N-Silyl Tethered Radical Cyclizations :

A New Synthesis of γ -Aminoalcohols

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General Remarks :

Reactions were carried out under an anhydrous atmosphere of Ar. Glassware was flame-dried under an argon gas flow prior to use. Anhydrous THF and Et₂O were obtained by distillation over sodium/benzophenone under nitrogen and used freshly distilled. Et₃N was dried then distilled from KOH ; benzene, toluene and CH₂Cl₂ from CaH₂. Other reagents were commercially available and used without further purification. TMSCl was freshly distilled before use. *n*-Butyllithium was purchased as 2.5 M solutions in hexanes and titrated before use. Methyllithium was purchased as 1.6 M low chloride solutions in Et₂O. ¹H NMR and ¹³C NMR spectra were recorded on 200 MHz AC 200 and 400 MHz ARX 400 Bruker spectrometers. ¹H NMR spectra are referenced at 7.26 ppm for CDCl₃ and 7.16 ppm for C₆D₆. ¹³C NMR spectra are referenced at 77.23 ppm for CDCl₃ and 128.62 ppm for C₆D₆. Chemical shifts are given in ppm. IR spectra were recorded with a Nicolet AVATAR 320 FT-IR or a Philips PYE UNICAM SP3-100 spectrophotometers. IR is reported as characteristic bands in their maximal intensity. The melting points reported were measured with a SMP3 Stuart Scientific melting point apparatus and are uncorrected. Photochemically induced radical cyclizations were run with a OSRAM ULTRA-VITALUX® sunlamp.

Synthesis of *N*-protected allyl- and propargylamines :

N-protected amines were prepared according to literature (**1a**¹, **1c**², **1d**³) or purchased from commercial source (**1b**). *N*-protected amines **6**, **8a** and **8b** were prepared as follows :

6

N-(*tert*-butoxycarbonyl)-methallylamine **6**⁴ :

To a stirred solution of PPh₃ (3.94 g, 14.9 mmol, 1.0 equiv.), *N*-(*tert*-butoxycarbonyl)-*p*-toluenesulfonamide (4.07 g, 15.0 mmol, 1.0 equiv.) and methallyl alcohol (1.28 mL, 14.9 mmol, 1.0 equiv.) in THF (50 mL) was added dropwise DIAD (3.15 mL, 15.0 mmol, 1.0 equiv.) at rt. After reaction completion, THF was evaporated and the yellow residue was purified by flash column chromatography on silica gel (PE/Et₂O gradient) to afford *p*-toluenesulfonamido-*N*-(*tert*-butoxycarbonyl)-methallylamine : white solid (4.05 g, 83%), mp = 89-90 °C ; ¹H NMR (CDCl₃, 400 MHz) δ 7.81 (d, *J* = 8.1 Hz, 2H, arom.), 7.30 (d, *J* = 8.1 Hz, 2H, arom.), 4.93 (s, 1H, =C/H), 4.90 (s, 1H, =C/H), 4.39 (s, 2H, CH₂N), 2.44 (s, 3H, CCH₃), 1.75 (s, 3H, H₂C=CCH₃), 1.35 (s, 9H, C(CH₃)₃) ; ¹³C NMR (CDCl₃, 100 MHz) δ 151.1, 144.3, 140.8, 137.3, 129.3, 128.4, 111.9, 84.4, 52.0, 28.0, 21.8, 20.3 ; IR (neat) 3080, 1730, 1660, 1350, 1160 cm⁻¹ ; MS (CI NH₃, *m/z*) 343 (MNH₄⁺), 326 (MH⁺), 287 (MNH₄⁺ - C₄H₈), 270 (MH⁺ - C₄H₈), 243 (MNH₄⁺ - C₅H₈O₂), 226 (MH⁺ - C₅H₈O₂) ; Anal. calcd. for : C₁₆H₂₃NO₄S : C, 59.05 ; H, 7.12 ; N, 4.30 ; Found : C, 58.97 ; H, 7.28 ; N, 4.23.

The latter (1.68 g, 5.2 mmol, 1.0 equiv.) was diluted with MeOH (50 mL) and Mg turnings (0.63 g, 25.9 mmol, 5 equiv.) were added at rt. The resulting suspension was sonicated⁵ for 30 min then submitted to a CH₂Cl₂/1 M HCl extraction. The combined organic layers were washed with aqueous saturated NaHCO₃ solution then brine, dried over anhydrous Na₂SO₄, filtered and evaporated *in vacuo* to afford **6** as a colorless oil (876 mg, 99%). No further purification was necessary. **6**⁴ : ¹H NMR (CDCl₃, 400 MHz) δ 4.80 (s, 1H, =C/H), 4.78 (s, 1H, =C/H), 4.75 (brs, 1H, NH), 3.62 (brd, *J* = 5.6 Hz, 2H, CH₂N), 1.69 (s, 3H, H₂C=CCH₃), 1.41 (s, 9H, C(CH₃)₃) ; ¹³C NMR (CDCl₃, 100 MHz) δ 156.1, 142.7, 110.4, 79.4, 46.4, 28.5, 20.2.

1-*p*-toluenesulfonamido hept-2-yne 8a :

