Synthesis of Substituted Pyridines and Pyridazines via Ring Closing Metathesis

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Electronic Supplementary Information

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General Experimental Details. All solvents and reagents requiring purification were purified using standard laboratory techniques according to methods published by Perrin, Armarego, and Perrin (Pergamon Press, 1966) apart from CH_2Cl_2, PhMe, THF and Et_2O which were dried by filtration through an activated alumina purification column. Petrol refers to petroleum ether in the boiling range 40–60 ^oC. Flash column chromatography (FCC) was performed using oven dried Merck Kieselgel 60 (40–63 μm). Proton nuclear magnetic resonance spectra (NMR) were recorded at 400 MHz or 500 MHz. ^{13}C NMR spectra were recorded at 100 MHz or 125 MHz as stated. Coupling constants are quoted to the nearest 0.5 Hz. Where mixtures of isomers (*e.g.* diastereoisomers and rotamers) have been characterized together integrals are normalized to the major isomer. Mass spectra under the conditions of electrospray ionisation (ESI) were recorded on a Fisons Platform II. Mass spectra under the conditions of field ionisation (FI) were recorded on a Micromass LCT. Mass spectra under the conditions of chemical ionisation (CI) were recorded on a Fisons Autospec-oaTof. Infrared spectra (IR) were recorded as evaporated films or KBr discs. Melting points were obtained using a Leica VMTG heated-stage microscope and are uncorrected.

Experimental Procedures and Data for the Synthesis of Pyridines

Procedure A for the formation of 2-bromo-*N*-methoxy-*N*-methylamides:[1] The corresponding acid bromide (230 mol%) was added dropwise to a stirred suspension of *N*,*O*-dimethylhydroxylamine hydrochloride (100 mol%) and K_2CO_3 (500 mol%) in MeCN (1 mL/mmol) at room temperature. After 1 hour the reaction mixture concentrated *in vacuo*. The residue was dissolved in water (2 mL/mmol) and extracted with CH_2Cl_2 (3 × 2 mL/mmol). The organic extracts were combined, dried (Na_2SO_4) and concentrated *in vacuo* to afford the crude product that was used without further purification.

Procedure B for the formation of 2-(*N*-4-methylphenylsulfonamido)-*N*-methoxy-*N*-methylamides: The corresponding *p*-toluenesulfonamide (100 mol%) was added to a stirred suspension of 2-bromo-*N*-methoxy-*N*-methylamide (100 mol%) and K_2CO_3 (500 mol%) in MeCN (3 mL/mmol) and the reaction mixture was heated at reflux until TLC analysis indicated that the starting material was consumed. The mixture was then cooled to room temperature, filtered and concentrated *in vacuo*. Purification of the residue by FCC, under the conditions noted, afforded the corresponding amide.

Procedure C for the formation of α,β-unsaturated ketones using 2-bromopropene: *t*-BuLi (1.7 M in pentane, 400 mol%) was added dropwise to a stirred solution of 2-bromopropene (200 mol%) in THF (4 mL/mmol) at –78 °C and stirring was continued for 30 minutes. Theis solution was then transferred dropwise, *via* cannula (approximately one drop per second), to a stirred solution of the corresponding amide (100 mol%) in THF (8 mL/mmol) at –78 °C. The reaction mixture was stirred for 1 hour at –78 C and was then quenched at this temperature with saturated aq. NH_4Cl (10 mL/mmol) and extracted with Et_2O (3 × 10 mL/mmol). The organic portions were combined, dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by FCC, under the conditions noted, afforded the corresponding α,β-unsaturated ketones.

Procedure D for ring-closing metathesis: Hoveyda-Grubbs 2nd generation catalyst (1.5-10 mol%) was added to a stirred solution of α,β-unsaturated amide (100 mol%) in argon sparged CH_2Cl_2 or toluene (25 mL/mmol), and the mixture was heated at the specified temperature until TLC analysis indicated that the starting material was consumed. The mixture was then concentrated *in vacuo* and purified by FCC, under the conditions noted, to afford the corresponding product.

Procedure E for base-mediated aromatisation: DBU (500 mol%) was added to a stirred solution of dihydropyridone (100 mol%) in THF (2 mL/mmol) and stirring was continued at room temperature until TLC analysis indicated complete consumption of starting material. The reaction mixture was filtered through a small plug of silica, eluting with EtOAc-*i*-PrOH-20% aq. NH_3 (12:7:1). The solvent was concentrated *in vacuo* and the residue was purified by FCC, under the conditions noted, to afford the corresponding 3-hydroxypyridine.

[1] M. F. Mechelke, A. I. Meyers, *Tetrahedron Lett.* 2000, **41**, 4339-4342.

Procedure F for allylic amination under Mitsunobu conditions: To a solution of the corresponding allylic alcohol (200 mol%), PPh_3 (300 mol%), and sulfonamide **11** (1 mmol) in THF (10 mL/mmol) was added dropwise DIAD (260 mol%). After 16 hours the reaction mixture concentrated *in vacuo*. Purification of the residue by FCC, under the conditions noted, afforded the corresponding product.

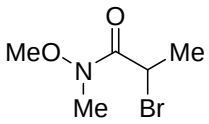
Procedure G for acetal deprotection: To a solution of the corresponding acetal (100 mol%) in acetone (15 mL/mmol) was added 6 M aq. HCl (3 mL/mmol) at 0 ºC and the reaction mixture was stirred for 4 hours at room temperature. The reaction mixture was then diluted with EtOAc (70 mL/mmol) and washed with saturated aq. $NaHCO_3$ (50 mL/mmol) and brine (50 mL/mmol). The organic portion was then dried ($MgSO_4$) and concentrated *in vacuo* to afford the corresponding aldehyde which was used without further purification.

Procedure H for the formation of allylic alcohols using vinylmagnesium bromide: To a solution of the corresponding aldehyde (100 mol%) in THF (20 mL/mmol) at -78 ºC, was added dropwise vinylmagnesium bromide (1.0 M in THF, 150 mol%). After 30 minutes the reaction mixture was warmed to 0 ºC. After 2 hours saturated aq. NH_4Cl (20 mL/mmol). The mixture was then extracted with EtOAc (2 × 50 mL/mmol). The organic extracts were combined, washed with brine (50 mL/mmol), dried ($MgSO_4$) and concentrated *in vacuo* to afford the product which was used without further purification.

Procedure I for the oxidation of allylic alcohols with Jones reagent: To a solution of the corresponding cyclic alcohol (100 mol%) in acetone (10 mL/mmol) at 0 ºC, was added dropwise Jones reagent (100 mol%). After 30 minutes 2-propanol (0.3 mL/mmol) was added. After a further 15 minutes the reaction mixture was diluted with EtOAc (50 mL/mmol) and washed with saturated aq. $NaHCO_3$ (50 mL/mmol). The aqueous layer was then back extracted with EtOAc (25 mL/mmol). The organic extracts were combined, washed with brine (30 mL/mmol), dried ($MgSO_4$) and concentrated *in vacuo* to afford the product which was used without further purification.

Procedure J for one-pot aromatization and triflation: A solution of the corresponding enone (100 mol%) in THF (20 mL/mmol) was treated with DBU (500 mol%) and stirred until all the starting material was consumed (TLC monitoring). *N*-Phenyltriflimide (150 mol%) was added and the reaction mixture was stirred for 6 hours. The reaction mixture was then concentrated *in vacuo* and the residue was purified by FCC, under the conditions noted, to afford the corresponding pyridine triflate.

2-Bromo-*N*-methoxy-*N*-methylpropanamide (1a)



General Procedure A: 2-Bromopropionyl bromide (2.40 mL, 23.0 mmol) was employed to afford the title compound (2.02 g, 100%) as an analytically pure, colourless oil.

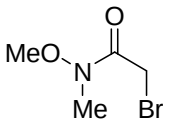
^{1}H NMR (400 MHz, $CDCl_3$): 4.90 (1H, q, J = 7.0 Hz), 3.80 (3H, s), 3.23 (3H, s), 1.79 (3H, d, J = 7.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): 166.5, 61.6, 36.6, 32.6, 21.3.

MS *m/z* (CI) 196.0 ($[M+H]^+$, 100%), 198.0 ($[M+H]^+$, 98%); HRMS: (CI) Calcd. for $C_5H_{11}NO_2{}^{79}Br$ $[M+H]^+$: 195.9969, Found: 195.9973.

FTIR 2976, 2939, 1671, 1447, 1420, 1388, 1296, 1176, 1114, 1065 cm^{-1}.

2-Bromo-*N*-methoxy-*N*-methylacetamide (1b)



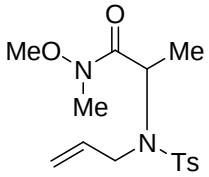
General Procedure A: Bromoacetyl bromide (2.00 mL, 23.1 mmol) was employed to afford the title compound (1.70 g, 100%) as an analytically, pure colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): 3.99 (2H, s), 3.78 (3H, s), 3.22 (3H, s).

^{13}C NMR (100 MHz, $CDCl_3$): 167.6, 61.6, 32.5, 25.1.

The spectroscopic properties of this compound were consistent with the data reported in the literature.[2]

2-(*N*-Allyl-4-methylphenylsulfonamido)-*N*-methoxy-*N*-methylpropanamide (2a)



[2] M. Groesbeek, *Rec. Trav. Chim.* 1992, **8**, 149-154.

General Procedure B: Amide **1a** (2.02 g, 10.3 mmol) and *p*-toluenesulfonamide (2.18 g, 10.3mmol) were employed. Purification by FCC (2:1 petrol-EtOAc) afforded the title compound (2.51 g, 74%) as a colourless oil.

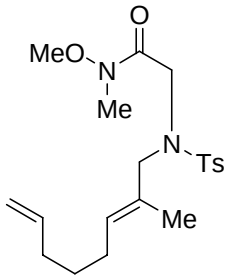
^{1}H NMR (400 MHz, $CDCl_3$): 7.69 (2H, d, J = 8.5 Hz), 7.27 (2H, d, J = 8.5 Hz), 5.88 (1H, ddt, J = 17.0, 10.5, 6.0 Hz), 5.19 (1H, dd, J = 17.0, 1.5 Hz), 5.16-5.09 (1H, m), 5.08 (1H, dd, J = 10.5, 1.5 Hz), 4.12 (1H, dd, J = 16.5, 6.0 Hz), 3.99 (1H, dd, J = 16.5, 6.0 Hz), 3.76 (3H, s), 3.06 (3H, s), 2.41 (3H, s), 1.27 (3H, d, J = 7.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): 172.2, 143.3, 137.2, 136.2, 129.5, 127.4, 116.5, 61.7, 51.1, 47.1, 32.0, 21.5, 16.0.

MS (ESI$^+$) Calcd. for $C_{15}H_{22}N_2NaO_4S$ $[M+Na]^+$: 349.1192. Found: 349.1198.

FTIR 2980, 2939, 1668, 1598, 1446, 1331, 1161, 1093, 1066 cm^{-1}.

(*E*)-*N*-Methoxy-*N*-methyl-2-(4-methyl-*N*-(2-methylocta-2,7-dienyl)phenylsulfonamido)acetamide (2b)



General Procedure B: Amide **1b** (145 mg, 0.80 mmol) and (*E*)-4-Methyl-*N*-(2-methylocta-2,7-dienyl)benzenesulfonamide (230 mg, 0.80 mmol) were employed. Purification by FCC (3:1 petrol-EtOAc) afforded the title compound (206 mg, 66%) as a colourless oil.

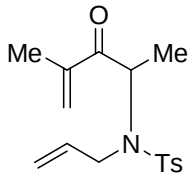
^{1}H NMR (400 MHz, $CDCl_3$): 7.75 (2H, d, J = 8.0 Hz), 7.26 (2H, d, J = 8.0 Hz), 5.75 (1H, ddt, J = 17.0, 10.5, 7.0 Hz), 5.27 (1H, t, J = 7.0 Hz), 5.00-4.90 (2H, m), 4.16 (2H, s), 3.83 (2H, s), 3.65 (3H, s), 3.07 (3H, s), 2.39 (3H, s), 2.03-1.96 (4H, m), 1.56 (3H, s), 1.38 (2H, app quintet, J = 7.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): 169.2, 143.0, 138.5, 137.4, 130.7, 130.0, 129.3, 127.6, 114.7, 61.4, 55.6, 45.0, 33.3, 32.3, 28.6, 27.3, 21.6, 14.0.

