, found 390.2.

**(2*S*)-5-Oxo-4,4-bis(pent-3-ynyl)pyrrolidine-1,2-dicarboxylic Acid Di-*tert*-butyl Ester (39).** With use of the same procedure as for **33**, compound **31** (0.500 g, 2.06 mmol) was converted into **39** (0.554 g, 72%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.52−4.45 (m, 1H), 3.75 (s, 3H), 2.34 (dd, 1H, $J$ = 9.8 Hz, $J$ = 3.7 Hz), 2.16−2.10 (m, 4H), 1.96 (dd, 1H, $J$ = 6.1 Hz, $J$ = 13.8 Hz), 1.80−1.70 (m, 10H), 1.46 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 176.3, 172.4, 149.6, 84.1, 56.4, 52.9, 48.5, 35.6, 35.3, 31.7, 28.2, 14.4, 14.2, 3.8; $[\alpha]_D$ −21.1 (*c* 1.00, $CHCl_3$); FAB/MS for $C_{21}H_{30}NO_5$ calculated ($M + H^+$) 376.2, found 376.2.

**(2*S*,3a*S*,6*S*,7a*S*)-3a-But-3-enyl-6-chlorooctahydroindole-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (47).** with use of the general procedure described above with $SnCl_4$, compound **33** (0.200 g, 0.569 mmol) was converted (via **40**) into **47** (0.087 g, 41%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (rotamers) 5.80−5.63 (m, 1H), 5.05−4.87 (m, 2H), 4.30 (d, 0.5H, $J$ = 8.7 Hz), 4.22 (d, 0.5H, $J$ = 8.7 Hz), 3.77−3.57 (m, 4.5H), 3.53−3.45 (m, 0.5H), 2.77−2.65 (m, 0.5H), 2.58−2.46 (m, 0.5H), 2.10−1.57 (m, 8H), 1.55−1.36 (m, 11H), 1.36−1.20 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (rotamers) 174.1, 173.8, 154.4, 153.6, 138.5, 138.4, 115.5, 115.4, 80.8, 80.7, 63.0, 62.7, 58.4, 57.9, 56.5, 56.4, 52.7, 52.6, 42.8, 42.0, 39.6, 39.1, 38.9, 38.8, 34.8, 34.1, 32.7, 32.5, 30.8, 28.9, 28.7, 28.6, 28.4; $[\alpha]_D$ +9.2 (*c* 0.60, $CHCl_3$); HRMS for $C_{16}H_{28}NO_6$ calculated ($M^+$) 371.186336, found 371.186682.

**(2*S*,3a*S*,6*S*,7a*S*)-6-Bromo-3a-but-3-enyloctahydroindole-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (48).** With use of the general procedure described above with

$SnBr_4$, compound **33** (0.200 g, 0.569 mmol) was converted (via **40**) into **48** (0.113 g, 48%). $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ (rotamers) 5.81−5.69 (m, 1H), 5.04−4.93 (m, 2H), 4.32−4.18 (m, 1H), 3.86−3.68 (m, 4H), 3.64−3.58 (m, 0.5H), 3.52−3.47 (m, 0.5H), 2.84−2.79 (m, 0.5H), 2.68−2.59 (m, 0.5), 2.16−1.73 (m, 8H), 1.53−1.21 (m, 12H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ (rotamers) 174.0, 173.7, 154.4, 153.6, 138.5, 138.4, 115.4, 115.3, 80.8, 80.7, 63.3, 63.1, 58.4, 57.9, 52.7, 52.5, 47.5, 47.4, 42.7, 41.9, 40.4, 40.0, 39.0, 38.9, 34.9, 34.2, 33.5, 33.4, 31.9, 28.8, 28.6, 28.5, 28.4; $[\alpha]_D$ +10.9 (*c* 1.05, $CHCl_3$); HRMS for $C_{19}H_{30}NO_4Br$ calculated ($M^+$) 415.135820, found 415.136412.

**(2*S*,3a*S*,6*S*,7a*S*)-3a-But-3-enyl-6-chlorooctahydroindole-1,2-dicarboxylic Acid Di-*tert*-butyl Ester (49).** With use of the general procedure described above with $SnCl_4$, compound **34** (0.200 g, 0.508 mmol) was converted (via **41**) into **49** (0.142 g, 68%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (rotamers) 5.82−5.70 (m, 1H), 5.09−4.83 (m, 2H), 4.20−4.06 (m, 1H), 3.74−3.67 (m, 1.6H), 3.51−3.46 (m, 0.4H), 2.72−2.65 (m, 0.6H), 2.60−2.50 (m, 0.4H), 2.17−1.65 (m, 8H), 1.58−1.38 (m, 20H), 1.35−1.23 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (rotamers) 172.5, 172.3, 154.2, 153.9, 138.6, 138.5, 115.4, 115.2, 81.6, 80.5, 80.3, 62.9, 62.8, 59.2, 59.1, 56.7, 56.5, 42.7, 41.9, 39.5, 39.2, 39.0, 35.2, 34.0, 32.8, 32.7, 30.9, 30.8, 28.8, 28.7, 28.5, 28.4, 28.3; $[\alpha]_D$ −10.6 (*c* 1.33, $CHCl_3$); FAB/MS for $C_{22}H_{37}ClNO_5$ calculated ($M + H^+$) 414.2, found 414.2.

