Sulfur-Based Chiral Iodoarenes: An Underexplored Class of Chiral Hypervalent Iodine Reagents

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Abstract Chiral hypervalent iodine reagents are active players in modern stereoselective organic synthesis.1–4 They are extensively studied in a wide range of stereoselective transformations under stoichiometric and catalytic conditions. Stereoselective synthesis of chiral sulfur compounds,5,6 oxidative phenol dearomatisation,7–11 α-functionalisation of carbonyl compounds,12–15 difunctionalisation of alkenes,16–20 and oxidative rearrangement reactions21–24 are efficiently achieved with high degree of stereochemical control using diverse chiral hypervalent iodine reagents.

The incorporation of chirality into hypervalent iodine reagents is typically achieved through substituents of the iodoarene moiety containing a stereogenic centre (Figure 1). Using chiral ligands to the iodine is another strategy, even though limited.25–27 The vast majority of chiral hypervalent iodine reagent are synthesised by the oxidation of chiral iodoarenes containing chiral tetrahedral carbon centres I, II or C–C axis of chirality III. C–N axially chiral hypervalent iodine reagents of type IV are also gaining interest lately.28,29 On the other hand, the synthesis of hypervalent iodine reagents with chiral sulfur moieties is scarcely developed, even though there are a few examples known.30,31 To the best of our knowledge only one report on the synthesis and reactions of diaryliodonium salts containing chiral sulfoxide moiety has been published.32 Herein, we report our efforts towards the synthesis of this challenging class of chiral hypervalent iodine reagents from precursors of types V and VI (Figure 1).

Figure 1 Strategies of introducing chirality into iodoarene scaffolds

The main challenge of synthesis of hypervalent iodine reagents with chiral sulf oxide moiety is the loss of chirality due to the possible oxidation of sulfoxides to sulfones under...
the oxidation conditions to prepare iodine(III) reagents.\textsuperscript{32} We envisaged that the introduction of a chiral sulfinamide (type V) or sulfoximine (type VI) and adjusting the substitution pattern around the central sulfur could alleviate this problem.

A first set of sulfinamide-based precursors was easily obtained from 2-iodobenzaldehyde (1) and (R)-tert-butanemethyl derivative in 85% yield.\textsuperscript{37} The absolute configuration of domethane. Addition of phenylmagnesium bromide to the stereochemical control delivering ety, precursors and Koser's reagent [PhI(OH)OTs] were investigated; in addition, oxidation protocols. Many oxidants typical for preparing io-duct of the chiral sulfinamide moiety with a chiral sulfoxide moiety or the latter is solely oxidised and hence the chirali-

To probe the potential of selective oxidation of the iodine centre without affecting the sensitive sulfoxide moiety, precursors 3–7 were subjected to oxidation using various oxidants and conditions. It is not surprising that the labile sulfoxide group was not tolerated under most of the oxidation protocols. Many oxidants typical for preparing iodine(III) compounds such as Selectfluor, Oxone, perborates, and Koser’s reagent [PhI(OH)OTs] were investigated; in addition, anodic oxidation was also attempted.\textsuperscript{39,40} The iodine precursors 3–7 were not reactive under many reaction conditions, only sodium perborate oxidation was productive (Scheme 2). Generally, the selective oxidation of the iodine centre was not possible under the reaction conditions investigated and is either oxidised along with the sulfoxide moiety or the latter is solely oxidised and hence the chirality is lost. Oxidation of the chiral imine 3 with sodium per-

In view of these results, we envisaged that a replacement of the chiral sulfoximate moiety with a chiral sulfox-}

