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Development of a [3+3] approach to tetrahydropyridines and its application in indolizidine alkaloid synthesis

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Abstract

A stepwise [3+3] annelation sequence is described that generates tetrahydropyridines from the corresponding aziridines. The scope of this process is described and its potential for the stereoselective synthesis of indolizidines is highlighted by the synthesis of (−)-monomorine.

1. Introduction

Aziridines are extremely useful building blocks in organic synthesis because of their ability to function as reactive electrophilic substrates.[1] Recent work in our laboratory[2,7] has focused on the exploitation of aziridines in [3+3] annelation processes for the stereoselective synthesis of piperidines[3,4] by the addition of a suitable conjunctive reagent. Specifically, we have shown that trimethylenemethane (TMM; **1**) equivalents **2** and **3** can serve as useful reagents for the synthesis of piperidines bearing an exomethylene motif. In an effort of expanding the scope of the [3+3] annelation manifold, we have been investigating alternative conjunctive reagents with a view to prepare piperidines with the potential for alternative modes of functionalisation. Indeed, we anticipated that synthon **4** would allow us to generate tetrahydropyridines by a manner akin to the sulfone based three-carbon homologating reagent **5** developed by Craig and co-workers.[5] Our preliminary studies demonstrated that the Büchi Grignard reagent **6**[6] served as a suitable reagent for this purpose,[7] we report herein a full account of the development of this [3+3] methodology and the exemplification of its employment in the stereoselective preparation of indolizidines by the total synthesis of (−)-monomorine (Fig. 1).

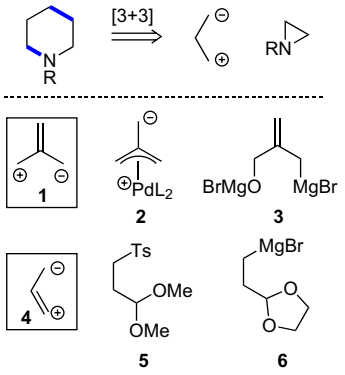

Figure 1. A [3+3] annelation strategy to piperidines.

2. Results and discussion

Previous studies on annelation reactions of aziridines highlighted that *N*-tosyl 2-alkylaziridines were generally most reactive towards TMM-based conjunctive reagents and we therefore began our investigations with these substrates. With regard to the Grignard reagent, Büchi had reported that **6** decomposes at temperatures above 35 °C,[6,8] in contrast, however, 1,3-dioxane reagent **7**[9] has been reported to be more thermally stable. We therefore set out to compare the efficiency of the tetrahydropyridine forming reaction with each of these reagents and our results are shown in Scheme 1.

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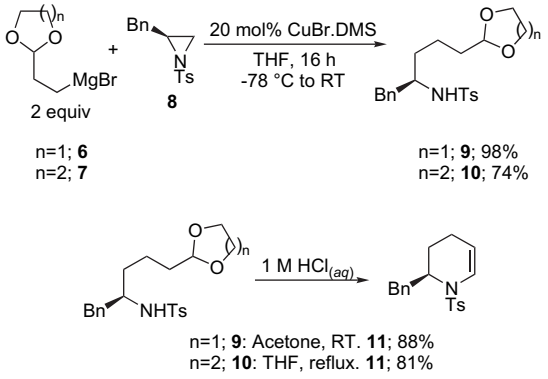
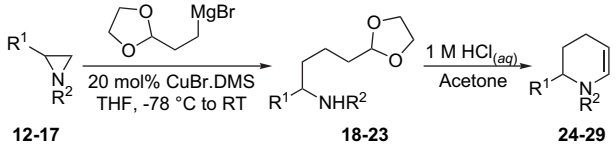


Scheme 1. Addition of functionalised Grignard reagents to aziridines.

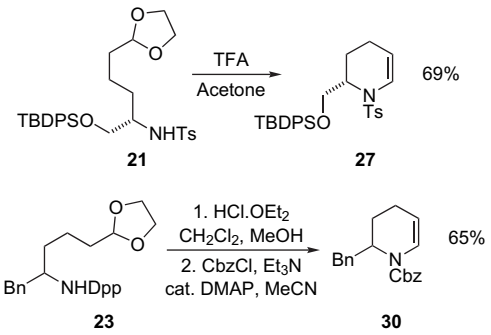
Addition of 2 equiv of reagents **6** and **7** to aziridine **8** resulted in formation of the corresponding adducts in good to excellent yield. In addition, acid catalysed cyclisation took place in good yield in both cases to provide the desired tetrahydropyridine **11**. Whilst these studies highlighted that both Grignard reagents were suitable for the formation of tetrahydropyridines, the higher yields observed when using **6** coupled with the milder cyclisation conditions required in the case of **9** prompted us to continue our investigations with 1,3-dioxolane **6**. Accordingly, the scope of the stepwise annelation with regard to 2-alkylaziridines is highlighted in Table 1. We found that Ts-protected substrates bearing simple alkyl substituents underwent smooth addition and cyclisation reactions to deliver the corresponding heterocycles in good yield (entries 1 and 2). Bn-protected alcohol **14** also efficiently delivered the corresponding tetrahydropyridine **26**, in contrast, however, silyl protected analogue **15** underwent high yielding addition to **6** but the subsequent cyclisation proceeded in low yield (entries 3 and 4). We undertook a brief study of alternative *N*-protecting groups and found the SES-group to be compatible with this process (entry 5), unfortunately, however, the Dpp-protected substrate **17** was incompatible with the cyclisation conditions albeit after a very high yielding reaction with Grignard **6**.

Table 1
[3+3] Annelation reactions



Entry	R^1	R^2		Addition product (%)	Piperidine (%)
1	(*S*)-Me	Ts	**12**	**18** (70)	**24** (84)
2	^{i}Pr	Ts	**13**	**19** (82)	**25** (98)
3	CH_2OBn	Ts	**14**	**20** (87)	**26** (73)
4	(*S*)-$CH_2OTBDPS$	Ts	**15**	**21** (87)	**27** (8)
5	(*S*)-Me	SES	**16**	**22** (88)	**28** (62)
6	Bn	Dpp	**17**	**23** (94)	**29** (0)

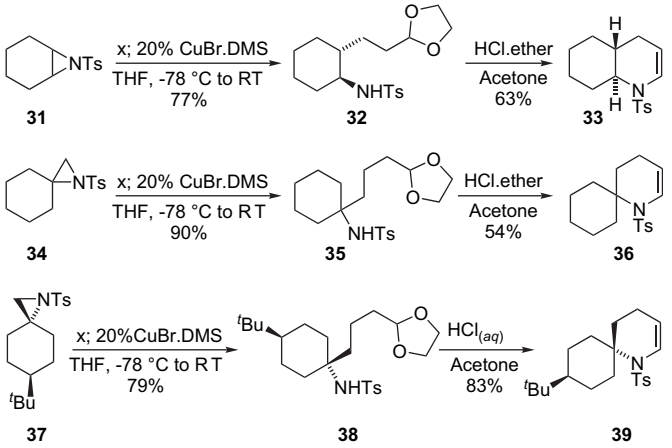
The studies outlined in Table 1 highlighted that the Cu-catalysed Grignard addition chemistry showed good generality but that limitations could arise during the cyclisation step when acid labile groups were introduced (silyl ether and *N*-Dpp, entries 4 and 6, respectively). We decided to exploit these specific substrates to develop some alternative cyclisation protocols that would allow such functional groups to be included in this annelation process, our results are outlined in Scheme 2. In the case of silyl ether **21**, simply switching from HCl $_{(aq)}$ to TFA allowed us to isolate the desired heterocycle **27** in significantly improved yield. Carrying out similar Brønsted acid screening in the case of **23** failed to uncover conditions for cyclisation without cleavage of the Dpp-group. We therefore endeavoured to carry out a tandem deprotection of the acetal and Dpp-groups. We hoped that these conditions would also promote cyclisation such that the enamine could be N-protected with Cbz. In the event, we were able to telescope this process and deliver **30** in good yield over two steps.



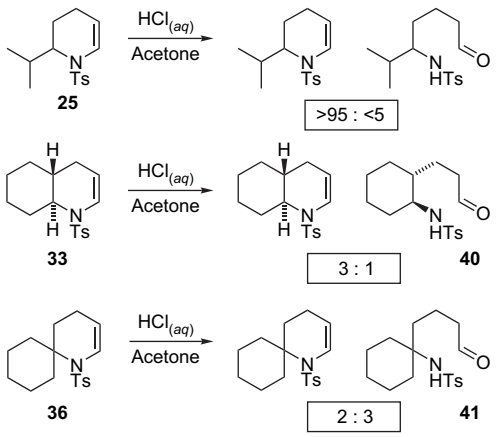
Scheme 2. Alternative cyclisation conditions.

We next turned our attention to the [3+3] annelation of bicyclic and spirocyclic aziridines in an effort to obtain more heavily substituted piperidine derivatives, our results are shown in Scheme 3. Once again, we found that the Cu-catalysed alkylation step proceeded in high yield in all cases, but we were disappointed to find that the cyclisation step provided only modest yields of tetrahydropyridines **33** and **36**.

During these studies we noted that spiropiperidine **39** crystallised from solution during cyclisation and that this product was generated in excellent yield. This observation prompted us to speculate that enamide formation could be taking place



Scheme 3. Synthesis of bicycles and spirocycles.



Scheme 4. Tetrahydropyridine stability.

reversibly in solution in these cases. In order to probe this possibility, we subjected tetrahydropyridines **25**, **33** and **36** to 1 M $HCl_{(aq)}$ and examined the crude reaction mixtures by ^1H NMR spectroscopy. The 6-alkyl substituted heterocycle **25** was found to be stable towards hydrolysis, even after prolonged reaction times (up to 28 h). In contrast, however, bicycle **33** and spirocycle **36** were both found to readily hydrolyse to the corresponding aldehydes **40**[10] and **41** (Scheme 4).

