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Regioselective Mo-Catalyzed Hydrostannations as Key Steps in the Synthesis of Functionalized Amino Alcohols and Heterocycles

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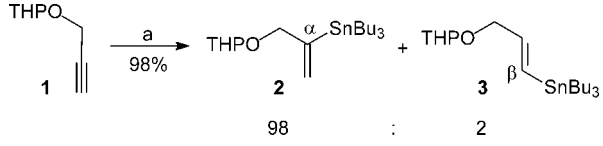
Dedicated to Prof. P. Hofmann on the occasion of 60th birthday

Keywords: Cross coupling / Hydrostannation / Metathesis / Molybdenum / Stannanes

Molybdenum catalyzed hydrostannation of suitable protected propargylic amino alcohols provides the corresponding functionalized vinyl stannanes, which are useful synthetic intermediates for the combinatorial synthesis of amino alcohols and heterocycles.

Introduction

Vinylstannanes are interesting building blocks in organic synthesis, easily available for example by hydrostannations of alkynes.[1] For this purpose either radical or transition metal catalyzed versions have been developed during the last decades.[2] A major drawback of both protocols results form the difficulties to control the stereo- and regioselective outcome of the reaction in case of unsymmetrical alkynes. Recently, our group has developed a new catalyst based on molybdenum.[3] $Mo(CO)_3(CNtBu)_3$ ($MoBl_3$) was found to be an excellent catalyst for highly regio- and stereoselective hydrostannations of functionalized alkynes such as **1** (Scheme 1), preferentially affording the α-stannylated products **2**.[4]



Scheme 1. Hydrostannation of alkyne **1**. Reaction conditions: a) Bu_3SnH (3 equiv.), hydroquinone (10 mol-%), $Mo(CO)_3(CNtBu)_3$ (2 mol-%), THF, 60 °C, 4 h.

These α-regioisomers are not available under radical conditions or by using other metal catalysts, at least not with these yields and selectivities. This protocol has been successfully applied to the synthesis of protected (PG: protecting group) stannylated γ,δ-unsaturated amino acids **4** (Figure 1), which can be further modified, e.g. by Stille coupling reactions giving rise to amino acids with interesting functionalized side chains.[5]

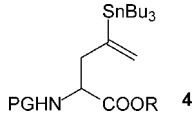


Figure 1. Stannylated amino acid.

Results and Discussion

In principle, these amino acids can easily be reduced to the corresponding amino alcohols, which are also valuable building blocks. But we were also interested to see, if we can obtain suitable protected derivatives such as **6** directly from chiral alkynes such as **5**. This alkyne can easily be obtained from L-serine in 5 steps.[6] Reginato et al. could show, that the β-isomer **7** can selectively be obtained via the addition of $Bu_3Sn(Bu)Cu(CN)Li$ and subsequent partial hydrolysis.[7] To get access to the other regioisomer **6** we subjected alkyne **5** to our molybdenum-catalyzed hydrostannation conditions (Scheme 2). Hydroquinone was added to the reaction mixture to suppress radical hydrostannation. And indeed, in the presence of 2% $MoBl_3$ the reaction was finished after 24 h (THF, 60 °C), and the stannylated products were obtained in high yield as a 9:1 regioisomeric mixture, which could easily be separated by flash chromatography.[8]

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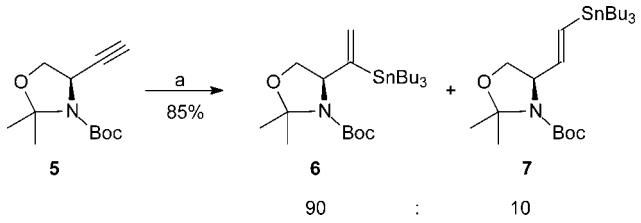
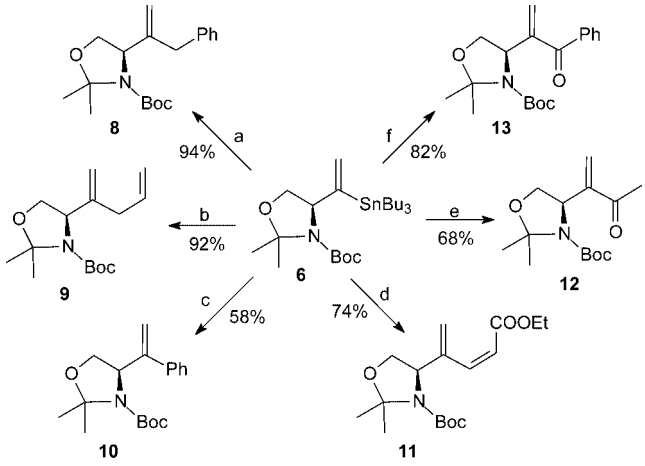


