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Preparation of γ-siloxyallyltributylstannanes and their use in the synthesis of (±)-1-deoxy-6,8a-di-*epi*-castanospermine

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γ-Siloxyallyltributylstannanes were selectively obtained as *E* or *Z* isomers from β-tributylstannylacrolein upon reaction with lithium or magnesium alkylcyanocuprates. The ability of the reagents to give a high *syn* selectivity when added to iminium salts has been used for the efficient synthesis of (±)-1-deoxy-6,8a-di-*epi*-castanospermine from succinimide. The key step of the synthesis was the allylstannation of the *N*-allyliminium intermediate followed by ring closing metathesis.

Introduction

In the course of our studies involving γ-alkoxyallylstannanes and γ-siloxyallylstannanes in allylstannation reaction of aldehydes and iminium salts, we pointed out possible effects of an α-substituent relative to tin[1] or stereoconvergent effects when reactions were performed on chiral α-alkoxyaldehydes.[2] These behaviours of heterosubstituted allylstannanes have been reviewed by several groups with a special emphasis on the crucial importance of the experimental conditions on the stereochemistry of the reaction[3–5] and exploited for syntheses in sugar series.[6,7] As far as we are concerned, we have recently been interested in the allylstannation of glyceraldehyde derivatives through aldopentose syntheses[2] and in the already known allylstannation of iminium salts.[8,9] We successfully applied these methods for the synthesis of polyhydroxypiperidines.[10] In the present paper, we report an efficient synthesis of γ-siloxyallyltributylstannanes and an aspect of their use for the synthesis of (±)-1-deoxy-6,8a-di-*epi*-castanospermine starting from succinimide.

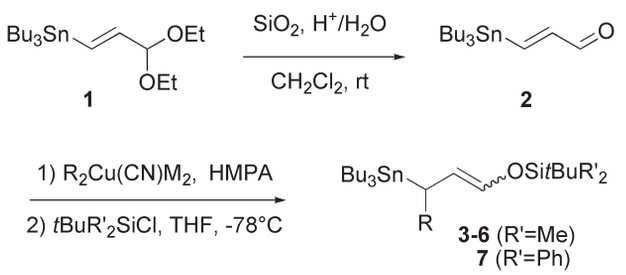
Results and discussion

1. Synthesis of γ-siloxyallyltributylstannanes

γ-Siloxyallyltributylstannanes were previously obtained by Marshall[11] using the reaction of $Bu_3Sn(Bu)CuCNLi_2$ (Lipshutz reagent)[12] on α,β-enals and this reaction was shown to be also possible when this organostannane reagent was allowed to react with β-tributylstannylacrolein.[13] Taking advantage of the easy synthesis of β-tributylstannylacrolein diethylacetal[14,15] which can be very efficiently deprotected upon treatment on acidified silica, we extended this preparation to several γ-siloxyallylstannanes using 1,4-addition of cyanocuprates on β-tributylstannylacrolein followed by subsequent quenching with chlorosilanes (Scheme 1).

The obtained results are reported in Table 1 and demonstrate an easier 1,4-addition of the cyanocuprates on β-tributylstannylacrolein when compared to the possible transmetalation reaction of the Csp^2–Sn bond.[16,17]

High yields were obtained with lithium cyanocuprates (entries 1,3,4,6), with a preference for *E*-siloxyallyltributylstannanes, while magnesium cyanocuprates led to poor yields with a reversed stereoselectivity (*Z*-siloxytributylstannanes were obtained as major isomers) (entries 2,5). It must be noted

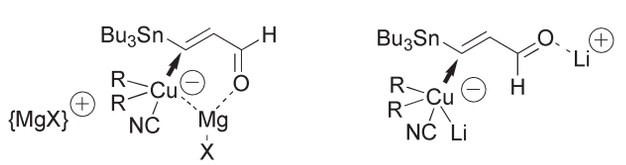


Scheme 1

Table 1 Synthesis of γ-siloxyallyltributylstannanes

Entry	$R_2Cu(CN)M_2$	R′	Compound	Yield (*E*/*Z*)
1	$Me_2Cu(CN)Li_2$	Me	**3**	70% (92/8)
2	$iPr_2Cu(CN)(MgCl)_2$	Me	**4**	35% (20/80)
3	$nBu_2Cu(CN)Li_2$	Me	**5**	90% (75/25)
4	$tBu_2Cu(CN)Li_2$	Me	**6**	85% (85/15)
5	$tBu_2Cu(CN)(MgCl)_2$	Me	**6**	35% (15/85)
6	$tBu_2Cu(CN)Li_2$	Ph	**7**	89% (90/10)

that the use of TBDPS (entry 6) does not change strongly the stereoselectivity. These results could be explained by considering the initial geometry of the intermediate adduct. The bidentate nature of the magnesium might induce the *Z* isomer formation through a chelation of **2** in a cisoid conformation while the stereochemistry might essentially be controlled by steric effects when lithium cuprates are involved (Scheme 2).



