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Creation of quaternary stereocenters by the addition of allyltributyltin to chiral cyclic *N*-acyliminium ions

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Abstract

5,5-Disubstituted pyrrolidinones and 5-substituted pyrrolidinones were obtained with moderate to good diastereoisomeric excess through the *cis* addition of allyltributyltin and triethylsilane, respectively, to the 4-OTBS group in the *N*-acyliminium ion prepared from the corresponding 5-hydroxy lactams. Cyclization of an *N*-allyl-5-propargyl pyrrolidinone and *N*-allyl-5-allyl-5-substituted pyrrolidinones using Grubbs' catalyst led to the preparation of a dehydropyrrolizinone and dehydroindolizinones containing a quaternary stereocenter. © 2000 Elsevier Science Ltd. All rights reserved.

1. Introduction

Despite the great interest in the asymmetric construction of molecules with quaternary stereocenters,[1,2] there are few methods available to prepare compounds containing four different non-hydrogen substituents at the α-nitrogen position of 5- and 6-membered nitrogen heterocycles. The methodology developed by Meyers and Burgess[3] afforded GABA analogues and 2,2-disubstituted pyrrolidines with good diastereoselectivities. The alkylation of tricyclic *N*,*O*-acetals with some organometallic reagents was utilized for the synthesis of the core ring of the alkaloid FR901483.[4] The construction of α-nitrogen spiro rings through the reduction of hydroxy amides derived from 5- and 6-membered imides was successfully achieved by Speckamp and Schoemaker[5] for the synthesis of perhydrohistrionicotoxin.

The addition of Grignard reagents to chiral imide derivatives from tartaric acid, followed by the reduction with Et_3SiH mediated by $BF_3 \cdot OEt_2$, has been extensively studied by Yoda et al.[6–10] and applied in the synthesis of some indolizidine alkaloids. In spite of high levels of diastereoselection observed in the reduction of *N*-acyliminium ion derived from tartaric and malic acids,[11] to the best of our knowledge, efforts regarding the creation of a quaternary stereocenter through the addition of a second carbon nucleophile have not been reported.

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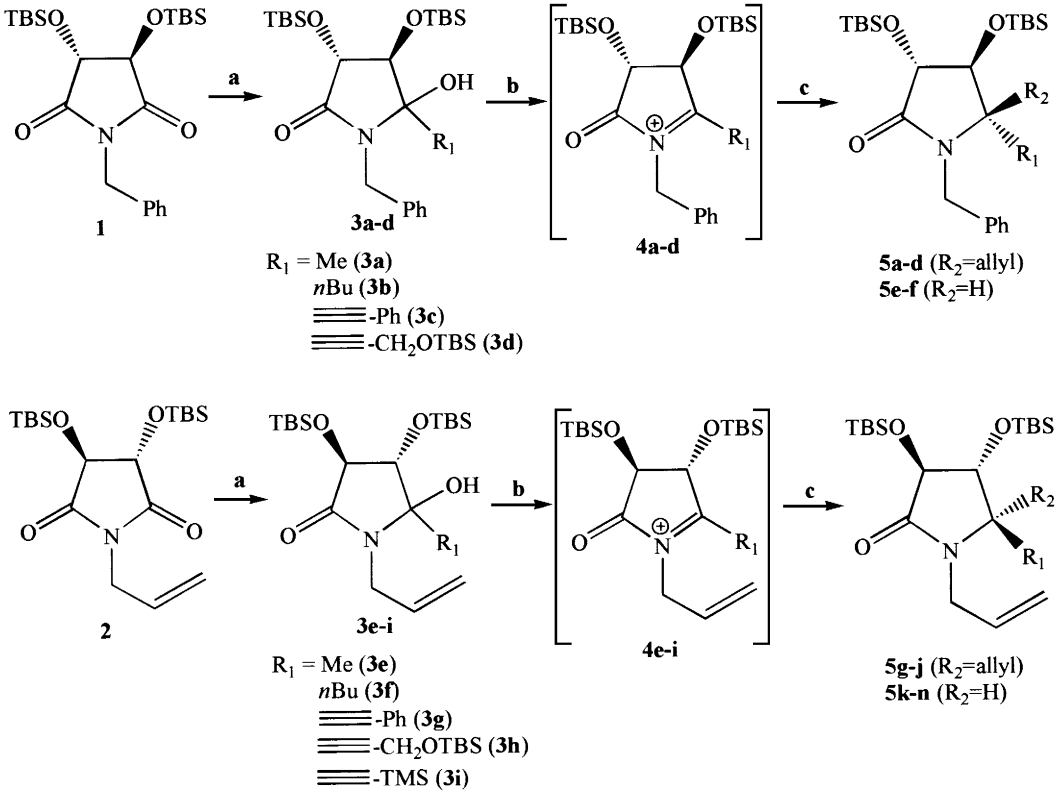
We report here the results for the addition of organolithium species to chiral imide derivatives from tartaric acid and the transformation of the resulting α-hydroxy quaternary lactams in highly functionalized 5,5-disubstituted pyrrolidinones.[12] For this purpose we employed $BF_3 \cdot OEt_2$ to promote the formation of *N*-acyliminium ions[13,14] and allyltributyltin as the nucleophile. We also carried out a systematic study on the reduction of α-hydroxy quaternary pyrrolidinones to afford 5-acetylenic and 5-alkylated lactams. Our results include the synthesis of a dehydropyrrolizinone ring and some dehydroindolizinones containing an α-nitrogen quaternary stereocenter by ring-closing metathesis (RCM) of olefins[15,16] and an enyne[17,18] promoted by Grubbs' catalyst.

2. Results and discussion

Imides **1** and **2** were readily obtained from tartaric acid in 63 and 83% yields, respectively, after five steps. Addition of organolithium to chiral imides **1** and **2** in THF at −78°C afforded α-hydroxy lactams **3a–i** as diastereoisomeric mixtures, which were used in the next step without purification. The addition of allyltributyltin, mediated by $BF_3 \cdot OEt_2$, afforded 5,5-disubstituted pyrrolidinones **5a–d** and **5g–j** in 36–66% yields from imides **1** and **2** (Scheme 1). Using the same procedure, the addition of triethylsilane mediated by $BF_3 \cdot OEt_2$ afforded 5-substituted pyrrolidinones **5e–f** and **5k–n** in 50–66% yields after two steps (Scheme 1).

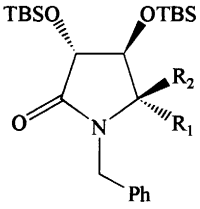
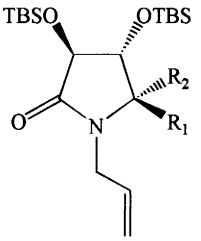


Scheme 1. (a) R_1–Li, THF, −78°C; (b) $BF_3 \cdot OEt_2$, CH_2Cl_2, −78°C; (c) allyltributyltin (R_2=allyl) or Et_3SiH (R_2=H), −78°C to 0°C

The addition of methyllithium, butyllithium, and lithium acetylides to imides **1** and **2**, followed by allyltributyltin to the corresponding *N*-acyliminium ion **4**, resulted in 5,5-disubstituted pyrrolidinones

