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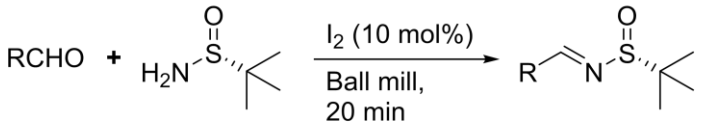

Mechanochemical Synthesis of *N*-tert-Butanesulfinyl Imines Under Metal-Free Conditions

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1. Introduction

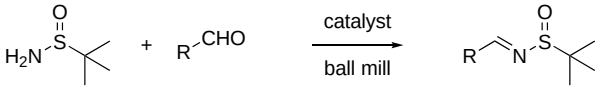
Chiral *N*-sulfinyl imines are valuable synthetic intermediates that undergo diverse transformations with a high degree of stereoselectivity. Some examples are the palladium-catalyzed α-allylation of ketones,[1] asymmetric fluoroalkylation,[2] diastereoselective alkylation,[3,4] asymmetric Strecker synthesis,[5] and asymmetric synthesis of amine derivatives such as α- and β-aminophosphonic acids,[6] α- and β-amino acids,[7] α-branched amines,[8,9] and aziridines.[10] They also find applications in the total synthesis of natural products and biologically active molecules.[11-13] Chiral *N*-sulfinyl imines are the condensation products of carbonyl compounds with commercially available chiral sulfinamides such as *p*-toluenesulfinamide and *tert*-butanesulfinamide. However, such condensations typically require the utilization of excess amounts (2-5 equivalents) of metal reagents such as Ti(IV) derivatives and $CuSO_4$ that act as Lewis acids and dehydrating agents at the same time.[14-16]

Lately, mechanochemistry is gaining increased attention of synthetic chemists and is becoming a useful tool in some laboratories rather than being a side-line in organic synthesis. Mechanochemistry typically provides a solvent-free and, hence, green alternative to the conventional solution-based chemistry. Mechanochemical reactions are often cleaner, rapid and the workup is usually simple.[17-28] These advantages of mechanochemistry promoted us to investigate the condensation of *tert*-butanesulfinamide with carbonyl compounds under grinding conditions as a metal-free, solvent-free and greener approach for accessing the synthetically valuable *tert*-butanesulfinyl imines.

2. Results and Discussion

We initially examined the condensation of 2-iodobenzaldehyde with (*R*)-(+)-2-methyl-2-propanesulfinamide [(*R*)-(+)-*tert*-butanesulfinamide] under solvent free conditions using agate mortar and pestle without any additives. Under these conditions, there was no reaction observed even after grinding for one hour. Repeating the reaction in presence of iodine (1 equivalent) lead to the formation of the desired sulfinylimine (80% ^{1}H NMR conversion) in 20 minutes. After finding that this condensation is possible mechanochemically without a metal catalyst, we started a systematic study of the reaction with benzaldehyde and racemic *tert*-butanesulfinamide using a ball mill (Retsch MM400 ball mill at 30 Hz). We found that in contrast to grinding using a mortar and pestle, the reaction proceeds without any catalyst in the ball mill (table 1, entry 1). Addition of 10 mol% of iodine enhanced the reaction (80% conversion) in 15 minutes (Table 1, entry 2). We examined different copper and zinc salts as catalysts for this reaction (Table 1, entries 3-8), but none of these catalysts was as efficient as iodine. Increasing the reaction time from 15 to 20 minutes lead to a slight enhancement of the yield, but any further increase of the reaction time (> 20 min) led to a slight decrease in the reaction yield (Table 1, entries 9-11). Decreasing the iodine loading from 10 mol% to 2 mol% lead to a significant decrease in the conversion of benzaldehyde to the desired sulfinylimine, while increasing the catalyst loading over 10% showed no significant effect on the reaction outcome (Table 1, entries 12-15). Addition of anhydrous sodium sulfate (1 equivalent) had no impact on the reaction outcome (Table 1, entry 16). From these results, we conclude that the optimum reaction conditions are milling the substrates in the presence of 10 mol% of iodine as a catalyst for 20 minutes.

