Supplementary Material for Organic & Biomolecular Chemistry

Supplementary data

Asymmetrized tris(hydroxymethyl)methane as precursor of *N*- and *O*-containing 6-membered heterocycles through ring closing metathesis

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Note: the employed analytical instruments as well as analysis conditions and some general experimental procedures are reported in the paper.

General procedure for the protection of primary alcoholic functions as THP-ethers

A solution of alcohol (10.95 mmol) in dry CH_2Cl_2 (35 ml) was cooled to 0°C and treated with 3,4-dihydro-2*H*-pyran (2.0 ml, 21.92 mmol) and *p*-TSA (0.1 M sol in THF, 1.1 ml, 110 μmol). After 2 h at 0°C, saturated aq $NaHCO_3$ solution was added and, after dilution with H_2O/Et_2O, the reaction mixture was extracted with ether. The solvent was removed under reduced pressure and, depending upon the product, the crude was directly submitted to the following reaction, or purified by chromatography.

(*R,E)*- and (*S,E)*-5-methyl-2-[(tetrahydro-2*H*-pyran-2-yloxy)methyl]hex-3-enyl acetate

Both enantiomers have been synthesised from **(*R*)-** or **(*S*)-3**. Due to the difficulty to separate products from by-products, the crude was directly submitted to the following tansformations. The structure of them was however confirmed on a not completely purified sample obtained after chromatography with PE/Et_2O 95:5 → 8:2. R_f 0.66 (PE/Et_2O 6:4, B). IR: ν_{max} 2951, 1727, 1249, 1028. GC-MS: R_t 6.53; *m/z* 186 (M^+, 0.015), 109 (6.0), 96 (6.1), 86 (5.9), 81 (5.9), 67 (14), 57 (7.2), 55 (7.1), 43 (34), 41 (10). ^{1}H NMR: 0.95 [6H, d, $(CH_3)_2CH$, J 6.6]; 1.42-1.95 [6H, m, 3 CH_2 of THP]; 2.03 [3H, s, $COCH_3$]; 2.22 [1H, octuplet, $(CH_3)_2CH$, J 6.4]; 2.61 [1H, quintuplet, $CHCH_2OTHP$, J 6.6]; 3.28-3.94 [2H, m, CH_2OTHP]; 4.12 [2H, dd, CH_2OAc, J 2.2, 6.4]; 4.58 [1H, broad dd, $OCHO$, J 4.2, 7.9]; 5.26 [1H, ddt, CH=CH*i*Pr, J 1.2, 8.0, 15.8]; 5.52 [1H, dd, CH=CH*i*Pr, J 6.6, 15.8].

(*S,E*)-5-Methyl-2-[(tetrahydro-2*H*-pyran-2-yloxy)methyl]hex-3-enyl methanesulfonate 11

It was prepared starting from **10**. Chromatography with PE/Et_2O 7:3 → 1:1 gave **11** as a colourless oil in 80% yield. R_f 0.36 (PE/Et_2O 6:4, B). Anal. found C, 54.70; H, 8.65. $C_{14}H_{26}O_5S$ requires C, 54.88; H, 8.55. $[\alpha]_D$ = + 5.5 ($CHCl_3$, c 1.14). IR: ν_{max} 2951, 1356, 1120, 971. GC-MS: R_t 8.08; *m/z* 291 (M^+-15, 0.021), 109 (10), 101 (6.9), 96 (8.0), 93 (5.3), 86 (6.0), 85 (100), 84 (5.8), 81 (11), 79 (7.2), 67 (19), 57 (7.7), 55 (9.5), 43 (9.9), 41 (15). ^{1}H NMR: 0.97 [6H, d, $(CH_3)_2CH$, J 6.6]; 1.55-1.88 [6H, m, 3 CH_2 of THP]; 2.27 [1H, octuplet, $(CH_3)_2CH$, J 6.6]; 2.69 [1H, quintuplet, $CHCH_2OTHP$, J 6.5]; 3.00 [3H, s, SO_2CH_3]; 3.33-3.56 and 3.69-3.90 [4H, 2 m, 2H each, CH_2OTHP and $OCHOCH_2$]; 4.20-4.36 [2H, m, CH_2OMs]; 4.58 [1H, broad dd, $OCHO$, J 4.2, 7.4]; 5.30

[1H, apparent dddd, C*H*=CH*i*Pr, J 1.2, 4.0, 8.2, 15.6]; 5.60 [1H, dd, CH=C*Hi*Pr, J 6.6, 15.4]. ^{13}C NMR: 19.28 and 19.40 [$CH_2CH_2(CH_2)_2O$]; 22.44 and 22.26 [2C, $CH(CH_3)_2$]; 25.33 [$(CH_2)_2CH_2CH_2O$]; 30.45 [$CH_2(CH_2)_3O$]; 31.10 [$CH(CH_3)_2$]; 37.11 [SO_2CH_3]; 42.06 and 42.16 [$CHCH_2OTHP$]; 62.03 and 62.25, 66.93 and 67.07, 70.32 and 70.35 [3C, CH_2OTHP, CH_2OMs, $(CH_2)_3CH_2O$]; 98.62 and 99.22 [OCHO]; 122.65 and 141.71 [2C, C=C].

2-[(*R*,*E*)-2-(Azidomethyl)-5-methylhex-3-enyloxy]-tetrahydro-2*H*-pyran 19

It was prepared starting from **18** and it was usually used as such for the following transformation (see paragraph 4.2.1). The structure of it was however confirmed on a not completely purified sample obtained after chromatography with PE/Et_2O 98:2 → 8:2. R_f 0.58 (PE/Et_2O 7:3, B). IR: ν_{max} 2955, 2099, 1121, 1023. GC-MS: R_t 6.36; *m/z* 225 (M^+-28, 0.016), 86 (5.9), 85 (100), 81 (5.6), 67 (13), 57 (9.3), 55 (11), 43 (14), 41 (17), ^{1}H NMR: 0.98 [6H, d, $(CH_3)_2CH$, J 6.6]; 1.14-1.92 [6H, m, 3 CH_2 of THP]; 2.28 [1H, octuplet, $(CH_3)_2CH$, J 6.6]; 2.48-2.64 [1H, m, $CHCH_2OTHP$]; 3.57-3.97 [6H, m, CH_2OTHP, $OCHOCH_2$, CH_2N_3]; 4.59 [1H, broad dd, OC*H*O, J 3.8, 7.0]; 5.29 [1H, apparent ddq, C*H*=CH*i*Pr, J 1.1, 8.0, 15.4]; 5.59 [1H, dd, CH=C*Hi*Pr, J 6.6, 15.4]. ^{13}C NMR: 19.22 and 19.35 [$CH_2CH_2(CH_2)_2O$]; 22.25 [2C, $CH(CH_3)_2$]; 25.39 [$(CH_2)_2CH_2CH_2O$]; 30.48 [$CH_2(CH_2)_3O$]; 31.13 [$CH(CH_3)_2$]; 42.96 [$CHCH_2OTHP$]; 53.05 [CH_2N_3]; 61.89 and 62.09, 67.92 and 68.28 [2C, CH_2OTHP, $(CH_2)_3CH_2O$]; 98.45 and 99.02 [OCHO]; 124.36 and 141.00 [2C, C=C].

(*R*,*E*)-[5-Methyl-2-{(tetrahydropyran-2-yloxy)methyl]-hex-3-enyl} carbamic acid *tert*-butyl ester 20

It was prepared starting from **21**. Chromatography with PE/Et_2O 9:1 → 8:2 gave **20** as a gold-brown oil in 95% yield. R_f 0.20 (PE/Et_2O 85:15, B). Anal. found C, 65.90; H, 10.25; N, 4.20. $C_{18}H_{33}NO_4$ requires C, 66.02; H, 10.16; N, 4.28. $[\alpha]_D$ = + 3.0 ($CHCl_3$, c 0.97). IR: ν_{max} 3442, 2956, 1697, 1366, 1159, 1120. GC-MS: R_t 8.21; *m/z* 254 (M^+-73, 0.11), 170 (5.2), 169 (7.8), 157 (5.8), 114 (11), 109 (7.8), 108 (6.3), 97 (5.1), 96 (45), 86 (6.3), 85 (100), 82 (7.4), 81 (20), 74 (6.0), 67 (11.7), 57 (60), 55 (8.7), 43 (9.8), 41 (18). ^{1}H NMR: 0.97 [6H, d, $(CH_3)_2CH$, J 7.0]; 1.12-1.88 [6H, m, 3 CH_2 of THP]; 1.44 [9H, s, $C(CH_3)_3$]; 2.26 [1H, octuplet, $(CH_3)_2CH$, J 6.6]; 2.45 [1H, centre of m, $CHCH_2OTHP$]; 3.09-3.91 [6H, m, CH_2OTHP, $OCHOCH_2$, CH_2NH]; 4.55-4.61 [1H, m, OC*H*O]; 4.92 [1H, broad s, N*H*]; 5.22 [1H, broad ddd, C*H*=CH*i*Pr, J 1.0, 8.0, 16.4]; 5.53 [1H, dd, CH=C*Hi*Pr, J 6.6, 15.8]. ^{13}C NMR: 19.11 and 19.33 [$CH_2CH_2(CH_2)_2O$]; 22.40 and 22.45 [2C, $CH(CH_3)_2$]; 25.38 [$(CH_2)_2CH_2CH_2O$]; 28.39 [3C, $C(CH_3)_3$]; 30.43 and 30.50 [$CH_2(CH_2)_3O$]; 31.12 [$CH(CH_3)_2$]; 42.51 [$CHCH_2OTHP$]; 42.73 and 43.03 [CH_2NHBoc]; 61.80 and 62.13, 69.70 [2C, CH_2OTHP, $(CH_2)_3CH_2O$]; 78.81 [$C(CH_3)_3$]; 98.44 and 99.02 [OCHO]; 124.79 and 125.01, 140.62 [2C, C=C]; 156.97 [CO].