<table>
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<tr>
<th>Scheme 1</th>
<th>Synthesis of sulfinamide-based chiral iodoarenes</th>
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<tbody>
<tr>
<td>1</td>
<td>CHO</td>
</tr>
<tr>
<td>2</td>
<td>1.8 equiv NaH</td>
</tr>
<tr>
<td>3</td>
<td>1.8 equiv NaH</td>
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<tr>
<td>4</td>
<td>R = H, 93%</td>
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<tr>
<td>5</td>
<td>R = Me, 84%</td>
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<tr>
<td>6</td>
<td>NaBH₄</td>
</tr>
<tr>
<td>7</td>
<td>R = H, 85%</td>
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<tr>
<td>8</td>
<td>NaBH₄</td>
</tr>
<tr>
<td>9</td>
<td>95%</td>
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<tr>
<td>10</td>
<td>10 mol%</td>
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</tbody>
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| 11 | tert-Butane-2-sulfinamide with the iodine centre untouched, which could not be further oxidised using perborate or Koser’s reagent, while with Oxone in the presence of trifluoroacetic acid the tert-butanemethyl derivative was additionally confirmed by X-ray crystallography.\textsuperscript{38} Oxidation of precursors 4 and 5 with sodium perborate led to sulfone 12 in 95% yield in 2.5 hours. Extended reaction times (12 h) or further oxidation of 12 formed the cyclic iodine(III) compound 13, which is chiral, but does no longer have a stereogenic sulfur centre. On the other hand, attempted oxidation of 7 via iodine metathesis\textsuperscript{41,42} using Koser’s reagent led to the cleavage of the tert-butanemethyl moiety and formed salt 14.

<table>
<thead>
<tr>
<th>Scheme 2</th>
<th>Oxidation of sulfinamide-based iodoarenes 3–7</th>
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<tbody>
<tr>
<td>3</td>
<td>3</td>
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<tr>
<td>4</td>
<td>5</td>
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<tr>
<td>6</td>
<td>NaBO3·4H2O</td>
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<tr>
<td>7</td>
<td>NaBO3·4H2O</td>
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<td>8</td>
<td>95%</td>
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<td>9</td>
<td>90%</td>
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<td>10</td>
<td>86%</td>
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<tr>
<td>11</td>
<td>R = Me, 70%</td>
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<td>12</td>
<td>92%</td>
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<td>13</td>
<td>82%</td>
</tr>
<tr>
<td>14</td>
<td>83%</td>
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</tbody>
</table>
amide proved that the t-Bu group is not tolerated under the reaction conditions used to convert sulfinamides into sulfoximines.

To avoid the difficulties encountered during the oxidation of the above compounds, the synthesis of different sulfoximine containing chiral iodoarenes was attempted (Scheme 3). Relying on the oxidation of thioanisole (15) and 2-iodothioanisole (16) to sulfoximines 17 and 18 followed by chiral resolution with (+)-camphorsulfonic acid (CSA), the chiral sulfoximine derivatives (S)-17 and (S)-18 were obtained and converted into the N-substituted derivatives 20–22 in high yields.

The oxidation of (S)-20 to the corresponding chiral hypervalent iodine reagent using Selectfluor in the presence of acetic acid was unsuccessful, leaving the starting material unreacted. Sodium perborate as oxidant or aerobic oxidation in the presence of a CoCl$_2$ catalyst$^{16}$ led to complex reaction mixtures with 2-iodobenzoic acid identified as one of the products. Similar outcomes were obtained upon oxidation of compounds (S)-18, (S)-21, and (S)-22 using Selectfluor or the CoCl$_2$-catalysed aerobic oxidation protocol.

With sodium perborate the formation of a cyclic chiral hypervalent iodine reagent (S)-24 was observed as a major product in the case of precursors (S)-18 and (S)-22 and as a minor product in the case of precursor (S)-21 (Scheme 4). The $^1$H NMR analysis of the crude reaction mixture showed the formation of the hypervalent iodine reagent (S)-23 along with the cyclic product (S)-24 that is formed most likely through cyclization of (S)-23.