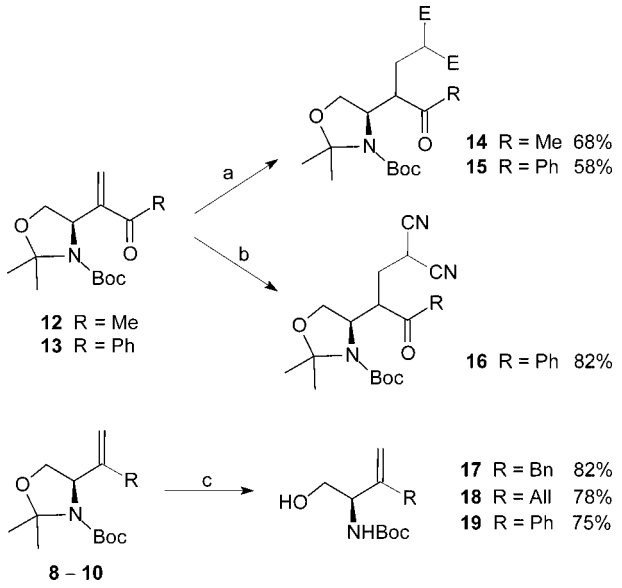
Scheme 2. Hydrostannation of alkyne **5**. Reaction conditions: (a) Bu_3SnH (3 equiv.), hydroquinone (10 mol-%), $Mo(CO)_3(CNtBu)_3$ (2 mol-%), THF, 60 °C, 24 h.

With pure stannane **6** in hand, we subjected it to several cross coupling reactions (Scheme 3). Excellent yields were obtained with benzyl and allyl bromide giving rise to **8** and **9** in a very clean conversion. Different is the situation with aryl halides which show a tendency to undergo *ipso*-substitution via a Heck-type mechanism.[5b,9] Therefore, in the case of **10** the yield dropped to around 60%. Iodoalkenes are also versatile substrates as shown with the coupling of (*Z*)-β-iodoacrylate,[10] which provided the conjugated diene **11** as a single isomer in good yield.[11] In principle, further modifications at the double bonds should be possible, which is also true for the coupling products obtained with acyl halides. Both aromatic and aliphatic acyl chlorides are suitable coupling partners and the vinylogeous ketones **12** and **13** are good candidates for subsequent Michael additions.



Scheme 3. Cross coupling reactions of stannylated amino alcohol derivative **6**. General reaction conditions: 2 mol-% $[(allyl)PdCl]_2$, 4 mol-% PPh_3, 2 equiv. halide, THF, 60 °C, overnight; a) BnBr; b) Allyl bromide; c) PhI; d) (*Z*)-ethyl 3-iodoacrylate; e) acetyl chloride; f) PhCOCl.

For example, in the presence of LiI malonates and malononitrile could be added to these ketones under neutral conditions,[12] but without significant diastereoselectivity (Scheme 4). The best yield was obtained in the addition of malononitrile, and in this case the diastereomers of **16** could be separated by chromatography.

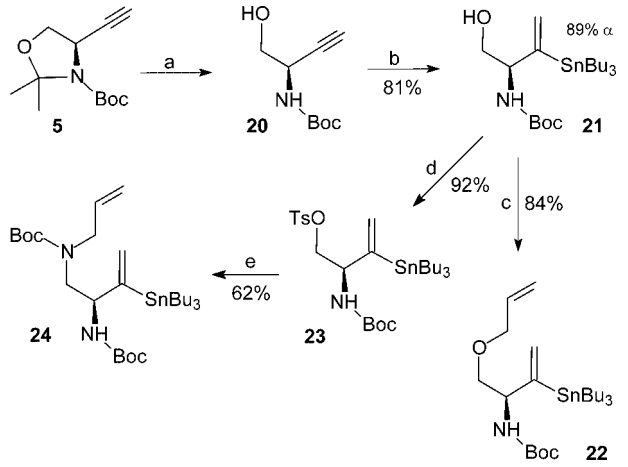


Scheme 4. Modifications of cross coupling products. Reaction conditions: a) $CH_2(COOEt)_2$ (2 equiv.), LiI (2 equiv.), DME, Δ, 24 h; b) $CH_2(CN)_2$ (2 equiv.), LiI (2 equiv.), DME, Δ, 24 h; c) 1) 20 mol-% *p*TsOH, MeOH, H_2O, Δ, 48 h; 2) NEt_3 (1 equiv.), Boc_2O (1 equiv.).

The ketale unit of the coupling products in principle can selectively be removed without affecting the Boc-protecting group (68% yield for the cleavage of **8**), but the yields was slightly better (82%) if some additional Boc_2O was added after the reaction.