The stark difference in hydrolytic stability of tetrahydropyridines **25**, **33** and **36** can be rationalised based on relative allylic strain present in each case.[11] As outlined in Figure 2, piperidine **25** can adopt a conformation whereby the alkyl substituent is orientated in a *pseudo*-axial position to avoid a steric interaction with the S–O moiety.[5a] In contrast, both the bicycle **33** and spirocycle **36** require *pseudo*-equatorial alkyl substituents and therefore the $A^{1,3}$ clash cannot be avoided in either case.

In order to gather some evidence for this proposal we decided to obtain solid state structures of these compounds. In the event, compounds **25** and **39** provided suitable crystals for X-ray crystallographic analysis and these are outlined in Figure 3. The ^{i}Pr-substituted piperidine derivative **25** displayed a *pseudo*-axial alkyl group and showed the expected sulfonamide conformation whereby the nitrogen-lone pair adopts a *gauche* orientation with respect to the O–S–O unit.[12] Moreover, the N-atom showed a reasonable degree of pyramidalisation, the sum of internal bond angles were found to be 352.8°. In contrast, the sulfonamide conformation present in the spiropiperidine **39** was found to deviate from the expected antiperiplanar arrangement (with respect to the *N*-lone pair and S–C bond) such that one S–O bond eclipses a N–C bond. This conformation presumably minimises unfavourable $A^{1,3}$ interactions outlined in Figure 2. Moreover, the length of the C–N bond bearing the spiro substituted ring is longer than that bearing the ^{i}Pr-moiety (cf. N(1)–C(1) in **39**

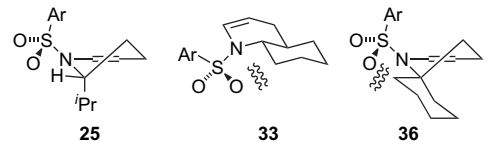


Figure 2. Proposed origin of hydrolytic stability.

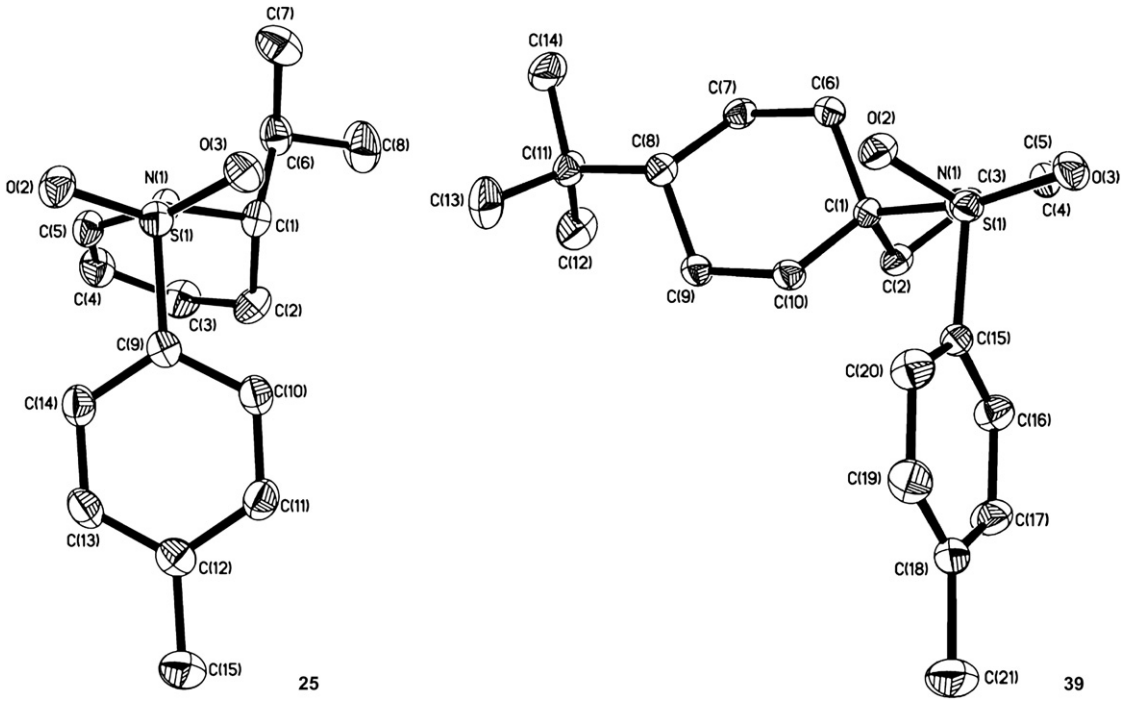
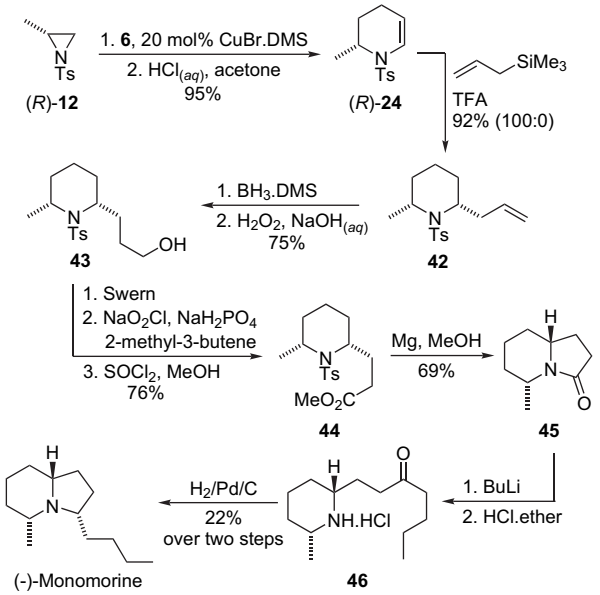


Figure 3. ORTEP diagrams of **25** and **39**; selected bond distances [Å] and angles [°]. Compound **25**: S(1)–O(2) 1.4317 (12), S(1)–O(3) 1.4349 (12), S(1)–C(9) 1.7616 (16), S(1)–N(1) 1.6451 (13), N(1)–C(5) 1.4225 (19), N(1)–C(1) 1.4879 (19), C(5)–C(4) 1.323 (2); O(2)–S(1)–O(3) 120.36 (7), N(1)–S(1)–C(9) 106.22 (7), C(1)–N(1)–S(1) 118.84 (10), C(5)–N(1)–S(1) 117.41 (11), C(1)–N(1)–C(5) 116.58 (12). Compound **39**: S(1)–O(2) 1.4373 (13), S(1)–O(3) 1.4377 (13), S(1)–C(15) 1.7685 (18), S(1)–N(1) 1.6353 (15), N(1)–C(5) 1.422 (2), N(1)–C(1) 1.516 (2), C(5)–C(4) 1.323 (3); O(2)–S(1)–O(3) 117.77 (8), N(1)–S(1)–C(15) 106.02 (8), C(1)–N(1)–S(1) 124.23 (12), C(5)–N(1)–S(1) 117.69 (13), C(1)–N(1)–C(5) 117.32 (14).

vs **25**). Finally, the N-atom is unusually planar[13] in this case, the sum of the internal bond angles were found to be 358.8°.

Having established the scope of the [3+3] annelation process, we decided to employ this methodology in the synthesis of indolizidine alkaloids. Specifically, we opted to prepare (−)-monomorine, the unnatural antipode of (+)-monomorine, the trail-laying pheromone of the ant, *Monomorium pharaonis* L. that has also been found recently in amphibian skin extracts.[14] Our synthetic route is outlined in Scheme 5.



Scheme 5. Synthesis of (−)-monomorine.

We began by performing the [3+3] annelation sequence on aziridine (*R*)-**12**. This process was conveniently carried out on multigram scale without purification of the intermediate Grignard adduct to provide the piperidine (*R*)-**24** in high yield over the two steps. Acid catalysed allylation at C-2 took place in excellent yield and diastereoselectivity to furnish *cis*-**42**, which was subjected to hydroboration to provide alcohol **43**. Previous work within our group had shown that indolizidinones could be prepared by a one-pot Ts-deprotection cyclisation sequence on to an appended ester,[15] hence we decided to explore this strategy. Accordingly, sequential oxidation and esterification of **43** proceeded uneventfully. Pleasingly, treatment of **44** with Mg/MeOH provided lactam **45** in 69% yield (83% based on recovered starting material). Lactam **45** had previously been converted to monomorine by Shono and co-workers by addition of BuLi, followed by $NaBH_4$ reduction, but with poor diastereocontrol.[16] In an effort to improve on this, we isolated **46** after BuLi addition and subjected this to the more selective (>95:5)[17] hydrogenation to furnish (−)-monomorine in 22% yield over two steps.

3. Conclusion

We report a two step annelation process that delivers functionalised piperidine derivatives from readily available aziridines. These compounds can be further elaborated towards indolizidine derivatives with excellent levels of diastereocontrol. The potential exploitation of this methodology in the preparation of alkaloids has been highlighted by a short stereocontrolled synthesis of (−)-monomorine.

