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Diastereo- and enantioselective synthesis of protected vicinal silylamines via 1,2-addition to α-silyl-hydrazones †

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Abstract: Nucleophilic 1,2-addition of MeLi/$CeCl_3$ to α-silylaldehyde-SAMP-hydrazones **2** and subsequent reductive NN bond cleavage affords protected vicinal silylamines **4** in good yields with high diastereomeric and enantiomeric excesses. © 1997 Elsevier Science Ltd

The asymmetric synthesis of β-silylamines is not well established. To our knowledge there are only two stereoselective routes to this type of compound reported in the literature, which both describe the diastereoselective synthesis of racemic vicinal silylamines.[1,2] The asymmetric 1,2-addition of organometallic reagents to the CN double bond constitutes a powerful method for the preparation of chiral amines,[3] which are important substrates for the synthesis of bioactive compounds. In continuation with our studies on the asymmetric synthesis of chiral amines[4] based on the (−)-(*S*)-1-amino-2-(methoxymethyl)pyrrolidine (SAMP)/(+)-(*R*)-1-amino-2-(methoxymethyl)pyrrolidine (RAMP)-hydrazone method,[5] we now wish to report a highly diastereo- and enantioselective synthesis of protected vicinal silylamines.

The first key step is the diastereoselective nucleophilic 1,2-addition of MeLi/$CeCl_3$ to the CN double bond of the α-silylaldehyde-SAMP-hydrazones (*S,S*)-**2**, which occurs giving high asymmetric induction. The second key step is the reductive cleavage of the *N*-protected hydrazines **3**, followed by a reprotection of the amine function, affording the protected α-silylamines **4**.

The α-*tert*-butyldimethylsilylaldehyde-SAMP-hydrazones (*S,S*)-**2a–f** are readily available in three steps (54–74% overall yield) from the acetaldehyde **1**.[6] As shown in Scheme 1, the condensation of **1** with SAMP, followed by α-silylation and subsequent α-alkylation affords hydrazones (*S,S*)-**2a–f** with high diastereomeric excesses (*de* ≥95%).

The 1,2-addition of the *in situ* prepared methyl cerium reagent according to Imamoto *et al.*[7] to the CN double bond of the hydrazones (*S,S*)-**2a–f** occurs with good yields (70–91%) and with high diastereoselectivities (*de*=85–≥96%). The unstable intermediate β-silyl-hydrazines were protected as their trifluoroacetamides. This protection step allowed the isolation of the β-silyl-hydrazines and helped facilitate NN bond cleavage in the subsequent step. The absolute configuration of compounds **3** is derived from the assumption that the attack is to the *re*-face. One equivalent of the MeLi/$CeCl_3$ reagent may coordinate to the methoxymethyl group and to the nitrogen of the auxiliary. Then an excess of the organometallic reagent delivers the methyl group to the less hindered *re* face. The (*R*)-configuration of the new stereocentre was confirmed by N.O.E. experiments on compound **3c** (R=*i*-Pr) (Figure 1).

After chromatography, the N-protected hydrazines (*R,S,S*)-**3a–f** were cleaved by treatment with lithium in liquid ammonia[8] with *tert*-butylalcohol as proton source affording, after protection with acetyl chloride, the vicinal silylamines (*R,S*)-**4a–f** in good yields and without detectable epimerisation or racemisation (*de*=83–>99%, *ee*≥99%). The *ee* and *de* values of the protected amines (*R,S*)-**4a–f**

† Key words: SAMP-hydrazone/nucleophilic 1,2-addition/vicinal silylamine/asymmetric synthesis.

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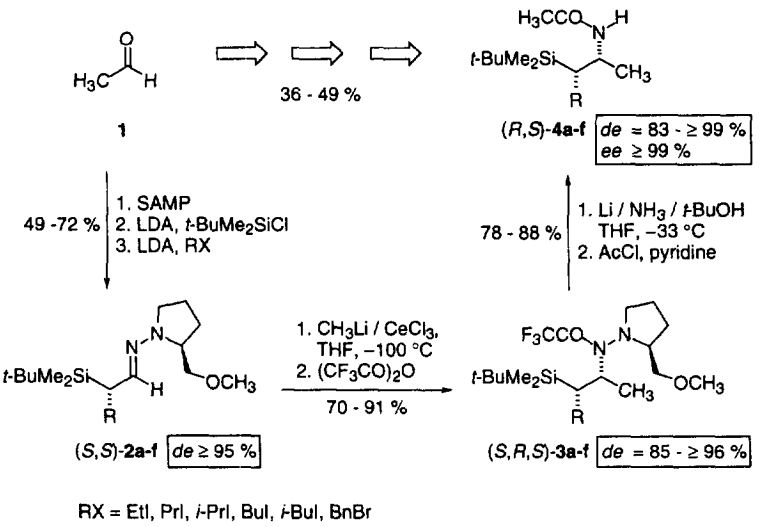

Scheme 1.