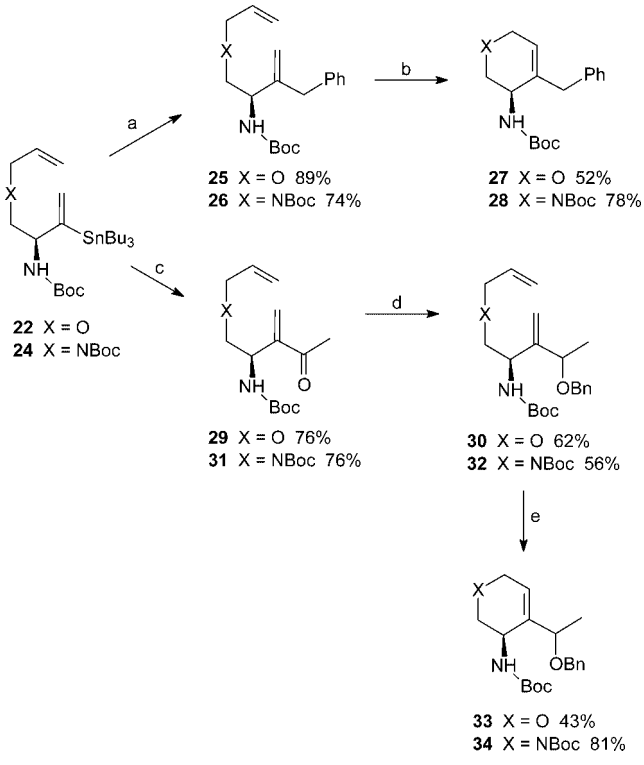
To have an even more flexible access towards these unsaturated alcohols it might be interesting to carry out the Stille couplings directly with the stannylated free alcohol. Because the stannylated ketale **6** would definitely not survive the acidic cleavage conditions, we subjected alcohol **20** also to our hydrostannation conditions (Scheme 5). And indeed, a similar yield and regioselectivity of **21** was obtained as with ketale **6**. The alcohol **21** was afterwards converted into several other derivatives, such as allyl ether **22** and the tosylated **23**, which was further transformed into protected stannylated diamine **24**. Interestingly, no decomposition of the vinyl stannane subunit was observed under all these reaction conditions, probably because all reactions were carried out in a basic medium.

Attempts to subject the stannylated dienes to a ring closing metathesis (RCM) using either "Grubbs I" or "Grubbs II" catalyst failed.[13] Only migration of the double bond was observed,[14] but no cyclization. With respect to the sterically demanding tin substituent, this result is not really surprising. The chances to get the heterocyclic systems should increase if the Stille coupling is carried out prior to the ring closing metathesis. Therefore, both dienes **22** and **24** were coupled (Scheme 6), each with benzyl bromide and acetyl chloride to get two different types of alkenes. Both types of Stille couplings proceeded with good yields, but only the substrates **25** and **26** with the electron rich double bond underwent RCM, while the vinylogeous ketones **29** and **30** did not. This can be explained by electronic factors,



Scheme 5. Synthesis and conversions of stannylated amino alcohol **20**. Reaction conditions: a) 1) 20 mol-% *p*TsOH, MeOH, H_2O, Δ, 48 h; 2) NEt_3 (1 equiv.), Boc_2O (1 equiv.); b) Bu_3SnH (3 equiv.), hydroquinone (10 mol-%), $Mo(CO)_3(CNtBu)_3$ (2 mol-%), THF, 55 °C, 16 h; c) 1) NaH, DMF, 0 °C, 30 min; 2) allyl bromide, room temp., 3 h; (d) TsCl, NEt_3, THF, Δ, 3 h; d) allylamine, Δ, 5 h.

and electron poor alkenes are generally unsuited substrates for RCM.[15] But after reduction of the ketones under "Luche conditions",[16] and protection of the allylic alcohol obtained, the cyclization products **33** and **34** were obtained in acceptable to good yields.



Scheme 6. Synthesis of unsaturated heterocycles via ring closing metathesis. Reaction conditions: (a) BnBr, $Pd(PPh_3)_4$ (2 mol-%), THF, 60 °C, overnight; (b) Grubbs II catalyst, (20 mol-%), CH_2Cl_2, room temp., 2d; (c) acetyl chloride, $[(allyl)PdCl]_2$ (2 mol-%), PPh_3 (4 mol-%), THF, 60 °C, 16 h; (d) 1) $NaBH_4$, $CeCl_3 \cdot 7H_2O$, MeOH, 10 min; 2) $PhCH_2Br$, Bu_4NI, NaH, THF, room temp., 16 h.

Conclusions

In conclusion, we have shown that hydrostannation of alkynes such as **5** gives rise to synthetically interesting intermediates, which can easily be converted into functionalized amino alcohols and heterocyclic structures. The vinylstannanes **6** obtained can be subjected to various Stille-type couplings, including the reactions with acyl halides. The coupling products themselves can be further modified as exemplified with Michael additions and ring closing metatheses.

