Asymmetric Syntheses of *S*,*S*-Dialkyl-Substituted Sulfoximines and Related Heterocycles

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Abstract: Enantiomerically enriched forms of a sulfoximine-based myristic acid analogue are prepared using either an asymmetric desymmetrization with a chiral base, or an enantioselective oxidation procedure as key steps. Additionally, a variety of 2-oxa-2-alkyl 3,4-dihydro 2,1-benzothiazines are synthesized via intramolecular metal-catalyzed N-arylation of appropriately functionalized sulfoximines with tethered 2-bromoaryl substituents. In turn, the sulfoximines are prepared by lithiation–alkylation sequences including enantioselective deprotonation steps or the use of an optically active sulfoxide. Using this methodology, the range of accessible 3,4-dihydro 2,1-benzothiazine derivatives is expanded.

Key words: alkyl sulfoximines, dihydro benzothiazines, desymmetrization, cyclizations, copper

In recent years, the potential of sulfoximines as versatile compounds in asymmetric synthesis has been recognized,[1] and several derivatives have found interest in medicinal and crop protection chemistry.[2] Since the first report on methionine sulfoximine [(*S*,*S*)-**1**, Figure 1] in 1950,[3] various strategies for the preparation of enantiomerically enriched sulfoximines with a stereogenic center at the sulfur atom have been developed. These synthetic activities, however, have largely been focused on the preparation of *S*-alkyl-*S*-aryl sulfoximines.[1,4] In contrast, approaches toward stereochemically homogeneous *S*,*S*-dialkyl-substituted derivatives, which would also be of interest for methionine sulfoximine, have seldom been considered despite the fact that several sulfoximines with two alkyl substituents on sulfur have shown pronounced bioactivities.[5] Mostly, these have been applied as racemates,[6] presumably due to preparative difficulties, which hampered their accessibility in enantiopure form. Consequently, the effect of the absolute configuration at sulfur on the potency of such compounds is often unknown. Two examples are depicted in Figure 1. In replication studies of the Moloney leukemia virus (MoLV), myristic acid analogue **2** was found to be a functional myrsitoylation antagonist,[7] and 2-oxa-2-methyl 1,2-benzoisothiazole **3** proved to be a central nervous system (CNS) depressant agent.[8] In the respective studies, both sulfoximines were applied as racemates.

Our general interest in sulfoximine chemistry[1d] motivated us to focus our attention on the preparative access of enantiomerically enriched forms of such compounds. Thus, asymmetric syntheses of *S*,*S*-dialkyl-substituted sulfoximines and related heterocycles with potential biological relevance became prime targets of choice.

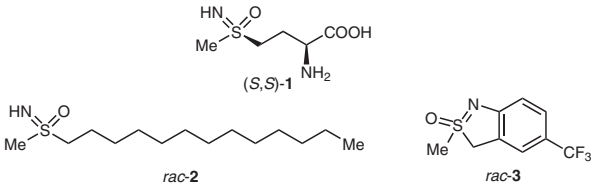
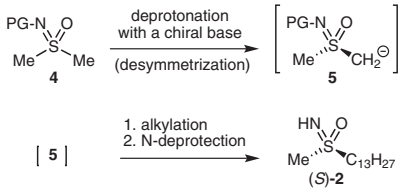


Figure 1 Bioactive *S*,*S*-dialkyl sulfoximines and a related heterocycle

In the study reported here, two main synthetic strategies were followed: the first utilized a desymmetrization of N-protected dimethyl sulfoximine **4** with a chiral base,[9] opening direct access to enantioenriched methyl alkyl sulfoximines [such as (*S*)-**2**] by formal alkylation of chiral carbanion **5** (Scheme 1).