Table 1. Optimization of the reaction conditions



1 **2** **3**

No[a]	Catalyst	Catalyst [mol%]	Time [min]	Conversion [%][b]
1[c]	------	-----	60	47
2	I_2	10	15	80
3	CuBr	10	15	18
4	CuI	10	15	16
5	$ZnCl_2$	10	15	20
6	ZnF_2	10	15	16
7	$Cu(OAc)_2$	10	15	12
8	$Cu(OTf)_2$	10	15	31
9	I_2	10	20	84
10	I_2	10	25	81
11	I_2	10	30	80
12	I_2	2	20	55
13	I_2	5	20	80
14	I_2	12	20	81
15	I_2	15	20	80
16[d]	I_2	10	20	83

[a] PhCHO (0.5 mmol), *t*-Bu-sulfinamide (0.5 mmol), Retsch MM400 ball mill, 5 mL stainless steel jar, one 10 mm stainless steel ball, 30 Hz; [b] Determined by ^{1}H NMR of the crude mixture; [c] Performed with agate mortar and pestle: 0% conversion; [d] Na_2SO_4 (1 eq) was added.

With the optimized reaction conditions we studied the scope of the reaction using different aldehydes by varying electronic and steric properties (Table 2). Aromatic, heteroaromatic and aliphatic aldehydes afforded the corresponding sulfinylimines in moderate to excellent yields, while paraformaldehyde showed no reactivity at all. Under the same conditions neither acetophenone nor 2,2,2-trifluoroacetophene were converted to the corresponding sulfinylimines indicating that ketones are unreactive under these conditions. This could be considered as a limitation of this methodology, but shows that the reaction is selective for aldehydes, which is beneficial especially with complex molecules having different carbonyl functionalities. Most of the aldehyde substrates were used without purification but the purification of the aldehydes prior to the reaction had a great impact on the reaction yield as expected, where the yields of the products **3k**, **3q**, **3t**, and **3u** for example is significantly increased upon purification of the starting materials. We noticed that electronic factors affect the reaction outcome more than steric factors. Aromatic aldehydes with an electron-withdrawing group such as 4-nitrobenzaldehyde and 4-cyanobenzaldehyde gave the corresponding products in low yields. This could be attributed to the reactivity of the formed sulfinylimines and that iodine also can catalyze the backward reaction. To test this hypothesis, we performed the reaction of 4-cyanobenzaldehyde and 4-nitrobenzaldehyde under the optimized condition conditions but reducing the reaction time from 20 to 10 minutes. This reduction in the reaction time showed an increase in the yield of 4-cyanobenzaldehyde (49% to 76%), while no effect was observed with 4-nitrobenzaldehyde. By reducing the reaction time in the case of 4-nitrobenzaldehyde to only two minutes, the yield of the product **3p** increased from 40% (20 min reaction time) to 53% proving our hypothesis.

In case of the 1,3-isophthaldicarboxaldehyde the starting material was quantitatively converted into products giving the bissufinylimine **3r** as major product (85%) in addition to **3s** in 14%. The condensation of citral (*cis*/*trans* mixture) with **(*R*)-1** lead to the formation of the two-corresponding isomeric sulfinylimine products **3z-1** and **3z-2** in a 1:1 ratio as indicated by the ^{1}H NMR of the crude mixture. The two isomeric products were isolated by flash column chromatography (10% EtOAc/*n*-hexane). The compound of the lower R_f (0.25) (**3z-2**) was characterized as the product of the *trans*-citral as its NOESY spectrum showed a NOE signal between the azomethine proton and the nearby methyl group. This NOE signal is absent in the NOESY spectrum of the product with the higher R_f (0.31) indicating that the product **3z-1** has the *Z*-configuration.