Scheme 2

2. Use for an expedious synthesis of (±)-1-deoxy-6,8a-di-*epi*-castanospermine

The naturally occurring polyhydroxylated indolizine alkaloids, represented by (+)-castanospermine **8** and (+)-6-*epi*-castanospermine **9** (Scheme 3), have been isolated from *Castanospermum*

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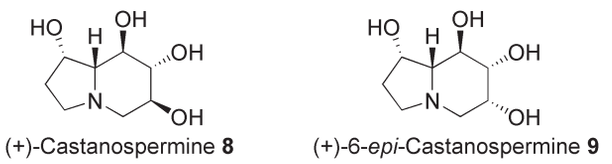
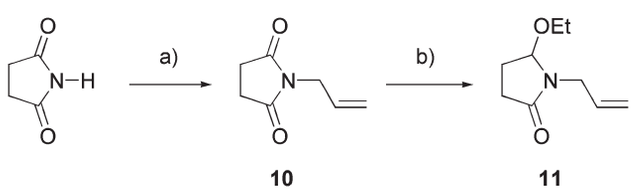
australe[18] and *Alexa leiopetala.*[19] These indolizine alkaloids and their derivatives were reported to display glycosidase inhibition activity[20,21] and are considered as potential antiviral, antitumor and immunomodulating agents.[22,23] With regards to their unique properties, (+)-castanospermine **8** and (+)-6-*epi*-castanospermine **9** and their analogues have recently been synthesized by several groups.[24–28] Among these compounds (+)-1-deoxy-6,8a-di-*epi*-castanospermine was shown to be an inhibitor of α-L-fucosidase.[29]



Scheme 3

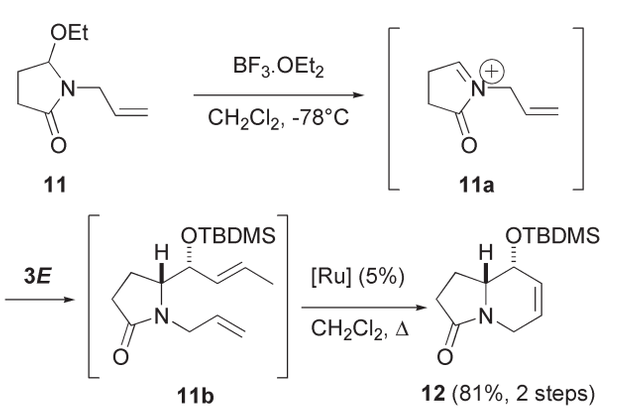
In order to learn more about this type of molecule both in terms of recognition and structure/reactivity relationships in the area of glycosidase inhibitors, it appears of high interest to synthesise natural and unnatural species in this series with perfect control of the stereochemistry. Taking advantage of the expected *syn* addition of γ-siloxyallylstannanes on iminium salts, this kind of skeleton seems likely to be obtained through a combined allylstannation/ring closing metathesis sequence starting from an *N*-allyl succinimide derivative. 1-Allyl-5-ethoxy pyrrolidinone **11** was prepared in two steps from commercially available succinimide (Scheme 4) according to literature procedures.[30,31] The succinimide was alkylated under Mitsunobu conditions[32] to furnish the corresponding imide **10**, which was reduced by $NaBH_4$ in dry ethanol to give the intermediate α-ethoxy amide **11**.[33]



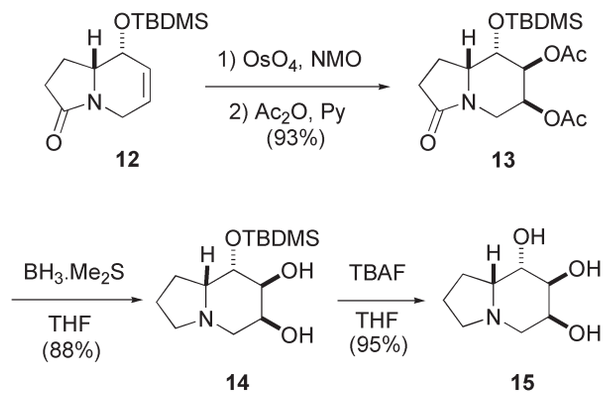
Scheme 4 a) PPh_3, DEAD, CH_2=CH–CH_2OH, THF (82%). b) $NaBH_4$, EtOH (65%).

The addition of γ-siloxyallyltributylstannane **3*E*** to the iminium salt **11a** formed *in situ* from the ethoxy amide **11** in the presence of $BF_3{\cdot}OEt_2$ (3 equiv.) in CH_2Cl_2 at −78 °C afforded after 1 h, selectively, the expected adduct as a crude product **11b** after neutralization with $NaHCO_3$ and washing (Scheme 5). The use of γ-siloxyallyltributylstannane **3*E*** was preferred to the others due to the ring-closing metathesis reaction facilitated by the volatility of the rejected olefin.

This crude product (**11b**) upon treatment with Grubbs' catalyst [$(PCy_3)_2RuCl_2$(=CHPh)] in refluxed CH_2Cl_2 during 24 h, allowed construction of the tetrahydro-indolizinone **12** in over 80% yield. Subsequent dihydroxylation of **12** with OsO_4/*N*-methylmorpholine *N*-oxide at room temperature[34] provided the corresponding diol which was directly acetylated with Ac_2O in pyridine to afford **13** (purified by flash chromatography and fully characterized) as shown in Scheme 6. The stereochemistry of **13** was fully established on the basis of ^{1}H NMR spectra, COSY and NOESY homonuclear shift correlation spectra.



Scheme 5



Scheme 6

A NOE interaction between 8a-H and 5-H (Fig. 1) and a vicinal coupling constant $^3J_{ax\text{-}ax}$ = 12 Hz (Fig. 2) strongly support the stereochemistry of the obtained compound and the *syn* selectivity of the allystannation reaction.

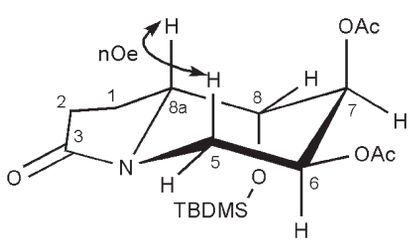


Fig. 1 NOE interaction observed on **13**.