General procedure for basic hydrolysis of the acetyl group

A solution of acetate (11.95 mmol) was dissolved in MeOH (30 ml) and, after cooling to 0°C, KOH (1 N sol. in MeOH, 17.5 ml, 17.52 mmol) was added. After 2.5 h at 0°C, the pH was adjusted to 7 by addition of 5% aq $(NH_4)H_2PO_4$. After concentration under reduced pressure, the residue was diluted with water and extracted with Et_2O.

(2*S*,*E*)- and (2*R*,*E*)-5-Methyl-2-[(tetrahydro-2*H*-pyran-2-yloxy)methyl]hex-3-en-1-ol 4

It was obtained starting from crude THP ether prepared from **(*R*)-** or **(*S*)-3**. Chromatography with PE/Et_2O 9:1 → 1:1 gave **4 [(*S*)-** from **(*R*)-3** and **(*R*)-** from **(*S*)-3**] as a colourless oil in 84% overall yield. R_f 0.29 (PE/Et_2O 6:4, B). Anal. found C, 68.55; H, 10.63. $C_{13}H_{24}O_3$ requires C, 68.38; H, 10.59. $[\alpha]_D$ (2*S*-4) = - 22.2 ($CHCl_3$, c 1.22); $[\alpha]_D$ (2*R*-4) = + 23.0 ($CHCl_3$, c 1.05). IR: ν_{max} 3514, 2950, 1120, 1021. GC-MS: R_t 5.96; *m/z* 213 (M^+-15, 0.021), 101 (7.4), 96 (26), 86 (5.8), 85 (100), 81 (11), 67 (15), 57 (19), 55 (11), 43 (14), 41 (14). ^{1}H NMR: 0.97 [6H, d, (CH_3)$_2$CH, J 7.0]; 1.48-1.85 [6H, m, 3 CH_2 of THP]; 2.26 [1H, octuplet, (CH_3)$_2$C*H*, J 6.8]; 2.45-2.65 [2H, m, C*H*CH_2O*H*]; 3.38-3.92 [6H, m, CH_2OTHP, OCHOCH_2, CH_2OH]; 4.56-4.62 [1H, m, OC*H*O]; 5.24 [1H, apparent ddt, C*H*=CH*i*Pr, J 1.2, 8.0, 15.6]; 5.56 [1H, apparent ddd, CH=C*Hi*Pr, J 0.8, 6.6, 15.8]. ^{13}C NMR: 19.46 [$CH_2CH_2(CH_2)_2O$]; 22.39 and 22.44 [2C, $CH(CH_3)_2$]; 25.25 and 25.28 [$(CH_2)_2CH_2CH_2O$]; 30.50 [$CH_2(CH_2)_3O$]; 31.16 [$CH(CH_3)_2$]; 44.34 and 44.56 [*C*HCH_2OTHP]; 62.37, 65.10 and 65.23, 69.80 and 69.94 [3C, CH_2OTHP, $(CH_2)_3CH_2O$, CH_2OH]; 98.87 and 99.17 [O*C*HO]; 123.72 and 123.93, 140.82 [2C, *C*=*C*].

(2*S*,*E*)-2-(Hydroxy)methyl-5-methylhex-3-enyl methanesulfonate 10

It was prepared starting from **8**. Chromatography with PE/Et_2O 2:8 gave **10** as a colourless oil in 87% yield. R_f 0.42 (PE/Et_2O 1:9, B). Anal. found C, 48.50; H, 8.20. $C_9H_{18}O_4S$ requires C, 48.63; H, 8.16. $[\alpha]_D$ = - 13.6 ($CHCl_3$, c 1.73). IR: ν_{max} 3603, 2955, 1354, 1167, 972. GC-MS: R_t 5.83; *m/z* 126 (M^+-96, 6.7), 108 (5.7), 97 (7.8), 96 (58), 95 (49), 93 (21), 83 (6.4), 82 (17), 81 (100), 79 (26), 70 (5.5), 69 (21), 68 (8.8), 67 (24), 57 (9.4), 56 (10), 55 (28), 54 (7.0), 53 (9.3), 43 (17), 41 (35), 39 (12). ^{1}H NMR: 0.99 [6H, d, (CH_3)$_2$CH, J 6.8]; 1.71 [1H, broad s, O*H*]; 2.30 [1H, d of octuplets, (CH_3)$_2$C*H*, J 1.0, 6.7]; 2.61 [1H, centre of m, C*H*CH_2OH]; 3.03 [3H, s, SO_2CH_3]; 3.68 [2H, broad d, CH_2OH, J 5.4]; 4.26 and 4.30 [2H, AB part of ABX system, CH_2OMs, J_{AB} 10.0, J_{AX} 6.8, J_{BX} 5.3]; 5.27 [1H, ddd, C*H*=CH*i*Pr, J 1.2, 8.0, 15.8]; 5.65 [1H, ddd, CH=C*Hi*Pr, J 0.8, 6.6, 15.8]. ^{13}C NMR: 22.28 [2C, $CH(CH_3)_2$]; 31.20 [$CH(CH_3)_2$]; 37.21 [SO_2CH_3]; 44.25 [*C*HCH_2OH]; 62.11 and 69.80 [2C, CH_2OH, CH_2OMs]; 121.99 and 142.76 [2C, *C*=*C*].

General procedure for *O*- and *N*-allylation

Sodium hydride (60% in mineral oil, 552 mg, 13.80 mmol) was poured into the reaction flask and washed twice with dry pentane (10 ml). After addition of dry DMF (10 ml) the suspension was cooled to 0°C and treated with a solution of substrate (9.20 mmol) in dry DMF (5 ml) and allyl bromide (1.3 ml, 13.80 mmol). After 10 min the reaction was allowed to stir at rt untile complete (3-4 h). On nitrogen derivatives sometimes an addition of both reagents was required in order the reaction to go to completion. Quenching with sat. aq NH_4Cl solution, was followed by extractive work-up with water and ether.

(*S*,*E*)- and (*R*,*E*)-2-(2-Allyloxymethyl-5-methylhex-3-enyloxy)tetrahydro-2*H*-pyran 5

It was prepared starting from both enantiomers of **4**. Chromatography with PE/Et_2O 9:1 → 8:2 gave **5** [**(*S*)-** from **(*S*)-4** and **(*R*)-** from **(*R*)-4**] as a colourless oil in 98% yield. R_f 0.57 (PE/Et_2O 8:2, B). Anal. found C, 71.10; H, 10.58. $C_{16}H_{28}O_3$ requires C, 71.60; H, 10.52. $[\alpha]_D \cong 0$. IR: ν_{max} 2951, 2869, 1382, 1190, 1073, 1019. GC-MS: R_t 6.41; *m/z* 253 (M^+-15, 0.030), 101 (5.2), 96 (18), 86 (5.6), 85 (100), 84 (11), 81 (12), 69 (3.3), 67 (12), 57 (7.2), 55 (9.1), 43 (9.8), 41 (20).^{1}H NMR: 0.96 [6H, d, (CH_3)$_2$CH, J 7.0]; 1.45-1.95 [6H, m, 3 CH_2 of THP]; 2.26 [1H, octuplet, (CH_3)$_2$C*H*, J 6.9]; 2.56 [2H, centre of m, C*H*CH_2O*H*]; 3.50-3.90 [6H, m, CH_2OTHP,

OCHOCH_2, CH_2OAllyl]; 3.97 [2H, dt, CH_2CH=CH_2, J 1.2, 5.4]; 4.58 [1H, broad t, OC*H*O, J 3.1]; 5.11-5.40 [3H, m, C*H*=CH*i*Pr, OCH$_2$CH=CH_2]; 5.53 [1H, dd, CH=C*Hi*Pr, J 6.2, 15.8]; 5.90 [1H, ddt, OCH$_2$C*H*=CH$_2$, J 5.4, 10.3, 17.3]. ^{13}C NMR: 19.27 and 19.31 [CH$_2$*C*H$_2$(CH$_2$)$_2$O]; 22.46 and 22.52 [2C, CH(*C*H$_3$)$_2$]; 25.49 [(CH$_2$)$_2$*C*H$_2$CH$_2$O]; 30.53 [*C*H$_2$(CH$_2$)$_3$O]; 31.13 [*C*H(CH$_3$)$_2$]; 42.90 [*C*HCH$_2$OTHP]; 61.77 and 61.82, 68.11 and 68.24 [2C, *C*H$_2$OTHP, (CH$_2$)$_3$*C*H$_2$O]; 71.14 and 71.18, 71.92 [2C, *C*H$_2$O*C*H$_2$CH=CH$_2$]; 98.61 [O*C*HO]; 116.44 [OCH$_2$CH=*C*H$_2$]; 125.43 and 139.68 [2C, *C*=*C*]; 135.01 [OCH$_2$*C*H=CH$_2$].