**(2*S*,3a*S*,6*S*,7a*S*)-6-Bromo-3a-but-3-enyloctahydroindole-1,2-dicarboxylic Acid Di-*tert*-butyl Ester (50).** With use of the general procedure described above with $SnBr_4$, compound **34** (0.200 g, 0.508 mmol) was converted (via **41**) into **50** (0.165 g, 71%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (rotamers) 5.81−5.71 (m, 1H), 5.10−4.92 (m, 2H), 4.18−4.05 (m, 1H), 3.86−3.75 (m, 1H), 3.65−3.60 (m, 0.6H), 3.50−3.45 (m, 0.4H), 2.80−2.75 (m, 0.6H), 2.65−2.60 (m, 0.4H), 2.20−1.71 (m, 8H), 2.50−1.37 (m, 20H), 1.31−1.22 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (rotamers) 174.4, 174.2, 154.2, 153.8, 138.6, 138.5, 115.4, 115.3, 81.7, 80.5, 80.3, 63.3, 63.2, 59.2, 59.1, 47.8, 47.5, 42.6, 41.7, 40.4, 40.0, 39.1, 35.1, 34.0, 33.6, 33.5, 31.9, 31.8, 28.8, 28.7, 28.5, 28.4, 28.3; $[\alpha]_D$ −0.84 (*c* 0.95, $CHCl_3$); FAB/MS for $C_{22}H_{37}BrNO_5$ calculated ($M + H^+$) 458.2, found 458.2.

**(2*S*,3a*S*,7a*S*)-3a-But-3-ynyl-6-chloro-2,3,3a,4,5,7a-hexahydroindole-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (51).** With use of the general procedure described above with $SnCl_4$, compound **36** (0.200 g, 0.576 mmol) was converted (via **43**) into **51** (0.134 g, 57%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (rotamers) 6.00 (s, 0.6H), 5.88 (s, 0.4H), 4.38−4.20 (m, 1H), 4.10 (s, 0.6H), 4.05 (s, 0.4H), 3.70 (s, 3H), 2.37−2.26 (m, 2H), 2.21−2.10 (m, 2H), 2.03−1.80 (m, 3H), 1.78−1.60 (m, 4H), 1.47 (s, 4.5H), 1.40 (s, 4.5H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (rotamers) 173.5, 173.1, 154.5, 154.0, 132.7, 132.3, 130.8, 124.5, 124.3, 84.1, 84.0, 81.1, 80.9, 80.8, 69.5, 62.9, 62.8, 62.4, 58.5, 58.0, 57.6, 52.7, 52.5, 42.5, 41.7, 37.4, 37.0, 35.3, 34.7, 34.0, 29.8, 29.3, 28.8, 28.7, 28.1, 28.0, 14.2, 14.0; $[\alpha]_D$ +21.7 (*c* 0.850, $CHCl_3$); HRMS for $C_{19}H_{27}ClNO_4$ calculated ($M + H^+$) 368.162861, found 368.161400.

**(2*S*,3a*S*,7a*S*)-3a-But-3-ynyl-6-chloro-2,3,3a,4,5,7a-hexahydroindole-1,2-dicarboxylic Acid Di-*tert*-butyl Ester (53).** With use of the general procedure described above with $SnCl_4$, compound **38** (0.200 g, 0.513 mmol) was converted (via **45**) into **53** (0.147 g, 63%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (rotamers) 5.96 (s, 0.6H), 5.83 (s, 0.4H), 4.20−4.00 (m, 2H), 2.35−2.25 (m, 2H), 2.20−2.10 (m, 2H), 2.05−1.90 (m, 2H), 1.85−55 (m, 5H), 1.50−1.35 (m, 18H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (rotamers) 171.4, 153.5, 131.7, 131.3, 124.3, 124.1, 83.6, 83.6, 80.9, 80.8, 80.2, 80.1, 68.8, 61.9, 61.8, 58.2, 41.9, 41.0, 37.2, 37.1, 34.4, 33.2, 29.1, 28.7, 28.3, 28.2, 27.8, 27.7, 14.0, 13.5; $[\alpha]_D$ +4.64 (*c* 1.25, $CHCl_3$); FAB/MS for $C_{22}H_{33}ClNO_4$ calculated ($M + H^+$) 410.2, found 410.2.