To a stirred solution of ***N,N*-bis(trimethylsilyl)-propargylamine**⁶ (3.0 g, 15.0 mmol, 1.0 equiv.) in THF (38 mL) was added dropwise *n*-BuLi (2.15 M, 7.7 mL, 16.5 mmol, 1.1 equiv.) at -78 °C. After addition, the solution was allowed to warm to rt then stirred for 30 min. *n*-BuBr (1.9 mL, 17.5 mmol, 1.2 equiv.) was added then the solution refluxed for 65 h. The reaction was quenched with brine and the aqueous layer was extracted with Et₂O. The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered and evaporated *in vacuo* to give 4.0 g of crude ***N,N*-bis(trimethylsilyl)-hept-2-yn-amine**⁷ as a yellow-orange oil. The latter was diluted with MeOH (30 mL) and KF (87 mg, 1.5 mmol, 0.1 equiv.)⁷ was added at rt. After completion, the reaction was quenched with 0.5 M NaOH and the aqueous layer was extracted with CH₂Cl₂. The combined organic layers were washed with 0.5 M NaOH, dried over anhydrous Na₂SO₄, filtered and evaporated *in vacuo* to give crude **hept-2-yn-amine** as an orange-brown oil. The latter was diluted with CH₂Cl₂ and concentrated HCl was added with vigorous stirring. The resulting aqueous layer was collected and pH was carefully adjusted to 10-11 by addition of NaOH pellets at 0 °C. The resulting aqueous layer was extracted several times with CH₂Cl₂. The combined organic layers were dried over anhydrous Na₂SO₄, filtered and evaporated *in vacuo* to give 1.27 g of pure **hept-2-yn-amine**⁸ as a yellow oil. To a stirred solution of the latter (1.27 g, 11.4 mmol, 1.0 equiv.) in CH₂Cl₂ (15 mL) was added dropwise a solution of Et₃N (1.8 mL, 12.8 mmol, 1.1 equiv.), 4-DMAP (15 mg, 0.1 mmol, 0.01 equiv.) and tosyl chloride (2.09 g, 10.8 mmol, 0.95 equiv.) in CH₂Cl₂ (15 mL) at 0 °C. After addition, the solution was allowed to warm to rt then stirred for 1 h. The reaction was quenched with aqueous saturated NH₄Cl solution and the aqueous layer was extracted with CH₂Cl₂. The combined organic layers were washed with aqueous saturated NH₄Cl solution, dried over anhydrous Na₂SO₄, filtered and evaporated *in vacuo* to give 2.8 g of an orange oil. Purification was achieved by flash column chromatography on silica gel (PE/Et₂O gradient). **8a** : white solid (2.7 g, 67% for 3 steps) ; mp = 36-38 °C ; ¹H NMR (CDCl₃, 400 MHz) δ 7.77 (d, *J* = 8.4 Hz, 2H, arom.), 7.28 (d, *J* = 8.4 Hz, 2H, arom.), 4.92 (brs, 1H, NH), 3.78 (m, 2H, CH₂N), 2.41 (s, 3H, CCH₃), 1.93 (m, 2H, CH₃-(CH₂)₂-CH₂-), 1.25 (m, 4H, CH₃-(CH₂)₂-CH₂-), 0.83 (t, *J* = 6.9 Hz, 3H, CH₃-(CH₂)₂-CH₂-) ; ¹³C NMR (CDCl₃, 100 MHz) δ 143.6, 137.1, 129.7, 127.6, 85.6, 74.2, 33.5, 30.5, 21.9, 21.6, 18.3, 13.6 ; IR (CDCl₃) 3280 (br), 3030, 2250, 1330, 1160 cm⁻¹ ; MS (CI NH₃, *m/z*) 283 (MNH₄⁺), 266 (MH⁺) ; Anal. calcd. for : C₁₄H₁₉NO₂S : C, 63.36 ; H, 7.22 ; N, 5.28 ; Found : C, 63.23 ; H, 7.34 ; N, 5.47.

8b

N-(tert-butoxycarbonyl) hept-2-yn-1-amine 8b :

To a stirred solution of **8a** (1.31 g, 4.9 mmol, 1.0 equiv.), Et₃N (1.5 mL, 10.6 mmol, 2.0 equiv.), 4-DMAP (60 mg, 0.5 mmol, 0.1 equiv.) in THF (10 mL) was added di-*tert*-butyl dicarbonate (1.1 g, 4.9 mmol, 1.0 equiv.) at rt. After stirring for 1.5 h, the reaction was quenched with aqueous saturated NH₄Cl solution and the aqueous layer was extracted with Et₂O. The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered and evaporated *in vacuo* to give 1.87 g of ***p*-toluenesulfonamido-*N*-(*tert*-butoxycarbonyl)-hept-2-yn-amine** as a beige solid : ¹H NMR (CDCl₃, 200 MHz) δ 7.93 (d, *J* = 8.4 Hz, 2H, arom.), 7.30 (d, *J* = 8.4 Hz, 2H, arom.), 4.60 (t, *J* = 2.2 Hz, 2H, CH₂N), 2.45 (s, 3H, CCH₃), 2.20 (m, 2H, CH₃-(CH₂)₂-CH₂), 1.45 (m, 4H, CH₃-(CH₂)₂-CH₂-), 1.35 (s, 9H, C(CH₃)₃), 0.89 (t, *J* = 6.9 Hz, 3H, CH₃-(CH₂)₂-CH₂-). The latter was diluted with MeOH (60 mL) and Mg turnings (0.6 g, 24.6 mmol, 5 equiv.) were added at rt. The resulting suspension was sonicated for 30 min⁵ then submitted to a CH₂Cl₂/1 M HCl extraction. The combined organic layers were washed with aqueous saturated NaHCO₃ solution then brine, dried over anhydrous Na₂SO₄, filtered and evaporated *in vacuo* to give 1.05 g of a pale yellow oil. Purification was achieved by flash column chromatography on silica gel (PE/Et₂O gradient). **8b** : pale yellow oil (1.0 g, 95% for 2 steps) ; ¹H NMR (CDCl₃, 200 MHz) δ 4.63 (brs, 1H, NH), 3.88 (brs, 2H, CH₂N), 2.16 (m, 2H, CH₃-(CH₂)₂-CH₂), 1.45 (m, 4H, CH₃-(CH₂)₂-CH₂-), 1.45 (s, 9H, C(CH₃)₃), 0.90 (t, *J* = 6.9 Hz, 3H, CH₃-(CH₂)₂-CH₂-) ; ¹³C NMR (CDCl₃, 100 MHz) δ 155.5, 83.7, 79.7, 76.1, 30.9, 30.8, 28.4, 22.0, 18.4, 13.6 ; IR (neat) 3450-3200, 2280, 1700 cm⁻¹ ; MS (CI NH₃, *m/z*) 229 (MNH₄⁺), 212 (MH⁺), 173 (MNH₄⁺ - C₄H₈), 156 (MH⁺ - C₄H₈) ; Anal. calcd. for : C₁₂H₂₁NO₂ : C, 68.21 ; H, 10.02 ; N, 6.63 ; Found : C, 68.08 ; H, 10.20 ; N, 6.44.