(*R*,*E*)-Allyl-{5-methyl-2-[(tetrahydropyran-2-yloxy)methyl]hex-3-enyl} carbamic acid *tert*-butyl ester 15

It was prepared starting from **20**. Chromatography with PE/Et$_2$O 85:15 → 7:3 gave **15** as a colourless oil in 22% yield. R$_f$ (two diast. slightly separated) 0.47 and 0.51 (PE/Et$_2$O 7:3, B). Anal. found C, 68.60; H, 10.20; N, 3.85. C$_{21}$H$_{37}$NO$_4$ requires C, 68.63; H, 10.15; N, 3.81. [α]$_D$ = + 14.2 (CHCl$_3$, c 1.69). IR: ν$_{max}$ 2952, 2867, 1678, 1409, 1366, 1192, 1157, 1019. GC-MS: R$_t$ 8.48; *m/z* 294 (M$^+$-73, 0.062), 170 (19), 114 (24), 96 (15), 85 (28), 81 (11), 71 (5.0), 70 (100), 67 (7.0), 57 (79), 55 (6.4), 43 (8.2), 41 (25). ^{1}H NMR: 0.96 [6H, d, (C*H*$_3$)$_2$CH, J 6.6]; 1.43 [9H, s, C(C*H*$_3$)$_3$]; 1.14-1.83 [6H, m, 3 C*H*$_2$ of THP]; 2.24 [1H, octuplet, (CH$_3$)$_2$C*H*, J 6.6]; 2.62 [1H, centre of m, C*H*CH$_2$OTHP]; 3.02-3.88 [8H, m, C*H*$_2$OTHP, OCHOC*H*$_2$, C*H*$_2$N(Boc)C*H*$_2$C=CH$_2$]; 4.57 [1H, apparent broad d, OC*H*O, J 3.0]; 5.01-5.89 [5H, m, C*H*=C*Hi*Pr, NCH$_2$C*H*=C*H*$_2$]. ^{13}C NMR: 19.29 [CH$_2$*C*H$_2$(CH$_2$)$_2$O]; 22.45 [2C, CH(*C*H$_3$)$_2$]; 25.48 [(CH$_2$)$_2$*C*H$_2$CH$_2$O]; 28.42 [3C, C(*C*H$_3$)$_3$]; 30.54 [*C*H$_2$(CH$_2$)$_3$O]; 31.11 [*C*H(CH$_3$)$_2$]; 42.03 and 42.62 [2C, *C*HCH$_2$OTHP, *C*HCH$_2$N]; 48.56, 50.05 and 50.26 [2C, *C*H$_2$N*C*H$_2$CH=CH$_2$]; 61.92 [*C*H$_2$OTHP]; 68.99 and 69.29 [(CH$_2$)$_3$*C*H$_2$O]; 79.19 [*C*(CH$_3$)$_3$]; 98.66 and 98.75 [O*C*HO]; 115.69 and 116.11 [NCH$_2$CH=*C*H$_2$]; 125.82 and 125.93, and 140.14 [2C, *C*=*C*]; 134.20 [NCH$_2$*C*H=CH$_2$]; 155.65 [*C*O].

(*R*,*E*)-Allyl-{2-[(*tert*-butyldimethylsilyloxy)methyl]-5-methylhex-3-enyl} carbamic acid *tert*-butyl ester 24

It was prepared starting from **22**. Chromatography with PE → PE/Et$_2$O 95:5 gave **24** as a pale yellow oil in 53% yield. R$_f$ 0.33 (PE/Et$_2$O 97:3, B). Anal. found C, 66.55; H, 10.80; N, 3.45. C$_{22}$H$_{43}$NO$_3$Si requires C, 66.45; H, 10.90; N, 3.52. [α]$_D$ = + 6.3 (CHCl$_3$, c 1.41). IR: ν$_{max}$ 2955, 2924, 1675, 1154, 1104. GC-MS: R$_t$ 7.90; *m/z* 341 (M$^+$-56, 0.036), 284 (16), 170 (15), 114 (23), 81 (5.1), 75 (24), 73 (19), 71 (5.2), 70 (100), 57 (74), 41 (21). ^{1}H NMR (DMSO-d$_6$; temp=100°C): 0.039 [6H, s, Si(C*H*$_3$)$_2$*t*Bu]; 0.89 [9H, s, SiMe$_2$C(C*H*$_3$)$_3$]; 0.96 [6H, d, (C*H*$_3$)$_2$CH, J 7.0]; 1.40 [9H, s, OC(C*H*$_3$)$_3$]; 2.40 [1H, octuplet, (CH$_3$)$_2$C*H*, J 6.7]; 2.45 [1H, centre of m, C*H*CH$_2$O]; 3.19 [2H, broad d, C*H*$_2$N, J 7.4]; 3.53 [2H, broad d, C*H*$_2$OSi, J 5.0]; 3.76 [2H, broad s, C*H*$_2$CH=CH$_2$]; 5.04-5.13 [2H, m, NCH$_2$CH=C*H*$_2$]; 5.27 and 5.45 [2H, AB part of ABX system, C*H*=C*Hi*Pr, J$_{AB}$ 15.4, J$_{AX}$ 8.2, J$_{BX}$ 6.1]; 5.68-5.87 [1H, m, NCH$_2$C*H*=CH$_2$]. ^{13}C NMR: –5.45 and –5.37 [2C, Si(*C*H$_3$)$_2$C(CH$_3$)$_3$]; 18.28 [Si(CH$_3$)$_2$*C*(CH$_3$)$_3$]; 22.43 [2C, CH(*C*H$_3$)$_2$]; 25.88 [3C, Si(CH$_3$)$_2$C(*C*H$_3$)$_3$]; 28.44 [3C, OC(*C*H$_3$)$_3$]; 31.09 [*C*H(CH$_3$)$_2$]; 44.33 and 44.84 [*C*HCH$_2$N]; 48.17, 49.83 and 50.31 [2C, *C*H$_2$N*C*H$_2$CH=CH$_2$]; 64.83 [*C*H$_2$OSi]; 79.17 [*C*(CH$_3$)$_3$]; 115.68 and 116.02 [NCH$_2$CH=*C*H$_2$]; 126.04 and 139.95 [2C, *C*=*C*]; 134.25 [NCH$_2$*C*H=CH$_2$]; 155.70 [*C*O].

(*R*,*E*)-Allyl-5-methyl-2-[(triisopropylsilyloxy)methyl]hex-3-enyl carbamic acid *tert*-butyl ester 25

It was prepared starting from **23**. Chromatography with PE → PE/Et$_2$O 9:1 gave **25** as a pale yellow oil in 93% yield. R$_f$ 0.61 (PE/Et$_2$O 9:1, B). Anal. found C, 68.35; H, 11.20; N, 3.25. C$_{25}$H$_{49}$NO$_3$Si requires C, 68.28; H,

11.23; N, 3.19. $[\alpha]_D$ = + 8.6 ($CHCl_3$, c 1.44). IR: ν_{max} 2955, 2863, 1677, 1206, 1101. GC-MS: R_t 9.22; *m/z* 396 (M^+-43, 0.038), 340 (67), 170 (19), 131 (5.4), 114 (26), 103 (8.3), 81 (6.3), 75 (22), 73 (8.0), 71 (5.9), 70 (100.), 61 (15), 59 (15), 57 (84), 55 (7.7), 45 (5.5), 43 (6.7), 41 (32). ^{1}H NMR (DMSO-d_6; temp=100°C): 0.96 [6H, d, (CH_3)$_2$CH, J 7.0]; 1.03-1.06 [21H, m, TIPS]; 1.41 [9H, s, OC(CH_3)$_3$]; 2.32 [1H, octuplet, (CH_3)$_2$C*H*, J 6.7]; 2.50 [1H, centre of m, C*H*CH_2O]; 3.22 [2H, d, CH_2N, J 6.8]; 3.65 [2H, broad d, CH_2OSi, J 5.6]; 3.76 [2H, broad d, CH_2CH=CH_2, J 4.4]; 5.00 [2H, apparent broad d, NCH_2CH=CH_2, J 12.0]; 5.32 and 5.47 [2H, AB part of ABX system, C*H*=C*Hi*Pr, J_{AB} 15.4, J_{AX} 8.2, J_{BX} 5.4]; 5.68-5.90 [1H, m, NCH_2C*H*=CH_2]. ^{13}C NMR: 11.96 [3C, Si(*C*H(CH_3)$_2$)$_3$]; 18.02 [6C, Si(CH(*C*H_3)$_2$)$_3$]; 22.40 [2C, CH(*C*H_3)$_2$]; 28.44 [3C, OC(*C*H_3)$_3$]; 31.08 [*C*H(CH_3)$_2$]; 44.68 and 45.21 [*C*HCH_2N]; 48.29, 49.88 and 50.35 [2C, *C*H_2N*C*H_2CH=CH_2]; 65.43 [*C*H_2OSi]; 79.20 [*C*(CH_3)$_3$]; 115.69 and 116.02 [NCH_2CH=*C*H_2]; 126.20 and 139.82 [2C, *C*=*C*]; 134.31 [NCH_2*C*H=CH_2]; 155.70 [*C*O].

(*R*,*E*)-Allyl-5-methyl-2-[(triisopropylsilyloxy)methyl]hex-3-enyl carbamic acid benzyl ester 31

It was prepared starting from **30**. Chromatography with PE/Et_2O 98:2 → PE/Et_2O 95:5 gave **31** as a pale yellow oil in 81% yield. R_f 0.39 (PE/Et_2O 9:1, A, B). Anal. found C, 70.75; H, 10.15; N, 3.05. $C_{28}H_{47}NO_3Si$ requires C, 70.98; H, 10.00; N, 2.96. $[\alpha]_D$ = + 17.3 ($CHCl_3$, c 1.17). IR: ν_{max} 2946, 2962, 1686, 1459, 1108. GC-MS: R_t 11.53; *m/z* 446 (M^+-27, 0.062), 431 (6.7), 430 (21), 160 (17), 100 (5.0), 92 (7.8), 91 (100), 75 (7.7), 59 (5.2). ^{1}H NMR (DMSO-d_6; temp=100°C): 0.92 [6H, d, (CH_3)$_2$CH, J 7.0]; 1.03-1.06 [21H, m, TIPS]; 2.20 [1H, octuplet, (CH_3)$_2$C*H*, J 6.6]; 2.54 [1H, centre of m, C*H*CH_2O]; 3.31 [2H, d, CH_2N, J 7.8]; 3.64 [2H, d, CH_2OSi, J 5.4]; 3.85 [2H, broad d, CH_2CH=CH_2, J 5.6]; 5.07-5.18 [4H, m, NCH_2CH=CH_2 and OCH_2Ph]; 5.30 and 5.43 [2H, AB part of ABX system, C*H*=C*Hi*Pr, J_{AB} 15.7, J_{AX} 8.1, J_{BX} 5.5]; 5.67-5.89 [1H, m, NCH_2C*H*=CH_2]; 7.21-7.47 [5H, m, Ph]. ^{13}C NMR: 11.91 [3C, Si(*C*H(CH_3)$_2$)$_3$]; 18.00 [6C, Si(CH(*C*H_3)$_2$)$_3$]; 22.37 [2C, CH(*C*H_3)$_2$]; 31.04 [*C*H(CH_3)$_2$]; 44.56 and 45.12 [*C*HCH_2N]; 47.95 and 48.69, 50.01 and 50.39 [2C, *C*H_2N*C*H_2CH=CH_2]; 65.25 [*C*H_2OSi]; 66.92 [O*C*H_2Ph]; 116.24 and 116.65 [NCH_2CH=*C*H_2]; 125.75 and 125.93, 140.08 and 140.18 [3C, *C*=*C* and *C ipso* of Ph]; 127.64 [*C para* of Ph]; 127.78 [2C, *C para* of Ph]; 128.38 [2C, *C meta* of Ph]; 133.72 and 133.89 [NCH_2*C*H=CH_2]; 156.25 and 156.34 [*C*O].