MS (ESI$^+$) Calcd. for $C_{20}H_{30}N_2NaO_4S$ $[M+Na]^+$: 417.1818. Found: 417.1808.

FTIR 2928, 1685, 1598, 1444, 1339, 1157, 1092 cm^{-1}.

***N*-Allyl-4-methyl-*N*-(4-methyl-3-oxopent-4-en-2-yl)benzenesulfonamide (3a)**



General Procedure C: Amide **2a** (1.28 g, 3.93 mmol) was employed. Purification by FCC (15:1 petrol-EtOAc) afforded the title compound (1.04 g, 86%) as a colourless oil.

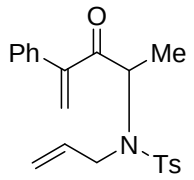
^{1}H NMR (400 MHz, $CDCl_3$): 7.68 (2H, d, *J* = 9.0 Hz), 7.28 (2H, d, *J* = 9.0 Hz), 6.27 (1H, s), 5.90 (1H, s), 5.75 (1H, ddt, *J* = 17.0, 10.0, 6.0 Hz), 5.37 (1H, q, *J* = 7.0 Hz), 5.10 (1H, dd, *J* = 17.0, 1.0 Hz), 5.06 (1H, dd, *J* = 10.0, 1.0 Hz), 3.90 (1H, dd, *J* = 17.0, 6.0 Hz), 3.72 (1H, dd, *J* = 17.0, 6.0 Hz), 2.42 (3H, s), 1.80 (3H, s), 1.15 (3H, d, *J* = 7.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): 199.4, 143.5, 142.3, 137.1, 135.2, 129.7, 127.4, 126.5, 117.4, 54.3, 47.1, 21.5, 17.9, 14.4.

MS (ESI^+) Calcd. for $C_{16}H_{21}NNaO_3S$ $[M+Na]^+$: 330.1134. Found: 330.1135.

FTIR 2985, 1682, 1597, 1453, 1344, 1161, 1091, 1013 cm^{-1}.

***N*-Allyl-4-methyl-*N*-(3-oxo-4-phenylpent-4-en-2-yl)benzenesulfonamide (3b)**



n-BuLi (1.6 M in hexanes, 4.88 mmol) was added dropwise to a stirred solution of α-bromostyrene (318 μL, 2.45 mmol) in THF (10 mL) at -78 °C and stirring was continued for 1 hour. The solution was then added dropwise *via* cannula (approximately one drop per second) to a stirred solution of amide **2a** (400 mg, 1.22 mmol) in THF (10 mL) at -78 °C. The reaction mixture was stirred for 3 hours at -78 °C then quenched at this temperature with saturated aq. NH_4Cl (20 mL). The aqueous layer was extracted with Et_2O (3 × 20 mL). The organic layers were combined, dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by FCC (10:1 petrol-EtOAc) afforded the title compound (263 mg, 58%) a colourless oil.

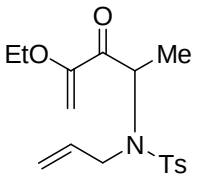
^{1}H NMR (400 MHz, $CDCl_3$): 7.70 (2H, d, *J* = 8.0 Hz), 7.24–7.38 (7H, m), 6.29 (1H, s), 6.00 (1H, s), 5.76 (1H, ddt, *J* = 17.0, 10.0, 6.0 Hz), 5.27 (1H, q, *J* = 7.0 Hz), 5.13 (1H, dd, *J* = 17.0, 1.0 Hz), 5.05 (1H, dd, *J* = 10.0, 1.0 Hz), 3.93-3.80 (2H, m), 2.42 (3H, s), 1.27 (3H, d, *J* = 7.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): 199.9, 147.3, 143.6, 137.1, 136.7, 135.2, 129.7, 128.4, 128.1, 127.5, 127.3, 125.6, 117.7, 57.0, 47.9, 21.5, 14.9.

MS (ESI^+) Calcd. for $C_{21}H_{23}NNaO_3S$ $[M+Na]^+$: 392.1291. Found: 392.1296.

FTIR 3421, 1688, 1340, 1200, 1160, 1006 cm^{-1}.

***N*-Allyl-*N*-(4-ethoxy-3-oxopent-4-en-2-yl)-*p*-toluenesulfonamide (3c)**



t-BuLi (1.7 M in pentane, 2.67 mmol) was added dropwise to a stirred solution of ethyl vinyl ether (264 μL, 2.75 mmol) in THF (10 mL) at -78 °C and stirring was continued at 0 °C for 15 minutes. The solution was then added dropwise *via* cannula (approximately one drop per second) to a stirred solution of amide **2a** (300 mg, 0.92 mmol) in THF (10 mL) at -78 °C. The reaction mixture was stirred for 3 hours at -78 °C before quenching at this temperature with saturated aq. NH_4Cl solution (20 mL). The aqueous layer was extracted with Et_2O (3 × 20 mL). The organic layers were combined, dried (Na_2SO_4) and concentrated *in vacuo* to afford the crude product. Purification by FCC (9:1 petrol-EtOAc) afforded the title compound (271 mg, 88%) as a colourless oil.

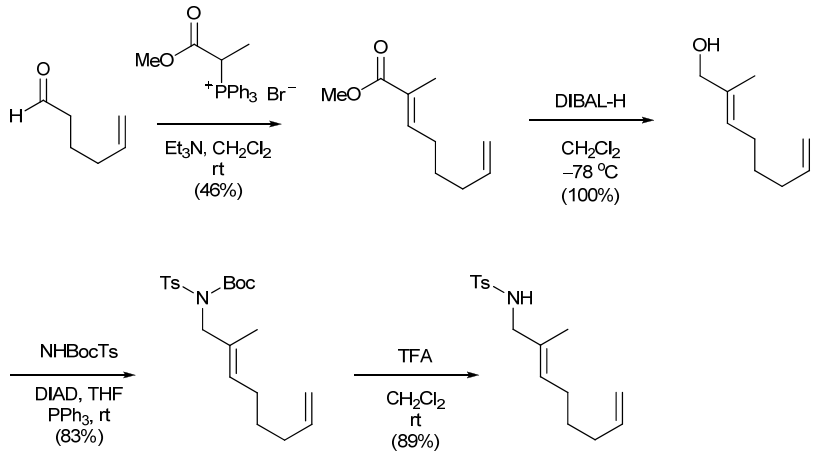
^{1}H NMR (400 MHz, $CDCl_3$): 7.66 (2H, d, *J* = 8.5 Hz), 7.25 (2H, d, *J* = 8.5 Hz), 5.91-5.80 (1H, m), 5.32 (1H, q, *J* = 7.0 Hz), 5.15 (1H, d, *J* = 3.0 Hz), 5.21-5.05 (2H, m), 4.45 (1H, d, *J* = 3.0 Hz), 4.02-3.86 (2H, m), 3.82 (2H, q, *J* = 7.0 Hz), 2.41 (3H, s), 1.40 (3H, t, *J* = 7.0 Hz), 1.31 (3H, d, *J* = 7.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): 195.7, 156.3, 143.2, 137.2, 135.9, 129.5, 127.3, 116.9, 92.3, 63.9, 56.0, 47.9, 21.5, 15.3, 14.2.

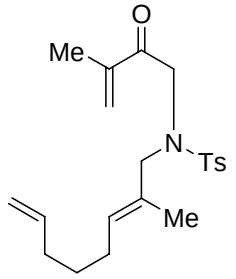
MS (ESI^+) Calcd. for $C_{17}H_{23}NNaO_4S$ $[M+Na]^+$: 360.1240. Found: 360.1245.

FTIR 2983, 2940, 1715, 1608, 1494, 1446, 1341, 1304, 1160, 1091, 1057 cm^{-1}.

Scheme for the synthesis of the sulfonamide precursor to 10.



(*E*)-4-Methyl-*N*-(3-methyl-2-oxobut-3-enyl)-*N*-(2-methylocta-2,7-dienyl)benzene-sulfonamide (3d)



General Procedure C: Amide **2b** (200 mg, 0.51 mmol) was employed. Purification by FCC (10:1 petrol-EtOAc) to give the title compound (82 mg, 43%) as a colourless oil.

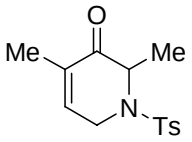
^{1}H NMR (400 MHz, $CDCl_3$): 7.70 (2H, d, J = 8.5 Hz), 7.28 (2H, d, J = 8.5 Hz), 5.91 (1H, s), 5.79-5.77 (1H, m), 5.74 (1H, ddt, J = 17.0, 10.0, 6.5 Hz), 5.17 (1H, t, J = 7.0 Hz) 4.99-4.90 (2H, m), 4.36 (2H, s), 3.75 (2H, s), 2.42 (3H, s), 2.00-1.93 (4H, m), 1.80 (3H, s), 1.56 (3H, s), 1.35 (2H, app quintet, J = 7.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): 195.4, 143.2, 142.7, 138.5, 137.1, 131.1, 129.8, 129.4, 127.4, 125.0, 114.7, 55.9, 50.4, 33.2, 28.5, 27.3, 21.6, 17.7, 14.0.

MS (ESI^+) Calcd. for $[M+Na]^+$: $C_{21}H_{29}NNaO_3S$. Found: 398.1760.

FTIR 2925, 2857, 1694, 1639, 1598, 1495, 1453, 1338, 1157, 1092, 1068 cm^{-1}.

2,4-Dimethyl-1-tosyl-1,2-dihydropyridin-3(6*H*)-one (4a)



General Procedure D: Enone **3a** (1.04 g, 3.39 mmol) and Hoveyda-Grubbs 2nd generation catalyst (32 mg, 1.5 mol%) were employed using CH_2Cl_2 (85 mL) at reflux for 16 hours. Purification by FCC (4:1 petrol-EtOAc) afforded the title compound (926 mg, 98%) as a colourless oil.

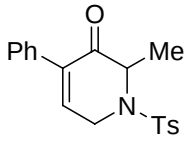
^{1}H NMR (400 MHz, $CDCl_3$): 7.63 (2H, d, J = 7.5 Hz), 7.26 (2H, d, J = 7.5 Hz), 6.48-6.45 (1H, ddq, J = 5.0, 2.0, 1.5 Hz), 4.53 (1H, q, J = 7.0 Hz), 4.37 (1H, ddq, J = 20.0, 5.0, 1.5 Hz), 3.98 (1H, ddq, J = 20.0, 2.0, 2.0 Hz), 2.40 (3H, s), 1.58-1.56 (3H, ddd, J = 2.0, 2.0, 1.5 Hz), 1.27 (3H, d, J = 7.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): 195.6, 143.8, 138.5, 136.4, 133.0, 129.9, 127.1, 57.3, 40.9, 21.5, 15.4, 15.1.

MS (ESI^+) Calcd. for $C_{14}H_{17}NNaO_3S$ $[M+Na]^+$: 302.0821. Found: 302.0831.

FTIR 2920, 1682, 1349, 1164, 1094, 1007 cm^{-1}.

2-Methyl-4-phenyl-1-tosyl-1,2-dihydropyridin-3(6*H*)-one (4b)



General Procedure D: Enone **3b** (260 mg, 0.70 mmol) and Hoveyda-Grubbs 2nd generation catalyst (44 mg, 10 mol%) were employed and the reaction mixture was heated in PhMe (18 mL) at 65 °C for 16 hours. Purification by FCC (4:1 petrol-EtOAc) afforded the title compound (229 mg, 95%) as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$): 7.68 (2H, d, J = 8.5 Hz), 7.31-7.25 (5H, m), 6.98-6.94 (2H, m), 6.69 (1H, dd, J = 5.5, 2.0 Hz), 4.67 (1H, q, J = 7.0 Hz), 4.62 (1H, dd, J = 21.0, 5.5 Hz), 4.20 (1H, dd, J = 21.0, 2.0 Hz), 2.37 (3H, s), 1.41 (3H, d, J = 7.0 Hz).

