JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

One-Pot Synthesis of Chiral Nonracemic Amines

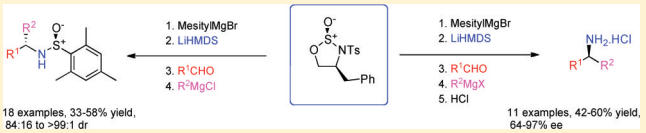
Caroline Roe,[†] Heather Hobbs,[‡] and Robert A. Stockman*,[†]

[†]School of Chemistry, University of Nottingham, Nottingham NG7 2RD, U.K.

[‡]GlaxoSmithKline, Gunnels Wood Road, Stevenage SG1 2NY, U.K.

Supporting Information

ABSTRACT: One-pot five-component reactions of oxathiazolidine-*S*-oxides with mesitylmagnesium bromide, lithium bis(trimethylsilyl)amide, aldehydes and Grignard reagents afford chiral nonracemic amines or sulfinamides in good yields and high stereoselectivities.

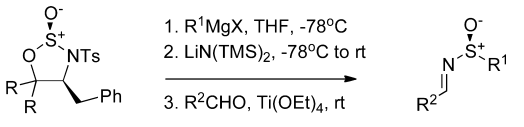


INTRODUCTION

Multicomponent reactions are one of the most powerful methods for the construction of molecules, assembling multiple starting materials and forming numerous bonds in a one-pot process.[1] This single-pot operation involving many bond-forming steps eliminates several purifications, reduces the use of solvent, minimizes chemical waste, and reduces the amount of time chemical synthesis requires.[2] Thus in the ever-important quest for more sustainable chemistry,[3] the development of new multicomponent sequences, especially those that induce stereoselectivity, remains a high priority for synthetic chemists.[4]

Chiral amines are high value materials that form the basis of many pharmaceutical ingredients (e.g., Plavix, Alna, Sifrol, and Januvia) and serve as auxiliaries[5] and as ligands for homogeneous catalysis.[6] They are also commonplace in many natural products. This has spurred much interest in the synthesis of α-chiral amines, and there are now a multitude of practical methods for their formation, including catalytic asymmetric reduction of ketimines, enamines and enamides,[7] asymmetric reductive amination[8] and the asymmetric addition of organometallic reagents to imines,[9] or the addition of organometallic reagents to chiral sulfinimines.[10] In many of these cases multiple steps are required for the formation of the enamide or imine and the chiral ligand/catalyst, or the chiral sulfinimine, thus necessitating multiple synthetic operations, workups, and purifications. Of these methods, organometallic addition to imines and reductive amination combine connectivity with the formation of the new stereogenic center. We wished to investigate an approach that included a high degree of connectivity, with a one-pot process for the simple and convenient formation of α-chiral amines from readily available precursors. Recently we reported the use of a chiral oxathiazolidine oxide (readily prepared in just two steps from simple commercially available chemicals in >90% yield) as a template to prepare chiral sulfinimines in a four-component, one-pot reaction in high yields and enantioselectivities (Scheme 1).[11] Additionally we recently described the nucleophilic addition of Grignard reagents to mesityl sulfinimines, which we found to give excellent yields and high diastereoselectivities via an open transition state, allowing a wide range of chiral amines to be prepared.[12] We describe herein the combination of these two high-yielding and highly stereoselective reactions into a sequential five-component, one-pot process, enabling the facile preparation of chiral sulfinamides and chiral amines in a connective manner, from cheap commodity chemicals in an efficient single operation which minimizes waste and time. This process, which forms both a C−C bond and a C−N bond, is complementary to the asymmetric reduction of imines/enamines and derivatives.

Scheme 1. Four-Component Synthesis of Chiral Sulfinimines



R = H, Me

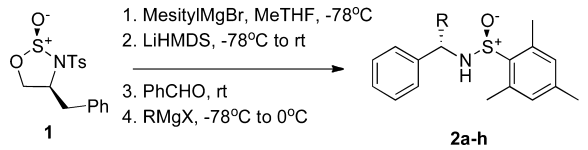
38 examples
12-85% yield, 66.3-100% ee

RESULTS AND DISCUSSION

Initially, we concentrated our efforts into extending our previous four-component sulfinimine synthesis into a five-component sulfinamide synthesis protocol, using benzaldehyde as the fourth component (Table 1). This consisted of adding a series of additional Grignard reagents, as the fifth component, to the reactions after sulfinimine formation had been observed by LC−MS or TLC. A range of mesityl sulfinamides was produced in yields ranging from 36% to 58% (equivalent to an average 76−87% per step over the four-step process) and excellent diastereoselectivities. The whole process involves the formation of four new bonds and two stereogenic centers in a single-pot operation. It is noteworthy that diastereoselectivities were improved over the equivalent single-step reaction from the mesityl sulfinimine (e.g., entry 8, BnMgCl gave 70:30 dr in the stepwise reaction).[12] We found that allyl magnesium bromide gave the opposite stereoselectivity to all other Grignard reagents, and thus in this case we surmise that

Received: September 12, 2011
Published: October 12, 2011

Table 1. Five-Component Synthesis of Sulfinamides

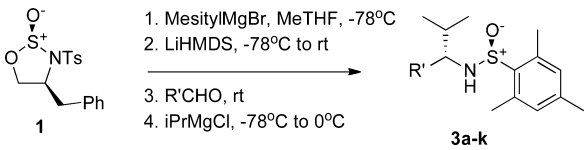


entry	RMgX	2	yield (%)	dr
1	EtMgCl	**2a**	46	93:7
2	^{n}PrMgCl	**2b**	46	95:5
3	^{i}PrMgCl	**2c**	43	>99:1
4	^{i}BuMgCl	**2d**	44	94:6
5	^{n}hexylMgBr	**2e**	34	86:14
6	CyMgCl	**2f**	39	>99:1
7	allylMgBr	**2g**	36	95:5
8	BnMgCl	**2h**	58	84:16

reaction is proceeding via a chelated S_E2' pathway, rather than an open transition state, which has been shown by Ellman to induce the opposite sense of stereochemistry in the addition of Grignard reagents to *tert*-butanesulfinimines.[13] The reactions were carried out in 2-methyltetrahydrofuran, and it was found important to exclude all tetrahydrofuran from the reaction in order to maximize stereoselectivity, as we had found in the stepwise reaction study.[12] Thus the commercial Grignard reagents used were in solution in diethyl ether, and the lithium hexamethyldisilazide was used as a solution in toluene. The diastereomeric ratios were generally very high, except for lipophilic and sterically unencumbered Grignard reagents (e.g., *n*-hexyl, *n*-Bn), which follows the same profile as the earlier single-step study.[12] This may be due to increased aggregation in these reagents.[14]

In order to further explore the scope of the one-pot synthesis of sulfinamides, a range of aldehydes was explored as the fourth component, while using isopropylmagnesium chloride as the fifth component of the one-pot reaction (Table 2). Once again,

Table 2. One-Pot Synthesis of Isopropyl-*S*-mesitylsulfinamides



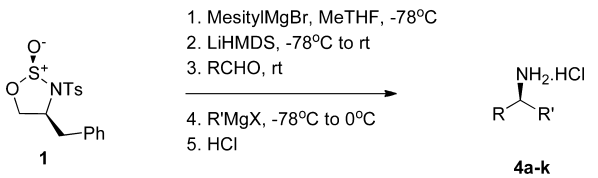
entry	R′	3	yield (%)	dr
1	Ph	**3a**	43	>99:1
2	4-MeOPh	**3b**	48	>99:1
3	mesityl	**3c**	33	>99:1
4	4-ClPh	**3d**	45	98:2
5	6-MeO-naphthalen-2-yl	**3e**	38	>99:1
6	1-Boc-1*H*-indol-3-yl	**3f**	40	99:1
7	2-furanyl	**3g**	48	97:3
8	1-benzofuran-2-yl	**3h**	44	97:3
9	5-bromo-2-thienyl	**3i**	40	98:2
10	1,3-thiazol-5-yl	**3j**	36	90:10
11	Ph(CC)-	**3k**	34	94:6

we were pleased to note the generality of the reaction, with mesityl sulfinamides being produced in good yields (for a four-step sequence) and excellent diastereoselectivities. Notably entry 11 using the aldehyde 3-phenyl-2-propynal gave much-improved diastereoselectivity from a 50:50 dr in the single step[12] to 94:6 dr in the one-pot reaction. This may be due to the presence of lithium counterions in the one-pot reaction or the increased amount of metal counterions compared to the single-step reaction. Entry 3 using mesitaldehyde required the addition of magnesium sulfate alongside the aldehyde in step 3 to aid in the sulfinimine formation, whereas all of the other sulfinimines formed without the need for any extra desiccant. Also noteworthy is the tolerance of an aryl bromide in entry 9, although it was necessary to quench the reaction quickly after the isopropyl Grignard addition, once the reaction was judged to be complete, or debromination was observed in increasing yield over time.

The diastereomeric ratios of the mesityl sulfinamides were determined from the chiral HPLC of the purified sulfinamides and confirmed by the ^{1}H NMR spectra. The absolute configuration of the major diastereoisomer was deduced, as in our previous communication,[12] by the removal of the *N*-sulfinyl group and comparison of the sign of the specific rotation of the free primary amines (or hydrochloride salt) with the reported data.

We next turned our attention to the in situ removal of the mesitylsulfinyl auxiliary, which would give an asymmetric synthesis of unprotected amines by formation of an imine with a temporary chiral stereodirecting and activating group, diastereoselective addition, and removal of the stereodirecting group, all in a single-pot operation from simple starting materials. The removal of the mesitylsulfinyl group was achieved by addition of 2 M HCl in the final stage of the workup, which allowed precipitation of the amine hydrochlorides and isolation by filtration without any further purification required, rendering the whole process very operationally simple and reducing the solvent requirement still further. The amino-alcohol template could be recovered by chromatography of the filtrate in >90% recovery. The enantiomeric excess of the products was determined by conversion to the corresponding benzamides and analysis by chiral HPLC. Our findings are shown in Table 3.

