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PAPER

Bismuth(III) triflate promoted intramolecular hydroamination of unactivated alkenyl sulfonamides in the preparation of pyrrolidines†

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$Bi(OTf)_3 \cdot nH_2O$ was found to be an efficient promoter of the cyclisative hydroamination of unactivated alkenyl sulfonamides, giving rise to the *N*-protected 2-methyl pyrrolidines in good to excellent yields (up to 95%). Based on control experiments, a joint Lewis acid–Brønsted acid catalysis might be in operation, or triflic acid itself, generated *in situ* by hydrolysis of metal triflate, could be the true hydroamination catalyst.

Introduction

Owing to the atom-economy and efficiency, hydroamination[1] is a prominent synthetic method for the preparation of amines. The intramolecular version of metal-catalysed[2,31] hydroamination is an attractive method for the synthesis of saturated nitrogen heterocycles. While there are some very active hydroamination metal catalysts already established, many of them suffer from air and/or water intolerance.[3,33] Moreover, most of the successful cyclisative hydroaminations so far are restricted to either highly reactive unsaturated amines (dienes, allenes, alkynes)[4] or alkenyl amines–amides activated[5] *via gem*-dialkyl/aryl-substitution (Thorpe–Ingold effect).[6]

On the other hand, bismuth(III) triflate is a non-toxic and air-tolerant Lewis acid, which has been widely applied as green catalyst in diverse organic syntheses over the past years.[7] Among such applications, there are only few cases of hydroamination using $Bi(OTf)_3$. However, most of them were only successful with activated olefines like dienes[8] and/or vinyl arenes[9]. Such a cyclisative transformation with non-conjugated terminal alkenes was achieved only very recently.[10] However, the reported hydroamination was only successful with substrates activated *via gem*-dimethyl-substitution. Herein, we report an efficient bismuth(III) triflate promoted intramolecular hydroamination of unactivated alkenyl sulfonamides to produce methyl-substituted pyrrolidines in excellent yields up to 95%.

Results and discussion

Catalyst screening

In order to find a suitable (pre)catalyst for the cyclisative hydroamination, various metal salts were first screened for the reaction of simple *N*-tosylalkenylamine **1** (Scheme 1). Bismuth(III) triflate turned out to be superior to all other Lewis acids tested (Table 1). Stirring the substrate **1** with 20 mol% $Bi(OTf)_3 \cdot nH_2O$ in 1,2-dichloroethane at 40 °C delivered the *N*-tosyl-2-methyl-pyrrolidine **2**, which was essentially pure by ^{1}H NMR of crude reaction mixture (entry 1, Table 1). Scandium(III) triflate, iron(III) and indium(III) chloride also furnished the desired product **2** in high yields, however, the complete conversion of substrate **1** took substantially longer in these cases (entries 5–7, Table 1). On the other hand, cerium(III) chloride and manganese(II) chloride caused only partial isomerisation of the substrate's double with no formation of pyrrolidine **2** (entries 8–9, Table 1). Thus, having identified the bismuth as a suitable metallic atom, we have next searched for the optimal type of bismuth(III) salt. It turned out, that the hardness of the anion is the key parameter determining the activity of Bi-containing Lewis acids[11] tested in the hydroamination of **1**. Thus, bismuth(III) triflate (entry 1, Table 1) was superior again in comparison to all three halides (entries 10–12) as it delivered the pyrrolidine **2** in highest yield and shortest reaction time. On the other hand, the nitrate performed only poorly (entry 13), while the carbonate (entry 14) and acetate (entry 15) did not furnish the desired product **2** at all. The minimum catalytic loading of $Bi(OTf)_3 \cdot nH_2O$ for the

1 2

Scheme 1 Screening of Lewis acids in the hydroamination of **1**.

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† Electronic supplementary information (ESI) available: Spectra of compounds **3** and **10**, chiral GC analyses of crude reaction mixtures from attempted enantioselective hydroaminations of **1**, and list of chiral ligands used. See DOI: 10.1039/c2ob07064b

Table 1 Screening of various Lewis acids in the hydroamination of **1**

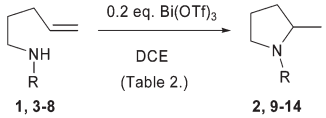
Entry	Lewis acid	Temp., Time	Conversion[a] of **1** (%)	Yield[a] of **2** (%)
1	$Bi(OTf)_3{\cdot}nH_2O$ (0.2 eq.)	40 °C, 3 d	>95	>95
2	$Bi(OTf)_3{\cdot}nH_2O$ (0.1 eq.)	40 °C, 5 d	>95	>95
3	$Bi(OTf)_3{\cdot}nH_2O$ (0.05 eq.)	40 °C, 8 d	>95	>95
4	$Bi(OTf)_3{\cdot}nH_2O$ (0.01 eq.)	40 °C, 14 d	72[b]	72[b]
5	$Sc(OTf)_3$ (0.2 eq.)	60 °C, 8 d	>95	>95
6	$FeCl_3$ (0.2 eq.)	100 °C, 12 d	>95	>95
7	$InCl_3$ (0.2 eq.)	100 °C, 12 d	>95	>95
8	$CeCl_3$ (0.2 eq.)	100 °C, 19 d	<5	<5
9	$MnCl_2$ (0.2 eq.)	100 °C, 19 d	<5	<5
10	BiF_3 (0.2 eq.)	100 °C, 14 d	<5	<5
11	$BiCl_3$ (0.2 eq.)	100 °C, 14 d	50[b]	50[b]
12	$BiBr_3$ (0.2 eq.)	100 °C, 8 d	>95	>95
13	$Bi(NO_3)_3{\cdot}5H_2O$ (0.2 eq.)	100 °C, 14 d	12[b]	<5
14	$(BiO)_2CO_3$ (0.1 eq.)	100 °C, 14 d	<5	<5
15	$Bi(OAc)_3$ (0.2 eq.)	100 °C, 14 d	<5	<5
16	TfOH (0.2 eq.)	40 °C, 2 d	>95	>95
17	Tf_2NH (0.2 eq.)	60 °C, 5 d	>95	>95
18	$In(OTf)_3$ (0.2 eq.)	80 °C, 7 d	>95	>95
19	$Cu(OTf)_2$ (0.2 eq.)	100 °C, 8 d	>95	84
20	$Al(OTf)_3$ (0.2 eq.)	100 °C, 9 d	>95	>95
21	$Hg(OTf)_2$ (0.2 eq.)	100 °C, 12 d	>95	>95
22	$Y(OTf)_3{\cdot}H_2O$ (0.2 eq.)	100 °C, 14 d	>95	>95
23	$Zn(OTf)_2$ (0.2 eq.)	100 °C, 14 d	<5	<5

[a] Based on ^{1}H NMR analysis of crude reaction mixture. [b] DCM was used as an internal standard.

efficient hydroamination of **1** was found to be as low as 0.05 mol% (entry 3). Interestingly, both triflic acid and triflic imide were also capable of delivering the product of cyclisative hydroamination of **1** in high yields (entries 16–17). Finally, the screening of various metal triflates revealed that indium(III), copper(II), aluminium(III), mercury(II) and yttrium(III) triflates also promote the intramolecular hydroamination of alkenyl amine **1** to the 2-methylpyrrolidine **2**. However, these transformations were substantially slower and required prolonged reaction time to reach the full conversion of the substrate in comparison to the $Bi(OTf)_3{\cdot}nH_2O$ (entries 18–22 *vs.* entry 1). Eventually, the catalytic amount of zinc(II) triflate was incapable to hydroaminate the substrate **1** even after 14 days at 100 °C (entry 23).

Influence of *N*-protecting group

Having identified the best metal catalyst, the influence of *N*-protecting group on the hydroamination was scrutinised next. Thus, substrates **1** and **3–7** bearing various electron-withdrawing substituents on the nitrogen atom were prepared and submitted to the $Bi(OTf)_3$-catalysed cyclisation in dry dichloroethane



Scheme 2 Influence of *N*-protecting group on the hydroamination course.