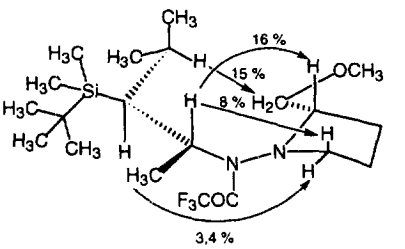

Figure 1. Configuration of **3c** by N.O.E. experiments.

were determined by GC-analysis. The results are shown in Table 1. In the case of **3f** (R=Bn), the phenyl group underwent a *Birch* reduction and was transformed into the 1,4-cyclohexadienyl group.

In summary, we have developed an efficient asymmetric synthesis of 1,2-silylamines starting from acetaldehyde with acceptable overall yields and high diastereomeric and enantiomeric excesses. The extention of this method employing other silyl groups and other organometallic reagents is currently being investigated in our laboratory.

Experimental

Apparatus

The melting points (Büchi-apparatus, system Dr. Tottoli) are uncorrected. Optical rotation values were measured using a Perkin-Elmer P 241 polarimeter. The ^{1}H- and ^{13}C-NMR spectra were recorded in deuteriochloroform on a Varian VXR 300 (300 and 75 MHz). All chemical shifts are quoted in parts per million relative to tetramethylsilane and coupling constants (J) are measured in Hertz. IR spectra were obtained with a Perkin-Elmer FT 1750 spectrometer. Mass spectra were recorded on a Varian Mat 212 (70 eV, 1 mA) spectrometer with DEI ionisation and are represented as m/z (%). Microanalyses were obtained using a Heraeus CHN-O-RAPID element analyser.

Chemicals

All reactions were carried out under argon with magnetic stirring. The reagents were of commercial quality from freshly opened containers or purified prior to use. Methyllithium (1.6 N in

Table 1. Synthesis of *N*-protected hydrazines (*S,R,S*)-**3a–f** and silylamines (*R,S*)-**4a–f**

3 / 4	R	Yield 2→3 [%]	*de* 3[a] [%]	$[\alpha]_D^{RT}$ 3 (c, $CHCl_3$)	Yield 3→4 [%]	*de* 4[b] [%]	*ee* 4[b] [%]	$[\alpha]_D^{RT}$ 4 (c, $CHCl_3$)
a	Et	86	≥96	- 69.3 (0.98)	78	97	≥99	+46.0 (1.04)
b	Pr	79	90	-70.8 (1.03)	84	≥99	≥99	+32.5 (0.98)
c	*i*-Pr	90	≥96	-63.8 (0.95)	87	≥99	99	+20.6 (1.11)
d	Bu	70	94	-66.7 (1.05)	80	94	99	+22.1(1.02)
e	*i*-Bu	79	≥96	-72.5 (1.13)	79	≥99	≥99	+43.0 (1,01)
f	Bn[c]	91	85	-40.6 (1.03)	88	83	≥99	+46.5 (1,04)

[a] Determined by ^{13}C and ^1H NMR spectroscopy.
[b] Determined by GC-analysis on a chiral stationary phase (CP-Chirasil-L-Val).
[c] The phenyl group was reduced to the 1,4-cyclohexadienyl group in the case of compound **4f**.

diethylether) was purchased from Merck. The chiral auxiliary SAMP was prepared according to the literature procedure.[9] Tetrahydrofuran was freshly distilled from potassium–benzophenone–ketyl. Dichloromethane was distilled from calcium hydride. Flash column chromatography was carried out using Merck (230–400 mesh) silica gel. Reactions were monitored by thin-layer chromatography using Merck plates (silica gel F_{254}) and visualized using phosphomolybdic acid 10% or ninhydrin 0.2% in ethanol, followed by heat.