Table 3. Asymmetric One-Pot Synthesis of Chiral Amines



entry	R	R′MgX	4	yield (%)	ee[a] (%)
1	Ph	EtMgCl	**4a**	60	84
2	Ph	^{n}PrMgCl	**4b**	53	88
3	Ph	^{i}PrMgCl	**4c**	59	97
4	Ph	^{i}BuMgCl	**4d**	57	89
5	Ph	allylMgBr	**4e**	52	86
6	Ph	BnMgCl	**4f**	58	64
7	2-furanyl	^{i}PrMgCl	**4g**	49	88
8	4-MeOPh	^{i}PrMgCl	**4h**	54	96
9	4-ClPh	^{i}PrMgCl	**4i**	42	94
10	6-MeO-naphthalen-2-yl	^{i}PrMgCl	**4j**	47	97
11	1-benzo-furan-2-yl	^{i}PrMgCl	**4k**	53	80

[a]Enantiomeric excesses were determined by chiral HPLC of the corresponding benzamides.

dx.doi.org/10.1021/jo201849j | *J. Org. Chem.* 2011, 76, 9452–9459

The procedure was successful with a range of Grignard and aldehyde components, giving amine hydrochlorides in very good yields (over five steps, equivalent to 84−90% per step) and excellent enantioselectivities, with no column chromatography required. The yields of the one-pot reaction to the amines were improved over the yields of the one-pot reaction to the sulfinamides, even with the additional sulfinyl removal step, probably due to the simplicity of the workup with no column chromatography needed. 2-Methyltetrahydrofuran, which is a green solvent, was used in this one-pot reaction, and no chlorinated solvents were used in the workup, so this protocol has a high degree of sustainability. As before we observed that the allyl example (entry 5) gave the *R* enantiome,r whereas all the others gave the opposite, *S* enantiomer. It was found necessary to introduce an aqueous ammonium chloride wash during the workup before the acidic sulfinyl cleavage to ensure the removal of any racemic amine that could have formed from the reaction of excess aldehyde, LiHMDS, and Grignard reagent, which would result in the reduction of enantiomeric excess of the final product if not removed.

CONCLUSION

In conclusion, we have developed a one-pot five-component reaction capable of producing chiral amine hydrochlorides in high yields and high enantioselectivities from the simple template **1** (itself available in just two steps from phenylalaninol in >90% yield)[11a] and cheap commodity chemicals, under green conditions with no column chomatography, that is applicable to carry out in an array format.

EXPERIMENTAL SECTION

General Information. All reactions were carried out under an environment of nitrogen. Dry solvents were purchased from commercial suppliers. Unless otherwise noted, all reagents and solvents were obtained commercially and used without further purification. All reactions were stirred with a magnetic stirrer bar. Chemical shifts are quoted with the deuterated solvent as the reference. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, oct = octet, m = multiplet or unresolved, coupling constant(s) in Hz, integration). Melting points are uncorrected. The diastereomeric ratios (dr's) of the mesityl sulfinamides were determined by chiral HPLC analysis in comparison with the authentic racemates (containing the four diastereomers) and confirmed by the ^{1}H NMR spectra of the purified product in acetone-d_6. The only exception to this was for the mesityl sulfinamides prepared by hydride reduction of the mesityl sulfinyl ketimine, for which the dr's were determined from the crude ^{1}H NMR spectra. The enantiomeric excesses of the amine hydrochlorides were determined by chiral HPLC analysis of the benzoyl protected amines in comparison with the authentic racemates

General Procedure A: Four-Step One-Pot Reaction to Sulfinamides. Mesitylmagnesium bromide (1 M in diethyl ether) (0.427 mL, 0.427 mmol) was added dropwise to a solution of (4*S*)-3-[(4-methylphenyl)sulfonyl]-4-(phenylmethyl)-1,2,3-oxathiazolidine 2-oxide (**1**) (0.15 g, 0.427 mmol) in dry 2-MeTHF (1.5 mL) at −78 °C and stirred for 20−45 min. Lithium hexamethyldisilazide (1 M in toluene) (0.854 mL, 0.854 mmol) was added to the reaction mixture at −78 °C, then the dry ice bath was removed, and the reaction mixture was allowed to warm to room temperature (20 °C) and stirred for 2.6−5.6 h. The aldehyde (0.854 mmol) was added to the reaction mixture, and it was stirred overnight (16−18 h) at room temperature. The reaction mixture was cooled to −78 °C, a Grignard solution (3.41 mmol) was added slowly, and the mixture was left to stir for 3.3−8 h while warming to −10−20 °C. The cooled reaction mixture (0 °C) was quenched with saturated sodium bicarbonate solution and DCM, filtered through a frit, and extracted a further two times with DCM. The combined organic phase was dried using a hydrophobic frit, and the solvent was evaporated to give the crude sulfinamide, which was purified by flash chromatography.

General Procedure B: Five-Step One-Pot Reaction to Amine Hydrochlorides. Mesitylmagnesium bromide (1 M in diethyl ether) (0.427 mL, 0.427 mmol) was added dropwise to a solution of (4*S*)-3-[(4-methylphenyl)sulfonyl]-4-(phenylmethyl)-1,2,3-oxathiazolidine 2-oxide (**1**) (0.15 g, 0.427 mmol) in dry MeTHF (1.5 mL) at −78 °C and stirred for 20−40 min. Lithium hexamethyldisilazide (1 M in toluene) (0.854 mL, 0.854 mmol) was added to the reaction mixture at −78 °C, then the dry ice bath was removed, and the reaction mixture was allowed to warm to room temperature (20 °C) and stirred for 5−5.6 h. The aldehyde (0.854 mmol) was added to the reaction mixture, and it was stirred overnight (17 h) at room temperature. The reaction mixture was cooled to −78 °C, a Grignard solution (3.41 mmol) was added slowly, and the mixture was left to stir for 5−6.3 h while warming to 0−5 °C. The cooled reaction mixture (0 °C) was quenched with saturated sodium bicarbonate solution and diethyl ether, filtered through a frit, and extracted a further two times with diethyl ether. The combined organic phase was washed twice with ammonium chloride solution, then with water, then 2 M HCl in diethyl ether (0.50 mL, 1.00 mmol) was added, and the mixture was left for 10 min. Next, 2 M HCl (aq) (6 mL) was added, the aqueous layer was separated and extracted with diethyl ether, and then the combined organic phase was discarded. The acidic aqueous layer was basified (to pH 12) with solid sodium hydroxide and then extracted twice with diethyl ether. The combined organic phase was dried using a hydrophobic frit, then 2 M HCl in diethyl ether (0.50 mL, 1.00 mmol) was added, and after 5 min the solvent was evaporated to give the product, which where required was further purified by trituration with diethyl ether.

(*S*)-2,4,6-Trimethyl-*N*-((*S*)-1-phenylpropyl)-benzenesulfinamide (2a). General procedure A was followed using benzaldehyde (0.087 mL, 0.854 mmol) and ethylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−50% ethyl acetate/cyclohexane) gave the *title compound* (59 mg, 0.195 mmol, 46%) as a pale yellow oil. Diastereomeric ratio: 92.8:7.2, determined by HPLC [Chiralcel OJ (heptane/ethanol 95:5, flow rate 1.0 mL/min, λ = 215 nm, retention time: 12.441 min (R,S_S, minor), 14.773 min (S,S_S, major)]; $[\alpha]^{20}_D$ +192 (*c* 1.0, $CHCl_3$); IR (ATR) 3213, 2964, 2928, 1602, 1453, 1378, 1071, 1047; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 7.16−7.34 (m, 5 H), 6.82 (s, 2 H), 5.69 (d, J = 6.5 Hz, 1 H), 4.29 (q, J = 7.1 Hz, 1 H), 2.50 (s, 6 H), 2.23 (s, 3 H), 1.92−2.03 (m, 1 H), 1.74−1.87 (m, 1 H), 0.87 ppm (t, J = 7.3 Hz, 3 H); minor diastereoisomer δ 7.16−7.42 (m, 5 H), 6.85 (s, 2 H), 5.56 (d, J = 4.0 Hz, 1 H), 4.25−4.34 (m, 1 H), 2.42 (s, 6 H), 2.25 (s, 3 H), 1.92−2.03 (m, 1 H), 1.74−1.87 (m, 1 H), 0.83−0.90 ppm (m, 3 H); ^{13}C NMR (acetone-d_6, 101 MHz) major diastereomer δ 144.6, 140.7, 139.5, 137.5, 131.4, 129.0, 127.8, 127.8, 62.1, 31.3, 21.0, 19.7, 11.3 ppm; *m*/*z* (ES+) 324 ([M + Na]$^+$, 100%), 302 ([M + H]$^+$, 16), 237 (8), 167 (9); HRMS found, 324.1386 $C_{18}H_{23}NONaS$ 324.1398.

(*S*)-2,4,6-Trimethyl-*N*-((*S*)-1-phenylbutyl)-benzenesulfinamide (2b). General procedure A was followed using benzaldehyde (0.087 mL, 0.854 mmol) and *n*-propylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−50% ethyl acetate/cyclohexane) gave the *title compound* (62 mg, 0.196 mmol, 46%) as a pale yellow oil. Diastereomeric ratio: 95.2:4.8, determined by HPLC [Chiralcel OJ (heptane/ethanol 98:2, flow rate 1.0 mL/min, λ = 215 nm, retention time: 10.839 (S,S_S, major), 12.862 (R,S_S, minor)]; $[\alpha]^{20}_D$ +188 (*c* 1.0, $CHCl_3$); IR (ATR) 3213, 2958, 2929, 2870, 1602, 1454, 1378, 1070, 1047; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 7.16−7.34 (m, 5 H), 6.81 (s, 2 H), 5.70 (d, J = 6.8 Hz, 1 H), 4.38 (q, J = 7.1 Hz, 1 H), 2.50 (s, 6 H), 2.23 (s, 3 H), 1.88−2.00 (m, 1 H), 1.69−1.81 (m, 1 H), 1.20−1.45 (m, 2 H), 0.90 ppm (t, J = 7.4 Hz, 3 H); minor diastereomer δ 7.16−7.43 (m, 5 H), 6.84 (s, 2 H), 5.54 (d, J = 4.3 Hz, 1 H), 4.34−4.44 (m, 1 H), 2.42 (s, 6 H), 2.25 (s, 3 H), 1.88−2.00 (m, 1 H), 1.69−1.81 (m, 1 H), 1.20−1.45

dx.doi.org/10.1021/jo201849j | *J. Org. Chem.* 2011, 76, 9452−9459

(m, 2 H), 0.87 ppm (t, J = 7.6 Hz, 3 H); ^{13}C NMR (acetone-d_6, 101 MHz) major diastereoisomer δ 144.9, 140.7, 139.6, 137.5, 131.4, 129.0, 127.7, 127.7, 60.3, 40.7, 21.0, 20.3, 19.7, 14.2 ppm; m/z (ES+) 338 ([M + Na]$^+$, 100%), 316 ([M + H]$^+$, 8), 167 (10); HRMS found, 338.1544 $C_{19}H_{25}NONaS$ 338.1555.