4. Experimental

4.1. General

Aziridines **12**–**17**, **31**, **34**, **37** were prepared according to reported procedures.[2e,5a] Reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of dry nitrogen. Flash chromatography was performed on silica gel (BDH Silica Gel 60 43–60, or Fluorochem Davisil silica gel 43–60). Thin layer chromatography (TLC) was performed on aluminium backed plates pre-coated with silica (0.2 mm, Merck DC-alufolien Kieselgel 60 F254) and were developed using standard visualising agents: ultraviolet light or potassium permanganate. $^1H/^{13}C$ NMR spectra were recorded on Bruker AC-250 or Av1-250 instrument or AMX-400 or AV1-400 instrument. ^1H NMR: chemical shifts are reported in parts per million with the solvent resonance as the internal standard ($CHCl_3$: δ 7.27 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, br=broad, m=multiplet), coupling constants (J) in hertz, and assignment. ^{13}C NMR spectra were recorded with complete proton decoupling. Chemical shifts are reported in parts per million with the solvent resonance as the internal standard ($CDCl_3$: δ 77.0 ppm). Infrared (FTIR) spectra were recorded on a Perkin–Elmer Paragon 100 FTIR spectrophotometer, ν_{max} in cm^{-1}. Low resolution mass spectra were recorded on Micromass Autospec, operating in E.I., C.I. or FAB mode; or a Perkin–Elmer Turbomass Benchtop GC–MS operating in either EI or CI mode. High-resolution mass spectra (HRMS) recorded for accurate mass analysis, were performed on either a MicroMass LCT operating in Electrospray mode (TOF ES^+) or a MicroMass Prospec operating in either FAB (FAB^+), EI (EI^+) or CI (CI^+) mode. Elemental microanalysis were performed using a Perkin–Elmer 2400 CHNS/O Series II Elemental Analyser. Melting points were performed on recrystallised solids and recorded on a Gallenkamp melting point apparatus and are uncorrected. All solvents and reagents were purified using standard laboratory techniques according to methods published in Ref. 18 .

4.1.1. Preparation of the Büchi Grignard reagent (*6*)

To a 50 mL two-necked flask fitted with a reflux condenser were added magnesium turnings (484 mg, 17.25 mmol, 1.7 equiv) and THF (10 mL), then 2-(2-bromoethyl)-[1,3]dioxolane (1.2 mL, 10.2 mmol, 1 equiv) was added slowly. The solution was allowed to cool to room temperature and the concentration of the Büchi Grignard solution assessed by titration.[19]

4.1.2. Preparation of the Grignard reagent (*7*)

To a 10 mL two-necked flask fitted with a reflux condenser were added magnesium turnings (212 mg, 8.82 mmol, 2 equiv) and THF (4.5 mL), then 2-(2-bromoethyl)-[1,3]dioxane (0.6 mL, 4.41 mmol, 1 equiv) was added. The solution was

heated gently until reflux then the mixture was allowed to cool to room temperature and the concentration of the Grignard solution assessed by titration.[19]

4.2. General procedure for the synthesis of acetal adducts

A solution of CuBr·DMS (0.4 equiv) in DMS was added to an aliquot of Grignard solution (0.3–0.4 M, 2 equiv) at −78 °C and stirred for 1 h. Then a solution of aziridine (1 equiv) in THF was added at −78 °C and the reaction mixture stirred for 10 min. The solution was allowed to warm to room temperature overnight. The reaction was quenched with water and the organic layer was separated. The aqueous layer was re-extracted with EtOAc, the organic layers were combined and washed with brine. The solution was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography.

4.2.1. (R)-N-(1-Benzyl-4-[1,3]dioxolan-2-yl-butyl)-4-methyl-benzenesulfonamide (**9**)

Following the general procedure, a solution of CuBr·DMS (93 mg, 0.45 mmol, 0.4 equiv) in DMS (1 mL) was added to the Büchi Grignard (**6**) solution (1.8 mL, 0.4 M, 0.72 mmol, 2 equiv), followed by (**8**) (103 mg, 0.36 mmol, 1 equiv) in THF (1 mL). Purification by column chromatography (using a continuous gradient from petroleum ether and ending with 5:1 petroleum ether/EtOAc) yielded (**9**) as a colourless solid, 138 mg, 98%. Mp 115–116 °C; $[\alpha]_D^{25}$ −13 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): *δ* 1.13–1.51 (6H, m, $CH_2CH_2CH_2$), 2.33 (3H, s, Ar–CH_3), 2.59 (2H, d, *J*=6.5 Hz, Ar–CH_2), 3.25–3.45 (1H, m, NHC*H*), 3.67–3.89 (4H, m, OCH_2CH_2O), 4.51 (1H, d, *J*=8.0 Hz, N*H*), 4.64 (1H, t, *J*=4.5 Hz, OC*H*CH_2), 6.87–6.98 (2H, m, Ar–*H*), 7.06–7.21 (5H, m, Ar–*H*), 7.57 (2H, d, *J*=8.0 Hz, Ar–*H*); ^{13}C NMR (62.9 MHz, $CDCl_3$): *δ* 19.8, 21.5, 33.3, 34.1, 41.2, 54.9, 64.8, 104.2, 126.5, 127.0, 128.5, 129.5, 129.6, 137.2, 137.8, 143.1; FTIR (thin film): 3279 (br), 2950 (s), 2877 (s), 1599 (m), 1495 (m), 1454 (s), 1417 (s), 1327 (s), 1158 (s), 1091 (s), 1030 (s) cm^{-1}; HRMS (TOF ES) calcd for $C_{21}H_{27}NO_4SNa$: 412.1559, found: 412.1553. Anal. Calcd for $C_{21}H_{27}NO_4S$: C, 64.75; H, 6.99; N, 3.60; S, 8.23. Found: C, 64.48; H, 7.25; N, 3.56; S, 8.35.

4.2.2. N-(1-Benzyl-4-[1,3]dioxan-2-yl-butyl)-benzenesulfonamide (**10**)

Following the general procedure, a solution of CuBr·DMS (23 mg, 0.11 mmol, 0.4 equiv) in DMS (0.5 mL) was added to the Grignard solution (**7**) (1.4 mL, 0.4 M, mmol, 2 equiv) followed by (**8**) (80 mg, 0.28 mmol, 1 equiv) in THF (1.5 mL). Purification by column chromatography (using a continuous gradient from petroleum ether and ending with 5:1 petroleum ether/EtOAc) yielded (**10**) as a colourless solid, 84 mg, 74%. Mp 108–110 °C; $[\alpha]_D^{25}$ −12 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): *δ* 1.11–1.25 (8H, m, CH_2), 2.40 (3H, s, Ar–CH_3), 2.66 (2H, d, *J*=6.5 Hz, Ar–CH_2), 3.31–3.47 (1H, m, C*H*N), 3.69 (2H, dd, *J*=12.0, 2.0 Hz, OCH_2), 4.06 (2H, ddd, *J*=12.0, 5.0, 1.5 Hz, OCH_2), 4.32 (1H, d, *J*=8.0 Hz, N*H*), 4.37 (1H, t, *J*=5.0 Hz, OC*H*CH_2), 6.95–7.03 (2H, m, Ar–*H*), 7.15–7.28 (5H, m, Ar–*H*), 7.63 (2H, d, *J*=8.0 Hz, Ar–*H*); ^{13}C NMR (62.9 MHz, $CDCl_3$): *δ* 19.8, 21.5, 25.8, 33.3, 34.5, 41.0, 54.9, 66.8, 101.9, 126.5, 127.0, 128.5, 129.5, 129.6, 137.2, 137.8, 143.0; FTIR (thin film): 3279 (br), 2954 (s), 2857 (s), 1599 (m), 1495 (m), 1434 (s), 1378 (s), 1327 (s), 1288 (s), 1145 (s), 1091 (s) cm^{-1}; HRMS (TOF ES) calcd for $C_{22}H_{29}NO_4SNa$: 426.1715, found: 426.1730. Anal. Calcd for $C_{22}H_{29}NO_4S$: C, 65.48; H, 7.24; N, 3.47; S, 7.95. Found: C, 65.24; H, 7.30; N, 3.37; S, 7.97.

4.2.3. (S)-N-(4-[1,3]Dioxolan-2-yl-1-methyl-butyl)-4-methyl-benzenesulfonamide (**18**)

Following the general procedure, a solution of CuBr·DMS (135 mg, 0.66 mmol, 0.4 equiv) in DMS (2 mL) was added to the Büchi Grignard solution (**6**) (7 mL, 0.47 M, 3.29 mmol, 2 equiv) followed by (**12**) (347 mg, 1.65 mmol, 1 equiv) in THF (3 mL). Purification by column chromatography (using a continuous gradient from petroleum ether and ending with 5:1 petroleum ether/EtOAc) yielded (**18**) as a colourless solid, 360 mg, 70%. Mp 89–93 °C; $[\alpha]_D^{25}$ −27 (*c* 0.009, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): *δ* 1.03 (3H, d, *J*=6.5 Hz, $CHCH_3$), 1.21–1.71 (6H, m, CH_2), 2.42 (3H, s, Ar–CH_3), 3.21–3.39 (1H, m, NHC*H*), 3.78–3.97 (4H, m, OCH_2CH_2O), 4.33 (1H, d, *J*=8.0 Hz, N*H*), 4.75 (1H, t, *J*=4.5 Hz, OC*H*CH_2), 7.26–7.32 (2H, m, Ar–*H*), 7.72–7.78 (2H, m, Ar–*H*); ^{13}C NMR (62.9 MHz, $CDCl_3$): *δ* 20.0, 21.5, 21.6, 33.3, 37.2, 49.9, 64.8, 10.2, 127.0, 129.6, 138.2, 143.1; FTIR (thin film): 3272 (br), 2950 (m), 1323 (m), 1160 (s), 1092 (m), 1030 (w) cm^{-1}; *m/z* (TOF ES): 252, 320, 336 (MNa^+); HRMS (TOF ES) calcd for $C_{15}H_{23}NO_4SNa$: 336.1245, found: 336.1259.