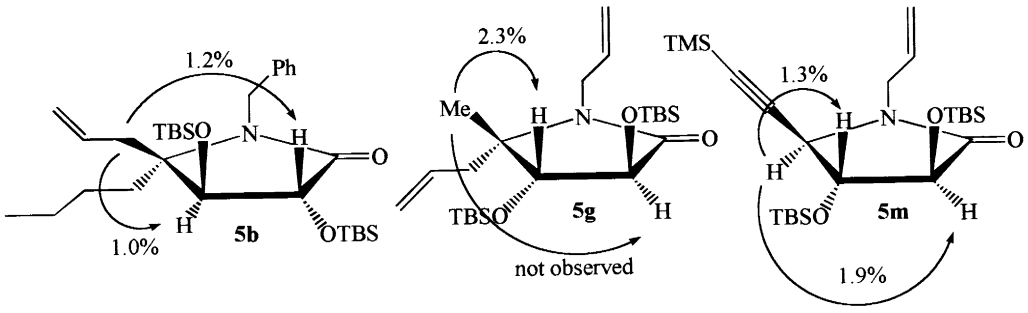
5a–d and **5g–j** (Table 1, entries 1–4 and 7–10) in good yields and moderate diastereoselectivities, except for *n*-butyllithium which afforded a single diastereoisomer (entries 2 and 8). The addition of *n*-butyllithium to imides **1** and **2**, followed by reduction, afforded 5-butyl pyrrolidinones **5e** and **5k** in 89 and 80% d.e., respectively (entries 5 and 11, Table 1), while the addition of lithium acetylides afforded 5-acetylenic pyrrolidinones (entries 6 and 12–14) with excellent diastereoselectivity and moderate to good yields.

Table 1
Addition of allyltributyltin and Et_3SiH to chiral cyclic *N*-acyliminium ions **4a–i**

Entry	Major Product		R_1	R_2	J_{trans} (Hz)	Yield[a]	d.e.[b]
1		**5a**	Me	allyl	$J_{3,4}$=7.1	45%	50%
2		**5b**	Bu	allyl	$J_{3,4}$=6.6	65%	>95%
3		**5c**	≡-Ph	allyl	$J_{3,4}$=7.8	56%	60%
4		**5d**	≡-CH_2OTBS	allyl	$J_{3,4}$=7.7	36%	67%
5		**5e**	Bu	H	$J_{3,4}$=$J_{4,5}$=2.0	61%	89%
6		**5f**	≡-Ph	H	$J_{3,4}$=6.4; $J_{4,5}$=6.1	62%	>95%
7		**5g**	Me	allyl	$J_{3,4}$=7.3	65%	33%
8		**5h**	Bu	allyl	$J_{3,4}$=7.0	66%	>95%
9		**5i**	≡-Ph	allyl	$J_{3,4}$=7.8	63%	44%
10		**5j**	≡-CH_2OTBS	allyl	$J_{3,4}$=7.7	48%	46%
11		**5k**	Bu	H	$J_{3,4}$=$J_{4,5}$=2.4	60%	80%
12		**5l**	≡-Ph	H	$J_{3,4}$=$J_{4,5}$=6.3	66%	>95%
13		**5m**	≡-TMS	H	$J_{3,4}$=6.6; $J_{4,5}$=6.3	50%	>95%
14		**5n**	≡-CH_2OTBS	H	$J_{3,4}$=6.2; $J_{4,5}$=5.6	52%	>95%

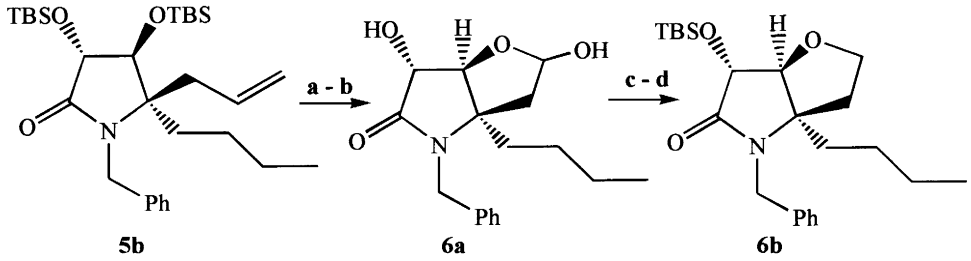
[a] Yields (2 steps) are reported after purification of the crude mixture by column chromatography on silica gel; [b] Diastereomeric ratio determined by ^{1}H-NMR (300 MHz).

The stereochemical assignment of 5,5-disubstituted pyrrolidinones **5a–d** and **5g–j** was carried out using NOE studies, as illustrated for compound **5b** in Scheme 2: irradiation of one of the allylic hydrogens led to a 1.0% increment in the H4 signal and a 1.2% increment in the H3 signal. Accordingly, irradiation of the methyl group at C5 of **5g** led to a 2.3% increment in the H4 signal and no increment in the H3 signal.



Scheme 2.

The *cis* relative stereochemistry between the OTBS group at C4 and the allyl group at C5 in **5b** was unambiguously established after its conversion to **6b**, as depicted in Scheme 3.



5b **6a** **6b**

Scheme 3. (a) **(**i) O_3/O_2, MeOH, −78°C; (ii) DMS, 12 h, rt; (b) HF/MeCN, 5 h, rt (80%, two steps); (c) Et_3SiH, $BF_3 \cdot OEt_2$, CH_2Cl_2, −78°C; (d) TBSCl, im., DMF, rt, 5 h (62%, two steps)

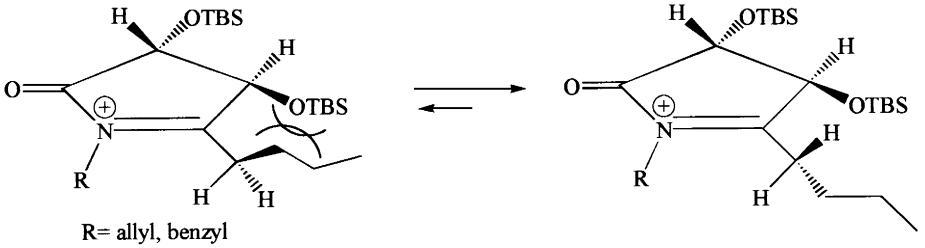
The *trans* stereochemistry of 5-butyl pyrrolidinones **5e** and **5k** was assigned according to the observed vicinal coupling constants ($J_{4,5}$=2.0 and 2.4 Hz, respectively), as described by Yoda et al.[8] The stereochemistry for compounds **5f** and **5l**–**n** was assigned from NOE studies which provided higher increments in the H3 signal rather than in the H4 signal upon irradiation of H5, as depicted for **5m** (Scheme 2). The unexpected increase in the $J_{3,4}$ and $J_{4,5}$ values observed for compounds **5f** and **5l**–**n** was assigned to a conformational change in the pyrrolidinone ring due to the relief, in these cases, of the steric interactions between the nitrogen protecting group and the *n*-butyl side chain present in **5e** and **5k**. Such conformational change is supported by the deshielding effect observed for H3, H4 and H5 signals in 5-*trans*-acetylenic pyrrolidinones (**5f** and **5l**–**n**) relative to 5-*trans*-butyl pyrrolidinones (**5e** and **5k**). Additionally, H4 is less shielded than H3 in **5f** and **5l**–**n**, in contrast to the behavior observed for **5e** and **5k**. Accordingly, the hydrogenation of **5l** ($J_{3,4}=J_{4,5}$=6.3 Hz) afforded the corresponding perhydrolactam with coupling constants for the carbinolic protons ($J_{3,4}=J_{4,5}$=2.4 Hz) in the same range as observed for **5e** and **5k**.