The ratio of 23:24 varies with the reaction time and the equivalents of sodium perborate, but 24 was the major product in all cases. The non-cyclic product 23 was only detected in the crude reaction mixture, but could not be isolated, while the cyclic product 24 was isolated and crystallised. The structure of (S)-24 was proven by single crystal X-ray crystallography (Figure 2). Analysis of the X-ray data of compound 24 showed a strong interaction (2.100 Å) between the sulfoximine nitrogen [(N(1))] and the iodine centre [(I(1)]), which is shorter than the iodine–oxygen bond [(I(1)–O(2)], 2.249 Å. The observed angle [N(1)–I(1)–O(2)] of compound 24 (167.15°) is in the range of the distorted T-shaped geometry characteristic to $\lambda^3$-iodanes.$^{30,46}$

In conclusion, various sulfur-based chiral iodoarenes were synthesised starting with readily available chemicals. Chiral iodoarenes containing sulfinamide units and compounds containing sulfoximine unit have been prepared. Oxidation of both categories to the corresponding chiral hypervalent iodine reagents was cumbersome. All sulfinamide derivatives underwent overoxidation and, hence, the chirality is lost. Chiral sulfoximine units are more robust and cannot undergo further oxidation. However, the oxidation of the sulfoximines to the corresponding chiral hypervalent iodine reagents was not easy due to the degradation of some precursors. Only the oxidation of chiral 1-iodo-2-(S-methylsulfonimidoyl)benzene derivatives was successful and led to a cyclic chiral-at-sulfur iodine(III) reagent. Applications of sulfur-based chiral hypervalent iodine reagents in stereoselective oxidative transformations are ongoing in our laboratory.

All starting materials were purchased from commercial suppliers and used without further purification and all solvents used were dried and purified by standard techniques. Reactions requiring the exclusion of moisture were carried out under an atmosphere of argon or N$_2$.
in oven-dried glassware. Flash chromatography was carried out using Merck silica gel (35–70 μm) or on a Biotage Isolera Four platform using SNAP Ultra (25 μm) cartridges. Melting points were recorded on a Gallenkamp MPD350 apparatus. IR measurements were taken using a PerkinElmer 1600 FTIR spectrometer. NMR spectra were recorded on Bruker DPX 300, Bruker DPX 400, or Bruker DPX 500. ¹H NMR spectra were measured at 300, 400, and 500 MHz. ¹³C (¹H) NMR spectra were recorded at 75, 100, and 125 MHz using CDCl₃ as the solvent and internal reference. Coupling constants J are given in hertz (Hz). Standard abbreviations were used for denoting multiplicity. High-resolution mass spectrometry (HRMS) was carried out using a Waters LCT Premier XE mass spectrometer using electrospray ionisation (ESI). Optical rotations were measured with a UniPol L polarimeter at 20 °C. High-performance liquid chromatography (HPLC) analysis was conducted using Shimadzu LC-10 AD coupled diode array-detector SPD-MAX-10A-VP.

2-Iodobenzaldehyde (1)
Pyridinium chlorochromate (9.1 hexane:EtOAc; yield: 2.15 g (5.26 mmol, 74%); white solid; mp 74.5–74.6 °C (Lit. mp 74 °C).

1H NMR (400 MHz, CDCl₃): δ = 10.07 (1H), 7.69 (d, J = 7.9 Hz, 1H), 7.89 (d, J = 7.7 Hz, 1H), 7.47 (t, J = 7.5 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H).

13C NMR (101 MHz, CDCl₃): δ = 196.0, 140.8, 135.6, 135.3, 130.4, 128.9, 100.9.

The spectral data are in agreement with literature.

(R,E)-N-(2-Iodobenzylidene)-2-methylpropane-2-sulfonamide (3)
A solution of 2-iodobenzaldehyde [1 (1.12 g, 4.82 mmol) and Ti(OEt)₄ (1.05 mL) in anhyd CH₂Cl₂ (48 mL)] was stirred for 5 min under N₂. Then, (R)-(+)-2-methyl-2-propanesulfonylamine (2; 0.58 g, 4.82 mmol) was added portionwise. The reaction mixture was stirred at rt for 20 h. Sat. aq NaHCO₃ (30 mL) was added until white titanium salt stopped precipitating. The suspension was filtered off a short pad of Celite washing with small portions of EtOAc. The aqueous filtrate was extracted with EtOAc and the combined organic layers were washed with brine (anhyd MgSO₄) and concentrated in vacuo. The crude product (yellow oil) was purified by flash chromatography (silica gel, 9:1 hexane:EtOAc) to give the pure sulfonamide 3 as a yellow solid; yield: 1.53 g (4.58 mmol, 95%); mp 77.5–77.7 °C; [α]D = -179.18 (c 1.23, CHCl₃).