General procedure for the 1,2 addition to the hydrazones ***2a–f***

4 equiv. $CeCl_3 \cdot 7H_2O$ were dried at 140°C/0.1 torr for 2 h, suspended in THF (3 mL/mmol), stirred for 1 h at room temperature and then placed in an ultrasonic bath[10] for 1 h. The suspension was cooled to −78°C and 5 equiv. of methyllithium in Et_2O were slowly added and the mixture stirred for a further 2 h at this temperature. After cooling to −100°C a solution of SAMP-hydrazone (*S,S*)-**2** in THF (3 mL/mmol) was dropped very slowly (10 mL/h) into the suspension. The mixture was then stirred for 1 h at −78°C and was allowed to warm up to room temperature overnight. The solution was then cooled to 0°C and quenched with trifluoroacetic anhydride. After aqueous workup and extraction with Et_2O (3×30 mL) the crude hydrazines **3a–f** were purified by flash chromatography on silica gel (Et_2O/pentane, 1:10)

*(2R,3S,2′S)-N-(3-*tert*-butyldimethylsilylpent-2-yl)-N-(2′-methoxymethylpyrrolidin-1′-yl)-trifluoroacetamide* ***3a***

Starting from 895 mg of (*S,S*) **2a** (3 mmol), 1.06 g of **3a** was obtained. Yield: 86%; Colourless oil; $[\alpha]_D^{25} = -69.3$ (c=1.03, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 0.06 (s, 3H), 0.09 (s, 3H), 0.92 (t, J=7.1, 3H), 0.95 (s, 9H), 1.28–1.41 (m, 2H), 1.49 (d, J=6.4, 3H), 1.52–1.62 (m, 1H), 1.68–1.80 (m, 2H), 1.80–1.87 (m, 1H), 1.92–2.02 (m, 1H), 2.96 (m, 1H), 3.03–3.20 (m, 3H), 3.33 (s, 3H), 3.37–3.51 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.4, −4.1, 16.2, 17.8, 21.2, 21.6, 22.4, 27.8, 28.0, 30.2, 53.4, 57.0, 58.2, 59.2, 75.0, 116.4 (q, $^1J_{CF}$=287.5), 158.9 (q, $^2J_{CF}$=33.0); IR (film) ν_{max} 2958, 2932, 2881, 2859, 1700, 1465, 1378, 1255, 1219, 1160, 1128, 864 cm^{-1}; MS (70 eV) *m/z* 353 (1), 295 (42), 185 (10), 133 (44), 115 (57), 73 (100); Anal. Calcd. for $C_{19}H_{37}F_3N_2O_2Si$: C, 55.58; H, 9.08; N, 6.82%. Found: C, 55.49; H, 9.21; N, 6.92%.

*(2R,3S,2′S)-N-(3-*tert*-butyldimethylsilylhex-2-yl)-N-(2′-methoxymethylpyrrolidin-1′-yl)-trifluoroacetamide* ***3b***

Starting from 644 mg of (*S,S*)-**2b** (2 mmol), 610 mg of **3b** was obtained. Yield: 79%; Colourless oil; $[\alpha]_D^{25} = -70.8$ (c=1.03, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ −0.04 (s, 3H), −0.01 (s, 3H),

0.81 (t, J=6.9, 3H), 0.89 (s, 9H), 1.13–1.34 (m, 4H), 1.49 (d, J=6.6, 3H), 1.54–1.82 (m, 4H), 1.89–1.97 (m, 1H), 2.91 (m, 1H), 2.98–3.06 (m, 1H), 3.07–3.13 (m, 2H), 3.28 (s, 3H), 3.36 (m, 1H), 3.43 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −3.9, −3.7, 15.0, 18.2, 21.6, 22.0, 24.9, 28.2, 28.5, 28.6, 32.7, 53.9, 57.5, 58.4, 59.6, 75.6, 116.0 (q, $^1J_{CF}$=287.4), 159.3 (q, $^2J_{CF}$=33.2); IR (film) ν_{max} 2958, 2932, 2876, 2860, 1700, 1466, 1190, 1161, 1128, 834 cm^{-1}; MS (70 eV) *m/z* 409 (1), 295 (98), 199 (25), 133 (65), 115 (98), 73 (100); Anal. Calcd. for $C_{20}H_{39}F_3N_2O_2Si$: C,56.57; H, 9.26; N, 6.60%. Found: C, 56.60; H, 9.18; N, 6.38%.