Table 2 Influence of *N*-protecting group on the hydroamination course

Entry	Substrate (R)	Temp., Time	Conversion[a] (%)	Product[a] (Yield)
1	**1** (Ts)	40 °C, 3 d	>95	**2** (>95%)
2	**3** (Ms)	60 °C, 4 d	>95	**9** (88%)[b]
3	**4** (Tf)	80 °C, 8 d	>95	**10** (68%)[b]
4	**5** (Cbz)	100 °C, 5 d	<5	**11** (<5%)
5	**6** (Boc)	100 °C, 5 d	<5	**12** (<5%)
6	**7** (Ac)	100 °C, 9 d	>95	**13** (<5%)[c]
7	**8** (H)	100 °C, 5 d	>95	**14** (<5%)[c]

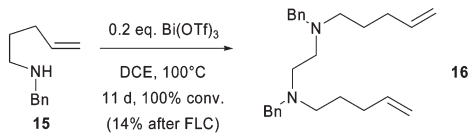
[a] Based on ^{1}H NMR analysis of crude reaction mixture. [b] DCM was used as an internal standard. [c] Substrate decomposition and/or formation of complex reaction mixture.

(Scheme 2, Table 2). The tosyl group in **1** was found to be superior in promoting hydroamination and delivering the pyrrolidine **2** after 3 days stirring at 40 °C as the single compound in quantitative yield (Table 1 and 2, entry 1). Slightly lower yield of cyclic product **9** (88%) was obtained with the use of mesyl group on the nitrogen of **3** (entry 2), while the conversion of triflate **4** took substantially longer (8 days at 80 °C) but finally delivered the hydroamination product **10** in 68% yield. On the other hand, attempts to cyclise carbamates **5** (*N*-Cbz) and **6** (*N*-Boc) resulted in zero conversion of substrates after 5 days at 100 °C (entries 4 and 5). Employment of acetamide **7** led to the complex reaction mixture only (entry 6), and the attempted hydroamination of unprotected alkenylamine **8** gave the same result (entry 7).

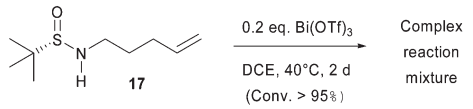
Interestingly, the $Bi(OTf)_3$-catalysed hydroamination of *N*-benzyl protected substrate **15** led to a mixture of compounds with 1,2-diamine **16** as a major product and no formation of the desired 2-methylpyrrolidine. Apparently, the dichloroethane used as a solvent played a dual role in this case – acting also as an electrophile, and thus bridging two electron-rich *N*-atoms intermolecularly (Scheme 3). In a control experiment, the attempted hydroamination of **15** with 0.2 eq. $Bi(OTf)_3{\cdot}nH_2O$ in toluene gave less than 5% conversion of substrate even after 12 days at 100 °C.

Finally, the employment of sulfinamide **17** led to the formation of complex reaction mixture without any trace of the desired product of hydroamination (Scheme 4). This is a rather surprising result bearing in mind the excellent performance of similar protecting groups (Ts, Ms, and Tf *cf.* Table 2, entries 1–3).

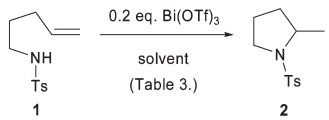
Altogether, results of this screening clearly indicated the necessity of significantly diminished *N*-basicity as a key parameter for the successful intramolecular hydroamination of unactivated alkenyl amines. Thus, (less basic) sulfonamides **1–3** are far superior substrates for the cyclisation than (more basic)



Scheme 3 $Bi(OTf)_3$-catalysed hydroamination of *N*-benzyl protected **15**.



Scheme 4 $Bi(OTf)_3$-catalysed hydroamination of sulfinamide **17**.



Scheme 5 Solvent screening in $Bi(OTf)_3$-catalysed hydroamination of **1**.

Table 3 Solvent screening in $Bi(OTf)_3$-catalysed hydroamination of **1**

Entry	Solvent	Temp./Time	Conversion[a] of **1** (%)	Yield[a] of **2** (%)
1	DCE	40 °C, 3 d	>95	>95
2	DCM	60 °C, 5 d	>95	>95
3	Toluene	60 °C, 6 d	>95	>95
4	THF	100 °C, 14 d	>95	79[b]
5	Dioxane	100 °C, 14 d	80[b]	72[b]
6	MeCN	100 °C, 14 d	73[b]	68[b]
7	Acetone	100 °C, 14 d	75[b]	56[b]
8	DMF	100 °C, 7 d	<5	<5
9	MeOH	80 °C, 5 d	>95	>95
10	^{i}PrOH	100 °C, 7 d	~20	n.d.[c]
11	H_2O	80 °C, 5 d	>95	>95

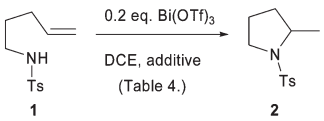
[a] Based on ^{1}H NMR analysis of crude reaction mixture. [b] DCM was used as an internal standard. [c] Not determined.

carbamates **5–6**, amide **7**, and (the most basic) amines **8**, **15**. This empirical observation subsequently raised the question about the nature of the true catalytic species in such $Bi(OTf)_3$-catalysed cyclisative intramolecular hydroamination.

Solvent screening

With the tosylate as an optimal *N*-protecting group, the effect of solvent on the hydroamination course was tested next. Thus, the substrate **1** underwent the $Bi(OTf)_3$-catalysed cyclisation in various reaction media (Scheme 5, Table 3).

The use of chlorinated hydrocarbons gave the best results, while the hydroamination was faster in dichloroethane (3 days at 40 °C) in comparison to dichloromethane (5 days at 60 °C), and thus, delivering the *N*-tosyl-2-methyl-pyrrolidine **2** in excellent yield in both cases (entries 1–2, Table 3). Interestingly, similar



Scheme 6 Influence of additives on the hydroamination of **1**.

Table 4 Influence of various additives on the hydroamination of **1**

Entry	Additive	Temp., Time	Conversion[a] of **1** (%)	Yield[a] of **2** (%)
1	4 Å MS	100 °C, 14 d	12[b]	7[b]
2	Na_2SO_4	100 °C, 14 d	<5	<5
3	H_2O (0.2 eq.)	60 °C, 5 d	>95	>95
4	K_2CO_3 (0.2 eq.)	100 °C, 14 d	<5	<5
5	H^+ Sponge (0.2 eq.)	80 °C, 12 d	>95	>95
6	H^+ Sponge (0.3 eq.)	100 °C, 12 d	>95	>95
7	H^+ Sponge (0.6 eq.)	100 °C, 14 d	<5	<5
8	H^+ Sponge (1.0 eq.)	100 °C, 14 d	<5	<5

[a] Based on ^{1}H NMR analysis of crude reaction mixture. [b] DCM was used as an internal standard.

results were obtained using aprotic and non-polar toluene, though the reaction was slightly slower in this case (entry 3). The employment of either oxygenated solvents like tetrahydrofuran, 1,4-dioxane, and acetone or highly polar acetonitrile led to the incomplete conversions (except of THF) of substrate **1** even after 4 days at 100 °C, and hence, to diminished yields of *N*-tosyl-2-methylpyrrolidine **2** (56–79%, entries 4–7). The use of dimethylformamide as solvent resulted in zero conversion of **1** after 7 days at 100 °C. On the other hand, the cyclisative hydroamination of **1** with 0.2 eq. $Bi(OTf)_3{\cdot}nH_2O$ in protic solvents like methanol and/or water proceeded smoothly delivering the desired pyrrolidine **2** after 5 days at 80 °C (entries 9 and 11, Table 3). These latter, rather unexpected results indicated that either the joint Lewis acid–Brønsted acid catalysis might be in operation, or triflic acid itself (generated *in situ* by hydrolysis of metal triflate) could be the true hydroamination catalyst.

Effect of additives

Thus, we have further investigated the influence of various additives (dehydrating agent, water, base) on the course of cyclisative hydroamination of **1** under the optimised reaction conditions with DCE as a solvent (Scheme 6, Table 4).

In accordance with previous observations regarding protic media including water, the addition of either activated 4 Å molecular sieves or anhydrous sodium sulphate to the reaction mixture led to the (in)complete suppression of the hydroamination, resulting in a negligible or zero conversion of substrate **1** even after 14 days at 100 °C (entries 1–2, Table 4). On the other hand, the addition of a catalytic amount of water (an equimolar amount to $Bi(OTf)_3$) resulted in a smooth cyclisation affording the desired *N*-tosyl-2-methylpyrrolidine **2** in 95% yield (entry 3).