4.2.4. N-(4-[1,3]Dioxolan-2-yl-1-isopropyl-butyl)-4-methyl-benzenesulfonamide (**19**)

Following the general procedure, a solution of CuBr·DMS (137 mg, 0.67 mmol, 0.4 equiv) in DMS (2 mL) was added to the Büchi Grignard solution (8 mL, 0.4 M, 3.33 mmol, 2 equiv) followed by (**13**) (396 mg, 1.67 mmol, 1 equiv) in THF (2 mL). Purification by column chromatography (using a continuous gradient from petroleum ether and ending with 5:1 petroleum ether/EtOAc) yielded (**19**) as a colourless solid, 469 mg, 82%. Mp 117–120 °C; ^{1}H NMR (250 MHz, $CDCl_3$): *δ* 0.78 (6H, d, *J*=6.5 Hz, $CH(CH_3)_2$), 1.04–1.80 (7H, m, $CH_2CH_2CH_2CH(CH_3)_3$), 2.41 (3H, s, Ar–CH_3), 3.01–3.13 (1H, m, NC*H*), 3.75–3.96 (4H, m, OCH_2CH_2O), 4.30 (1H, d, *J*=9.0 Hz, N*H*), 4.69 (1H, t, *J*=4.5 Hz, OC*H*CH_2), 7.29 (2H, d, *J*=8.5 Hz, Ar–*H*), 7.75 (2H, d, *J*=8.5 Hz, Ar–*H*); ^{13}C NMR (62.9 MHz, $CDCl_3$): *δ* 17.5, 18.3, 20.1, 21.5, 31.0, 31.4, 33.4, 59.1, 64.8, 104.2, 127.0, 129.5, 138.6, 142.9; FTIR (thin film): 3281 (w), 2958 (m), 2875 (m), 1323 (s), 1160 (s), 1093 (s), 1029 (s) cm^{-1}; *m/z* (TOF ES): 280, 364 (MNa^+); HRMS (TOF ES) calcd for $C_{17}H_{27}NO_4SNa$: 364.1559, found: 364.1553.

4.2.5. N-(1-Benzyloxymethyl-4-[1,3]dioxolan-2-yl-butyl)-4-methyl-benzenesulfonamide (**20**)

Following the general procedure, a solution of CuBr·DMS (51 mg, 0.25 mmol, 0.4 equiv) in DMS (1 mL) was added to

the Büchi Grignard solution (**6**) (3.3 mL, 0.38 M, 1.25 mmol, 2 equiv), followed by (**14**) (199 mg, 0.63 mmol, 1 equiv) in THF (1.5 mL). The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 2:1 petroleum ether/EtOAc) yielded (**20**) as a clear oil, 215 mg, 82%. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.20–1.63 (6H, m, CH_2), 2.39 (3H, s, Ar–CH_3), 3.16–3.37 (3H, m, OCH_2CHN), 3.74–3.97 (4H, m, OCH_2CH_2O), 4.33 (2H, s, Ar–CH_2O), 4.73 (1H, t, J=4.5 Hz, OCHCH$_2$), 4.87 (1H, d, J=7.5 Hz, NH), 7.16–7.37 (7H, m, Ar–H), 7.71 (2H, d, J=8.5 Hz, Ar–H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 20.1, 21.5, 32.3, 33.3, 53.5, 64.8, 71.0, 73.1, 104.2, 127.0, 127.6, 127.7, 128.4, 129.5, 137.7, 138.0, 143.1; FTIR (thin film): 3278 (br), 2952 (m), 2870 (m), 1454 (w), 1330 (m), 1161 (s), 1121 (m), 1092 (s) cm^{-1}; *m/z* (TOF ES): 203, 358, 442 (MNa$^+$); HRMS (TOF ES) calcd for $C_{22}H_{29}NO_5NaS$: 442.1664, found: 442.1645.

4.2.6. *N-[1-(tert-Butyl-diphenyl-silanyloxymethyl)-4-[1,3]-dioxolan-2-yl-butyl]-4-methyl-benzenesulfonamide (**21**)*

Following the general procedure, a solution of CuBr·DMS (119 mg, 0.58 mmol, 0.4 equiv) in DMS (1 mL) was added to the Büchi Grignard solution (**6**) (7.4 mL, 0.4 M, 2.96 mmol, 2 equiv) followed by (**15**) (689 mg, 1.45 mmol, 1 equiv) in THF (2 mL). Purification by column chromatography (using a continuous gradient from petroleum ether and ending with 2:1 petroleum ether/EtOAc) yielded (**21**) as a clear oil, 716 mg, 87%. $[\alpha]_D^{21}$ −10 (*c* 0.01, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.02 (9H, s, SiC(CH_3)$_3$), 1.19–1.40 (2H, m, CH_2), 1.51–1.64 (4H, m, CH_2), 2.41 (3H, s, Ar–CH_3), 3.16–3.29 (1H, m, CHNH), 3.38 (1H, dd, J=4.0, 10.5 Hz, OCH_2CHN), 3.46 (1H, dd, J=3.5, 10.5 Hz, OCH_2CHN), 3.78–3.97 (4H, m, OCH_2CH_2O), 4.74 (1H, t, J=4.5 Hz, OCHCH$_2$), 4.83 (1H, d, J=8.0 Hz, NH), 7.24 (2H, d, J=8.0 Hz, Ar–H), 7.32–7.58 (10H, m, Ar–H), 7.70 (2H, d, J=8.0 Hz, Ar–H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 19.1, 19.9, 21.4, 26.7, 31.9, 33.3, 54.8, 64.6, 64.7, 104.1, 126.8, 127.6, 129.5, 129.7, 132.7, 135.4, 138.0, 142.9; FTIR (thin film): 3271 (br), 2931 (m), 2858 (m), 1427 (m), 1331 (m), 1162 (s), 1113 (s), 1090 (s) cm^{-1}; *m/z* (TOF ES): 428, 506, 590 (MNa$^+$); HRMS (TOF ES) calcd for $C_{31}H_{41}NO_5NaSiS$: 590.2372, found: 590.2374.

4.2.7. *(S)-2-Trimethylsilanyl-ethanesulfonic acid (4-[1,3]dioxolan-2-yl-1-methyl-butyl)-amide (**22**)*

Following the general procedure, a solution of CuBr·DMS (37 mg, 0.18 mmol, 0.5 equiv) in DMS (2 mL) was added to the Büchi Grignard solution (**6**) (2.8 mL, 0.34 M, 0.91 mmol, 2.5 equiv) followed by (**16**) (79 mg, 0.36 mmol, 1 equiv) in THF (1 mL). Purification by column chromatography (using a continuous gradient from petroleum ether and ending with 5:1 petroleum ether/EtOAc) yielded (**22**) as a colourless solid, 102 mg, 88%. Mp 76–78 °C; $[\alpha]_D^{25}$ +40 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ −0.30 to 0.04 (9H, m, Si(CH_3)$_3$), 0.93–1.03 (2H, m, SCH$_2$CH_2Si), 1.19 (3H, d, J=6.5 Hz, NCHCH_3), 1.35–1.69 (6H, m, CH_2), 2.82–2.92 (2H, m, SCH_2CH$_2$Si), 3.34–3.47 (1H, m, CHNH), 3.75–3.95 (4H, m, OCH_2CH_2O), 4.79 (1H, t, J=4.5 Hz, OCHCH$_2$); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ −2.0, 10.7, 20.3, 22.5, 33.4, 37.7, 50.0, 50.2, 64.8, 104.2; FTIR (thin film): 3544 (w, br), 3278 (br), 2953 (s), 2895 (m), 1316 (s), 1250 (s), 1134 (s), 1027 (m) cm^{-1}; *m/z* (TOF ES): 346 (MNa$^+$), 363 (MK$^+$); HRMS (TOF ES) calcd for $C_{13}H_{29}NO_4SiSNa$: 346.1484, found: 346.1497.

4.2.8. *N-(1-Benzyl-4-[1,3]dioxolan-2-yl-butyl)-diphenyl-phosphinamide (**23**)*

Following the general procedure, a solution of CuBr·DMS (36 mg, 0.76 mmol, 0.4 equiv) in DMS (0.5 mL) was added to the Büchi Grignard solution (**6**) (1.8 mL, 0.5 M, 0.88 mmol, 2 equiv) followed by (**17**) (146 mg, 0.44 mmol, 1 equiv) in THF (1 mL). Purification by column chromatography (using a continuous gradient from petroleum ether to EtOAc followed by 1:9 MeOH/CH_2Cl_2) yielded (**23**) as a colourless solid, 180 mg, 94%. Mp 144–146 °C; ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.53–1.84 (6H, m, CH_2), 2.72 (1H, dd, J=5.0, 10.5 Hz, NH), 2.82 (1H, dd, J=6.5, 13.5 Hz, Ar–CH_2), 2.93 (1H, dd, J=6.0, 13.5 Hz, Ar–CH_2), 3.20–3.35 (1H, m, NHCH), 3.80–3.99 (4H, m, OCH_2CH_2O), 4.67–4.81 (1H, m, OCHCH$_2$), 7.12–7.55 (11H, m, Ar–H), 7.60–7.71 (2H, m, Ar–H), 7.81–7.92 (2H, m, Ar–H); ^{31}P NMR (250 MHz, $CDCl_3$): δ 21.5; ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 20.1, 33.5, 36.4 (d, J=3 Hz), 42.8 (d, J=5 Hz), 53.0, 64.7, 104.2, 126.3, 128.2, 128.4 (d, J=9 Hz), 129.8, 131.6 (d, J=9 Hz), 132.1 (d, J=9 Hz), 133.9 (d, J=32 Hz), 138.3; FTIR (thin film): 3187 (br), 2947 (w), 1438 (s), 1187 (s), 1110 (s) cm^{-1}; *m/z* (TOF ES): 436 (MH$^+$); HRMS (TOF ES) calcd for $C_{26}H_{31}NO_3P$: 436.2042, found: 436.2037.