**(2*S*,4*RS*)-4-But-3-enyl-5-oxo-4-(4-(trimethylsilanyl)but-3-ynyl)pyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (59).** To a solution of (2*S*,4*S*)-4-but-3-enyl-5-oxo-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester (0.500 g, 1.68 mmol) in THF (11 mL) at −78 °C was added LiHMDS (2.02 mL, 1.0 N in THF). After the mixtue was stirred for 30 min, a solution of 4-(trimethylsilyl)but-3-ynol-*O*-Tf (0.600 g, 2.19 mmol) in THF (5 mL) at −78 °C was added dropwise via cannula. After the solution was warmed slowly to −35 °C over a period of 3 h, the mixture was quenched with $NH_4Cl$ (2 N), warmed to RT, and concentrated under vacuum. The resulting aqueous solution was extracted with $CH_2Cl_2$, and the combined organic extracts were washed with brine and dried over $Na_2SO_4$. The solvent was removed under vacuum and the resulting oil was purified by flash chromatography (EtOAc/hexanes 10:90 to 15:85) to give the corresponding 4,4′-bis-alkylated product **59** (0.552 g, 78%) as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (mixture of diastereoisomers) 5.80−5.70 (m, 1H), 5.03−4.90 (m, 2H), 4.55−4.40 (m, 1H), 3.78 (s, 1.5H), 3.77 (s, 1.5H), 2.40−2.18 (m, 3H), 2.18−1.78 (m, 5H), 1.70−1.58 (m, 2H), 1.49 (s, 9H), 0.13 (s, 4.5H), 0.12 (s, 4.5H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (mixture of diastereoisomers) 176.7, 176.5, 172.5, 172.4, 149.7, 137.9, 137.7, 115.7, 115.5, 106.7, 106.3, 85.9, 85.6, 84.2, 84.1, 56.5, 56.4, 52.9, 52.8, 48.7, 35.9, 35.5, 35.4, 35.2, 32.2, 32.0, 28.6, 28.5, 28.3, 15.5, 15.4, 0.4; FAB/MS for $C_{22}H_{36}NO_5Si$ calculated ($M + H^+$) 422.2, found 422.2.

**(2*S*,4*RS*)-4-But-3-enyl-4-but-3-ynyl-5-oxo-pyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (60).** With use of the same procedure as for **36**, compound **59** (0.250 g, 0.593 mmol) was converted into **60** (0.186 g, 90%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (mixture of diastereoisomers) 5.75−5.62 (m, 1H), 5.02−4.89 (m, 2H), 4.51−4.42 (m, 1H), 3.74 (s, 1.5H), 3.73 (s, 1.5H), 2.35−1.75 (m, 9H), 1.65−1.57 (m, 2H), 1.45 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (mixture of diastereoisomers) 176.0, 175.9, 171.8, 149.0, 137.3, 137.1, 115.2, 115.0, 83.7, 83.6, 83.4, 83.0, 69.0, 68.7, 60.2, 55.9, 55.8, 52.4, 48.0, 35.4, 34.8, 34.7, 34.6, 31.5, 31.3, 28.0, 27.8, 27.7, 13.5, 13.4; FAB/MS for $C_{19}H_{28}NO_5$ calculated ($M + H^+$) 350.2, found 350.2.

**(2*S*,3a*S*,6*S*,7a*S*)-3a-But-3-ynyl-6-chlorooctahydroindole-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (61) and (2*S*,3a*S*,7a*S*)-3a-But-3-ynyl-6-chloro-2,3,3a,4,5,-7a-hexahydroindole-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (62).** With use of the general procedure described above with $SnCl_4$, compound **60** (0.180 g, 0.427 mmol) was converted into **61** (0.021 g, 13%, 3 steps) and **62** (0.063 g, 40%, 3 steps) which were separated by flash chromatography.

Data for **61**: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ (rotamers) 4.40−4.25 (m, 1H), 3.78−3.63 (m, 4.6H), 3.59−3.53 (m, 0.4H), 2.77−2.72 (m, 0.6H), 2.21−2.16 (m, 0.4H), 2.09−1.92 (m, 2H), 1.91−1.63 (m, 8H), 1.60−1.30 (m, 11H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ (rotamers) 173.9, 173.7, 154.3, 153.5, 84.2, 80.9, 80.8, 69.5, 69.4, 62.8, 62.5, 58.3, 57.9, 56.3, 56.2, 52.8, 52.6, 42.9, 42.1, 39.4, 39.0, 38.3, 34.7, 34.0, 32.5, 32.4, 30.6, 30.5, 28.9, 28.7, 13.8; $[\alpha]_D$ +1.6 (*c* 1.0, $CHCl_3$); FAB/MS for $C_{19}H_{29}ClNO_4$ calculated ($M + H^+$) 370.2, found 370.2.

Data for **62**: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (rotamers) 6.05 (s, 0.6H), 5.88 (s, 0.4H), 5.85−5.70 (m, 1H), 5.08−4.92 (m, 2H), 4.37−4.21 (m, 1H), 4.13 (s, 0.6H), 4.03 (s, 0.4H), 3.73 (s, 3H), 2.37−2.24 (m, 2H), 2.10−1.83 (m, 3H), 1.80−1.70 (m, 2H), 1.52−1.34 (m, 12H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (rotamers) 173.7, 173.2, 154.6, 154.1, 138.5, 132.8, 132.4, 124.7, 124.5, 115.4, 115.2, 81.0, 80.8, 80.7, 63.0, 62.6, 58.1, 57.6, 52.6, 52.5, 42.5, 41.7, 38.0, 34.9, 34.1, 29.4, 28.9, 28.8, 28.7, 28.5, 28.3; $[\alpha]_D$ +11.4 (*c* 1.00, $CHCl_3$); FAB/MS for $C_{19}H_{29}ClNO_4$ calculated ($M + H^+$) 370.2, found 370.2.