IR (neat): 3158, 3080, 2981, 2956, 1583, 1564, 1458, 1345, 1359, 1274, 1155, 1104, 1039, 738 cm⁻¹.

1H NMR (400 MHz, CDCl₃): δ = 7.81 (dd, J = 7.9, 1.1, Hz, 1H), 7.39 (dd, J = 7.7, 1.7 Hz, 1H), 7.33 (dd, J = 7.5, 1.2 Hz, 1H), 6.95 (td, J = 7.8, 1.8 Hz, 1H), 4.27 (d, J = 15.8 Hz, 1H), 4.18 (d, J = 15.9 Hz, 1H), 2.66 (s, 3H).

13C NMR (101 MHz, CDCl₃): δ = 193.8, 139.4, 129.2, 129.8, 129.5, 77.4, 61.7, 59.0, 23.6.


(R)-N-(2-Iodobenzyl)-2-methylpropane-2-sulfonamide (4)
Sulfonamide 3 (1.71 g, 5.11 mmol) was dissolved in 98:2 THF:H₂O (15 mL) and cooled down to 0 °C. NaN₃ (0.579 g, 15.32 mmol, 3 equiv) was added and the resulting solution was warmed to rt and monitored by TLC (7:3 hexane:EtOAc). After 1 h, the TLC showed the consumption of the starting material. Then, H₂O (20 mL) was added, and the mixture was stirred at rt for 5 min. THF was evaporated off before extracting with CH₂Cl₂ (3 × 10 mL). The combined CH₂Cl₂ layers were dried (anhyd MgSO₄) and evaporated off to give the crude product, which was purified by flash chromatography (silica gel, 9:1 hexane:EtOAc) to give the pure reduced imine 4 as a white solid; yield: 1.61 g (4.77 mmol, 93%); mp 134.6–135.1 °C; [α]D = -15.45 (c 1.03, CHCl₃).

IR (neat): 3194, 3059, 2976, 2360, 1583, 1564, 1436, 1363, 1074, 1040, 744, 428 cm⁻¹.

(R)-N-(2-Iodobenzyl)-N,2-dimethylpropane-2-sulfonamide (5)
To a solution of the sulfonamide 4 (317 mg, 0.94 mmol) in anhyd THF (5.5 mL) were added 60% NaH in mineral oil (68 mg, 1.69 mmol, 1.8 equiv) and Mel (760 mg, 5.33 mL, 5.36 mmol, 5.7 equiv). The reaction mixture was stirred at rt under N₂ for 1 h, and the solvent was removed under reduced pressure. The residue was dissolved in Et₂O (5 mL) and washed with H₂O (5 mL). The aqueous phase was extracted with Et₂O (3 × 5 mL). The combined Et₂O extracts were washed with 10% aq Na₂S₂O₃ (5 mL) and H₂O (5 mL), dried (MgSO₄), filtered. The filtrate was evaporated under vacuum to give methylated product 5 as a pale-yellow oil; yield: 277 mg (0.879 mmol, 84%); [α]D = +20.54 (c 0.73, CHCl₃).

IR (neat): 2953, 2864, 2360, 2331, 1562, 1508, 1458, 1435, 1359, 1068, 1012, 748, 432 cm⁻¹.

1H NMR (400 MHz, CDCl₃): δ = 7.71 (d, J = 7.9, 1.1 Hz, 1H), 7.39 (dd, J = 7.7, 1.7 Hz, 1H), 7.33 (dd, J = 7.5, 1.2 Hz, 1H), 6.95 (td, J = 7.8, 1.8 Hz, 1H), 4.27 (d, J = 15.8 Hz, 1H), 4.18 (d, J = 15.9 Hz, 1H), 2.66 (s, 3H).

13C NMR (101 MHz, CDCl₃): δ = 193.8, 139.4, 129.2, 129.8, 129.5, 77.4, 61.7, 58.8, 23.6.