(*S*,*E*)-2-(methanesulfonyloxy)methyl-5-methylhex-3-enyl acetate 8

A solution of **(*R*)-3** (1.00 g, 53.69 mmol) in dry CH_2Cl_2 (16 ml) was cooled to –30°C and treated with triethyl amine (1.0 ml, 7.3 mmol) and MsCl (500 µl, 6.46 mmol). After 1 h quenching with sat. aq NH_4Cl was followed by dilution with H_2O/Et_2O and extraction with ether. Chromatography with PE/CH_2Cl_2/Et_2O 2:2:1 gave **8** (1.31 g, 92%) as a pale yellow oil. R_f 0.54 (PE/CH_2Cl_2/Et_2O 2:2:1, B). Anal. found C, 49.80; H, 7.65. $C_{11}H_{20}O_5S$ requires C, 49.98; H, 7.63. $[\alpha]_D$ = - 0.45 ($CHCl_3$, c 1.22). IR: ν_{max} 2955, 2867, 1736, 1359, 1220, 1170, 973. GC-MS: R_t 6.42; *m/z* 205 (M^+-59, 0.092), 109 (10), 108 (49), 96 (7.8), 95 (17), 94 (8.0), 93 (100), 91 (6.7), 82 (6.2), 81 (34), 79 (22), 77 (6.5), 69 (8.0), 68 (5.5), 67 (15), 55 (14), 53 (5.8), 43 (95), 41 (19), 39 (6.9). ^{1}H NMR: 0.98 [6H, d, (CH_3)$_2$CH, J 6.6]; 2.07 [3H, s, COCH_3]; 2.30 [1H, d of octuplets, (CH_3)$_2$C*H*, J 0.8, 7.4]; 2.61 [1H, hexuplet, C*H*CH_2OAc, J 6.4]; 3.02 [3H, s, SO_2CH_3]; 4.07 and 4.16 [2H, AB part of ABX system, CH_2OMs or CH_2OAc, J_{AB} 11.0, J_{AX} 6.5, J_{BX} 5.6]; 4.21 and 4.24 [2H, AB part of ABX system, CH_2OMs or CH_2OAc, J_{AB} 9.6, J_{AX} 6.1, J_{BX} 5.5]; 5.24 [1H, ddd, C*H*=CH*i*Pr, J 1.2, 8.0, 15.8]; 5.63 [1H, dd, CH=C*Hi*Pr, J 6.6, 15.8]. ^{13}C NMR:

20.71 [CO*C*H$_3$]; 22.13 and 22.15 [2C, CH(*C*H$_3$)$_2$]; 31.11 [*C*H(CH$_3$)$_2$]; 37.26 [SO$_2$*C*H$_3$]; 41.15 [*C*HCH$_2$OAc]; 63.48 and 69.27 [2C, *C*H$_2$OH, *C*H$_2$OMs]; 121.33 and 142.70 [2C, *C*=*C*]; 170.67 [*C*O].

General procedure for the nucleophilic displacement of the mesylate by means of allyl amine

A 0.2-0.4 M solution of **8**, **11** or **12** in allylamine was heated at 80°C in sealed tube (8, 11) for 20-24 h and 120°C (12) for 2 h. Excess amine was removed under vacuo and the crude was directly purified by chromatography.

(*R*,*E*)-2-[(Allylamino)methyl]-5-methylhex-3-enyl acetate 9

It was prepared starting from **8**. Chromatography with PE/AcOEt 1:1 → AcOEtMeOH 1:1 gave **9** as a yellow oil (42%). R$_f$ 0.36 (AcOEt, B). Anal. found C, 69.50; H, 10.20; N, 6.20. C$_{13}$H$_{23}$NO$_2$ requires C, 69.29; H, 10.29; N, 6.22. [α]$_D$ = - 9.0 (CHCl$_3$, c 1.74). IR: ν$_{max}$ 2997, 2953, 1621, 1245. GC-MS: R$_t$ 6.43; *m/z* 205 (M$^+$, 0.21), 112 (32), 81 (6.3), 70 (100), 43 (18), 41 (17). ^{1}H NMR: 0.98 [6H, d, (C*H*$_3$)$_2$CH, J 7.0]; 2.12 [3H, s, COC*H*$_3$]; 2.18-2.40 [2H, m, (CH$_3$)$_2$C*H* and C*H*CH$_2$OAc]; 3.11 and 3.72 [2H, AB part of ABX system, C*H*$_2$NHAllyl, J$_{AB}$ 12.7, J$_{AX}$ 4.9, J$_{BX}$ 6.5]; 3.38-3.58 [2H, m, NHC*H*$_2$CH=CH$_2$]; 3.86-4.01 [2H, m, C*H*$_2$OAc]; 5.07-5.87 [5H, m, *H* on sp^2 C]; ^{13}C NMR: 21.23 [CO*C*H$_3$]; 22.27 and 22.40 [2C, CH(*C*H$_3$)$_2$]; 31.09 [*C*H(CH$_3$)$_2$]; 43.59 [*C*HCH$_2$OAc]; 47.05 and 51.85 [2C, 2 *C*H$_2$N]; 62.37 [*C*H$_2$OAc]; 116.85 [CH=*C*H$_2$]; 125.49 and 140.09 [2C, *C*H=*C*H]; 132.15 [*C*H=CH$_2$]; 172.52 [*C*O].

(*R*,*E*)-Allyl-5-methyl-2-[(tetrahydro-2*H*-pyran-2-yloxy)methyl]hex-3-enyl amine 13

It was prepared starting from **11**. Chromatography with Et$_2$O + 2% Et$_3$N gave **13** as a yellow oil (92%). R$_f$ 0.41 (Et$_2$O + 2% Et$_3$N, B). Anal. found C, 71.95; H, 10.85; N, 5.15. C$_{16}$H$_{29}$NO$_2$ requires C, 71.86; H, 10.93; N, 5.24. [α]$_D$ = + 18.19 (CHCl$_3$, c 1.41). IR: ν$_{max}$ 3079, 2952, 2865, 1451, 1118, 1072, 1019. GC-MS: R$_t$ 5.28; *m/z* 2267 (M$^+$, 0.092), 96 (10), 85 (20), 81 (12), 71 (5.3), 70 (100), 67 (5.1), 43 (5.0), 41 (17). ^{1}H NMR: 0.97 [6H, d, (C*H*$_3$)$_2$CH, J 6.6]; 1.38-1.85 [6H, m, 3 C*H*$_2$ of THP]; 2.18-2.35 [1H, m, (CH$_3$)$_2$C*H*]; 2.48-2.58 [2H, m, C*H*$_2$NHAllyl]; 2.70-2.85 [1H, m, C*H*CH$_2$OTHP]; 3.23-3.91 [6H, m, 2 C*H*$_2$O and NC*H*$_2$CH=CH$_2$]; 4.58 [1H, broad apparent s, OC*H*O]; 5.01-5.26 [3H, m, CH=C*H*$_2$ and C*H*=CH]; 5.55 [1H, dd, CH=C*H*, J 6.6, 15.4]; 5.81-6.00 [1H, m, C*H*=CH$_2$]. ^{13}C NMR: 19.31 and 19.38 [CH$_2$*C*H$_2$(CH$_2$)$_2$O]; 22.63 and 22.53 [2C, CH*C*H$_3$)$_2$]; 25.49 [(CH$_2$)$_2$*C*H$_2$CH$_2$O]; 30.57 [*C*H$_2$(CH$_2$)$_3$O]; 31.17 [*C*H(CH$_3$)$_2$]; 42.89 and 42.95 [*C*HCH$_2$OTHP]; 51.22, 51.48, 52.35 and 52.42 [2C, 2 *C*H$_2$N]; 61.95, 61.99 and 70.02 [2C, 2 *C*H$_2$O]; 98.56 and 98.73 [O*C*HO]; 115.54 [CH=*C*H$_2$]; 126.05, 126.28, 140.49 and 140.56 [2C, *C*H=*C*H]; 136.99 [*C*H=CH$_2$].

(*R*,*E*)-Allyl-5-methyl-2-[(triisopropylsilyloxy)methyl]hex-3-enylamine 14

It was prepared starting from **12**. Chromatography with PE/AcOEt 1:1 + 2% Et$_3$N → AcOEt/Et$_3$N 9:1 gave **14** as a yellow oil (54%). R$_f$ 0.55 (PE/AcOEt 1:1 + 2% Et$_3$N, B). Anal. found C, 70.50; H, 12.25; N, 4.25. C$_{20}$H$_{41}$NOSi requires C, 70.73; H, 12.17; N, 4.12. [α]$_D$ = + 5.1 (CHCl$_3$, c 0.82). IR: ν$_{max}$ 2927, 2862, 1458, 1222, 1096. GC-MS: R$_t$ 7.70; *m/z* 339 (M$^+$, 0.66), 296 (11), 131 (5.3), 75 (6.5), 71 (5.2), 70 (100), 41 (5.6). ^{1}H NMR: 0.97 [6H, d, (C*H*$_3$)$_2$CH, J 6.6]; 1.04-1.10 [21H, m, TIPS]; 2.17-2.61 [2H, m, (CH$_3$)$_2$C*H* and C*H*CH$_2$OSi]; 2.53 and 2.80 [2H, AB part of ABX system, C*H*$_2$NHAllyl, J$_{AB}$ 11.0, J$_{AX}$ 8.0, J$_{BX}$ 4.8]; 3.24 [2H, centre of m,

NHC*H*$_2$CH=CH$_2$]; 3.60 and 3.68 [2H, AB part of ABX system, C*H*$_2$OTIPS, J_{AB} 9.5, J_{AX} 6.8, J_{BX} 5.0]; 5.05-5.26 [2H, m, CH=C*H*$_2$]; 5.36 [1H, dd, C*H*=CH*i*Pr, J 6.0, 11.4]; 5.53 [1H, dd, CH=C*Hi*Pr, J 6.2, 15.4]; 5.90 [1H, centre of m, C*H*=CH$_2$]. ^{13}C NMR: 11.96 [3C, Si(*C*H(CH$_3$)$_2$)$_3$]; 18.04 [6C, Si(CH(*C*H$_3$)$_2$)$_3$]; 22.52 and 22.63 [2C, CH(*C*H$_3$)$_2$]; 29.71 [*C*H(CH$_3$)$_2$]; 45.56 [*C*HCH$_2$OSi]; 51.18 and 52.51 [2C, 2 *C*H$_2$N]; 66.38 [*C*H$_2$OSi]; 115.58 [CH=*C*H$_2$]; 126.43 and 140.37 [2C, *C*H=*C*H]; 137.06 [*C*H=CH$_2$].

