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. Structurally diverse chiral hypervalent iodine reagents have been synthesised and extensively studied, but hypervalent iodine reagents containing chiral sulfur stereogenic centre are scarce and their synthesis is challenging. A small library of iodoarenes containing chiral sulfonamide and chiral sulfoximine moieties has been synthesised using commercially available reagents. The oxidation of the chiral iodoarene precursors to iodine(III) reagents was cumbersome due to facile overoxidation of the sulfoxide moiety and hence loss of chirality under various oxidation conditions. Oxidation of chiral sulfonimidoyl derivatives to the corresponding hypervalent iodine reagents was successful and led to novel sulfur-based chiral iodine(III) reagents.

Key words hypervalent iodine, oxidation, stereoselective synthesis, sulfoximines, sulfur derivatives

Chiral hypervalent iodine reagents are widely used as active reagents in stereoselective 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 substitutions 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 sulfoxide 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 sulfamidine (type V) or sulfoximine (type VI) and adjusting the substitution pattern around the central sulfur could alleviate this problem.

A first set of sulfamidine-based precursors was easily obtained from 2-iodobenzaldehyde (1) and (R)-tert-butanesulfinamide (2) (Scheme 1). Condensation of 1 and 2 in the presence of excess Lewis acids such as titanium(IV) alkoxides\textsuperscript{13,14} or under iodine-catalysed solvent-free mechanochemical conditions\textsuperscript{15} provided imine 3 in high yields (95% and 73%). Reduction of imine 3 with NaBH4 led to sulfimide 4 in 93% yield,\textsuperscript{36} which was then converted into the N-methyl derivative 5 upon treatment with NaH and iodomethane. Addition of phenylmagnesium bromide to the chiral imine 3 proceeded smoothly with a high degree of stereocchemical control delivering 6 as a single diastereomer (dr >20:1) in 85% yield.\textsuperscript{37} The absolute configuration of compound 6 was determined by X-ray crystallography.\textsuperscript{38} Treatment of 6 with NaH/Mel led to the N-methyl derivative 7 in 82% yield.

![Scheme 1 Synthesis of sulfamidine-based chiral iodoarenes](image)

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 perborate in acetic acid led to the achiral cyclic hypervalent iodine reagent 8 in 85% yield. The chemical constitution of compound 8 was additionally confirmed by X-ray crystallography.\textsuperscript{38} Oxidation of precursors 4 and 5 with sodium perborate led to the corresponding achiral sulfoxones 9\textsuperscript{38} and 10 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-butanesulfoxide moiety was cleaved to form 11. Similarly, the oxidation of precursor 6 with 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 stereo- genic 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-butanesulfoxide moiety and formed salt 14.

![Scheme 2 Oxidation of sulfamidine-based iodoarenes 3–7](image)

In view of these results, we envisaged that a replacement of the chiral sulfoxide moiety with a chiral sulfoximine would lead to chiral sulfur-based iodoarene derivatives that could be oxidised to the corresponding hypervalent iodine reagents without loss of chirality. Initially, oxidation of compounds 3, 4, and 5 to the corresponding sulfoximines was attempted. However, oxidations using typical procedures such as [Rb2(OAc)]\textsubscript{4} and (diacetoxyiodo)benzene\textsuperscript{43} or t-BuOCl\textsuperscript{43} in the presence of an amine were unsuccessful and led to complex reaction mixtures. The \textsuperscript{1}H NMR spectra of the crude reaction mixtures showed the absence of the t-Bu moiety suggesting that it cleaved under these conditions. Also, the oxidation of (R)-N,2-dimethylpropane-2-sulfamidine with tBuOCl in the presence of aniline resulted in the formation of N-methyl-N’-phenyl-sulf-
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 CoCl₂ catalyst led to complex reaction mixtures with 2-iodobenzoic acid identified as one of the products. Similar outcomes were obtained upon oxidation of thioanisole using Selectfluor in the presence of moisture were carried out under an atmosphere of argon or N₂.

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 ¹H 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 λ₃-iiodanes.

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-methylsulfinimidoyl)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 N₂.
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-MA-10A-VP.