Scheme 1 Desymmetrization strategy for the synthesis of *S*,*S*-dialkyl sulfoximine (*S*)-**2**

The second approach made use of readily available enantiopure sulfoxide **6**,[10] which was converted into the desired *S*,*S*-dialkyl sulfoximines **7** by sequential stereospecific substitution and imination. Both strategies allowed the preparation of functionalized sulfoximines **8**, which proved useful for syntheses of 3,4-dihydro 2,1-benzothiazines **9** via metal-catalyzed intramolecular N-arylations (Scheme 2).[11,12]

Our initial studies focused on the preparation of enantiomerically enriched myristic acid analogue **2**. Following our previously reported desymmetrization methodology,[9] treatment of N-silylated dimethyl sulfoximine **4a** with lithium (*S*,*S*)-bis(α-methylbenzyl)amide [(*S*,*S*-**10**)] in the presence of lithium chloride at –105 °C, followed by trapping of the resulting anion with dodecyl iodide, gave N-protected sulfoximine **7a** (Scheme 3). To our disappointment, however, the product was racemic.

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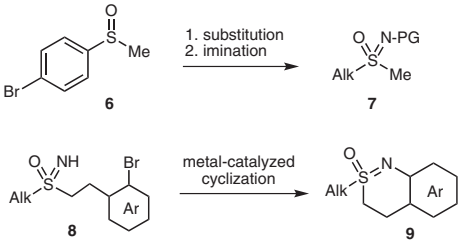
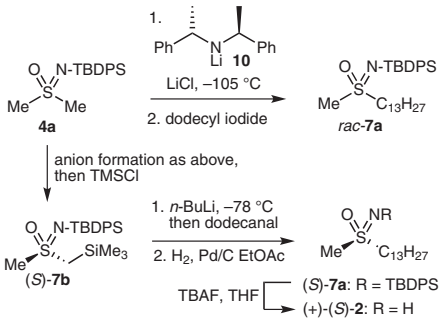


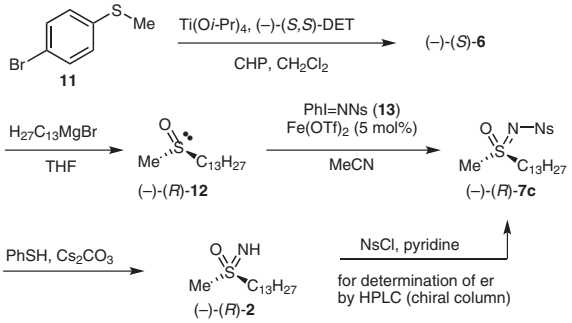
Scheme 2 General strategies for the syntheses of *S*,*S*-dialkyl sulfoximines and 3,4-dihydro 2,1-benzothiazines

Taking earlier observations[9] into account the desymmetrization strategy was modified. The intermediate anion, which was prepared as described above, was first trapped with trimethylsilyl chloride to give α-silylated sulfoximine **7b** in 81% yield. Pleasingly, an enantiomeric ratio (er) of 79:21 was found. Based on the previous assignment,[9] the *S*-enantiomer was formed in excess. Treatment of this product with *n*-butyllithium followed by dodecanal led to an olefin with mixed double bond geometry via a Peterson-type reaction. Subsequent palladium-catalyzed hydrogenation afforded saturated sulfoximine (*S*)-**7a** in 37% yield over two steps. This product had an enantiomeric ratio of 79:21. Desilylation with tetrabutylammonium fluoride in tetrahydrofuran then completed the reaction sequence providing myristic acid analogue (+)-(*S*)-**2** in 53% yield (Scheme 3).