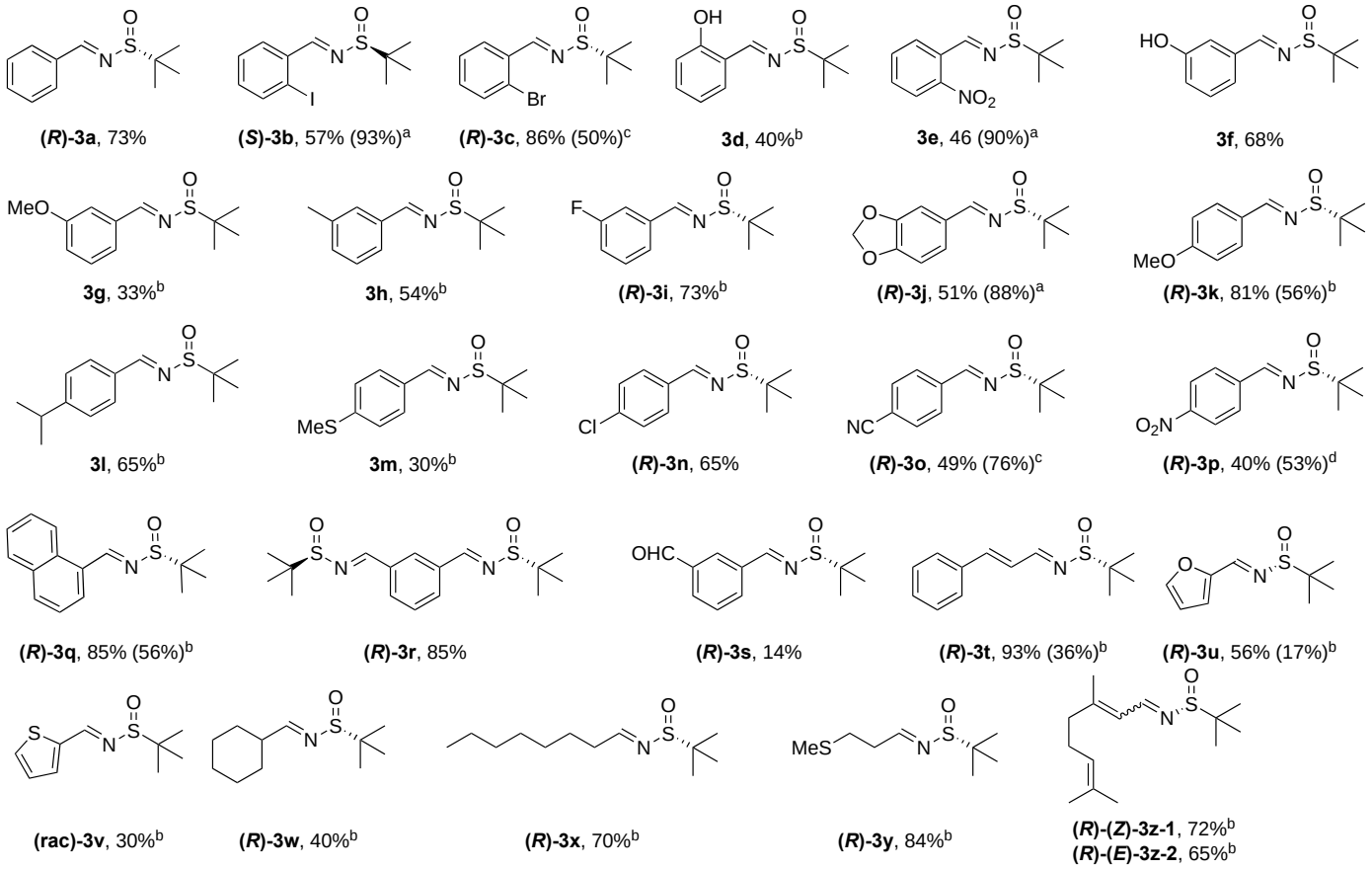


Table 2. Substrate scope of the mechanochemical condensation of aldehydes and *tert*-butanesulfinamide.

[a] Yield calculated based on the recovered aldehyde; [b] Aldehyde used without purification; [c] reaction time 10 min; [d] reaction time 2 min.

3. Conclusion

In summary, we have developed a simple, rapid, efficient, and green method for the introduction of the valuable chiral auxiliary *tert*-butansulfinamide into aldehydes under metal- and solvent-free reaction conditions. The reaction is performed using a ball mill and catalyzed by 10 mol% iodine. The reaction is applicable to a wide range of aldehydes and shows good function group tolerance.

Synthetic organic chemists should pay more attention to mechanochemistry as a promising, efficient, simpler and greener alternative to the conventional solution-based chemistry. There is an urgent need for developing elegant engineering solutions to make mechanochemistry more reliable and to open a window on monitoring the reaction during its progress.