***N*-BMDMS precursor characterization :**

Precursors **2a** (PG = Ts) and **2d** (PG = Boc) were characterized by ^1H NMR of aliquots prepared by cannulation of reaction mixture in flame-dried NMR tubes and under argon. Anhydrous CDCl_3 or C_6D_6 were used as NMR solvents. Precursors were synthesized as follows : in a 25 mL round-bottomed flask filled with *N*-protected allylamine (2.0 mmol, 1 equiv.) in Et_2O (10 mL) was added dropwise *n*-BuLi (2.0 mmol, 1 equiv.) at 0 °C. The solution was allowed to warm to rt then stirred for 15 min. After cooling to 0 °C, BMDMSCl (0.27 mL, 1.94 mmol, 0.97 equiv.) was added dropwise. The solution was allowed to warm to rt then stirred for 1 h. After ^1H NMR experiment, the reaction was quenched with aqueous saturated NaHCO_3 solution and the aqueous layer was extracted with Et_2O . The combined organic layers were washed with aqueous saturated NaHCO_3 solution, dried over anhydrous Na_2SO_4 , filtered and evaporated. Depending on the nature of the PG group, crude NMR spectra exhibited partial (PG = Ts) or complete BMDMdesilylation (PG = Boc) into starting *N*-protected allylamines. Precursor **2c** (PG = Bn) could not be obviously evidenced by that ^1H NMR experiment. Precursor **2b** (PG = Ph) was insensitive to that aqueous treatment and was purified further by column distillation. Precursor **2e** was synthesized in two steps using a sequence of one-pot bisilylation.

2d

1d

N*-bromomethyldimethylsilyl-*N*-(*tert*-butoxycarbonyl)-allylamine **2d* : ^1H NMR (C_6D_6 , 200 MHz) δ 5.70 (m, 1H, $\text{CH}=\text{CH}_2$), 4.96 (m, 2H, $\text{CH}=\text{CH}_2$), 3.67 (brs, 2H, CH_2N), 2.51 (brs, 2H, CH_2Br), 1.31 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.27 (brs, 6H, $\text{Si}(\text{CH}_3)_2$). Reaction treatment recovered quantitatively starting ***N*-(*tert*-butoxycarbonyl)-allylamine **1d**** : ^1H NMR (C_6D_6 , 200 MHz) δ 5.58 (m, 1H, $\text{CH}=\text{CH}_2$), 4.92 (m, 2H, $\text{CH}=\text{CH}_2$), 4.50 (brs, 1H, NH), 3.57 (brt, J = 5.4 Hz, 2H, CH_2N), 1.42 (s, 9H, $\text{C}(\text{CH}_3)_3$) ; ^{13}C NMR (C_6D_6 , 50 MHz) δ 156.3, 136.2, 115.7, 79.2, 43.8, 29.1. Procedure run with trimethylsilyl chloride afforded ***N*-trimethylsilyl-*N*-(*tert*-butoxycarbonyl)-allylamine** as a colorless oil. Purification was achieved by flash column chromatography on silica gel (PE/ Et_2O 9/1) : (321 mg, 70%). ^1H NMR (C_6D_6 , 400 MHz) δ 5.79 (m, 1H, $\text{CH}=\text{CH}_2$), 5.01 (m, 2H, $\text{CH}=\text{CH}_2$), 3.75 (brs, 2H, CH_2N), 1.41 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.20 (brs, 9H, $\text{Si}(\text{CH}_3)_3$) ; ^{13}C NMR (C_6D_6 , 100 MHz) δ 158.2, 137.9, 114.8, 80.1, 47.2, 29.0, 1.4 ; IR (neat) 3080, 1705 (br), 1645, 1250, 1170, 845 cm^{-1} ; MS (CI NH_3 , m/z) 230 (MH^+), 174 ($\text{MH}^+ - \text{C}_4\text{H}_8$), 158 ($\text{MH}^+ - \text{Si}(\text{CH}_3)_3$) ; Anal. calcd. for : $\text{C}_{11}\text{H}_{23}\text{NO}_2\text{Si}$: C, 57.60 ; H, 10.11 ; N, 6.11 ; Found : C, 57.45 ; H, 10.28 ; N, 6.21.

2a

1a

***N*-bromomethyldimethylsilyl-*N*-(*p*-toluenesulfonyl) allylamine 2a** : ^1H NMR (C_6D_6 , 200 MHz) δ 7.70 (d, $J = 8.1$ Hz, 2H, arom.), 6.81 (d, $J = 8.1$ Hz, 2H, arom.), 5.65 (m, 1H, $\text{C}=\text{CH}_2$), 4.80 (m, 2H, $\text{CH}=\text{CH}_2$), 3.44 (m, 2H, CH_2N), 2.72 (s, 2H, CH_2Br), 1.93 (s, 3H, CCH_3), 0.39 (s, 6H, $\text{Si}(\text{CH}_3)_2$). Reaction treatment led to partial BMDMdesilylation into starting ***N*-(*p*-toluenesulfonyl)-allylamine 1a** : ^1H NMR (C_6D_6 , 200 MHz) δ 7.84 (d, $J = 7.9$ Hz, 2H, arom.), 6.82 (d, $J = 7.9$ Hz, 2H, arom.), 5.46 (m, 1H, $\text{C}=\text{CH}_2$), 5.20 (brs, 1H, NH), 4.83 (m, 2H, $\text{CH}=\text{CH}_2$), 3.35 (brs, 2H, CH_2N), 1.91 (s, 3H, CCH_3).