Experimental Section

General Remarks: All reactions were carried out in oven-dried glassware (100 °C) under argon. All solvents were dried before use. THF was distilled from $LiAlH_4$ and stored over molecular sieves. The products were purified by flash chromatography on silica gel. Mixtures of EtOAc and hexanes were generally used as eluents. TLC: commercially precoated Polygram® SIL-G/UV 254 plates. Visualization was accomplished with UV-light and $KMnO_4$ solution. Melting points are uncorrected. NMR spectra were recorded in $CDCl_3$ using a Bruker DRX 500 NMR spectrometer. The formation of rotamers causes broad signals in some cases and/or a second set of signals. Selected signals in the NMR spectra for the minor isomers are extracted from the spectra of the isomeric mixture. CI-MS analyses were performed using a Finnigan MAT 95. Elemental analyses were carried out at the department of chemistry, University of Saarbrücken.

***N*-(*tert*-Butyloxycarbonyl)-2,2-dimethyl-4-[(1-tributylstannyl)vinyl]-oxazolidine (6):** The alkyne **5** (450 mg, 2.0 mmol), hydroquinone (22.4 mg, 0.20 mmol) and $Mo(CO)_3(CNtBu)_3$ ($MoBI_3$) (17.2 mg, 0.04 mmol) were dissolved in THF (1.6 mL) in a Schlenk tube under argon. Bu_3SnH (1.6 mL, 6.0 mmol) was added slowly and the mixture was warmed to 60 °C until all starting material was consumed (determined by TLC). After cooling to room temperature, the reaction mixture was subjected to flash chromatography. Excess Bu_3SnH was removed using hexane as eluent. The two isomers were separated by chromatography (hexane/ether, 100:1) giving rise to **6** (879 mg, 1.7 mmol, 85%) as a colorless oil. ^1H NMR (500 Hz, $CDCl_3$): δ = 0.88 (t, J = 7.5 Hz, 9 H), 0.93 (t, J = 8.5 Hz, 6 H), 1.31 (m, 6 H), 1.36–1.56 (m, 21 H), 3.58 (dd, J = 8.5, 1.5 Hz, 1 H), 4.06 (dd, J = 6.5, 6.0 Hz, 1 H), 4.50 (m, 1 H), 5.24 (s, $J_{Sn\text{-}H}$ = 59.0 Hz, 1 H), 5.75 (s, $J_{Sn\text{-}H}$ = 126.0 Hz, 1 H) ppm. ^{13}C NMR (500 Hz, $CDCl_3$): δ = 9.7, 13.6, 23.2, 25.8, 27.4, 28.4, 29.0, 64.4, 68.4, 79.4, 94.4, 123.4, 152.4, 152.6 ppm. Selected signals of the minor rotamer: ^{13}C NMR (500 Hz, $CDCl_3$): δ = 9.7, 13.6, 23.2, 25.8, 27.4, 28.4, 29.0, 65.2, 68.4, 79.9, 94.1, 123.5, 152.4, 152.6 ppm. $C_{24}H_{47}NO_3Sn$ (516.33): C 55.83, H 9.17, N 2.71; found C 55.03, H 8.81, N 3.04. HRMS calcd. for $C_{24}H_{48}NO_3Sn$ $[M + H]^+$: 517.2578, found 517.2614.

General Procedures for the Stille Coupling of Vinylstannanes 6: A mixture of vinylstannane **6** (258 mg, 0.50 mmol) and RX (1.0 mmol) was solved in dry THF (2 mL) in a Schlenk tube under argon. A solution of allyl palladium chloride dimer (3.7 mg, 0.01 mmol) and PPh_3 (5.3 mg, 0.02 mmol) was added in THF (2 mL) and the mixture was warmed to 60 °C overnight. After removal of the solvent, the residue was worked up using the "DBU procedure" developed by Curran[17] to remove the tin compound. Therefore, the residue was dissolved in diethyl ether (5 mL) and an excess of DBU was added, while some white solid precipitated. After stirring for a few minutes, a solution of iodide in ether was

added until the iodine colour remains. The solution was transferred to a short column (SiO_2) and after elution of the product with diethyl ether (40 mL), the solvent was removed. The residue was almost tin-free and the product was purified by flash chromatography (silica gel, acetate/hexanes).