**(2*S*,3a*S*,6*S*,7a*S*)-6-Bromo-3a-(4-(trimethylsilanyl)but-3-ynyl)octahydroindole-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (63).** With use of the general procedure described above with $SnBr_4$, compound **59** (0.250 g, 0.593 mmol) was converted into **63** (0.069 g, 24%, 3 steps), **64**, and **65**.

Data for **63**: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (rotamers) 4.32−4.25 (m, 1H), 3.85−3.70 (m, 4H), 3.68−3.60 (m, 0.6H), 3.52−3.47 (m, 0.4H), 2.88−2.78 (m, 0.6H), 2.68−2.60 (m, 0.4H),

2.30−1.95 (m, 6H), 1.88−1.75 (m, 2H), 1.70−1.63 (m, 1H), 1.56−1.33 (m, 11H), 0.20 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (rotamers) 174.0, 173.7, 154.4, 153.6, 107.0, 106.8, 85.8, 80.9, 80.8, 77.6, 63.5, 63.2, 58.3, 57.9, 52.7, 52.6, 47.3, 47.2, 42.8, 42.1, 40.3, 39.8, 38.5, 38.4, 34.5, 33.7, 33.4, 33.3, 31.7, 28.9, 28.7, 15.2, 0.4; $[\alpha]_D$ +3.0 (*c* 0.50, $CHCl_3$); FAB/MS for $C_{22}H_{37}BrNO_4Si$ calculated (M + $H^+$) 486.2, found 486.2.

**(2*S*,4*RS*)-4-But-3-enyl-5-oxo-4-(pent-3-ynyl)pyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (66).** With use of the same procedure as for **59**, compound (2*S*,4*S*)-4-but-3-enyl-5-oxo-pyrrolidine-1,2-dicarboxylic acid 1-*tert*-butyl ester 2-methyl ester (0.500 g, 1.68 mmol) was converted into **66** (0.476 g, 78%), using 3-pentynol-*O*-Tf as electrophile. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (mixture of diastereoisomers) 5.74−5.65 (m, 1H), 5.01−4.83 (m, 2H), 4.50−4.38 (m, 1H), 3.73 (s, 1.5H), 3.72 (s, 1.5H), 2.32−1.99 (m, 4H), 1.98−1.80 (m, 2H), 1.76−1.65 (m, 5H), 1.63−1.50 (m, 2H), 1.43 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (mixture of diastereoisomers) 176.7, 176.6, 172.5, 172.4, 149.6, 138.0, 137.7, 115.6, 115.4, 84.0, 83.9, 78.5, 78.2, 76.8, 76.6, 56.4, 52.8, 48.6, 36.0, 35.8, 35.6, 35.4, 31.9, 31.7, 28.6, 28.4, 28.2, 14.4, 14.2, 3.8; FAB/MS for $C_{20}H_{30}NO_5$ calculated (M + $H^+$) 364.2, found 364.2.

**(2a*R*,4*S*,7b*R*)-2a-But-3-enyl-7-methyl-5-oxo-1,2,2a,3,4,-7b-hexahydro-6-oxa-4a-aza-cyclopenta[*cd*]indene-4-carboxylic Acid Methyl Ester (67) and (2a*R*,4*S*,7b*R*)-2a-But-3-enyl-7-methyl-5-oxo-1,2,2a,3,4,7b-hexahydro-6-oxa-4a-aza-cyclopenta[*cd*]indene-4-carboxylic Acid Methyl Ester (68).** With use of the general procedure described above with $SnCl_4$, compound **66** (0.400 g, 1.10 mmol) was converted into **67** (0.106 g, 33%) and **68** (0.106 g, 33%, 3 steps), which were separated by flash chromatography.

Data for **67**: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.85−5.75 (m, 1H), 5.08−4.92 (m, 2H), 4.55 (dd, 1H, $J$ = 3.9 Hz, $J$ = 9.9 Hz), 3.95 (s, 1H), 3.74 (s, 3H), 2.55−2.43 (m, 2H), 2.36 (dd, 1H, $J$ = 9.9 Hz, $J$ = 13.9 Hz), 2.17−2.00 (m, 3H), 1.99−1.87 (m, 4H), 1.74−1.62 (m, 2H), 1.57−1.47 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.9, 153.2, 144.7, 138.2, 119.3, 115.5, 70.0, 62.0, 53.0, 52.5, 40.7, 38.3, 37.6, 30.1, 29.0, 16.5; $[\alpha]_D$ +13 (*c* 0.95, $CHCl_3$); FAB/MS for $C_{16}H_{22}NO_4$ calculated (M + $H^+$) 292.2, found 292.1.