**2-Iodobenzaldehyde (1)**

Pyridinium chlorochromate (3.11 g, 14.45 mmol) and Celite (13.12 g, 21.84 mmol, 1.74 equiv) were dried under vacuum in a 3-necked round-bottomed flask and then flushed with N2 and suspended in anhyd CH2Cl2 (145 mL). A solution of 2-iodobenzyl alcohol (2.92 g, 12.5 mmol) in anhyd CH2Cl2 (40 mL) was added dropwise at rt. The reaction mixture turned from red to brown to black and is stirred at rt overnight. After filtration through Celite, the solvent was removed under reduced pressure. The crude product was purified by flash chromatography (9:1 hexane:EtOAc) to give the pure sulfinamide (6).

**2-(Iodobenzyl)-2-methylpropane-2-sulfinamide (4)**

Sulfinamide 3 (1.71 g, 5.1 mmol) was dissolved in 98:2 THF:H2O (15 mL) and cooled down to 0 °C. NaBH4 (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 °C; [α]D –15.45 (c 0.73, CHCl3).

IR (neat): 2953, 2864, 2360, 1562, 1508, 1458, 1359, 1299, 1174, 1012, 748, 432 cm–1.


The spectral data are in agreement with literature.

**2-(Iodobenzylidene)-2-methylpropane-2-sulfinamide (3)**

A solution of 2-iodobenzaldehyde (1; 1.12 g, 4.82 mmol) and Ti(OEt)4 (5.05 mL) in anhyd CH2Cl2 (48 mL) was stirred for 5 min under N2. Then, (R)-(+)−2-methyl-2-propanesulfinamide (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, 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), dried (MgSO4), filtered. The filtrate was evaporated under vacuum to give methylated product 5 as a pale-yellow oil; yield: 277 mg (0.79 mmol, 84%); [α]D +20.54 (c 0.73, CHCl3).

IR (neat): 2953, 2864, 2360, 1577, 1554, 1460, 1074, 1012, 771, 740, 441 cm–1.


(R)-N-(2-iodobenzyl)-2-methylpropane-2-sulfonamide (4)

To a solution of the sulfinamide 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, 0.33 mmol, 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 (0.79 mmol, 84%); [α]D +20.54 (c 0.73, CHCl3).

IR (neat): 2953, 2864, 2360, 1577, 1554, 1460, 1074, 1012, 771, 740, 441 cm–1.


**N-(3,5-Dihydroxypheyl)(phenyl)methyl]-2-methylpropane-2-sulfonamide (6)**

To a solution of the imine 3 (322 mg, 0.96 mmol) in CH2Cl2 (5.8 mL) was added phenylmagnesium bromide (348 mg, 0.69 mL, 1.92 mmol, 2 equiv) at −48 °C. The reaction mixture was stirred at −48 °C for 6 h and then allowed to warm to rt and stirred overnight. The mixture was quenched with sat. aq NH4Cl (2 mL) and the aqueous layer was extracted with EtOAc (3 × 3 mL). The combined organic layers were dried (Na2SO4) and concentrated to provide the crude product, which was purified by flash chromatography (silica gel, 9:1 hexane:CH2Cl2) to give the pure product 6 as colourless crystals; yield: 337 mg (0.82 mmol, 85%); mp 145–146 °C; [α]D –68.14 (c 0.66, CHCl3).

IR (neat): 3213, 2981, 2962, 1540, 1494, 1465, 1448, 1357, 1033, 391 cm–1.
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). The reaction mixture was stirred at 40–45 °C for 4 h. The solvent was removed under reduced pressure and the white solid left was partitioned between H₂O (5 mL) and CH₂Cl₂ (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) and dried (anhyd MgSO₄), filtered, and concentrated under pressure to give the sulfonamide 9 as a pale-yellow solid; yield: 128 mg (0.36 mmol, 96%); mp 77–78 °C.

IR (neat): 3277, 2976, 2879, 2360, 1683, 1456, 1436, 1398, 1300, 1112, 1010, 742, 511 cm⁻¹.