Several studies in the literature report on the preferential *cis* addition of nucleophiles to *N*-acyliminium ions **4**, revealing that the stereochemical outcome is not ruled by steric effects. Although the reasons for this unexpected approach remain unknown,[8] a stereoelectronic effect analogous to the one proposed by Cieplak[19] and others[20,21] may not be ruled out at this moment.[22]

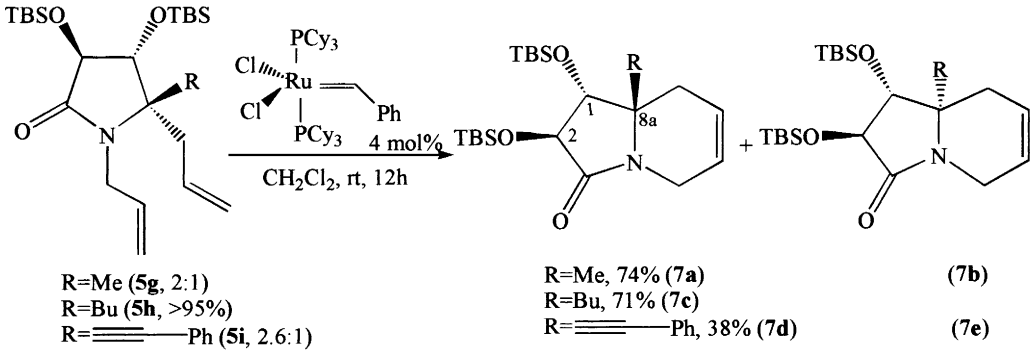
We have observed the same stereochemical preference in the addition of triethylsilane and allyltributyltin to *N*-acyliminium ions **4a**–**i**. A comparison among the products with a quaternary stereocenter at C5 showed that best selectivities were attained with 5-*n*-butyl-substituted *N*-acyliminium ions, in contrast to 5-methyl and 5-acetylenic substituted ones. Additionally, *N*-benzyl protected *N*-acyliminium ions were more selective than the *N*-allyl protected ones. These results led us to invoke the allylic $A^{1,3}$ strain involving the substituent at C5 and the nitrogen protecting group as a control element favoring the *cis* approach of the nucleophile in **4b** and **4f** due to an additional steric hindrance of the *si* face, as depicted in Scheme 4. In cases where this effect is less important, the *cis* approach of the nucleophile occurred with lower diastereoselection.

Good to excellent diastereoselection was observed in the reduction of 5-acetylenic *N*-acyliminium ions with the sterically more demanding triethylsilane, in accordance with previous reports in the literature.[6–11]

N-Allyl-5-allyl pyrrolidinones **5g**–**i** were submitted to ring-closing metathesis with Grubbs' catalyst (4 mol%) at room temperature to afford dehydroindolizinones **7a**–**e** in moderate to good yields (Scheme 5). The stereochemistry of the major diastereoisomer **7a** obtained from a 2:1 mixture of **5g** and its C5 epimer was confirmed by NOE experiments: the irradiation of the angular methyl group at C8a led to a 2.0% increment in the H1 signal and no increment in the H2 signal.

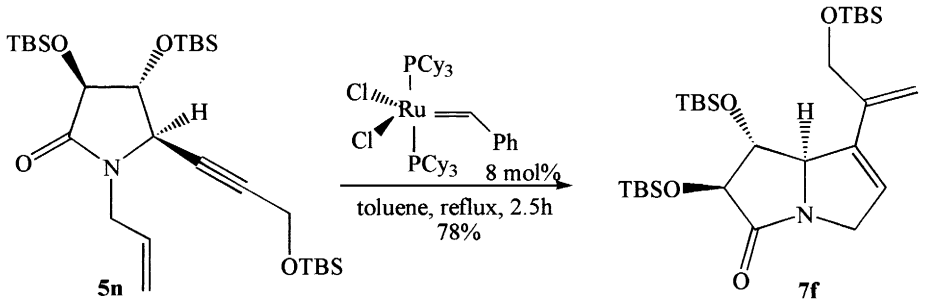


Scheme 4.



Scheme 5.

The enyne metathesis protocol was applied to **5n** to afford the highly functionalized dehydropyrrolizinone **7f** in 78% yield as a single stereoisomer (Scheme 6).



Scheme 6.

However, when pyrrolidinone **5l** was submitted to the same conditions the starting material was recovered in almost quantitative yield, probably due to severe steric strain which develops in the formation of the intermediate metalacycle required in the reaction mechanism.

3. Conclusion

The $BF_3 \cdot OEt_2$ promoted addition of allyltributyltin to α-hydroxy lactams **3a–i**, prepared from the reaction of alkyl or alkynyl lithium reagents and imides **1** and **2**, occurred *cis* to the 4-OTBS group to afford 5,5-disubstituted pyrrolidinones **5a**, **5c–d** and **5g**, **5i–j** with moderate diastereoisomeric excess (33–67%), except for **5b** and **5h** where a single diastereoisomer was formed (d.e. >95%). The same stereochemical trend was observed in the triethylsilane reduction of **3b**, **3c**, and **3f–i** mediated by $BF_3 \cdot OEt_2$, in accordance with previous reports in the literature.[6–11] The relative stereochemistry of

the major pyrrolidinones was assigned by ^{1}H NMR spectroscopy (NOE studies) and for **5b** upon its conversion to the corresponding oxa-azabicyclo[3.3.0]octan-3-one **6b**. *N*-Allyl-5,5-disubstituted pyrrolidinones **5g–i** and enyne **5n** were submitted to ring-closing metathesis with Grubbs' catalyst to afford the corresponding bicyclic compounds **7a–f** in good yields.

Studies are underway to synthesize 5,5-disubstituted pyrrolidinones derived from malic acid in order to investigate their utilization in the total synthesis of natural compounds.

4. Experimental

4.1. General

All solvents and reagents were purchased from commercial suppliers and used as received, unless otherwise indicated. Imide **1** was synthesized from L-(+)-tartaric acid as indicated in the literature.[7] Imide **2** was synthesized from D-(−)-tartaric acid as a colorless oil, in 83% overall yield. Commercial solutions of *n*BuLi (2.5 M in hexane) and MeLi (1.0 M in ether) were employed. Tetrahydrofuran (THF) and toluene were distilled from Na–benzophenone ketyl. Dichloromethane was distilled from calcium hydride. All reactions were performed under a positive argon pressure. The normal processing of organic extracts consisted of drying over $MgSO_4$, filtration and concentration with a rotary evaporator. ^{1}H NMR and ^{13}C NMR data were recorded on a Varian Gemini 300, Bruker AC 300P (7.05 T) or Varian Inova (11.7 T) spectrometer. Chemical shifts are reported in δ ppm relative to $(CH_3)_4Si$ for ^{1}H and $CDCl_3$ for ^{13}C NMR. Coupling constants *J* are reported in hertz. IR spectra were obtained on Nicolet Impact 410 FT (film and KBr). High resolution mass spectra (HRMS) were measured on a VG Autospec-Micromass spectrometer. Chromatographic separations were performed using 70–230 or 230–400 mesh (E. Merck) silica gel. Thin-layer chromatography was carried out on Macherey–Nagel precoated silica plates (0.25 mm layer thickness). GC analyses were performed with a HP-5890 chromatograph with a HP-5 (30 m×0.53 mm×1.3 μm) column. Optical rotations were measured at 25°C with a Polamat A instrument at the mercury line and converted to the values for the sodium D line (rotation at the Hg line=1.17 543×rotation at the Na line).

*4.2. General procedure for the addition of organolithium to imides **1** and **2***

*4.2.1. Synthesis of hydroxylactams **3a–i***

To a solution of organolithium reagent (0.7 mmol) in THF (1 mL) at −78°C was added a solution of imide **1** or **2** (0.35 mmol) in THF (1 mL) dropwise. After complete consumption of the imide, the reaction was quenched with H_2O (1 mL) and the mixture was allowed to stir for 10 min at room temperature, when it was diluted with CH_2Cl_2 (10 mL) and washed with brine (5 mL). The organic phase was dried over $MgSO_4$, filtered, and the solvent was removed under reduced pressure. The resultant oil was employed in the next step without further purification.