(*S*)-2,4,6-Trimethyl-*N*-((*S*)-2-methyl-1-phenylpropyl)-benzenesulfinamide (2c). General procedure A was followed using benzaldehyde (0.087 mL, 0.854 mmol) and isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−50% ethyl acetate/cyclohexane) gave impure product that was further purified by flash chromatography on silica gel (elution with 0−25% ethyl acetate/DCM) to give the *title compound* (58 mg, 0.184 mmol, 43%) as a white solid. Mp 99−101 °C; diastereomeric ratio: 99.2:0.8, determined by HPLC [Chiralcel OJ (heptane/ethanol 90:10, flow rate 1.0 mL/min, λ = 215 nm, retention time: 7.475 min (S,S_S, major), 10.460 min (R,S_S, minor)]; $[\alpha]^{20}_D$ +208 (c 1.0, $CHCl_3$); IR (ATR) 3257, 2949, 2920, 2865, 1602, 1456, 1383, 1064, 1045; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 7.15−7.31 (m, 5 H), 6.79 (s, 2 H), 5.79 (d, J = 8.3 Hz, 1 H), 4.07 (t, J = 7.9 Hz, 1 H), 2.47 (s, 6 H), 2.22 (s, 3 H), 2.01−2.12 (m, 1 H), 0.99 (d, J = 6.5 Hz, 3 H), 0.77 ppm (d, J = 6.8 Hz, 3 H); ^{13}C NMR (acetone-d_6, 101 MHz) major diastereomer δ 143.9, 140.6, 139.6, 137.4, 131.3, 128.7, 128.1, 127.5, 67.2, 35.1, 21.0, 20.0, 20.0, 19.7 ppm; m/z (ES+) 338 ([M + Na]$^+$, 100%), 316 ([M + H]$^+$, 11), 299 (5), 167 (9); HRMS found, 338.1546 $C_{19}H_{25}NONaS$ 338.1555.

(*S*)-2,4,6-Trimethyl-*N*-((*S*)-3-methyl-1-phenylbutyl)-benzenesulfinamide (2d). General procedure A was followed using benzaldehyde (0.087 mL, 0.854 mmol) and isobutylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−50% ethyl acetate/cyclohexane) gave the *title compound* (62 mg, 0.189 mmol, 44%) as a pale yellow oil. Diastereomeric ratio: 93.9:6.1, determined by HPLC [Chiralpak IA (heptane/ethanol 95:5, flow rate 1.0 mL/min, λ = 215 nm, retention time: 7.406 min (S,S_S, major), 8.744 min (R,S_S, minor)]; $[\alpha]^{20}_D$ +187 (c 1.0, $CHCl_3$); IR (ATR) 3212, 2955, 2926, 2868, 1602, 1454, 1382, 1070, 1048; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 7.15−7.34 (m, 5 H), 6.80 (s, 2 H), 5.73 (d, J = 7.3 Hz, 1 H), 4.46 (q, J = 7.4 Hz, 1 H), 2.50 (s, 6 H), 2.22 (s, 3 H), 1.78−1.90 (m, 1 H), 1.55−1.67 (m, 2 H), 0.95 (d, J = 6.3 Hz, 3 H), 0.90 ppm (d, J = 6.5 Hz, 3 H); minor diastereomer δ 7.15−7.44 (m, 5 H), 6.84 (s, 2 H), 5.54 (d, J = 4.8 Hz, 1 H), 4.40−4.51 (m, 1 H), 2.41 (s, 6 H), 2.25 (s, 3 H), 1.71−1.90 (m, 1 H), 1.52−1.69 (m, 2 H), 0.92−0.96 (m, 3 H), 0.87 ppm (d, J = 6.3 Hz, 3 H); ^{13}C NMR (acetone-d_6, 101 MHz) major diastereomer δ 145.3, 140.7, 139.7, 137.5, 131.4, 129.0, 127.7, 127.6, 58.8, 48.1, 25.6, 23.0, 22.7, 21.0, 19.7 ppm; m/z (ES+) 352 ([M + Na]$^+$, 100%), 330 ([M + H]$^+$, 12), 313 (12), 167 (12), 164 (13); HRMS found, 352.1699 $C_{20}H_{27}NONaS$ 352.1711.

(*S*)-2,4,6-Trimethyl-*N*-((*S*)-1-phenylheptyl)-benzenesulfinamide (2e). General procedure A was followed using benzaldehyde (0.087 mL, 0.854 mmol) and hexylmagnesium bromide (2 M in diethyl ether) (1.707 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−50% ethyl acetate/cyclohexane) gave impure product which was further purified by flash chromatography on silica gel (elution with 0−25% ethyl acetate/DCM) to give the *title compound* (52 mg, 0.145 mmol, 34%) as a pale yellow solid. Mp 45−47 °C; diastereomeric ratio: 85.6:14.4, determined by HPLC [Chiralpak IA (heptane/ethanol 98:2, flow rate 1.0 mL/min, λ = 215 nm, retention time: 13.222 min (S,S_S, major), 16.900 min (R,S_S, minor)]; $[\alpha]^{20}_D$ +167 (c 1.0, $CHCl_3$); IR (ATR) 3209, 2926, 2856, 1602, 1454, 1378, 1071, 1048; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 7.15−7.35 (m, 5 H), 6.81 (s, 2 H), 5.76 (d, J = 7.1 Hz, 1 H), 4.37 (q, J = 7.1 Hz, 1 H), 2.50 (s, 6 H), 2.23 (s, 3 H), 1.88−2.02 (m, 1 H), 1.71−1.87 (m, 1 H), 1.14−1.44 (m, 8 H), 0.85 ppm (t, J = 6.9 Hz, 3 H); minor diastereomer δ 7.15−7.44 (m, 5 H), 6.85 (s, 2 H), 5.61 (d, J = 3.8 Hz, 1 H), 4.32−4.43 (m, 1 H), 2.42 (s, 6 H), 2.25 (s, 3 H), 1.88−2.02 (m, 1 H), 1.71−1.87 (m, 1 H), 1.14−1.44 (m, 8 H), 0.81−0.90 ppm (m, 3 H); ^{13}C NMR (acetone-d_6, 101 MHz) major diastereomer δ 144.9, 140.7, 139.5, 137.5, 131.3, 129.0, 127.7, 127.7, 60.6, 38.5, 32.6, 29.8, 27.1, 23.3, 21.0, 19.7, 14.4 ppm; m/z (ES+) 380 ([M + Na]$^+$, 100%), 341 (12), 192 (7), 166 (6); HRMS found, 380.2024 $C_{22}H_{31}NONaS$ 380.2024.

(*S*)-*N*-((*S*)-Cyclohexyl(phenyl)methyl)-2,4,6-trimethylbenzenesulfinamide (2f). General procedure A was followed using benzaldehyde (0.087 mL, 0.854 mmol) and cyclohexylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−50% ethyl acetate/cyclohexane) gave impure product that was further purified by flash chromatography on silica gel (elution with 0−25% ethyl acetate/DCM) to give the *title compound* (59 mg, 0.166 mol, 39%) as a cream solid. Mp 119−121 °C; diastereomeric ratio: 99.7:0.3, determined by HPLC [Whelk-o 1 (heptane/ethanol 95:5, flow rate 1.0 mL/min, λ = 215 nm, retention time: 15.118 min (R,S_S, minor), 21.620 min (S,S_S, major)]; $[\alpha]^{21}_D$ +173 (c 1.0, $CHCl_3$); IR (ATR) 3272, 2934, 2853, 1600, 1448, 1421, 1070, 1047; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 7.14−7.29 (m, 5 H), 6.78 (s, 2 H), 5.78 (d, J = 8.6 Hz, 1 H), 4.07 (t, J = 8.3 Hz, 1 H), 2.46 (s, 6 H), 2.22 (s, 3 H), 1.98−2.07 (m, 1 H), 1.54−1.77 (m, 4 H), 1.33−1.43 (m, 1 H), 0.81−1.24 ppm (m, 5 H); ^{13}C NMR (acetone-d_6, 101 MHz) major diastereomer δ 144.0, 140.6, 139.7, 137.4, 131.3, 128.8, 128.1, 127.5, 66.5, 44.7, 30.9, 30.9, 27.2, 26.9, 26.8, 21.0, 19.7 ppm; m/z (ES+) 378 ([M + Na]$^+$, 100%), 356 ([M + H]$^+$, 9), 339 (15), 190 (7); HRMS found, 378.1857 $C_{22}H_{29}NONaS$ 378.1868.

(*S*)-2,4,6-Trimethyl-*N*-((*R*)-1-phenylbut-3-en-1-yl)-benzenesulfinamide (2g). General procedure A was followed using benzaldehyde (0.087 mL, 0.854 mmol) and allylmagnesium bromide (1 M in diethyl ether) (3.41 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−25% ethyl acetate/cyclohexane) gave impure product that was further purified by flash chromatography on silica gel (elution with 0−13% ethyl acetate/DCM) to give the *title compound* (48 mg, 0.153 mmol, 36%) as a colorless oil. Diastereomeric ratio: 94.8:5.2, determined by HPLC [Chiralcel OJ (heptane/ethanol 98:2, flow rate 1.0 mL/min, λ = 215 nm, retention time: 10.658 min (R,S_S, major), 16.579 min (S,S_S, minor)]; $[\alpha]^{20}_D$ +150 (c 1.0, $CHCl_3$); IR (ATR) 3212, 3029, 2922, 1601, 1454, 1380, 1071, 1048; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 7.43 (d, J = 7.1 Hz, 2 H), 7.36 (t, J = 7.4 Hz, 2 H), 7.24−7.31 (m, 1 H), 6.87 (s, 2 H), 5.77 (ddt, J = 17.2, 10.2, 7.0 Hz, 1 H), 5.40 (d, J = 3.6 Hz, 1 H), 5.02−5.14 (m, 2 H), 4.50 (td, J = 7.0, 3.6 Hz, 1 H), 2.59 (t, J = 7.0 Hz, 2 H), 2.43 (s, 6 H), 2.25 ppm (s, 3 H); minor diastereomer δ 7.16−7.46 (m, 5 H), 6.82 (s, 2 H), 5.69−5.83 (m, 2 H), 4.95−5.03 (m, 2 H), 4.43−4.53 (m, 1 H), 2.56−2.63 (m, 2 H), 2.50 (s, 6 H), 2.23 ppm (s, 3 H); ^{13}C NMR (acetone-d_6, 101 MHz) major diastereomer δ 143.3, 141.1, 139.7, 137.6, 135.9, 131.5, 129.2, 128.5, 128.4, 118.5, 58.8, 43.5, 21.0, 19.4 ppm; m/z (ES+) 336 ([M + Na]$^+$, 93%), 314 (100), 287 (53), 261 (39), 217 (27); HRMS found, 314.1569 $C_{19}H_{24}NOS$ 314.1579.