4.2.9. *N-[2-(2-[1,3]Dioxolan-2-yl-ethyl)-cyclohexyl]-4-methyl-benzenesulfonamide (**32**)*

Following the general procedure, a solution of CuBr·DMS (70 mg, 0.34 mmol, 0.4 equiv) in DMS (1 mL) was added to the Büchi Grignard solution (**6**) (4 mL, 0.43 M, 1.70 mmol, 2 equiv), followed by (**31**) (215 mg, 0.85 mmol, 1 equiv) in THF (1 mL). Purification by column chromatography (using a continuous gradient from petroleum ether and ending with 5:1 petroleum ether/EtOAc) yielded (**32**) as a colourless solid, 234 mg, 78%. Mp 170–174 °C; ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.81–1.28 (6H, m, CH_2), 1.34–1.88 (7H, m, CH_2), 2.40 (3H, s, Ar–CH_3), 2.73–2.91 (1H, m, CHN), 3.74–3.99 (4H, m, OCH_2CH_2O) 4.50 (1H, d, J=8.5 Hz, NH), 4.68 (1H, t, J=4.5 Hz, OCHCH$_2$), 7.29 (2H, d, J=8.0 Hz, Ar–H), 7.76 (2H, d, J=8.0 Hz, Ar–H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 21.5, 25.0 (×2), 26.4, 30.7, 30.8, 34.6, 42.7, 57.3, 64.8, 104.7, 127.0, 129.6, 138.6, 143.0; FTIR (thin film): 3268 (br), 2929 (m), 2857 (m), 1325 (m), 1160 (s), 1092 (m), 1072 (w) cm^{-1}; *m/z* (ES): 292, 376 (MNa$^+$), 392 (MK$^+$), 729 (2MNa$^+$); HRMS (ES) calcd for $C_{18}H_{27}O_4SNa$: 376.1559, found: 376.1543.

4.2.10. *N-[1-(3-[1,3]Dioxolan-2-yl-propyl)-cyclohexyl]-4-methyl-benzenesulfonamide (**35**)*

Following general procedure, a solution of CuBr·DMS (35 mg, 0.17 mmol, 0.4 equiv) in DMS (0.5 mL) was added

to the Buchi Grignard solution (**6**) (2 mL, 0.43 M, 0.85 mmol, 2 equiv) followed by (**34**) (113 mg, 0.43 mmol, 1 equiv) in THF (0.5 mL). Purification by column chromatography (using a continuous gradient from petroleum ether and ending with 5:1 petroleum ether/EtOAc) yielded (**35**) as a colourless solid, 141 mg, 90%. Mp 109–111 °C; ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.16–1.79 (16H, m, CH_2), 2.40 (3H, s, Ar–CH_3), 3.78–3.96 (4H, m, OCH_2CH_2O), 4.38 (1H, s, N*H*), 4.68 (1H, t, *J*=5.0 Hz, OC*H*CH$_2$), 7.28 (2H, d, *J*=8.5 Hz, Ar–*H*), 7.78 (2H, d, *J*=8.5 Hz, Ar–*H*); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 17.5, 21.4, 21.5, 25.3, 33.7, 35.9, 38.3, 59.7, 64.7, 104.4, 126.9, 129.4, 140.6, 142.7; FTIR (thin film): 3280 (br), 2935 (m), 2864 (m), 1329 (m), 1152 (s), 1094 (m) cm^{-1}; *m*/*z* (TOF ES): 306, 390 (MNa^+), 406; HRMS (TOF ES) calcd for $C_{19}H_{29}NO_4SNa$: 390.1715, found: 390.1700.

4.2.11. N-[4-tert-Butyl-1-(3-[1,3]dioxolan-2-yl-propyl)-cyclohexyl]-4-methyl-benzenesulfonamide (*38*)

Following the general procedure, a solution of CuBr·DMS (45 mg, 0.22 mmol, 0.4 equiv) in DMS (1 mL) was added to the Buchi Grignard solution (**6**) (4 mL, 0.28 M, 1.12 mmol, 2 equiv), followed by (**37**) (180 mg, 0.56 mmol, 1 equiv) in THF (2 mL). Purification by column chromatography (using a continuous gradient from petroleum ether and ending with 3:1 petroleum ether/EtOAc) yielded (**38**) as a colourless solid, 189 mg, 79%. Mp 133–134 °C; ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.80–1.10 (2H, m), 0.78 (9H, s, C(CH_3)$_3$), 1.18–1.65 (11H, m, CH_2), 1.75–1.86 (2H, m, CH_2), 2.41 (3H, s, Ar–CH_3), 3.79–3.99 (4H, m, OCH_2CH_2O), 4.47 (1H, s, N*H*), 4.74 (1H, t, *J*=4.5 Hz, OC*H*CH$_2$), 7.28 (2H, d, *J*=8.5 Hz, Ar–*H*), 7.77 (2H, d, *J*=8.5 Hz, Ar–*H*); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 17.3, 21.5, 23.0, 27.5, 32.2, 33.3, 33.7, 36.2, 47.0, 59.9, 64.8, 104.5, 126.9, 129.4, 141.0, 142.7; FTIR (thin film): 3273 (br), 2948 (s), 2868 (m), 1331 (m), 1156 (s), 1094 (m), 1032 (w) cm^{-1}; *m*/*z* (TOF ES): 446 (MNa^+); HRMS (TOF ES) calcd for $C_{23}H_{37}NO_4SNa$: 446.2341, found: 446.2357.

4.3. General procedure for the synthesis of tetrahydropyridines

$HCl_{(aq)}$ (1 M, 7.5 equiv) was added to a solution of acetal adduct (1 equiv) in acetone and the reaction mixture stirred overnight at room temperature. The reaction was quenched with a saturated solution of K_2CO_3 and the product was extracted with EtOAc, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/EtOAc) to give the tetrahydropyridine.

4.3.1. (R)-2-Benzyl-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydropyridine (*11*) from (*9*)

Following the general procedure, $HCl_{(aq)}$ (1 M, 2 mL, 2.0 mmol, 7.5 equiv) was added to a solution of (**9**) (104 mg, 0.267 mmol, 1 equiv) in acetone (2 mL). Purification by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/EtOAc) yielded (**11**) as a colourless solid, 77 mg, 88%. Mp 106–108 °C; $[\alpha]_D^{25}$ +290 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.72–0.90 (1H, m, CH_2), 1.28–1.42 (1H, m, CH_2), 1.74 (1H, dt, *J*=18.5, 5.5 Hz, CH_2), 1.92–2.12 (1H, m, CH_2), 2.33 (3H, s Ar–CH_3), 2.66 (1H, dd, *J*=13.5, 10.5 Hz, Ar–CH_2), 2.92 (1H, dd, *J*=13.5, 5.0 Hz, Ar–CH_2), 3.98–4.10 (1H, m, NC*H*CH$_2$), 4.94–5.05 (1H, m, NCH=C*H*CH$_2$), 6.62 (1H, d, *J*=8.0 Hz, NC*H*=CHCH$_2$), 7.09–7.29 (7H, m, Ar–*H*), 7.60 (2H, d, *J*=8.0 Hz, Ar–*H*); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 17.1, 20.9, 21.5, 38.1, 54.3, 108.2, 123.6, 126.5, 126.9, 128.5, 129.4, 129.7, 136.3, 138.0, 143.4; FTIR (thin film): 3086 (m), 3063 (m), 3028 (s), 2927 (s), 2857 (s), 1917 (w), 1807 (w), 1737 (m), 1646 (s), 1597 (s), 1495 (s), 1455 (s), 1401 (s), 1344 (s), 1305 (s), 1261 (s), 1167 (s), 1098 (s), 1049 (s), 1018 (s) cm^{-1}; HRMS (TOF ES) calcd for $C_{19}H_{23}NO_2S$: 328.1371, found: 328.1386. Anal. Calcd for $C_{19}H_{22}NO_2S$: C, 69.69; H, 6.46; N, 4.28; S, 9.79. Found: C, 69.53; H, 6.53; N, 4.26; S, 9.84.

4.3.2. (R)-2-Benzyl-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydropyridine (*11*) from (*10*)

To (**10**) (50 mg, 0.12 mmol, 1 equiv), was added THF (2 mL) and 1 M $HCl_{(aq)}$ (2 mL). The reaction was heated to reflux and allowed to stir for 16 h. The mixture was then cooled to room temperature, quenched with $K_2CO_{3(aq)}$, and the product extracted with EtOAc. The organic layer was separated, dried over $MgSO_4$ and the solvent removed under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/EtOAc) yielded (**10**) as a colourless solid, 32 mg, 78%.

4.3.3. (S)-2-Methyl-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydropyridine (*24*)

Following the general procedure, $HCl_{(aq)}$ (1 M, 1.4 mL, 1.40 mmol, 7.7 equiv) was added to a solution of (**18**) (56 mg, 0.18 mmol, 1 equiv) in acetone (3.6 mL). Purification by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/EtOAc) yielded (**24**) as a yellow oil, 38 mg, 84%. $[\alpha]_D^{25}$ +511 (*c* 0.009, CH_2Cl_2); ^{1} H NMR (250 MHz, $CDCl_3$): δ 0.99–1.12 (1H, m, CH_2), 1.17 (3H, d, *J*=6.5 Hz, CHCH_3), 1.38–1.49 (1H, m, CH_2), 1.56–1.89 (1H, m, CH_2), 1.75–2.08 (1H, m, CH_2), 2.41 (3H, s, Ar–CH_3), 4.02–4.15 (1H, m, CH$_2$C*H*N), 4.94–5.02 (1H, m, NCHC=C*H*), 6.58–6.65 (1H, m, NC*H*=CH), 7.29 (2H, d, *J*=8.0 Hz, Ar–*H*), 7.68 (2H, d, *J*=8.0 Hz, Ar–*H*); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 16.9, 18.2, 21.5, 25.2, 48.5, 107.7, 123.2, 126.8, 129.6, 136.4, 143.3; FTIR (thin film): 3063 (w), 2977 (m), 2929 (m), 2848 (w), 1645 (m), 1362 (s), 1340 (s), 1262 (m), 1170 (s), 1136 (m), 1103 (s) cm^{-1}; *m*/*z* (TOF ES): 252 (MH^+), 274 (MNa^+); HRMS (TOF ES) calcd for $C_{13}H_{18}NO_2S$: 252.1058, found: 252.1048.