*(2R,3S,2′S)-N-(3-*tert*-butyldimethylsilyl-4-methylpent-2-yl)-N-(2′-methoxymethylpyrrolidin-1′-yl)-trifluoroacetamide* ***3c***

Starting from 781 mg of (*S,S*)-**2c** (2.5 mmol), 960 mg of **3c** was obtained. Yield: 90%; Colourless crystals: mp.=51°C; $[\alpha]_D^{25}$ = −63.8 (c=0.95, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.12 (s, 3H), 0.27 (s, 3H), 1.00 (s, 9H), 1.05 (d, J=7.0, 3H), 1.10 (d, J=7.3, 3H), 1.58 (d, J=6.4, 3H), 1.75–1.87 (m, 3H), 1.96 (dhept, J=7.0, J=2.1, 1H), 2.03–2.12 (m, 1H), 2.17 (dd, J=11.6, J=1.8, 1H), 3.08 (m, 2H), 3.18–3.27 (m, 2H), 3.39 (s, 3H), 3.49 (m, 1H), 3.59 (dq, J=6.4, J=11.6, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −2.6, 0.4, 18.0, 20.3, 21.2, 21.3, 24.2, 27.7, 27.8, 28.4, 35.4, 53.7, 55.9, 57.5, 59.3, 75.4, 116.4 (q, $^1J_{CF}$=287.4), 158.9 (q, $^2J_{CF}$=33.2); IR (KBr) ν_{max} 2962, 2936, 2897, 2862, 1698, 1466, 1368, 1260, 1187, 1163, 1124, 843 cm^{-1}; MS (70 eV) *m/z* 409 (1), 393 (1), 367 (7), 295 (50), 133 (45), 115 (56), 73 (100); Anal. Calcd. for $C_{20}H_{39}F_3N_2O_2Si$: C, 56.57; H, 9.26; N, 6.60%. Found: C, 56.46; H, 9.20; N, 6.65%.

*(2R,3S,2′S)-N-(3-*tert*-butyldimethylsilylhept-2-yl)-N-(2′-methoxymethylpyrrolidin-1′-yl)-trifluoroacetamide* ***3d***

Starting from 980 mg of (*S,S*)-**2d** (3 mmol), 921 mg of **3d** was obtained. Yield: 70%; Colourless oil; $[\alpha]_D^{25}$ = −66.7 (c=1.05, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.05 (s, 3H), 0.09 (s, 3H), 0.87 (t, J=6.4, 3H), 0.94 (s, 9H), 1.15–1.39 (m, 6H), 1.49 (d, J=6.4, 3H), 1.56–1.68 (m, 1H), 1.70–1.87 (m, 3H), 1.91–2.10 (m, 1H), 2.96 (m, 1H), 3.06 (m, 1H), 3.15 (m, 2H), 3.33 (s, 3H), 3.40 (m, 1H), 3.49 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.4, −4.1, 13.9, 17.7, 21.2, 21.6, 23.2, 27.8, 28.0, 29.5, 33.5, 53.5, 57.1, 58.0, 59.1, 75.1, 116.4 (q, $^1J_{CF}$=288.1), 158.8 (q, $^2J_{CF}$=33.6); IR (film) ν_{max} 2957, 2932, 2897, 2860, 1700, 1464, 1380, 1255, 1190, 1161, 1128, 834 cm^{-1}; MS (70 eV) *m/z* 428 (1), 295 (72), 213 (18), 199 (25), 133 (39), 115 (75), 73 (100); Anal. Calcd. for $C_{21}H_{41}F_3N_2O_2Si$: C, 57.50; H, 9.42; N, 6.39%. Found: C, 57.32; H, 9.41; N,6.43%.