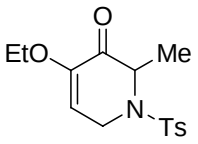
^{13}C NMR (100 MHz, $CDCl_3$): 193.6, 144.1, 140.2, 137.2, 136.2, 134.2, 130.1, 128.3, 128.3, 128.0, 127.2, 57.8, 41.4, 21.5, 15.5.

MS (ESI^+) Calcd. for $C_{19}H_{19}NNaO_3S$ $[M+Na]^+$: 364.0978. Found: 364.0973.

FTIR 2983, 1685, 1597, 1493, 1445, 1349, 1163, 1105, 1042 cm^{-1}.

M.P. 127–130 °C.

4-Ethoxy-2-methyl-1-tosyl-1,2-dihydropyridin-3(6*H*)-one (4c)



General Procedure D: Enone **3c** (248 mg, 0.74 mmol) and Hoveyda-Grubbs 2nd generation catalyst (44 mg, 10 mol%) were employed and the reaction mixture was heated in PhMe (18 mL) at 60 °C for 16 hours. Purification by FCC (3:2 petrol:-EtOAc) afforded the title compound (203 mg, 89%) as a colourless oil.

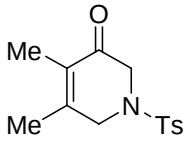
^{1}H NMR (400 MHz, $CDCl_3$): 7.63 (2H, d, *J* = 8.5 Hz), 7.26 (2H, d, *J* = 8.5 Hz), 5.53 (1H, dd, *J* = 6.5, 3.0 Hz), 4.61 (1H, q, *J* = 7.0 Hz), 4.47 (1H, dd, *J* = 19.5, 6.5 Hz), 4.09 (1H, dd, *J* = 19.5, 3.0 Hz), 3.67-3.45 (2H, m), 2.39 (3H, s), 1.32 (3H, d, *J* = 7.0 Hz), 1.25 (3H, t, *J* = 7.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): 190.6, 147.7, 143.9, 136.4, 130.0, 127.1, 110.9, 63.5, 58.1, 39.9, 21.5, 15.4, 14.1

MS (ESI^+) Calcd. For $C_{15}H_{19}NNaO_4S$ $[M+Na]^+$: 332.0927. Found: 332.0918.

FTIR 2982, 1698, 1633, 1445, 1350, 1254, 1158, 1101, 1055 cm^{-1}.

4,5-Dimethyl-1-tosyl-1,2-dihydropyridin-3(6*H*)-one (4d)



General Procedure D: Enone **3d** (80 mg, 0.21 mmol) and Hoveyda-Grubbs 2nd generation catalyst (13 mg, 10 mol%) were employed and the reaction mixture was heated in PhMe (50 mL) at 60 °C for 16 hours. Purification by FCC (3:1 petrol-EtOAc) afforded the title compound (48 mg, 84%) as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$): 7.64 (2H, d, J = 8.0 Hz), 7.33 (2H, d, J = 8.0 Hz), 3.84 (2H, s), 3.73 (2H, s), 2.42 (3H, s), 1.88 (3H, s), 1.64 (3H, s).

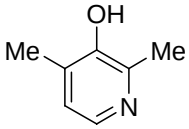
^{13}C NMR (100 MHz, $CDCl_3$): 190.9, 149.9, 144.3, 132.7, 130.4, 130.0, 127.7, 52.2, 49.3, 21.5, 18.5, 10.0.

MS (ESI^+) Calcd. for $C_{14}H_{17}NNaO_3S$ $[M+Na]^+$: 302.0821. Found: 302.0822.

FTIR 2922, 1672, 1644, 1596, 1445, 1396, 1344, 1290, 1242, 1168, 1140, 1022 cm^{-1}.

M.P. 100-104 °C.

2,4-Dimethylpyridin-3-ol (5)



General Procedure E: Enone **4a** (300 mg, 1.08 mmol) was employed. Purification by FCC (10:1 EtOAc-MeOH) afforded the title compound (116 mg, 88%) as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$): 10.40 (1H, br s), 7.79 (1H, d, J = 5.0 Hz), 6.96 (1H, d, J = 5.0 Hz), 2.45 (3H, s), 2.28 (3H, s).

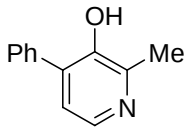
^{13}C NMR (100 MHz, $CDCl_3$): 152.0, 146.1, 137.3, 135.9, 124.3, 18.5, 16.6.

M.P. 92-95 °C [lit. 105–106 °C].[3]

The spectroscopic properties of this compound were consistent with the data reported in the literature.[3]

[3] Y. Wang, M. C. Liu, T. S. Lin, A. C. Sartorelli, *J. Med. Chem.* 1992, **35**, 3667-3671.

2-Methyl-4-phenylpyridin-3-ol (6)



General Procedure E: Enone **4b** (229 mg, 0.67 mmol) was employed. Purification by FCC (20:1 EtOAc-MeOH) afforded the title compound (108 mg, 87%) as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$): 7.92 (1H, d, *J* = 5.0 Hz), 7.51-7.40 (5H, m), 7.00 (1H, d, *J* = 5.0 Hz), 5.76 (1H, br s), 2.52 (3H, s)

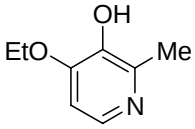
^{13}C NMR (100 MHz, $CDCl_3$): 147.8, 147.7, 139.9, 135.6, 135.5, 129.1, 128.8, 128.5, 122.5, 19.1.

MS (ESI^+) Calcd. for $C_{12}H_{12}NO$ $[M+H]^+$: 186.0913. Found: 186.0911.

FTIR 2934, 1596, 1498, 1206, 1110 cm^{-1}.

M.P. 108-111 °C.

4-Ethoxy-2-methylpyridin-3-ol (7)



General Procedure E: Enone **4c** (193 mg, 0.62 mmol) was employed. Purification by FCC (10:1 EtOAc-MeOH) afforded the title compound (73 mg, 77%) as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$): 7.97 (1H, d, *J* = 6.0 Hz), 6.65 (1H, d, *J* = 6.0 Hz), 6.07 (1H, br s), 4.14 (2H, q, *J* = 7.0 Hz), 2.48 (3H, s), 1.44 (3H, t, *J* = 7.0 Hz).

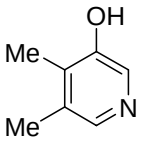
^{13}C NMR: (100 MHz, $CDCl_3$): 151.3, 145.1, 141.3, 140.3, 104.9, 64.4, 18.4, 14.6.

MS (ESI^+) Calcd. for $C_8H_{12}NO$ $[M+H]^+$: 154.0863. Found: 154.0862.

FTIR 1593, 1495, 1470, 1392, 1270, 1216, 1122, 1076 cm^{-1}.

M.P. 130-134 °C.

4,5-Dimethylpyridin-3-ol (8)



General Procedure E: Enone **4d** (42 mg, 0.15 mmol) was employed. Purification by FCC (10:1 EtOAc-MeOH) afforded the title compound as a colourless solid (15 mg, 79%).

^{1}H NMR (400 MHz, $CDCl_3$): 9.32 (1H, br s), 8.09 (1H, s), 7.86 (1H, s), 2.26 (3H, s), 2.24 (3H, s).

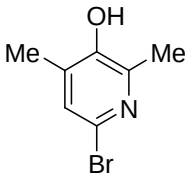
^{13}C NMR (100 MHz, $CDCl_3$): 153.8, 139.2, 134.9, 134.0, 132.6, 16.6, 11.6.

MS (ESI^+) Calcd. for $C_7H_{10}NO$ $[M+H]^+$: 124.0757. Found: 124.0752.

FTIR 2923, 1573, 1457, 1418, 1297, 1200, 1147, 1099, 1021 cm^{-1}.

M.P. 144-148 °C (decomp.)

6-Bromo-2,4-dimethylpyridin-3-ol (9)



N-Bromosuccinimide (159 mg, 0.89 mmol) was added to a solution of 3-hydroxy pyridine **5** (100 mg, 0.81 mmol) in MeCN (5 mL) and the mixture was heated at reflux for 1 hour. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. Purification by FCC (EtOAc) afforded the title compound (100 mg, 61%) as a red solid.

^{1}H NMR (400 MHz, $CDCl_3$): 7.11 (1H, app s), 6.35 (1H, br s), 2.44 (3H, s), 2.24 (3H, app d, J = 0.5 Hz).

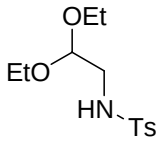
^{13}C NMR (100 MHz, $CDCl_3$): 149.2, 146.3, 136.8, 130.2, 127.4, 18.6, 15.8.

MS (ESI^+) Calcd. $C_7H_9{}^{79}BrNO$ for $[M+H]^+$: 201.9862. Found: 201.9862.

FTIR 3241, 2360, 2341, 1596, 1455, 1295, 1227, 1127, 1029 cm^{-1}.

M.P. 127-127 °C

***N*-(2,2-Diethoxyethyl)-4-methylbenzenesulfonamide (11)**



To a stirred solution of aminoacetaldehyde diethyl acetal (7.26 mL, 50.0 mmol) and anhydrous Et_3N (14.0 mL, 100 mmol) in CH_2Cl_2 (100 mL) was added dropwise a solution of *p*-toluenesulfonyl chloride (10.5 g, 55.0 mmol) in CH_2Cl_2 (100 mL) over 30 min at 0 ºC. After 1 hour the reaction mixture was diluted with water (200 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (100 mL). The organic extracts were combined, washed with 1 M aq. HCl (50 mL), water (100 mL), and saturated aq. $NaHCO_3$ (100 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification of the residue by FCC (4:1 petrol-EtOAc) afforded the title compound (13.7 g, 94%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$): 7.74 (2H, d, J = 8.0 Hz), 7.30 (2H, d, J = 8.0 Hz), 4.77 (1H, t, J = 6.0 Hz), 4.45 (1H, t, J = 6.0 Hz), 3.62 (2H, dq, J = 9.0, 7.0 Hz), 3.45 (2H, dq, J = 9.0, 7.0 Hz), 3.02 (2H, t, J = 6.0 Hz), 2.41 (3H, s), 1.15 (6H, t, J = 7.0 Hz).

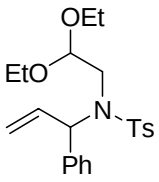
^{13}C NMR (100 MHz, $CDCl_3$): 143.4, 136.7, 129.6, 127.0, 100.6, 63.0, 45.4, 21.4, 15.1.

M.P. 67-68 ºC (CH_2Cl_2) [Lit. 66-67 ºC].[4]

The spectroscopic properties of this compound were consistent with the data reported in the literature.[5]

[4] V. P. Semenov, S. V. Ozernaya, I. M. Stroiman, K. A. Oglobin, *Chem. Het. Comp*. 1977, **12**, 1327-1331.
[5] R. J. Hall, P. Dharmasena, J. Marchant, A. F. Oliveira-Campos, M. R. P. Queiroz, M. M. Raposo, P. V. R. Shannon, *J. Chem. Soc. Perkin Trans. 1* 1993, 1879-1889.

_N_-(2,2-Diethoxyethyl)-4-methyl-_N_-(1-phenylprop-2-en-1-yl)benzenesulfonamide (12a)



$P(OMe)_3$ (0.17 mL, 1.44 mmol) was added to a solution of Wilkinson's catalyst (332 mg, 0.36 mmol) in THF (10 mL) at 30 ºC, under argon. In a separate vessel, sulfonamide **11** (3.00 g, 10.4 mmol) in THF (30 mL) was treated with LiHMDS (1.0 M in THF, 10.4 mmol) at room temperature. After 30 minutes this solution was added *via* cannula to the catalyst solution. 1-Phenylallyl acetate[6] (1.06 g, 5.53 mmol) was then added and the mixture was heated at 30 ºC for 16 hours. The reaction mixture was then cooled and diluted with EtOAc (200 mL). The organic layer was washed with a saturated aq. NH_4Cl (50 mL), brine (50 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the residue by FCC (9:1, petrol-EtOAc) afforded the title compound (1.72 g, 77%) as a clear oil.