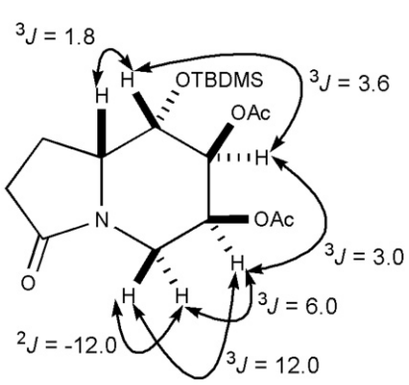


Fig. 2 Meaningful coupling constants for compound **13**.

This *syn* selectivity obtained from a cyclic iminium salt generated from α-ethoxy amide appears to be similar to that observed with *N*-acyl iminiums derived from non-cyclic α-ethoxy carbamates.[10] The NMR investigations were also indicative of a dihydroxylation of **12** occurring on the face of the double bond having a *syn* relationship to 8a-H and driven by an *anti* effect of the TBDMS group. In addition, suitable single crystals for an X-ray analysis were obtained for **13** from a saturated ethyl acetate solution at room temperature (Fig. 3).[35] The structural determination from radiocrystallographic analysis was in full agreement with the stereochemistry determined in solution. Finally, treatment of **13** by $BH_3{\cdot}Me_2S$ in THF reduced the amide function and removed the acetyl protecting groups to afford the indolizine **14** in 88% yield. The latter was converted

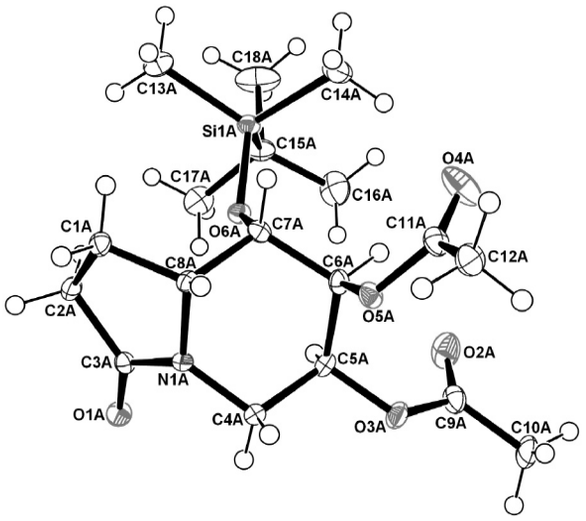


Fig. 3 An ORTEP[36] view of compound **13** with thermal ellipsoids drawn at the 50% probability level (for clarity, only one of the two independent molecules is shown).

into (±)-1-deoxy-6,8a-di-*epi*-castanospermine **15** upon treatment with tetrabutyl ammonium fluoride (95% yield).

Conclusion

The present work outlines an efficient route for the preparation of γ-siloxyallyltributylstannanes and underlines the usefulness of these tools to achieve syntheses in polyhydroxylated indolizine alkaloids series. This point was illustrated by the synthesis of (±)-1-deoxy-6,8a-di-*epi*-castanospermine which was obtained through a *syn* allylstannation of a cyclic iminium salt followed by a ring closing metathesis. A 34% overall yield through the 8 steps was obtained from commercial succinimide (63% on the last 6 steps). The stereochemistry of the obtained product was unambiguously determined both by NMR analyses and X-ray diffraction.

Experimental

General remarks

^{1}H, ^{13}C and ^{119}Sn spectra were recorded on Bruker AC 200, Bruker Avance 300 or Bruker ARX 400 spectrometers. Chemical shifts are given in ppm as δ values relative to tetramethylsilane (^{1}H, ^{13}C) or tetramethylstannane (^{119}Sn) and coupling constants are given in Hz. NMR data are given for spectra recorded at 300 K. Mass spectra were obtained in CI or in EI mode (70 eV) with an HP apparatus (Engine 5989A) in direct introduction mode and when high resolution was desired HRMS data were obtained from the CRUS in Rouen (Centre Régional Universitaire de Spectroscopie de l'Université de Rouen). IR spectra were recorded on a Bruker IFS Vector 22 apparatus. Diethyl ether and THF were distilled over sodium/benzophenone and CH_2Cl_2 was distilled over CaH_2 prior to use. Liquid chromatography separations were achieved on silica gel Merck Geduran Si 60 (40–63 mesh), TLC analyses on silica-coated plates (Merck Kieselgel $60F_{254}$). The tributyltin hydride allowing the synthesis of the γ-siloxyallylstannane was a Crompton product while *n*-butyllithium was a Chemetall product.

General procedure for the synthesis of γ-siloxyallyltributylstannanes 3–7

The reagents were prepared in two different Schlenk tubes A and B.

- Schlenk A: CuCN (62.7 mg, 0.7 mmol) was dried under vacuum (0.1 mmHg, flame heater ≈250 °C, 15 min) before addition of THF (10 mL). The mixture was cooled to −78 °C and degassed. The alkyllithium or alkylmagnesium solution in hexanes or ether (1.39 mmol) was slowly added and HMPA (208 mg, 1.16 mmol) was added 30 min later.

- Schlenk B: To a stirred, cooled (−78 °C) solution of β-tributylstannylacrolein (200 mg, 0.58 mmol) in THF (15 mL) was added triorganosilyl chloride (1.74 mmol). The solution A was cannulated on B, the mixture was stirred from −78 °C to −50 °C for 2 hours and quenched by a $NaHCO_3$ saturated aqueous solution. The mixture was extracted with diethyl ether and the combined organic layers were washed with saturated aqueous NaCl, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The colourless oily product was purified by flash chromatography on silica gel (hexanes–Et_3N 98 : 2).