These results suggested again, that triflic acid (in a low but steady equilibrium concentration) formed *in situ* by the reversible hydrolysis of bismuth(III) triflate[12] (eqn (1) and (2)), may actually catalyse the hydroamination[13] of **1** (*cf.* Table 1, entry 16).

$$Bi(OTf)_3 + H_2O \rightleftharpoons Bi(OTf)_2OH + TfOH \quad (1)$$

$$Bi(OTf)_3 + 2\ H_2O \rightleftharpoons [Bi(OH)_2]^+\ TfO^- + 2\ TfOH \quad (2)$$

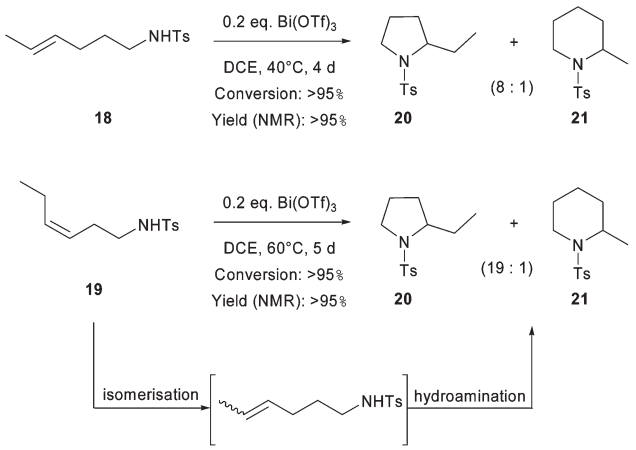
To test such an option,[14] we treated the reaction mixture[15] with the proton scavenger (1,8-bis(dimethylamino)naphthalene, Proton Sponge®) with variable stoichiometry relative to Bi $(OTf)_3$. The addition of equimolar ratio(s) of base to the catalyst (0.2 and/or 0.3 eq.) resulted in full conversion of **1** and quantitative formation of **2** (entries 5–6, Table 4). However, raising the amount of Proton Sponge® to 0.6 and/or 1 eq. completely suppressed the hydroamination and zero conversion of **1** was observed even after 14 days stirring at 100 °C (entries 7–8, Table 4). Again, these results strongly supported the hypothesis that the actual hydroamination catalyst might be the triflic acid generated from $Bi(OTf)_3{\cdot}nH_2O$ during the course of reaction.

Finally, the most convincing (though indirect) evidence favouring that option came from the attempted asymmetric hydroaminations of substrate **1**. We have tested a structurally diverse set of 17 chiral ligands (see ESI†) in order to determine the level of stereoinduction during the cyclisation step. Much to our surprise, none of the commercially available chiral ligands were capable of delivering the non-racemic product **2** (the determined enantioselectivities were in the range 0–2% ee in all cases). This was very probably due to the fact that the (chiral) bismuth complex did not catalysed the hydroamination, but rather served as a promotor generating (achiral) TfOH *in situ* as a truly catalytic species.

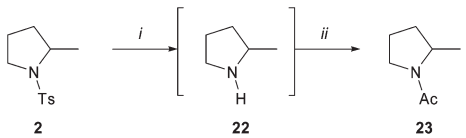
Influence of alkene substitution

Lastly, we determined the influence of an alkene substitution and its geometry on the course of cyclisative hydroamination. Thus, we exposed the (*E*)- and (*Z*)-1,2-disubstituted alkenylamines **18** and **19** to the optimised $Bi(OTf)_3$-catalysed hydroamination conditions (Scheme 7).

In comparison to monosubstituted *N*-tosylalkenylamine **1**, which exclusively underwent the *5-exo-trig* mode of cyclisation producing the pyrrolidine **2** as a single product (Scheme 1, Table 1), the intramolecular hydroamination of (*E*)-1,2-disubstituted alkenylamine **18** under identical reaction conditions afforded the chromatographically inseparable mixture of *N*-tosyl-2-ethylpyrrolidine **20** (*5-exo-trig* product) and *N*-tosyl-2-methylpiperidine **21** (*6-endo-trig* product) in the ratio of 8 : 1 (Scheme 7). Surprisingly, the formation of the same products was observed during the hydroamination of (*Z*)-1,2-disubstituted alkenylamine **19**, which was originally designed to test the feasibility of (favoured) *4-exo-trig* cyclisation in competition with (disfavoured) *5-endo-trig* cyclisation. Apparently, the substrate **19** initially underwent a double bond shift/isomerisation under the reaction conditions, followed by the desired intramolecular hydroamination. However, now being of (both favoured) *5-exo-trig vs. 6-endo-trig* nature again, the hydroamination resulted in the formation of mixture of **20** and **21** in the ratio of 19 : 1 (Scheme 7).



Scheme 7 Intramolecular hydroamination of disubstituted alkenes **18**, **19**. Compounds **20** and **21** were identified in crude reaction mixtures and their structures were assigned by comparison with known ^{1}H NMR data. The ratio of **20** : **21** was determined by the integration of respective CH_3-protons. For 2-ethyl-1-tosylpyrrolidine **20**: δ = 0.90 ppm (3H, *t*);[16] for 2-methyl-1-tosylpiperidine **21** : **21** : δ = 1.06 ppm (3H, *d*).[17]



Scheme 8 Deprotection of *N*-tosyl-2-methylpyrrolidine **2**: (i) 3 eq. $LiAlH_4$, Et_2O, r.t., overnight, **22** (crude); (ii) 1.2 eq. Ac_2O, 1.4 eq. Et_3N, Et_2O, 0 °C –r.t., overnight, **23** (68% over 2 steps).

Reductive *N*-detosylation

With the aim of developing the $Bi(OTf)_3$-promoted intramolecular hydroamination as an operationally simple, yet powerful synthetic methodology for the efficient preparation of complex pyrrolidine-containing targets, we have searched for an easy and reliable deprotection of *N*-tosyl-2-methylpyrrolidine **2** (Scheme 8).

There are numerous methods for the reductive *N*-detosylation of pyrrolidines.[18] We had found that treatment[19,39] of **2** with an excess of lithium aluminium hydride cleanly afforded the semi-volatile 2-methylpyrrolidine **22** (bp 93 °C), which was isolated and characterised after the derivatisation to its *N*-acetate **23** (68% overall yield).

Conclusions

In summary, we have developed a catalytic intramolecular hydroamination of unactivated alkenyl sulfonamides using the commercially available[20] $Bi(OTf)_3{\cdot}nH_2O$ as an air and water tolerant Lewis acid. This efficient transformation proceeds under operationally simple conditions and provides an easy and straightforward access to the 2-methylpyrrolidines in yields up to 95%.

Based on the control experiments, a joint Lewis acid–Brønsted acid catalysis might be in operation, or triflic acid itself, generated *in situ* by hydrolysis of metal triflate, could be the true hydroamination catalyst (so-called 'hidden Brønsted catalysis').[21] However, since TfOH is extremely corrosive and difficult to handle, the practical use of $Bi(OTf)_3 \cdot nH_2O$ makes our methodology particularly valuable.

Experimental

All commercial reagents were purchased from Alfa Aesar. 5-Bromo-1-pentene was obtained from VÚP a.s. (Prievidza, Slovakia) as a generous gift. All solvents were distilled before use: diethylether, THF and dioxane from Na/benzophenone, MeOH from MeONa, dichloro(m)ethane from P_2O_5 and stored over activated 4 Å molecular sieves. Thin layer chromatography (TLC) was performed on aluminium plates pre-coated with 0.2 mm silica gel 60 F_{254} (Merck). Flash column liquid chromatography (FLC) was performed on silica gel [Kieselgel 60 (40–63 μm)]. MPLC chromatography was performed on silica gel [Kieselgel 60 (15–40 μm)] with standard eluent flow 30 mL min^{-1}. Infrared (IR) spectra were recorded on a Nicolet 5700 FTIR spectrometer as films on KBr window. NMR spectra were recorded on Varian VXR-300 (300 MHz) and Varian Inova 600 (600 MHz) spectrometers, respectively. Chemical shifts (δ) are quoted in ppm and the residual protic solvent was used as internal reference. The COSY technique was used in assignment of ^1H–^1H relationships and the determination of relative configuration. The multiplicities of carbons were assigned from a broadband decoupled analysis used in conjunction with APT. The HSQC technique was used throughout for the assignment of the ^1H–^{13}C relationships. Liquid chromatography-mass spectrometry (LC-MS) analyses were performed on an Agilent 1200 Series instrument equipped with a multimode MS detector using the MM ESI/APCI$^+$ ionisation method (Column: Zorbax SB C-8 12.5 × 2.1 mm, particle size 5 μm, eluent: acetonitrile–water with 0.1% HCO_2H, gradient 0–100% of CH_3CN for 7 min, flow 1.5 mL min^{-1}).