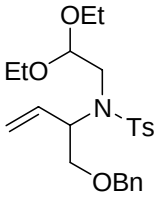
^{1}H NMR (400 MHz, $CDCl_3$): 7.68 (2H, d, J = 8.0 Hz), 7.22 (7H, m), 6.21 (1H, ddd, J = 17.0, 10.0, 7.5 Hz), 5.54 (1H, d, J = 7.5 Hz), 5.26 (1H, d, J = 10.0 Hz), 5.07 (1H, dd, J = 17.0), 4.51 (1H, t, J = 5.0 Hz), 3.64 (1H, app quintet, J = 7.0 Hz), 3.54 (1H, app quintet, J = 7.0 Hz), 3.39 (1H, app quintet, J = 7.0 Hz), 3.30 (2H, m), 3.19 (1H, dd, J = 15.0, 5.0 Hz), 2.43 (3H, s), 1.17 (3H, t, J = 7.0 Hz), 1.04 (3H, t, J = 6.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): 143.0, 138.4, 137.4, 135.2, 129.2, 128.1, 128.1, 127.4, 127.3, 118.8, 102.0, 64.2, 63.3, 62.9, 48.4, 21.3, 15.0, 15.0.

MS (ESI^+) Calcd. for $C_{22}H_{29}NNaO_4S$ $[M+Na]^+$: 426.1710, Found: 426.1710.

FTIR 3529, 3063, 3031, 2976, 2929, 1917, 1599, 1495, 1451, 1342, 1161, 1092, 1020 cm^{-1}.

_N_-[1-(Benzyloxy)but-3-en-2-yl]-_N_-(2,2-diethoxyethyl)-4-methylbenzenesulfonamide (12b)



[6] S. Shekhar, B. Trantow, A. Leitner, J. F. Hartwig, *J. Am. Chem. Soc*. 2006, **128**, 11770-11771.

General Procedure F: Sulfonamide **11** (302 mg, 1.05 mmol) and 1-(benzyloxy)but-3-en-2-ol[7] (382 mg, 2.14 mmol) were employed. Purification by FCC (10:0:0 to 1:1:0 to 0:0:1 petrol-EtOAc- CH_2Cl_2) afforded the title compound (355 g, 74%) as a colourless oil.

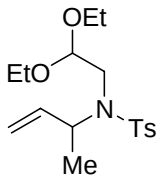
^{1}H NMR (500 MHz, $CDCl_3$): 7.73 (2H, d, *J* = 8.5 Hz), 7.27 (7H, m), 5.64 (1H, ddd, *J* = 17.0, 11.0, 6.0 Hz), 5.15 (1H, d, *J* = 11.0 Hz), 5.08 (1H, d, *J* = 17.0 Hz), 4.70 (1H, dd, *J* = 6.0, 4.5 Hz), 4.53 (1H, m), 4.46 (2H, s), 3.69 (4H, m), 3.53 (2H, dd, *J* = 9.5, 2.5 Hz), 3.27 (1H, dd, *J* = 15.5, 4.5 Hz) 3.13 (1H, dd, *J* = 15.5, 6.0 Hz) 2.40 (3H, s) 1.20 (3H, t, *J* = 7.0 Hz) 1.17 (3H, t, *J* = 7.0 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): 143.2, 138.0, 137.2, 134.0, 129.4, 128.2, 127.5 (2 signals), 127.4, 118.8, 102.9, 72.9, 70.8, 64.0, 63.4, 59.6, 48.4, 21.5, 15.3, 15.2.

MS (ESI^+) Calcd. for $C_{24}H_{33}NNaO_5S$ $[M+Na]^+$: 470.1972, Found: 470.1983.

FTIR 3306, 3031, 2979, 2873, 1808, 1751, 1599, 1496, 1376, 1340, 1110, 1027 cm^{-1}.

***N*-(But-3-en-2-yl)-*N*-(2,2-diethoxyethyl)-4-methylbenzenesulfonamide (12c)**



General Procedure F: Sulfonamide **11** (1.48g, 5.16 mmol) and 3-buten-2-ol (0.77 g, 8.9 mmol) were employed. Purification by FCC (1:0 to 9:1 petrol-EtOAc) afforded the title compound (1.54 g, 88%) as a colourless oil.

^{1}H NMR (500 MHz, $CHCl_3$) 7.74 (2H, d, *J* = 8.0 Hz), 7.30 (2H, d, *J* = 8.0 Hz), 5.52 (1H, ddd, *J* = 17.5, 11.0, 4.5 Hz), 5.04 (2H, m), 4.80 (1H, dd, *J* = 6.5, 4.0 Hz), 4.44 (1H, dq, *J* = 6.5, 4.5 Hz), 3.76 (2H, m), 3.59 (2H, m), 3.17 (1H, dd, *J* = 15.0, 4.5 Hz), 3.04 (1H, dd, *J* = 15.0, 6.5 Hz), 2.43 (3H, s), 1.22 (9H, m).

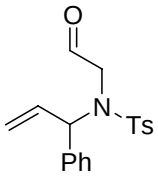
^{13}C NMR (125 MHz, $CHCl_3$) 143.3, 137.6, 137.4, 129.6, 127.3, 116.8, 102.9, 64.4, 63.6, 55.6, 47.5, 21.5, 17.7, 15.3, 15.2.

MS (ESI^+) Calcd. for $C_{17}H_{27}NNaO_4S$ $[M+Na]^+$: 364.1553, Found: 364.1551.

FTIR 2977, 2931, 2879, 1922, 1758, 1639, 1598, 1493, 1453, 1375, 1339, 1305, 1230, 1156, 1129, 1063 cm^{-1}.

[7] S. C. Bergmeier, D. M. Stanchina, *J. Org. Chem.* 1997, **62**, 4449-4456.

4-methyl-*N*-(2-oxoethyl)-*N*-(1-phenylprop-2-en-1-yl)benzenesulfonamide (13a)



General Procedure G: Acetal **12a** (619 mg, 1.53 mmol) was employed. Purification by FCC (4:1 petrol-EtOAc) afforded the title compound (391 mg, 78%) as a clear oil.

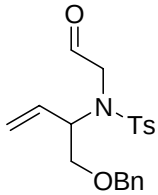
^{1}H NMR (500 MHz, $CDCl_3$): 9.13 (1H, dd, *J* = 2.0, 2.0 Hz), 7.72 (2H, d, *J* = 8.5 Hz), 7.30 (7H, m), 5.86 (2H, m), 5.27 (1H, d, *J* = 8.5 Hz), 5.10 (1H, m), 3.75 (1H, dd, *J* = 18.5, 2.0 Hz), 3.61 (1H, dd, *J* = 18.5, 2.0 Hz), 2.45 (3H, s).

^{13}C NMR (125 MHz, $CDCl_3$): 199.2, 143.9, 137.4, 136.5, 133.0, 129.7, 128.9, 128.5, 128.3, 127.6, 119.6, 62.9, 53.0, 21.6.

MS (ESI^+) Calcd. for $C_{19}H_{23}NNaO_4S$ $[M+CH_3OH+Na]^+$: 384.1240, Found: 384.1224.

FTIR 3661, 3447, 3088, 3063, 3031, 2828, 2723, 2586, 1734, 1643, 1598, 1494, 1452, 1340, 1155, 1095, 1019, 942 cm^{-1}.

***N*-[1-(Benzyloxy)but-3-en-2-yl]-4-methyl-*N*-(2-oxoethyl)benzenesulfonamide (13b)**



General Procedure G: Acetal **12b** (1.00 g, 2.23 mmol) was employed. Purification by FCC (10:0 to 3:1 petrol-EtOAc) afforded the title compound (715 mg, 86%) as a clear oil.

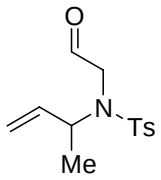
^{1}H NMR (500 MHz, $CDCl_3$): 9.54 (1H, s), 7.72 (2H, d, *J* = 8.0 Hz), 7.31 (5H, m), 7.21 (2H, d, *J* = 6.0 Hz), 5.58 (1H, ddd, *J* = 17.0, 11.0, 5.5 Hz), 5.19 (1H, d, *J* = 11.0 Hz), 5.08 (1H, d, *J* = 17.0 Hz), 4.71 (1H, m), 4.44 (1H, d, *J* = 12.0 Hz), 4.35 (1H, d, *J* = 12.0 Hz), 3.86 (1H, dd, *J* = 19.0, 1.5 Hz), 3.79 (1H, dd, *J* = 19.0, 1.5 Hz), 3.66 (1H, dd, *J* = 10.0, 4.5 Hz), 3.56 (1H, dd, *J* = 10.0, 4.5 Hz), 2.42 (3H, s).

^{13}C NMR (125 MHz, $CDCl_3$): 200.0, 143.8, 137.1, 136.8, 132.5, 129.7, 128.4, 127.9, 127.8, 127.4, 119.5, 73.3, 71.0, 58.4, 53.3, 21.5.

MS (ESI^+) Calcd. for $C_{21}H_{27}NNaO_5S$ $[M+CH_3OH+Na]^+$: 428.1502, Found: 428.1496.

FTIR 3444, 3088, 3054, 2919, 2862, 2721, 1733, 1641, 1598, 1341, 1157, 1099 cm^{-1}.

***N*-(But-3-en-2-yl)-4-methyl-*N*-(2-oxoethyl)benzenesulfonamide (13c)**



General Procedure G: Acetal **12c** (1.28 g, 4.1 mmol) was employed. Purification by FCC (10:0 to 7.5:2.5 petrol-EtOAc) afforded the title compound (1.10 g, 95%) as a clear oil.

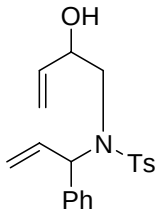
^{1}H NMR (400 MHz, $CHCl_3$) 9.61 (1H, dd, *J* = 2.0, 2.0 Hz), 7.74 (2H, dt, *J* = 8.5, 2.0 Hz), 7.32 (2H, dd, *J* = 8.5, 1.0 Hz), 5.57 (1H, ddd, *J* = 17.5, 10.5, 4.5 Hz), 5.16 (1H, ddd, *J* = 10.5, 2.0, 1.0 Hz), 5.09 (1H, ddd, *J* = 17.5, 2.0, 1.0 Hz), 4.63 (1H, dddq, *J* = 7.0, 4.5, 2.0, 2.0 Hz), 3.71 (1H, dd, *J* = 18.5, 1.5 Hz), 3.62 (1H, dd, *J* = 18.5, 1.5 Hz), 2.44 (3H, s), 1.13 (3H, d, *J* = 7.0 Hz).

^{13}C NMR (100 MHz, $CHCl_3$) 199.6, 143.9, 136.7, 136.6, 129.9, 127.3, 118.0, 54.1, 51.7, 21.5, 16.4.

MS (ESI^-) Calcd. for $C_{13}H_{16}NO_3S$ $[M-H]^-$: 266.0856, Found: 266.0861.

FTIR 3089, 2979, 2945, 2722, 1785, 1735, 1378, 1154, 1020 cm^{-1}.

***N*-(2-Hydroxybut-3-en-1-yl)-4-methyl-*N*-(1-phenylprop-2-en-1-yl)benzenesulfonamide (14a)**



General Procedure H: Aldehyde **13a** (358 mg, 1.08 mmol) was employed. Purification by FCC (9:1 to 8:1 petrol-EtOAc) gave the title compound (295 g, 77%, 1:0.7 dr) as a clear oil.