To a solution of the sulfinamide 2-sulfinamide (7) (52 mg, 0.125 mmol) in glacial AcOH (4 mL) was added NaBO₃·4H₂O (289 mg, 1.88 mmol, 15 equiv). The reaction mixture was stirred at rt and monitored by TLC. After completion of reaction, the solvent was evaporated under reduced pressure and the residue was treated with CHCl₃ (2 mL). The crude product 8 as a white solid, which was purified by recrystallisation from hexane:AcOH (8:2) to obtain 8 as a white solid; yield: 73 mg (0.17 mmol, 85%).

1H NMR (400 MHz, acetone-d₆): δ = 8.17 (dd, J = 7.6, 1.1 Hz, 1 H), 8.13 (d, J = 8.4 Hz, 1 H), 8.03 (t, J = 7.2 Hz, 1 H), 7.84 (t, J = 7.5 Hz, 1 H), 2.19 (s, 3 H), 1.54 (s, 9 H).

13C NMR (101 MHz, acetone-d₆): δ = 176.4, 163.2, 137.2, 134.5, 132.9, 132.0, 130.6, 117.8, 64.0, 25.1, 20.5.

N-(2-Iodobenzyl)-2-methylpropane-2-sulfonamide (9)

To a solution of sulfinamide 4 (135 mg, 0.4 mmol) in glacial AcOH (6 mL) was added NaBO₃·4H₂O (615 mg, 4 mmol, 10 equiv) and the reaction mixture was stirred at 40–45 °C. After 1 h, the TLC (hexane:EtOAc 7:3) showed the consumption of the starting material. The solvent was removed under reduced pressure and the white solid left was partitioned between CH₂Cl₂ (5 mL) and CHCl₃ (5 mL). The two layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 × 5 mL). The combined organic layers were washed with brine (5 mL), dried (anhyd MgSO₄), filtered, and concentrated under pressure to give the sulfonamide 9 as a pale-yellow solid; yield: 128 mg (0.36 mmol, 90%); mp 77–78 °C.

IR (neat): 793, 1605, 1670, 1778, 2920, 2954, 428 cm⁻¹.


N-(2-Iodo phenyl)-N-methylaniline (11)

To a solution of 10 (43 mg, 0.12 mmol) in a mixture of trifluoroacetic acid (1.2 mL) and CHCl₃ (10 mL) was added Oxone (111 mg, 0.18 mmol, 1.5 equiv). The reaction mixture was stirred at rt and monitored by TLC. After completion of reaction, the solvent was evaporated under vacuum and the residue was treated with CHCl₃ (2 mL). The insoluble residue of inorganic salts was collected by filtration, washed with CHCl₃ (2 mL), and discarded. Evaporation of combined CHCl₃ layers under reduced pressure afforded amino compound 11 as a pale-yellow oil; yield: 21 mg (0.0841 mmol, 70%).

IR (neat): 3014, 2818, 2742, 2358, 2331, 1778, 1670, 1176, 1138, 1014, 798, 756, 403 cm⁻¹.

was added (NH₄)₂CO₃ (1.50 g, 15.6 mmol, 1.5 equiv). After the dissolution racemic 1.15 (s, 1 H). Hz, 2 H), 7.20–7.13 (m, 1 H), 5.71 (s, 1 H), 2.72 (s, 3 H), 2.37 (s, 3 H), dried (anhyd MgSO₄), filtered, and concentrated under pressure to give the sulfonamide 12 as a white solid; yield: 51 mg (0.12 mmol, 95%).

1H NMR (300 MHz, CDCl₃): δ = 7.87 (dd, J = 7.9, 0.7 Hz, 1 H), 7.53–7.40 (m, 2 H), 7.36–7.19 (m, 5 H), 7.04 (dd, J = 7.9, 6.7, 2.4 Hz, 1 H), 6.03 (d, J = 9.0 Hz, 1 H), 4.81 (d, J = 8.9 Hz, 1 H), 1.32 (s, 9 H).

13C NMR (101 MHz, CDCl₃): δ = 146.0, 140.6, 140.3, 129.6, 128.9, 128.8, 128.00, 127.97, 99.1, 65.3, 60.3, 24.3.

IR (neat): 3287, 1564, 1422, 1314, 1204, 1080, 986, 932, 754, 700, 509 cm⁻¹.