4-[(2-Benzyl)vinyl]-*N*-(*tert*-butyloxycarbonyl)-2,2-dimethyloxazolidine (8): According to the general procedure for Stille couplings, **8** was obtained from vinylstannane **6** (256 mg, 0.50 mmol) and benzyl bromide (171 mg, 1.0 mmol) as a colourless oil (149 mg, 0.47 mmol, 94%). ^{1}H NMR (500 Hz, $CDCl_3$): δ = 1.30–1.76 (m, 15 H), 3.27–3.47 (m, 2 H), 3.66 (m, 0.4 H), 3.74 (m, 0.6 H), 4.00 (m, 1 H), 4.27 (m, 0.6 H), 4.42 (m, 0.4 H), 4.75 (s, 1 H), 5.00 (s, 0.6 H), 5.08 (s, 0.4 H), 7.14–7.25 (m, 3 H), 7.28 (dd, J = 7.0, 7.5 Hz, 2 H) ppm. The major conformation: ^{13}C NMR (500 Hz, $CDCl_3$): δ = 23.2, 25.9, 28.4, 39.8, 61.3, 67.8, 79.6, 94.3, 111.9, 126.3, 128.4, 129.3, 138.7, 147.7, 152.1 ppm. Selected signals of the minor rotamer: ^{13}C NMR (500 Hz, $CDCl_3$): δ = 24.6, 26.6, 28.4, 39.4, 62.0, 67.8, 80.2, 94.3, 112.4, 126.3, 128.4, 129.3, 138.7, 147.2, 152.1 ppm. HRMS for $C_{19}H_{27}NO_3$ [M$^+$], 317.1991, found 317.2023.

4-[(1-Benzoyl)vinyl]-*N*-(*tert*-butyloxycarbonyl)-2,2-dimethyloxazolidine (13): According to the general procedure for Stille couplings, **13** was obtained from vinylstannane **6** (256 mg, 0.50 mmol) and benzoyl chloride (141 mg, 1.0 mmol) as a colorless solid (136 mg, 0.41 mmol, 82%), m.p. 71–73 °C. ^{1}H NMR (500 Hz, $CDCl_3$): δ = 1.24–1.83 (m, 15 H), 3.86 (d, J = 9.0 Hz, 0.6 H), 3.91 (d, J = 8.5 Hz, 0.4 H), 4.24 (dd, J = 8.5, 6.5 Hz, 1 H), 4.90 (d, J = 7.0 Hz, 0.6 H), 4.96 (d, J = 5.5 Hz, 0.4 H), 5.78 (s, 0.4 H), 5.83 (s, 0.6 H), 5.95 (s, 0.4 H), 6.06 (s, 0.6 H), 7.38–7.49 (m, 2 H), 7.55 (m, 1 H), 7.75 (d, J = 7.5 Hz, 2 H) ppm. ^{13}C NMR (500 Hz, $CDCl_3$): δ = 22.9, 26.4, 28.4, 57.4, 68.9, 80.0, 94.4, 125.8, 128.3, 129.4, 132.5, 137.5, 147.5, 151.8, 197.3 ppm. Selected signals of the minor rotamer: ^{13}C NMR (500 Hz, $CDCl_3$): δ = 24.4, 27.0, 28.4, 58.3, 68.4, 80.5, 93.9, 125.3, 128.2, 129.5, 132.2, 137.8, 146.2, 152.0, 197.6 ppm. HRMS calcd. for $C_{19}H_{25}NO_4$[M$^+$]: 331.1784, found 331.1751.

The General Procedure for Micheal Additions Towards Vinyl Ketones 12 and 13: A solution of **12** or **13** (0.2 mmol), diethyl malonate (0.4 mmol) or malononitrile (0.4 mmol) and lithium iodide (0.4 mmol) in dimethoxyethane (5 mL) was stirred at reflux for 24 h. After cooling to room temperature, the solvent was evaporated and the residue was purified by flash chromatography (silica, EtOAc/hexanes) to give addition products.