2b

***N*-bromomethyldimethylsilyl-*N*-allyl-aniline 2b** : reaction run on a 32 mmol scale (Et_2O : 60 mL) afforded **2b** as a pale yellow oil after column distillation (6.6 g, 71%) : ^1H NMR (CDCl_3 , 400 MHz) δ 7.22 (t, $J = 7.6$ Hz, 2H, arom.), 6.95 (d, $J = 7.6$ Hz, 2H, arom.), 6.90 (t, $J = 7.6$ Hz, 1H, arom.), 5.87 (m, 1H, $\text{C}=\text{CH}_2$), 5.10 (m, 2H, $\text{CH}=\text{CH}_2$), 3.96 (m, 2H, CH_2N), 2.67 (s, 2H, CH_2Br), 0.42 (s, 6H, $\text{Si}(\text{CH}_3)_2$) ; ^{13}C (CDCl_3 , 100 MHz) δ 148.8, 137.2, 128.9, 121.3, 120.8, 115.4, 51.8, 17.6, -1.9 ; IR (neat) 3060, 3020, 1640, 1255, 840, 750, 695 cm^{-1} ; HRMS (CI CH_4 , m/z) calcd for $\text{C}_{12}\text{H}_{19}\text{NSiBr}$ (MH^+) 284.0470 (^{79}Br) and 286.0450 (^{81}Br), found 284.0463 (^{79}Br) and 286.0439 (^{81}Br).

2e

***N*-bromomethyldimethyldimethylsilyl-*N*-trimethylsilyl allylamine **2e** :**

N-BMDMS precursor **2e** was synthesized in two steps from commercially available allylamine using a sequence of one pot bisilylation.

To a stirred solution of allylamine (3 mL, 39.2 mmol, 1.0 equiv.) in THF (40 mL) was added dropwise *n*-BuLi (2.30 M, 17 mL, 39.1 mmol, 1.0 equiv.) at -78 °C. After addition, the solution was allowed to warm to rt then stirred for 20 min. After cooling to 0 °C, TMSCl (5 mL, 39.1 mmol, 1.0 equiv.) was added dropwise and the solution was allowed to warm to rt then stirred for 30 min. After cooling to -78 °C, *n*-BuLi (17 mL, 39.1 mmol, 1.0 equiv.) was added dropwise. The solution was allowed to slowly reach rt then stirred for 30 min. After cooling to 0 °C, BMDMSCl (5.4 mL, 38.8 mmol, 1.0 equiv.) was added dropwise. The reaction mixture was stirred for 15 min at 0 °C, allowed to warm to rt then stirred for 45 min. The reaction was quenched with brine and the aqueous layer was extracted with Et₂O. The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered and evaporated *in vacuo* to give a yellow-orange oil (10.0 g, 91%). ¹H NMR spectrum exhibited a fairly pure compound. Further purification by column distillation gave **2e** as the unique distillating compound (7.9 g, 72%) : bp < 74 °C (0.02 torr). Redistillation (0.02-0.03 torr) gave stabilized bp = 58-59 °C. Colorless oil, ¹H NMR (CDCl₃, 400 MHz) δ 5.79 (m, 1H, H₂C=CH), 5.11 and 5.02 (m, 2H, H₂C=CH), 3.49 (m, 2H, CH₂N), 2.48 (s, 2H, CH₂Br), 0.27 (s, 6H, Si(CH₃)₂-CH₂Br), 0.12 (s, 9H, Si(CH₃)₃) ; ¹³C NMR (CDCl₃, 50 MHz) δ 140.8, 114.0, 47.6, 19.1, 2.1, -1.0 ; IR (neat) 3100, 1650, 1260, 930, 890, 850, 825, 765, 695 cm⁻¹ ; HRMS (CI CH₄, *m/z*) calcd for C₉H₂₃NSi₂Br (MH⁺) 280.0552 (⁷⁹Br) and 282.0532 (⁸¹Br), found 280.0544 (⁷⁹Br) and 282.0525 (⁸¹Br).

One-pot radical cyclizations :

Cyclization products **4a**, **5a**, **5b**, **5d**, **7**, **11a** and **11b** were synthesized by a one-pot sequence including the *in situ* synthesis of *N*-BMDMS precursors, a thermally or photochemically induced radical cyclization and a heterocycle treatment (MeLi or Tamao oxidation).

In situ synthesis of N-BMDMS precursors :

***n*-BuLi as base :** in a 50 mL round-bottomed flask filled with *N*-protected amine (0.5 mmol, 1 equiv.) in Et₂O (3 mL) was added dropwise *n*-BuLi (0.5 mmol, 1 equiv.) at 0°C. The solution was allowed to warm to rt then stirred for 15 min. After cooling to 0°C, BMDMSCl (70 µL, 0.5 mmol, 1 equiv.) was added dropwise. The solution was allowed to warm to rt then stirred for 1 h.

***Et₃N*/4-DMAP as base :** in a 50 mL round-bottomed flask filled with *N*-protected amine (0.5 mmol, 1 equiv.), Et₃N (0.07 mL, 0.5 mmol, 1 equiv.) and 4-DMAP (8 mg, 0.06 mmol, 0.1 equiv.) in Et₂O (1 mL) was added dropwise BMDMSCl (70 µL, 0.5 mmol, 1 equiv.) at rt. After addition, the solution was stirred for 1 h.

Radical cyclizations :

Photochemical initiation : to the resulting solution of *in situ* prepared *N*-BMDMS precursor was added AIBN (8 mg, 0.05 mmol, 0.1 equiv.) and toluene or benzene (20 mL, 0.025 M). A solution of AIBN (16 mg, 0.10 mmol, 0.2 equiv.) and *n*-Bu₃SnH (0.18 mL, 0.65 mmol, 1.3 equiv.) in toluene or benzene (7 mL) was added dropwise *via* syringe-pump ($2 \cdot 10^{-4}$ mol.h⁻¹) at -10 °C (toluene) or 10 °C (benzene) under sunlamp irradiation. After addition, sunlamp irradiation was maintained for 30 min.