General procedure for the introduction of silylated (TBDMS or TIPS) protecting groups on primary alcohols using $R^1_2R^2SiCl$

A solution of alcohol (7.76 mmol) in dry DMF (10 ml) was treated with imidazole (13.19 mmol, 898 mg) and the appropriate $R^1_2R^2SiCl$ (10.10 mmol). The solution was stirred at rt for 1-2 h and then diluted with water. After extraction with ether, the organic layers were washed with water and finally with brine. After solvent removal the crude was purified by chromatography as reported for each compound.

(*S*,*E*)-5-Methyl-2-[(triisopropylsilyloxy)methyl]hex-3-enyl methanesulfonate 12
It was prepared starting from **10** using TIPS-Cl. Chromatography with PE/Et$_2$O 8:2 gave **32** as a colourless oil in 73% yield. R_f 0.54 (PE/Et$_2$O 8:2, B). Anal. found C, 57.25; H, 10.10. $C_{18}H_{38}O_4SSi$ requires C, 57.10; H, 10.12. $[\alpha]_D$ = + 3.2 ($CHCl_3$, c 1.02). IR: ν_{max} 2952, 2866, 1356, 1198, 1167. GC-MS: R_t 8.88; *m/z* 283 (M^+-95, 0 .21), 211 (8.7), 210 (13), 209 (94), 181 (11), 153 (10), 139 (6.5), 110 (8.8), 109 (100), 81 (11), 79 (6.9), 77 (5.5) , 75 (17), 73 (7.2), 67 (32), 61 (13), 59 (16), 55 (14), 45 (8.9), 43 (15), 41 (14). ^{1}H NMR: 0.97 [6H, d, (C*H*$_3$)$_2$CH, J 6.6]; 1.02-1.12 [21H, m, TIPS]; 2.64 [1H, centre of m, (CH$_3$)$_2$C*H*]; 2.56 [1H, centre of m, C*H*CH$_2$Si]; 2.99 [3H, s, SO$_2$C*H*$_3$]; 3.67 and 3.77 [2H, AB part of ABX system, C*H*$_2$OTIPS, J_{AB} 9.7, J_{AX} 6.5, J_{BX} 4.3]; 4.27 and 4.33 [2H, AB part of ABX system, C*H*$_2$OMs, J_{AB} 9.3, J_{AX} 5.2, J_{BX} 6.6]; 5.31 [1H, ddd, C*H*=CH*i*Pr, J 1.0, 8.0, 15.8]; 5.59 [1H, dd, CH=C*Hi*Pr, J 6.6, 15.8]. ^{13}C NMR: 11.90 [3C, Si(*C*H(CH$_3$)$_2$)$_3$]; 17.98 [6C, Si(CH(*C*H$_3$)$_2$)$_3$]; 22.28 [2C, CH(*C*H$_3$)$_2$]; 31.16 [*C*H(CH$_3$)$_2$]; 37.09 [SO$_2$*C*H$_3$]; 44.68 [*C*HCH$_2$OTIPS]; 63.12 and 70.25 [2C, *C*H$_2$OSi, *C*H$_2$OMs]; 122.86 and 141.64 [2C, *C*=*C*].

(*R*,*E*)-{2-[(*tert*-Butyldimethylsilyloxy)methyl]-5-methylhex-3-enyl} carbamic acid *tert*-butyl ester 22
It was prepared starting from **21** using TBDMS-Cl. Chromatography with PE/Et$_2$O 95:5 → 9:1 gave **22** as a pale yellow oil in 84% yield. R_f 0.50 (PE/Et$_2$O 9:1, B). Anal. found C, 63.85; H, 10.95; N, 3.85. $C_{19}H_{39}NO_3Si$ requires C, 63.81; H, 10.99; N, 3.92. $[\alpha]_D$ = + 13.5 ($CHCl_3$, c 1.41). IR: ν_{max} 3441, 2955, 2858, 1699, 1462, 1388, 1365, 1160, 1103. GC-MS: R_t 7.62; *m/z* 341 (M^+-57, 0.14), 284 (5.0), 246 (5.5), 245 (18), 244 (100), 200 (5.7), 169 (5.4), 118 (15), 109 (11), 108 (5.8), 104 (9.7), 100 (5.6), 96 (25), 95 (8.2), 89 (12), 82 (8.9), 81 (17), 75 (53), 74 (14), 73 (37), 67 (12), 59 (10), 58 (5.2), 57 (71), 55 (13), 41 (17). ^{1}H NMR: 0.049 [6H, s, Si(C*H*$_3$)$_2$*t*Bu]; 0.90 [9H, s, SiMe$_2$C(C*H*$_3$)$_3$]; 0.96 [6H, d, (C*H*$_3$)$_2$CH, J 7.0]; 1.43 [9H, s, OC(C*H*$_3$)$_3$]; 2.13-2.40 [2H, m, (CH$_3$)$_2$C*H*, C*H*CH$_2$O]; 3.19 [2H, broad t, C*H*$_2$N, J 6.1]; 3.52 and 3.63 [2H, AB part of ABX system, C*H*$_2$OSi, J_{AB} 10.0, J_{AX} 7.4, J_{BX} 4.5]; 5.06 [1H, broad s, N*H*];]; 5.18 [1H, dd, C*H*=CH*i*Pr, J 8.0, 15.8]; 5.51 [1H, dd, CH=C*Hi*Pr, J 6.2, 15.4]. ^{13}C NMR: –5.57 and –5.51 [2C, Si(*C*H$_3$)$_2$C(CH$_3$)$_3$]; 18.16 [Si(CH$_3$)$_2$*C*(CH$_3$)$_3$]; 22.40 and 22.46 [2C, CH(*C*H$_3$)$_2$]; 25.84 [3C, Si(CH$_3$)$_2$C(*C*H$_3$)$_3$]; 28.39 [3C, OC(*C*H$_3$)$_3$]; 31.13 [*C*H(CH$_3$)$_2$]; 44.35 [CH*C*H$_2$N]; 44.48 [*C*HCH$_2$N]; 66.29 [*C*H$_2$OSi]; 78.67 [*C*(CH$_3$)$_3$]; 124.93 and 140.40 [2C, *C*=*C*]; 155.98

[*C*O].

(*R*,*E*)-5-Methyl-2-[(triisopropylsilyloxy)methyl]hex-3-enyl carbamic acid *tert*-butyl ester 23

It was prepared starting from **21** using TIPS-Cl. Chromatography with PE/Et_2O 95:5 → 9:1 gave **23** as a pale yellow oil in 88% yield. R_f 0.51 (PE/Et_2O 9:1, B). Anal. found C, 66.25; H, 11.40; N, 3.45. $C_{22}H_{45}NO_3Si$ requires C, 66.11; H, 11.35; N, 3.50. $[\alpha]_D$ = + 21.3 ($CHCl_3$, c 1.08). IR: ν_{max} 3443, 2937, 2863, 1694, 1365, 1199, 1161, 1111. GC-MS: R_t 8.99; *m/z* 326 (M^+-57, 3.3), 302 (6.1), 301 (22), 300 (100), 131 (9.6), 130 (5.9), 1 09 (10), 96 (5.1), 81 (5.2), 75 (13), 67 (6.8), 61 (7.4), 59 (9.3), 57 (21), 55 (7.4), 41 (6.3). ^{1}H NMR: 0.96 [6H, d, (CH_3)$_2$CH, J 7.0]; 1.04-1.28 [21H, m, TIPS]; 1.43 [9H, s, OC(CH_3)$_3$]; 2.16-2.42 [2H, m, (CH_3)$_2$C*H*, C*H*CH_2O]; 3.23 [2H, broad t, CH_2N, J 5.9]; 3.62 and 3.74 [2H, AB part of ABX system, CH_2OSi, J_{AB} 9.8, J_{AX} 7.2, J_{BX} 4.6]; 5.16 [1H, broad s, N*H*];]; 5.22 [1H, dd, C*H*=CH*i*Pr, J 7.6, 15.6]; 5.51 [1H, dd, CH=C*Hi*Pr, J 6.6, 15.4]. ^{13}C NMR: 11.82 [3C, Si(*C*H(CH_3)$_2$)$_3$]; 17.98 [6C, Si(CH(*C*H_3)$_2$)$_3$]; 22.35 and 22.43 [2C, CH(*C*H_3)$_2$]; 28.39 [3C, OC(*C*H_3)$_3$]; 31.11 [*C*H(CH_3)$_2$]; 43.59 [CH*C*H_2N]; 44.65 [*C*HCH_2N]; 67.01 [*C*H_2OSi]; 78.63 [*C*(CH_3)$_3$]; 125.03 and 140.28 [2C, *C*=*C*]; 156.02 [*C*O].