4-(1-Benzoyl-3,3-dicyanopropyl)-*N*-(*tert*-butyloxycarbonyl)-2,2-dimethyloxazolidine (16): According to the general procedure for Michael additions, **16** was obtained from vinyl ketone **13** (61 mg, 0.20 mmol) and malononitrile (26 mg, 0.40 mmol) as a diastereomeric mixture which could be separated by chromatography (EtOAc/hexanes, 10:1, 5:1). The *anti*-isomer was obtained as colorless crystals (27 mg, 0.068 mmol, 34%), m.p. 130–132 °C. ^{1}H NMR (500 Hz, $CDCl_3$): δ = 1.34–1.75 (m, 15 H), 2.28 (m, 1 H), 2.76 (m, 1 H), 3.61–3.93 (m, 3 H), 4.34 (m, 0.4 H), 4.42 (m, 0.6 H), 4.51 (m, 0.4 H), 4.57 (d, J = 10.0 Hz, 0.6 H), 7.41–7.58 (m, 2 H), 7.67 (m, 1 H), 8.06 (m, 1 H), 8.26 (d, J = 7.0 Hz, 1 H) ppm. ^{13}C NMR (500 Hz, $CDCl_3$): δ = 21.1, 23.4, 25.8, 26.8, 28.7, 45.4, 58.0, 62.5, 81.5, 94.2, 112.0, 128.7, 129.1, 134.5, 135.1, 152.7, 199.1 ppm. Selected signals of the minor rotamer: ^{13}C NMR (500 Hz, $CDCl_3$): δ = 21.1, 22.1, 25.8, 26.8, 28.3, 46.5, 56.8, 63.1, 82.0, 95.4, 112.6, 128.7, 129.1, 134.5, 135.1, 151.8, 199.1. The *syn*-isomer was obtained as a colorless oil (38 mg, 0.096 mmol, 48%) ppm. ^{1}H NMR (500 Hz, $CDCl_3$): δ = 0.94 (s, 3 H), 1.33 (s, 3 H), 1.39–1.70 (m, 9 H), 2.18 (m, 1 H), 2.59 (m, 1 H), 3.63 (m, 0.4 H), 3.85 (m, 0.6 H), 3.91 (m, 2 H), 4.08 (m, 0.4 H), 4.25 (m, 0.6 H), 4.43 (m, 1 H), 7.48 (dd, J = 8.0, 7.5 Hz, 2 H), 7.62 (dd, J = 8.0, 7.0 Hz, 1 H), 7.99 (d, J = 8.5 Hz, 2 H) ppm. ^{13}C NMR (500 Hz, $CDCl_3$): δ = 20.6, 23.5, 25.9, 28.3, 30.7, 44.3, 59.9, 63.8, 81.2, 94.2, 111.9, 128.8, 128.9, 134.4, 137.1, 153.0, 199.8 ppm. Selected signals of the minor rotamer: ^{13}C NMR (500 Hz, $CDCl_3$): δ = 20.6, 22.3, 24.7, 28.3, 31.4, 44.3, 60.2, 63.8, 81.2, 94.2, 112.5, 128.8, 128.9, 134.4, 137.1, 153.0, 199.8 ppm. HRMS calcd. for $C_{22}H_{28}N_3O_4$ [M + H]$^+$: 398.2080, found 398.2063.

(2*R*)-2-(*tert*-Butyloxycarbonylamino)-3-methylene-4-phenyl-1-butanol (17): A solution of **8** (137 mg, 0.43 mmol) and PTSA (17 mg, 0.10 mmol) in methanol (5 mL) and H_2O (1 mL) was heated at reflux for 48 h. After cooling to room temperature, Et_3N (61 μL) and Boc_2O (48 mg) was added and stirring was continued at room temperature for additional 2 h. The solvent was evaporated and the residue was purified by flash chromatography (silica, EtOAc/hexanes, 1:2) to give **17** (98 mg, 0.35 mmol, 82%) as white solid, m.p. 73–75 °C. ^{1}H NMR (500 Hz, $CDCl_3$): δ = 1.43 (s, 9 H), 2.06 (br., OH), 3.42 (s, 2 H), 3.63 (m, 2 H), 4.16 (m, 1 H), 4.93 (br., 1 H, NH), 4.94 (s, 1 H), 5.10 (s, 1 H), 7.18–7.24 (m, 3 H), 7.30 (ddd, J = 7.5, 5.5, 1.5 Hz, 2 H) ppm. ^{13}C NMR (500 Hz, $CDCl_3$): δ = 28.4, 41.0, 56.4, 64.3, 79.8, 113.7, 126.5, 128.6, 129.0, 138.5, 146.4, 156.0 ppm. HRMS calcd. for $C_{16}H_{24}NO_3$ [M + H]$^+$: 278.1756, found 278.1767.

(2*R*)-2-(*tert*-Butyloxycarbonylamino)-3-tributylstannyl-3-buten-1-ol (21): According to the synthesis of stannane **6**, **21** was obtained by hydrostannation of alcohol **20** (370 mg, 2.0 mmol) as a colourless oil (774 mg, 1.6 mmol, 81%). ^{1}H NMR (500 Hz, $CDCl_3$): δ = 0.89 (t, J = 7.0 Hz, 9 H), 0.90–0.96 (m, 6 H), 1.27–1.35 (m, 6 H), 1.44 (s, 9 H), 1.45–1.52 (m, 6 H), 2.17 (br., OH), 3.67 (m, 2 H), 4.33 (br., NH), 4.85 (d, J = 7.0 Hz, 1 H), 5.35 (s, J_{Sn-H} = 61.0 Hz, 1 H), 5.89 (s, J_{Sn-H} = 128.0 Hz, 1 H) ppm. ^{13}C NMR (500 Hz, $CDCl_3$): δ = 9.96, 13.6, 27.3, 28.4, 29.0, 60.2, 65.5, 79.7, 126.5, 152.5, 156.0 ppm. HRMS calcd. for $C_{21}H_{44}NO_3Sn$[M + 1]$^+$: 478.2343, found 478.2308.