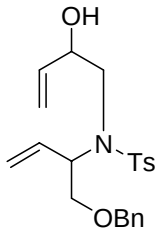
^{1}H NMR (500 MHz, $CDCl_3$): 7.75 (2H, d, *J* = 8.5 Hz), 7.69 (1.4H, d, *J* = 8.5 Hz), 7.31 (10H, m), 7.15 (1.7H, m), 6.08 (0.7H, ddd, *J* = 17.0, 10.5, 6.5 Hz), 5.92 (1H, ddd, *J* = 17.0, 10.5, 6.5 Hz), 5.78 (1H, d, *J* = 6.5 Hz), 5.64 (1.4H, m), 5.47 (1H, ddd, *J* = 17.0, 10.5, 6.0 Hz), 5.33 (0.7H, d, *J* = 10.5 Hz), 5.23 (2.4H, m), 5.03 (3.7H, m), 4.28 (0.7H, m), 3.50 (1H, m), 3.33 (1H, d, *J* = 3.0 Hz), 3.15 (3.4H, m), 2.62 (0.7H, d, *J* = 4.0 Hz), 2.45 (3H, s), 2.44 (2H, s).

^{13}C NMR (125 MHz, $CDCl_3$): 143.7, 143.6, 138.4, 137.9, 137.3, 137.3, 136.7, 136.5, 134.7, 133.0, 129.6, 129.5, 128.7 (2 signals), 128.5, 128.4, 128.3, 128.1, 127.8, 127.6, 119.8, 119.5, 116.1, 116.0, 71.9, 71.6, 64.0, 63.6, 51.6, 51.5, 21.5 (2 signals).

MS (ESI^+) Calcd. for $C_{20}H_{23}NNaO_3S$ $[M+Na]^+$: 380.1291, Found: 380.1291.

FTIR 3500, 3071, 3054, 3021, 1604, 1406, 1330, 1158 cm^{-1}.

***N*-[1-(Benzyloxy)but-3-en-2-yl]-*N*-(2-hydroxybut-3-en-1-yl)-4-methylbenzenesulfonamide (14b)**



General Procedure H: Aldehyde **13b** (300 mg, 0.80 mmol) was employed to afford the title compound (297 mg, 92%, 1:1 dr) as an analytically pure clear oil.

^{1}H NMR (400 MHz, $CDCl_3$) 7.73 (4H, d, *J* = 8.0 Hz), 7.29 (12H, m), 7.17 (2H, d, *J* = 8.0 Hz), 5.74 (3H, m), 5.57 (1H, ddd, *J* = 17.5, 11.0, 5.5 Hz), 5.37 (1H, dt, *J* = 17.0, 1.5 Hz), 5.28 (1H, dt, *J* = 17.0, 1.5 Hz), 5.14 (6H, m), 4.71 (1H, m), 4.51 (6H, m), 4.29 (1H, dddd,

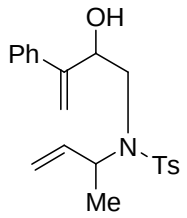
J = 6.0, 4.5, 2.5, 1.5 Hz), 3.93 (1H, d, *J* = 1.5 Hz), 3.83 (1H, m), 3.73 (1H, d, *J* = 3.0 Hz), 3.65 (3H, m), 3.41 (1H, dd, *J* = 15.0, 2.5 Hz), 3.23 (1H, m), 3.12 (1H, m), 2.84 (1H, dd, *J* = 15.0, 10.0 Hz), 2.41 (3H, s), 2.38 (3H, s).

^{13}C NMR (125 MHz, $CDCl_3$) 143.5, 143.4, 137.3, 137.2, 137.1, 137.0, 137.0, 136.9, 133.0, 132.6, 129.5, 129.5, 128.4 (2 signals), 128.0, 127.9 (2 signals), 127.8, 127.6, 127.5, 119.5, 119.2, 116.3, 116.0, 73.3, 72.7, 72.0, 71.3, 71.2, 69.1, 61.4, 58.9, 52.4, 50.9, 21.5 (2 signals).

MS (ESI^+) Calcd. for $C_{22}H_{27}NNaO_4S$ $[M+Na]^+$: 424.1553, Found: 424.1556.

FTIR 3468, 3087, 3064, 3031, 2982, 2923, 2866, 1875, 1805, 1643, 1495, 1336, 1156 cm^{-1}.

***N*-(But-3-en-2-yl)-*N*-(2-hydroxy-3-phenylbut-3-enyl)-4-methylbenzenesulfonamide (14c)**



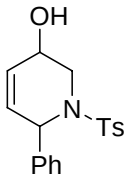
A solution of 1-phenylvinyl bromide (0.36 mL, 2.8 mmol) in THF (4 mL) was added dropwise to a mixture of magnesium turnings (0.14 g, 5.6 mmol), iodine (1 crystal) and THF (1 mL) and the reaction was stirred at room temperature for 30 min. The resulting Grignard was added to a solution of aldehyde **13c** (369 mg, 1.38 mmol) in THF at -78 ºC. After 1 hour the reaction mixture was warmed to 0 ºC. After a further 3 hours the reaction mixture was diluted with saturated aq. NH_4Cl (60 mL) and EtOAc (100 mL). The aqueous layer was extracted with EtOAc (2 × 30 mL). The organic extracts were combined, washed with brine (30 mL), then dried ($MgSO_4$), and concentrated *in vacuo*. Purification by FCC (1:0 to 5:1 petrol-EtOAc) afforded the title compound (444 mg, 68%, 1:1 dr) as a colourless oil. This material was contaminated with *ca.* 22% of starting aldehyde.

^{1}H NMR (400 MHz, $CDCl_3$) 7.68 (2H, dt, *J* = 8.5, 2.0 Hz), 7.65 (2H, dt, *J* = 8.5, 2.0 Hz), 7.32 (14H, m), 5.68 (1H, ddd, *J* = 17.5, 10.5, 4.5 Hz), 5.57 (2H, m), 5.37 (3H, m), 5.08 (2H, m), 4.99 (2H, m), 4.87 (2H, m), 4.54 (2H, m), 3.81 (1H, d, *J* = 3.0 Hz), 3.38 (1H, d, *J* = 3.0 Hz), 3.01 (4H, m), 2.41 (6H, m), 1.16 (3H, d, *J* = 7.0 Hz), 1.04 (3H, d, *J* = 7.0 Hz).

^{13}C NMR (101 MHz, $CDCl_3$) 148.8, 148.7, 143.6 (2 signals), 139.6, 139.3, 138.0, 136.5, 129.7 (2 signals), 128.4 (2 signals), 127.8, 127.3 (2 signals), 126.9, 126.8, 117.7, 116.9,

113.8, 113.6, 73.7, 72.2, 55.6, 54.9, 50.0, 49.6, 21.4 (2 signals), 17.9, 15.8. Only 31 signals were observed.

1-[(4-Methylphenyl)sulfonyl]-6-phenyl-1,2,3,6-tetrahydropyridin-3-ol (15a)



General Procedure D: Alcohol **14a** (515 mg, 1.44 mmol) and Hoveyda-Grubbs 2nd generation catalyst (44 mg, 5 mol%) were employed and the reaction mixture was stirred in CH_2Cl_2 at room temperature for 16 hours. Purification by FCC (4:1 to 1:1 petrol-EtOAc) afforded the title compound (440 mg, 91%, 1:0.5 dr) as a pale brown oil.

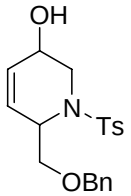
^{1}H NMR (400 MHz, $CDCl_3$): 7.62 (1H, d, J = 8.5 Hz), 7.57 (2H, d, J = 8.0 Hz), 7.38 (3H, m), 7.31 (4.5H, m), 7.21 (3H, m), 6.18 (0.5H, dd, J = 10.5, 4.5 Hz), 6.11 (0.5H, dd, J = 10.0, 4.5 Hz), 5.89 (2H, m), 5.67 (0.5H, d, J = 4.0 Hz), 5.52 (1H, br s), 4.11 (1H, m), 4.02 (0.5H, m), 3.92 (1H, dd, J = 13.5, 6.0 Hz), 3.70 (0.5H, d, J = 15.0 Hz), 3.24 (0.5H, m), 2.86 (1H, dd, J = 14.0, 10.0 Hz), 2.44 (0.5H, s), 2.39 (4.5H, s), 1.71 (1H, d, J = 7.0 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): 143.6, 143.3, 138.2, 137.5, 137.3, 136.4, 130.7, 130.2, 129.5 (2 signals), 128.5 (2 signals), 128.2, 128.1 (3 signals), 128.0, 127.9, 127.6, 127.0, 62.4, 62.0, 56.0, 55.1, 46.3, 44.8, 21.5 (2 signals).

MS (ESI^+) Calcd. for $C_{18}H_{19}NNaO_3S$ $[M+Na]^+$: 352.0978, Found: 352.0972.

FTIR 3497, 3061, 3032, 2922, 2873, 1653, 1493, 1371, 1183 cm^{-1}.

6-[(Benzyloxy)methyl]-1-[(4-methylphenyl)sulfonyl]-1,2,3,6-tetrahydropyridin-3-ol (15b)



General Procedure D: Alcohol **14b** (297 mg, 0.74 mmol) and Hoveyda-Grubbs 2nd generation catalyst (23 mg, 5 mol%) were employed using CH_2Cl_2 (15 mL) at room

temperature for 24 hours. Purification by FCC (4:1 to 1:1 petrol-EtOAc) afforded the title compound (258 mg, 93%, 1:1 dr) as a pale brown oil.

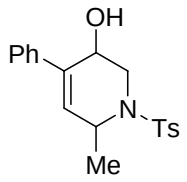
^{1}H NMR (400 MHz, $CDCl_3$): 7.78 (2H, d, *J* = 8.5 Hz), 7.70 (2H, d, *J* = 8.5 Hz), 7.33 (8H, m), 7.23 (6H, m), 6.06 (1H, ddt, *J* = 10.0, 5.5, 1.5 Hz), 5.94 (1H, dd, *J* = 10.0, 4.5 Hz), 5.84 (1H, m), 5.78 (1H, ddt, *J* = 10.5, 4.0, 1.5 Hz), 4.65 (1H, m), 4.47 (5H, m), 3.95 (2H, m), 3.86 (2H, m), 3.63 (2H, m), 3.54 (2H, m), 3.43 (1H, dd, *J* = 14.5, 3.0 Hz), 3.02 (1H, dd, *J* = 13.0, 9.0 Hz), 2.40 (6H, m), 2.18 (1H, d, *J* = 10.0 Hz), 1.76 (1 H, d, *J* = 8.0 Hz).

^{13}C NMR (125 MHz, $CDCl_3$): 143.5, 143.4, 137.7 (2 signals), 137.5, 137.2, 131.4, 129.7, 129.6, 129.1, 128.4 (3 signals), 127.7, 127.6 (3 signals), 127.0 (2 signals), 73.3, 73.2, 71.7, 70.5, 62.2, 61.9, 52.8, 52.3, 47.2, 46.5, 21.5 (2 signals). Only 31 signals were observed.

MS (ESI^+) Calcd. for $C_{20}H_{23}NNaO_4S$ $[M+Na]^+$: 396.1240, Found: 396.1229.

FTIR 3496, 3032, 2923, 2864, 1723, 1597, 1495, 1454, 1212, 1194, 1068 cm^{-1}.

6-Methyl-4-phenyl-1-tosyl-1,2,3,6-tetrahydropyridin-3-ol (15c)



General Procedure D: Alcohol **14c** (418 mg, 78% purity, 0.88 mmol) and Hoveyda-Grubbs 2nd generation catalyst (25 mg, 5 mol%) were employed using CH_2Cl_2 (25 mL) at 70 ºC, in a sealed tube for 3 hours. Purification by FCC (4:1 to 3:2 petrol-EtOAc) afforded the title compound (240 mg, 80%, 1:1 dr) as pale brown solid. *N.B.* Yield is based on a purity of 78% for alcohol **14c** as judged by ^{1}H NMR (*vide supra*). The overall yield from aldehyde **13c** is 54%.