4. Experimental section

4.1. General

Commercially available aldehydes were used in all reactions without purification unless specifically indicated. The mechanochemical reactions are performed in Retsch MM400 vibrating mill at a frequency of 30 Hz in a stainless steel 10 mL vial with one steel ball of 10 mm diameter. Thin-layer chromatography (TLC) was performed on pre-coated aluminium sheets of Merck silica gel 60 F254 (0.20 mm) and visualized by UV radiation (254 nm). Automated column chromatography was performed on a Biotage® Isolera Four using Biotage® cartridges SNAP Ultra 10 g. ^{1}H NMR and ^{13}C NMR spectra were measured on Bruker DPX 300, 400 or 500 apparatus and were referenced to the residual proton solvent peak (^{1}H: $CDCl_3$, δ 7.26 ppm) and solvent ^{13}C signal ($CDCl_3$, δ 77.2 ppm). Chemical shifts δ were reported in ppm, multiplicity of the signals was declared as followed: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sex = sextet, hep = septet, dd = doublet of doublets, m = multiplet, b = broad; and coupling constants (*J*) in Hertz. Mass spectrometric measurements were performed by the EPSRC Mass Spectrometry Facility in Swansea University on a Waters Xevo G2-S. Ions were generated by the Atmospheric Pressure Ionisation Techniques (APCI). The molecular ion peaks values quoted for molecular ion plus hydrogen $[M+H]^+$. IR spectra were recorded on a Shimadzu FTIR Affinity-1S apparatus.

Wavenumbers are quoted in cm^{-1}. All compounds were measured neat directly on the crystal of the IR machine.

4.2. Typical procedure for ball milling imine formation

A mixture of 2-methyl-2-propanesulfinamide (0.5 mmol, 1 eq), the appropriate aldehyde (0.5 mmol, 1 eq), and elemental iodine (10 mol%) was placed in a 5 mL grinding steel jar and milled for 20 min at 30 Hz. The reaction mixture was dissolved in dichloromethane (20 mL) and washed with a saturated solution of $Na_2S_2O_8$ (10 mL), then with brine (10 mL). The organic phase was dried over anhydrous $MgSO_4$, filtered and evaporated under reduced pressure. The residue was purified by flash column chromatography.

*4.3. (R)-(–)-N-(Benzylidene)-2-methylpropane-2-sulfinamide [**(R)-3a**][14,15,29]*

The general procedure was followed using benzaldehyde (53.1 mg, 51 µL, 0.5 mmol), (*R*)-(+)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (17% EtOAc/*n*-hexane) to give **(*R*)-3a** (77 mg, 73%) as a colourless solid; $[\alpha]_D^{20}$ = –213 (*c* 0.67, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 8.59 (s, 1H), 7.89 – 7.79 (m, 2H), 7.55 – 7.43 (m, 3H), 1.27 (s, 9H).

*4.4. (R)-(+)-N-(2-Iodobenzylidene)-2-methylpropane-2-sulfinamide [**(S)-3b**][2]*

The general procedure was followed using 2-iodobenzaldehyde (116 mg, 0.5 mmol), (*S*)-(-)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (10% EtOAc/*n*-hexane) to give **(*S*)-3b** (96 mg, 57%) as a yellowish solid; $[\alpha]_D^{20}$ = 164 (*c* 0.77, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 8.78 (s, 1H), 7.99 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.94 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.47 – 7.37 (m, 1H), 7.18 (ddd, *J* = 7.9, 7.4, 1.8 Hz, 1H), 1.28 (s, 9H).

*4.5. (R)-(–)-N-(2-Bromobenzylidene)-2-methylpropane-2-sulfinamide [**(R)-3c**][29,30]*

The general procedure was followed using purified 2-bromobenzaldehyde (93 mg, 59 µL, 0.5 mmol), (*R*)-(+)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (14% EtOAc/*n*-hexane) to give **(*R*)-3c** (124 mg, 86%) as a colourless oil; $[\alpha]_D^{20}$-227 (*c* 0.7, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 8.98 (s, 1H), 8.04 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.65 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.43 – 7.30 (m, 2H), 1.28 (s, 9H).

*4.6. N-(2-Hydroxybenzylidene)-2-methylpropane-2-sulfinamide [**3d**][31]*

The general procedure was followed using salicylaldehyde (61.1 mg, 53 µL, 0.5 mmol), (*rac*)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (20% EtOAc/*n*-hexane) to give **3d** (45 mg, 40%) as a white solid; δ_H (500 MHz, $CDCl_3$) 11.04 (s, 1H), 8.70 (s, 1H), 7.52 – 7.38 (m, 2H), 7.06 – 6.93 (m, 2H), 1.26 (s, 9H).