1-(*tert*-Butyldimethylsiloxy)-3-(tributylstannyl)-but-1-ene (*E*/*Z* 92/8, 193 mg, 70% yield) (3)[11]

IR ν_{max}/cm^{-1} (neat): 2955, 2872, 1588, 1465, 1378, 1251, 980, 831, 768, 672. ^{1}H NMR ($CDCl_3$): *Z* isomer: 0.10 (6H, s), 0.80–0.91 (15H, m), 0.95 (9H, s), 1.20–1.60 (12H, m), 1.28 (3H, d, ^{3}J = 7.5), 2.53 (1H, m, ^{4}J = 1.0 ^{3}J = 7.5 and ^{3}J = 10.9, $^{2}J_{Sn}$ = 58), 4.47 (1H, dd, ^{3}J = 5.7 and ^{3}J = 10.9, $^{3}J_{Sn}$ = 18), 5.97 (1H, dd, ^{3}J = 5.7 and ^{4}J = 1.1, $^{4}J_{Sn}$ = 22). *E* isomer: 0.10 (6H, s), 0.80–0.91 (15H, m), 0.92 (9H, s), 1.20–1.60 (12H, m), 1.26 (3H, d, ^{3}J = 7.5), 1.97 (1H, m, ^{3}J = 9.0 ^{3}J = 7.5 and ^{4}J = 1.3, $^{2}J_{Sn}$ = 61), 5.24 (1H, dd, ^{3}J = 9.0 and ^{3}J = 11.8, $^{3}J_{Sn}$ = 22), 6.10 (1H, dd, ^{3}J = 11.8 and ^{4}J = 1.3, $^{4}J_{Sn}$ = 18). ^{13}C NMR ($CDCl_3$): *Z* isomer: −5.3, −5.0, 8.8 (3C, $^{1}J_{Sn}$ = 293/284), 13.9 (3C), 16.4 ($^{1}J_{Sn}$ = 311), 18.5, 18.9 ($^{2}J_{Sn}$ = 18), 25.9 (3C), 27.7 (3C, $^{3}J_{Sn}$ = 55), 29.5 (3C, $^{2}J_{Sn}$ = 18), 117.3 ($^{2}J_{Sn}$ = 38), 133.4 ($^{3}J_{Sn}$ = 46). *E* isomer: −5.2 (2C), 8.5 (3C, $^{1}J_{Sn}$ = 285/299), 13.7 (3C), 18.2, 18.4, 18.6 ($^{1}J_{Sn}$ = 304/318), 25.8 (3C), 27.6 (3C, $^{3}J_{Sn}$ = 51), 29.3 (3C, $^{2}J_{Sn}$ = 19), 118.2 ($^{2}J_{Sn}$ = 30), 135.6 ($^{3}J_{Sn}$ = 50). ^{119}Sn NMR ($CDCl_3$): *Z* isomer: −15.8. *E* isomer: −17.9. MS (EI): organostannyl fragments: *m*/*z* (%) = 476 ($M^{+\bullet}$) (1), 419 (32), 291 (26), 235 (30), 179 (29); organic fragments: *m*/*z* (%) = 185 (62), 73 (100).

1-(*tert*-Butyldimethylsiloxy)-3-(tributylstannyl)-4-methyl-pent-1-ene (*E*/*Z* 20/80, 102 mg, 35% yield) (4)

IR ν_{max}/cm^{-1} (neat): 3020, 2957, 2929, 2857, 1640, 1464, 1258, 1093, 859, 837, 780, 673 cm^{-1}. ^{1}H NMR ($CDCl_3$): *Z* isomer: 0.10 (6H, s), 0.70–1.00 (21H, m), 0.90 (9H, s), 1.20–1.60 (12H, m), 1.88 (1H, m, ^{3}J = 6.4), 2.49 (1H, dd, ^{3}J = 7.8 and 11.7, $^{2}J_{Sn}$ = 61), 4.48 (1H, dd, ^{3}J = 5.8 and 11.7, $^{3}J_{Sn}$ = 19), 6.05 (1H, d, ^{3}J = 5.8, $^{4}J_{Sn}$ = 20). *E* isomer: 0.10 (6H, s), 0.80–1.00 (30H, m), 1.20–1.70 (14H, m), 5.21 (1H, dd, ^{3}J = 11.4 and 12.3), 6.10 (1H, d, ^{3}J = 11.4). ^{13}C NMR ($CDCl_3$): *Z* isomer: −5.3, −5.0, 8.9, 9.9 (3C, $^{1}J_{Sn}$ = 282/296), 10.1, 13.9 (3C), 18.4, 25.9 (3C), 27.7 (3C, $^{3}J_{Sn}$ = 55), 29.5 (3C, $^{2}J_{Sn}$ = 19), 31.5 ($^{2}J_{Sn}$ = 14), 33.1 ($^{1}J_{Sn}$ = 300), 113.0 ($^{2}J_{Sn}$ = 39), 134.7 ($^{3}J_{Sn}$ = 50). *E* isomer: −5.04 (2C), 10.3 (3C, $^{1}J_{Sn}$ = 300), 13.8 (3C), 18.5, 25.7 (2C), 25.8, 26.0 (3C), 27.7 (3C, $^{3}J_{Sn}$ = 55), 29.4 (3C, $^{2}J_{Sn}$ = 20), 114.9, 135.5. ^{119}Sn NMR ($CDCl_3$): *Z* isomer: −23.9. *E* isomer: −24.1. MS (EI): organostannyl fragments: *m*/*z* (%) = 504 ($M^{+\bullet}$) (1), 447 (4), 365 (1), 291 (17), 235 (34), 179 (37); organic fragments: *m*/*z* (%) = 213 (70), 81 (16), 73 (100).