(*S*)-*N*-((*S*)-1,2-Diphenylethyl)-2,4,6-trimethylbenzenesulfinamide (2h). General procedure A was followed using benzaldehyde (0.087 mL, 0.854 mmol) and benzylmagnesium chloride (1 M in diethyl ether) (3.41 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−25% ethyl acetate/cyclohexane) gave impure product that was further purified by flash chromatography on silica gel (elution with 0−13% ethyl acetate/DCM) to give the *title compound* (90 mg, 0.248 mmol, 58%) as a cream solid. Mp 113−116 °C; diastereomeric ratio: 84.0:16.0, determined by HPLC [Chiralcel OD-H (heptane/ethanol 98:2, flow rate 1.0 mL/min, λ = 215 nm, retention time: 9.904 min (R,S_S, minor), 14.684 min (S,S_S, major)]; $[\alpha]^{20}_D$ +176 (c 1.0, $CHCl_3$); IR (ATR) 3257, 3028, 2926, 1602, 1495, 1454, 1410, 1066, 1045; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 7.08−7.48 (m, 10 H), 6.77 (s, 2 H), 5.79 (d, J = 7.1 Hz, 1 H), 4.65 (q, J = 7.3 Hz, 1 H), 3.21 (dd, J = 13.6, 8.1 Hz, 1 H), 3.10 (dd, J = 13.6, 6.4 Hz, 1 H), 2.32 (s, 6 H), 2.22 ppm (s, 3 H); minor diastereomer δ 7.08−7.48 (m, 10 H), 6.83 (s, 2 H), 5.20−5.29 (m, 1 H), 4.69−4.75 (m, 1 H), 3.00−3.26 (m, 2 H), 2.27 (s, 6 H), 2.24 ppm (s, 3 H); ^{13}C NMR (acetone-d_6, 101 MHz) major diastereomer δ 144.3, 140.7, 139.7, 139.7, 137.5, 131.2, 130.4, 129.0, 129.0, 128.0, 127.9, 127.1, 62.8, 45.1, 21.0, 19.5 ppm; $m/$

z (ES+) 386 ([M + Na]$^+$, 100%), 364 ([M + H]$^+$, 19); HRMS found, 386.1544 $C_{23}H_{25}NNaOS$ 386.1549.

(*S*)-*N*-((*S*)-1-(4-Methoxyphenyl)-2-methylpropyl)-2,4,6-trimethylbenzenesulfinamide (3b). General procedure A was followed using 4-methoxybenzaldehyde (0.104 mL, 0.854 mmol) and isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−50% ethyl acetate/cyclohexane) gave the *title compound* (71 mg, 0.205 mmol, 48%) as a cream solid. Mp 108−110 °C; diastereomeric ratio: 99.3:0.7, determined by HPLC [Chiralpak AD (heptane/ethanol 95:5, flow rate 1.0 mL/min, λ = 215 nm, retention time: 9.470 min (R,S_S, minor), 10.818 min (S,S_S, major)]; $[\alpha]^{21}_D$ +197 (*c* 1.0, $CHCl_3$); IR (ATR) 3236, 2949, 2917, 2866, 1614, 1517, 1460, 1383, 1252, 1181, 1064, 1024; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 7.20 (d, J = 8.8 Hz, 2 H), 6.81 (d, J = 8.8 Hz, 2 H), 6.80 (s, 2 H), 5.67 (d, J = 7.8 Hz, 1 H), 4.02 (t, J = 7.8 Hz, 1 H), 3.76 (s, 3 H), 2.47 (s, 6 H), 2.23 (s, 3 H), 2.05 (dqq, J = 7.8, 6.8, 6.8 Hz, 1 H), 0.98 (d, J = 6.8 Hz, 3 H), 0.76 ppm (d, J = 6.8 Hz, 3 H); ^{13}C NMR (acetone-d_6, 101 MHz) δ 159.5, 140.6, 139.7, 137.4, 135.8, 131.3, 129.2, 114.1, 66.6, 55.5, 35.0, 21.0, 20.1, 19.9, 19.7 ppm; *m*/*z* (ES+) 368 ([M + Na]$^+$, 100%), 346 ([M + H]$^+$, 8), 329 (13), 163 (15); HRMS found, 368.1646 $C_{20}H_{27}NO_2NaS$ 368.1660.

(*S*)-*N*-((*S*)-1-Mesityl-2-methylpropyl)-2,4,6-trimethylbenzenesulfinamide (3c). General procedure A was followed using mesitaldehyde (0.126 mL, 0.854 mmol) (and magnesium sulfate (0.205 g, 1.707 mmol) was also added with the aldehyde and it was stirred for 41 h) isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−50% ethyl acetate/cyclohexane) gave impure product, which was dissolved in THF (2 mL). TBAF (1 M in THF) (0.2 mL) was added and stirred for 20 min (to deprotect the TMS group from the impurity) and then evaporated. Further purification by flash chromatography on silica gel (elution with 0−50% ethyl acetate/cyclohexane) gave the *title compound* (51 mg, 0.141 mmol, 33%) as a white solid. Mp 123−125 °C; diastereomeric ratio: 99.3:0.7, determined by HPLC [Chiralpak IA (heptane/ethanol 95:5, flow rate 1.0 mL/min, λ = 215 nm, retention time: 4.877 min (R,S_S, minor), 8.158 min (S,S_S, major)]; $[\alpha]^{21}_D$ +251 (*c* 1.0, $CHCl_3$); IR (ATR) 3252, 2959, 2865, 1605, 1464, 1378, 1071, 1050; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 6.85 (s, 2 H), 6.80 (s, 1 H), 6.79 (s, 1 H), 5.24 (d, J = 7.9 Hz, 1 H), 4.40 (dd, J = 10.4, 7.9 Hz, 1 H), 2.47 (s, 6 H), 2.43 (s, 3 H), 2.34 (s, 3 H), 2.25 (s, 3 H), 2.23−2.37 (m, 1 H), 2.20 (s, 3 H), 1.17 (d, J = 6.5 Hz, 3 H), 0.67 ppm (d, J = 6.8 Hz, 3 H); ^{13}C NMR (acetone-d_6, 101 MHz) major diastereomer δ 140.9, 140.5, 137.3, 137.3, 137.2, 137.2, 137.1, 136.7, 136.0, 131.9, 131.4, 130.0, 64.2, 33.8, 21.9, 21.8, 21.6, 21.0, 20.9, 20.1, 19.6 ppm; *m*/*z* (ES+) 380 ([M + Na]$^+$, 100%), 358 ([M + H]$^+$, 12), 341 (5); HRMS found, 380.2017 $C_{22}H_{31}NONaS$ 380.2024.

(*S*)-*N*-((*S*)-1-(4-Chlorophenyl)-2-methylpropyl)-2,4,6-trimethylbenzenesulfinamide (3d). General procedure A was followed using 4-chlorobenzaldehyde (0.120 g, 0.854 mmol) and isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−50% ethyl acetate/cyclohexane) gave impure product that was further purified by flash chromatography on silica gel (elution with 0−25% methanol/DCM) to give the *title compound* (68 mg, 0.193 mmol, 45%) as a pale yellow oil. Mp 111−113 °C; diastereomeric ratio: 97.6:2.4, determined by HPLC [Chiralpak IA (heptane/ethanol 95:5, flow rate 1.0 mL/min, λ = 215 nm, retention time: 9.254 min (S,S_S, major), 11.965 min (R,S_S, minor)]; $[\alpha]^{21}_D$ +170 (*c* 1.0, $CHCl_3$); IR (ATR) 3188, 2965, 2927, 2868, 1599, 1493, 1441, 1381, 1064, 1044; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 7.29 (d, J = 8.7 Hz, 2 H), 7.25 (d, J = 8.7 Hz, 2 H), 6.78 (s, 2 H), 5.88 (d, J = 8.3 Hz, 1 H), 4.10 (t, J = 7.9 Hz, 1 H), 2.46 (s, 6 H), 2.22 (s, 3 H), 1.96−2.08 (m, 1 H), 0.98 (d, J = 6.8 Hz, 3 H), 0.77 ppm (d, J = 6.8 Hz, 3 H); minor diastereomer δ 7.33−7.42 (m, 4 H), 6.85 (s, 2 H), 5.65 (d, J = 5.3 Hz, 1 H), 4.16 (dd, J = 6.9, 5.3 Hz, 1 H), 2.41 (s, 6 H), 2.25 (s, 3 H), 1.97−2.08 (m, 1 H), 0.95−1.02 (m, 3 H), 0.74−0.80 ppm (m, 3 H); ^{13}C NMR (acetone-d_6, 101 MHz) major diastereomer δ 143.1, 140.7, 139.3, 137.5, 132.7, 131.3, 129.9, 128.7, 66.2, 35.1, 20.9, 20.0, 19.9, 19.7 ppm; *m*/*z* (ES+) 372 ([M + Na]$^+$, 100%), 350 ([M + H]$^+$, 10), 151 (12); HRMS found, 372.1176 $C_{19}H_{24}NONaSCl$ 372.1165.