*4.7. N-(2-Nitrobenzylidene)-2-methylpropane-2-sulfinamide [**3e**][32]*

The general procedure was followed using 2-nitrobenzaldehyde (76 mg, 0.5 mmol), (*rac*)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (17% EtOAc/*n*-hexane) to give **3e** (59 mg, 46%) as a yellow solid; δ_H (400 MHz, $CDCl_3$) 8.99 (s, 1H), 8.07 – 7.98 (m, 2H), 7.73 (ddd, *J* = 7.7, 1.3, 0.6 Hz, 1H), 7.66 (td, *J* = 7.8, 1.5 Hz, 1H), 1.30 (s, 9H).

*4.8. N-(3-Hydroxybenzylidene)-2-methylpropane-2-sulfinamide [**3f**][33]*

The general procedure was followed using 3-hydroxybenzaldehyde (61 mg, 0.5 mmol), (*rac*)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol), and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (20% EtOAc/*n*-hexane) to give **3f** (77 mg, 63%) as a white solid; δ_H (400 MHz, $CDCl_3$) 8.59 (s, 1H), 7.46 (dt, *J* = 7.6, 1.1 Hz, 1H), 7.41 (dd, *J* = 2.5, 1.5 Hz, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 7.05 (ddd, *J* = 8.1, 2.6, 1.0 Hz, 1H), 1.28 (s, 9H).

*4.9. N-(3-Methoxybenzylidene)-2-methylpropane-2-sulfinamide [**3g**][34]*

The general procedure was followed using *m*-anisaldehyde (68 mg, 61 µL, 0.5 mmol), (*rac*)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (17% EtOAc/*n*-hexane) to give **3g** (40 mg, 33%) as a colourless oil; δ_H (400 MHz, $CDCl_3$) 8.55 (s, 1H), 7.44 – 7.34 (m, 3H), 7.10 – 7.03 (m, 1H), 3.86 (s, 3H), 1.26 (s, 9H).

*4.10. N-(3-Methylbenzylidene)-2-methylpropane-2-sulfinamide [**3h**][35]*

The general procedure was followed using *m*-tolualdehyde (60 mg, 59 µL, 0.5 mmol), (*rac*)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (14% EtOAc/*n*-hexane) to give **3h** (60 mg, 54%) as a colourless oil; δ_H (400 MHz, $CDCl_3$) 8.56 (s, 1H), 7.67 (s, 1H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.36 (dd, *J* = 9.1, 5.7 Hz, 1H), 7.34 – 7.31 (m, 1H), 2.41 (s, 3H), 1.27 (s, 9H).

*4.11. (R)-(–)-N-(3-Fluorobenzylidene)-2-methylpropane-2-sulfinamide [**(R)-3i**][36]*

The general procedure was followed using 3-fluorobenzaldehyde (62 mg, 53 µL, 0.5 mmol), (*R*)-(+)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (11% EtOAc/*n*-hexane) to give **(*R*)-3i** (83 mg, 73%) as a colourless oil; $[\alpha]_D^{20}$ = –4 (*c* 0.5, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 8.56 (d, *J* = 1.3 Hz, 1H), 7.63 – 7.55 (m, 2H), 7.46 (ddd, *J* = 11.2, 6.7, 3.1 Hz, 1H), 7.25 – 7.18 (m, 1H), 1.27 (s, 9H).

*4.12. (R)-(–)-N-(Benzo[d][1,3]dioxol-5-ylmethylene)-2-methylpropane-2-sulfinamide [**(R)-3j**][36]*

The general procedure was followed using piperonal (75 mg, 0.5 mmol), (*R*)-(+)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (20% EtOAc/*n*-hexane) to give **(*R*)-3j** (65 mg, 51%) as a white solid; $[\alpha]_D^{20}$ = –18 (*c* 0.66, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 8.44 (s, 1H), 7.40 (d, *J* = 1.6 Hz, 1H), 7.28 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.05 (q, *J* = 1.3 Hz, 2H), 1.24 (s, 9H).

*4.13. (R)-(–)-N-(4-Methoxybenzylidene)-2-methylpropane-2-sulfinamide [**(R)-3k**][14,15]*

The general procedure was followed using purified *p*-anisaldehyde (68 mg, 61 µL, 0.5 mmol), (*R*)-(+)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (20% EtOAc/*n*-hexane) to give **(*R*)-3k** (97 mg, 81%) as a white solid; $[\alpha]_D^{20}$ = –68 (*c* 0.73, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 8.51 (s, 1H), 7.85 – 7.73 (m, 2H), 7.01 – 6.92 (m, 2H), 3.87 (s, 3H), 1.25 (s, 9H).