^{1}H NMR (400 MHz, $CDCl_3$): 7.81 (2H, dt, *J* = 8.5, 2.0 Hz), 7.75 (2H, dt, *J* = 8.5, 2.0 Hz), 7.50 (2H, m), 7.32 (8H, m), 7.20 (4H, m), 6.10 (1H, d, *J* = 4.5 Hz), 5.81 (1H, dd, *J* = 4.0, 1.0 Hz), 4.69 (1H, qd, *J* = 7.0, 4.5 Hz), 4.48 (3H, m), 4.00 (2H, m), 3.34 (1H, dd, *J* = 14.0, 2.5 Hz), 3.18 (1H, dd, *J* = 13.5, 9.0 Hz), 2.43 (3H, s), 2.42 (3H, s), 2.05 (1H, d, *J* = 10.0 Hz), 1.74 (1H, d, *J* = 5.5 Hz), 1.37 (3H, d, *J* = 7.0 Hz), 1.22 (3H, d, *J* = 7.0 Hz).

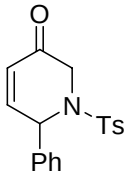
^{13}C NMR (100 MHz, $CDCl_3$): 143.5, 143.4, 139.4, 138.2, 137.4, 137.3, 136.5, 129.7 (2 signals), 128.9, 128.7, 128.6 (2 signals), 127.9, 127.7, 127.3, 127.0, 126.4, 125.6, 64.3, 63.1, 50.3, 49.7, 45.8, 45.0, 21.5 (2 signals), 19.6, 17.6. Only 29 signals were observed.

MS (ESI^+) Calcd. for $C_{19}H_{21}NKO_3S$ $[M+K]^+$: 382.0874, Found: 382.0874.

FTIR 3566, 3538, 3064, 2979, 2901, 1598, 1494, 1446, 1370, 1329, 1280, 1193, 1019 cm^{-1}.

M.P. 102-103ºC (CH_2Cl_2).

1-[(4-Methylphenyl)sulfonyl]-6-phenyl-1,6-dihydropyridin-3(2*H*)-one (16a)



General Procedure I: Alcohol **15a** (426 mg, 1.29 mmol) was employed to afford the title compound (358 mg, 85%) as an analytically pure colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$): 7.59 (2H, d, *J* = 8.0 Hz), 7.38 (5H, s), 7.25 (2H, m, *J* = 8.0 Hz), 6.97 (1H, dd, *J* = 10.5, 5.0 Hz), 5.99 (1H, d, *J* = 10.0 Hz), 5.82 (1H, d, *J* = 5.0 Hz), 4.32 (1H, d, *J* = 18.5 Hz), 3.70 (1H, d, *J* = 18.5 Hz), 2.40 (3H, s).

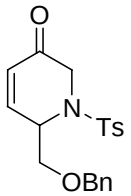
^{13}C NMR (100 MHz, $CDCl_3$): 191.4, 146.6, 143.9, 135.7, 134.5, 129.9, 128.9, 128.8, 128.2, 127.9, 127.1, 56.2, 49.4, 21.5.

MS *m/z* (EI) 327 ($[M]^+$, 100%); HRMS: (EI) Calcd. for $C_{18}H_{17}NO_3S$ $[M]^+$: 327.0929, Found: 327.0929.

FTIR 3441, 3062, 3032, 2967, 1917, 1687, 1375, 1289, 1163, 925 cm^{-1}.

M.P. 159-160 ºC (CH_2Cl_2-pentane).

6-[(Benzyloxy)methyl]-1-[(4-methylphenyl)sulfonyl]-1,6-dihydropyridin-3(2*H*)-one (16b)



General Procedure I: Alcohol **15b** (264 mg, 0.70 mmol) was employed. Purification by FCC (4:1 to 1:1 petrol-EtOAc) afforded the title compound (219 mg, 84%) as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$): 7.62 (2H, d, *J* = 8.0 Hz), 7.34 (3H, m), 7.24 (4H, m), 6.79 (1H, dd, *J* = 10.5, 5.0 Hz), 5.92 (1H, dd, *J* = 10.5, 2.0 Hz), 4.75 (1H, dddd, *J* = 5.0, 5.0, 4.0, 2.0 Hz), 4.53 (1H, d, *J* = 12.0 Hz), 4.46 (1H, d, *J* = 12.0 Hz), 4.36 (1H, d, *J* = 18.5 Hz), 4.09 (1H, d, *J* = 18.5 Hz), 3.84 (1H, dd, *J* = 10.0, 4.5 Hz), 3.74 (1H, dd, *J* = 10.0, 4.5 Hz), 2.40 (3H, s).

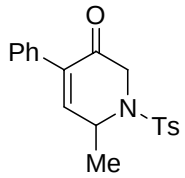
^{13}C NMR (100 MHz, $CDCl_3$): 191.5, 146.2, 143.8, 137.1, 135.7, 129.7, 128.2, 128.0, 127.6, 127.2, 126.8, 73.1, 70.7, 53.3, 50.8, 21.3.

FTIR 3357, 3026, 2921, 2867, 1683, 1598, 1495, 1421, 1260, 1167, 1092 cm^{-1}.

MS (ESI^+) Calcd. for $C_{20}H_{21}NKO_4S$ $[M+K]^+$: 410.0823, Found: 410.0819.

M.P. 78-79 ºC (CH_2Cl_2-pentane).

6-Methyl-4-phenyl-1-tosyl-1,2-dihydropyridin-3(6H)-one (16c)



To a solution of alcohol **15c** (212 mg, 0.62 mmol) in CH_2Cl_2 at 0 ºC was added $NaHCO_3$ (262 mg, 3.12 mmol) and then Dess-Martin Periodinane (406 mg, 0.96 mmol). After 3 hours further Dess-Martin Periodinane (200 mg, 0.47 mmol) was added. After 5 hours the mixture was concentrated *in vacuo* (at 20 ºC). Purification of the residue by FCC (7:3 petrol-EtOAc) afforded the title compound (142 mg, 67%) as a white solid.

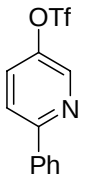
^{1}H NMR (400 MHz, $CHCl_3$) 7.69 (2H, d, *J* = 8.5 Hz), 7.28 (5H, m), 6.94 (2H, m), 6.72 (1H, d, *J* = 5.0 Hz), 4.92 (1H, qd, *J* = 7.0, 5.0 Hz), 4.53 (1H, d, *J* = 18.5 Hz), 4.08 (1H, d, *J* = 18.5 Hz), 2.38 (3H, s), 1.52 (3H, d, *J* = 7.0 Hz).

^{13}C NMR (100 MHz, $CHCl_3$) 190.2, 146.5, 144.0, 137.2, 135.9, 133.7, 130.0, 128.2, 128.0 (2 signals), 127.2, 50.4, 49.2, 21.4, 17.7.

FTIR 3442, 2982, 1744, 1676, 1344, 1186, 1017 cm^{-1}.

M.P. 143-144 ºC (CH_2Cl_2).

6-Phenylpyridin-3-yl trifluoromethanesulfonate (17)



General Procedure J: Enone **16a** (275 mg, 0.84 mmol) was employed. Purification by FCC (4:1 to 1:1 petrol-EtOAc) afforded the title compound (220 mg, 86%) as white solid.

^{1}H NMR (400 MHz, $CDCl_3$): 8.66 (1H, d, J = 3.0 Hz), 8.00 (2H, dd, J = 8.0, 1.5 Hz), 7.84 (1H, d, J = 9.0 Hz), 7.70 (1H, dd, J = 9.0, 3.0 Hz), 7.44-7.55 (3H, m).

^{13}C NMR (100 MHz, $CDCl_3$): 157.4, 145.6, 142.4, 137.4, 129.8, 129.6, 128.9, 127.0, 121.2, 118.7 (q, J = 321.0 Hz).

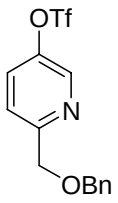
^{19}F NMR (377 MHz, $CDCl_3$): -72.5 (s).

MS *m/z* (CI) 304.0 ($[M+H]^+$, 100%); HRMS: (CI) Calcd. for $C_{12}H_9NO_3F_3S$ $[M+H]^+$: 304.0255, Found: 304.0255.

FTIR 3080, 1964, 1590, 1579, 1471, 1450, 1426, 1250, 1226, 1168, 1135, 1074, 1016, 938 cm^{-1}.

M.P. 88-89 ºC (CH_2Cl_2-pentane).

6-[(Benzyloxy)methyl]pyridin-3-yl trifluoromethanesulfonate (18)



General Procedure J: Enone **16b** (239 mg, 0.64 mmol) was employed. Purification by FCC (1:1 to 0:1 petrol-CH_2Cl_2) afforded the title compound (98 mg, 44%) as a clear oil.

^{1}H NMR (400 MHz, C_6D_6) 8.28 (1H, d, J = 2.5 Hz), 7.25-7.31 (2H, m), 7.23 (2H, m), 7.19 (2H, m), 6.88 (1H, dd, J = 8.5, 2.5 Hz), 4.51 (2H, s), 4.32 (2H, s).

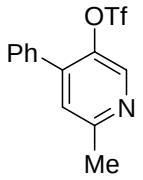
^{113}C NMR (125 MHz, $CDCl_3$): 159.2, 145.6, 141.9, 137.5, 129.5, 128.5, 128.0, 127.8, 122.3, 118.6 (q, J = 320.0 Hz), 73.1, 72.1.

^{19}F NMR (377 MHz, $CDCl_3$): -72.5 (s).

MS *m/z* (CI) 348 ($[M+H]^+$, 100%); HRMS: (CI) Calcd. for $C_{14}H_{13}NO_4F_3S$ $[M+H]^+$: 348.0517, Found: 348.0505.

FTIR 3066, 3033, 2862, 1812, 1481, 1454, 1428, 1215, 1161, 1140, 1103, 1019 cm^{-1}

6-Methyl-4-phenylpyridin-3-yl trifluoromethanesulfonate (19)



General Procedure J: Enone **16c** (42 mg, 0.12 mmol) was employed. Purification by FCC (1:0 to 1:20 petrol-EtOAc) afforded the title compound (30 mg, 77%) as clear oil.

^{1}H NMR (500 MHz, $CDCl_3$) 8.53 (1H, s), 7.50 (5H, s), 7.29 (1H, s), 2.65 (3H, s).

^{13}C NMR (125 MHz, $CHCl_3$) 159.0, 143.0, 142.8, 142.4, 133.3, 129.6, 128.9, 128.8, 125.2, 118.3 (q, J = 320.0 Hz), 24.0.

^{19}F NMR (377 MHz, $CDCl_3$): -73.6 (s).

MS *m/z* (CI) 318 ($[M+H]^+$, 100%); HRMS: (CI) Calcd. for $C_{13}H_{11}NO_3F_3S$ $[M+H]^+$: 318.0412, Found: 318.04089.

FTIR 3662, 3062, 1725, 1599, 1500, 1248, 1212, 1042 cm^{-1}.

Experimental Procedures and Data for the Synthesis of Pyridazinones

General Procedure A for the Preparation of Allylated Tosyl Hydrazides:[8] To a vigorously stirred solution of *p*-toluene sulfonylhydrazide (100 mol%) in anhydrous DMSO (2.5 mL/mmol) at room temperature was added, in one portion, NaH (60 % dispersion in mineral oil, 100 mol%). The resulting mixture was stirred for 2 hours, whereupon a colourless precipitate formed, and was then cooled to 0 ^{o}C. The corresponding allyl halide (101 mol%) was then added in one portion and the mixture was warmed to room temperature. After stirring at room temperature for 1-3 hours (until complete dissolution of the precipitate was observed) the mixture was poured into ice-water (15 ml/mmol). The product was then isolated by vacuum filtration, washed with water (3 × 1mL/mmol) and dried under vacuum on the filter bed to afford the corresponding allylated adduct.

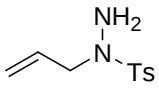
General Procedure B for the Acylation of Allylated Tosyl Hydrazides: To a solution of the appropriate allylated *p*-toluene sulfonylhydrazide (100 mol%) in anhydrous THF (10 ml/mmol) at 0 ^{o}C was added freshly distilled acid chloride (110 mol%) and then Hünig's base (110 mol%). The mixture was stirred at 0 ^{o}C for one hour and then at room temperature overnight. The mixture was then concentrated *in vacuo* and the residue was dissolved in EtOAc (25 ml/mmol). This solution was washed with water (20 mL/mmol), aq. 1 M HCl (20 mL/mmol) and saturated aq. $NaHCO_3$ (20 mL/mmol). The organic portion was then dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by FCC, under the conditions noted, afforded the corresponding acylated adduct.