Preparation[22–27] of alkenylamines (1), (3–8), and (15–19)

4-Methyl-*N*-pent-4-enyl-benzenesulfonamide (1). Anhydrous DMF solution (3 mL) of tosylamine (1362 mg, 7.8 mmol) and 5-bromo-1-pentene (593 mg, 3.90 mmol) was stirred in closed pressure tube under Ar at 38 °C for 4 days. The reaction mixture was cooled to 0 °C, water (30 mL) was added and the solution was extracted with Et_2O (3 × 30 mL). The combined org. layers were dried over anhydrous $MgSO_4$, and evaporated *in vacuo* to leave an orange-brown oil (1.58 g) that solidified upon standing at r.t. over 30 min. The purification by MPLC (50 g SiO_2, hexanes–Et_2O = 3 : 2) afforded pure *N*-tosylalkenylamine **1** (734 mg, 79%) as a pale yellow viscous oil.

R_f 0.27 (Hex–Et_2O 1 : 1); $C_{12}H_{17}NO_3S$ (239.33); ^1H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 8.3 Hz, 2H, H-2′), 7.31 (d, J = 8.0 Hz, 2H, H-3′), 5.71 (ddt, J = 17.0, 10.2, 6.7 Hz, 1H, H-4), 4.98 (ddd, J = 11.1, 6.4, 1.3 Hz, 2H, H-5), 4.45 (t, J = 5.6 Hz, 1H, exchangeable with D_2O, NH), 2.95 (dd, J = 13.5, 6.9 Hz, 2H, H-1), 2.43 (s, 3H, Ar–CH_3), 2.04 (dd, J = 14.4, 7.0 Hz, 2H, H-3), 1.63–1.50 (m, 2H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.51 (C_q, C-4′), 137.35 (CH, C-4), 137.13 (C–H, C-1′), 129.83 (CH, C-3′), 127.22 (CH, C-2′), 115.71 (CH_2, C-5), 42.78 (CH_2, C-1), 30.79 (CH_2, C-3), 28.84 (CH_2, C-2), 21.65 (CH_3, Tol). LC-MS: m/z 240 (28%) $[M + 1]^+$, 80 (100%), 102 (19%). All analytical data are in perfect accordance with the literature.[28]

5-Azido-pent-1-ene. Anhydrous DMF solution (2 mL) of sodium azide (844 mg, 13 mmol, 1.3 eq.) and 5-bromo-1-pentene (1.49 g, 10 mmol) was stirred in closed pressure tube under Ar at 30 °C for 18 h. The ice (5 g) was added and the mixture was stirred until its dissolution, then water (10 mL) and n-pentane (15 mL) were added. The org. layer was separated and washed with water (2 × 5 mL), separated again, filtered through short pad of silica gel (3 cm) and solids washed with n-pentane. Due to the high volatility of 5-azido-pent-1-ene, the solution was carefully evaporated *in vacuo* (200 mbar/5 °C) to obtain its stock solution (10.8 g) containing *ca.* 87% of a product (based on NMR), which was further used in the synthesis as such. An aliquot was further evaporated *in vacuo* (200 mbar/5 °C) in order to obtain the sample for analysis.

R_f 0.40 (Hexanes); $C_5H_9N_3$ (111.15); ^1H NMR (300 MHz, $CDCl_3$) δ 5.79 (1H, ddt, J = 16.9, 10.2, 6.7 Hz, H-4), 5.12–4.95 (2H, m, H-5), 3.29 (2H, t, J = 6.9 Hz, H-1), 2.15 (2H, ddd, J = 7.6, 6.8, 1.3 Hz, H-3), 1.79–1.61 (2H, m, H-2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.23 (CH, C-4), 115.78 (CH_2, C-5), 50.88 (CH_2, C-1), 30.84 (CH_2, C-3), 28.17 (CH_2, C-2). LC-MS: m/z 112 (18%) $[M + 1]^+$, 86 (100%). All analytical data are in perfect accordance with the literature.[29]

***N*-Pent-4-enyl-methanesulfonamide (3).** THF (12 mL) and water (108 mg, 6 mmol, 4 eq.) were added to a cold (0 °C) stock solution of 5-azido-pent-1-ene in n-pentane (166 mg, 1.5 mmol) followed by the addition of PPh_3 (635 mg, 2.4 mmol, 1.6 eq.) all at once. The resulting mixture was stirred at 0 °C for 1 h, then cooling bath was removed and the reaction mixture was stirred at r.t. for 48 h. Triethylamine (464 mg, 4.5 mmol) was added dropwise at 0 °C, stirred for 5 min and then MsCl (208 mg, 1.8 mmol) was added dropwise. The cloudy reaction mixture was clarified by the addition of DCM (10 mL) and stirred at 0 °C overnight. Water (15 mL) and DCM (10 mL) were added, layers were separated and the water phase was extracted with DCM (2 × 10 mL). The combined org. layers were dried over anhydrous $MgSO_4$, and evaporated *in vacuo* to leave an oil (780 mg), which solidified upon standing at r.t. Purification by MPLC (SiO_2, hexanes–Et_2O = 1 : 1 + 2% aq. NH_4OH) afforded pure **3** as an oil (54 mg, 22%).

R_f 0.6 (Et_2O); $C_6H_{13}NO_2S$ (163.24); IR (film on KBr) ν_{max} 3291, 3078, 2935, 2870, 1641, 1439, 1414, 1320, 1152, 1081, 975, 776 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.79 (1H, ddt, J = 16.9, 10.2, 6.7 Hz, H-4), 5.05 (2H, ddd, J = 10.2, 5.2, 3.6 Hz, H-5), 4.25 (1H, brs, exchangeable with D_2O, NH), 3.16 (2H, dd, J = 13.5, 6.9 Hz, H-1), 2.96 (3H, s, Me), 2.15 (2H, dd, J = 14.1, 7.2 Hz, H-3), 1.77–1.61 (2H, m, H-2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.28 (CH, C-4), 115.97 (CH_2, C-5), 42.88 (CH_2, C-1), 40.55 (CH_3, Me), 30.83 (CH_2, C-3), 29.37 (CH_2, C-2). LC-MS: m/z 164 (4%) $[M + 1]^+$, 102 (11%), 80 (100%), 160 (8%).

***C*,*C*,*C*-Trifluoro-*N*-pent-4-enyl-methanesulfonamide (4).** Anhydrous Et_2O (10 mL) was added to a cold (0 °C) stock solution of 5-azido-pent-1-ene in n-pentane (166 mg, 1.5 mmol) After 10 min stirring $LiAlH_4$ (85 mg, 2.25 mmol, 1.5 eq.) was added in portions and the resulting mixture was stirred at 0 °C for 3 h. Glauber's salt (*ca.* 2 g) was added in small portions with vigorous stirring resulting in intensive foaming. The cooling bath was removed and the suspension was stirred at r.t. overnight. The liquid over the white solid was decanted, the residue was washed with Et_2O (5 mL) and the combined org. phases were dried over the activated molecular sieves. The solution was transferred to the dry flask *via* canula, anhydrous DCM (15 mL) was added and the mixture was cooled to −5 °C. Anhydrous Et_3N (174 mg, 1.725 mmol, 1.15 eq.) was added followed by the dropwise addition of Tf_2O (444 mg, 1.575 mmol, 1.05 eq.) over 5 min. The resulting mixture was stirred at 0 °C overnight and then evaporated *in vacuo* (100 mbar, 30 °C) to leave an orange-brown. Aq. soln. of NaOH (4M, 10 mL) was added, the mixture was extracted with DCM (3 × 30 mL) and dried over anhydrous $MgSO_4$. The evaporation *in vacuo* furnished a brown oil (238 mg), which was purified by FLC (7.5 g SiO_2, hexanes–Et_2O = 2 : 1 + 2% aq. NH_4OH) to afford a pure **4** (171 mg, 52%) as a pale orange oil.