*4.14. N-(4-Isopropylbenzylidene)-2-methylpropane-2-sulfinamide [**3l**][37]*

The general procedure was followed using cuminaldehyde (74 mg, 76 μL, 0.5 mmol), (*rac*)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (14% EtOAc/*n*-hexane) to give **3l** (82 mg, 65%) as a colourless oil; δ_H (400 MHz, $CDCl_3$) 8.56 (s, 1H), 7.78 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.3 Hz, 2H), 2.96 (hept, *J* = 6.9 Hz, 1H), 1.27 (s, *J* = 6.9 Hz, 6H), 1.26 (s, 9H).

*4.15. N-(4-(Methylthio)benzylidene)-2-methylpropane-2-sulfinamide [**3m**][38]*

The general procedure was followed using 4-(methylthio)benzaldehyde (76 mg, 67 μL, 0.5 mmol), (*rac*)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (14% EtOAc/*n*-hexane) to give **3m** (38 mg, 30%) as a colourless oil; δ_H (400 MHz, $CDCl_3$) 8.52 (s, 1H), 7.77 – 7.72 (m, 2H), 7.31 – 7.27 (m, 2H), 2.52 (s, 3H), 1.25 (s, 9H).

*4.16. (R)-(–)-N-(4-Chlorobenzylidene)-2-methylpropane-2-sulfinamide [**(R)-3n**][15,36]*

The general procedure was followed using 4-chlorobenzaldehyde (70 mg, 0.5 mmol), (*R*)-(+)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (10% EtOAc/*n*-hexane) to give **(*R*)-3n** (79 mg, 65%) as a white solid; $[\alpha]_D^{20}$ = –68 (*c* 0.73, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 8.54 (s, 1H), 7.83 – 7.74 (m, 2H), 7.49 – 7.40 (m, 2H), 1.26 (s, 9H).

*4.17. (R)-(–)-N-(4-Cyanobenzylidene)-2-methylpropane-2-sulfinamide [**(R)-3o**][38]*

The general procedure was followed using 4-cyanobenzaldehyde (66 mg, 0.5 mmol), (*R*)-(+)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (17% EtOAc/*n*-hexane) to give **(*R*)-3o** (57 mg, 49%) as a white solid; $[\alpha]_D^{20}$ = –70 (*c* 0.77, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 8.6 (s, 1H), 7.98 – 7.91 (m, 2H), 7.80 – 7.72 (m, 2H), 1.26 (s, 9H).

*4.18. (R)-(–)-N-(4-Nitrobenzylidene)-2-methylpropane-2-sulfinamide [**(R)-3p**][30]*

The general procedure was followed using 4-nitrobenzaldehyde (76 mg, 0.5 mmol), (*R*)-(+)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (17% EtOAc/*n*-hexane) to give **(*R*)-3p** (51 mg, 40%) as a yellow solid; $[\alpha]_D^{20}$ = –70 (*c* 0.77, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 8.67 (s, 1H), 8.37 – 8.29 (m, 2H), 8.06 – 7.99 (m, 2H), 1.29 (s, 9H).

*4.19. ((R)-(–)-2-Methyl-N-(naphthalen-1-ylmethylene)propane-2-sulfinamide [**(R)-3q**][15,39]*

The general procedure was followed using purified 1-naphthaldehyde (78 mg, 68 μL, 0.5 mmol), (*R*)-(+)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (10% EtOAc/*n*-hexane) to give **(*R*)-3q** (110 mg, 85%) as a yellow oil; $[\alpha]_D^{20}$ = –6 (*c* 0.66, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 9.16 (s, 1H), 9.04 (d, *J* = 8.3 Hz, 1H), 8.08 – 7.99 (m, 2H), 7.93 (d, *J* = 7.6 Hz, 1H), 7.65 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.62 – 7.54 (m, 2H), 1.33 (s, 9H).

*4.20. (R,R)-(–)-N,N'-Bis-(tert-butylsulfinyl)-isophthaldimine [**(R)-3r**][40]*

The general procedure was followed using isophthalaldehyde (34 mg, 0.25 mmol), (*R*)-(+)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (20% EtOAc/*n*-hexane) to give **(*R*)-3r** (R_f = 0.24) (72 mg, 85%) as a white solid; $[\alpha]_D^{20}$ = –28 (*c* 0.50, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 8.65 (s, 2H), 8.31 (t, *J* = 1.5 Hz, 1H), 8.00 (dd, *J* = 7.7, 1.7 Hz, 2H), 7.61 (dd, *J* = 9.5, 5.8 Hz, 1H), 1.29 (s, 18H).