*4.2.2. General procedure for the synthesis of 5,5-disubstituted pyrrolidinones **5a–d** and **5g–j***

To a solution of hydroxylactam **3a–i** (0.35 mmol) in CH_2Cl_2 (3.5 mL), under an argon atmosphere at −78°C, was added allyltributyltin (0.42 mL, 1.4 mmol) followed by $BF_3 \cdot OEt_2$ (0.08 mL, 0.7 mmol) dropwise. Stirring was continued for 15 min at −78°C, followed by 2 h at 0°C. The reaction was quenched with 10% aq. KF solution (2 mL) and allowed to stir 1 h at rt. The mixture was diluted with CH_2Cl_2 (10 mL) and washed with brine (5 mL), dried over $MgSO_4$, and the solvent was removed under reduced

pressure. Purification by column chromatography on silica gel (4% EtOAc/hexane, v/v) afforded 5,5-disubstituted pyrrolidinones **5a**–**d** and **5g**–**j** as colorless oils (Table 1).

*4.2.2.1. (3*R,*4*S,*5*R*)-3,4-Bis[(*tert-*butyldimethylsilyl)oxy]-1-benzyl-5-allyl-5-methyl-2-pyrrolidinone.* Colorless oil; 45% yield as a 3:1 mixture. Data for the major isomer **5a**: ^{1}H NMR (300 MHz): 0.09 (s, 3H), 0.15 (s, 3H), 0.18 (s, 3H), 0.24 (s, 3H), 0.93 (s, 9H), 0.95 (s, 9H), 1.12 (s, 3H), 2.21 (dd, *J*=7.3 and 14.2, 1H), 2.36 (dd, *J*=7.3 and 14.2, 1H), 3.90 (d, *J*=7.1, 1H), 4.16 (d, *J*=15.4, 1H), 4.36 (d, *J*=7.1, 1H), 4.72 (d, *J*=15.4, 1H), 4.95 (dd, *J*=2.0 and 17.3, 1H), 5.04 (dd, *J*=2.0 and 10.3, 1H), 5.72 (m, 1H), 7.27 (m, 5H). ^{13}C NMR (75.5 MHz): −4.7, −4.3, −3.8, −3.7, 17.9, 18.4, 25.8, 25.9, 26.0, 39.3, 43.2, 64.3, 76.4, 83.0, 119.3, 127.1, 127.8, 128.4, 133.6, 138.6, 171.6. IR (film, cm^{-1}): 3076, 3030, 2954, 2929, 2856, 1709. HRMS $C_{27}H_{47}NO_3Si_2$ ($M^+-C_4H_9$, calcd): 432.23903; ($M^+-C_4H_9$, found): 432.23903.

*4.2.2.2. (3*R,*4*S,*5*R*)-3,4-Bis[(*tert-*butyldimethylsilyl)oxy]-1-benzyl-5-allyl-5-*n*-butyl-2-pyrrolidinone **5b**.* Colorless oil; 65% yield. ^{1}H NMR (300 MHz): 0.09 (s, 3H), 0.15 (s, 3H), 0.19 (s, 3H), 0.24 (s, 3H), 0.69 (t, *J*=7.0, 3H), 0.92 (s, 9H), 0.95 (s, 9H), 0.87–0.96 (m, 4H), 1.40–1.55 (m, 2H), 2.15 (dd, *J*=7.7 and 14.3, 1H), 2.43 (dd, *J*=6.6 and 14.3, 1H), 4.05 (d, *J*=6.6, 1H), 4.19 (d, *J*=15.4, 1H), 4.36 (d, *J*=6.6, 1H), 4.55 (d, *J*=15.4, 1H), 4.84 (dd, *J*=1.5 and 19.0, 1H), 4.98 (dd, *J*=1.5 and 10.3, 1H), 5.64 (m, 1H), 7.27 (m, 5H). ^{13}C NMR (75.5 MHz): −4.7, −4.4, −4.0, −3.7, 13.7, 17.9, 18.4, 22.6, 25.5, 25.8, 26.0, 36.5, 39.1, 43.6, 67.3, 76.9, 78.5, 119.2, 127.3, 128.4, 128.7, 133.9, 138.6, 172.5. IR (film, cm^{-1}): 3078, 2954, 2929, 2853, 1709. HRMS $C_{30}H_{53}NO_3Si_2$ ($M^+-C_4H_9$, calcd): 474.28598; ($M^+-C_4H_9$, found): 474.28603. $[\alpha]_D$=+64.9 (*c* 1.18, $CHCl_3$).

*4.2.2.3. (3*R,*4*S,*5*S*)-3,4-Bis[(*tert-*butyldimethylsilyl)oxy]-1-benzyl-5-allyl-5-(2-phenyl-1-ethynyl)-2-pyrrolidinone.* Colorless oil; 56% yield as a 4:1 mixture. Major isomer **5c** was isolated by column chromatography on silica gel (4% EtOAc/hexane, v/v). ^{1}H NMR (300 MHz): 0.16 (s, 3H), 0.18 (s, 3H), 0.23 (s, 3H), 0.24 (s, 3H), 0.95 (s, 18H), 2.56 (dd, *J*=6.6 and 14.3, 1H), 2.60 (dd, *J*=7.3 and 14.3, 1H), 4.35 (d, *J*=7.8, 1H), 4.47 (d, *J*=7.8, 1H), 4.65 (d, *J*=2.0, 2H), 4.84 (dd, *J*=1.8 and 17.2, 1H), 5.04 (dd, *J*=1.8 and 10.2, 1H), 5.70 (m, 1H), 7.30 (m, 10H). ^{13}C NMR (75.5 MHz): −4.7, −4.5, −4.1, −3.9, 17.8, 18.2, 25.7, 25.8, 40.1, 44.8, 62.8, 75.4, 82.9, 86.9, 89.1, 120.3, 122.0, 127.3, 128.3, 128.4, 128.7, 131.6, 132.5, 138.0, 170.8. IR (film, cm^{-1}): 3408, 3080, 3030, 2954, 2929, 2856, 2229, 1714. HRMS $C_{34}H_{49}NO_3Si_2$ ($M^+-C_4H_9$, calcd): 518.25468; ($M^+-C_4H_9$, found): 518.25461. $[\alpha]_D$=+24.1 (*c* 1.06, $CHCl_3$).

*4.2.2.4. (3*R,*4*S,*5*S*)-3,4-Bis[(*tert-*butyldimethylsilyl)oxy]-1-benzyl-5-allyl-5-[(*tert-*butyldimethylsilyl)-oxy]propargyl-2-pyrrolidinone.* Colorless oil; 36% yield as a 5:1 mixture. Data for the major isomer **5d**: ^{1}H NMR (300 MHz): 0.12 (s, 6H), 0.17 (s, 3H), 0.19 (s, 3H), 0.23 (s, 3H), 0.25 (s, 3H), 0.93 (s, 9H), 0.96 (s, 9H), 0.97 (s, 9H), 2.41 (dd, *J*=7.0 and 14.3, 1H), 2.55 (dd, *J*=7.0 and 14.3, 1H), 4.26 (s, 2H), 4.31 (d, *J*=7.7, 1H), 4.36 (d, *J*=7.7, 1H), 4.50 (d, *J*=15.0, 1H), 4.73 (d, *J*=15.0, 1H), 5.00 (dd, *J*=1.8 and 12.1, 1H), 5.09 (m, 1H), 5.60 (m, 1H), 7.29 (m, 5H). ^{13}C NMR (75.5 MHz): −5.3, −4.6, −4.5, −4.0, −3.9, 17.9, 18.2, 18.3, 25.7, 25.8, 40.0, 44.7, 51.4, 62.6, 75.3, 82.7, 84.3, 85.8, 120.2, 127.3, 128.3, 128.9, 132.3, 137.9, 170.6. IR (film, cm^{-1}): 3502, 3064, 3032, 2960, 2929, 2856, 1716. HRMS $C_{35}H_{61}NO_4Si_3$ ($M^+-C_4H_9$, calcd): 586.32042; ($M^+-C_4H_9$, found): 586.32034.