R_f 0.5 (Hexanes–Et_2O = 2 : 3); $C_6H_{10}F_3NO_2S$ (217.21); ^1H NMR (300 MHz, $CDCl_3$) δ 5.78 (1H, ddt, J = 16.9, 10.2, 6.7 Hz, H-4), 5.16–4.99 (2H, m, H-5), 3.32 (2H, t, J = 7.1 Hz, H-1), 2.15 (2H, dd, J = 14.2, 7.1 Hz, H-3), 1.78–1.66 (2H, m, H-2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.79 (CH, C-4), 119.76 (C_q, J = 320.9 Hz, CF_3), 113.38 (CH_2, C-5), 44.09 (CH_2, C-1), 30.52 (CH_2, C-3), 29.34 (CH_2, C-2). LC-MS: *m*/*z* 102 (100%), 130.2 (14%). All analytical data are in perfect accordance with the literature.[30]

Pent-4-enyl-carbamic acid benzyl ester (5). To a cold (0 °C) stock solution of 5-azido-pent-1-ene in n-pentane (229 mg, 2.06 mmol) was added THF (15.6 mL) and PPh_3 (635 mg, 2.4 mmol, 1.2 eq.). After the complete dissolution water was added (148 µl, 8.64 mmol, 4 eq.) and the resulting mixture was stirred at r.t. for 48 h. Then, triethylamine (416 mg, 4.12 mmol, 2 eq.) was added at once followed by the dropwise addition of CbzCl (457 mg, 2.68 mmol, 1.3 eq.) at −2 °C. After 6 h of stirring the mixture was evaporated *in vacuo* and DCM (30 mL) and H_2O (30 mL) were added. The separated water layer was extracted with DCM (20 mL), combined org. extracts were dried over anhydrous $MgSO_4$ and evaporated *in vacuo* to leave a white semi-crystalline oil (1.556 g). Purification by MPLC (SiO_2, 25 × 110 mm, hexanes–Et_2O = 84 : 16 + 2% aq. NH_4OH, 30 mL min^{-1}) yielded pure **5** as a colourless clear oil (370 mg, 82%).

R_f 0.26 (Hexanes–Et_2O = 4 : 1); $C_{13}H_{17}NO_2$ (219.28); ^1H NMR (300 MHz, $CDCl_3$) δ 7.46–7.19 (m, 5H, Ph), 5.79 (ddt, J = 16.9, 10.1, 6.6 Hz, 1H, H-4), 5.14–4.91 (m, 4H, H-5, CH_2Ph), 4.80 (1H, brs, exchangeable with D_2O, NH), 3.20 (dd, J = 13.3, 6.7 Hz, 2H, H-1), 2.08 (dd, J = 14.4, 7.0 Hz, 2H, H-3), 1.65–1.54 (m, 2H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.50 (C_q, C═O), 137.80 (CH, C-4), 136.75 (C_q, C-1′), 128.62, 128.20 (CH, Ph), 115.34 (CH_2, C-5), 66.73 (CH_2, CH_2Ph), 40.68 (CH_2, C-1), 31.01 (CH_2, C-3), 29.21 (CH_2, C-2). LC-MS: *m*/*z* 220 (70%) $[M + 1]^+$, 176 (39%), 91 (8%), 86 (100%). All analytical data are in perfect accordance with the literature.[31]

Pent-4-enyl-carbamic acid *tert*-butyl ester (6). THF (15.6 mL) and PPh_3 (864 mg, 3.3 mmol, 1.6 eq.) were added to a cold (0 °C) stock solution of 5-azido-pent-1-ene in n-pentane (229 mg, 2.06 mmol). After complete dissolution water was added (148 µL, 8.64 mmol, 4 eq.) and the resulting mixture was stirred at r.t. for 48 h. Then, triethylamine (416 mg, 4.12 mmol, 2 eq.) was added and after 5 min Boc_2O (485 mg, 2.27 mmol, 1.1 eq.) was added all at once while the mixture slightly warmed up. After 6 h stirring at r.t. the mixture was evaporated *in vacuo* and DCM (30 mL) and H_2O (20 mL) were added. The separated water layer was extracted with DCM (20 mL), combined org. extracts were dried over anhydrous $MgSO_4$ and evaporated *in vacuo* to leave a white semi-crystalline oil (1.222 g). Purification by MPLC (SiO_2, 25 × 110 mm, hexanes–Et_2O = 92 : 8 + 2% aq. NH_4OH, 30 mL min^{-1}) yielded pure **6** as a colourless clear oil (230 mg, 82%).

R_f 0.5 (Hexanes–Et_2O = 4 : 1); $C_{10}H_{19}NO_2$ (185.26); ^1H NMR (300 MHz, $CDCl_3$) δ 5.80 (1H, ddt, J = 16.9, 10.2, 6.6 Hz, H-4), 5.14–4.85 (2H, m, H-5), 4.55 (1H, brs, J = 41.0 Hz, exchangeable with D_2O, NH), 3.13 (2H, dd, J = 13.1, 6.5 Hz, H-1), 2.08 (2H, dd, J = 14.4, 7.1 Hz, H-3), 1.65–1.49 (2H, m, H-2), 1.44 (9H, s, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.01 (C_q, C═O) 137.97 (CH, C-4), 115.21 (CH_2, C-5), 79.22 (C_q, **C**$(CH_3)_3$), 40.22 (CH_2, C-1), 31.11 (CH_2, C-4), 29.38 (CH_2, C-2), 28.56 (CH_3, C(**C**$H_3)_3$). LC-MS, *m*/*z* $(M + 1)^+$ 186 (4%), 86 (100%). All analytical data are in perfect accordance with the literature.[32]

***N*-Pent-4-enyl-acetamide (7).** To a cold (0 °C) stock solution of 5-azido-pent-1-ene in n-pentane (166 mg, 1.5 mmol) was added anhydrous Et_2O (10 mL). After 10 min stirring $LiAlH_4$ (85 mg, 2.25 mmol, 1.5 eq.) was carefully added in portions and the resulting grey mixture was stirred at 0 °C over 3 h. Glauber's salt (*ca.* 2 g) was added in small portions with vigorous stirring resulting in intensive foaming. The cooling bath was removed and the suspension was stirred at r.t. overnight. The liquid over the white solid was decanted, the residue was washed with Et_2O (5 mL) and the combined org. phases were dried over the activated molecular sieves. The solution was transferred to the dry flask *via* canula and cooled to −1 °C. Acetic anhydride (459 mg, 4.50 mmol, 3 eq.) was added dropwise and the resulting yellow mixture was stirred at r.t. under Ar overnight. Then, aq. soln. of KOH (1 M, 5 mL) was added at 0 °C and the mixture was stirred for 50 min at r.t. The separated water layer was extracted with AcOEt (2 × 25 mL) and combined org. phases were dried over anhydrous $MgSO_4$. The evaporation *in vacuo* furnished an orange-brown oil (202 mg), which was purified by FLC (6.5 g SiO_2, hexanes–Et_2O = 9 : 1 + 2% aq. NH_4OH) to afford a pure **7** (117 mg, 61%) as a pale orange oil.

R_f 0.35 (Et_2O); $C_7H_{13}NO$ (127.18); ^1H NMR (300 MHz, $CDCl_3$) δ 5.80 (1H, ddt, J = 16.9, 10.2, 6.6 Hz, H-4), 5.72–5.52 (1H, brs, exchangeable with D_2O, NH), 5.03 (2H, dd, J = 24.0, 6.7 Hz, H-5), 3.26 (2H, dd, J = 13.2, 7.0 Hz, H-1), 2.10 (2H, dd, J = 14.6, 6.9 Hz, H-3), 1.97 (3H, s, Me), 1.68–1.53 (2H, m, H-2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.10 (C_q, C═O), 137.73 (CH, C-4), 115.17 (CH_2, C-5), 39.17 (CH_2, C-1), 31.09 (CH_2, C-3), 28.71 (CH_2, C-2), 23.29 (CH_3, Me). LC-MS: *m*/*z* 128 (100%) $[M + 1]^+$, 86 (8%). All analytical data are in perfect accordance with the literature.[25]

1-Amino-pent-4-ene (8). To a cold (−5 °C) stock solution of 5-azido-pent-1-ene (333 mg, 3 mmol) in n-pentane was added anhydrous Et_2O (14 mL). After 10 min stirring $LiAlH_4$ (171 mg, 4.5 mmol, 1.5 eq.) was carefully added in 3 portions under Ar, cooling bath was removed and the resulting suspension was stirred at r.t. over 2 h. Glauber's salt (*ca.* 2 g) was added in small portions to a cold (−3 °C) mixture over 5 min. The cooling bath was removed and the suspension was vigorously stirred at r.t. overnight. The liquid over the white solid was decanted and carefully evaporated *in vacuo* (100 mbar, 0 °C) yielding yellow clear stinking solution containing 1-amino-pent-4-ene **8** (41% yield based on ^{1}H NMR).