4.3.4. 2-Isopropyl-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydropyridine (*25*)

Following the general procedure, $HCl_{(aq)}$ (1 M, 4 mL, 4.0 mmol, 7.1 equiv) was added to a solution of (**19**) (190 mg,

0.56 mmol, 1 equiv) in acetone (4 mL) and stirred overnight at room temperature. Purification by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/EtOAc) yielded (**25**) as a colourless solid, 154 mg, 98%. Mp 84–88 °C; ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.61–0.78 (1H, m, $CH_3(CH_3)CH$), 0.90 (3H, d, J=6.5 Hz, $CH_3(CH_3)CH$), 1.11 (3H, d, J=6.5 Hz, $CH_3(CH_3)CH$), 1.55–1.97 (4H, m, CH_2), 2.42 (3H, s, Ar–CH_3), 3.52 (1H, dt, J=10.0, 2.5 Hz, $CH_2(CH)CH$N) 5.05–5.13 (1H, m, NCH=CH), 6.54–6.61 (1H, m, NCH=CH), 7.31 (2H, d, J=8.0 Hz, Ar–H), 7.68 (2H, d, J=8.0 Hz, Ar–H); ^{13}C NMR (62.9 MHz, $CDCl_3$): 17.6, 19.0, 20.6, 20.8, 21.5, 27.5, 59.13, 111.4, 123.9, 127.0, 129.6, 136.0, 143.2; FTIR (thin film): 2961 (m), 1644 (w), 1354 (w), 1340 (s), 1171 (s), 1092 (m) cm^{-1}; *m/z* (ES): 280 (MH^+). HRMS (ES) calcd for $C_{15}H_{22}O_2S$: 280.1371, found: 280.1364.

4.3.5. 2-Benzyloxymethyl-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydropyridine (*26*)

Following the general procedure, $HCl_{(aq)}$ (1 M, 1.6 mL, 1.6 mmol, 7.5 equiv) was added to a solution of (**20**) (90 mg, 0.22 mmol, 1 equiv) in acetone (2.2 mL). Purification by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/EtOAc) yielded (**26**) as a clear oil, 56 mg, 73%. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.82–1.01 (1H, m, CH_2), 1.69–1.97 (3H, m, CH_2), 2.41 (3H, s, Ar–CH_3), 3.45 (1H, dd, J=9.5, 9.5 Hz, OCH_2CH), 3.57 (1H, dd, J=5.5, 9.5 Hz, OCH_2CH), 4.09–4.19 (1H, m, CH_2CHN), 4.49 (1H, d, J=12.0 Hz, Ar–CH_2O), 4.59 (1H, d, J=12.0 Hz, Ar–CH_2O), 4.93–5.01 (1H, m, NCH=CH), 6.58–6.64 (1H, m, NCH=CH), 7.24–7.38 (7H, m, Ar–H), 7.68 (2H, d, J=8.5 Hz, Ar–H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 16.9, 19.9, 21.5, 51.5, 68.4, 73.2, 108.4, 123.6, 126.9, 127.6 (×2), 128.4, 129.6, 135.9, 138.1, 143.5; FTIR (thin film): 2926 (m), 1719 (w), 1648 (w), 1453 (w), 1344 (m), 1167 (s), 1102 (s) cm^{-1}; *m/z* (TOF ES): 275, 358 (MH^+), 380 (MNa^+); HRMS (TOF ES) calcd for $C_{20}H_{24}NO_3S$: 358.1477, found: 358.1486.

4.3.6. 2-(tert-Butyl-diphenyl-silanyloxymethyl)-1-(toluene-4-sulfonyl)-1,2,3,4-tetrahydropyridine (*27*)

Trifluoroacetic acid (90 μL, 1.135 mmol, 5 equiv) was added to a solution of (**21**) (129 mg, 0.227 mmol, 1 equiv) in acetone (distilled) (2.3 mL) at room temperature and left stirring overnight. The reaction was quenched with $NaHCO_3$, extracted with EtOAc. The organic layers were combined, washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/EtOAc) to give (**27**) as a colourless oil, 79 mg, 69%. $[\alpha]_D^{21}$ −34 (*c* 0.01, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.80–1.12 (1H, m, CH_2), 1.07 (9H, s, SiC(CH_3)$_3$), 1.70–1.81 (2H, m, CH_2), 1.95–2.08 (1H, m, CH_2), 2.42 (3H, s, Ar–CH_3), 3.57 (1H, dd, J=10.0, 10.0 Hz, OCH_2), 3.80 (1H, dd, J=5.0, 10.0 Hz, OCH_2), 3.98–4.10 (1H, m, NCH), 4.87–4.97 (1H, m, NCH=CH), 6.57 (1H, m, NCH=CH), 7.24–7.31 (2H, m, Ar–H), 7.35–7.49 (6H, m, Ar–H), 7.59–7.70 (6H, m, Ar–H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 16.8, 19.2, 19.5, 21.5, 26.9, 53.3, 61.9, 108.4, 123.6, 126.9, 127.7, 129.6, 129.7, 133.4, 135.6, 136.0, 143.3; FTIR (thin film): 3071 (w), 2931 (m), 2858 (m), 1650 (w), 1428 (m), 1361 (m), 1169 (s), 1106 (s), 814 (w), 703 (s) cm^{-1}; *m/z* (TOF ES): 428, 506 (MH^+), 528 (MNa^+); HRMS (TOF ES) calcd for $C_{29}H_{36}NO_3SiS$: 506.2185, found: 506.2194.

4.3.7. (S)-2-Methyl-1-(2-trimethylsilanylethane-sulfonyl)-1,2,3,4-tetrahydropyridine (*28*)

Following the general procedure, $HCl_{(aq)}$ (1 M, 1.1 mL, 1.1 mmol, 8.3 equiv) was added to a solution of (**22**) (42 mg, 0.13 mmol, 1 equiv) in acetone (1.3 mL). Purification by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/EtOAc) gave (**28**) as a colourless oil, 20 mg, 62%. $[\alpha]_D^{25}$ +271 (*c* 0.009, CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ −0.10 to 0.10 (9H, m, Si(CH_3)$_3$), 0.90–1.03 (2H, m, SCH_2CH_2Si), 1.20 (3H, d, J=6.5 Hz, NCHCH_3), 1.62–1.77 (2H, m, CH_2), 1.89–2.17 (2H, m, CH_2), 2.81–2.95 (2H, m, SCH_2CH_2Si), 4.09–4.21 (1H, m, CH_3CHN), 4.83–4.91 (1H, m, NCH=CH), 6.39–6.46 (1H, m, NCH=CH); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ −2.0, 10.4, 16.9, 18.4, 26.8, 48.8, 48.9, 105.2, 125.9; FTIR (thin film): 3508 (br), 2952 (s), 1648 (m), 1337 (s), 1251 (s), 1156 (s), 1100 (m), 1000 (s) cm^{-1}; *m/z* (TOF ES): 262 (MH^+); HRMS (TOF ES) calcd for $C_{11}H_{24}NO_2SiS$: 262.1297, found: 262.1305.

4.3.8. 2-Benzyl-3,4-dihydro-2H-pyridine-1-carboxylic acid benzyl ester (*30*)

An ether solution of HCl (1 M, 1.0 mL, 1.00 mmol, 3 equiv) was added to a solution of (**23**) (145 mg, 0.33 mmol, 1 equiv) in CH_2Cl_2 (3 mL) and MeOH (0.3 mL). The solution was stirred at room temperature overnight and concentrated under reduced pressure.

The crude mixture was redissolved in MeCN (3.3 mL) followed by the addition of benzyl chloroformate (188 μL, 1.32 mmol, 4 equiv), Et_3N (97 μL, 0.72 mmol, 2.1 equiv) and DMAP (8 mg, 0.07 mmol, 0.2 equiv) at room temperature and stirred for 24 h. The reaction mixture was concentrated under reduced pressure. The crude mixture was diluted with Et_2O then washed with $K_2CO_{3(aq)}$ solution. The aqueous layer was extracted with Et_2O. The organic layers were combined, washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/EtOAc) to yield (**30**) as a colourless oil, 66 mg, 65%. ^{1}H NMR (250 MHz, $CDCl_3$) two rotamers: δ 1.61–1.78 (2H, m, CH_2), 1.93–2.10 (1H, m, CH_2), 2.15–2.33 (1H, m, CH_2), 2.62–2.76 (1H, m, Ar–CH_2), 2.83–3.00 (1H, m, Ar–CH_2), 4.38–4.60 (1H, m, NCH), 4.93 (0.5H, d, J=12.0 Hz, Ar–CH_2O), 4.87–4.97 (0.5H, m, NCH=CH), 5.00–5.09 (0.5H, m, NCH=CH), 5.15 (0.5H, d, J=12.0 Hz, Ar–CH_2O), 5.19 (1H, s, Ar–CH_2O), 6.79–6.87 (0.5H, d, J=8.5 Hz, NCH=CH), 6.91–6.98 (0.5H, d, J=8.5 Hz, NCH=CH), 7.07–7.42 (10H, m, Ar–H); ^{13}C

NMR (100.6 MHz, $CDCl_3$) two rotamers: δ 17.4, 17.4, 22.2, 23.2, 36.5, 37.2, 52.0, 52.4, 67.4, 67.4, 105.6, 106.1, 123.6, 124.0, 126.3, 128.0, 128.1, 128.4, 128.5, 129.2, 129.3, 136.1, 136.4, 138.4, 138.6, 152.7, 153.3; FTIR (thin film): 3401 (br), 3029 (w), 2929 (w), 2845 (w), 1704 (s), 1654 (s), 1414 (s), 1330 (s), 1234 (m), 1111 (m), 1076 (m), 699 (s) cm^{-1}; *m/z* (TOF ES): 308 (MH^+), 330 (MNa^+); HRMS (TOF ES) calcd for $C_{20}H_{22}NO_2$: 308.1651, found: 308.1636.