(*S*)-*N*-((*S*)-1-(6-Methoxynaphthalen-2-yl)-2-methylpropyl)-2,4,6-trimethylbenzenesulfinamide (3e). General procedure A was followed using 6-methoxy-2-naphthalenecarbaldehyde (0.159 g, 0.854 mmol) and isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−50% ethyl acetate/cyclohexane) gave impure product that was further purified by flash chromatography on silica gel (elution with 0−25% ethyl acetate/DCM) to give the *title compound* (64 mg, 0.162 mmol, 38%) as a cream solid. Mp 143−145 °C; diastereomeric ratio: 99.3:0.7, determined by HPLC [Chiralpak IA (heptane/ethanol 95:5, flow rate 1.0 mL/min, λ = 215 nm, retention time: 13.404 min (S,S_S, major), 14.460 min (R,S_S, minor)]; $[\alpha]^{21}_D$ +167 (*c* 1.0, $CHCl_3$); IR (ATR) 3266, 2949, 2920, 2864, 1606, 1487, 1462, 1382, 1272, 1229, 1173, 1069, 1048; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 7.70 (d, J = 8.5 Hz, 1 H), 7.68 (d, J = 8.9 Hz, 1 H), 7.55 (d, J = 1.6 Hz, 1 H), 7.46 (dd, J = 8.5, 1.6 Hz, 1 H), 7.24 (d, J = 2.4 Hz, 1 H), 7.11 (dd, J = 8.9, 2.4 Hz, 1 H), 6.74 (s, 2 H), 5.86 (d, J = 8.1 Hz, 1 H), 4.19 (t, J = 8.1 Hz, 1 H), 3.90 (s, 3 H), 2.46 (s, 6 H), 2.17 (s, 3 H), 2.16 (dqq, J = 8.1, 6.8, 6.8 Hz, 1 H), 1.05 (d, J = 6.8 Hz, 3 H), 0.79 ppm (d, J = 6.8 Hz, 3 H); ^{13}C NMR (acetone-d_6, 101 MHz) major diastereomer δ 158.5, 140.6, 139.4, 139.0, 137.5, 134.8, 131.3, 130.1, 129.6, 127.4, 126.8, 126.8, 119.5, 106.5, 67.1, 55.6, 34.9, 20.9, 20.1, 19.7 ppm; *m*/*z* (ES+) 418 ([M + Na]$^+$, 100%), 396 ([M + H]$^+$, 11), 380 (34); HRMS found, 418.1810 $C_{24}H_{29}NO_2NaS$ 418.1817.

***tert*-Butyl 3-((*S*)-2-Methyl-1-((*S*)-2,4,6-trimethylphenylsulfinamido)propyl)-1*H*-indole-1-carboxylate (3f).** General procedure A was followed using 1,1-dimethylethyl 3-formyl-1H-indole-1-carboxylate (0.209 g, 0.854 mmol) and isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−25% ethyl acetate/cyclohexane) gave impure product that was further purified by flash chromatography on silica gel (elution with 5−15% ethyl acetate/DCM) to give the *title compound* (77 mg, 0.170 mmol, 40%) as a pale yellow oil. Diastereomeric ratio: 98.8:1.2, determined by HPLC [Chiralpak IC (heptane/ethanol 95:5, flow rate 1.0 mL/min, λ = 215 nm, retention time: 12.231 min (R,S_S, minor), 13.290 min (S,S_S, major)]; $[\alpha]^{21}_D$ +139 (*c* 1.0, $CHCl_3$); IR (ATR) 3218, 2972, 2929, 1730, 1603, 1453, 1370, 1247, 1156, 1073; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 8.11 (d, J = 7.8 Hz, 1 H), 7.72 (d, J = 8.0 Hz, 1 H), 7.56 (s, 1 H), 7.29 (dd, J = 7.8, 7.3 Hz, 1 H), 7.20 (dd, J = 8.0, 7.3 Hz, 1 H), 6.73 (s, 2 H), 5.78 (d, J = 7.6 Hz, 1 H), 4.50 (dd, J = 7.6, 6.8 Hz, 1 H), 2.47 (s, 6 H), 2.24−2.38 (dqq, J = 6.8, 6.8, 6.5 Hz, 1 H), 2.19 (s, 3 H), 1.68 (s, 9 H), 1.02 (d, J = 6.8 Hz, 3 H), 0.96 ppm (d, J = 6.5 Hz, 3 H); ^{13}C NMR (acetone-d_6, 101 MHz) δ 150.3, 140.6, 139.2, 137.6, 136.5, 131.3, 130.3, 125.0, 124.5, 123.2, 120.7, 120.5, 115.9, 84.2, 58.6, 34.1, 28.4, 21.0, 20.2, 19.7, 19.6 ppm; *m*/*z* (ES+) 477 ([M + Na]$^+$, 100%), 455 ([M + H]$^+$, 29), 421 (15); HRMS found, 477.2184 $C_{26}H_{34}N_2O_3NaS$ 477.2182.

(*S*)-*N*-((*S*)-1-(Furan-2-yl)-2-methylpropyl)-2,4,6-trimethylbenzenesulfinamide (3g). General procedure A was followed using furfural (0.071 mL, 0.854 mmol) and isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−50% ethyl acetate/cyclohexane) gave impure product that was further purified by flash chromatography on silica gel (elution with 0−25% ethyl acetate/DCM) to give the *title compound* (63 mg, 0.206 mmol, 48%) as a pale yellow solid. Mp 70−73 °C; diastereomeric ratio: 97.3:2.7, determined by HPLC [Chiralpak AD (heptane/isopropanol 95:5, flow rate 1.0 mL/min, λ = 215 nm, retention time: 11.686 min (R,S_S, minor), 13.877 min (S,S_S, major)]; $[\alpha]^{21}_D$ +197 (*c* 1.0, $CHCl_3$); IR (ATR) 3198, 2952, 2925, 2865, 1602, 1441, 1380, 1068, 1047; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 7.44 (d, J = 1.5 Hz, 1 H), 6.85 (s, 2 H), 6.32 (dd, J = 3.2, 1.5 Hz, 1 H), 6.24 (d, J = 3.2 Hz, 1 H), 5.66 (d, J = 8.6 Hz, 1 H), 4.19 (dd, J = 8.6, 6.8 Hz, 1 H), 2.51 (s, 6 H), 2.25 (s, 3 H), 2.19 (dqq, J = 6.8, 6.8, 6.5 Hz, 1 H), 0.93 (d, J = 6.5 Hz, 3 H), 0.88 ppm (d, J = 6.8 Hz, 3 H); ^{13}C NMR (acetone-d_6, 101 MHz) major diastereomer δ 156.6, 142.3, 140.8, 139.7, 137.4, 131.4,

110.9, 107.6, 60.9, 33.7, 21.0, 19.6, 19.2 ppm; *m/z* (ES+) 328 ([M + Na]$^+$, 100%), 306 ([M + H]$^+$, 10), 167 (16); HRMS found, 328.1335 $C_{17}H_{23}NO_2NaS$ 328.1347.

(*S*)-*N*-((*S*)-1-(Benzofuran-2-yl)-2-methylpropyl)-2,4,6-trimethylbenzenesulfinamide (3h). General procedure A was followed using 1-benzofuran-2-carbaldehyde (0.103 mL, 0.854 mmol) and isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−25% ethyl acetate/cyclohexane) gave impure product that was further purified by flash chromatography on silica gel (elution with 0−13% ethyl acetate/DCM) to give the *title compound* (67 mg, 0.188 mmol, 44%) as a pale yellow oil. Diastereomeric ratio: 97.1:2.9, determined by HPLC [Chiralpak IA (heptane/ethanol 97:3, flow rate 1.0 mL/min, λ = 215 nm, retention time: 14.418 min (S,S_S, major), 20.705 min (R,S_S, minor)]; $[\alpha]^{21}_D$ +159 (*c* 1.0, $CHCl_3$); IR (ATR) 3211, 2962, 2928, 2872, 1601, 1454, 1384, 1252, 1075, 1048; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 7.54 (dd, *J* = 7.2, 1.5 Hz, 1 H), 7.44 (d, *J* = 8.1 Hz, 1 H), 7.24 (ddd, *J* = 8.1, 7.5, 1.5 Hz, 1 H), 7.19 (ddd, *J* = 7.5, 7.2, 1.1 Hz, 1 H), 6.81 (s, 2 H), 6.67 (s, 1 H), 5.87 (d, *J* = 8.7 Hz, 1 H), 4.37 (dd, *J* = 8.7, 6.8 Hz, 1 H), 2.53 (s, 6 H), 2.31 (oct, *J* = 6.8 Hz, 1 H), 2.21 (s, 3 H), 1.00 (d, *J* = 6.8 Hz, 3 H), 0.96 ppm (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (acetone-d_6, 101 MHz) major diastereomer δ 159.8, 155.6, 140.9, 139.4, 137.6, 131.4, 129.5, 124.6, 123.6, 121.7, 111.7, 104.6, 61.0, 33.6, 21.0, 19.8, 19.7, 19.2 ppm; *m/z* (ES+) 378 ([M + Na]$^+$, 100%), 356 ([M + H]$^+$, 21); HRMS found, 378.1498 $C_{21}H_{25}NO_2NaS$ 378.1498.

(*S*)-*N*-((*S*)-1-(5-Bromothiophen-2-yl)-2-methylpropyl)-2,4,6-trimethylbenzenesulfinamide (3i). General procedure A was followed using 5-bromo-2-thiophenecarbaldehyde (0.101 mL, 0.854 mmol) and isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol), which was stirred for only 2 h while warming to −45 °C and then immediately quenched (to prevent debromination of the product). Purification by flash chromatography on silica gel (elution with 0−25% ethyl acetate/cyclohexane) gave impure product that was further purified by flash chromatography on silica gel (elution with 0−13% ethyl acetate/DCM) to give the *title compound* (69 mg, 0.172 mmol, 40%) as a colorless oil. Diastereomeric ratio: 98.1:1.9, determined by HPLC [Chiralpak AY-H (heptane/ethanol 80:20, flow rate 1.0 mL/min, λ = 215 nm, retention time: 8.594 min (S,S_S, major), 22.311 min (R,S_S, minor)]; $[\alpha]^{21}_D$ +123 (*c* 1.0, $CHCl_3$); IR (ATR) 3203, 2960, 2923, 2871, 1602, 1441, 1380, 1070, 1046; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 6.93 (d, *J* = 3.8 Hz, 1 H), 6.83 (s, 2 H), 6.79 (d, *J* = 3.8 Hz, 1 H), 5.82 (d, *J* = 7.8 Hz, 1 H), 4.40 (t, *J* = 7.3 Hz, 1 H), 2.52 (s, 6 H), 2.24 (s, 3 H), 2.05−2.16 (m, 1 H), 0.97 (d, *J* = 6.8 Hz, 3 H), 0.93 ppm (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (acetone-d_6, 101 MHz) major diastereomer δ 150.0, 141.0, 139.2, 137.6, 131.4, 130.4, 126.4, 110.7, 62.4, 35.5, 21.0, 19.9, 19.8, 19.2 ppm; *m/z* (ES+) 424 ([^{81}Br, M + Na]$^+$, 100%), 422 ([^{79}Br, M + Na]$^+$, 92), 402 ([^{81}Br, M + H]$^+$, 32), 400 ([^{79}Br, M + H]$^+$, 30); HRMS found, 422.0222 $C_{17}H_{22}{}^{79}BrNONaS_2$ 422.0218.