(2*R*)-2-(*tert*-Butyloxycarbonylamino)-3-tributylstannyl-3-butenyl Tosylate (23): A solution of **21** (1.61 g, 3.38 mmol), *p*-toluenesulfonyl chloride (0.77 g, 4.0 mmol) and Et_3N (0.41 g, 4.0 mmol) in CH_2Cl_2 (15 mL) was heated to reflux for 4 h. After cooling, the solvent was evaporated and the residue was purified by flash chromatography (silica gel, ether/hexanes, 1:80) to give **23** (1.95 g, 3.1 mmol, 92%) as a colorless oil. ^{1}H NMR (500 Hz, $CDCl_3$): δ = 0.72–0.92 (m, 15 H), 1.24–1.33 (m, 6 H), 1.36–1.50 (m, 15 H), 2.43 (s, 3 H), 3.98 (m, 1 H), 4.07 (m, 1 H), 4.42 (m, 1 H), 4.70 (m, 1 H), 5.31 (s, J_{Sn-H} = 60.0 Hz, 1 H), 5.81 (s, J_{Sn-H} = 123.0 Hz, 1 H), 7.35 (d, J = 8.5 Hz, 2 H), 7.77 (d, J = 9.0 Hz, 2 H) ppm. ^{13}C NMR (500 Hz, $CDCl_3$): δ = 9.9, 13.6, 21.6, 27.3, 28.3, 28.9, 56.5, 70.7, 79.7, 127.1, 128.0, 129.9, 132.7, 144.9, 150.0, 154.8 ppm.

(2*S*)-*N*-Allyl-*N*-(*tert*-butyloxycarbonyl)-2-(*tert*-butyloxycarbonylamino)-3-tributylstannyl-3-butenyl-1-amine (24): A solution of crude **23** (475 mg, 0.75 mmol) in allylamine (3 mL) was heated at reflux for 5 h. The excess allylamine was removed by evaporation in vacuo. The residue was dissolved in CH_2Cl_2 (5 mL) and Boc_2O (329 mg, 1.5 mmol) and Et_3N (0.25 mL) was added. The resulting solution was stirred at room temperature for 4 h. The solvent was evaporated and the residue was purified by flash chromatography (silica gel, ether/hexanes, 1:100) to give the product **24** (288 mg, 0.46 mmol, 62%) as a colourless oil. ^{1}H NMR (500 Hz, $CDCl_3$): δ = 0.83–0.98 (m, 15 H), 1.27–1.37 (m, 6 H), 1.38–1.55 (m, 24 H), 2.75 (d, J = 13.5 Hz, 0.6 H), 2.88 (d, J = 14.0 Hz, 0.4 H), 3.43 (m, 0.4 H), 3.57–3.77 (m, 1.6 H), 3.98 (d, J = 15.0 Hz, 0.6 H), 4.14 (d, J = 14.0 Hz, 0.4 H), 4.34 (m, 1 H), 5.10 (m, 2 H), 5.26 (s, J_{Sn-H} = 61.5 Hz, 1 H), 5.55 (br., NH), 5.74 (m, 1 H), 5.86 (s, J_{Sn-H} = 128.0 Hz, 1 H) ppm. ^{13}C NMR (500 Hz, $CDCl_3$): δ = 10.0, 13.7, 27.4, 28.3, 28.4, 29.0, 49.5, 50.0, 58.8, 78.6, 80.0, 116.3, 125.7,

133.9, 154.3, 155.0, 157.0 ppm. $C_{29}H_{56}N_2O_4Sn$ (615.46): C, 56.59; H, 9.17; N, 4.55, found C 56.84, H 8.84, N 4.57. HRMS calcd. for $C_{29}H_{56}N_2O_4Sn$ [M^+]: 616.3262, found 616.3285.