General Procedure C for the Synthesis of Pyridazinones *via* Olefin Metathesis: To an argon purged, resealable reaction tube containing the appropriate metathesis precursor (100 mol%) and Hoveyda-Grubbs 2nd generation catalyst (10 mol%) was added anhydrous, argon sparged CH_2Cl_2 (10 mL/mmol). The reaction tube was sealed and then heated at 40 ^{o}C for the time stated. The mixture was then cooled to room temperature and DBU (500 mol%) was added. The mixture was stirred until complete elimination had occurred (TLC monitoring) and was then concentrated *in vacuo*. Purification by FCC, under the conditions noted, afforded the corresponding pyridazinone.

General Procedure D for the Triflation of Pyridazinones:[9] To a solution of the appropriate pyridazinone (100 mol%) in anhydrous pyridine (2 mL/mmol) at 0 ^{o}C was added dropwise Tf_2O (130 mol%). The resulting solution was warmed slowly to room temperature over two hours. The mixture was then concentrated *in vacuo* (at 20 ^{o}C) and purified by FCC, under the conditions noted, to afford the corresponding pyridazine triflate (**24-27**).

[8] T. Sato, I. Homma, *Bull. Chem. Soc. Jpn.* 1971, **44**, 1885-1891.
[9] D. Toussaint, J. Suffert, C. G. Wermuth, *Heterocycles*, 1994, **38**, 1273-1286.

_N_-Allyl-4-methylbenzenesulfonohydrazide[8]



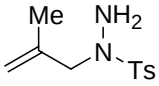
General Procedure A: *p*-Toluene sulfonylhydrazide (3.72 g, 20.0 mmol) and allyl bromide (1.75 mL, 20.2 mmol) were employed to afford the title compound (3.75 g, 83%) as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$): 7.76 (2H, d, J = 8.5 Hz), 7.36 (2H, d, J = 8.5 Hz), 5.80 (1H, m), 5.26 (1H, m), 5.22 (1H, m), 3.75 (2H, ddd, J = 6.5, 1.5, 1.5 Hz), 2.86 (2H, br s), 2.45 (3H, s).

M.P. 86-88 ^{o}C (EtOAc-petrol) [Lit. 87-89 ^{o}C (PhH-petrol)].[8]

The spectroscopic properties of this compound were consistent with the data reported in the literature.[8]

4-Methyl-*N*-(2-methylallyl)benzenesulfonohydrazide



General Procedure A: *p*-Toluene sulfonylhydrazide (1.86 g, 10.0 mmol) and 3-chloro-2-methyl-1-propene (1.10 mL, 10.1 mmol) were employed to afford the title compound (1.21 g, 92%) as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$): 7.76 (2H, d, J = 8.5 Hz), 7.37 (2H, d, J = 8.5 Hz), 4.97 (1H, s), 4.88 (1H, s), 3.61 (2H, s), 3.21 (2H, br s), 2.46 (3H, s), 1.82 (3H, s).

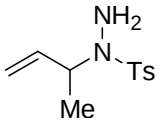
^{13}C NMR (100 MHz, $CDCl_3$): 144.3, 139.9, 131.4, 129.8, 128.6, 115.1, 58.9, 21.6, 19.9.

MS *m/z* (FI) 240 ($[M]^+$, 100%); HRMS: (FI) Calcd. for $C_{11}H_{16}N_2O_2S$ $[M]^+$: 240.0932, Found: 240.0939.

FTIR 3374, 2922, 1338, 1160, 1092 cm^{-1}.

M.P. 69-71 ^{o}C (EtOAc-petrol).

***N*-(But-3-en-2-yl)-4-methylbenzenesulfonohydrazide**



General Procedure A: *p*-Toluene sulfonylhydrazide (1.86 g, 10.0 mmol) and 3-chloro-1-butene (1.02 mL, 10.1 mmol) were employed. In a modification to the general procedure, after quenching with ice-water, the mixture was extracted with Et_2O (2 × 150 mL). The organic extracts were combined, washed with water (2 × 100 mL) and then brine (100 mL), dried (Na_2SO_4) and concentrated *in vacuo* (at 20 ^oC) to afford a yellow oil. This residue was purified by FCC (2:1 petrol-EtOAc) to afford the title compound (538 mg, 22%) as a colourless, viscous oil.

An alternative Mitsunobu protocol can be employed: To a solution of *p*-toluene sulfonylhydrazide (1.43 g, 7.66 mmol) and PPh_3 (2.00 g, 7.63 mmol) in anhydrous PhMe (35 mL) at 0 ^oC was added 3-buten-2-ol (500 μL, 5.78 mmol) and then DIAD (1.50 mL, 7.63 mmol). The mixture was stirred at 0 ^oC for 2 hours and then concentrated *in vacuo* (at 20 ^oC). The residue was purified by FCC (1:1 Et_2O-petrol) to afford the title compound (807 mg, 58%) as a colourless, viscous oil.

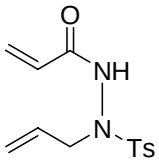
^{1}H NMR (400 MHz, $CDCl_3$): 7.78 (2H, d, J = 8.5 Hz), 7.31 (2H, d, J = 8.5 Hz), 5.70 (1H, ddd, J = 17.5, 10.5, 5.5 Hz), 5.16 (1H, ddd, J = 17.5, 1.5, 1.5 Hz), 5.14 (1H, ddd, J = 10.5, 1.5, 1.5 Hz), 3.85 (2H, br s), 4.73 (1H, qddd, J = 7.0, 5.5, 1.5, 1.5 Hz), 2.43 (3H, s), 1.23 (3H, d, J = 7.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): 144.0, 136.3, 134.4, 129.7, 128.3, 117.5, 55.8, 21.6, 16.3.

MS *m/z* (FI) 240 ($[M]^+$, 20%), 210 (100); HRMS: (FI) Calcd. for $C_{11}H_{16}N_2O_2S$ $[M]^+$: 240.0932, Found: 240.0939.

FTIR 2923, 1741, 1596, 1493, 1371, 1172, 1123 cm^{-1}.

***N*'-Acryloyl-*N*-allyl-4-methylbenzenesulfonohydrazide**



General Procedure B: *N*-Allyl-4-methylbenzenesulfonohydrazide (150 mg, 0.66 mmol) was employed. Purification by FCC (2:1 petrol-EtOAc) afforded the title compound (163 mg, 88%, 1:0.5 rotamer ratio) as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$): 8.12 (0.5H, br s), 7.78-7.69 (4H, m), 7.40-7.25 (3H, m), 6.77 (1H, dd, J = 17.0, 10.0 Hz), 6.30-6.18 (1.5H, m), 6.12-5.96 (0.5H, dd, J = 16.5, 10.0 Hz), 5.94-5.61 (3H, m), 5.30-5.17 (3H, m), 4.33 (1H, dd, J = 13.5, 6.0 Hz), 4.15 (1H, d, J = 6.5 Hz), 3.32 (1H, dd, J = 13.5, 8.0 Hz), 2.41 (4.5 H, s). *N.B.* Rotamers were still observed under high temperature NMR conditions (100 ^{o}C in DMSO-d_6).

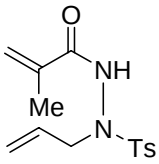
^{13}C NMR (100 MHz, $CDCl_3$): 170.0, 163.7, 145.2, 144.5, 134.5, 131.4, 130.8, 130.2, 130.1, 129.7, 129.6, 128.8, 128.3, 127.7, 125.7, 122.6, 120.6, 55.3, 52.3, 21.7 (2 signals). Only 21 signals were observed.

MS (ESI^+) Calcd. for $C_{13}H_{16}N_2NaO_3S$ $[M+Na]^+$: 303.0774, Found: 303.0772.

FTIR 3205, 3038, 1682, 1549, 1407, 1359, 1166 cm^{-1}.

M.P. 143-144 ^{o}C (CH_2Cl_2-petrol).

***N*-Allyl-*N*'-methacryloyl-4-methylbenzenesulfonohydrazide**



General Procedure B: *N*-Allyl-4-methylbenzenesulfonohydrazide (320 mg, 1.33 mmol) was employed. Purification by FCC (3:1 petrol-EtOAc) afforded the title compound (292 mg, 75%) as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$): 7.78 (2H, d, J = 8.5 Hz), 7.56 (1H, br s), 7.30 (2H, d, J = 8.5 Hz), 5.87 (1H, ddt, J =17.0, 10.0, 6.5 Hz), 5.58 (1H, s), 5.35 (1H, m), 5.26 (1H, m), 5.23 (1H, m), 4.18 (2H, d, J = 6.5 Hz), 2.42 (3H, s), 1.83 (3H, s).

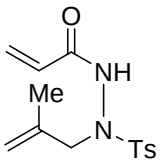
^{13}C NMR (100 MHz, $CDCl_3$): 166.6, 144.5, 138.2, 134.5, 131.5, 129.6, 128.3, 120.9, 120.8, 52.4, 21.7, 18.6.

MS *m/z* (FI) 294 ($[M]^+$, 100%); HRMS: (FI) Calcd. for $C_{14}H_{18}N_2O_3S$ $[M]^+$: 294.1038, Found: 294.1036.

FTIR 3236, 3027, 1680, 1633, 1597, 1360, 1167, 1090 cm^{-1}.

M.P. 110-112 ^oC (CH_2Cl_2-petrol).

***N*'-Acryloyl-4-methyl-*N*-(2-methylallyl)benzenesulfonohydrazide**



General Procedure B: 4-Methyl-*N*-(2-methylallyl)benzenesulfonohydrazide (320 mg, 1.33 mmol) was employed. Purification by FCC (3:1 petrol-EtOAc) afforded the title compound (313 mg, 80%, 1:1 rotamer ratio) as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$): 8.03 (1H, br s), 7.76-7.70 (4H, m), 7.54 (1H, br s), 7.36 (2H, d, *J* = 8.0 Hz), 7.29 (2H, d, *J* = 8.0 Hz), 6.80 (1H, dd, *J* = 17.0, 10.5 Hz), 6.30 (1H, dd, *J* = 17.0, 1.5 Hz), 6.21 (1H, d, *J* = 17.0 Hz), 6.04 (1H, dd, *J* = 17.0, 10.5 Hz), 5.77 (1H, d, *J* = 10.5 Hz), 5.66 (1H, d, *J* = 10.5 Hz), 4.98-4.91 (2H, m), 4.86 (2H, s), 4.26 (1H, d, *J* = 13.0 Hz), 4.10 (2H, s), 3.05 (1H, d, *J* = 13.0 Hz), 2.45-2.41 (6H, m), 1.85-1.77 (6H, m).

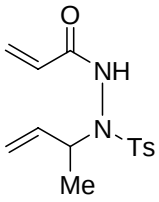
^{13}C NMR (100 MHz, $CDCl_3$): 170.0, 163.5, 145.3, 144.3, 139.1, 137.4, 134.8, 130.5, 130.2, 130.1, 129.5, 128.8, 128.7, 128.2, 127.7, 125.6, 118.7, 116.1, 59.2, 55.3, 21.7, 20.5, 19.9. Only 23 signals were observed.

MS (ESI^+) Calcd. for $C_{14}H_{18}N_2NaO_3S$ $[M+Na]^+$: 317.0930, Found: 317.0930.

FTIR 3209, 3044, 1683, 1550, 1359, 1165 cm^{-1}.

M.P. 160-161 ^oC (CH_2Cl_2-petrol).