*(2R,3S,2′S)-N-(3-*tert*-butyldimethylsilyl-5-methylhex-2-yl)-N-(2′-methoxymethylpyrrolidin-1′-yl)-trifluoroacetamide* ***3e***

Starting from 1.15 g of (*S,S*)-**2e** (3,5 mmol), 1.21 g of **3e** was obtained. Yield: 79%; Colourless crystals: mp=39°C; $[\alpha]_D^{25}$ = −72.5 (c=1.13, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ −0.05 (s, 3H), −0.02 (s, 3H), 0.79 (d, J=6.0, 3H), 0.81 (d, J=6.0, 3H), 0.89 (s, 9H), 1.29–1.34 (m, 1H), 1.38–1.44 (m, 1H), 1.46 (d, J=6.4, 3H), 1.62–1.83 (m, 4H), 1.85–1.96 (m, 1H), 2.91 (m, 1H), 3.00 (m, 1H), 3.10 (m, 1H), 3.20 (m, 2H), 3.30 (s, 3H), 3.30–3.38 (m, 1H), 3.47 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.4, −4.0, 13.9, 18.6, 21.0, 21.6, 21.7, 23.7, 26.0, 27.6, 27.7, 28.1, 39.4, 53.5, 57.0, 57.9, 59.1, 75.2, 116.4 (q, $^1J_{CF}$=287.5), 158.0 (q, $^2J_{CF}$=33.0); IR (Et_2O) ν_{max} 2956, 2932, 2898, 2863, 1701, 1466, 1387, 1254, 1191, 1161, 1128, 835 cm^{-1}; MS (70 eV) *m/z* 423 (1), 295 (53), 213 (21), 133 (49), 115 (97), 73 (100); Anal. Calcd. for $C_{21}H_{41}F_3N_2O_2Si$: C, 57.50; H, 9.42; N, 6.39%. Found: C, 57.63; H, 9.40; N, 6.22%.

*(2R,3S,2′S)-N-(3-*tert*-butyldimethylsilyl-4-phenylbut-2-yl)-N-(2′-methoxymethylpyrrolidin-1-yl)-trifluoroacetamide* ***3f***

Starting from 1.08 g of (*S,S*)-**2f** (3 mmol), 1.30 g of **3f** was obtained. Yield: 91%; Colourless oil; $[\alpha]_D^{25}$ = −40.6 (c=1.03, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ −0.04 (s, 3H), 0.05 (s, 3H), 0.70 (s, 9H), 1.59 (s, 3H), 1.69–1.80 (m, 2H), 1.80–1.87 (m, 1H), 1.90–2.05 (m, 1H), 2.20 (dt, J=11.5, J=2.7,

1H), 2.60 (m, 1H), 2.81–2.90 (m, 1H), 2.98 (m, 1H), 3.07–3.18 (m, 3H), 3.30 (s, 3H), 3.40–3.48 (m, 1H), 3.48 (dq, J=11.5, J=6.6, 1H), 7.10–7.17 (m, 1H), 7.20–7.32 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −4.1, −3.2, 17.4, 20.7, 21.7, 27.4, 28.1, 29.6, 35.2, 53.3, 56.7, 58.5, 59.2, 75.0, 116.4 (q, $^1J_{CF}$=287.5), 125.9, 128.1, 128.7, 129.3, 141.6, 159.8 (q, $^2J_{CF}$=33.5); IR (film) ν_{max} 2953, 2930, 2882, 2858, 1698, 1464, 1454, 1191, 1162, 1126, 835 cm^{-1}; MS (70 eV) *m/z* 472 (1), 295 (53), 213 (21), 133 (49), 115 (97), 73 (100); Anal. Calcd. for $C_{24}H_{39}F_3N_2O_2Si$: C, 60.99; H, 8.32; N,5.93%. Found: C, 61.23; H, 8.36; N, 5.81%.

General procedure for the reductive cleavage of the N-protected hydrazines ***4a–f***

To anhydrous liquid ammonia (10 mL/mmol) was added lithium metal (20 equiv.) and dry THF (12.5 mL/mmol). A solution of **3** (1 equiv.) and *tert*-butylalcohol (12 equiv.) in dry THF (12.5 mL/mmol) was then added dropwise to the reaction mixture. The reaction temperature was maintained below −33°C during the addition by an external cooling bath. After the addition was complete, the cooling bath was removed and the reaction mixture was stirred for 4 h at reflux. The reaction mixture was then cooled and quenched *via* the addition of saturated aqueous ammonium chloride solution (0.5 mL/mmol). The ammonia was allowed to evaporate and the residue was dissolved in water, extracted with Et_2O (5×30mL) and washed with a pH 7 buffer. The organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The amines were purified by filtration on silica gel (Et_2O), dissolved in dry CH_2Cl_2 and the solution was cooled to 0°C. Acetyl chloride (10 equiv.) and pyridine (20 equiv.) were added, the mixture was stirred at 0°C for 2 h then ice-water was added. Usual extractive work-up with CH_2Cl_2 and purification by column chromatography (Et_2O) gave the *N*-protected hydrazines **4a–f**.