Data for **68**: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.88−5.70 (m, 1H), 5.08−4.92 (m, 2H), 4.82 (dd, 1H, $J$ = 1.6 Hz, $J$ = 9.3 Hz), 4.12 (s, 1H), 3.77 (s, 3H), 2.54−2.38 (m, 2H), 2.25 (dd, 1H, $J$ = 2.0 Hz, $J$ = 13.8 Hz), 2.12−2.00 (m, 4H), 1.92 (s, 3H), 1.66−1.50 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 172.5, 151.9, 142.9, 138.2, 117.6, 115.4, 68.8, 63.1, 54.0, 53.0, 42.4, 40.7, 38.7, 35.2, 32.9, 30.1, 30.0, 16.4, 6.0; $[\alpha]_D$ −97 (*c* 0.72, $CHCl_3$); FAB/MS for $C_{16}H_{22}NO_4$ calculated (M + $H^+$) 292.2, found 292.1.

**(2*S*,4*RS*)-5-Oxo-4-pent-3-ynyl-4-(4-(trimethylsilanyl)-but-3-ynyl)pyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (69).** With use of the same procedure as for **59**, compound **19** (0.800 g, 2.59 mmol) was converted into **69** (0.740 g, 66%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (mixture of diastereoisomers) 4.50−4.40 (m, 1H), 3.71 (s, 3H), 2.38−2.25 (m, 1H), 2.23−2.18 (m, 2H), 2.18−2.05 (m, 2H), 1.95−1.88 (m, 1H), 1.80−1.62 (m, 7H), 1.41 (s, 9H), 0.06 (s, 4.5H), 0.04 (s, 0.4H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (mixture of diastereoisomers) 176.2, 176.1, 172.3, 172.2, 149.5, 106.6, 106.2, 85.8, 85.6, 84.1, 78.3, 78.0, 76.9, 76.8, 56.4, 56.3, 52.9, 48.6, 48.5, 35.3, 35.1, 34.9, 34.8, 32.0, 31.9, 28.2, 15.4, 15.3, 14.4, 14.2, 3.8, 0.3; FAB/MS for $C_{23}H_{35}NO_5Si$ calculated (M + $H^+$) 434.2, found 434.2.

**(2*S*,4*RS*)-4-But-3-ynyl-5-oxo-4-pent-3-ynylpyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (70).** With use of the same procedure as for **36**, compound **69** (0.370 g, 0.853 mmol) was converted into **70** (0.293 g, 95%). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (mixture of diastereoisomers) 4.49 (dd, 1H, $J$ = 5.9 Hz, $J$ = 9.5 Hz), 3.75 (s, 3H), 2.40−2.30 (m, 1H), 2.30−2.05 (m, 4H), 2.03−1.90 (m, 2H), 1.84−1.69 (m, 7H), 1.45 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (mixture of diastereoisomers) 176.2, 172.4, 172.3, 149.6, 84.2, 83.9, 83.5, 78.3, 78.0, 77.1, 76.9, 69.6, 69.4, 56.4, 56.3, 53.0, 48.5, 35.4, 35.1, 35.0, 34.9, 32.0, 31.9, 28.2, 14.4, 14.2, 14.1, 14.0, 3.8; FAB/MS for $C_{16}H_{28}NO_6$ calculated (M + $H^+$) 362.2, found 362.1.

**(2a*R*,4*S*,7b*R*)-7-Methyl-5-oxo-2a-(4-(trimethylsilanyl)-but-3-ynyl)-1,2,2a,3,4,7b-hexahydro-6-oxa-4a-aza-cyclopenta[*cd*]indene-4-carboxylic Acid Methyl Ester (71) and (2a*S*,4*S*,7b*R*)-7-Methyl-5-oxo-2a-(4-(trimethylsilanyl)but-3-ynyl)-1,2,2a,3,4,7b-hexahydro-6-oxa-4a-aza-cyclopenta[*cd*]indene-4-carboxylic Acid Methyl Ester (73).** With use of the general procedure described above with $SnBr_4$, compound **69** (0.340 g, 0.853 mmol) was converted into **71** (0.114 g, 37%) and **73** (0.114 g, 37%) which were separated by flash chromatography.

Data for **71**: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.56 (dd, 1H, $J$ = 3.7 Hz, $J$ = 9.9 Hz), 4.00 (s, 1H), 3.73 (s, 3H), 2.54−2.38 (m, 3H), 2.35−2.22 (m, 2H), 2.04 (dd, 1H, $J$ = 3.7 Hz, $J$ = 13.9 Hz), 1.98−1.80 (m, 5H), 1.79−1.58 (m, 2H), 0.14 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.9, 153.2, 144.9, 119.2, 106.4, 86.2, 69.9, 61.9, 53.0, 52.5, 40.5, 39.8, 37.7, 37.3, 29.0, 16.8, 16.5, 0.4; $[\alpha]_D$ +32.2 (*c* 1.00, $CHCl_3$); FAB/MS for $C_{19}H_{28}NO_4Si$ calculated (M + $H^+$) 362.1, found 362.0.