(*S*)-2,4,6-Trimethyl-*N*-((*S*)-2-methyl-1-(thiazol-5-yl)propyl)-benzenesulfinamide (3j). General procedure A was followed using 1,3-thiazole-5-carbaldehyde (0.074 mL, 0.854 mmol) and isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−50% ethyl acetate/cyclohexane) gave impure product that was further purified by flash chromatography on silica gel (elution with 0−100% ethyl acetate/DCM) to give the *title compound* (50 mg, 0.155 mmol, 36%) as a pale yellow oil. Diastereomeric ratio: 89.7:10.3, determined by HPLC [Chiralpak IA (heptane/ethanol 95:5, flow rate 1.0 mL/min, λ = 215 nm, retention time: 22.571 min (R,S_S, minor), 24.335 min (S,S_S, major)]; $[\alpha]^{21}_D$ +183 (*c* 1.0, $CHCl_3$); IR (ATR) 3194, 2960, 2926, 2873, 1603, 1459, 1382, 1066, 1034; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 8.80 (s, 1 H), 7.70 (s, 1 H), 6.82 (s, 2 H), 5.91 (d, *J* = 8.1 Hz, 1 H), 4.57 (t, *J* = 7.6 Hz, 1 H), 2.51 (s, 6 H), 2.23 (s, 3 H), 2.07−2.20 (m, 1 H), 1.00 (d, *J* = 6.8 Hz, 3 H), 0.92 ppm (d, *J* = 6.8 Hz, 3 H); minor diastereomer δ 8.92 (s, 1 H), 7.86 (s, 1 H), 6.87 (s, 2 H), 5.73 (d, *J* = 5.2 Hz, 1 H), 4.61 (dd, *J* = 6.0, 5.2 Hz, 1 H), 2.45 (s, 6 H), 2.26 (s, 3 H), 2.08−2.20 (m, 1 H), 1.00−1.04 (m, 3 H), 0.87 ppm (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (acetone-d_6, 101 MHz) major diastereomer δ 153.2, 142.1, 141.9, 141.0, 139.1, 137.6, 131.4, 60.0, 35.9, 21.0, 19.9, 19.7, 19.4 ppm; *m/z* (ES+) 345 ([M + Na]$^+$, 100%), 323 ([M + H]$^+$, 74); HRMS found, 345.1057 $C_{16}H_{22}N_2ONaS_2$ 345.1066.

(*S*)-2,4,6-Trimethyl-*N*-((*S*)-4-methyl-1-phenylpent-1-yn-3-yl)-benzenesulfinamide (3k). General procedure A was followed using 3-phenyl-2-propynal (0.104 mL, 0.854 mmol) and isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol). Purification by flash chromatography on silica gel (elution with 0−25% ethyl acetate/cyclohexane) gave impure product that was further purified by flash chromatography on silica gel (elution with 0−13% ethyl acetate/DCM) to give the *title compound* (50 mg, 0.147 mmol, 34%) as a yellow oil. Diastereomeric ratio: 94.4:5.6, determined by HPLC [Chiralpak AY-H (heptane/ethanol 95:5, flow rate 1.0 mL/min, λ = 215 nm, retention time: 26.249 min (R,S_S, minor), 30.222 min (S,S_S, major)]; $[\alpha]^{21}_D$ +138 (*c* 1.0, $CHCl_3$); IR (ATR) 2960, 2923, 2870, 1600, 1490, 1463, 1380, 1071, 1049; ^{1}H NMR (acetone-d_6, 400 MHz) major diastereomer δ 7.32−7.42 (m, 5 H), 6.88 (s, 2 H), 5.71 (d, *J* = 7.1 Hz, 1 H), 4.13 (dd, *J* = 7.1, 6.3 Hz, 1 H), 2.58 (s, 6 H), 2.26 (s, 3 H), 2.09 (qqd, *J* = 6.8, 6.6, 6.3 Hz, 1 H), 1.11 (d, *J* = 6.6 Hz, 3 H), 1.09 ppm (d, *J* = 6.8 Hz, 3 H); minor diastereomer δ 7.28−7.47 (m, 5 H), 6.85−6.91 (m, 2 H), 5.63 (d, *J* = 7.1 Hz, 1 H), 4.23 (dd, *J* = 6.7, 5.2 Hz, 1 H), 2.58 (s, 6 H), 2.26 (s, 3 H), 1.95−2.07 (m, 1 H), 1.02−1.09 ppm (m, 6 H); ^{13}C NMR (acetone-d_6, 101 MHz) major diastereomer δ 141.0, 139.4, 137.8, 132.4, 131.5, 129.3, 129.2, 124.2, 89.5, 85.4, 54.7, 35.2, 21.0, 19.7, 19.7, 18.7 ppm; *m/z* (ES+) 362 ([M + Na]$^+$, 100%), 340 ([M + H]$^+$, 29); HRMS found, 362.1542 $C_{21}H_{25}NONaS$ 362.1549.

(*S*)-1-Phenylpropan-1-amine Hydrochloride (4a).[15] General procedure B was followed using benzaldehyde (0.087 mL, 0.854 mmol) and ethylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol), which gave the title compound (44 mg, 0.256 mmol, 60%) as a cream solid. Mp 226−229 °C (decomp) [lit.[15] mp 192−193 °C]; $[\alpha]^{20}_D$ +16 (*c* 1.0, EtOH) [lit.[15b] $[\alpha]^{23}_D$ +17.8 (*c* 2.08, EtOH) (*S*)]; IR (ATR) 2964, 2880, 1600, 1516, 1458, 1395; ^{1}H NMR (MeOH-d_4, 400 MHz) δ 7.39−7.51 (m, 5 H), 4.16 (dd, *J* = 9.2, 5.9 Hz, 1 H), 1.89−2.11 (m, 2 H), 0.90 ppm (t, *J* = 7.4 Hz, 3 H); ^{13}C NMR (MeOH-d_4, 101 MHz) δ 138.2, 130.5, 130.5, 128.5, 58.5, 28.9, 10.6 ppm; *m/z* (ES+) 136 ([M − Cl]$^+$, 100%), 119 ([M − NH_3Cl]$^+$, 46); HRMS found, 136.1126 $C_9H_{14}N$ 136.1126. All analytical data are in accordance with the literature.[15c]

(*S*)-1-Phenylbutan-1-amine Hydrochloride (4b).[16] General procedure B was followed using benzaldehyde (0.087 mL, 0.854 mmol) and *n*-propylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol), which gave the title compound (42 mg, 0.226 mmol, 53%) as a cream solid. Mp 277−280 °C (decomp) [lit.[16a] mp 299 °C (decomp)]; $[\alpha]^{21}_D$ +20 (*c* 1.0, EtOH); IR (ATR) 2961, 2876, 1601, 1515, 1458, 1392; ^{1}H NMR (MeOH-d_4, 400 MHz) δ 7.37−7.51 (m, 5 H), 4.24 (dd, *J* = 8.5, 6.7 Hz, 1 H), 1.88−2.02 (m, 2 H), 1.15−1.39 (m, 2 H), 0.95 ppm (t, *J* = 7.3 Hz, 3 H); ^{13}C NMR (MeOH-d_4, 101 MHz) δ 138.4, 130.5, 130.4, 128.5, 56.9, 37.7, 20.2, 14.0 ppm; *m/z* (ES+) 150 ([M − Cl]$^+$, 29%), 133 ([M − NH_3Cl]$^+$, 100); HRMS found, 150.1272 $C_{10}H_{16}N$ 150.1277. All analytical data are in accordance with the literature.[16b] The amine hydrochloride was converted to the free amine by treatment with sodium hydroxide. $[\alpha]^{22}_D$ −4 (*c* 0.9, EtOH) [lit.[17] $[\alpha]^{25}_D$ −2.8 (*c* 1.0, EtOH) (*S*)].

(*S*)-2-Methyl-1-phenylpropan-1-amine Hydrochloride (4c).[15a,c] General procedure B was followed using benzaldehyde (0.087 mL, 0.854 mmol) and isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol), which gave the title compound (47 mg, 0.253 mmol, 59%) as a cream solid. Mp 266−269 °C (decomp) [lit.[15a] mp 265−267 °C (decomp)]; $[\alpha]^{22}_D$ +12 (*c* 0.4, EtOH); IR (ATR) 2963, 2893, 1600, 1515, 1460, 1395; ^{1}H NMR (MeOH-d_4, 400 MHz) δ 7.36−7.51 (m, 5 H), 3.93 (d, *J* = 9.1 Hz, 1 H), 2.12−2.27 (m, 1 H), 1.15 (d, *J* = 6.6 Hz, 3 H), 0.81 ppm (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (MeOH-d_4, 101 MHz) δ 138.2, 130.4, 130.3, 128.7, 63.3, 34.0, 19.8, 19.6 ppm; *m/z* (ES+) 150 ([M − Cl]$^+$, 15%), 133 ([M − NH_3Cl]$^+$, 100); HRMS found, 150.1273 $C_{10}H_{16}N$ 150.1277. All analytical data are in accordance with the literature.[15a,c] The amine hydrochloride was converted to the free amine by

dx.doi.org/10.1021/jo201849j | *J. Org. Chem.* 2011, 76, 9452−9459

treatment with sodium hydroxide. $[\alpha]^{22}_{D}$ −12 (*c* 1.1, $CHCl_3$) [lit.[18] $[\alpha]^{23}_{D}$ −12.4 (*c* 0.97, $CHCl_3$) (*S*)].