R_f 0.17 (DCM–MeOH = 4 : 1); $C_5H_{11}N$ (85.15); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82 (1H, ddt, J = 16.9, 10.1, 6.7 Hz, H-4), 4.99 (2H, ddd, J = 13.7, 11.2, 1.4 Hz, H-5), 2.71 (2H, t, J = 7.1 Hz, H-1), 2.10 (2H, dd, J = 14.4, 7.2 Hz, H-3), 1.54 (2H, dt, J = 14.6, 7.2 Hz, H-2), 1.40 (2H, brs, exchangeable with D_2O, NH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.51 (CH, C-4), 114.84 (CH_2, C-5), 41.72 (CH_2, C-1), 32.80 (CH_2, C-3), 31.25 (CH_2, C-2). LC-MS: m/z 86 (100%) $[M + 1]^+$. All analytical data are in perfect accordance with the literature.[33]

Benzyl-pent-4-enyl-amine (15). To a solution of benzylamine (1607 mg, 15 mmol, 5 eq.) in dry EtOH (7.5 mL) 5-bromo-1-pentene (447 mg, 3 mmol, 1 eq.) and NaI (22.5 mg, 0.15 mmol, 0.05 eq.) were added. The reaction mixture was stirred at 80 °C overnight and the solvent was evaporated. Dichloromethane (20 mL) and 1 N aq. KOH (10 mL) were added and layers were separated. The water phase was extracted with DCM (2 × 10 mL) and combined organic phases were dried over $MgSO_4$, concentrated *in vacuo*, and the resulting yellowish oil (914 mg) was purified by FLC (29 g SiO_2, hexanes–AcOEt = 3 : 1 + 2% aq. NH_4OH) to afford pure **15** (322 mg, 61%) as colorless oil.

R_f 0.37 (Hexanes–AcOEt = 1 : 1 + 2% aq. NH_4OH); $C_{12}H_{17}N$ (175.14); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.20 (5H, m, Ph), 5.83 (1H, ddt, J = 16.9, 10.2, 6.6 Hz, H-4), 5.09–4.91 (2H, m, H-5), 3.80 (2H, s, PhCH_2), 2.71–2.62 (2H, m, H-3), 2.12 (2H, dd, J = 14.7, 6.9 Hz, H-1), 1.63 (2H, dt, J = 14.7, 7.4 Hz, H-2), 1.51 (1H, brs, exchangeable with D_2O, NH). ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.62 (C_q, Ph), 138.74 (CH, C-4), 128.50, 128.22, 127.00 (3 × CH, Ph), 114.75 (CH_2, C-5), 54.17 (CH_2, PhCH_2), 49.04 (CH_2, C-1), 31.69 (CH_2, C-3), 29.39 (CH_2, C-2). LC-MS: m/z 177 (13%), 176 (100%) $[M + 1]^+$. All analytical data are in perfect accordance with the literature.[34]

(*R*)-2-Methyl-*N*-(pent-4-enylidene)propane-2-sulfinamide. To a stirred suspension of PCC (1.207 g, 5.6 mmol, 1.4 eq.) in dry DCM (12 mL) a solution of 1-pentenol (345 mg, 4 mmol, 1 eq.) in dry DCM (8 mL) was added dropwise at 0 °C during 20 min. The reaction mixture was stirred overnight at r.t., filtered through the pad of silica gel (8 × 1 cm), washed with dry DCM (20 mL) and concentrated *in vacuo* to approx. half-volume. To the resulting solution of crude pentenal, $Ti(OEt)_4$ (1.825 g, 8 mmol, 2 eq.) was added and the mixture was stirred until the clear solution was obtained. (*R*)-2-Methylpropane-2-sulfinamide (519 mg, 4.28 mmol, 1.07 eq.) was added in one portion and the reaction was refluxed overnight. After completion, brine was added and mixture was vigorously stirred for 15 min, filtered through short plug of Celite and washed with AcOEt (2 × 30 mL). After the separation of layers, the organic phase was washed with brine, and combined water phases were back-extracted with AcOEt (2 × 30 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The obtained yellow viscous liquid (724 mg) was purified by FLC (24 g SiO_2, hexanes–AcOEt = 5 : 1) affording the desired product as colourless oil (514 mg, 69%).

R_f 0.56 (Hexanes–AcOEt = 3 : 1); $C_9H_{17}NOS$ (187.30); IR (ATR) ν_{max} 3078, 2959, 1621, 1474, 1456, 1415, 1363, 1184, 1084, 992, 913, 792, 678, 581 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (1H, t, J = 4.4 Hz, H-1), 5.85 (1H, ddt, J = 16.7, 10.2, 6.4 Hz, H-4), 5.15–4.99 (2H, m, H-5), 2.64 (2H, td, J = 7.2, 4.5 Hz, H-3), 2.41 (2H, q, J = 6.7 Hz, H-2), 1.20 (9H, s, Me_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.94 (CH, C-1) 136.78 (CH, C-4), 115.96 (CH_2, C-5) 56.69 (C_q, C-*t*Bu), 35.39 (CH_2, C-3), 29.47(CH_2, C-2), 22.47 (CH_3, 3 × Me). $[\alpha]_D^{25}$ = −273.0 (c 1.00, $CHCl_3$), LC-MS: m/z 188 (100%) $[M + 1]^+$, 132 (20%), 122 (26%), 84 (12%). All analytical data are in perfect accordance with the literature.[35]

(*R*)-2-Methyl-propane-2-sulfinic acid pent-4-enylamide (17). $NaBH_4$ (13 mg, 0.35 mmol, 0.5 eq.) at −40 °C was added to a solution of (*R*)-2-methyl-*N*-(pent-4-enylidene)propane-2-sulfinamide (131 mg, 0.7 mmol, 1 eq.) in dry THF (7 mL) in one portion. After stirring for 90 min at this temperature, the solvent was evaporated, and the residue was partitioned between Et_2O (20 mL) and water (15 mL). The water phase was back-extracted with Et_2O (2 × 15 mL), combined organic extracts were dried over $MgSO_4$ and solvent evaporated *in vacuo*. The resulting oil (120 mg) was purified by FLC (4 g SiO_2, hexanes–AcOEt = 3 : 2) affording pure **17** as colourless oil (83 mg, 63%).

R_f 0.18 (Hexanes–AcOEt = 2 : 1 + 2% aq. NH_4OH); $C_9H_{19}NOS$ (189.32); IR (ATR) ν_{max} 3419, 3205, 3076, 2925, 1641, 1473, 1456, 1363, 1178, 1048, 993, 909, 796, 599, 505 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80 (1H, ddt, J = 16.9, 10.2, 6.7 Hz, H-4), 5.03 (2H, ddd, J = 11.8, 6.7, 1.6 Hz, H-5), 3.29–3.04 (3H, m, H-1 + NH), 2.13 (2H, dd, J = 14.4, 6.8 Hz, H-3), 1.67 (2H, p, J = 7.1 Hz, H-2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.84 (CH, C-4), 115.38 (CH_2, C-5), 55.65 (C_q, C-*t*Bu), 45.22 (CH_2, C-1), 30.99, 30.21 (2 × CH_2, C-2, C-3), 22.71 (CH_3, 3 × Me). $[\alpha]_D^{25}$ = −69.1 (c 1.00, $CHCl_3$), LC-MS: m/z 379 (59%) $[2M + 1]^+$, 190 (100%) $[M + 1]^+$, 116 (15%), 86 (7%). All analytical data are in perfect accordance with the literature.[36]

(*Z*)-*N*-Boc-*N*-hex-4-enyl-4′-methyl-benzenesulfonamide. DIAD (356 mg, 1.76 mmol, 1.1 eq.) was added dropwise to a cold (0 °C) solution of (*Z*)-hex-4-ene-1-ol (160 mg, 1.6 mmol), BocNHTs (434 mg, 1.6 mmol, 1 eq.), PPh_3 (461 mg, 1.76 mmol, 1.1 eq.) in anhydrous THF (10 mL). The slightly yellow clear reaction mixture was stirred at r.t. for 9 days. The evaporation *in vacuo* (100 mbar) provided a thick oil, which was dissolved in DCM (20 mL) and washed with H_2O (10 mL). The water layer was extracted with DCM (2 × 10 mL) and combined org. phases were dried over anhydrous $MgSO_4$. The evaporation *in vacuo* furnished a viscous slightly yellow clear oil (1.619 g), which was purified by MPLC (SiO_2, 25 × 100 mm, hexanes–Et_2O = 3 : 1, 30 mL min^{-1}) yielding colourless clear viscous oil (485 mg, 85%).