To a solution of racemic 12 (50 mg, 0.12 mmol, 1.1 equiv) in anhyd CH₂Cl₂ (1 mL) at rt. The reaction was stirred and monitored by TLC. After the completion of the reaction, the solvent was removed under reduced pressure and the crude product was collected by filtration and washed thoroughly with acetone. The obtained solid was then suspended in CH₂Cl₂ (30 mL). Sat. aq K₂CO₃ (0.5 M) was added with stirring. Stirring was continued at rt for 1 h. The organic phase was separated, and the aqueous phase was extracted with CH₂Cl₂ (3 × 5 mL). The combined organic layers were washed with brine (5 mL) and dried (anhyd MgSO₄), filtered, and concentrated under pressure to give the sulfonic acid (1.2 g, 5.1 mmol 0.55 equiv) in acetone (14 mL). The reaction mixture was stirred at rt overnight. The crude precipitate was collected by filtration and washed thoroughly with acetone. The obtained solid was then suspended in CH₂Cl₂ (30 mL). Sat. aq K₂CO₃ (30 mL) was added with stirring. Stirring was continued at rt for 1 h. The organic phase was separated, and the aqueous phase was extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layers were dried (anhyd MgSO₄) and evaporated to dryness affording pure (S)-17 as a colourless oil that solidified after a few days; yield: 0.46 g (2.95 mmol, 32%).

1H NMR (400 MHz, CDCl₃): δ = 8.04–7.99 (m, 1 H), 7.65–7.60 (m, 1 H), 7.58–7.53 (m, 1 H), 3.11 (s, 3 H).

13C NMR (101 MHz, CDCl₃): δ = 145.6, 143.1, 133.9, 130.6, 129.0, 93.3, 42.6.

HRMS: m/z [M + H]+ calcd for [C₁₄H₁₅INO₅S]: 371.9914; found: 371.9916.

(+)-(S)-Methyl-S-phenylsulfoximine ([S]-17)

To a solution of racemic S-methyl-S-phenylsulfoximine (rac-17; 1.43 g, 9.2 mmol) in acetonitrile (6 mL) was added a solution of (+)-camphorsulfonyl acid (1.2 g, 5.1 mmol 0.55 equiv) in acetone (14 mL). The reaction mixture was stirred at rt overnight. The reaction mixture was stirred at rt overnight.

Koser’s reagent (42 mg, 0.11 mmol) was added to a stirred solution of 12 (50 mg, 0.12 mmol, 1.1 equiv) in anhyd CH₂Cl₂ (1 mL) at rt. The reaction was stirred and monitored by TLC. After the completion of the reaction, the solvent was removed under reduced pressure and the solid residue was filtered and washed with Et₂O several times, then dried in vacuum to give 14 as a white solid; yield: 48 mg (0.114 mmol, 83%).

1H NMR (300 MHz, CDCl₃): δ = 7.90 (d, J = 9.4 Hz, 1 H), 7.50–7.46 (m, 1 H), 7.46–7.43 (m, 1 H), 7.42–7.38 (m, 5 H), 6.23 (s, 1 H), 2.13 (s, 3 H), 1.26 (s, 9 H).

13C NMR (101 MHz, CDCl₃): δ = 143.7, 140.7, 140.4, 129.6, 129.0, 128.9, 128.8, 128.00, 127.97, 99.1, 65.3, 60.3, 24.3.

(1,2-Iodophenyl)-N-methyl-1-phenylmethanamine 4-Methylbenzenesulfonate (14)

Prepared following the above procedure (for compound 16) starting with 6 or 12 but using 11 as reaction time leading to 13 as a white solid; yield: 40 mg (0.082 mmol, 82%); mp 144–146 °C; [α]D = +29.67 (c 0.4, CHCl₃).

1H NMR (400 MHz, CDCl₃): δ = 7.95 (d, J = 7.9 Hz, 1 H), 8.12 (d, J = 7.8 Hz, 1 H), 7.54 (t, J = 7.6 Hz, 1 H), 7.21 (t, J = 7.6 Hz, 1 H), 3.28 (s, 3 H), 2.75 (s, 3 H).