(R)-N-((2-Iodophenyl)(phenyl)methyl)-N,2-dimethylpropane-2-sulfonamide (7)

To a solution of 2-sulfinamide (7) (135 mg, 0.4 mmol, 1 equiv) in glacial AcOH (6 mL) was added NaBO₃·4H₂O (615 mg, 4 mmol, 10 equiv). The reaction mixture was stirred at 40–45 °C for 4 h. The solvent was removed under reduced pressure and the white solid left was partitioned between H₂O (5 mL) and CH₂Cl₂ (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) and dried (anhyd MgSO₄), filtered, and concentrated under pressure to give the sulfonamide 9 as a pale-yellow solid; yield: 128 mg (0.36 mmol, 96%); mp 77–78 °C.

IR (neat): 3277, 2976, 2879, 2360, 1683, 1456, 1436, 1398, 1300, 1112, 1010, 742, 511 cm⁻¹.


(N-2-Iodobenzyl)-N,2-dimethylpropane-2-sulfonamide (10)

To a solution of sulfinamide 5 (140 mg, 0.4 mmol, 1 equiv) in glacial AcOH (6 mL) was added NaBO₃·4H₂O (615 mg, 4 mmol, 10 equiv). 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 residue was treated 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 sulfonamide 10 as a pale-yellow solid; yield: 126 mg (0.34 mmol, 86%); mp 82–83 °C.

IR (neat): 2360, 1695, 1581, 1436, 1317, 1261, 1120, 1016, 790, 511, 418 cm⁻¹.


1-(2-Iodophenyl)-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 treated with H₂O (5 mL) and CH₂Cl₂ (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, 96%); mp 77–78 °C.

IR (neat): 3277, 2976, 2879, 2360, 1683, 1456, 1436, 1398, 1300, 1112, 1010, 742, 511 cm⁻¹.

The solvent was removed under reduced pressure and the white solid left was treated with H2O (5 mL) and CH2Cl2 (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) and dried (anh 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 (ddd, 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 = 141.0, 139.7, 139.3, 129.8, 129.7, 129.9, 128.9, 128.8, 128.0, 127.97, 99.1, 65.3, 60.3, 24.3.

(5)-1-(2-Iodophenyl)-N-methyl-1-phenylmethanamine 4-Methylbenzenesulfonate (14)

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, CD3OD): δ = 8.02 (d, J = 7.80 Hz, 1 H), 7.70 (d, J = 8.02 Hz, 2 H), 7.66–7.57 (m, 1 H), 7.53–7.39 (m, 5 H), 7.23 (d, J = 7.78 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), 1.15 (s, 1 H).

rac-S-Methyl-S-phenylsulfoximine (17)

To a solution of thioanisole 15 (1.24 g, 10.0 mmol) in MeOH (100 mL) was added (NH4)2CO3 (1.50 g, 15.6 mmol, 1.5 equiv). After the dissolution of (NH4)2CO3, (diacetoxycarbonyl)benzene (7.43 g, 23.1 mmol, 2.3 equiv) was added. The reaction mixture was stirred at rt overnight, then evaporated to dryness and purified by column chromatography (hexane:EtOAc 1:1) affording pure 17 as a yellow oil that solidified after a few days; yield: 1.43 g (9.20 mmol, 92%); mp 33–34 °C (Lit. 48 mp 371.9916).

1H NMR (400 MHz, CDCl3): δ = 8.05–8.00 (m, 2 H), 7.66–7.60 (m, 1 H), 7.59–7.53 (m, 2 H), 3.13 (s, 3 H).

The spectral data are in agreement with literature.

rac-S-Methyl-S-2-iodophenylsulfoximine (18)

Prepared following the above procedure (for 17), starting with 2-iodothiaoanisole (16; 1.0 g, 4.0 mmol). Compound 18 was obtained as a yellow oil that solidified after a few days; yield: 0.765 g (2.72 mmol, 68%); mp 64–66 °C.

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

1H NMR (400 MHz, CDCl3): δ = 8.30 (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, 1 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 [C10H9INOS]: 281.9444; found: 281.9452.

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

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

(+)-(S)-Methyl-S-2-iodophenylsulfoximine ([S]-18)

Obtained following the above procedure [for (S)-17], starting with racemic S-methyl-S-2-iodophenylsulfoximine (rac-18; 0.764 g, 2.72 mmol) and (+)-camphorsulfonic acid (0.32 g, 1.36 mmol 0.5 equiv). Compound (S)-18 was obtained as a colourless oil that solidified after a few days; yield: 0.36 mg (1.28 mmol, 47%); mp 63–65 °C; [α]D +30 (c 2.6, CHCl3).