*4.3.9. 1-(Toluene-4-sulfonyl)-1,4,4a,5,6,7,8,8a-octahydro-qunoline (**33**)*

HCl in ether (1 M, 1.2 mL, 1.23 mol, 5 equiv) was added to a solution of (**32**) (87.2 mg, 0.25 mmol, 1 equiv) in ether (2.5 mL) and acetone (1 mL). Then THF (2 mL) was added and stirred at room temperature for 4 h. The reaction mixture was poured into a saturated solution of K_2CO_3 (10 mL) and the product was extracted with EtOAc, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/EtOAc) yielded (**33**) as a colourless solid, 45 mg, 63%. Mp 71–73 °C; ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.84–1.03 (1H, m, C*H*), 1.14–1.65 (6H, m, CH_2), 1.68–1.87 (3H, m, CH_2), 2.42 (3H, s, Ar–CH_3), 2.63–2.76 (2H, m, CH_2), 5.00–5.10 (1H, m, NCH=C*H*), 6.67–6.74 (1H, m, NC*H*=CH), 7.31 (2H, d, *J*=8.5 Hz, Ar–*H*), 7.66 (2H, d, *J*=8.5 Hz, Ar–*H*); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 21.6, 25.3 (×2), 28.6, 32.7, 33.3, 39.3, 61.6, 109.1, 127.1, 127.4, 129.5, 135.7, 143.4; FTIR (thin film): 2927 (m), 2855 (m), 1658 (w), 1346 (m), 1241 (w), 1170 (s), 1092 (m) cm^{-1}; *m/z* (TOF ES): 292 (MH^+), 314 (MNa^+); HRMS (TOF ES) calcd for $C_{16}H_{22}NO_2S$: 292.1371, found: 292.1359.

*4.3.10. 1-(Toluene-4-sulfonyl)-1-aza-spiro[5.5]undec-2-ene (**36**)*

HCl in ether (1 M, 0.3 mL, 0.27 mol, 2.1 equiv) was added to a solution of (**35**) (50 mg, 0.14 mmol, 1 equiv) in acetone (1.4 mL). The mixture was stirred at room temperature overnight. Reaction was quenched with a saturated solution of K_2CO_3 and the product was extracted with EtOAc, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/EtOAc) yielded (**36**) as a colourless solid, 23 mg, 54%. Mp 119–122 °C; ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.34–1.42 (4H, m, CH_2), 1.50–1.66 (4H, m, CH_2), 1.74 (2H, t, *J*=6.5 Hz, CH_2), 1.93–2.02 (2H, m, CH_2), 2.04–2.18 (2H, m, CH_2), 2.41 (3H, s, Ar–CH_3), 4.96 (1H, dt, *J*=4.0, 8.5 Hz, NCH=C*H*), 6.97 (1H, dt, *J*=2.0, 8.5 Hz, NC*H*=CH), 7.23–7.29 (2H, m, Ar–*H*), 7.69 (2H, d, *J*=8.5 Hz, Ar–*H*); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 18.6, 21.5, 22.4, 25.2, 28.1, 32.9, 62.3, 105.1, 126.4 (×2), 129.5, 140.9, 142.8; FTIR (thin film): 2928 (m), 2864 (w), 1656 (m), 1332 (s), 1252 (m), 1161 (s), 1103 (s) cm^{-1}; *m/z* (TOF ES): 306 (MH^+), 328 (MNa^+); HRMS (TOF ES) calcd for $C_{17}H_{24}NO_2S$: 306.1528, found: 306.1521.

*4.3.11. 9-tert-Butyl-1-(toluene-4-sulfonyl)-1-aza-spiro-[5.5]undec-2-ene (**39**)*

Following the general procedure, $HCl_{(aq)}$ (1 M, 1.7 mL, 1.7 mol, 7.1 equiv) was added to a solution of (**38**) (100 mg, 0.24 mmol, 1 equiv) in acetone (2.4 mL). Purification by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/EtOAc) gave (**29**) as a colourless solid, 69 mg, 83%. Mp 139–142 °C; ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.74 (9H, s, C(CH_3)$_3$), 0.89–1.09 (3H, m, CH_2), 1.44–1.65 (6H, m, CH_2), 1.86–1.95 (2H, m, CH_2), 1.99–2.15 (2H, m, CH_2), 2.34 (3H, s, Ar–CH_3), 4.83–4.91 (1H, m, NCH=C*H*), 6.86–6.92 (1H, m, NC*H*=CH), 7.20 (2H, d, *J*=8.0 Hz, Ar–*H*), 7.62 (2H, d, *J*=8.0 Hz, Ar–*H*); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 18.6, 21.5, 23.1, 27.5, 28.1, 32.2, 33.0, 46.9, 62.1, 105.0, 126.5 (×2), 129.5, 140.9, 142.8; FTIR (thin film): 2943 (s), 1657 (m), 1325 (m), 1255 (m), 1162 (s), 1098 (s) cm^{-1}; *m/z* (TOF ES): 384 (MNa^+); HRMS (TOF ES) calcd for $C_{21}H_{31}NO_2SNa$: 384.1973, found: 384.1965.

*4.3.12. 4-Methyl-N-[1-(4-oxo-butyl)-cyclohexyl]-benzene-sulfonamide (**41**)*

A hydrogen chloride solution in ether (1 M, 0.9 mL, 0.9 mol, 6.9 equiv) was added to a solution of (**36**) (40 mg, 0.13 mmol, 1 equiv) in acetone (2.6 mL). The mixture was stirred at room temperature overnight. The reaction was quenched with a saturated solution of K_2CO_3, the product was extracted with ethyl acetate, dried over $MgSO_4$ and concentrated under reduced pressure. Data for (**41**): ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.21–1.77 (14H, m, CH_2), 2.25 (2H, dt, *J*=1.5, 7.0 Hz, CH_2C(O)H), 2.42 (3H, s, Ar–CH_3), 4.31 (1H, s, N*H*), 7.26–7.31 (2H, m, Ar–*H*), 7.79 (2H, d, *J*=8.5 Hz, Ar–*H*), 9.68 (1H, t, *J*=1.5 Hz); ^{13}C (100.6 MHz): δ 15.6, 21.5 (×2), 25.3, 33.0, 36.0, 43.8, 59.6, 126.9, 129.5, 140.5, 142.9, 202.4; FTIR (thin film): 3288 (br), 2936 (m), 2862 (m), 1723 (m), 1598 (w), 1330 (m), 1318 (m), 1288 (m), 1152 (s), 1094 (m) cm^{-1}; *m/z* (TOF ES): 346 (MNa^+), 362 (MK^+); HRMS (TOF ES) calcd for $C_{17}H_{25}NO_3SNa$: 346.1453, found: 346.1440.

*4.3.13. (R)-2-Methyl-1-(toluene-4-sulfonyl)-1,2,3,4-tetra-hydropyridine (**24**)*

Following the general procedure explained in Section 4.2, a solution of CuBr·DMS (1.2 g, 5.85 mmol, 0.4 equiv) in DMS (6 mL) was added to the Büchi Grignard (**6**) solution (73 mL, 0.4 M, 29.28 mmol, 2 equiv), followed by ((*R*)-**12**) (3.09 g, 14.63 mmol, 1 equiv) in THF (15 mL). Following the general procedure explained in Section 4.3, $HCl_{(aq)}$ (1 M, 100 mL, 100.0 mmol, 6.8 equiv) was added to a solution of crude residue in acetone (150 mL). Purification by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/EtOAc) yielded ((*R*)-**24**) as a yellow oil, 3.49 g, 95%. $[\alpha]_D^{25}$ −508 (*c* 0.01, CH_2Cl_2).

*4.3.14. (R)-2-Allyl-6-methyl-1-(toluene-4-sulfonyl)-piper-idine (**42**)*

To a solution of (*R*)-**24** (5.02 g, 19.97 mmol, 1 equiv) in CH_2Cl_2 (375 mL) at −20 °C was added allyltrimethylsilane (12.7 mL,

79.89 mmol, 6 equiv) and TFA (9.2 mL, 119.83 mmol, 4 equiv). The reaction mixture was stirred at −20 °C for 2 h and was then allowed to warm to room temperature overnight. The reaction was quenched with $NaHCO_3$ and extracted using CH_2Cl_2 (×3 portions). The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (using a continuous gradient from petroleum ether and ending with 19:1 petroleum ether/EtOAc) to give (**42**) as a colourless solid, 5.40 g, 92%. Mp 66–70 °C; $[\alpha]_D^{25}$ +32 (*c* 0.010, CH_2Cl_2); ^1H NMR (250 MHz, $CDCl_3$): δ 1.11–1.45 (4H, m, CH_2), 1.32 (3H, d, *J*=7.0 Hz, CH_3CH), 1.51–1.77 (2H, m, CH_2), 2.31–2.57 (2H, m, CHCH_2CHCH), 2.40 (3H, s, Ar–CH_3), 3.96–4.22 (2H, m, C*H*NC*H*), 4.99–5.13 (2H, m, CH=CH_2), 5.69–5.88 (1H, m, C*H*=CH_2), 7.27 (2H, d, *J*=8.0 Hz, Ar–*H*), 7.71 (2H, d, *J*=8.0 Hz, Ar–*H*); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 13.4, 21.5, 21.9, 26.2, 29.4, 40.1, 47.9, 52.1, 117.2, 126.7, 129.5, 136.0, 138.9, 142.6; FTIR (thin film): 2939 (m), 2361 (m), 1332 (m), 1221 (w), 1165 (s), 1105 (m) cm^{-1}; *m/z* (TOF ES): 294 (MH^+); HRMS (TOF ES) calcd for $C_{16}H_{24}NO_2S$: 294.1528, found: 294.1535.