13C NMR (101 MHz, CDCl₃): δ = 145.6, 143.1, 133.9, 130.6, 129.0, 93.3, 42.6.

HRMS: m/z [M + H]+ calcd for [C₁₄H₁₄INOS]: 311.0944; found: 311.0942.

(+)-(S)-Methyl-S-2-isodobenzylsulfoximine ([S]-20)

To a solution of (S)-methyl-S-2-isodobenzylsulfoximine ([S]-17; 0.459 g, 2.95 mmol) in DMSO (1.5 mL) was added KOH (0.33 g, 5.9 mmol, 2.0 equiv). The reaction was stirred at rt under argon for 5 min. 2-Iodobenzyl bromide (19; 1.13 g, 4.42 mmol, 1.5 equiv) was added and stirring was continued at rt overnight. The reaction was quenched by the addition of H₂O (5 mL) and the aqueous phase was extracted with CH₂Cl₂ (3 × 5 mL). The combined organic layers were dried (anhyd MgSO₄) and evaporated under reduced pressure. The crude product was purified by column chromatography (hexane:EtOAc 9:1) affording pure 20 as a dark yellow oil; yield: 0.73 g (1.95 mmol, 66%); [α]D = +1.23 (c 0.6, CHCl₃).

IR (neat): 1445, 1221, 1104, 711, 692, 613 cm⁻¹.

1H NMR (400 MHz, CDCl₃): δ = 7.95 (d, J = 7.6 Hz, 2 H), 7.75 (d, J = 7.8 Hz, 1 H), 7.67 (d, J = 7.6 Hz, 1 H), 7.62 (t, J = 7.2 Hz, 1 H), 7.56 (t, J = 7.5 Hz, 2 H), 7.33 (t, J = 7.4 Hz, 1 H), 6.91 (t, J = 7.5 Hz, 1 H), 4.15 (d, J = 15.5 Hz, 1 H), 4.05 (d, J = 15.5 Hz, 1 H), 3.20 (s, 3 H).

13C NMR (101 MHz, CDCl₃): δ = 143.0, 139.3, 139.1, 133.3, 129.7, 129.3, 128.8, 128.5, 128.4, 98.8, 52.4, 45.4.

HRMS: m/z [M + H]+ for [C₁₄H₁₄INOS]: 371.9914; found: 371.9916.
To a solution of (S)-S-methyl-S-2-iodophenylsulfoxime \((S)-21\) in DMSO (1.5 mL) at 0 °C was added KOH (90 mg, 1.6 mmol, 2.2 equiv). The reaction was stirred at rt under argon for 5 min. EtBr (0.10 mL, 1.34 mmol, 2.1 equiv) was added and stirring was continued at rt overnight. The reaction was quenched by the addition of H2O (5 mL) and the aqueous phase was extracted with CH2Cl2 (3 × 10 mL). The combined organic layers were dried (anhyd MgSO4), filtered, and evaporated under reduced pressure. The crude product was purified by column chromatography (hexane:EtOAc 1:1) affording pure \((S)-22\) as a white solid; yield: 0.145 g (0.49 mmol, 81%); mp 53–55 °C; \([\alpha]_D^21 +11.5 (c 0.59, CHCl3).

IR (neat): 3001, 2365, 1717, 1603, 1312, 1208, 991, 754 cm⁻¹.

1H NMR (400 MHz, CDCl3): \(\delta = 8.35\) (d, \(J = 7.6\) Hz, 1 H), 7.90 (dd, \(J = 7.0, 1.9\) Hz, 1 H), 7.86–7.80 (m, 2 H), 3.40 (s, 3 H), 2.11 (s, 3 H).

13C NMR (101 MHz, CDCl3): \(\delta = 178.1, 134.4, 133.9, 132.3, 131.3, 128.2, 117.5, 47.7, 22.2.

**Conflict of Interest**

The authors declare no conflict of interest

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**Supporting Information**

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(38) CCDC-2074473 (6), CCDC-2074474 (8), CCDC-2074476 (9), and CCDC-2074475 (24) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.