*4.2.2.5. (3*S*,4*R*,5*S*)-3,4-Bis[(*tert*-butyldimethylsilyl)oxy]-1,5-diallyl-5-methyl-2-pyrrolidinone.* Colorless oil; 65% yield as a 2:1 mixture. Major isomer **5g** was isolated by column chromatography on silica gel (4% EtOAc/hexane, v/v): ^{1}H NMR (500 MHz): 0.13 (s, 3H), 0.15 (s, 3H), 0.16 (s, 3H), 0.21 (s, 3H), 0.94 (s, 9H), 0.95 (s, 9H), 1.27 (s, 3H), 2.25 (dd, *J*=7.6 and 14.2, 1H), 2.40 (dd, *J*=7.3 and 14.2, 1H), 3.68 (dd, *J*=6.1 and 15.9, 1H), 3.89 (d, *J*=7.3, 1H), 4.00 (ddt, *J*=1.5, 5.6 and 15.9, 1H), 4.30 (d, *J*=7.3, 1H), 5.13 (m, 4H), 5.80 (m, 2H). ^{13}C NMR (75.5 MHz): −4.3, −4.2, −3.8, −3.7, 18.0, 18.4, 25.7, 25.9, 26.0, 39.6, 42.5, 63.9, 76.2, 83.2, 116.7, 119.3, 133.7, 134.4, 171.0. IR (film, cm^{-1}): 3080, 2954, 2924, 2853, 1709, 1641. HRMS $C_{23}H_{45}NO_3Si_2$ ($M^+-C_4H_9$, calcd): 382.22338; ($M^+-C_4H_9$, found): 382.22325. $[\alpha]_D$=−60.8 (*c* 0.56, $CHCl_3$).

*4.2.2.6. (3*S*,4*R*,5*S*)-3,4-Bis[(*tert*-butyldimethylsilyl)oxy]-1,5-diallyl-5-*n*-butyl-2-pyrrolidinone **5h**.* Colorless oil; 66% yield. ^{1}H NMR (300 MHz): 0.12 (s, 3H), 0.16 (s, 6H), 0.20 (s, 3H), 0.88–1.00 (s, br, 21H), 1.2–1.6 (m, 6H), 2.17 (dd, *J*=14.3 and 8.0, 1H), 2.46 (dd, *J*=14.3 and 7.0, 1H), 3.77 (t, br, *J*=6.6, 2H), 4.04 (d, *J*=7.0, 1H), 4.31 (d, *J*=7.0, 1H), 5.07 (dd, *J*=14.3 and 1.8, 2H), 5.13 (dd, *J*=10.2 and 1.5, 1H), 5.18 (dd, *J*=17.2 and 1.5, 1H), 5.7–5.9 (m, 2H). ^{13}C NMR (75.5 MHz): −4.7, −4.4, −4.0, −3.7, 13.8, 17.8, 18.3, 22.6, 25.3, 25.8, 26.0, 36.0, 39.5, 43.0, 66.6, 76.7, 78.6, 116.9, 119.2, 134.0, 134.3, 171.7. IR (film, cm^{-1}): 3078, 2954, 2929, 2853, 1709, 1641. HRMS $C_{26}H_{51}NO_3Si_2$ ($M^+-C_4H_9$, calcd): 424.74980; ($M^+-C_4H_9$, found): 424.74956. $[\alpha]_D$=−57.5 (*c* 2.81, $CHCl_3$).

*4.2.2.7. (3*S*,4*R*,5*R*)-3,4-Bis[(*tert*-butyldimethylsilyl)oxy]-1,5-diallyl-5-(2-phenyl-1-ethynyl)-2-pyrrolidinone.* Colorless oil; 63% yield as a 2.6:1 mixture. Data for the major isomer **5i**: ^{1}H NMR (500 MHz): 0.15 (s, 3H), 0.18 (s, 3H), 0.22 (s, 3H), 0.25 (s, 3H), 0.94 (s, 9H), 0.96 (s, 9H), 2.67 (dd, *J*=7.6 and 16.6, 1H), 2.72 (m, 1H), 4.06 (m, 2H), 4.28 (d, *J*=7.8, 1H), 4.44 (d, *J*=7.8, 1H), 5.16 (m, 4H), 5.92 (m, 2H), 7.32 (m, 5H). ^{13}C NMR (125.5 MHz): −4.6, −4.4, −3.9, −3.8, 18.0, 18.3, 25.8 25.9, 40.3, 44.4, 62.6, 75.3, 82.8, 86.3, 89.0, 117.4, 120.3, 122.1, 128.4, 128.7, 131.4, 132.6, 133.6, 170.2. IR (film, cm^{-1}): 3080, 2954, 2929, 2865, 1722, 1643. HRMS $C_{30}H_{47}NO_3Si_2$ ($M^+-C_4H_9$, calcd): 468.23903; ($M^+-C_4H_9$, found): 468.23929.

*4.2.2.8. (3*S*,4*R*,5*R*)-3,4-Bis[(*tert*-butyldimethylsilyl)oxy]-1,5-diallyl-5-[(*tert*-butyldimethylsilyl)oxy]-propargyl-2-pyrrolidinone.* Colorless oil; 48% yield as a 2.7:1 mixture. Data for the major isomer **5j**: ^{1}H NMR (300 MHz): 0.11 (s, 6H), 0.13 (s, 3H), 0.17 (s, 3H), 0.20 (s, 3H), 0.21 (s, 3H), 0.91 (s, 9H), 0.93 (s, 9H), 0.96 (s, 9H), 2.57 (d, *J*=7.3, 2H), 3.96 (m, 2H), 4.23 (d, *J*=7.7, 1H), 4.32 (d, *J*=7.7 Hz, 1H), 4.34 (s, 2H), 5.17 (m, 4H), 5.83 (m, 2H). ^{13}C NMR (75.5 MHz): −5.2, −4.5 −4.4, −4.1, −3.9, −3.8, 17.9, 18.2, 18.3, 25.7, 25.8, 25.9, 40.1, 44.2, 51.5, 62.2, 75.3, 82.7, 84.3, 85.1, 117.4, 120.3, 132.6, 133.6, 170.1. IR (film, cm^{-1}): 3080, 2954, 2929, 2865, 1722, 1643. HRMS $C_{31}H_{59}NO_4Si_3$ ($M^+-C_4H_9$, calcd): 536.30477; ($M^+-C_4H_9$, found): 536.30461.