1-(*tert*-Butyldimethylsiloxy)-3-(tributylstannyl)-hept-1-ene (*E*/*Z* 75/25, 270 mg, 90% yield) (5)

IR ν_{max}/cm^{-1} (neat): 3025, 2957, 2929, 2872, 2856, 1465, 1253, 1073, 837, 779, 664 cm^{-1}. ^{1}H NMR ($CDCl_3$): *Z* isomer: 0.10 (6H, s), 0.70–1.00 (27H, m), 1.20–1.60 (18H, m), 2.55 (1H, dt, ^{3}J = 5.8 and ^{3}J = 11.1, $^{4}J_{Sn}$ = 61), 4.42 (1H, dd, ^{3}J = 5.7 and 11.1, $^{3}J_{Sn}$ = 19), 6.01 (1H, d, ^{3}J = 5.7, $^{4}J_{Sn}$ = 21). *E* isomer: 0.10 (6H, s), 0.70–1.00 (18H, m), 0.9 (9H, s), 1.20–1.60 (18H, m), 1.92 (1H, dt, ^{3}J = 5.8 and ^{3}J = 10.0, $^{2}J_{Sn}$ = 58), 5.07 (1H, dd, ^{3}J = 10.0 and 11.5, $^{3}J_{Sn}$ = 23), 6.10 (1H, d, ^{3}J = 11.5, $^{4}J_{Sn}$ = 20). ^{13}C NMR ($CDCl_3$): *Z* isomer: −5.3, −5.0, 9.1 (3C), 13.9 (3C), 14.3, 18.4, 22.5, 23.0, 27.9 (3C), 29.5 (3C), 32.9, 33.2, 115.3, 134.2. *E* isomer: −5.1 (2C), 8.8 (3C, $^{1}J_{Sn}$ = 284/298), 13.8 (3C), 14.2, 18.5,

22.5, 25.2 ($^1J_{Sn}$ = 280), 25.7 (3C), 27.6 (3C, $^3J_{Sn}$ = 53), 29.4 (3C, $^2J_{Sn}$ = 20), 32.3, 33.0, 116.5 ($^2J_{Sn}$ = 39), 136.4 ($^3J_{Sn}$ = 54). ^{119}Sn NMR ($CDCl_3$): *Z* isomer: −19.7. *E* isomer: −20.2. MS (EI): organostannyl fragments: *m*/*z* (%) = 518 ($M^{+\bullet}$, 1), 461 (1), 365 (30), 291 (59), 235 (78), 179 (87), 121 (29); organic fragments: *m*/*z* (%) = 75 (100).

1-(*tert*-Butyldimethylsiloxy)-3-(tributylstannyl)-4,4-dimethyl-pent-1-ene (*E*/*Z* = 85/15, 255 mg, 85% yield) (6)

IR ν_{max}/cm^{-1} (neat): 3023, 2956, 2928, 2858, 1464, 1149, 854, 780, 676 cm^{-1}. ^{1}H NMR ($CDCl_3$): *Z* isomer: 0.10 (6H, s), 0.70–1.00 (24H, m), 1.15 (9H, s), 1.20–1.45 (12H, m), 2.71 (1H, d, ^3J = 12.3, $^2J_{Sn}$ = 64), 4.58 (1H, dd, ^3J = 6.0 and ^3J = 12.3, $^3J_{Sn}$ = 28), 6.11 (1H, d, ^3J = 6.0, $^4J_{Sn}$ = 20). *E* isomer: 0.13 (6H, s), 0.70–1.00 (33H, m), 1.25–1.53 (12H, m), 1.90 (1H, d, ^3J = 12.6, $^2J_{Sn}$ = 61), 5.13 (1H, dd, ^3J = 11.4 and ^3J = 12.6, $^3J_{Sn}$ = 25), 6.11 (1H, d, ^3J = 11.4, $^4J_{Sn}$ = 19). ^{13}C NMR ($CDCl_3$): *Z* isomer: −5.2, −4.9, 10.9 (3C, $^1J_{Sn}$ = 283/294), 13.9 (3C), 18.4, 25.9 (3C), 27.9 (3C), 29.7 (3C), 30.9 (3C), 34.1, 39.6 ($^1J_{Sn}$ = 302), 112.0 ($^2J_{Sn}$ = 38), 135.1 ($^3J_{Sn}$ = 49). *E* isomer: −5.0, −4.9, 10.7 (3C, $^1J_{Sn}$ = 283/294), 13.9 (3C), 18.5, 26.0 (3C), 27.8 (3C, $^3J_{Sn}$ = 55), 29.5 (3C, $^2J_{Sn}$ = 19), 30.9 (3C, $^3J_{Sn}$ = 25), 34.2, 42.7 ($^1J_{Sn}$ = 313/326), 113.1 ($^2J_{Sn}$ = 35), 137.7 ($^3J_{Sn}$ = 59). ^{119}Sn NMR ($CDCl_3$): *Z* isomer: −28.3. *E* isomer: −27.3. MS (EI): organostannyl fragments: *m*/*z* (%) = 518 ($M^{+\bullet}$, 1), 461 (4), 365 (1), 291 (30), 235 (33), 179 (28); organic fragments: *m*/*z* (%) = 227 (92), 95 (31), 73 (100).