Thermal initiation : to the resulting solution of *in situ* prepared *N*-BMDMS precursor was added AIBN (8 mg, 0.05 mmol, 0.1 equiv.) and benzene (20 mL, 0.025 M). To that refluxing solution was added dropwise *via* syringe-pump ($2 \cdot 10^{-4}$ mol.h⁻¹) a solution of AIBN (16 mg, 0.10 mmol, 0.2 equiv.) and *n*-Bu₃SnH (0.18 mL, 0.65 mmol, 1.3 equiv.) in benzene (7 mL). After addition, reflux was maintained for 30 min.

Heterocycle treatments :

MeLi treatment : after cyclization, the resulting solution was treated with MeLi (6.0 mL, 9.6 mmol, 19 equiv.) at 10 °C. After stirring for 30 min, the solution was allowed to warm to rt then stirred for 15 min. The reaction was carefully quenched with aqueous saturated NH₄Cl solution at 0 °C and the aqueous layer was extracted with Et₂O. The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered and evaporated *in vacuo* to give a yellow oil. Purification was achieved by flash column chromatography on silica gel (PE/Et₂O gradient).

4a

***N*-(2-methyl-3-trimethylsilyl-prop-1-yl)-*p*-toluenesulfonamide 4a** : pale yellow oil (104 mg, 69% (scheme 2, entry 3)) ; ¹H NMR (CDCl₃, 200 MHz) δ 7.77 (d, *J* = 8.4 Hz, 2H, arom.), 7.31 (d, *J* = 8.4 Hz, 2H, arom.), 5.00 (t, *J* = 6.4 Hz, 1H, NH), 2.74 (m, 2H, CH₂N), 2.43 (s, 3H, CCH₃), 1.70 (m, 1H, CHCH₃), 0.88 (d, *J* = 6.9 Hz, 3H, CHCH₃), 0.58 (dd, *J* = 14.8, 4.4 Hz, 1H, CHHSi), 0.28 (dd, *J* = 14.8, 9.8 Hz, 1H, CHHSi), -0.04 (s, 9H, Si(CH₃)₃) ; ¹³C NMR (CDCl₃, 50 MHz) δ 143.4, 137.3, 129.8, 127.2, 52.2, 30.2, 22.1, 21.7, 20.3, -0.6 ; IR (neat) 3300 (br), 3070, 1330, 1275, 1170, 845, 750 cm⁻¹ ; HRMS (CI CH₄, *m/z*) calcd for C₁₄H₂₆NO₂SSi (MH⁺) 300.1454, found 300.1451.

Tamao oxidation treatment : after cyclization, the resulting solution was allowed to warm to rt. Toluene was evaporated *in vacuo* then THF (2 mL), MeOH (2 mL), KHCO₃ (150 mg, 1.5 mmol, 3 equiv.), KF (58 mg, 1.0 mmol, 2 equiv.) and 30% H₂O₂ (0.6 mL, 5.9 mmol, 12 equiv.) were successively added. The resulting solution was stirred at rt for 20 h then diluted with Et₂O, filtered over celite® (Et₂O washings) and concentrated *in vacuo*. The residue was submitted to a CHCl₃/1 M NaOH extraction. The combined organic layers were washed with 1 M NaOH, dried over anhydrous Na₂SO₄, filtered and evaporated *in vacuo* to give a pasty beige oil. Purification was achieved by flash column chromatography on silica gel (PE/Et₂O gradient).

5a

3-(*p*-toluenesulfonamido)-2-methyl-propan-1-ol 5a : Colorless oil (77 mg, 63% (table 1, entry 2 (see also 54% HBF₄, OEt₂ treatment))) ; ¹H NMR (CDCl₃, 400 MHz) δ 7.75 (d, *J* = 8.1 Hz, 2H, arom.), 7.32 (d, *J* = 8.1 Hz, 2H, arom.), 5.15 (brs, 1H, NH), 3.67 (m, 1H, CHHO), 3.47 (m, 1H, CHHO), 3.02 (m, 1H, CHHN), 2.88 (m, 1H, CHHN), 2.44 (s, 3H, CCH₃), 2.04 (brs, 1H, OH), 1.85 (m, 1H, CHCH₃), 0.86 (d, *J* = 6.6 Hz, 3H, CHCH₃) ; ¹³C NMR (CDCl₃, 50 MHz) δ 143.6, 137.0, 130.0, 127.2, 66.1, 46.9, 35.4, 21.7, 14.5 ; IR (CDCl₃) 3500 (br), 3300 (br), 3070, 1330, 1170 cm⁻¹ ; HRMS (CI CH₄, *m/z*) calcd for C₁₁H₁₈NO₃S (MH⁺) 244.1007, found 244.1011.

Oxidation reluctant siloxane : mixture of diastereomers ; colorless oil (65 mg, 44%, (table 1, entry 1)) ; ¹H NMR (CDCl₃, 200 MHz) δ 7.75 (d, *J* = 8.4 Hz, 4H, arom.), 7.29 (d, *J* = 8.4 Hz, 4H, arom.), 4.92 (brs, 2H, NH), 2.74 (apparent triplet, *J* = 6.4 Hz, 4H, CH₂N), 2.42 (s, 6H, CCH₃), 1.75 (m, 2H, CHCH₃), 0.89 (d, *J* = 6.4 Hz, 6H, CHCH₃), 0.68 (m, 2H, CHHSi), 0.32 (dd, *J* = 14.7, 9.4 Hz, 2H, CHHSi), 0.04 (s, 6H, Si(CH₃)(CH₃)), 0.03 (s, 6H, Si(CH₃)(CH₃)) ; ¹³C NMR (CDCl₃, 100 MHz) δ 143.4, 137.4, 129.8, 127.3, 51.9, 29.8, 23.9-23.8 (2 diastereomers), 21.7, 20.5, 1.6, 1.4 ; IR (neat) 3400 (br), 3300 (br), 3050, 1330, 1260, 1160, 1060 (br), 845, 820 cm⁻¹ ; MS (CI NH₃, *m/z*) 602 (MNH₄⁺), 585 (MH⁺), 431 (MH⁺ - Ts), 284 (MH⁺ - TsNHCH₂CH(CH₃)CH₂Si(CH₃)₂-OH).