***N*'-Acryloyl-*N*-(but-3-en-2-yl)-4-methylbenzenesulfonohydrazide**



General Procedure B: *N*-(But-3-en-2-yl)-4-methylbenzenesulfonohydrazide (320 mg, 1.33 mmol) was employed. Purification by FCC (3:1 petrol-EtOAc) afforded the title compound (285 mg, 73%, 1:0.5:0.5 rotamer ratio) as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$): 7.98 (0.5 H, br s), 7.84 (1H, d, J = 8.5 Hz), 7.78-7.71 (3H, m), 7.35-7.25 (5.5 H, m), 6.64-6.55 (1.5H, m), 6.33-6.17 (2H, m), 6.10 (0.5H, dd, J = 17.0, 10.0 Hz), 5.93 (0.5H, ddd, J = 17.5, 10.5, 5.5 Hz), 5.82 (0.5H, J = 17.0, 10.5, 6.0 Hz), 5.71-5.65 (2H, m), 5.49 (1H, ddd, J = 17.0, 10.5, 6.0 Hz), 5.26-5.12 (4H, m), 4.89-4.70 (2H, m), 2.39 (6H, s), 1.30-1.23 (4.5 H, m), 1.02 (1.5H, d, J = 7.0 Hz).

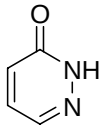
^{13}C NMR (100 MHz, $CDCl_3$): 170.4, 170.0, 164.5, 145.0, 144.9, 144.4, 137.8, 136.1, 135.0, 133.5, 133.1 (2 signals), 130.2, 130.1, 129.9, 129.8, 129.7, 129.4, 128.8, 128.6, 128.5, 128.2, 127.8, 125.5, 125.1, 120.1, 118.2, 57.6, 57.4, 57.1, 21.7, 21.6 (2 signals), 17.4, 16.3, 13.7.

MS (ESI^+) Calcd. for $C_{14}H_{18}N_2NaO_3S$ $[M+Na]^+$: 317.0930, Found: 317.0930.

FTIR 3263, 3028, 1680, 1450, 1359, 1185, 1090 cm^{-1}.

M.P. 141-142 ^oC (CH_2Cl_2-petrol).

2*H*-Pyridazin-3-one



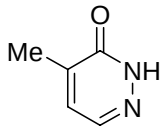
General Procedure C: *N*'-Acryloyl-*N*-allyl-4-methylbenzenesulfonohydrazide (100 mg, 0.36 mmol) was employed. Heating was continued for 36 hours. Purification by FCC (1:0 to 40:1 EtOAc-MeOH) afforded the title compound (30 mg, 87%) as a colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$): 7.84 (1H, dd, J = 4.0, 1.5 Hz), 7.27 (1H, dd, J = 9.5, 4.0 Hz), 7.00 (1H, dd, J = 9.5, 1.5 Hz). A signal attributable to NH was not observed.

M.P. 103-105 °C (CH_2Cl_2-hexane) [Lit. 103 °C (sublimed)].[10]

The spectroscopic properties of this compound were consistent with the data reported in the literature.[10]

4-Methyl-2*H*-pyridazin-3-one



General Procedure C: *N*-Allyl-*N*'-methacryloyl-4-methylbenzenesulfonohydrazide (108 mg, 0.36 mmol) was employed. Heating was continued for 36 hours. Purification by FCC (1:0 to 19:1 EtOAc-MeOH) afforded the title compound (36 mg, 91%) as a pale yellow solid.

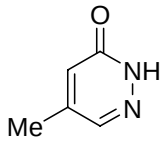
^{1}H NMR (400 MHz, $CDCl_3$): 12.10 (1H, br s), 7.73 (1H, d, J = 4.0 Hz), 7.11 (1H, dq, J = 4.0, 1.5 Hz), 2.23 (3H, d, J = 1.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): 163.5, 141.0, 137.4, 129.9, 16.3.

M.P. 149-152 °C (CH_2Cl_2-petrol) [Lit. 153-155 °C (PhH)]. [11]

The spectroscopic properties of this compound were consistent with the data reported in the literature.[11]

5-Methyl-2*H*-pyridazin-3-one



General Procedure C: *N*'-Acryloyl-4-methyl-*N*-(2-methylallyl)benzenesulfonohydrazide (105 mg, 0.36 mmol) was employed. In a modification to the metathesis step of the general procedure, Zhan 1B (10 mol%) was employed as catalyst and the reaction was run at increased dilution (40 mL/mmol) and temperature (70 °C) for 72 hours. After completion of the RCM the reaction concentration was adjusted to 10 mL/mmol prior to the elimination step. Purification by FCC (3:1:0 to 1:0:0 to 19:0:1 EtOAc-petrol-MeOH) afforded the title compound (28 mg, 70%) as a cream solid.

[10] H. McNab, I. Stobie, *J. Chem. Soc., Perkin Trans.1.* 1982, 1845-1853.
[11] H. McNab, *J. Chem. Soc., Perkin Trans.1.* 1983, 1203-1208.

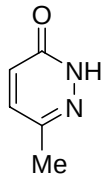
^{1}H NMR (400 MHz, $CDCl_3$): 12.00 (1H, br s), 7.68 (1H, d, *J* = 1.5 Hz), 6.74 (1H, m), 2.23 (3H, d, *J* = 1.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): 162.3, 144.3, 139.7, 127.5, 18.7.

M.P. 142-143 °C (CH_2Cl_2-petrol) [Lit. 151-153 °C (cyclohexane)].[10]

The spectroscopic properties of this compound were consistent with the data reported in the literature.[10]

6-Methyl-2*H*-pyridazin-3-one



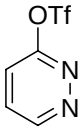
General Procedure C: *N*'-Acryloyl-*N*-(but-3-en-2-yl)-4-methylbenzenesulfonohydrazide (108 mg, 0.36 mmol) was employed. Heating was continued for 24 hours. Purification by FCC (1:0 to 19:1 EtOAc-MeOH) afforded the title compound (30 mg, 76%) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$): 7.16 (1H, d, *J* = 10.0 Hz), 6.92 (1H, d, *J* = 10.0 Hz), 2.33 (3H, s). A signal attributable to NH was not observed.

M.P. 134-136 °C (CH_2Cl_2-hexane) [Lit. 142-143 °C (cyclohexane)].[10]

The spectroscopic properties of this compound were consistent with the data reported in the literature.[10]

Trifluoromethanesulfonic acid pyridazin-3-yl ester (24)



General Procedure D: 2*H*-Pyridazin-3-one (26 mg, 0.27 mmol) was employed. Purification by FCC (2:1 petrol-EtOAc) afforded the title compound (37 mg, 60%) as a colourless oil. This material was contaminated with *ca.* 4% *O*□→*N* rearranged byproduct (see main paper).

^{1}H NMR (400 MHz, $CDCl_3$): 9.31 (1H, dd, *J* = 5.0, 1.5 Hz), 7.76 (1H, dd, *J* = 9.0, 5.0 Hz), 7.48 (1H, dd, *J* = 9.0, 1.5 Hz). Signals for rearranged byproduct: 7.98 (1H, dd, *J* = 3.5, 1.5 Hz), 7.30 (1H, dd, *J* = 9.5, 3.5 Hz), 7.02 (1H, dd, *J* = 9.0, 1.5 Hz).

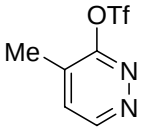
^{13}C NMR (100 MHz, $CDCl_3$): 160.3, 152.4, 131.1, 120.6, 118.6 (q, *J* = 321.0 Hz).

^{19}F NMR (377 MHz, $CDCl_3$): -72.4 (s). Signal for rearranged byproduct: -70.9 (s).

MS *m/z* (FI) 228 ($[M]^+$, 100%); HRMS: (FI) Calcd. for $C_5H_3F_3N_2O_3S$ $[M]^+$: 227.9816, Found: 227.9820.

FTIR 3074, 1721, 1572, 1425, 1215, 1132 cm^{-1}.

Trifluoromethanesulfonic acid 4-methylpyridazin-3-yl ester (25)



General Procedure D: 4-Methyl-2*H*-pyridazin-3-one (26 mg, 0.24 mmol) was employed. Purification by FCC (3:2 petrol-EtOAc) afforded the title compound (50 mg, 86%) as a pale yellow oil. This material was contaminated with *ca.* 8% *O→N* rearranged byproduct (see main paper).

^{1}H NMR (400 MHz, $CDCl_3$): 9.10 (1H, d, *J* = 5.0 Hz), 7.55 (1H, dq, *J* = 5.0, 1.0 Hz), 2.45 (3H, d, *J* = 1.0 Hz). Signals for rearranged byproduct: 7.86 (1H, d, *J* = 4.0 Hz), 7.11 (1H, d, *J* = 4.0, 1.5 Hz), 2.76 (3H, d, *J* = 1.5 Hz).

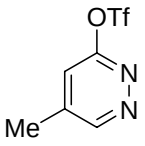
^{13}C NMR (100 MHz, $CDCl_3$): 160.4, 152.1, 131.9, 131.8, 118.5 (q, *J* = 321.0 Hz), 15.5. Characteristic signals for rearranged byproduct: 139.5, 129.7, 16.4.

^{19}F NMR (377 MHz, $CDCl_3$): -72.4 (s). Signal for rearranged byproduct: -70.7 (s).

MS *m/z* (FI) 242 ($[M]^+$, 100%); HRMS: (FI) Calcd. for $C_6H_5F_3N_2O_3S$ $[M]^+$: 241.9973, Found: 241.9974.

FTIR 3064, 1709, 1422, 1359, 1214, 1134 cm^{-1}.

Trifluoromethanesulfonic acid 5-methylpyridazin-3-yl ester (26)



General Procedure D: 5-Methyl-2*H*-pyridazin-3-one (30 mg, 0.27 mmol) was employed. Purification by FCC (2:1 petrol-EtOAc) afforded the title compound (47 mg, 72%) as a colourless oil. This material was contaminated with *ca.* 4% *O*→*N* rearranged byproduct (see main paper).

^{1}H NMR (400 MHz, $CDCl_3$): 9.11 (1H, d, *J* = 1.5 Hz), 7.26 (1H, m), 2.51 (3H, m). Signals for rearranged byproduct: 7.80 (1H, d, *J* = 2.0 Hz), 6.74 (1H, m), 2.31 (3H, d, *J* = 2.0 Hz).

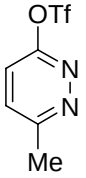
^{13}C NMR (100 MHz, $CDCl_3$): 160.1, 154.2, 143.7, 120.3, 118.6 (q, *J* = 321.0 Hz), 18.4.

^{19}F NMR (377 MHz, $CDCl_3$): -72.5 (s). Signal for rearranged byproduct: -71.0 (s).

MS (ESI^+) Calcd. for $C_6H_5F_3N_2NaO_3S$ $[M+Na]^+$: 264.9865, Found: 264.9867.

FTIR 3061, 1591, 1427, 1362, 1217, 1136 cm^{-1}.

Trifluoromethanesulfonic acid 6-methylpyridazin-3-yl ester (27)[9]



General Procedure D: 6-Methyl-2*H*-pyridazin-3-one (30 mg, 0.27 mmol) was employed. Purification by FCC (1:1 EtOAc-petrol) afforded the title compound (46 mg, 70%) as a pale yellow solid. This material was contaminated with *ca.* 3% *O*→*N* rearranged byproduct (see main paper).

^{1}H NMR (400 MHz, $CDCl_3$): 7.58 (1H, d, *J* = 9.0 Hz), 7.34 (1H, d, *J* = 9.0 Hz), 2.79 (3H, s). Signals for rearranged byproduct: 7.17 (1H, d, *J* = 9.5 Hz), 6.91 (1H, d, *J* = 9.5 Hz), 2.43 (3H, s).

^{13}C NMR (100 MHz, $CDCl_3$): 170.0, 159.0, 131.6, 120.3, 118.6 (q, *J* = 321.0 Hz), 21.7.

^{19}F NMR (377 MHz, $CDCl_3$): -72.4 (s). Signal for rearranged byproduct: -71.0 (s).

M.P. 48-49 ^{o}C (CH_2Cl_2-petrol) [Lit. 59 ^{o}C (no recrystallisation solvent quoted)].[9]

The spectroscopic properties of this compound were consistent with the data reported in the literature.[9]