R_f 0.55 (Hexanes–Et_2O = 7 : 3); $C_{18}H_{27}NO_4S$ (353.48); IR (film on KBr) ν_{max} 3011, 2980, 2935, 1728, 1657, 1456, 1356, 1158, 722, 675 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.78 (2H, d, J = 8.3 Hz, H-2′), 7.30 (2H, d, J = 8.4 Hz, H-3′), 5.60–5.34 (2H, m, H-4, H-5), 3.85–3.77 (2H, m, H-1), 2.44 (3H, s, H-5′), 2.11 (2H, dd, J = 14.5, 7.3 Hz, H-3), 1.88–1.76 (2H, m, H-2), 1.64–1.56 (3H, m, H-1), 1.33 (9H, s, ^{t}Bu); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.10 (C_q, C=O), 144.15 (C_q, C-4′), 137.66 (C_q, C-1′), 129.36 (CH, C-3′), 129.31 (CH, C-4), 127.93 (CH, C-2′), 124.92 (CH, C-5), 84.20 (C_q, $C(CH_3)_3$), 46.98 (CH_2, C-1), 30.05 (CH_2, C-3), 28.02 (CH_3, ^{t}Bu), 24.25 (CH_2, C-2), 21.76 (CH_3, C-5′), 12.96 (CH_3, C-6); LC-MS: m/z 354 (11%) $[M + 1]^+$, 242 (100%), 199 (10%), 102 (20%), 100 (18%).

(*E*)-*N*-Hex-4-enyl-4′-methyl-benzenesulfonamide (18). TFA (1.482 g, 13 mmol, 10 eq.) was added dropwise to a cold (0 °C) solution of (*Z*)-*N*-Boc-*N*-hex-4′-enyl-4-methyl-benzenesulfonamide (459 mg, 1.3 mmol) in anhydrous DCM (6.5 mL) and the reaction mixture was stirred at this temperature for 20 h. DCM (10 mL) was added followed by addition of aq. sol. Na_2CO_3 (2 M, 30 mL) and the biphasic system was stirred for 1 h. The separated water layer was extracted with DCM (2 × 15 mL) and the combined org. phases were dried over anhydrous $MgSO_4$. Evaporation *in vacuo* provided a clear yellow oil (333 mg), which was purified by FLC (10 g SiO_2, hexanes–Et_2O = 4 : 1 + 2% aq. NH_4OH) yielding pure **15** as a colourless viscous oil (293 mg, 88%).

R_f 0.2 (Hexanes–Et_2O = 3 : 1); $C_{13}H_{19}NO_2S$ (253.36); ^1H NMR (300 MHz, $CDCl_3$) δ 7.75 (2H, d, J = 8.3 Hz, H-2′), 7.31 (2H, d, J = 8.0 Hz, H-3′), 5.56–5.37 (1H, m, H-5), 5.35–5.19 (1H, m, H-4), 4.46 (1H, brs, exchangeable with D_2O, NH), 2.95 (2H, dd, J = 13.4, 6.9 Hz, H-1), 2.43 (3H, s, Ph-CH_3), 2.03 (2H, q, J = 7.3 Hz, H-3), 1.55 (5H, m, H-2, H-6). ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.49 (C_q, C-4′), 137.13 (C_q, C-1′), 129.82 (CH, C-3′), 128.99 (CH, C-4), 127.23 (CH, C-2′), 125.32 (CH, C-5), 43.05 (CH_2, C-1), 29.47 (CH_2, C-3), 24.06 (CH_2, C-2), 21.66 (CH_3, Ph-CH_3), 12.89 (CH_3, C-6). LC-MS: m/z 254 (65%) $[M + 1]^+$, 100 (9%), 94 (100%). All analytical data are in perfect accordance with the literature.[37]

(*Z*)-*N*-Boc-*N*-hex-3-enyl-4′-methyl-benzenesulfonamide. DIAD (356 mg, 1.76 mmol, 1.1 eq.) was added dropwise to a cold (0 °C) solution of (*Z*)-hex-3-ene-1-ol (160 mg, 1.6 mmol), BocNHTs (434 mg, 1.6 mmol, 1 eq.), PPh_3 (461 mg, 1.76 mmol, 1.1 eq.) in anhydrous THF (10 mL). The slightly yellow clear reaction mixture was stirred at r.t. for 9 d. The evaporation *in vacuo* (100 mbar) provided a thick oil, which was dissolved in DCM (20 mL) and washed with H_2O (10 mL). The water layer was extracted with DCM (2 × 10 mL) and combined org. phases were dried over anhydrous $MgSO_4$. The evaporation *in vacuo* furnished a slightly yellow clear oil (1.45 g), which solidified upon standing at r.t. The purification by MPLC (SiO_2, 25 × 100 mm, hexanes–Et_2O = 4 : 1, 30 mL min^{-1}) furnished colourless clear viscous oil (450 mg, 79%).

R_f 0.55 (Hexanes–Et_2O = 7 : 3); $C_{18}H_{27}NO_4S$ (353.48); ^1H NMR (300 MHz, $CDCl_3$) δ 7.79 (2H, d, J = 8.3 Hz, H-3′), 7.30 (2H, d, J = 8.1 Hz, H-4′), 5.52 (1H, dt, J = 10.7, 7.2 Hz, H-3), 5.35 (1H, dt, J = 9.0, 7.5 Hz, H-4), 3.89–3.73 (2H, m, H-1), 2.50 (2H, dd, J = 15.3, 7.7 Hz, H-2), 2.44 (3H, s, H-5′), 2.18–2.00 (2H, m, H-5), 1.35 (9H, s, J = 6.8 Hz, $C(CH_3)_3$), 0.97 (3H, t, J = 7.5 Hz, H-6); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.08 (C_q, C=O), 144.15 (C_q, C-4′), 137.66 (C_q, C-1′), 134.99 (CH, C-4), 129.34 (CH, C-3′), 127.98 (CH, C-2′), 124.20 (CH, C-3), 84.19 (C_q, $C(CH_3)_3$), 46.75 (CH_2, C-1), 28.32 (CH_2, C-2), 28.03 (CH_3, $C(CH_3)_3$), 21.76 (CH, C-5′), 20.75 (CH_2, C-5), 14.47 (CH_3, C-6). LC-MS: m/z 254 (42%), 94 (100%), 100 (9%), 172 (3%). All analytical data are in perfect accordance with the literature.[27]

(*Z*)-*N*-Hex-3-enyl-4′-methyl-benzenesulfonamide (19). TFA (1.368 g, 12 mmol, 10 eq.) was added dropwise to a cold (−1 °C) solution of (*Z*)-*N*-Boc-*N*-hex-4-enyl-4′-methyl-benzenesulfonamide (423 mg, 1.2 mmol) in anhydrous DCM (6 mL) and the reaction mixture was stirred at this temperature for 20 h. DCM (10 mL) was added followed by addition of aq. sol. Na_2CO_3 (2M, 30 mL) and the biphasic system was stirred for 1 h. The separated water layer was extracted with DCM (2 × 15 mL) and the combined org. phases were dried over anhydrous MgSO4. Evaporation *in vacuo* provided a clear yellow oil (303 mg), which was purified by FLC (9 g SiO_2, hexanes–Et_2O = 3 : 1 + 2% aq. NH_4OH) yielding pure **15** as a colourless viscous oil (282 mg, 92%).

R_f 0.15 (Hexanes–Et_2O = 3 : 1); $C_{13}H_{19}NO_2S$ (253.37); ^1H NMR (300 MHz, $CDCl_3$) δ 7.74 (2H, d, J = 8.3 Hz, H-3′), 7.31 (2H, d, J = 8.0 Hz, H-4′), 5.60–5.38 (1H, m, H-3), 5.20–5.04 (1H, m, H-4), 4.43 (1H, brs, exchangeable with D_2O, NH), 2.97 (2H, q, J = 6.7 Hz, H-1), 2.43 (3H, s, H-5′), 2.20 (2H, q, J = 6.8 Hz, H-2), 2.04–1.90 (2H, m, H-5), 0.93 (3H, t, J = 7.5 Hz, H-6); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.52 (C_q, C-4′), 137.10 (C_q, C-1′), 135.68 (CH, C-4), 129.82 (CH, C-2′), 127.25 (CH, C-3′), 124.10 (CH, C-3), 42.91 (CH_2, C-1), 27.44 (CH_2, C-2), 21.65 (CH_3, C-4′), 20.74 (CH_2, C-5), 14.33 (CH_3, C-6); LC-MS: m/z 254 (47%) $[M + 1]^+$, 108 (16%), 102 (18%), 100 (3%), 94 (100%). All analytical data are in perfect accordance with the literature.[27]

Representative procedure for the bismuth triflate-catalysed hydroamination

A solution of 4-methyl-*N*-pent-4-enyl-benzenesulfonamide **1** (107 mg, 0.45 mmol) and $Bi(OTf)_3{\cdot}nH_2O$ (59 mg, 0.09 mmol, 0.2 eq.) in anhydrous 1,2-dichloroethane (1.35 mL) was stirred in a closed pressure tube at 40 °C for 3 days under argon. Water (15 mL) was added and the mixture was extracted with Et_2O (15 mL containing 15 drops of 23% aq. NH_4OH). The layers were separated and the water phase was back-extracted with Et_2O (2 × 15 mL). Combined org. extracts were dried over anhydrous $MgSO_4$ and evaporated *in vacuo* to leave a yellow-brown oil (106 mg). Purification by FLC (3.5 g SiO_2, hexanes–Et_2O = 3 : 1 + 2% aq. NH_4OH) afforded pure *N*-tosyl-2-methylpyrrolidine **2** (98 mg, 91%) as a colourless oil that solidified upon standing at r.t.