1-(*tert*-Butyldiphenylsiloxy)-3-(tributylstannyl)-4,4-dimethyl-pent-1-ene (*E*/*Z* = 90/10, 331 mg, 89% yield) (7)

IR ν_{max}/cm^{-1} (neat): 3072, 2956, 2884, 2857, 1641, 1663, 1141, 1115, 823, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): *Z* isomer: 0.70–1.00 (15H, m), 0.99 (9H, s), 1.07 (9H, s), 1.31 (6H, m), 1.50 (6H, m), 2.90 (1H, d, ^3J = 12.3, , $^3J_{Sn}$ = 63), 4.58 (1H, dd, ^3J = 5.7 and 12.3, , $^3J_{Sn}$ = 22), 6.08 (1H, d, ^3J = 5.7, , $^4J_{Sn}$ = 18), 7.36–7.42 (6H, m), 7.70 (4H, d, ^3J = 4.0). *E* isomer: 0.70–0.90 (15H, m), 0.80 (9H, s), 1.06 (9H, s), 1.20–1.50 (12H, m), 1.79 (1H, d, ^3J = 12.0), 5.20 (1H, dd, ^3J = 11.5 and ^3J = 12.8, $^3J_{Sn}$ = 25), 6.13 (1H, d, ^3J = 11.5, $^4J_{Sn}$ = 19), 7.37–7.41 (6H, m), 7.68–7.72 (4H, m). ^{13}C NMR ($CDCl_3$): *Z* isomer: 11.1 (3C, $^1J_{Sn}$ = 282/294), 14.0 (3C), 19.6, 27.0 (3C), 28.1 (3C, $^3J_{Sn}$ = 57), 29.8 (3C, $^2J_{Sn}$ = 19), 31.2 (3C, $^3J_{Sn}$ = 27), 34.5, 40.1 ($^1J_{Sn}$ = 310), 112.3 ($^2J_{Sn}$ = 37), 128.1 (4C), 130.1, 133.2, 133.3, 135.8 (6C), 136.6 ($^3J_{Sn}$ = 35). *E* isomer: 10.8 (3C, $^1J_{Sn}$ = 284/296), 13.8(3C), 19.3, 26.6 (3C), 27.7 (3C, $^3J_{Sn}$ = 56), 29.4 (3C, $^2J_{Sn}$ = 18), 30.8 (3C, $^3J_{Sn}$ = 24), 34.0, 42.5 ($^1J_{Sn}$ = 318), 113.2 ($^2J_{Sn}$ = 35), 127.7 (4C), 129.8 (2C), 133.3, 133.4, 135.5 (4C), 137.4 ($^3J_{Sn}$ = 59). ^{119}Sn NMR ($CDCl_3$): *Z* isomer: −28.6. *E* isomer: −27.4. MS (EI): organostannyl fragments: *m*/*z* (%) = 642 ($M^{+\bullet}$, 3), 585 (100), 528 (6), 489 (16), 471 (13), 375 (15), 329 (11); organic fragments: *m*/*z* (%) = 351 (18), 230 (5), 173 (28), 75 (45).

***N*-Allyl-succinimide (10)[30,31]**

DEAD (2.28 g, 13.1 mmol) was added to a stirred solution of succinimide (1.00 g, 10.1 mmol), PPh_3 (3.44 g, 13.1 mmol) and allyl alcohol (0.70 g, 12.1 mmol) in THF (40 mL). After 24 h at room temperature, the reaction mixture was concentrated under reduced pressure and Et_2O (10 mL) was added. After precipitation of Ph_3PO, the mixture was filtered and the solvent was removed under reduced pressure. Purification by flash chromatography on silica gel (EtOAc–hexanes 4 : 6) afforded **10** (1.15 g, 82%) as a clear oil. ^{1}H NMR ($CDCl_3$): 2.65 (4H, s), 4.01 (2H, brd, ^3J = 6.0), 5.08 (1H, brd, ^3J = 9.0), 5.11 (1H, brd, ^3J = 17.4), 5.69 (1H, tdd, ^3J = 6.0 ^3J = 9.0 and ^3J = 17.4). ^{13}C NMR ($CDCl_3$): 28.1 (2C), 40.8, 118.1, 130.7, 176.8 (2C).

1-Allyl-5-ethoxy-pyrrolidin-2-one (11)[30,31]

To a stirred, cooled (−10 °C) solution of **10** (1.00 g, 7.19 mmol), $NaBH_4$ (1.09 g, 28.7 mmol) and bromocresol green indicator (2 drops) in EtOH (30 mL) were slowly added HCl (2 drops of a 2 M ethanol solution) every 10 min during a period of 2 h. The blue mixture was brought to pH 3–5 by addition of 6 M aqueous HCl and was diluted with water (10 mL). The mixture was extracted with CH_2Cl_2 and the combined organic layers were washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (EtOAc–hexanes 4 : 6) afforded **11** (0.79 g, 65%) as a clear oil. R_f = 0.20 (EtOAc–hexanes 4 : 6). IR ν_{max}/cm^{-1} (neat): 2977, 2930, 1700 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.21 (3H, t, ^3J = 6.9), 1.98–2.56 (4H, m), 3.48 (2H, q, ^3J = 6.9), 3.60 (1H, dd, ^3J = 6.9 and ^2J = −15.3), 4.24 (1H, dm, ^2J = −15.3), 4.93 (1H, brd, ^3J = 6.0), 5.17 (1H, brd, ^3J = 12.0), 5.24 (1H, brd, ^3J = 18.6), 5.70–5.80 (1H, m). ^{13}C NMR ($CDCl_3$): 15.2, 24.9, 28.9, 42.7, 61.7, 88.4, 117.7, 132.6, 174.7. MS (CI/NH_3): *m*/*z* (%) = 187 (M + NH_4^+, 18), 170 (M + H^+, 100), 124 [(M + H^+) − EtOH, 28]. HRMS: calcd for $C_9H_{15}NO_2$ 169.1103, found 169.1107.