(*R*,*E*)-5-Methyl-2-[(triisopropylsilyloxy)methyl]hex-3-enyl carbamic acid benzyl ester 30

It was prepared starting from **29** using TIPS-Cl. Chromatography with PE/CH_2Cl_2 6:4 → 3:7 gave **23** as a pale yellow oil in 89% yield. R_f 0.33 (PE/Et_2O 9:1, A, B). Anal. found C, 69.30; H, 9.85; N, 3.25. $C_{25}H_{43}NO_3Si$ requires C, 69.23; H, 9.99; N, 3.23. $[\alpha]_D$ = + 15.3 ($CHCl_3$, c 0.89). IR: ν_{max} 3439, 2949, 2862, 1708, 1497, 1458, 1197, 1108, 1011. GC-MS: R_t 11.30; *m/z* 390 (M^+-43, 1.42), 282 (5.4), 156 (9.7), 145 (8.2), 144 (16), 131 (6.9), 128 (20), 110 (8.6), 109 (100), 108 (25), 107 (19), 103 (7.8), 102 (7.7), 100 (37), 91 (9.5), 87 (5.1), 86 (13), 83 (39), 81 (9.2), 79 (31), 77 (22), 75 (19), 73 (7.0), 67 (28), 61 (13), 59 (11), 56 (5.8), 55 (36), 51 (83), 45 (8.1), 43 (9.4), 41 (10), 39 (5.3). ^{1}H NMR: 0.95 [6H, d, (CH_3)$_2$CH, J 7.0]; 1.04-1.20 [21H, m, TIPS]; 2.15-2.44 [2H, m, (CH_3)$_2$C*H*, C*H*CH_2O]; 3.25 and 3.37 [2H, ABX system, CH_2N, J_{AB} 13.5, J_{AX} 6.7, J_{BX} 6.6]; 3.62 and 3.74 [2H, AB part of ABX system, CH_2OSi, J_{AB} 9.7, J_{AX} 7.6, J_{BX} 4.5]; 5.09 [2H, s, OCH_2Ph]; 5.22 [1H, dd, C*H*=CH*i*Pr, J 8.4, 15.4]; 5.28 [1H, broad s, N*H*]; 5.51 [1H, dd, CH=C*Hi*Pr, J 6.4, 15.4]; 7.34 [5H, apparent broad s, Ph]. ^{13}C NMR: 11.84 [3C, Si(*C*H(CH_3)$_2$)$_3$]; 18.00 [6C, Si(CH(*C*H_3)$_2$)$_3$]; 22.35 and 22.45 [2C, CH(*C*H_3)$_2$]; 31.13 [*C*H(CH_3)$_2$]; 43.85 [CH*C*H_2N]; 44.80 [*C*HCH_2N]; 66.40 and 66.76 [2C, *C*H_2O]; 124.82 and 140.63 [2C, *C*=*C*]; 127.92 and 128.43 [5C, *C*H of Ph]; 136.86 [*C ipso* of Ph]; 156.41 [*C*O].

(*R*,*E*)-Allyl-{5-methyl-2-[(tetrahydropyran-2-yloxy)methyl]-hex-3-enyl} carbamic acid *tert*-butyl ester 15 from 14

A solution of **14** (109 mg, 407 μmol) in dry 1,2-dichloroethane (2 ml) was treated with di-*t*-butyl dicarbonate (103 μl, 448 μmol) and refluxed for 2.5 h. Chromatography was directly performed after solvent removal, using PE/Et_2O 8:2 → 7:3 as eluent, to give **15** (141 mg) in 94% yield. (Spectroscopic data have already been reported above).

(*R*,*E*)-2-azidomethyl-5-methylhex-3-enyl ester acetate 16

A solution of crude mesylate **8** (≤ 23.50 mmol) in dry DMF (25 ml) was treated with sodium azide (3.06 g, 47.07 mmol) and stirred at 50°C for 15-20 h. The reaction was partitioned between water/ether and extracted with ether. The organic layers were washed with water and finally with brine. After solvent removal chromatography with PE/Et_2O 95:5 → 9:1 gave **16** as colourless oil (4.43 g) in 90% overall yield from **(*R*)-3**. R_f 0.71 (PE/Et_2O 7:3, B). Anal. found C, 56.75; H, 8.15; N, 19.75. $C_{10}H_{17}N_3O_2$ requires C, 56.85; H, 8.11; N, 19.89. $[\alpha]_D$ = + 4.6 ($CHCl_3$, c 1.00). IR: ν_{max} 2956, 2100, 1731, 1598, 1451, 1382, 1364, 1233, 1031. GC-MS: R_t 4.39; *m/z* 182 (M^+-28, 0.14), 96 (6.8), 95 (29), 81 (17), 80 (8.4), 68 (9.6), 67 (11), 55 (12), 53 (5.1), 43 (100), 41 (16), 39 (8.0). ^{1}H NMR: 0.97 [6H, d, $(CH_3)_2CH$, J 6.2]; 2.06 [3H, s, $COCH_3$]; 2.28 [1H, d of octuplets, $(CH_3)_2CH$, J 0.8, 6.6]; 2.60 [1H, hexuplet, $CHCH_2OAc$, J 7.0]; 3.33 [2H, d, CH_2N_3, J 6.2]; 4.00 and 4.11 [2H, AB part of ABX system, CH_2OAc, J_{AB} 11.1, J_{AX} 7.3, J_{BX} 5.7]; 5.23 [1H, ddd, C*H*=CH*i*Pr, J 1.2, 8.2, 15.8]; 5.60 [1H, dd, CH=C*Hi*Pr, J 6.6, 15.4]. ^{13}C NMR: 20.77 [$COCH_3$]; 22.16 [2C, $CH(CH_3)_2$]; 31.13 [$CH(CH_3)_2$]; 41.95 [$CHCH_2OAc$]; 52.76 [CH_2N_3]; 64.73 [CH_2OAc]; 123.19 and 142.00 [2C, *C*=*C*]; 170.75 [*C*O].

(*R*,*E*)-*N*-(2-Hydroxymethyl-5-methylhex-3-enyl)acetamide 17

A solution of **16** (50 mg, 237 μmol) in THF/H_2O 9:1 (3 ml) was treated with triphenylphosphine (93 mg, 355 μmol) and heated at 55°C for 11 h. The solution was partitioned between water/Et_2O and extracted with ether. Chromatography with AcOEt → AcOEt/MeOH 8:2 gave **17** (23 mg) as a pale yellow oil in 52% yield. R_f 0.55 (AcOEt/MeOH 9:1, B). Anal. found C, 64.80; H, 10.40; N, 7.55. $C_{10}H_{19}NO_2$ requires C, 64.83; H, 10.34; N, 7.56. $[\alpha]_D$ = - 21.0 ($CHCl_3$, c 1.08). IR: ν_{max} 3449, 2956, 2923, 2868, 1657, 1506, 1193. GC-MS: R_t 5.59; *m/z* 1 85 (M^+, 0.42), 155 (17), 110 (6.8), 108 (19), 98 (5.5), 97 (6.4), 96 (65), 95 (12), 93 (17), 90 (8.8), 82 (11), 81 (1 00), 79 (8.5), 73 (16), 72 (59), 69 (9.0), 68 (5.3), 67 (11), 60 (27), 57 (6.0), 56 (9.1), 55 (13), 54 (6.3), 53 (6.8), 43 (60), 42 (6.2), 41 (25), 39 (9.8). ^{1}H NMR: 0.90 [6H, d, $(CH_3)_2CH$, J 6.6]; 1.94 [3H, s, $COCH_3$]; 2.11-2.33 [2H, m, $(CH_3)_2CH$, $CHCH_2OAc$]; 3.18 and 3.33 [2H, AB part of ABX system, CH_2O or CH_2N, J_{AB} 13.3, J_{AX} 5.8, J_{BX} 14.2]; 3.34-3.54 [3H, CH_2O or CH_2N, O*H*]; 5.17 [1H, ddd, C*H*=CH*i*Pr, J 1.0, 7.6, 15.4]; 5.46 [1H, dd, CH=C*Hi*Pr, J 0.8, 6.6, 15.4]; 5.94 [1H, broad s, N*H*]. ^{13}C NMR: 22.46 [2C, $CH(CH_3)_2$]; 23.07 [$COCH_3$]; 31.17 [$CH(CH_3)_2$]; 40.80 [$CHCH_2N$]; 44.82 [$CHCH_2O$]; 63.19 [CH_2O]; 124.79 and 140.83 [2C, *C*=*C*]; 171.38 [*C*O].

(*R*,*E*)-2-Azidomethyl-5-methylhex-3-en-1-ol 18

A solution of **16** (4.43 g, 20.97 mmol) in THF/0.079 M pH 7 phosphate buffer 3:1 (200 ml) was treated with lipase from *Pseudomonas cepacia* (PCL, 1.67 g) and stirred at rt for 19 h. The pH was maintained at 7 by constant addition of 1 N NaOH. The mixture was filtered over a celite pad and extracted with ether. Chromatography with PE/Et_2O 7:3: → 1:1 furnished **17** (3.45 g) as a yellow oil in 97% yield. R_f 0.41 (PE/Et_2O 6:4, B). Anal. found C, 56.70; H, 8.90; N, 25.00. $C_8H_{15}N_3O$ requires C, 56.78; H, 8.93; N, 24.83. $[\alpha]_D$ = - 21.0 ($CHCl_3$, c 1.08). IR: ν_{max} 3620, 2922, 3102, 1457, 1195, 1023. GC-MS: R_t 3.81; *m/z* 141 (M^+-28, 0.26), 126 (9. 9), 110 (10), 97 (5.0), 96 (25), 95 (56), 93 (6.3), 83 (16), 82 (6.1), 81 (41), 80 (8.0), 79 (10), 77 (5.7), 71 (5.0), 7 0 (14), 69 (78), 68 (41), 67 (31), 65 (5.2), 57 (32), 56 (16), 55 (49), 54 (7.4), 53 (18), 44 (5.0), 43 (66), 42 (11), 41 (100), 40 (83), 39 (31). ^{1}H NMR: 0.93 [6H, d, $(CH_3)_2CH$, J 7.0]; 2.33 [1H, d of octuplets, $(CH_3)_2CH$, J 0.8, 6.4]; 2.41 [1H, hexuplet, $CHCH_2O$, J 6.2]; 3.30 [2H, d, CH_2N_3, J 6.6]; 3.51 and 3.57 [2H, AB part of ABX system, CH_2O, J_{AB} 9.3, J_{AX} 4.9, J_{BX} 4.9]; 5.17 [1H, ddd, C*H*=CH*i*Pr, J 1.2, 8.0, 15.4]; 5.57 [1H, dd, CH=C*Hi*Pr, J 6.6, 15.4]. ^{13}C NMR: 22.27 and 22.35 [2C, $CH(CH_3)_2$]; 31.22 [$CH(CH_3)_2$]; 45.08 [$CHCH_2O$]; 52.83 [CH_2N_3];

63.74 [*C*H_2O]; 123.88 and 142.43 [2C, *C*=*C*].