*(2R,3S)-N-(3-*tert*-butyldimethylsilylpent-2-yl)-acetamide* ***4a***

Starting from 820 mg of **3a** (2 mmol), 380 g of **4a** was obtained. Yield: 78%; Colourless crystals: mp=63°C; $[\alpha]_D^{25}$ = +46.0 (c=1.05, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.01 (s, 3H), 0.06 (s, 3H), 0.90 (s, 9H), 1.04 (d, J=7.2, 3H), 1.19 (d, J=6.7, 3H), 1,40 (dq, J=7.4, J=7.1, 2H), 1.49–1.60 (m, 1H), 1.95 (s, 3H), 4.27 (m, 1H), 5.72 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −5.9, −4.9, 15.7, 17.3, 20.2, 20.3, 23.7, 27.1, 30.7, 46.3, 168.8; IR (Et_2O) ν_{max} 3301, 2957, 2931, 2857, 1644, 1547, 1465, 1416, 1374, 1282, 1251, 1147, 833, 807 cm^{-1}; MS (70 eV) 228 (1), 186 (12), 116 (100), 75 (47), 73 (29); Anal. Calcd. for $C_{13}C_{29}NOSi$: C, 64.13; H, 12.01; N, 5.75%. Found: C, 64.26; H, 12.21; N, 5.60%.

*(2R,3S)-N-(3-*tert*-butyldimethylsilylhex-2-yl)-acetamide* ***4b***

Starting from 848 mg of **3b** (2 mmol), 432 mg of **4b** was obtained. Yield: 84%; Colourless crystals: mp=173°C; $[\alpha]_D^{25}$ = +32.5 (c=0.98, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ −0.01 (s, 3H), 0.05 (s, 3H), 0.90 (s, 9H), 0.93 (t, J=6.8, 3H), 1.00 (m, 1H), 1.18 (d, J=6.7, 3H), 1.29–1.50 (m, 4H), 1.95 (s, 3H), 4.25 (m, 1H), 5.60 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −5.9, −4.9, 14.4, 17.3, 20.3, 23.6, 24.2, 27.1, 28.4, 29.4, 46.5, 168.8; IR (KBr) ν_{max} 3309, 2955, 2931, 2858, 1663, 1639, 1550, 1469, 1374, 1280, 1251, 834, 807 cm^{-1}; MS (70 eV) 228 (1), 200 (30), 116 (100), 75 (35), 73 (29); Anal. Calcd. for $C_{14}H_{31}NOSi$: C, 65.30; H, 12.13; N, 5.44%. Found: C, 66.62; H, 12.11; N, 5.32%.

*(2R,3S)-N-(3-*tert*-butyldimethylsilyl-4-methylpent-2-yl)-acetamide* ***4c***

Starting from 820 mg of **3c** (2 mmol), 447 mg of **4c** was obtained. Yield: 87%; Colourless oil; $[\alpha]_D^{25}$ = +20.6 (c=0.98, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.08 (s, 3H), 0.09 (s, 3H), 0.90 (s, 9H), 1.02 (d, J=7.0, 3H), 1.04 (m, 1H), 1.13 (d, J=7.0, 3H), 1.19 (d, J=6.7, 3H), 1.93 (s, 3H), 2.10 (m, 1H), 4.35 (m, 1H), 5.52 (m, 1H); ^{13}C NMR ($CDCl_3$, 75MHz) δ −4.0, −3.6, 17.5, 22.0, 22.4, 23.8, 24.9, 27.4, 27.8, 35.9, 45.6, 168.3; IR (film) ν_{max} 3299, 2957, 2932, 2858, 1644, 1548, 1465, 1373, 1289, 1258 cm^{-1}; MS (70 eV) 242 (3), 214 (7), 201 (25), 116 (100), 75 (48), 73 (36); Anal. Calcd. for $C_{14}H_{31}NOSi$: C, 65.30; H, 12.13; N, 5.44%. Found: C, 65.59; H, 12.14; N, 5.31%.