Data for **73**: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.80 (dd, 1H, $J$ = 1.9 Hz, $J$ = 9.4 Hz), 3.78 (s, 3H), 2.51−2.42 (m, 2H), 2.30−2.20 (m, 4H), 2.18−2.03 (m, 2H), 1.91 (s, 3H), 1.79−1.66 (m, 2H), 1.60−1.46 (m, 1H), 0.14 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 172.4, 151.8, 143.1, 117.4, 106.5, 85.9, 68.8, 63.0, 53.9, 53.1, 42.0, 40.4, 37.9, 30.2, 16.7, 16.5, 0.4; $[\alpha]_D$ −71 (*c* 0.90, $CHCl_3$); FAB/MS for $C_{19}H_{28}NO_4Si$ calculated (M + $H^+$) 362.1, found 362.0.

**(2a*S*,4*S*,7b*R*)-2a-But-3-ynyl-7-methyl-5-oxo-1,2,2a,3,4,-7b-hexahydro-6-oxa-4a-aza-cyclopenta[*cd*]indene-4-carboxylic Acid Methyl Ester (72) and (2a*R*,4*S*,7b*R*)-2a-But-3-ynyl-7-methyl-5-oxo-1,2,2a,3,4,7b-hexahydro-6-oxa-4a-aza-cyclopenta[*cd*]indene-4-carboxylic Acid Methyl Ester (74).** With use of the general procedure described above with $SnBr_4$, compound **70** (0.290 g, 0.802 mmol) was converted into **72** (0.086 g, 37%, 3 steps) and **74** (0.086 g, 37%) which were separated by flash chromatography;

Data for **72**: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.58 (dd, 1H, $J$ = 3.7 Hz, $J$ = 10.0 Hz), 3.98 (s, 1H), 3.74 (s, 3H), 2.43−2.30 (m, 3H), 2.25−2.16 (m, 2H), 2.10−1.88 (m, 7H), 1.80−1.50 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.9, 153.2, 145.0, 119.1, 83.8, 70.0, 69.7, 62.0, 53.1, 52.5, 40.2, 37.6, 37.2, 29.0, 16.6, 15.3; $[\alpha]_D$ +28.7 (*c* 1.00, $CHCl_3$); FAB/MS for $C_{16}H_{20}NO_4$ calculated (M + $H^+$) 290.1, found 290.1.

Data for **74**: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.82 (dd, 1H, $J$ = 1.6 Hz, $J$ = 9.4 Hz), 4.15 (s, 1H), 3.79 (s, 3H), 2.55−2.40 (m, 2H), 2.30−2.20 (m, 3H), 2.18−2.08 (m, 2H), 2.01−1.98 (m, 1H), 1.92 (s, 3H), 1.85−1.75 (m, 2H), 1.60−1.50 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 172.4, 151.7, 143.1, 117.2, 83.9, 69.7, 69.5, 68.8, 63.1, 53.9, 53.1, 41.9, 40.4, 37.9, 37.6, 30.1, 16.4, 15.3; $[\alpha]_D$ −93.0 (*c* 1.25, $CHCl_3$); FAB/MS for $C_{16}H_{20}NO_4$ calculated (M + $H^+$) 290.1, found 290.1.

**(2*S*)-5-Oxo-4,4-di(penta-3,4-dienyl)pyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (28a).** To a solution of **28** (0.470 g, 1.52 mmol) in THF (3 mL) at −78 °C was added LiHMDS (1.67 mL, 1.0 N in THF). After the mixture was stirred for 45 min, a solution of 3,4-dienylpentanol-*O*-Tf (0.427 g, 1.975 mmol) in THF (2 mL) at −78 °C was added dropwise via cannula. After being stirred at −78 °C for 30 min, the reaction was warmed to RT and quenched with saturated aqueous $NH_4Cl$. The resulting mixture was extracted with EtOAc and the combined organic extracts were washed with brine and dried over $Na_2SO_4$. The solvent was removed under vacuum and the resulting oil was purified by flash chromatography (EtOAc/hexanes 10:90) to give the corresponding 4,4′-bis-alkylated product **29a** (0.455 g, 80%) as a colorless oil. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 5.11 (m, 2H), 5.68 (m, 4H), 4.51 (dd, 1H, $J$ = 6.3 Hz, $J$ = 9.5 Hz), 3.78 (s, 3H), 2.23 (dd, 1H, $J$ = 9.5 Hz, $J$ = 13.6 Hz), 2.17−1.85 (m, 5H), 2.65 (m, 4H), 1.49 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 208.2, 208.1, 176.5, 171.9, 149.1, 89.3, 89.0, 83.5, 75.7, 75.5, 67.8, 55.9, 52.3, 48.1, 35.6, 35.0, 31.5, 27.7, 25.4, 22.4; $[\alpha]_D$ −11.6 (*c* 1.00,

$CHCl_3$); ESI/MS for $C_{21}H_{29}NO_5$ calculated (M + $H^+$) 376.2, found 376.2.