General procedure for the Staudinger reaction followed by protection of nitrogen as carbamate

a) Transformation of N_3 into NH_2: the same procedure described above for the preparation of **17** was employed, using 12 ml solvent/10 mmol substrate and stirring at rt for 8 h. In this case the crude mixture was directly N-protected, without performing an extractive work-up before. b) Protection as Boc (to give **20** and **21**): the solution was cooled to 0°C and treated with Et_3N (5 molar eq) and Boc-ON [(2-*t*-butoxycarbonyloxyimino)-2-phentlacetonitrile, 1.5 molar eq]. After 15 min the suspension was allowed to stirr a rt overnight. Dilution with water was followed by extraction with Et_2O. c) Protection as Cbz (to give **29**): the solution was cooled to 0°C and treated with benzyl chloroformate (1.5 molar eq), while pH was maintained at 9-10 by addition of 1N NaOH. Dilution with water was followed by extraction with Et_2O.

(*R*,*E*)-[5-Methyl-2-{(tetrahydropyran-2-yloxy)methyl]hex-3-enyl} carbamic acid *tert*-butyl ester 20 from 19

It was prepared starting from **19** in 74% overall yield. (Spectroscopic data have already been reported above).

(*R*,*E*)-(2-Hydroxymethyl-5-methylhex-3-enyl) carbamic acid *tert*-butyl ester 21

It was prepared starting from **18**. Chromatography with PE/Et_2O 9:1 → 4:6 gave **21** (usually a second chromatography was necessary in order to completely separate **21** from the oxime derived from Boc-ON) as a pale yellow oil in 96% yield. R_f 0.55 (PE/AcOEt 7:3, B). Anal. found C, 64.10; H, 10.30; N, 5.75. $C_{13}H_{25}NO_3$ requires C, 64.16; H, 10.36; N, 5.76. $[\alpha]_D$ = - 10.8 ($CHCl_3$, c 1.27). GC-MS: R_t 6.14; *m/z* 213 (M^+-30, 0.042), 1 70 (18), 169 (15), 157 (27), 130 (12), 109 (6.7), 108 (14), 97 (8.5), 96 (100.0), 95 (14), 93 (6.0), 92 (28), 82 (8. 5), 81 (50), 74 (9.6), 69 (5.5), 67 (6.0), 59 (12), 57 (88), 56 (5.9), 55 (7.8), 43 (5.4), 41 (19). ^{1}H NMR: 0.98 [6H, d, (C*H*$_3$)$_2$CH, J 6.6]; 1.45 [9H, s, C(C*H*$_3$)$_3$]; 2.16-2.38 [2H, m, (CH$_3$)$_2$C*H*, C*H*CH$_2$NHBoc]; 3.05-3.58 [5H, m, C*H*$_2$O*H*, C*H*$_2$NHBoc]; 4.74 [1H, broad s, N*H*]; 5.23 [1H, dd, C*H*=CH*i*Pr, J 8.0, 15.8]; 5.54 [1H, dd, CH=C*Hi*Pr, J 6.2, 15.4]. ^{13}C NMR: 22.44 [2C, CH*C*H$_3$)$_2$]; 28.32 [3C, C(*C*H$_3$)$_3$]; 31.15 [*C*H(CH$_3$)$_2$]; 41.37 [*C*H$_2$NHBoc]; 45.42 [C*H*CH$_2$NHBoc] 63.04 [*C*H$_2$OH]; 79.66 [*C*(CH$_3$)$_3$]; 124.82 and 140.94 [2C, *C*=*C*]; 157.10 [*C*O].

(*R*,*E*)-(2-Hydroxymethyl-5-methylhex-3-enyl) carbamic acid benzyl ester 29

It was prepared starting from **18**. Chromatography with PE/Et_2O 9:1 → 4:6 gave **29** as a pale yellow oil in 44% yield. R_f 0.26 (PE/Et_2O 4:6, A, B). Anal. found C, 69.35; H, 8.30; N, 5.15. $C_{16}H_{23}NO_3$ requires C, 69.29; H, 8.36; N, 5.05. $[\alpha]_D$ = - 11.2 ($CHCl_3$, c 1.54). IR: ν_{max} 3449, 2952, 2871, 1705, 1502, 1454, 1211. GC-MS: R_t 8.75; *m/z* 259 (M^+-18, 0.070), 168 (6.7), 108 (13), 107 (12), 96 (29), 95 (18), 92 (8.7), 91 (100), 81 (32), 79 (16), 77 (10), 67 (5.1), 65 (9.2), 41 (7.2). ^{1}H NMR: 0.97 [6H, d, (C*H*$_3$)$_2$CH, J 6.8]; 2.29 [2H, centre of m, (CH$_3$)$_2$C*H*, C*H*CH$_2$O]; 2.66 [1H, broad t, O*H*, J 6.8]; 3.24 and 3.36 [2H, ABX system, C*H*$_2$N, J_{AB} 14.0, J_{AX} 6.2, J_{BX} 6.2]; 3.46-3.60 [2H, m, C*H*$_2$O]; 4.97 [1H, broad s, N*H*]; 5.11 [2H, s, OC*H*$_2$Ph]; 5.21 [1H, dd, C*H*=CH*i*Pr, J 8.0, 15.8]; 5.55 [1H, dd, CH=C*Hi*Pr, J 6.2, 15.6]; 7.34-7.38 [5H, m, Ph]. ^{13}C NMR: 22.37 [2C, CH(*C*H$_3$)$_2$]; 31.11 [*C*H(CH$_3$)$_2$]; 41.98 [CH*C*H$_2$N]; 45.16 [*C*HCH$_2$N]; 63.24 and 66.85 [2C, *C*H$_2$O]; 124.50 and 141.23 [2C, *C*=*C*]; 128.05, 128.12 and 128.47 [5C, *C*H of Ph]; 136.34 [*C ipso* of Ph]; 157.28 [*C*O].

(*R*)-3-[(Triisopropylsilyloxy)methyl]-3,6-dihydro-2*H*-pyridine-1-carboxylic acid 2,2,2-trichloroethyl ester 41

a) Boc removal: a solution of 28 (94 mg, 261 μmol) in dry CH_2Cl_2 (1 ml) was cooled at 0°C and treated with CF_3CO_2H (1 ml). After 30 min the solvent was evaporated and all TFA was azeotropically removed with toluene. b) Troc introduction: the crude of the previuos reaction was dissolved in water (4 ml) and the pH was adjusted to 10 by addition of 1 N NaOH. 2,2,2-trichloroethyl chloroformate (72 μl, 522 μmol) was added and the mixture was stirred et rt for 3 h, maintaining the pH at 9-10 by additional introduction of 1 N NaOH. Extraction with Et_2O was followed by solvent removal. Chromatography with PE/Et_2O 95:5 gave **41** as a yellow oil. R_f 0.56 (PE/Et_2O 9:1, B). Anal. found C, 48.45; H, 7.15; N, 3.25. $C_{18}H_{32}Cl_3NO_3Si$ requires C, 48.59; H, 7.25; N, 3.15. $[\alpha]_D$ = - 19.4 ($CHCl_3$, c 1.05). IR: ν_{max} 2940, 2862, 2395, 1709, 1423, 1186, 1125. GC-MS: R_t 10.34; *m/z* 402 [M^+-43 (2 ^{36}Cl and 1 ^{35}Cl, 97)], 400 [M^+-43 (3 ^{35}Cl, 98)], 296 (13), 288 (7.4), 270 (5.8), 252 (9.7), 244 (5.9), 236 (23), 234 (36), 226 (6.6), 182 (12), 226 (6.6), 182 (12), 179 (12), 177 (11), 157 (10), 151 (6.6), 149 (18), 145 (25), 140 (9.0), 139 (10), 138 (5.6), 137 (19), 133 (13), 131 (30), 127 (7.9), 125 (8.4), 123 (9.9), 122 (11), 121 (83), 119 (14),115 (18), 113 (8.3), 111 (8.5), 109 (7.7), 103 (24), 101 (6.0), 99 (12), 97 (20), 96 (24), 95 (32), 94 (17), 93 (23), 89 (6.5), 88 (5.7), 87 (18), 85 (6.3), 82 (5.0), 81 (7.1), 80 (16), 79 (29), 77 (8.9), 75 (57), 73 (31), 71 (7.1), 69 (5.5), 68 (9.4), 67 (100), 65 (8.6), 61 (36), 60 (6.6), 59 (57), 56 (9.2), 45 (25), 44 (12), 43 (15), 42 (6.8), 41 (27), 39 (5.3). ^{1}H NMR: 0.95-2.20 [21H, m, TIPS]; 2.51 [1H, apparent broad s, C*H*CH_2O]; 3.31-4.32 [6H, m, C*H*$_2$O, C*H*$_2$NC*H*$_2$]; 4.77 [2H, centre of m, CO_2CH_2]; 5.68-5.84 [2H, m, C*H*=C*H*]. ^{13}C NMR (two rotamers): 11.94 [3C, Si(*C*H(CH_3)$_2$)$_3$]; 18.01 [6C, Si(CH(*C*H_3)$_2$)$_3$]; 38.15 and 38.56 [*C*HCH_2O]; 43.05, 43.56 and 44.05 [2C, *C*H_2N*C*H_2CH=CH]; 64.71 and 64.90 [*C*H_2OSi]; 75.02 [CO_2CH_2]; 95.72 [*C*Cl_3]; 124.32 and 124.94, 126.60 and 126.94 [2C, *C*=*C*]; 153.79 [*C*O].