*(2R,3S)-N-(3-*tert*-butyldimethylsilylhept-2-yl)-acetamide* ***4d***

Starting from 880 mg of **3d** (2 mmol), 444 mg of **4d** was obtained. Yield: 80%; Colourless crystals: mp=105°C; $[\alpha]_D^{25}$ = +22.1 (c=0.98, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.04 (s, 3H), 0.09 (s, 3H), 0.94 (s, 9H), 0.93–0.96 (m, 3H), 0.96–0.99 (m, 1H), 1.22 (d, J=6.7, 3H), 1.30–1.49 (m, 6H), 2.00 (s, 3H), 4.21–4.34 (m, 1H), 5.52–5.55 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −5.8, −4.9, 14.0,

17.3, 20.3, 23.1, 23.6, 27.0, 27.1, 28.6, 33.4, 46.5, 168.7; IR (KBr)ν_{max} 3304, 2959, 2930, 2856, 1640, 1551, 1467, 1374, 1284, 1252, 1146, 809 cm^{-1}; MS (70 eV) 256 (1), 228 (2), 214 (15), 116 (100), 75 (41), 73 (31); Anal. Calcd. for $C_{15}H_{33}NOSi$: C, 66.35; H, 12.25; N, 5.16%. Found: C, 66.39; H, 12.24; N, 5.10%.

*(2R,3S)-N-(3-*tert*-butyldimethylsilyl-5-methylhex-2-yl)-acetamide* ***4e***

Starting from 880 mg of **3e** (2 mmol), 430 mg of **4e** was obtained. Yield: 79%; Colourless crystals: mp=126°C; $[\alpha]_D^{25}$ = +43.0 (c=1.01, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ −0.01 (s, 3H), 0.07 (s, 3H), 0.90 (s, 9H), 0.92 (d, J=6.4, 3H), 0.96 (d, J=6.4, 3H), 1.17 (d, J=7.1, 3H), 1.23–1.28 (m, 3H), 1.69 (m, 1H), 1.94 (s, 3H), 4.26 (m, 1H), 5.57 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −5.7, −4.5, 17.4, 19.7, 22.0, 23.3, 23.6, 25.5, 27.1, 36.7, 46.3, 168.7; IR (KBr) ν_{max} 3307, 2959, 2931, 2865, 1664, 1639 1546, 1470, 1384, 1281, 1249, 970, 837 cm^{-1}; MS (70 eV) 256 (1), 214 (17), 116 (100), 75 (21), 73 (20); Anal. Calcd. for $C_{15}H_{33}NOSi$: C, 66.35; H, 12.25; N, 5.16%. Found: C, 66.61; H, 12.26; N, 4.98%.

*(2R,3S)-N-(3-*tert*-butyldimethylsilyl-4-cyclohexa-1,4-dienylbut-2-yl)-acetamide* ***4f***

Starting from 940 mg of **3f** (2 mmol), 540 mg of **4f** was obtained. Yield: 88%; Colourless crystals: mp=90°C; $[\alpha]_D^{25}$ = +46.5 (c=1.04, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ −0.01 (s, 3H), 0.10 (s, 3H), 0.90 (s, 9H), 1.14 (d, J=6.7, 3H), 1.58 (dt, J=11.9, J=6.9, 1H), 1.91 (s, 3H), 1.96–2.03 (m, 1H), 2.16–2.19 (m, 1H), 2.40–2.52 (m, 1H), 2.70 (m, 2H), 2.91–2.99 (m, 1H), 4.14 (m, 1H), 5.48–5.49 (m, 2H), 5.66–5.77 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −5.8, −4.1, 17.4, 19.4, 23.6, 24.0, 26.9, 27.1, 28.4, 36.7, 46.3, 119.6, 124.1, 124.4, 134.8, 168.7; IR (KBr) ν_{max} 3316, 2955, 2932, 2856, 1641, 1548, 1471, 1433, 1373, 1251, 959 cm^{-1}; MS (70 eV) 307 (M^+,1), 250 (28), 191 (4), 132 (14), 116 (100), 75 (45), 73 (69); Anal. Calcd. for $C_{18}H_{33}NOSi$: C, 70.30; H, 10.81; N, 4.55%. Found: C, 70.45; H, 10.80; N, 4.45%.

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