(*rel*-8*R*,8a*R*)-8-(*tert*-Butyldimethylsiloxy)-1,5,8,8a-tetrahydro-2*H*-indolizin-3-one (12)

To a stirred, cooled (−78 °C) solution of **11** (500 mg, 2.95 mmol) in dry CH_2Cl_2 (20 mL) were successively added $BF_3{\cdot}OEt_2$ (1.26 g, 8.86 mmol) and **3*E*** (1.40 g, 2.95 mmol). The reaction mixture was stirred for 1 h at −78 °C, quenched with saturated aqueous $NaHCO_3$ and allowed to warm to ambient temperature. The phases were separated and the aqueous phase was extracted with dichloromethane. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was dissolved in dry degassed dichloromethane and Grubbs' catalyst (122 mg, 5 mol%) was added. The mixture was refluxed for 24 h and then treated with DMSO (500 μL). After 12 h at room temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash chromatography on silica gel (EtOAc–hexanes 6 : 4) gave **12** (640 mg, 81%) as a clear oil. R_f = 0.18 (EtOAc–hexanes 6 : 4). IR ν_{max}/cm^{-1} (neat): 2928, 1639, 1356, 1079 cm^{-1}. ^{1}H NMR ($CDCl_3$): 0.04 (3H, s, SiCH_3), 0.08 (3H, s, SiCH_3), 0.87 (9H, s, (CH_3)$_3$), 2.00–2.17 (2H, m, $H_{1+1'}$), 2.33 (1H, m, ^5J = 1.3, ^3J = 4.4, ^2J = −10.4 and ^3J = 16.3, H_2), 2.49 (1H, m, ^5J = 1.5, ^4J = 1.5, ^3J = 7.8, ^3J = 18.1 and ^2J = −10.4, $H_{2'}$), 3.50 (1H, m, ^2J = −19.2, ^3J = 5.1 and ^5J = 1.5, H_5), 3.67 (1H, m, ^4J = 1.5, ^3J = 2.1, ^3J = 4.7 and ^3J = 8.7, H_{8a}), 4.04 (1H, m, ^4J = 1.6, ^3J = 2.5 and ^3J = 4.7, H_8), 4.40 (1H, ddd,^4J = 3.3, ^3J = 1.6 and ^2J = −19.2, H_5), 5.85 (1H, ddd, ^4J = 3.3, ^3J = 2.5 and ^3J = 10.1, H_7), 5.91 (1H, m, ^4J = 1.6, ^3J = 1.6, ^3J = 5.1 and ^3J = 10.1, H_6). ^{13}C NMR ($CDCl_3$): −4.6 (Si*C*H_3), −3.7 (*C*H_3Si), 18.2 (*C*(CH$_3$)$_3$), 19.8 (C_1), 25.9 (3C, C(*C*H$_3$)$_3$), 30.5 (C_2), 40.3 (C_5), 58.5 (C_{8a}), 65.9 (C_8), 127.2 and 127.5 (C_{6+7}), 174.9 (C_3). MS (CI/NH_3): *m*/*z* (%) = 285 (M + NH_4^+, 15), 268 (M + H^+, 100). HRMS: calcd for $C_{14}H_{26}NO_2Si$ (M + H^+) 268.1733, found 268.1726.

(*rel*-6*S*,7*S*,8*S*,8a*R*)-8-(*tert*-Butyldimethylsiloxy)-6,7-diacetoxy-hexahydro-indolizin-3-one (13)

To a stirred solution of **12** (200 mg, 0.75 mmol) in acetone (9 mL) and water (3 mL) was added NMO (431 mg, 3.74 mmol) and 2.5% OsO_4 in *t*-BuOH (76 mg, 1 mol%). After 24 h at room temperature, the reaction mixture was concentrated under reduced pressure. The crude product was dissolved in pyridine (4 mL) and acetic anhydride (2 mL) was added. After 1 h at room temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash chromatography on silica gel (EtOAc) afforded **13** (268 mg, 93%) as a white solid (mp 129 °C). R_f = 0.41 (EtOAc). IR ν_{max}/cm^{-1} (KBr) 2927, 2854, 1744, 1686, 1242 cm^{-1}. ^{1}H NMR ($CDCl_3$): 0.10 (3H, s, SiCH_3), 0.20 (3H, s, SiCH_3), 0.91 (9H, s, (CH_3)$_3$), 1.89 (1H, m, H_1), 2.00 (3H, s, CH_3CO), 2.06 (1H, m, $H_{1'}$), 2.13 (3H, s, CH_3CO), 2.39 (2H, m, H_2), 2.99 (1H, dd, ^2J = 12.0 and ^3J = 12.0, H_5), 3.77 (1H, dd, ^3J = 1.8 and ^3J = 3.6, H_8), 3.85 (1H, ddd, ^3J = 1.8, ^3J = 3.6 and ^3J = 8.7, H_{8a}), 4.16 (1H, dd, ^2J = 12.0 and ^3J = 6.0,

$H_{5'}$), 5.12 (1H, ddd, ^3J = 3.0, ^3J = 6.0 and ^3J = 12.0, H_6), 5.25 (1H, dd, ^3J = 3.0 and ^3J = 3.6, H_7). ^{13}C NMR ($CDCl_3$): −5.1 (SiCH_3), −4.7 (CH_3Si), 17.8 ($C(CH_3)_3$), 18.4 (C_1), 20.7 (CH_3CO), 20.9 (CH_3CO), 25.6 (3C, C(CH_3)$_3$), 30.6 (C_2), 37.8 (C_5), 55.7 (C_{8a}), 64.5 (C_6), 69.8 (C_8), 70.1 (C_7), 169.5 (CH_3CO), 169.7 (CH_3CO), 174.4 (C_3). MS (CI/NH_3): *m*/*z* (%) = 403 (M + NH_4^+, 61), 386 (M + H^+, 100). HRMS: calcd for $C_{18}H_{32}NO_6Si$ (M + H^+) 386.1999, found 386.1998.