**(2*S*,4*RS*)-4-But-3-enyl-5-oxo-4-(penta-3,4-dienyl)pyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (28b).** To a solution of **28** (0.235 g, 0.76 mmol) in THF (3 mL) at −78 °C was added LiHMDS (0.83 mL, 1.0 N in THF). After the mixture was stirred for 45 min, a solution of 3-buten-1-ol-*O*-Tf (0.273 g, 0.99 mmol) in THF (3 mL) at −78 °C was added dropwise via cannula. After being stirred at −78 °C for 30 min, the reaction was warmed to RT and quenched with saturated aqueous $NH_4Cl$. The resulting mixture was extracted with EtOAc and the combined organic extracts were washed with brine and dried over $Na_2SO_4$. The solvent was removed under vacuum and the resulting oil was purified by flash chromatography (EtOAc/hexanes 15:85) to give the corresponding 4,4′-bis-alkylated product **29b** (0.209 g, 75%) as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ (mixture of diastereomers) 5.77 (m, 1H), 5.12−4.83 (m, 3H), 4.61 (m, 2H), 4.45 (m, 1H), 3.76 (s, 3H), 2.20 (dd, 1H, $J$ = 9.6 Hz, $J$ = 13.6 Hz), 2.17−1.80 (m, 5H), 1.61 (m, 4H), 1.44 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (mixture of diastereomers) 208.17, 176.5, 171.9, 149.1, 137.5, 137.3, 115.0, 114.8, 89.3, 89.1, 83.5, 75.6, 75.5, 55.9, 52.3, 48.1, 35.8, 35.6, 35.1, 31.5, 28.1, 28.0, 27.7, 22.6, 22.4; ESI/MS for $C_{20}H_{29}NO_5$ calculated (M + $H^+$) 364.2, found 364.2.

**(2*S*,4*RS*)-4-But-3-ynyl-5-oxo-4-(penta-3,4-dienyl)pyrrolidine-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (28d).** To a solution of **28** (0.247 g, 0.80 mmol) in THF (3 mL) at −78 °C was added LiHMDS (0.88 mL, 1.0 N in THF). After the mixture was stirred for 45 min, a solution of 3-butyn-1-ol-*O*-Tf (0.285 g, 1.04 mmol) in THF (3 mL) at −78 °C was added dropwise via cannula. After being stirred at −78 °C for 30 min, the reaction was warmed to RT and quenched with saturated aqueous $NH_4Cl$. The resulting mixture was extracted with EtOAc and the combined organic extracts were washed with brine and dried over $Na_2SO_4$. The solvent was removed under vacuum and the resulting oil was treated directly with TBAF (0.50 mL, 1 M in THF) and allowed to stand at RT for 15 min. The mixture was then concentrated and purified by flash chromatography (EtOAc/hexanes 18:82) to give the corresponding 4,4′-bis-alkylated product **29d** (0.153 g, 53%) as a pale yellow oil. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ (mixture of diastereomers) 5.11 (m, 1H), 4.70 (m, 2H), 4.54 (m, 1H), 3.77 and 3.75 (2s, 3H), 2.25 (m, 3H), 2.17−1.77 (m, 6H), 1.63 (m, 2H), 1.49 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (mixture of diastereomers) 208.2, 175.9, 175.8, 171.8, 149.0, 105.0, 89.1, 88.9, 83.7, 83.6, 83.4, 83.0, 75.7, 75.6, 69.0, 68.8, 55.9, 52.4, 48.0, 35.2, 34.8, 34.7, 34.5, 31.6, 31.4, 27.7, 22.5, 22.3, 13.6; ESI/MS for $C_{20}H_{27}NO_5$ calculated (M + $H^+$) 361.2, found 362.2.

**(2a*S*,4*S*,7a*S*,7b*R*)-7-Methylene-5-oxo-2a-penta-3,4-dienyloctahydro-6-oxa-4a-aza-cyclopenta[*cd*]indene-4-carboxylic Acid Methyl Ester (30a).** With use of the general procedure described above with $SnCl_4$, **28a** (0.200 g, 0.53 mmol) was converted (via **29a**) into **30a**. $^1$H NMR of the crude residue indicated the presence of the minor diastereomer of **30a** in ca. 1:10 mol ratio (which was not isolated). The crude oil obtained was purified by flash chromatography (EtOAc/hexanes 25:75) to give **30a** (42%, 3 steps) as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ (rotamers) 5.12 (m, 1H), 4.72 (m, 2H), 4.58 (t, 1H, $J$ = 1.9 Hz), 4.51 (dd, 1H, $J$ = 6.9 Hz, $J$ = 10.1), 4.07 (t, 1H, $J$ = 2.0 Hz), 3.78 (s, 3H), 3.27 (d, 1H, $J$ = 11.1 Hz), 2.65 (m, 1H), 2.34 (dd, 1H, $J$ = 6.9 Hz, $J$ = 13.4 Hz), 2.15 (m, 2H), 2.10−1.93 (m, 5H), 1.79−1.60 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (rotamers) 208.1, 170.8, 157.0, 150.9, 89.2, 87.7, 73.1, 65.1, 52.7, 49.5, 44.9, 43.0, 39.3, 38.3, 27.1, 23.6; $[\alpha]_D$ +28 (*c* 1.00, $CHCl_3$); ESI/MS calculated for $C_{17}H_{21}NO_4$ calculated (M + $H^+$) 304.1, found 304.1.