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).

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

To a solution of (S)-methyl-S-phenylsulfoximine ([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; 1.31 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 organic layers were combined, dried (anh MgSO4) and evaporated under reduced pressure. The crude product was purified by column chromatography (hexane:EtOAc 9:1) affording pure (S)-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, 741, 689, 513 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 (d, 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]+ calcd for [C10H8INOS]: 297.9114; found: 297.9116.
(5)-N-Ethyl-S-methyl-S-2-iodophenylsulfoximine [(5)-21]
To a solution of (5)-S-methyl-S-2-iodophenylsulfoximine [(5)-18; 0.168 g, 0.6 mol] in DMSO (1.5 mL) 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 × 5 mL). The organic layers were combined, dried (anhyd MgSO4) and evaporated under reduced pressure. The crude product was purified by column chromatography (hexane:EtOAc 1:1) affording pure (5)-21 as a white solid; yield: 0.151 g (0.49 mmol, 81%); mp 137–139 °C; 

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\text{IR (neat): } 2928, 2850, 1533, 1419, 1281, 1234, 1209, 1165, 1120, 1043, 1019, 954, 751, 745, 644 \text{ cm}^{-1}.
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1H NMR (400 MHz, CDCl3): \( \delta = 8.22 \) (dd, \( J = 7.9, 1.4 \text{ Hz}, 1 \text{ H} \)), 8.12 (dd, \( J = 7.8, 1.2 \text{ Hz}, 1 \text{ H} \)), 7.56 (dd, \( J = 7.9, 7.4, 1.2 \text{ Hz}, 1 \text{ H} \)), 7.24–7.20 (m, 1 H), 3.26 (s, 3 H), 2.94 (dq, \( J = 7.2, 7.2 \text{ Hz}, 1 \text{ H} \)), 2.78 (dq, \( J = 12.2, 7.2 \text{ Hz}, 1 \text{ H} \)), 1.21 (t, \( J = 7.2 \text{ Hz}, 3 \text{ H} \)).

13C NMR (101 MHz, CDCl3): \( \delta = 143.1, 141.5, 133.8, 133.0, 129.2, 93.8, 42.1, 38.9, 18.0 \).

HRMS: m/z [M + H]+ calcd for [C9H13INOS]: 309.9751; found: 309.9751.

(5)-N-Acetyl-S-methyl-S-2-iodophenylsulfoximine [(5)-22]
To a solution of (5)-S-methyl-S-2-iodophenylsulfoximine [(5)-18; 309 mg, 1.09 mmol] in CH2Cl2 (8 mL) at 0 °C was added pyridine (0.12 mL, 1.3 equiv) followed by AcCl (77 µL, 1.09 mmol). The reaction mixture was stirred at 0 °C for 1 h, then allowed to warm to rt and stirring was continued overnight. The reaction was quenched with ice cold water (10 mL). The organic phase was separated, 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 9:1) affording pure [(5)-22] as white crystals; yield: 348 mg (1.08 mmol, 50%); mp 53–55 °C; mp 53–55 °C; 

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\text{IR (neat): } 3014, 2954, 2931, 2851, 1645, 1419, 1281, 1209, 1120, 1063, 1043, 1019, 954, 751, 745, 644 \text{ cm}^{-1}.
\]

1H NMR (400 MHz, CDCl3): \( \delta = 8.22 \) (dd, \( J = 8.0, 1.4 \text{ Hz}, 1 \text{ H} \)), 8.12 (dd, \( J = 7.8, 1.2 \text{ Hz}, 1 \text{ H} \)), 7.63–7.59 (m, 1 H), 7.30–7.26 (m, 1 H), 3.45 (s, 3 H), 2.16 (s, 3 H).

13C NMR (101 MHz, CDCl3): \( \delta = 178.9, 143.3, 140.9, 134.5, 131.5, 129.1, 91.6, 41.2, 25.6 \).

HRMS: m/z [M + H]+ calcd for [C9H14INO3S]: 323.9550; found: 323.9557.

The spectral data are in agreement with literature.50

Reference

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(26) Koposov, A. Y.; Boyarskikh, V. V.; Zhdankin, V. V. Org. Lett. 2004, 6, 3613.


(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.