(2*S*)-*N*-Allyl-3-benzyl-*N*-(*tert*-butyloxycarbonyl)-2-(*tert*-butyloxycarbonylamino)-3-butenyl-1-amine (26): Stannane **24** (120 mg, 0.195 mmol) and benzyl bromide (41 mg, 0.24 mmol) was solved in dry THF (1 mL) in a Schlenk tube under argon. $Pd(PPh_3)_4$ (1.7 mg) was added and the solution was warmed to 60 °C overnight. After removal of the solvent, the residue was worked up with DBU procedure to remove the tin compounds. The crude product was purified by flash chromatography on silica gel with acetate-hexane in an appropriate ratio as the eluent to give the coupling products **25** (61 mg, 0.146 mmol, 74%) as a colourless oil. ^{1}H NMR (500 Hz, $CDCl_3$): δ = 1.40 (s, 9 H), 1.44 (s, 6 H), 1.47 (s, 3 H), 2.78 (d, J = 13.0 Hz, 0.6 H), 2.94 (d, J = 13.0 Hz, 0.4 H), 3.35 (m, 0.4 H), 3.40 (s, 2 H), 3.54 (m, 1 H), 3.64 (m, 0.6 H), 3.82 (d, J = 14.5 Hz, 0.6 H), 3.97 (d, J = 13.5 Hz, 0.4 H), 4.23 (m, 1 H), 4.80 (s, 0.6 H), 4.86 (s, 0.4 H), 4.97–5.13 (m, 3 H), 5.58 (s, 1 H), 5.67 (m, 1 H), 7.15–7.23 (m, 3 H), 7.28 (dd, J = 8.5, 7.0 Hz, 2 H) ppm. ^{13}C NMR (500 Hz, $CDCl_3$): δ = 28.2, 28.3, 40.4, 49.0, 49.9, 54.8, 78.8, 80.1, 113.1, 116.4, 126.2, 128.3, 129.2, 133.6, 138.9, 147.6, 155.3, 155.7 ppm. Selected signals of the minor rotamer: ^{13}C NMR (500 Hz, $CDCl_3$): δ = 28.2, 28.3, 40.2, 49.0, 49.4, 54.1, 79.3, 80.1, 113.1, 116.9, 126.3, 128.4, 129.1, 133.6, 138.7, 147.6, 154.9, 157.0 ppm. HRMS calcd. for $C_{24}H_{36}N_2O_4$ [M^+]: 416.2675, found 416.2644.

The General Procedure of the RCM Reactions: The corresponding (**25**, 63 mg, 0.20 mmol) was solved in dry CH_2Cl_2 (10 mL) in a Schlenk tube under argon. Grubbs-II-type catalyst (34 mg, 0.04 mmol, 20%mmol) was added and the solution was stirred 2 d at room temperature. After evaporation of the solvent, and the crude product was purified by flash chromatography (silica gel, ether/hexanes = 1:10, 1:4) to give the cyclization products.

(3*R*)-4-Benzyl-3-(*tert*-butoxycarbonylamino)-1,2,3,6-tetrahydropyran (27): Pyran **27** was obtained from diene **25** (63 mg, 0.20 mmol) as a white solid (30 mg, 0.104 mmol, 52%), m.p. 82–84 °C. ^{1}H NMR (500 Hz, $CDCl_3$): δ = 1.43 (s, 9 H), 3.33 (d, J = 15.5 Hz, 1 H), 3.39 (d, J = 15.5 Hz, 1 H), 3.57 (dd, J = 11.5, 2.5 Hz, 1 H), 3.87 (d, J = 7.0 Hz, 1 H), 3.94 (d, J = 9.0 Hz, 1 H), 4.05 (m, 1 H), 4.13 (d, J = 16.5 Hz, 1 H), 4.86 (br., NH), 5.47 (m, 1 H), 7.16–7.24 (m, 3 H), 7.30 (dd, J = 7.5, 6.0 Hz, 2 H) ppm. ^{13}C NMR (500 Hz, $CDCl_3$): δ = 28.4, 40.4, 46.5, 65.5, 69.9, 79.4, 124.8, 126.3, 128.4, 129.2, 135.9, 138.6, 155.5 ppm. HRMS calcd. for $C_{17}H_{24}NO_3$ [M + 1]$^+$: 290.1756, found 290.1775.

(3*R*)-4-Benzyl-*N*-(*tert*-butoxycarbonyl)-3-(*tert*-butoxycarbonylamino)-1,2,3,6-tetrahydropyridine (28): According to the general procedure for RCM, **28** was obtained from diene **26** (56 mg, 0.13 mmol) as a colourless oil (39 mg, 0.10 mmol, 78%). ^{1}H NMR (500 Hz, $CDCl_3$): δ = 1.44 (s, 9 H), 1.45 (s, 9 H), 2.95 (m, 1 H), 3.35 (m, 2 H), 3.52 (m, 1 H), 4.03 (m, 2 H), 4.28 (s, 1 H), 4.58 (br., NH), 5.43 (m, 1 H), 7.10–7.43 (m, 5 H) ppm. ^{13}C NMR (500 Hz, $CDCl_3$): δ = 28.3, 28.4, 40.7, 42.8, 46.6, 47.4, 79.4, 79.9, 126.3, 128.3, 128.5, 129.2, 138.6, 142.5, 155.2, 155.3 ppm. HRMS calcd. for $C_{22}H_{32}N_2O_4$ [M^+]: 388.2362, found 388.2331.

Supporting Information (see also the footnote on the first page of this article): Analytical and NMR spectroscopic data of all new compounds).

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