*4.2.3. Reduction of hydroxy lactams **3a–i** with Et_3SiH, mediated by $BF_3\cdot OEt_2$*

To a solution of hydroxylactam **3a–i** (0.35 mmol) in CH_2Cl_2 (3.5 mL), under an argon atmosphere at −78°C, was added Et_3SiH (0.20 mL, 1.4 mmol) followed by $BF_3\cdot OEt_2$ (0.08 mL, 0.70 mmol) dropwise. Stirring was continued for 15 min at −78°C, followed by 30 min at 0°C. The reaction was quenched with H_2O (1 mL) and extracted with CH_2Cl_2 (2×5 mL). The organic phase was washed with brine (5 mL), dried over $MgSO_4$, and the solvent was removed under reduced pressure. Purification by column chromatography on silica gel (8% EtOAc/hexane, v/v) afforded pyrrolidinones **5e–f** and **5k–n** (Table 1).

*4.2.3.1. (3*R,*4*S,*5*S*)-3,4-Bis[(*tert-*butyldimethylsilyl)oxy]-1-benzyl-5-*n-*butyl-2-pyrrolidinone.* Colorless oil; 61% yield as a 17:1 mixture. Data for the major isomer **5e**: ^{1}H NMR (500 MHz): 0.00 (s, 3H), 0.09 (s, 3H), 0.20 (s, 3H), 0.22 (s, 3H), 0.85 (s, 9H), 0.94 (s, 9H), 0.90 (t, *J*=7.0, 3H), 1.2–1.3 (m, 4H), 1.6–1.7 (m, 2H), 3.15 (ddd, *J*=2.0, 2.9 and 4.5, 1H), 3.85 (t, *J*=2.0, 1H), 3.91 (d, *J*=15.4, 1H), 4.03 (d, *J*=2.0, 1H), 5.09 (d, *J*=15.4, 1H), 7.28 (m, 5H). ^{13}C NMR (75.5 MHz): −5.2, −4.9, −4.7, −4.5, 13.8, 17.7, 18.0, 22.6, 25.5, 25.7, 27.1, 29.7, 43.8, 64.6, 75.6, 78.4, 127.4, 127.8, 128.6, 136.4, 172.3. IR (film, cm^{-1}): 3064, 3030, 2954, 2924, 2856, 1705. HRMS $C_{27}H_{49}NO_3Si_2$ ($M^+-C_4H_9$, calcd): 434.74500; ($M^+-C_4H_9$, found): 434.74508.

*4.2.3.2. (3*R,*4*S,*5*R*)-3,4-Bis[(*tert-*butyldimethylsilyl)oxy]-1-benzyl-5-(2-phenyl-1-ethynyl)-2-pyrrolidinone **5f**.* Colorless oil; 62% yield. ^{1}H NMR (300 MHz): 0.15 (s, 3H), 0.17 (s, 3H), 0.18 (s, 3H), 0.26 (s, 3H), 0.89 (s, 9H), 0.96 (s, 9H), 4.00 (d, *J*=6.1, 1H), 4.16 (d, *J*=14.6, 1H), 4.19 (d, *J*=6.4, 1H), 4.32 (dd, *J*=6.1 and 6.4, 1H), 5.12 (d, *J*=14.7, 1H), 7.36 (m, 10H). ^{13}C NMR (75.5 MHz): −4.7, −4.5, −4.1, −4.0, 17.8, 18.3, 25.7, 25.8, 44.3, 53.6, 77.2, 80.4, 84.6, 87.4, 122.0, 127.6, 128.4, 128.5, 128.7, 128.8, 131.6, 136.1, 170.3. IR (film, cm^{-1}): 3061, 3032, 2954, 2930, 2856, 2225, 1716. HRMS $C_{31}H_{45}NO_3Si_2$ ($M^+-C_4H_9$, calcd): 478.22338; ($M^+-C_4H_9$, found): 478.22337. $[\alpha]_D$ = +58.4 (*c* 2.77, $CHCl_3$).

*4.2.3.3. (3*S,*4*R,*5*S*)-3,4-Bis[(*tert-*butyldimethylsilyl)oxy]-1-allyl-5-*n-*butyl-2-pyrrolidinone.* Colorless oil; 60% yield as a 9:1 mixture. Data for the major isomer **5k**: ^{1}H NMR (500 MHz): 0.08 (s, 3H), 0.10 (s, 3H), 0.16 (s, 3H), 0.17 (s, 3H), 0.88 (s, 9H), 0.90 (s, 9H), 0.92 (t, *J*=7.1, 3H), 1.31 (m, 4H), 1.61 (m, 2H), 3.28 (m, 1H), 3.42 (dd, *J*=6.8 and 15.9, 1H), 3.84 (t, *J*=2.4, 1H), 3.97 (d, *J*=2.4, 1H), 4.36 (ddd, *J*=2.0, 4.4 and 16.0, 1H), 5.15 (dq, *J*=1.2 and 10.4, 1H), 5.20 (dq, *J*=2.0 and 17.0, 1H), 5.70 (m, 1H). ^{13}C NMR (125.5 MHz): −5.2, −4.8, −4.5, −4.4, 13.8, 17.7, 18.0, 22.6, 25.5, 25.7, 27.0, 29.8, 42.6, 64.6, 76.1, 78.4, 117.3, 132.4, 171.9. IR (film, cm^{-1}): 3082, 2954, 2929, 2858, 1705, 1645. HRMS $C_{23}H_{47}NO_3Si_2$ ($M^+-C_4H_9$, calcd): 384.68520; ($M^+-C_4H_9$, found): 384.68400.

*4.2.3.4. (3*S,*4*R,*5*R*)-3,4-Bis[(*tert-*butyldimethylsilyl)oxy]-1-allyl-5-(2-phenyl-1-ethynyl)-2-pyrrolidinone **5l**.* Colorless oil; 66% yield. ^{1}H NMR (500 MHz): 0.17 (s, 3H), 0.18 (s, 3H), 0.22 (s, 3H), 0.24 (s, 3H), 0.94 (s, 9H), 0.95 (s, 9H), 3.71 (dd, *J*=7.6 and 15.1, 1H), 4.19 (d, *J*=6.3, 1H), 4.21 (d, *J*=6.3, 1H), 4.31 (t, *J*=6.3, 1H), 4.45 (ddt, *J*=1.5, 4.6 and 15.1, 1H), 5.26 (m, 2H), 5.78 (m, 1H), 7.3–7.4 (m, 5H). ^{13}C NMR (125.5 MHz): −4.8, −4.4, −4.1, −4.0, 17.9, 18.2, 25.7, 25.8, 43.1, 53.8, 77.1, 80.5, 84.6, 87.0, 118.7, 122.0, 128.4, 128.8, 131.6, 131.7, 170.1. IR (film, cm^{-1}): 3082, 2954, 2929, 2856, 2225, 1720, 1645. HRMS $C_{27}H_{43}NO_3Si_2$ ($M^+-C_4H_9$, calcd): 428.20773; ($M^+-C_4H_9$, found): 428.20774. $[\alpha]_D$=+5.6 (*c* 1.51, $CHCl_3$).

*4.2.3.5. (3*S,*4*R,*5*R*)-3,4-Bis[(*tert-*butyldimethylsilyl)oxy]-1-allyl-5-(2-trimethylsilyl-1-ethynyl)-2-pyrrolidinone **5m**.* Colorless oil; 50% yield. ^{1}H NMR (500 MHz): 0.15 (s, 3H), 0.16 (s, 3H), 0.18 (s, 9H), 0.19 (s, 3H), 0.21 (s, 3H), 0.92 (s, 9H), 0.94 (s, 9H), 3.60 (dd, *J*=7.8 and 15.1, 1H), 3.93 (d, *J*=6.3, 1H), 4.14 (d, *J*=6.6, 1H), 4.20 (dd, *J*=6.3 and 6.6, 1H), 4.39 (ddt, *J*=1.5, 4.9 and 15.1, 1H), 5.20 (dd, *J*=1.5 and 10.0, 1H), 5.23 (dd, *J*=1.5 and 14.2, 1H), 5.73 (m, 1H). ^{13}C NMR (125.5 MHz): −4.8, −4.4, −4.1, −4.0, −0.37, 17.9, 18.2, 25.8, 43.0, 53.8, 77.1, 80.5, 92.6, 100.8, 118.8, 131.6, 170.0. IR (film, cm^{-1}): 3311, 3238, 3084, 2956, 2930, 2858, 2177, 1722, 1645. HRMS $C_{24}H_{47}NO_3Si_3$ ($M^+-C_4H_9$, calcd): 424.21595; ($M^+-C_4H_9$, found): 424.21596. $[\alpha]_D$=+4.4 (*c* 1.95, $CHCl_3$).