Hydrolysis and re-esterification of **30a** was carried out as follows: A solution of **30a** (0.030 g, 0.099 mmol) in 2 mL of 1:1 MeCN:$H_2O$ was cooled to 0 °C, treated with (0.016 g, 0.398 mmol) LiOH·$H_2O$, and monitored by TLC for completion. After being strirred 1.5 h at 0 °C the reaction was diluted with $H_2O$ and washed with $Et_2O$. The aqueous layer was then carefully acidified to pH <4 with 1 M HCl, extracted with EtOAc, dried over $Na_2SO_4$, and evaporated to give the corresponding carboxylic acid as a white solid (0.028 g, 97%). This material was then taken up in 1.5 mL of 2:1 PhMe:MeOH and treated with $TMSCHN_2$ (2.0 M in) until a yellow color persisted. After the mixture was stirred for 30 min, the volatiles were removed under vacuum to afford the ester whose spectral data were identical in every respect to those of **30a**.

**(2a*S*,4*S*,7a*S*,7b*R*)-2a-But-3-enyl-7-methylene-5-oxo-octahydro-6-oxa-4a-aza-cyclopenta[*cd*]indene-4-carboxylic Acid Methyl Ester (30b).** With use of the general procedure described above with $SnCl_4$, **28b** (0.065 g, 0.19 mmol) was converted (via **29b**) into **30b** (0.018 g, 33% over 3 steps). $^1$H NMR of the crude residue also revealed the presence of the minor diastereomer of **30b** in ca. 1:10 mol ratio (which was not isolated). $^1$H NMR of **30b** (300 MHz, $CDCl_3$) $\delta$ (rotamers) 5.82 (m, 1H), 5.10 (m, 2H), 4.60 (t, 1H, $J$ = 2.0 Hz), 4.53 (dd, 1H, $J$ = 7.0 Hz, $J$ = 10.1 Hz), 4.12 (t, 1H, $J$ = 2.0 Hz), 3.82 (s, 3H), 3.29 (d, 1H, $J$ = 11.1 Hz), 2.67 (m, 1H), 2.40 (m, 1H), 2.30−2.20 (m, 6H), 1.80 (m, 1H), 1.63 (m, 4H); $[\alpha]_D$ +34 (*c* 1.00, $CHCl_3$); ESI/MS calculated for $C_{16}H_{21}NO_4$ (M + $H^+$) 292.1, found 292.1.

**(2a*S*,4*S*,7a*S*,7b*R*)-2a-But-3-ynyl-7-methylene-5-oxo-octahydro-6-oxa-4a-aza-cyclopenta[*cd*]indene-4-carboxylic Acid Methyl Ester (30d) and (2*S*,3a*R*,7a*R*)-6-Chloro-3a-penta-3,4-dienyl-2,3,3a,4,5,7a-hexahydroindole-1,2-dicarboxylic Acid 1-*tert*-Butyl Ester 2-Methyl Ester (30e).** With use of the general procedure described above with $SnCl_4$, compound **28d** (0.130 g, 0.36 mmol) was converted into **30d** (0.017 g, 17% yield over 3 steps) and **30e** (0.035, 35% yield) which were separated by flash chromatography.

Data for **30d**: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (rotamers) 4.62 (m, 1H), 4.55 (dd, 1H), 4.10 (m, 1H), 3.82(s, 3H), 3.30 (d, 1H), 2.67 (m, 1H), 2.42 (m, 1H), 2.31 (m, 2H), 2.21 (m, 2H), 2.05 (m, 3H), 1.89−1.71 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (rotamers) 171.3, 157.3, 151.4, 88.6, 83.7, 73.7, 69.7, 65.5, 53.4, 50.2, 45.4, 43.2, 39.4, 38.4, 27.7, 15.2; $[\alpha]_D$ +41 (*c* 1.00, $CHCl_3$); ESI/MS calculated for $C_{16}H_{19}NO_4$ (M + $H^+$) 290.1, found 290.1.

Data for **30e**: $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ (rotamers) 6.01 and 5.82 (2s, 1H), 5.13 (m, 1H), 4.61 (m, 2H), 4.38−4.22 (m, 1H), 4.16 and 4.05 (2s, 1H), 3.73 (s, 3H), 2.35 (m, 2H), 2.06−1.65 (m, 7H), 1.58−1.39 (m, 10H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ (rotamers) 208.7, 173.2, 132.4, 124.8, 124.7, 124.5, 90.1, 80.9, 70.0, 62.6, 58.1, 57.7, 52.7, 52.6, 41.7, 38.0, 37.8, 34.9, 29.4, 28.9, 28.7, 28.6, 23.1; $[\alpha]_D$ +5 (*c* 1.00, $CHCl_3$); ESI/MS calculated for $C_{20}H_{28}ClNO_4$ (M + $H^+$) 381.2, found 381.2.

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**Note Added after ASAP Publication.** The descriptions of compounds **33** and **34** and **33**−**39** were incorrect in the paragraph describing Scheme 5 in the version published ASAP May 20, 2005; the corrected version was published May 27, 2005.

**Supporting Information Available:** Selected NMR spectra and X-ray crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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