(*S*)-3-Methyl-1-phenylbutan-1-amine Hydrochloride (4d).[16] General procedure B was followed using benzaldehyde (0.087 mL, 0.854 mmol) and isobutylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol), which gave the title compound (49 mg, 0.245 mmol, 57%) as a white solid. Mp 272−275 °C (decomp) [lit.[16a] mp >310 °C]; $[\alpha]^{21}_{D}$ +22 (*c* 1.0, EtOH); IR (ATR) 2887, 1600, 1514, 1459, 1393; ^{1}H NMR (MeOH-d_4, 400 MHz) δ 7.38−7.51 (m, 5 H), 4.31 (dd, *J* = 10.0, 5.6 Hz, 1 H), 1.94 (ddd, *J* = 14.8, 10.0, 5.3 Hz, 1 H), 1.80 (ddd, *J* = 14.8, 8.6, 5.6 Hz, 1 H), 1.33−1.48 (m, 1 H), 0.96 (d, *J* = 6.5 Hz, 3 H), 0.92 ppm (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (MeOH-d_4, 101 MHz) δ 138.3, 130.5, 130.5, 128.6, 55.4, 44.4, 25.9, 23.5, 22.0 ppm; *m*/*z* (ES+) 164 ($[M - Cl]^+$, 70%), 147 ($[M - NH_3Cl]^+$, 100); HRMS found, 164.1444 $C_{11}H_{18}N$ 164.1439. All analytical data are in accordance with the literature.[16b]

(*R*)-1-Phenylbut-3-en-1-amine Hydrochloride (4e).[15a,19] General procedure B was followed using benzaldehyde (0.087 mL, 0.854 mmol) and allylmagnesium bromide (1 M in diethyl ether) (3.41 mL, 3.41 mmol), which gave the title compound (41 mg, 0.223 mmol, 52%) as a pale brown solid. Mp 208−211 °C (decomp) [lit.[15a] mp 223−225 °C (decomp)]; $[\alpha]^{21}_{D}$ +13 (*c* 1.1, $CHCl_3$) [lit.[17] $[\alpha]^{25}_{D}$ +36.2 (*c* 1.4, $CHCl_3$) (*R*)]; IR (ATR) 2885, 1597, 1511, 1459, 1438, 1395; ^{1}H NMR (MeOH-d_4, 400 MHz) δ 7.38−7.51 (m, 5 H), 5.63−5.77 (ddt, *J* = 17.1, 10.1, 7.1 Hz, 1 H), 5.11−5.25 (m, 2 H), 4.34 (t, *J* = 7.4 Hz, 1 H), 2.74 ppm (dd, *J* = 7.4, 7.1 Hz, 2 H); ^{13}C NMR (MeOH-d_4, 101 MHz) δ 138.1, 133.4, 130.4, 130.4, 128.4, 120.5, 56.4, 40.3 ppm; *m*/*z* (ES+) 148 ($[M - Cl]^+$, 8%), 131 ($[M - NH_3Cl]^+$, 100); HRMS found, 148.1125 $C_{10}H_{14}N$ 148.1121. All analytical data are in accordance with the literature.[15a]

(*S*)-1,2-Diphenylethanamine Hydrochloride (4f).[15c,20] General procedure B was followed using benzaldehyde (0.087 mL, 0.854 mmol) and benzylmagnesium chloride (1 M in diethyl ether) (3.41 mL, 3.41 mmol), which gave the title compound (58 mg, 0.248 mmol, 58%) as a cream solid. Mp 238−240 °C (decomp) [lit.[19] mp 259−260 °C]; $[\alpha]^{21}_{D}$ +83 (*c* 1.0, EtOH) [lit.[19] $[\alpha]^{20}_{D}$ +128.0 (*c* 0.99, EtOH) (*S*)]; IR (ATR) 3027, 2883, 1598, 1514, 1498, 1455, 1394; ^{1}H NMR (MeOH-d_4, 400 MHz) δ 7.32−7.46 (m, 5 H), 7.18−7.28 (m, 3 H), 7.07−7.13 (m, 2 H), 4.51 (dd, *J* = 9.0, 6.5 Hz, 1 H), 3.31 (dd, *J* = 13.6, 6.5 Hz, 1 H), 3.21 ppm (dd, *J* = 13.6, 9.0 Hz, 1 H); ^{13}C NMR (MeOH-d_4, 101 MHz) δ 137.8, 136.9, 130.6, 130.4, 130.3, 129.8, 128.6, 128.4, 58.5, 42.1 ppm; *m*/*z* (ES+) 198 ($[M - Cl]^+$, 43%), 181 ($[M - NH_3Cl]^+$, 100), 166 (11); HRMS found, 198.1279 $C_{14}H_{16}N$ 198.1283. All analytical data are in accordance with the literature.[15c]

(*S*)-1-(Furan-2-yl)-2-methylpropan-1-amine Hydrochloride (4g). General procedure B was followed using furfural (0.070 mL, 0.854 mmol) and isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol), which gave the title compound (37 mg, 0.211 mmol, 49%) as a brown solid. Mp 194−197 °C (decomp); IR (ATR) 2966, 2878, 1588, 1495, 1158; ^{1}H NMR (MeOH-d_4, 400 MHz) δ 7.60 (d, *J* = 1.7 Hz, 1 H), 6.51 (d, *J* = 3.2 Hz, 1 H), 6.48 (dd, *J* = 3.2, 1.7 Hz, 1 H), 4.17 (d, *J* = 8.0 Hz, 1 H), 2.28 (dqq, *J* = 8.0, 6.8, 6.8 Hz, 1 H), 1.09 (d, *J* = 6.8 Hz, 3 H), 0.92 ppm (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (MeOH-d_4, 101 MHz) δ 150.4, 144.9, 111.9, 111.3, 56.0, 32.4, 19.5, 19.0 ppm; *m*/*z* (ES+) 140 ($[M - Cl]^+$, 6%), 138 (27), 123 ($[M - NH_3Cl]^+$, 100); HRMS found, 123.0803 $C_8H_{11}O$ 123.0810. The amine hydrochloride was converted to the free amine by treatment with sodium hydroxide. $[\alpha]^{22}_{D}$ +16 (*c* 0.5, EtOH) [lit.[21] $[\alpha]^{20}_{D}$ +9.6 (*c* 1.0, EtOH) (*S*)].

(*S*)-1-(4-Methoxyphenyl)-2-methylpropan-1-amine Hydrochloride (4h).[15a] General procedure B was followed using 4-methoxybenzaldehyde (0.010 mL, 0.854 mmol) and isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol), which gave the title compound (50 mg, 0.232 mmol, 54%) as a pale brown solid. Mp 218−220 °C (decomp) [lit.[15a] mp 217−219 °C (decomp)]; $[\alpha]^{22}_{D}$ +8 (*c* 1.0, EtOH); IR (ATR) 2966, 2914, 1612, 1574, 1511, 1261, 1183, 1027; ^{1}H NMR (MeOH-d_4, 400 MHz) δ 7.31 (d, *J* = 8.8 Hz, 2 H), 7.00 (d, *J* = 8.8 Hz, 2 H), 3.86 (d, *J* = 9.8 Hz, 1 H), 3.82 (s, 3 H), 2.17 (dqq, *J* = 9.8, 6.8, 6.5 Hz, 1 H), 1.13 (d, *J* = 6.8 Hz, 3 H), 0.80 ppm (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (MeOH-d_4, 101 MHz) δ 161.8, 130.0, 130.0, 115.6, 62.9, 56.0, 34.0, 19.9, 19.7 ppm; *m*/*z* (ES+) 180 ($[M - Cl]^+$, 13%), 179 ($[M - HCl]^+$, 43), 163 ($[M - NH_3Cl]^+$, 100); HRMS found, 163.1120 $C_{11}H_{15}O$ 163.1123. All analytical data are in accordance with the literature.[15a]

(*S*)-1-(4-Chlorophenyl)-2-methylpropan-1-amine Hydrochloride (4i).[22] General procedure B was followed using 4-chlorobenzaldehyde (0.120 g, 0.854 mmol) and isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol), which gave the title compound (39 mg, 0.177 mmol, 42%) as a cream solid. Mp 276−279 °C (decomp) [lit.[22] mp 256−259 °C]; $[\alpha]^{21}_{D}$ +11 (*c* 1.0, EtOH); IR (ATR) 2962, 2878, 1609, 1512, 1469, 1394, 1090; ^{1}H NMR (MeOH-d_4, 400 MHz) δ 7.48 (d, *J* = 8.4 Hz, 2 H), 7.39 (d, *J* = 8.4 Hz, 2 H), 3.96 (d, *J* = 9.3 Hz, 1 H), 2.11−2.25 (dqq, *J* = 9.3, 6.8, 6.8 Hz, 1 H), 1.14 (d, *J* = 6.8 Hz, 3 H), 0.81 ppm (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (MeOH-d_4, 101 MHz) δ 136.9, 136.2, 130.5, 130.4, 62.5, 33.9, 19.8, 19.5 ppm; *m*/*z* (ES+) 184 ($[M - Cl]^+$, 8%), 169 (33), 167 ($[M - NH_3Cl]^+$, 100), 127 (23); HRMS found, 184.0887 $C_{10}H_{15}ClN$ 184.0888.

(*S*)-1-(6-Methoxynaphthalen-2-yl)-2-methylpropan-1-amine Hydrochloride (4j). General procedure B was followed using 6-methoxy-2-naphthaldehyde (0.159 g, 0.854 mmol) and isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol), which gave the *title compound* (53 mg, 0.199 mmol, 47%) as a cream solid. Mp 256−259 °C (decomp); $[\alpha]^{22}_{D}$ +13 (*c* 0.9, EtOH); IR (ATR) 2963, 2845, 1606, 1509, 1488, 1200, 1024; ^{1}H NMR (MeOH-d_4, 400 MHz) δ 7.88 (d, *J* = 8.5 Hz, 1 H), 7.80 (d, *J* = 8.5 Hz, 1 H), 7.79 (s, 1 H), 7.44 (dd, *J* = 8.5, 1.8 Hz, 1 H), 7.29 (d, *J* = 2.4 Hz, 1 H), 7.20 (dd, *J* = 8.5, 2.4 Hz, 1 H), 4.06 (d, *J* = 9.3 Hz, 1 H), 3.93 (s, 3 H), 2.24−2.36 (dqq, *J* = 9.3, 6.5, 6.5 Hz, 1 H), 1.19 (d, *J* = 6.5 Hz, 3 H), 0.84 ppm (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (MeOH-d_4, 101 MHz) δ 160.0, 136.4, 133.0, 130.7, 130.2, 129.2, 128.3, 126.0, 120.8, 106.9, 63.5, 56.0, 34.0, 19.9, 19.8 ppm; *m*/*z* (ES+) 213 ($[M - NH_3Cl]^+$, 100%), 178 (18); HRMS found, 213.1273 $C_{15}H_{17}O$ 213.1279.