*4.2.3.6. (3*S*,4*R*,5*R*)-3,4-Bis[(*tert*-butyldimethylsilyl)oxy]-1-allyl-5-[(*tert*-butyldimethylsilyl)oxy]-propargyl-2-pyrrolidinone **5n**.* Colorless oil; 52% yield. ^{1}H NMR (300 MHz): 0.11 (s, 6H), 0.15 (s, 6H), 0.18 (s, 3H), 0.21 (s, 3H), 0.91 (s, 18H), 0.93 (s, 9H), 3.59 (dd, *J*=7.6 and 15.4, 1H), 3.99 (d, br, *J*=5.6, 1H), 4.13 (d, *J*=6.2, 1H), 4.18 (dd, *J*=6.2 and 5.6, 1H), 4.35 (d, *J*=1.5, 2H), 4.41 (dd, *J*=4.6 and 15.4, 1H), 5.19 (m, 2H), 5.69 (m, 1H). ^{13}C NMR (75.5 MHz): −5.4, −4.9, −4.6, −4.3, 17.7, 18.1, 25.6, 25.8, 42.9, 51.5, 53.5, 77.2, 80.1, 80.2, 85.8, 118.6, 131.6, 170.3. IR (film, cm^{-1}): 3084, 2954, 2936, 2858, 2177, 1728. HRMS $C_{28}H_{55}NO_4Si_3$ ($M^+-C_4H_9$, calcd): 496.27347; ($M^+-C_4H_9$, found): 496.27340. $[\alpha]_D$=−11.2 (*c* 1.52, $CHCl_3$).

*4.3. Synthesis of (4*R*,7*R*,8*S*)-4-*n*-Butyl-5-benzyl-7-[(*tert*-butyldimethylsilyl)oxy]-1-oxa-5-azabicyclo-[3.3.0]octan-6-one **6b***

A solution of **5b** (0.097 g, 0.18 mmol) in MeOH (4 mL) was treated with O_3/O_2 stream at −78°C for 2 h. After argon purging, methyl sulfide (0.3 mL) was added to the colorless solution, stirred overnight, and evaporated to give an oil. This crude mixture was diluted with 3 mL of CH_3CN and a 40% aqueous solution of HF was added (0.3 mL). The mixture was vigorously stirred for 6 h at room temperature. After neutralization with solid $KHCO_3$ the organic layer was separated, dried over $MgSO_4$, and the solvent evaporated at reduced pressure. Lactol **6a** was obtained as a white powder (0.042 g, 0.14 mmol) in 80% yield and used in the next step without further purification. To a solution of **6a** (0.14 mmol) in dry CH_2Cl_2 under an argon atmosphere at −78°C was added Et_3SiH (0.05 mL, 0.35 mmol) followed by $BF_3\cdot OEt_2$ (0.02 mL, 0.18 mmol) dropwise. Stirring was continued for 1 h. The reaction was quenched with H_2O (0.5 mL) and extracted with $CHCl_3$ (3×5 mL). The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude oil was dissolved in DMF (0.5 mL), imidazole (0.010 g) was added, followed by a solution of TBSCl (0.030 g, 0.20 mmol) in DMF (0.2 mL). The stirring was continued for 5 h at room temperature. The reaction was quenched with H_2O, extracted with $CHCl_3$ (3×5 mL), and washed with brine. The organic phase was dried over $MgSO_4$ and the solvent removed under reduced pressure. Purification of the crude mixture by column chromatography on silica gel (10% EtOAc/hexane, v/v) afforded bicyclic compound **6b** as a colorless oil (0.035 g, 0.086 mmol) in 62% yield. ^{1}H NMR (500 MHz): 0.13 (s, 3H), 0.14 (s, 3H), 0.75 (t, *J*=7.1, 3H), 0.85 (s, 9H), 0.9–1.0 (m, 1H), 1.0–1.3 (m, 3H), 1.4–1.5 (m, 1H), 1.5–1.6 (m, 1H), 1.6–1.7 (m, 1H), 1.8–1.9 (m, 1H), 3.47 (dt, *J*=5.8 and 8.8, 1H), 3.65 (ddd, *J*=3.9, 7.4 and 8.8, 1H), 3.91 (s, 1H), 4.06 (d, *J*=15.1, 1H), 4.09 (s, 1H), 4.67 (d, *J*=15.1, 1H), 7.21 (m, 5H). ^{13}C NMR (125.5 MHz): −5.2, −4.6, 13.8, 18.2, 22.8, 25.6, 26.6, 35.9, 36.7, 44.0, 67.2, 73.6, 75.7, 87.3, 127.5, 128.2, 128.5, 138.1, 173.1. IR (film, cm^{-1}): 2954, 2929, 2858, 1699. HRMS $C_{23}H_{37}NO_3Si$ ($M^+-C_4H_9$, calcd): 346.18385; ($M^+-C_4H_9$, found): 346.18156. $[\alpha]_D$=+77.3 (*c* 0.22 , EtOAc).

4.4. General procedure for olefin metathesis

*4.4.1. Synthesis of dehydroindolizinones **7a–e***

To a solution of **5g**, **5h**, or **5i** (0.10 mmol) in CH_2Cl_2 (5 mL), under an argon atmosphere at rt, was added a solution of bis(tricyclohexylphosphine)benzylidine ruthenium(IV) dichloride (Grubbs' catalyst, 0.003 g, 0.004 mmol) in CH_2Cl_2 (0.4 mL) The mixture was stirred at rt for 12 h. The solvent was removed under reduced pressure and the oily residue was purified by column chromatography on silica gel (8% EtOAc/hexane, v/v) to afford dehydroindolizinones **7a–e**.