*4.21. (R)-(–)-N-(3-Formylbenzylidene)-2-methylpropane-2-sulfinamide [**(R)-3s**]*

Isolated as a colorless oil (8 mg, 14%) from the crude mixture of the previous reaction (isophthalaldehyde reaction) by flash chromatography (20% EtOAc/*n*-hexane) (R_f = 0.31); $[\alpha]_D^{20}$ = –68 (*c* 0.50, $CHCl_3$); IR (neat) ν_{max} 3024, 2970, 1737, 1700, 1604, 1084 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 10.09 (s, 1H), 8.66 (s, 1H), 8.35 (t, *J* = 1.5 Hz, 1H), 8.09 (dt, *J* = 7.7, 1.4 Hz, 1H), 8.06 – 7.99 (m, 1H), 7.67 (dd, *J* = 9.6, 5.7 Hz, 1H), 1.28 (m, 9H); δ_C (126 MHz, $CDCl_3$) 191.5, 161.7, 137.1, 135.1, 135.0, 132.8, 130.4, 129.9, 58.2, 22.8; HRMS (ASAP): MH^+, found 238.0900. $C_{12}H_{16}NO_2S$ requires 238.0902.

*4.22. (R)-2-Methyl-N-((1E,2E)-3-phenylallylidene)propane-2-sulfinamide [**(R)-3t**][15,39]*

The general procedure was followed using *trans*-cinnamaldehyde (66 mg, 63 μL, 0.5 mmol), (*R*)-(+)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (17% EtOAc/*n*-hexane) to give **(*R*)-3t** (109 mg, 93%) as a yellow solid; $[\alpha]_D^{20}$ = –142 (*c* 0.70, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 8.38 (d, *J* = 9.2 Hz, 1H), 7.58 – 7.51 (m, 2H), 7.44 – 7.36 (m, 3H), 7.25 (t, *J* = 7.9 Hz, 1H), 7.09 (dd, *J* = 15.9, 9.2 Hz, 1H), 1.24 (s, 9H).

*4.23. (R)-N-(Furan-2-ylmethylene)-2-methylpropane-2-sulfinamide [**(R)-3u**][14,15]*

The general procedure was followed using purified furfural (48 mg, 41 μL, 0.5 mmol), (*R*)-(+)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (14% EtOAc/*n*-hexane) to give **(*R*)-3u** (62 mg, 62%) as a colourless oil; $[\alpha]_D^{20}$ = –228 (*c* 0.67, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 8.40 (s, 1H), 7.64 (dd, *J* = 1.1, 0.6 Hz, 1H), 7.01 (dd, *J* = 3.5, 0.5 Hz, 1H), 6.57 (dd, *J* = 3.5, 1.8 Hz, 1H), 1.26 (s, 9H).

*4.24. 2-Methyl-N-(thiophen-2-ylmethylene)propane-2-sulfinamide [**(R)-3v**][15]*

The general procedure was followed using purified 2-thiophenecarboxaldehyde (56 mg, 47 μL, 0.5 mmol), 2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol), and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (14% EtOAc/*n*-hexane) to give **(*R*)-3v** (32 mg, 30%) as a white solid; δ_H (400 MHz, $CDCl_3$) 8.67 (s, 1H), 7.59 (dt, *J* = 5.0, 1.1 Hz, 1H), 7.55 – 7.52 (m, 1H), 7.18 – 7.10 (m, 1H), 1.25 (s, 9H).

*4.25. (R)-N-(Cyclohexylmethylene)-2-methylpropane-2-sulfinamide [**(R)-3w**][15,16]*

The general procedure was followed using cyclohexanecarboxaldehyde (56 mg, 61 μL, 0.5 mmol), (*R*)-(+)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (10% EtOAc/*n*-hexane) to give **(*R*)-3w** (43 mg, 62%) as a colourless oil; $[\alpha]_D^{20}$ = –180 (*c* 0.5, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.95 (d, *J* = 4.6 Hz, 1H), 2.54 – 2.33 (m, 1H), 1.96 – 1.60 (m, 6H), 1.32 (dt, *J* = 18.6, 4.8 Hz, 4H), 1.18 (s, 9H).