5b

2-methyl-3-phenylamino-propan-1-ol 5b : colorless oil (54 mg, 65% (table 1, entry 4 (see also KF/MeOH treatment))) ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.20 (t, J = 7.6 Hz, 2H, arom.), 6.75 (t, J = 7.6 Hz, 1H, arom.), 6.67 (d, J = 7.6 Hz, 2H, arom.), 3.68 (dd, J = 10.7, 4.6 Hz, 1H, CH/O), 3.61 (dd, J = 10.7, 7.1 Hz, 1H, CH/O), 3.17 (dd, J = 12.7, 7.6 Hz, 1H, CH/N), 3.10 (dd, J = 12.7, 5.6 Hz, 1H, CH/N), 3.10 (brs, 2H, NH and OH), 2.04 (m, 1H, CHCH_3), 0.99 (d, J = 7.1 Hz, 3H, CHCH_3) ; ^{13}C NMR (CDCl_3 , 50 MHz) δ 148.5, 129.4, 117.9, 113.4, 67.6, 48.9, 35.4, 15.2 ; IR (neat) 3600-3200, 3050, 750, 700 cm^{-1} ; HRMS (CI CH_4 , m/z) calcd for $\text{C}_{10}\text{H}_{16}\text{NO}$ (MH^+) 166.1232, found 166.1229.

p-5b

2-methyl-3-(p-bromo-phenylamino)-propan-1-ol p-5b : yellow oil (mixture with **5b**, 41 mg, 33% (table 1, entry 3)) ; ^1H NMR (CDCl_3 , 200 MHz) δ 7.25 (d, J = 8.8 Hz, 2H, arom.), 6.52 (d, J = 8.8 Hz, 2H, arom.), 3.64 (m, 2H, CH_2O), 3.12 (m, 2H, CH_2N), 2.03 (m, 1H, CHCH_3), 1.70 (brs, 1H, NH), 0.99 (d, J = 6.9 Hz, 3H, CHCH_3) ; ^{13}C NMR (CDCl_3 , 50 MHz) δ 147.6, 132.1, 114.7, 109.1, 67.3, 48.7, 35.3, 15.2 ; IR (neat) 3600-3100, 3050, 810, 690 cm^{-1} ; HRMS (CI CH_4 , m/z) calcd for $\text{C}_{10}\text{H}_{15}\text{NOBr}$ (MH^+) 244.0337 (^{79}Br) and 246.0317 (^{81}Br), found 244.0333 (^{79}Br) and 246.0310 (^{81}Br).

o-5b

2-methyl-3-(*o*-bromo-phenylamino)-propan-1-ol *o-5b* : Brown oil (13 mg, 11% (table 1, entry 3)) ; ^1H NMR (CDCl_3 , 200 MHz) δ 7.42 (d, J = 7.9 Hz, 1H, arom.), 7.18 (t, J = 7.9 Hz, 1H, arom.), 6.68 (d, J = 7.9 Hz, 1H, arom.), 6.56 (t, J = 7.9 Hz, 1H, arom.), 4.63 (brs, 1H, NH), 3.67 (m, 2H, CH_2O), 3.18 (m, 2H, CH_2N), 2.07 (m, 1H, CHCH_3), 1.03 (d, J = 6.9 Hz, 3H, CHCH_3) ; ^{13}C NMR (CDCl_3 , 50 MHz) δ 145.3, 132.6, 128.7, 118.0, 111.6, 110.2, 67.2, 48.1, 35.4, 15.2 ; IR (neat) 3500-3200, 3050, 735, 650 cm^{-1} ; HRMS (CI CH_4 , m/z) calcd for $\text{C}_{10}\text{H}_{15}\text{NOBr}$ (MH^+) 244.0337 (^{79}Br) and 246.0317 (^{81}Br), found 244.0343 (^{79}Br) and 246.0318 (^{81}Br).

5d

***N*-(*tert*-butoxycarbonyl)-2-methyl-3-hydroxy-prop-1-ylamine *5d*⁹** : Colorless oil (72 mg, 75% (table 1, entry 6)). Spectroscopic data were consistent with those reported in the literature⁹ : ^1H NMR (CDCl_3 , 400 MHz) δ 4.90 (brs, 1H, NH), 3.53 (m, 1H, CHHO), 3.44 (brs, 1H, OH), 3.29 (m, 2H, CHHO and CHHN), 3.02 (m, 1H, CHHN), 1.75 (m, 1H, CHCH_3), 1.43 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.87 (d, J = 7.1 Hz, 3H, CHCH_3) ; ^{13}C NMR (CDCl_3 , 50 MHz) δ 157.6, 79.9, 64.5, 42.7, 36.5, 28.5, 14.6.

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N*-(*tert*-butoxycarbonyl)-2,2-dimethyl-3-hydroxy-prop-1-ylamine *7 : white solid (43 mg, 42% (scheme 4)), mp = 82-84 $^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz) δ 5.02 (brs, 1H, NH), 3.87 (brs, 1H, OH), 3.17 (d, J = 5.6 Hz, 2H, CH_2O), 2.93 (d, J = 7.1 Hz, 2H, CH_2N), 1.42 (s, 9H, $\text{C}(\text{CH}_3)_3$), 0.83 (s, 6H, $\text{C}(\text{CH}_3)_2$) ; ^{13}C NMR (CDCl_3 , 100 MHz) δ 157.9, 80.0, 68.2, 47.3, 37.0, 28.5, 22.6 ; IR (CDCl_3) 3500-3200, 1690 cm^{-1} ; MS (CI NH_3 , m/z) 204 (MH^+), 148 ($\text{MH}^+ - \text{C}_4\text{H}_8$), 104 ($\text{MH}^+ - \text{C}_5\text{H}_8\text{O}_2$) ; Anal. calcd. for : $\text{C}_{10}\text{H}_{21}\text{NO}_3$: C, 59.08 ; H, 10.41 ; N, 6.89 ; Found : C, 59.15 ; H, 9.89 ; N, 6.42.