*4.4.1.1. (1*R,*2*S,*8a*S*)-1,2-Bis[(*tert-*butyldimethylsilyl)oxy]-8a-methyl-1,2,3,5,8,8a-hexahydro-3-indolizinone.* Colorless oil; 74% yield as a 2:1 mixture. The major isomer **7a** was isolated by column chromatography on silica gel (8% EtOAc/hexane, v/v). ^{1}H NMR (500 MHz): 0.13 (s, 3H), 0.15 (s, 3H), 0.16 (s, 3H), 0.22 (s, 3H), 0.92 (s, 9H), 0.93 (s, 9H), 1.32 (s, 3H), 1.82 (dd, *J*=5.9 and 17.6, 1H), 2.43 (d, *J*=17.6, 1H), 3.44 (dd, *J*=2.0 and 18.3, 1H), 3.93 (d, *J*=5.9, 1H), 4.10 (d, *J*=5.9, 1H), 4.36 (d, *J*=18.3, 1H), 5.66 (m, 1H), 5.76 (m, 1H). ^{13}C NMR (125.5 MHz): −4.6, −4.3, −4.1, −3.8, 18.0, 18.2, 23.4, 25.8, 25.9, 31.0, 38.0, 57.6, 77.8, 81.8, 122.8, 124.2, 169.9. IR (film, cm^{-1}): 3035, 2954, 2929, 2856, 1716, 1651. HRMS $C_{21}H_{41}NO_3Si_2$ ($M^+-C_4H_9$, calcd): 354.19208; ($M^+-C_4H_9$, found): 354.19209. $[\alpha]_D$=−52.4 (*c* 1.30, $CHCl_3$). Data for the minor isomer **7b**: ^{1}H NMR (500 MHz): 0.11 (s, 3H), 0.14 (s, 3H), 0.15 (s, 3H), 0.23 (s, 3H), 0.92 (s, 9H), 0.94 (s, 9H), 1.15 (s, 3H), 2.20 (m, 2H), 3.49 (d, br, *J*=19.5, 1H), 3.87 (d, *J*=7.1, 1H), 4.16 (dd, *J*=7.1 and 1.1, 1H), 4.24 (d, br, *J*=19.5, 1H), 5.68 (m, 2H). ^{13}C NMR (125.5 MHz): −4.8, −4.5, −4.2, −4.0, 17.8, 17.9, 18.5, 25.7, 25.8, 37.6, 37.7, 56.7, 76.3, 83.9, 121.5, 122.8, 170.0.

*4.4.1.2. (1*R,*2*S,*8a*S*)-1,2-Bis[(*tert-*butyldimethylsilyl)oxy]-8a-*n-*butyl-1,2,3,5,8,8a-hexahydro-3-indolizinone **7c**.* Colorless oil; 71% yield. ^{1}H NMR (300 MHz): 0.11 (s, 3H), 0.15 (s, 3H), 0.17 (s, 3H), 0.22 (s, 3H), 0.92 (s, br, 12H), 0.93 (s, 9H), 1.0–1.2 (m, 1H), 1.2–1.4 (m, 3H), 1.4–1.6 (m, 1H), 1.6–1.9 (m, 2H), 2.45 (d, br, *J*=17.6, 1H), 3.34 (dd, *J*=1.8 and 18.3, 1H), 4.10 (d, *J*=5.3, 1H), 4.13 (d, *J*=5.3, 1H), 4.36 (d, *J*=18.3, 1H), 5.70 (m, 2H). ^{13}C NMR (125.5 MHz): −4.6, −4.5, −4.0, −3.7, 14.0, 18.0, 18.3, 22.9, 25.4, 25.8, 26.0, 30.3, 33.4, 38.5, 60.3, 77.5, 78.2, 122.9, 124.3, 170.5. IR (film, cm^{-1}): 3035, 2956, 2929, 2858, 1720, 1651. HRMS $C_{24}H_{47}NO_3Si_2$ ($M^+-C_4H_9$, calcd): 396.23903; ($M^+-C_4H_9$, found): 396.23891. $[\alpha]_D$=−39.8 (*c* 1.71, $CHCl_3$).

*4.4.1.3. (1*R,*2*S,*8a*R*)-1,2-Bis[(*tert-*butyldimethylsilyl)oxy]-8a-(2-phenyl-1-ethynyl)-1,2,3,5,8,8a-hexahydro-3-indolizinone.* Colorless oil; 38% yield as a 4:1 mixture. The major isomer **7d** was isolated by column chromatography on silica gel (8% EtOAc/hexane, v/v). ^{1}H NMR (300 MHz): 0.16 (s, 3H), 0.19 (s, 3H), 0.24 (s, 3H), 0.25 (s, 3H), 0.94 (s, 9H), 0.95 (s, 9H), 2.32 (dd, *J*=2.4 and 17.4, 1H), 2.53 (d, br, *J*=17.4, 1H), 3.71 (d, br, *J*=17.9, 1H), 4.13 (d, *J*=6.8, 1H), 4.42 (d, br, *J*=16.5, 1H), 4.51 (d, *J*=6.8, 1H), 5.77 (m, 2H). 7.35 (m, 5H). ^{13}C NMR (75.5 MHz): −4.7, −4.5, −3.9, −3.9, 18.0, 18.2, 25.8, 32.0, 38.8, 56.3, 76.9, 81.7, 83.4, 89.4, 122.2, 123.4, 124.2, 128.3, 128.5, 131.5, 131.7, 168.9. IR (film, cm^{-1}): 3035, 2956, 2929, 2858, 1720, 1651. HRMS $C_{28}H_{43}NO_3Si_2$ ($M^+-C_4H_9$, calcd): 440.20773; ($M^+-C_4H_9$, found): 440.20775. $[\alpha]_D$=+25.0 (*c* 0.68, $CHCl_3$). Data for the minor isomer **7e**: colorless oil. ^{1}H NMR (500 MHz): 0.07 (s, 3H), 0.16 (s, 3H), 0.17 (s, 3H), 0.24 (s, 3H), 0.95 (s, 9H), 0.97 (s, 9H), 2.37 (d, br, *J*=17.3, 1H), 2.75 (d, br, *J*=17.3, 1H), 3.71 (d, br, *J*=17.1, 1H), 3.99 (d, *J*=7.3, 1H), 4.26 (d, br, *J*=17.1, 1H), 4.32 (dd, *J*=1.5 and 7.3, 1H), 5.80 (m, 2H), 7.35 (m, 5H). ^{13}C NMR (75.5 MHz): −4.6, −4.1, −4.0, −3.9, 18.0, 18.3, 25.8, 25.9, 37.5, 38.4, 56.3, 76.4, 83.3, 85.2, 86.2, 122.0, 122.3, 122.6, 128.2, 128.3, 131.7, 170.8.

*4.4.2. Synthesis of dehydropyrrolizinone **7f***

To a solution of **5n** (0.070 g, 0.14 mmol) in dry toluene (7 mL), under an argon atmosphere at rt, was added a solution of Grubbs' catalyst (0.009 g, 0.011 mmol) in toluene (1.1 mL). The mixture was heated at reflux for 2.5 h and cooled to rt. The solvent was removed under reduced pressure and the resultant oily residue was purified by column chromatography on silica gel (10% EtOAc/hexane, v/v) to afford **7f** (0.060 g, 0.11 mmol) in 78% yield, as a colorless oil. ^{1}H NMR (500 MHz, C_6D_6): 0.02 (s, 3H), 0.07 (s, 3H), 0.08 (s, 3H), 0.20 (s, 3H), 0.30 (s, 3H), 0.44 (s, 3H), 0.98 (s, 9H), 1.00 (s, 9H), 1.15 (s, 9H), 3.31 (d, br, *J*=16.4, 1H), 3.87 (dd, *J*=7.1 and 8.1, 1H), 4.06 (d, *J*=14.0, 1H), 4.20 (d, *J*=14.0, 1H), 4.26

(m, 1H), 4.36 (d, br, J=16.4, 1H), 4.45 (d, J=8.1, 1H), 5.05 (d, J=1.7, 1H), 5.49 (d, J=17.1, 2H). ^{13}C NMR (125.5 MHz, C_6D_6): −5.4, −5.3, −4.1, −3.9, −3.7, −2.7, 17.8, 18.3, 18.6, 25.9, 26.0, 26.2, 50.4, 63.7, 68.6, 79.1, 83.7, 115.2, 122.7, 139.3, 140.6, 173.4. IR (film, cm^{-1}): 3390, 2954, 2930, 2858, 1732. HRMS $C_{28}H_{55}NO_4Si_3$ ($M^+-C_4H_9$, calcd): 496.27347; ($M^+-C_4H_9$, found): 496.27340. $[\alpha]_D$=−25.5 (*c* 3.00, hexane).

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