(*S*)-1-(Benzofuran-2-yl)-2-methylpropan-1-amine Hydrochloride (4k). General procedure B was followed using benzofuran-2-carbaldehyde (0.100 mL, 0.854 mmol) and isopropylmagnesium chloride (2 M in diethyl ether) (1.707 mL, 3.41 mmol), which gave the *title compound* (51 mg, 0.226 mmol, 53%) as a brown solid. Mp 220−223 °C (decomp); $[\alpha]^{22}_{D}$ +21 (*c* 0.3, EtOH); IR (ATR) 2963, 2871, 1598, 1510, 1453, 1394, 1257, 1175, 1098; ^{1}H NMR (MeOH-d_4, 400 MHz) δ 7.63 (d, *J* = 7.5 Hz, 1 H), 7.53 (d, *J* = 8.3 Hz, 1 H), 7.35 (t, *J* = 7.4 Hz, 1 H), 7.27 (t, *J* = 7.3 Hz, 1 H), 6.95 (s, 1 H), 4.34 (d, *J* = 8.0 Hz, 1 H), 2.33−2.46 (dqq, *J* = 8.0, 6.5, 6.5 Hz, 1 H), 1.16 (d, *J* = 6.5 Hz, 3 H), 0.97 ppm (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (MeOH-d_4, 101 MHz) δ 156.6, 152.8, 129.0, 126.5, 124.7, 122.8, 112.3, 108.2, 56.4, 32.3, 19.5, 19.2 ppm; *m*/*z* (ES+) 188 (23%), 173 ($[M - NH_3Cl]^+$, 100), 145 (10); HRMS found, 173.0962 $C_{12}H_{13}O$ 173.0966.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details for synthesis of benzamides, NMR spectra, and HPLC analyses. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: robert.stockman@nottingham.ac.uk.

■ ACKNOWLEDGMENTS

This research was supported by EPSRC/GSK (EP/F068352/1). Eric Hortense (GSK) is thanked for carrying out chiral HPLC analyses and Bill Leavens (GSK) for accurate mass analyses.

■ REFERENCES

(1) (a) Nicolaou, K. C.; Montagnon, T.; Snyder, S. A. *Chem. Commun.* **2003**, 551. (b) Tietze, L. F.; Brasche, G.; Gericke, K. M.

Domino Reactions in Organic Synthesis; Wiley-VCH: Weinheim, 2006. (c) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 7134. (d) Enders, D.; Grondal, C.; Huettl, M. R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 1570. (e) Grondal, C.; Jeanty, M.; Enders, D. *Nat. Chem.* **2010**, *2*, 167.

(2) (a) Walji, A. M.; MacMillan, D. W. C. *Synlett* **2007**, 1447. (b) Clarke, P. A.; Santos, S.; Martin, W. H. C. *Green Chem.* **2007**, *9*, 438.

(3) Olah, G. A. *Angew. Chem., Int. Ed.* **2005**, *44*, 2636. (b) Armaroli, N.; Balzani, V. *Angew. Chem., Int. Ed.* **2007**, *46*, 52.

(4) Ranón, D. J.; Yus, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1602.

(5) Seyden-Penne, J. *Chiral Auxiliaries and Ligands in asymmetric Synthesis*; Wiley: New York, 1995.

(6) (a) Hashiguchi, S.; Fujii, A.; Takehara, J.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 7562. (b) Fujii, A.; Hashiguchi, S.; Uematsu, N.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1996**, *118*, 2521.

(7) For recent reviews, see: Xie, J.-H.; Zhu, S.-F.; Zhou, Q.-L. *Chem. Rev.* **2011**, *111*, 1713. For a recent review and perspective on the field, see: Nugent, T. C.; El-Shazly, M. *Adv. Synth. Catal.* **2010**, *352*, 753. Fleury-Brégeot, N.; de la Fuente, V.; Castillion, S.; Claver, C. *ChemCatChem* **2010**, *2*, 1346.

(8) For reviews see: Tripathi, R. P.; Verma, S. S.; Pandey, J.; Tiwari, V. K. *Curr. Org. Chem.* **2008**, *12*, 1093. Guillena, G.; Ramon, D. J.; Yus, M. *Tetrahedron: Asymmetry* **2007**, *18*, 693. You, S.-L. *Chem. Asian J.* **2007**, *2*, 820.

(9) (a) Hayashi, T.; Ishigedani, M. *J. Am. Chem. Soc.* **2000**, *122*, 976. (b) Hayashi, T.; Kawai, M.; Tokunaga, N. *Angew. Chem., Int. Ed.* **2004**, *43*, 6125. (c) Hermanns, N.; Dahmen, S.; Bolm, C.; Bräse, S. *Angew. Chem., Int. Ed.* **2002**, *41* (3692), 3694. (d) Kuriyama, M.; Soeta, T.; Hao, X. Y.; Chen, O.; Tomioka, K. *J. Am. Chem. Soc.* **2004**, *126*, 8128. (e) Tokunaga, N.; Otomaru, Y.; Okamoto, K.; Ueyama, K.; Shintani, R.; Hayashi, T. *J. Am. Chem. Soc.* **2004**, *126*, 13584. (f) Wang, Z. Q.; Feng, C. G.; Xu, M. H.; Lin, G. Q. *J. Am. Chem. Soc.* **2007**, *129*, 5336. (g) Duan, H. F.; Jia, X. Y.; Wang, L. X.; Zhou, Q. L. *Org. Lett.* **2006**, *8*, 2567. (h) Marques, C. S.; Burke, A. J. *Eur. J. Org. Chem.* **2010**, *9*, 1639. (i) Otomaru, Y.; Tokunaga, N.; Shintani, R.; Hayashi, T. *Org. Lett.* **2005**, *7*, 307. (j) Okamoto, K.; Hayashi, T.; Rawal, V. H. *Chem. Commun.* **2009**, 4815. (k) Kurihara, K.; Yamamoto, Y.; Miyaura, N. *Adv. Synth. Catal.* **2009**, *351*, 260. (l) Hao, X. Y.; Kuriyama, M.; Chen, Q.; Yamamoto, Y.; Yamada, K.; Tomioka, K. *Org. Lett.* **2009**, *11*, 4470. (m) Jagt, R. B. C.; Toullec, P. Y.; Geerdink, D.; de Vries, J. G.; Feringa, B. L.; Minnaard, A. D. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 2789. (n) Cao, Z. P.; Du, H. F. *Org. Lett.* **2010**, *12*, 2602. (o) Crampton, R.; Woodward, S.; Fox, M. *Adv. Synth. Catal.* **2011**, *353*, 903.

(10) For reviews on sulfinimine chemistry, see: (a) Robak, M. T.; Herbage, M. A.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 3600. (b) Ferreira, F.; Botuha, C.; Chemla, F.; Pérez-Luna, A. *Chem. Soc. Rev.* **2009**, *38*, 1162. (c) Morton, D.; Stockman, R. A. *Tetrahedron* **2006**, *62*, 8869. (d) Davis, F. A. *J. Org. Chem.* **2006**, *71*, 8993. (e) Senanayake, C. H.; Krishnamurthy, D.; Lu, Z.-H; Hou, Z.; Gallou, I. *Aldrichimica Acta* **2005**, *38*, 93. (f) Zhou, P.; Chen, B.-C.; Davis, F. A. *Tetrahedron* **2004**, *60*, 8003. (g) Ellman, J. A.; Owens, T. D.; Tang, T. P. *Acc. Chem. Res.* **2002**, *35*, 984. (h) Davis, F. A.; Zhou, P.; Chen, B.-C . *Chem. Soc. Rev.* **1998**, *27*, 13.

(11) (a) Roe, C.; Hobbs, H.; Stockman, R. A. *Chem.—Eur. J.* **2011**, *17*, 2704. (b) Sasraku-Neequaye, L.; MacPherson, D.; Stockman, R. A. *Tetrahedron Lett.* **2008**, *49*, 1129.

(12) Roe, C.; Moragas Solá, T.; Sasraku-Neequaye, L.; Hobbs, H.; Churcher, I.; MacPherson, D.; Stockman, R. A. *Chem. Commun.* **2011**, *47*, 7491.

(13) Liu, G.; Coogan, D. A.; Ellman, J. A. *J. Am. Chem. Soc.* **1997**, *119*, 9913.

(14) Westera, G.; Blomberg, C.; Bickelhaupt, F. *J. Organomet. Chem.* **1978**, *C55*, 155.

(15) (a) Zwierzak, A.; Napieraj, A. *Synthesis* **1999**, 930. (b) Côté, A.; Charette, A. B. *J. Org. Chem.* **2005**, *70*, 10864. (c) Coogan, D. A.; Liu, G.; Ellman, J. A. *Tetrahedron* **1999**, *55*, 8883.

(16) (a) de Roocker, A. *Bull. Soc. Chim. Belg* **1963**, *72*, 195. (b) Asada, M.; Obitsu, T.; Nagese, T.; Tanaka, M.; Yamaura, Y.; Takizawa, H.; Yoshikawa, K.; Sato, K.; Narita, M.; Ochuchida, S.; Nakai, H.; Toda, M. *Bioorg. Med. Chem.* **2010**, *18*, 80.

(17) Mereyala, H. B.; Koduru, S. R.; Cheemalapati, V. N. *Tetrahedron: Asymmetry* **2006**, *17*, 259.

(18) Shen, Z. L.; Loh, T. P. *Org. Lett.* **2007**, *9*, 5413.

(19) Wu, M. J.; Prigden, L. N. *Synlett* **1990**, 636.

(20) Sasaki, T.; Kanematsu, K. *J. Med. Chem.* **1966**, *9*, 847.

(21) Demir, A. S.; Sesenoglu, Ö.; Ülkü, D.; Arici, C. *Helv. Chim. Acta* **2003**, *86*, 91.

(22) Arrowsmith, J. E.; Cook, M. J.; Hardstone, D. J. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2364.