11a

(Z)- and (E)- 2-(p-toluenesulfonamidomethyl)-hept-2-en-1-ol (Z)-11a and (E)-11a : pale yellow oil (mixture of inseparable **(Z)-11a** and **(E)-11a** (7/3), 64 mg, 43% (scheme 5, entry 1)). **(Z)-11a :** ^1H NMR (CDCl_3 , 200 MHz) δ 7.75 (d, J = 8.6 Hz, 2H, arom.), 7.31 (d, J = 8.6 Hz, 2H, arom.), 5.39 (t, J = 7.4 Hz, 1H, $\text{CH}=\text{C}$), 5.28 (brs, 1H, NH), 4.15 (s, 2H, CH_2O), 3.60 (d, J = 6.9 Hz, 2H, CH_2N), 2.42 (s, 3H, CCH_3), 1.96 (m, 2H, $\text{CH}_2\text{CH}=\text{C}$), 1.26 (m, 4H, $-(\text{CH}_2)_2\text{CH}_3$), 0.86 (t, J = 6.9 Hz, 3H, $-(\text{CH}_2)_3\text{CH}_3$) ; ^{13}C NMR (CDCl_3 , 100 MHz) δ 143.6, 137.2, 133.6, 132.8, 129.9, 127.4, 59.1, 48.4, 31.8, 27.4, 22.4, 21.7, 14.1. **(E)-11a :** ^1H NMR (CDCl_3 , 200 MHz) δ 7.74 (d, J = 8.6 Hz, 2H, arom.), 7.30 (d, J = 8.6 Hz, 2H, arom.), 5.52 (t, J = 7.4 Hz, 1H, $\text{CH}=\text{C}$), 5.28 (brs, 1H, NH), 4.03 (s, 2H, CH_2O), 3.63 (d, J = 6.4 Hz, 2H, CH_2N), 2.42 (s, 3H, CCH_3), 1.96 (m, 2H, $\text{CH}_2\text{CH}=\text{C}$), 1.26 (m, 4H, $-(\text{CH}_2)_2\text{CH}_3$), 0.86 (t, J = 6.9 Hz, 3H, $-(\text{CH}_2)_3\text{CH}_3$) ; ^{13}C NMR (CDCl_3 , 100 MHz) δ 143.5, 136.9, 133.4, 132.6, 129.9, 127.4, 66.8, 41.0, 31.7, 27.4, 22.4, 21.7, 14.1 ; IR (neat) 3500 (br), 3300 (br), 3060, 3010, 1670, 1320, 1160 cm^{-1} ; HRMS (CI CH_4 , m/z) calcd for $\text{C}_{15}\text{H}_{24}\text{NO}_3\text{S}$ (MH^+) 298.1477, found 298.1476.

Oxidation reluctant siloxane : mixture of diastereomers (58 mg, 33%, (scheme 5, entry 1)), ^1H NMR (CDCl_3 , 400 MHz) δ 7.76 (m, 4H, arom.), 7.29 (m, 4H, arom.), 5.12 and 5.08 (t, J = 7.1 Hz each, 2H, $\text{CH}=\text{C}$, (*Z*) and (*E*) substitution of the double bond), 4.82 (brs, 2H, NH), 3.47 and 3.41 (m, 4H, CH_2N , (*E*) and (*Z*) substitution of the double bond), 2.41 (s, 6H, CCH_3), 1.83 (m, 4H, $\text{CH}_2\text{CH}=\text{C}$), 1.47 and 1.43 (s, 4H, CH_2Si , (*Z*) and (*E*) substitution of the double bond), 1.22 (m, 8H, $\text{CH}_3-(\text{CH}_2)_2$), 0.85 (m, 6H, $\text{CH}_3-(\text{CH}_2)_2$), 0.03 and 0.01 (s, 12H, $\text{Si}(\text{CH}_3)_2$, (*Z*) and (*E*) substitution of the double bond) ; IR (neat) 3400-3200, 3060, 3030, 1655, 1325, 1255, 1160, 1050, 840, 815 cm^{-1} ; MS (CI NH_3 , m/z) 710 (MNH_4^+), 693 (MH^+), 539 ($\text{MH}^+ - \text{Ts}$), 338 ($\text{MH}^+ - \text{TsNHCH}_2\text{C}(\text{CH}_2\text{Si}(\text{CH}_3)_2 - \text{OH})=\text{CH}(\text{n-Bu})$).

11b

(Z)- and (E)- N-(tert-butoxycarbonyl)-2-hydroxymethyl-hept-2-en-1-amine (Z)-11b and (E)-11b : colorless oil (mixture of inseparable **(Z)-11b** and **(E)-11b** (7/3), 80 mg, 65% (scheme 5, entry 2)). **(Z)-11b** : ^1H NMR (CDCl_3 , 400 MHz) δ 5.37 (t, J = 7.4 Hz, 1H, $\text{CH}=\text{C}$), 5.01 (brs, 1H, NH), 4.11 (s, 2H, CH_2O), 3.74 (d, J = 6.1 Hz, 2H, CH_2N), 2.03 (m, 2H, $\text{CH}_2\text{CH}=\text{C}$), 1.41 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.28 (m, 4H, $-(\text{CH}_2)_2\text{CH}_3$), 0.85 (t, J = 6.6 Hz, 3H, $-(\text{CH}_2)_3\text{CH}_3$) ; ^{13}C NMR (CDCl_3 , 100 MHz) δ 157.1, 136.1, 130.1, 79.8, 58.2, 44.9, 31.9, 28.5, 27.3, 22.4, 14.0. **(E)-11b** : ^1H NMR (CDCl_3 , 400 MHz) δ 5.50 (t, J = 7.4 Hz, 1H, $\text{CH}=\text{C}$), 5.01 (brs, 1H, NH), 4.00 (s, 2H, CH_2O), 3.81 (d, J = 6.1 Hz, 2H, CH_2N), 2.03 (m, 2H, $\text{CH}_2\text{CH}=\text{C}$), 1.41 (s, 9H, $\text{C}(\text{CH}_3)_3$), 1.28 (m, 4H, $-(\text{CH}_2)_2\text{CH}_3$), 0.85 (t, J = 6.6 Hz, 3H, $-(\text{CH}_2)_3\text{CH}_3$) ; ^{13}C NMR (CDCl_3 , 100 MHz) δ 157.1, 136.1, 130.9, 79.8, 66.4, 37.8, 31.9, 28.5, 27.3, 22.4, 14.0 ; IR (neat) 3600-3100, 3030, 1680 (br) cm^{-1} ; HRMS (CI CH_4 , m/z) calcd for $\text{C}_{13}\text{H}_{26}\text{NO}_3$ (MH^+) 244.1913, found 244.1916.