*4.3.15. Alcohol-3-((2R,6R)-6-methyl-1-tosylpiperidin-2-yl) propan-1-ol (**43**)*

Borane dimethylsulfide complex (1.20 mL, 12.65 mmol, 3 equiv) was added to a solution of (*R*)-**42** (1.24 g, 4.22 mmol, 1 equiv) in THF (45 mL), cooled to 0 °C and stirred for 3 h. $NaOH_{(aq)}$ (12.65 mL, 1.0 M, 12.65 mmol, 3 equiv) and H_2O_2 (30% w/w, 1.43 mL, 12.65 mmol, 3 equiv) were added at 0 °C and the mixture allowed to warm to room temperature over 1 h. The product was extracted with CH_2Cl_2 and the extracts were washed with water, brine then dried over $MgSO_4$, filtered and concentrated under reduced pressure. The alcohol was obtained by column chromatography in 1:1 petroleum ether/EtOAc to give (**43**) as a colourless oil, 984 mg, 75%. $[\alpha]_D^{25}$ +33.3 (*c* 0.0096, CH_2Cl_2); Mp 77–80 °C; ^1H NMR (250 MHz, $CDCl_3$): δ 1.18–1.91 (10H, m, CH_2), 1.35 (3H, d, *J*=7.0 Hz, CH_3CHN), 2.42 (3H, s, Ar–CH_3), 3.63–3.79 (2H, m, HOCH_2), 3.97–4.20 (2H, m, C*H*NC*H*), 7.29 (2H, d, *J*=8.0 Hz, Ar–*H*), 7.72 (2H, d, *J*=8.0 Hz, Ar–*H*); ^{13}C NMR: δ 13.5, 21.4, 21.8, 27.4, 29.1, 29.9, 31.7, 48.0, 52.1, 62.4, 126.5, 129.5, 138.7, 142.6; FTIR (thin film): 3520 (br), 2940 (s), 2871 (m), 1598 (w), 1329 (s), 1224 (m), 1163 (s), 1140 (m) cm^{-1}; *m/z* (TOF ES): 312 (MH^+); HRMS (TOF ES) calcd for $C_{16}H_{26}NO_3S$: 312.1633, found: 312.1639.

*4.3.16. 2,3-[6-Methyl-1-(toluene-4-sulfonyl)-piperidin-2-yl]-propionic acid methyl ester (**44**)*

Oxalyl chloride (2.16 mL, 24.77 mmol, 1.2 equiv) was added to CH_2Cl_2 (165 mL) at −78 °C then a solution of DMSO (3.7 mL, 51.61 mmol, 2.5 equiv) in CH_2Cl_2 (330 mL) was added and the reaction mixture stirred for 5 min. A solution of alcohol (6.43 g, 20.65 mmol, 1 equiv) in CH_2Cl_2 (165 mL) was added to the mixture. After 1 h, Et_3N (12.1 mL, 86.71 mmol, 4.2 equiv) was added and the mixture was allowed to warm to room temperature. The reaction was quenched with water and the product was extracted with CH_2Cl_2. The combined organic layers were washed with brine then dried over $MgSO_4$, filtered and concentrated under reduced pressure. With no further purification the aldehyde was obtained as a colourless oil, 7.04 g.

The aldehyde (3.54 g, 11.45 mmol, 1 equiv) was dissolved in *tert*-butanol (160 mL), THF (80 mL) and water (40 mL). 2-Methyl-3-butene (57.2 mL, 2 M, 114.45 mmol, 10 equiv), NaH_2PO_4 (8.24 g, 68.67 mmol, 6 equiv) and sodium chlorite (6.21 g, 68.67 mmol, 6 equiv) were added to the solution and the reaction mixture stirred for 30 min at room temperature. The reaction was quenched with brine and extracted with EtOAc. The extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was redissolved in methanol (40 mL) and thionyl chloride was added at 0 °C. The reaction mixture was allowed to warm to room temperature over night. The reaction was quenched with a saturated solution of potassium carbonate, then the product was extracted with CH_2Cl_2. The organic layers were combined and washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The ester was obtained by column chromatography in 8.5:1.5 petroleum ether/EtOAc to yield (**44**) as a colourless solid, 2.85 g, 76%. Mp 62–64 °C; $[\alpha]_D^{21}$ +21 (*c* 1.2, CH_2Cl_2); ^1H NMR (250 MHz, $CDCl_3$): δ 1.05–1.88 (7H, m, CH_2), 1.34 (3H, d, *J*=7.5 Hz, CH_3CHN), 2.02–2.19 (1H, m, CH_2), 2.41 (3H, s, Ar–CH_3), 2.49–2.58 (2H, m, CH_2C(O)OCH_3), 3.69 (3H, s, C(O)OCH_3), 3.98–4.18 (2H, m, C*H*NC*H*), 7.28 (2H, d, *J*=8.0 Hz, Ar–*H*), 7.70 (2H, d, *J*=8.0, Ar–*H*); ^{13}C NMR (100.6 MHz): δ 13.7, 21.5, 21.9, 27.9, 29.0, 30.2, 31.4, 48.1, 51.6×2, 126.7, 129.6, 138.7, 142.8, 174.0; FTIR (thin film): 2942 (s), 2872 (m), 1738 (s), 1598 (w), 1331 (s), 1286 (m), 1164 (s), 1104 (m) cm^{-1}; *m/z* (TOF ES): 308, 340 (MH^+); HRMS (TOF ES) calcd for $C_{17}H_{26}NO_4S$: 340.1583, found: 340.1568.

*4.3.17. 5-Methyl-hexahydro-indolizin-3-one (**45**)*

Magnesium turnings (934 mg, 38.91 mmol, 30 equiv) were flame dried in a two-neck flask fitted with a reflux condenser. The flask was placed under nitrogen and methanol (5.3 mL) was added followed by dropwise addition of a solution of the ester (422 mg, 1.30 mmol, 1 equiv) in methanol (10.6 mL). The solution was left at room temperature overnight then heated at reflux for 1 h. The reaction was allowed to cool to room temperature and was then quenched with 1 M $HCl_{(aq)}$ until all salts had dissolved. The product was extracted with EtOAc and the extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The lactam was obtained by column chromatography in EtOAc to give (**45**) a colourless oil, 138 mg (69%, recovered 17% ester). $[\alpha]_D^{20}$ −102 (*c* 0.01 g/mL, CH_2Cl_2); ^1H NMR (250 MHz, $CDCl_3$): δ 1.12–1.71 (5H, m, CH_2), 1.62 (3H, d, *J*=6.5 Hz, CH_3CH), 1.75–1.90 (2H, m, CH_2), 2.02–2.16 (1H, m, CH_2), 2.36–2.56 (2H, m, C(O)CH_2), 3.19–3.37 (2H, m, C*H*NC*H*); ^{13}C NMR: δ 19.8, 22.8, 25.5, 31.9, 32.6, 33.7, 52.5, 59.3, 175.6; FTIR (thin film): 2934 (s), 2860 (s), 1682 (s) cm^{-1}; *m/z* (EI): 138, 153 (M); HRMS (EI) calcd for $C_9H_{15}NO$: 153.1154, found: 153.1152.[15]

4.3.18. (−)-Monomorine

To a solution of (**44**) (18 mg, 0.177 mmol, 1 equiv) in hexane (2.3 mL) at −78 °C was added *n*-BuLi (2.2 M, 160 mL,

0.35 mmol, 3 equiv). The reaction was allowed to warm to 0 °C and stirred for 1.5 h. The reaction was quenched with water and warmed to room temperature. The organic layer was separated and the aqueous layer extracted with diethyl ether. The organic layers were combined and washed with $Na_2CO_{3(aq)}$ and brine. The organic layers were concentrated under reduced pressure to give (**46**) as a cream coloured solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.90 (3H, t, J=7.0 Hz, CH_2CH_3), 1.07–3.23 (21H, m), 9.18 (1H, br, N*H*), 9.39 (1H, br, N*H*); ^{13}C NMR: δ 13.8, 19.4, 22.3, 22.9, 25.8, 27.2, 28.0, 30.5, 38.4, 42.5, 54.6, 57.8, 210.0.

The crude residue was diluted in methanol (3.5 mL) and to this solution was added 10% Pd/C (12 mg). The reaction mixture was placed under hydrogen balloon and left to stir overnight. The reaction mixture was filtered through hyflo supercel with CH_2Cl_2, then concentrated under reduced pressure. (−)-Monomorine was obtained by column chromatography in 9:1 pentane/Et_2O as a colourless solid, 5 mg, 22%. $[\alpha]_D^{22}$ −30 (*c* 1, hexane), (lit. $[\alpha]_D^{20}$ −26.4 (*c* 1.0, hexane));[20] ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (3H, t, J=7.0 Hz, CH_2CH_3), 1.14 (3H, d, J=6.5 Hz, $CHCH_3$), 1.17–1.56 (10H, m, CH_2), 1.61–1.89 (6H, m, CH_2), 2.02–2.11 (1H, m, NC*H*), 2.16–2.26 (1H, m, NC*H*), 2.42–2.51 (1H, m, NC*H*); ^{13}C NMR (100.6 MHz): δ 14.2, 22.9×2, 24.9, 29.4, 29.8, 30.3, 30.9, 35.8, 39.7, 60.2, 62.9, 67.1; *m/z* (EI): 138, 149, 194; HRMS (TOF ES) calcd for $C_{13}H_{26}N$: 196.2065, found: 196.2068.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.01.071.

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