(±)-8-(*tert*-Butyldimethylsiloxy)-1-deoxy-6,8a-di-*epi*-castanospermine (14)

To a stirred solution of **13** (100 mg, 0.26 mmol) in THF (15 mL) was added $BH_3{\cdot}Me_2S$ (1.30 mL of a 2 M toluene solution, 2.60 mmol). The mixture was refluxed for 30 min and water was slowly added. The mixture was extracted with Et_2O and CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by flash chromatography on silica gel (EtOAc–hexanes 35 : 65) afforded **14** (66 mg, 88%) as a clear oil. R_f = 0.20 (EtOAc–hexanes 35 : 65). IR ν_{max}/cm^{-1} (neat): 3384, 2956, 2923, 2857, 1259, 1063 cm^{-1}. ^{1}H NMR ($CDCl_3$): 0.11 (3H, s, SiCH_3), 0.12 (3H, s, SiCH_3), 0.88 (9H, s, $(CH_3)_3$), 1.84 (2H, m, H_{1+2}), 2.05 (1H, m, $H_{2'}$), 2.30 (1H, m, $H_{1'}$), 3.02 (2H, m, H_{3+5}), 3.21 (2H, m, $H_{3'+5'}$), 3.45 (1H, m, H_{8a}), 3.73 (1H, dd, ^3J = 3.3 and ^3J = 6.6, H_7), 4.00 (1H, dd, ^3J = 4.6 and ^3J = 6.6, H_8), 4.09 (1H, m, H_6). ^{13}C NMR ($CDCl_3$): −4.8 (SiCH_3), −4.7 (CH_3Si), 18.0 ($C(CH_3)_3$), 20.9 (C_2), 24.5 (C_1), 25.8 (3C, C(CH_3)$_3$), 55.0 (C_5), 62.3 (C_3), 64.7 (C_6), 66.4 (C_{8a}), 69.9 (C_7), 71.4 (C_8). MS (CI/NH_3): *m*/*z* (%) = 288 (M + H^+, 100). HRMS: calcd for $C_{14}H_{30}NO_3Si$ (M + H^+) 288.1995, found 288.1995.

(±)-1-Deoxy-6,8a-di-*epi*-castanospermine (15)

To a stirred solution of **14** (50 mg, 0.17 mmol) in THF (2 mL) was added TBAF (170 µL of a 1 M THF solution, 0.17 mmol). After 1 h at room temperature, the reaction mixture was concentrated under reduced pressure. Purification by flash chromatography on silica gel (EtOAc–MeOH 8 : 2) gave **15** (29 mg, 95%) as a clear oil. R_f = 0.42 (EtOAc–MeOH 8 : 2). IR ν_{max}/cm^{-1} (neat): 3336, 2955, 2927, 2856, 1077 cm^{-1}. ^{1}H NMR (CD_3OD): 1.89–2.08 (3H, m, $H_{1+2+2'}$), 2.41 (1H, m, $H_{1'}$), 2.93 (2H, m, H_{3+5}), 3.27 (2H, m, $H_{3'+5'}$), 3.42 (1H, dd, ^3J = 3.4 and ^3J = 8.0, H_{8a}), 3.70 (1H, dd, ^3J = 3.4 and ^3J = 3.4, H_8), 3.83 (1H, dd, ^3J = 3.4 and ^3J = 4.5, H_7), 4.12 (1H, ddd, ^3J = 2.7, ^3J = 4.5 and ^3J = 11.4, H_6). ^{13}C NMR (CD_3OD): 23.4 (C_2), 26.1 (C_1), 55.4 (C_5), 59.7 (C_3), 62.2 (C_6), 64.9 (C_{8a}), 71.8 (C_7), 73.6 (C_8). MS (CI/NH_3): *m*/*z* (%) = 174 (M + H^+, 100). HRMS: calcd for $C_8H_{15}NO_3$ 173.1052, found 173.1042.

Single crystal X-ray structure determination

Suitable single crystals of **13** were obtained by slow evaporation of an ethyl acetate solution at room temperature. A first data collection, carried out at room temperature on a Bruker-Nonius KappaCCD diffractometer with graphite-monochromated MoK-$L_{2,3}$ radiation, led to a structure with very large atomic displacement parameters, especially for carbon and oxygen atoms of acetyl groups, suggesting static disorder. To improve the resolution, a second data collection was realized at 100 K, achieved by means of an Oxford cryostream cooler. A weak, two-fold superstructure along the *c* axis was detected, indicating possible resolution of the envisioned room temperature disorder. A model of the low temperature structure was found with the Sir2000[37] direct methods. All subsequent calculations were carried out with the Jana2000 program suite.[38] All non-H atoms were refined with anisotropic atomic displacement parameters. H atoms were fully retrained in geometry (angles and distances), except for those of four CH_3 groups (C10a, C10b, C12a and C12b) for which rotations around the C–C bonds were allowed. Riding isotropic displacement parameter (×1.2) was used for all H atoms. Meaningless residues in the [−0.40;0.64] e Å^{-3} range were observed in the last difference Fourier synthesis. Final refinement details are given in the crystallographic data.

CCDC reference numbers 241959. See http://www.rsc.org/suppdata/ob/b4/b409507c/ for crystallographic data in .cif or other electronic format.

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