HBF_4 , OEt_2 treatment (PG = Ts, (table 1, entry 2 ; scheme 5)) : after cyclization and toluene evaporation, the crude was diluted with CH_2Cl_2 (4 mL) and 54% HBF_4 , OEt_2 (0.14 mL, 1.0 mmol, 2 equiv.) was added dropwise at 0°C . After 15 min, the solution was allowed to warm to rt then stirred for 15 min. CH_2Cl_2 was removed *in vacuo* and the residue was submitted to Tamao oxidation conditions : THF (2 mL), MeOH (2 mL), KHCO_3 (250 mg, 2.5 mmol, 5 equiv.), no KF, 30% H_2O_2 (0.6 mL, 5.9 mmol, 12 equiv. (additional 30% H_2O_2 can possibly be required for oxidation completion)), rt, 18 h ; followed by usual treatment and purification.

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2-(*p*-toluenesulfonamidomethyl) hept-1-ene 12¹⁰ (PG = Ts, scheme 5) : colorless oil (65 mg, 46%, (scheme 5)) ; ¹H NMR (CDCl₃, 400 MHz) δ 7.76 (d, *J* = 8.3 Hz, 2H, arom.), 7.31 (d, *J* = 8.3 Hz, 2H, arom.), 4.88 (s, 1H, =CH*H*), 4.82 (s, 1H, =CH*H*), 4.60 (brs, 1H, NH), 3.49 (d, *J* = 6.1 Hz, 2H, CH₂N), 2.43 (s, 3H, CCH₃), 1.95 (t, *J* = 7.6 Hz, 2H, CH₃-(CH₂)₃-CH₂-), 1.25 (m, 6H, CH₃-(CH₂)₃-CH₂-), 0.86 (t, *J* = 7.1 Hz, 3H, CH₃-(CH₂)₃-CH₂-) ; ¹³C NMR (CDCl₃, 50 MHz) δ 144.9, 143.6, 137.0, 129.9, 127.3, 112.0, 48.0, 33.8, 31.6, 27.3, 22.6, 21.7, 14.2 ; IR (CDCl₃) 3400-3200, 3060, 3030, 1650, 1325, 1160, 815 cm⁻¹ ; Anal. calcd. for : C₁₅H₂₃NO₂S : C, 64.02 ; H, 8.24 ; N, 4.98 ; Found : C, 64.13 ; H, 8.37 ; N, 4.91.

KF/MeOH treatment (PG = Ph, (table 1, entry 4)) : after cyclization and toluene evaporation, the crude was diluted with MeOH (14 mL) and KF (194 mg, 3.3 mmol, 6.7 equiv.) was added at rt. After 16 h, MeOH was removed *in vacuo* and the residue was diluted with CH₂Cl₂ then filtered over celite® (CH₂Cl₂ washings). CH₂Cl₂ was removed *in vacuo* and the residue was submitted to usual Tamao oxidation conditions (6 equiv. of KF used), treatment and purification.

One pot *tert*-butoxycarbonylation (PG = TMS, scheme 3) : reaction run on a 1.17 mmol scale. After radical cyclization, benzene was partially evaporated (1-2 mL remaining). The residue was submitted to Tamao oxidation conditions : THF (3.5 mL), MeOH (3.5 mL), KHCO₃ (706 mg, 7.0 mmol, 6 equiv.), KF (273 mg, 4.7 mmol, 4 equiv.), 30% H₂O₂ (4.3 mL, 42.1 mmol, 36 equiv.), rt, 22 h ; then pH was adjusted to 9-10 by addition of 1 M NaOH. After THF dilution (7 mL) and cooling to 0 °C, di-*tert*-butyl dicarbonate (256 mg, 1.14 mmol, 1 equiv.) was added. The resulting mixture was stirred for 10 min, allowed to warm to rt, stirred for 2 h then finally submitted to usual treatment and purification.

3e

1,1,4-trimethyl-2-trimethylsilyl-2-aza-1-sila-cyclopentane 3e (scheme 3) : **3e** was characterized in PhH after radical cyclization and partial benzene evaporation : ^1H NMR (C_6D_6 , 200 MHz) δ 3.01 (m, 1H, CHHN), 2.47 (t, $J = 9.4$ Hz, 1H, CHN), 1.91 (m, 1H, CHCH_3), 0.98 (d, $J = 6.4$ Hz, 3H, CHCH_3), 0.84 (dd, $J = 14.2, 6.6$ Hz, 1H, CHHSi), 0.28 (dd, $J = 14.2, 10.7$ Hz, 1H, CHSi), 0.20 (s, 3H, $\text{Si}(\text{CH}_3)(\text{CH}_3)$), 0.16 (s, 3H, $\text{Si}(\text{CH}_3)(\text{CH}_3)$), 0.15 (s, 9H, $\text{Si}(\text{CH}_3)_3$) ; ^{13}C NMR (C_6D_6 , 50 MHz) δ 56.4, 35.2, 23.3, 21.7, 2.8, 2.7, 1.0.

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