General procedure for TIPS removal

A solution of substrate (1.00 mmol for 41 and 28; 36 μmol for 49 and 50) in dry THF (7 ml for 41 and 28; 1 ml for 49 and 50) was treated with *n*-Bu_4NF (0.5 M in THF, 6 ml for 41 and 28; 216 μl for 49 and 50) and stirred at rt for 2.5-3 h. The solution was partitioned between water/ether and extracted with ether.

(*R*)-3-Hydroxymethyl-3,6-dihydro-2*H*-pyridine-1-carboxylic acid 2,2,2-trichloroethyl ester 42

It was prepared starting from **41**. Chromatography with PE/Et_2O 1:1 → 1:9 gave **42** as a colourless oil in 74% yield. R_f 0.57 (PE/Et_2O 1:9, B, D). Anal. found C, 37.55; H, 4.10; N, 4.90; N, 3.25. $C_9H_{12}Cl_3NO_3$ requires C, 37.46; H, 4.19; N, 4.85. $[\alpha]_D$ = - 44.2 ($CHCl_3$, c 1.04). IR: ν_{max} 3459, 2920, 2851, 1706, 1428, 1238, 1127, 1030. GC-MS: R_t 7.38; *m/z* 289 [M^+ (2 ^{36}Cl and 1 ^{35}Cl, 2.4)], 287 [M^+ (3 ^{35}Cl, 2.6)], 271 (12), 270 (12), 269 (13), 268 (12), 261 (11), 260 (7.5), 259 (32), 258 (16), 257 (34), 256 (18), 254 (11), 206 (9.6), 204 (9.6), 156 (6.6), 141 (6.8), 140 (78), 139 (7.9), 138 (61), 135 (22), 133 (72), 131 (73), 127 (13), 126 (53), 125 (6.3), 124 (18), 113 (7.0), 112 (74), 111 (83), 110 (9.6), 109 (9.0), 108 (5.6), 99 (7.3), 98 (11), 97 (41), 96 (22), 95 (64), 94 (39), 84 (32), 83 (57), 82 (81), 81 (27), 80 (90), 79 (10), 78 (9.7), 74 (18), 69 (18), 68 (20), 67 (100), 66 (20), 65 (15), 63 (8.3), 62 (5.1), 61 (20), 57 (13), 56 (73), 55 (86), 54 (38), 53 (33), 52 (8.1), 51 (7.2), 44 (8.7), 43 (22), 42 (21), 41 (57), 40 (7.8), 39 (35). ^{1}H NMR (DMSO-d_6; temp=100°C); 2.38 [1H, centre of m, C*H*CH_2O]; 3.31 [1H, dd,

NC*H*HCHCH$_2$OH, J 7.0, 12.8]; 3.33 and 3.44 [2H, ABX system, NC*H*$_2$CH=CH, J_{AB} 10.4, J_{AX} 13.5, J_{BX} 5.1]; 3.76 [1H, dd, NCH*H*CHCH$_2$OH, J 5.2, 13.2]; 3.83-4.07 [2H, m, C*H*$_2$OH]; 4.34 [1H, broad t, O*H*, J 5.3]; 4.85 [2H, s, CO$_2$C*H*$_2$]; 5.73-5.84 [2H, m, C*H*=C*H*]. ^{13}C NMR (DMSO-d$_6$; two rotamers): 37.61 and 37.81 [*C*HCH$_2$O]; 42.78, 43.09 and 43.54 [2C, *C*H$_2$N*C*H$_2$CH=CH]; 62.27 and 62.45 [*C*H$_2$OSi]; 73.99 [CO$_2$*C*H$_2$]; 95.95 [*C*Cl$_3$]; 124.42 and 124.71, 126.78 [2C, *C*=*C*]; 152.90 and 153.16 [*C*O].

(*R*)-3-Hydroxymethyl-3,6-dihydro-2*H*-pyridine-1-carboxylic acid *tert*-butyl ester 43

It was prepared starting from **28**. Chromatography with PE/Et$_2$O 6:4 → 2:8 gave **43** as a yellow oil in 97% yield. R_f 0.57 (PE/Et$_2$O 1:9, C, D). Anal. found C, 62.05; H, 8.95; N, 6.50. $C_{11}H_{19}NO_3$ requires C, 61.95; H, 8.98; N, 6.57. $[\alpha]_D$ = - 38.1 ($CHCl_3$, c 0.55). IR: ν_{max} 3436, 2971, 1664, 1425, 1366, 1256, 1161, 1119. GC-MS: R_t 5.37; *m/z* 289 (M^+ -30, 1.2), 157 (10), 140 (8.7), 139 (6.7), 127 (19), 112 (11), 84 (6.9), 83 (6.1), 82 (23), 80 (8.0), 67 (12), 57 (100), 56 (13), 55 (7.6), 43 (6.3), 41 (26), 39 (6.4). ^{1}H NMR (DMSO-d$_6$; temp=100°C): 1.43 [9H, s, OC(C*H*$_3$)$_3$]; 2.30 [1H, centre of m, C*H*CH$_2$O]; 3.18 [1H, dd, NC*H*HCHCH$_2$OH, J 6.6, 13.0]; 3.30 and 3.40 [2H, ABX system, NC*H*$_2$CH=CH, J_{AB} 10.4, J_{AX} 8.2, J_{BX} 5.2]; 3.60 [1H, dd, NCH*H*CHCH$_2$OH, J 5.2, 12.8]; 3.39-3.93 [2H, m, C*H*$_2$OH]; 4.24-4.34 [1H, m, O*H*]; 5.68-5.79 [2H, m, C*H*=C*H*]. ^{13}C NMR (DMSO-d$_6$; temp=100°C): 28.00 [3C, OC(*C*H$_3$)$_3$]; 37.94 [*C*HCH$_2$O]; 42.87 [2C, *C*H$_2$N*C*H$_2$CH=CH]; 62.40 [*C*H$_2$OSi]; 78.57 [*C*(CH$_3$)$_3$]; 125.29 and 126.67 [2C, *C*=*C*]; 154.06 [*C*O].

(3*R*,4*R*,5*R*)-3,4-Dihydroxy-5-(hydroxymethyl)piperidine-1-carboxylic acid *tert*-butyl ester 51

It was prepared starting from **49** (36 μmol). Chromatography on preparative TLC with AcOEt/MeOH 9:1 gave **51** as a white foam in 44% yield. (Spectroscopic data have already been reported in the paper).

(3*S*,4*S*,5*R*)-3,4-Dihydroxy-5-(hydroxymethyl)piperidine-1-carboxylic acid *tert*-butyl ester 52

It was prepared starting from **50** (38 μmol). Chromatography on preparative TLC with AcOEt/MeOH 9:1 gave **52** as a white foam in 72% yield. (Spectroscopic data have already been reported in the paper).

(*S*)-(3,6-dihydro-2*H*-pyran-3-yl)methanol 48

A solution of **6** (240 mg, 1.21 mmol) in dry MeOH (5 ml) was cooled to 0°C. After *p*-TSA addition (16 mg, 84 μmol) the solution was allowed to stir at rt for 4 h. After addition of solid NaHCO$_3$ (10 mg, 119 μmol) the mixture was concentrated and the residue was partitioned between brine/AcOEt and extracted with AcOEt. Chromatography with PE/Et$_2$O 1:9 gave **48** (112 mg) in 81% yield as a colourless oil. R_f 0.46 (PE/Et$_2$O 1:9, B). Anal. found C, 63.20; H, 8.85. $C_6H_{10}O_2$ requires C, 63.14; H, 8.83. $[\alpha]_D$ = - 112.9 ($CHCl_3$, c 1.19). IR: ν_{max} 3451, 2935, 2873, 2834, 1602, 1114, 1084, 1018. GC-MS: R_t 1.30; *m/z* 114 (M^+, 0.38), 96 (38), 95 (28), 84 (31) , 83 (78), 82 (7.5), 81 (48), 71 (6.6), 70 (34), 69 (12), 68 (14), 67 (23), 66 (11), 65 (7.0), 57 (25), 56 (25), 55 (10 0), 54 (8.7), 53 (23), 51 (7.1), 50 (5.2), 43 (12), 42 (6.7), 41 (23), 40 (5.9), 39 (30). ^{1}H NMR: 1.96 [1H, broad s, O*H*]; 2.30-2.36 [1H, m, C*H*CH$_2$O]; 3.68 [2H, apparent broad s, C*H*$_2$OH]; 3.84 [2H, d, C*H*$_2$O, J 4.0]; 4.13 [2H, dd, C*H*$_2$O, J 2.4, 4.2]; 5.74-5.92 [2H, m, C*H*=C*H*]. ^{13}C NMR: 37.33 [*C*HCH$_2$O]; 63.42, 65.45 and 66.19 [3C, *C*H$_2$O]; 124.98 and 127.99 [2C, *C*=*C*].

(3*R*,4*R*,5*R*)- and (3*S*,4*R*,5*R*)-3,4-Dihydroxy-5-[(triisopropylsilyloxy)methyl]piperidine-1-carboxylic acid *tert*-butyl ester 49 and 50 from 51,52

Diastereomeric mixture **51,52** (6.8 mg, 27 μmol), prepared above, was dissolved in dry CH_2Cl_2 (1 ml) and cooled to 0°C. 2,6-Lutidine (8 μl, 69 μmol) and triisopropylsilyl triflate (12 μl, 45 μmol) were added and the solution was allowed to stir at 0°C for 5 h. After dilution with water/AcOEt, the reaction was extracted with AcOEt. Excess 2,6-lutidine was azeotropically removed with *n*-octane. After solvent removal, chromatography on preparative TLC with PE/Et_2O 25:75 gave the diastereomeric mixture **49,50** (6.5 mg, 59% yield) having the same d.r. of the starting epoxides **36,40** (by GC-MS).