*4.26. (R)-2-Methyl-N-octylidenepropane-2-sulfinamide [(**R**)-**3x**][41]*

The general procedure was followed using octanal (64 mg, 78 µL, 0.5 mmol), (*R*)-(+)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (10% EtOAc/*n*-hexane) to give **(*R*)-3x** (81 mg, 70%) as a yellow oil; $[\alpha]_D^{20}$ = –461 (*c* 0.77, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 8.06 (t, *J* = 4.8 Hz, 1H), 2.51 (td, *J* = 7.4, 4.8 Hz, 2H), 1.67 – 1.58 (m, 2H), 1.37 – 1.24 (m, 8H), 1.19 (s, 9H), 0.88 (t, *J* = 7.0 Hz, 3H).

*4.27. (R)-2-Methyl-N-(3-(methylthio)propylidene)propane-2-sulfinamide [(**R**)-**3y**][42]*

The general procedure was followed using 3-(methylthio)propionaldehyde (52 mg, 50 µL, 0.5 mmol), (*R*)-(+)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product was purified by flash chromatography (20% EtOAc/*n*-hexane) to give **(*R*)-3y** (87 mg, 84%) as a yellow oil; $[\alpha]_D^{20}$ = –292 (*c* 0.5, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 8.08 (dt, *J* = 5.3, 4.0 Hz, 1H), 2.93 – 2.66 (m, 4H), 2.13 (s, 3H), 1.20 (s, 9H).

4.28. Condensation of citral (cis/trans mixture) with (R)-(+)-2-methyl-2-propanesulfinamide

The general procedure was followed using citral (mixture of *cis*- and *trans*-isomers) (76 mg, 86 µL, 0.25 mmol), (*R*)-(+)-2-methyl-2-propanesulfinamide (61 mg, 0.5 mmol) and iodine (13 mg, 0.05 mmol). The crude product (1:1 mixture of *E*- and *Z*-isomers) was purified and the two isomeric products were separated by flash chromatography (10% EtOAc/*n*-hexane).

(R)-N-((1E,2Z)-3,7-Dimethylocta-2,6-dien-1-ylidene)-2-methylpropane-2-sulfinamide [**(*R*)-3z-1**]

R_f = 0.31 (46 mg, 72%) as a colourless oil; $[\alpha]_D^{20}$ = –530 (*c* 0.40, $CHCl_3$); IR (neat) ν_{max} 2960, 2918, 2864, 1633, 1568, 1082 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.5 (d, *J* = 9.9 Hz, 1H), 6.24 (d, *J* = 9.9 Hz, 1H), 5.07 (tdd, *J* = 5.9, 2.8, 1.4 Hz, 1H), 2.47 (t, *J* = 7.5 Hz, 2H), 2.19 (td, *J* = 14.9, 6.2 Hz, 2H), 1.96 (d, *J* = 1.3 Hz, 3H), 1.65 (d, *J* = 0.8 Hz, 3H), 1.59 (s, 3H), 1.19 (s, 9H); δ_C (126 MHz, $CDCl_3$) 160.4, 157.2, 133.3, 124.7, 122.8, 57.2, 33.1, 27.0, 25.8, 24.9, 22.6, 17.9; HRMS (ASAP): MH^+, found 256.1732. $C_{14}H_{26}NOS$ requires 256.1735.

(R)-N-((1E,2E)-3,7-Dimethylocta-2,6-dien-1-ylidene)-2-methylpropane-2-sulfinamide [**(*R*)-3z-2**]

Colourless oil; R_f = 0.25 (42 mg, 65%); $[\alpha]_D^{20}$ = –303 (*c* 0.50, $CHCl_3$); IR (neat) ν_{max} 2960, 2920, 2860, 1633, 1568, 1082 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.54 (d, *J* = 9.9 Hz, 1H), 6.23 (dd, *J* = 9.9, 1.0 Hz, 1H), 5.08 (dd, *J* = 8.9, 3.4 Hz, 1H), 2.29 – 2.12 (m, 4H), 2.04 (d, *J* = 1.0 Hz, 3H), 1.68 (s, 3H), 1.60 (s, 3H), 1.20 (s, 9H); δ_C (126 MHz, $CDCl_3$) 160.7, 157.3, 132.8, 123.6, 123.1, 57.2, 40.7, 28.3, 26.2, 25.8, 24.9, 22.6, 18.0, 17.9; HRMS (ASAP): MH^+, 256.1735. $C_{14}H_{26}NOS$ requires 256.1735.

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