***N*-(Toluene-4-sulfonyl)-2-methyl-pyrrolidine (2).** mp 91–93 °C; R_f 0.47 (Hexanes–Et_2O = 1 : 1); $C_{12}H_{17}NO_2S$ (239.33); ^1H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, J = 8.2 Hz, 2H, 2 × CH–Ph), 7.31 (d, J = 8.1 Hz, 2H, 2 × CH–Ph), 3.77–3.64 (m, 1H, H-2), 3.43 (ddd, J = 10.0, 6.8, 4.8 Hz, 1H, H_a-5), 3.15 (dt, J =

10.2, 7.1 Hz, 1H, H_b-5), 2.43 (s, 3H, Ph–CH_3), 1.92–1.42 (m, 4H, H-3, H-4), 1.31 (d, J = 6.4 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.3 (C_q, C-4′), 135.1 (C_q, C-1′), 129.7 (CH, C-3′), 127.6 (CH, C-2′), 56.2 (CH, C-2), 49.2 (CH_2, C-5), 33.6 (CH_2, C-3), 24.0 (CH_2, C-4), 23.0, (CH_3, C(2)-CH_3), 21.6 (CH_3, Ph–CH_3). LC-MS: m/z = 240 (100%) $[M + 1]^+$.

***N*-Methanesulfonyl-2-methylpyrrolidine (9).** R_f 0.3 (Hexanes–Et_2O = 1 : 4); $C_6H_{13}NO_2S$ (163.24); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.91–3.71 (H, m, H-2), 3.43 (1H, ddd, J = 10.2, 6.7, 5.5 Hz, H-5), 3.30 (1H, dt, J = 14.8, 5.9 Hz, H-5), 2.82 (3H, s, Ms), 2.14–1.59 (4H, m, H-3, H-4), 1.29 (3H, d, J = 6.3 Hz, Me). ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.18 (CH, C-2), 48.90 (CH_2,C-5), 35.64 (CH_3, Ms), 33.89 (CH_2, C-3), 24.45 (CH_2, C-4), 22.61 (CH_3, Me). LC-MS, m/z 164 (100%) $[M + 1]^+$, 186 (22%), 86 (2%). All analytical data are in perfect accordance with the literature.[38]

***N*-Trifluoromethanesulfonyl-2-methylpyrrolidine (10).** R_f 0.68 (Hexanes–Et_2O = 2 : 3); $C_6H_{10}F_3NO_2S$ (217.21); IR (film on KBr) ν_{max} = 3188, 2961, 2931, 2875, 1720, 1649, 1599, 1453, 1383, 1228, 1189, 1150, 1078, 1031, 814, 768, 606, 582 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.14 (1H, dd, J = 10.8, 6.4 Hz, H-2), 3.66–3.46 (2H, m, H-5), 2.22–1.88 (3H, m, H-3, H-4a), 1.70 (1H, tdd, J = 9.6, 5.8, 4.1 Hz, H-4b), 1.32 (3H, d, J = 6.4 Hz, Me); ^{13}C NMR (75 MHz, $CDCl_3$) δ 120.49 (C_q, J = 324.7 Hz, CF_3), 58.03 (CH, C-2), 49.43 (CH_2, C-5), 33.87 (CH_2, C-3), 24.40 (CH_2, C-4), 21.98 (CH_3, Me). LC-MS: m/z 218 (48%) $[M + 1]^+$, 102 (100%).

***N*,*N*′-Dibenzyl-*N*,*N*′-di-pent-4-enyl-ethane-1,2-diamine (16).** R_f 0.65 (Hexanes–AcOEt = 2 : 1 + 2% aq. NH_4OH); $C_{26}H_{36}N_2$ (376.58); IR (ATR) ν_{max} = 3062, 3026, 2929, 2794, 1639, 1495, 1452, 1367, 1028, 908, 732, 697 cm^{-1}; ^{1}H NMR (300 MHz, CDCl3) δ 7.34–7.16 (10H, m, 2 × Ph), 5.75 (2H, ddt, J = 16.9, 10.2, 6.6 Hz, H-4, H-4′), 5.03–4.85 (4H, m, H-5, H-5′), 3.53 (4H, s, 2 × PhCH_2), 2.54 (4H, s, NCH_2CH_2N), 2.45–2.35 (4H, m, H-1, H-1′), 2.00 (4H, dd, J = 14.7, 6.9 Hz, H-3, H-3′), 1.51 (4H, dt, J = 14.7, 7.4 Hz, H-2, H-2′). ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.99 (C_q, Ph) 138.88 (CH, C-4), 128.96, 128.23, 126.86, (3 × CH, Ph) 114.54 (CH_2, C-5), 59.18 (CH_2, PhCH_2), 53.96 (CH_2, C-1), 51.88 (CH_2, NCH_2CH_2N) 31.65 (CH_2, C-3), 26.53 (CH_2, C-2). LC-MS: m/z 378, (23%), 377 (100%) $[M + 1]^+$, 287 (8%).

Detosylation[39] of (2) and subsequent acetylation of (21)

***N*-Acetyl-2-methylpyrrolidine (22).** $LiAlH_4$ (46 mg, 1.2 mmol, 3 eq.) was added to a cold (−3 °C) solution of **2** (96 mg, 0.4 mmol) in anhydrous Et_2O (4 mL) in 2 portions under Ar, the cooling bath was removed and the resulting suspension was stirred at r.t. overnight. Glauber's salt (*ca.* 300 mg) was added in small portions to a cold (0 °C) mixture over 5 min. The cooling bath was removed and the suspension was vigorously stirred at r. t. for 24 h. The liquid over the white solid was transferred *via* canula to the dry flask containing activated 4 Å MS under Ar and stirred for 30 min. The solids were left to settle down, the liquid was transferred *via* canula to the dry flask, cooled to 0 °C and Et_3N (57 mg, 0.563 mmol, 1.4 eq.) was added followed by the dropwise addition of Ac_2O (53 mg, 0.52 mmol, 1.3 eq.). The cooling bath was removed and the reaction mixture was stirred at r.t. for 20 h. Water (10 mL) and Et_2O (5 mL) were added and the biphasic solution was stirred for 30 min at r.t. The layers were separated and the water phase was back-extracted with DCM (3 × 10 mL). Combined org. extracts were dried over anhydrous $MgSO_4$ and evaporated *in vacuo* to leave an yellow oil (57 mg) which was filtered through short pad of silica gel (300 mg, Et_2O) leaving pure **22** as a colourless oil (40 mg, 79%).

R_f 0.2 (Et_2O); $C_7H_{13}NO$ (127.19); ^{1}H NMR (300 MHz, $CDCl_3$) (2 rotamers) δ 4.26–4.12 (m) and 3.97 (dt, J = 12.7, 6.4 Hz) (1H sum, H-2), 3.48 (dd, J = 8.5, 5.9 Hz) and 3.38 (dt, J = 11.6, 8.5 Hz) (2H sum, H-5), 2.09 (s) and 2.03 (s) (3H sum, C(═O)Me), 2.01–1.80 (3H, m) and 1.76–1.55 (1H, m) (4H sum, H-3, H-4), 1.19 (3H, dd, J = 6.4, 1.9 Hz, H-1′). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.03 (C_q, C═O), 53.97, 52.66, (CH, C-1), 47.71, 45.52 (CH_2, C-5), 33.29, 32.11 (CH_2, C-2), 23.93, 22.16 (CH_2, C-4) 23.02, 22.04, 21.07, 19.60 (4 × CH_3, 2 × C-1′, 2 × C(═O)CH_3); LC-MS: m/z 128 (100%) $[M + 1]^+$, 129 (8%), 255 (29%). All analytical data are in perfect accordance with the literature.[40]

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