Scheme 3 Asymmetric synthesis of myristic acid analogue (+)-(*S*)-**2**

Although the desymmetrization protocol led to the desired *S*,*S*-dialkyl sulfoximine (*S*)-**2** in enantiomerically enriched form, the enantiomeric ratio remained unsatisfying. Consequently, an alternative approach had to be developed. A reaction sequence involving a metal-catalyzed asymmetric sulfide oxidation to provide enantiopure sulfoxide (*S*)-**6** as the key step (Scheme 4) appeared most attractive.[10] Thus, starting from the corresponding aryl methyl sulfide **11**, asymmetric oxidation with titanium tetraisopropoxide and cumyl hydroperoxide (CHP) in the presence of (–)-(*S*,*S*)-diethyl tartrate [(–)-(*S*,*S*)-DET] gave (–)-(*S*)-**6** in 77% yield. After recrystallization from hexane, the enantiomeric ratio of the product was 99.7:0.3 (chiral HPLC analysis).[10,13] Nucleophilic displacement of the 4-bromophenyl group with tridecylmagnesium bromide gave *S*,*S*-dialkyl sulfoxide (*R*)-**12** in 92% yield. After recrystallization, only one enantiomer (er >99.7:0.3) could be detected by HPLC analysis using a chiral column.[10b] Iron-catalyzed nitrogen transfer[14] with hypervalent iodine reagent **13**[15] provided *N*-nosyl sulfoximine (*R*)-**7c** in 65% yield (er >99.5:0.5). Cleavage of the nosyl group with thiophenol and cesium carbonate[16] afforded the desired myristic acid analogue (–)-(*R*)-**2** in 96% yield. As no adequate HLPC conditions for the determination of the enantiomeric ratio of *S*,*S*-dialkyl-substituted sulfoximine **2** were found, the final product was renosylated by treatment with nosyl chloride in pyridine (54% yield). The enantiomeric ratio of (*R*)-**7c** (er >99.5:0.5) revealed that no racemization had occurred in this reaction sequence, and we conclude that we have achieved the synthesis of essentially enantiopure[13] myristic acid analogue (–)-(*R*)-**2**.

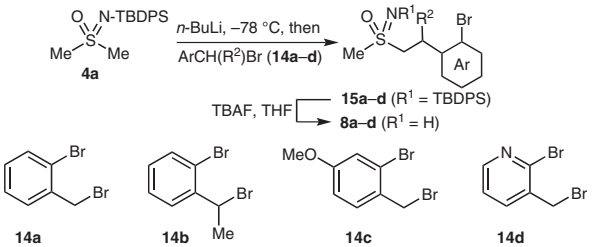


Scheme 4 Asymmetric synthesis of myristic acid analogue (–)-(*R*)-**2**

Using these two synthetic strategies, it was envisaged that aryl alkyl-substituted sulfoximines could be prepared, which would allow access to enantiomerically enriched 2-oxa-2-alkyl 3,4-dihydro 2,1-benzothiazines by metal-catalyzed cyclization. Initial optimization studies were performed with racemic *N*-silyl-protected dimethyl sulfoximine **4a** as starting material. Addition of *n*-butyllithium to **4a** at –78 °C and subsequent treatment of the resulting anion with benzyl bromides **14** afforded sulfoximines **15** in yields ranging from 39–70% (Table 1). Desilylations of these products with tetrabutylammonium fluoride gave NH-sulfoximines **8** in yields of up to 87%.

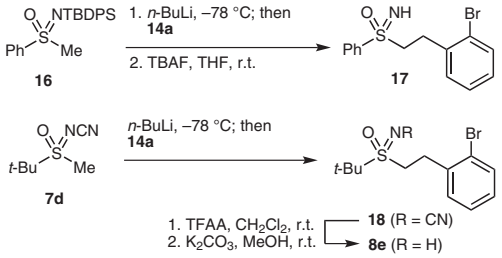
To enlarge the substrate range in the subsequent metal-catalyzed cyclization study, two further 2-bromophenylethyl substituted sulfoximines, **17** and **8e**, having a phenyl and a *tert*-butyl group at the sulfur atom, respectively, were synthesized (Scheme 5). Both compounds made use of known starting materials, and they were prepared in racemic form. Accordingly, *N*-silyl *S*-phenyl sulfoximine **16**[17] was lithiated with *n*-butyllithium, and trapping of the resulting anion with 1-bromo-2-(bromomethyl)benzene (**14a**), followed by reaction with tetrabutylammonium fluoride gave NH-sulfoximine **17** in 62% overall yield. An analogous approach was used for the conversion of *N*-cyano *S*-*tert*-butyl derivative **7d**.[18] Here, the alkylated *N*-cyano sulfoximine intermediate **18** was treated with trifluoroacetic anhydride followed by potassium carbonate in methanol to give *tert*-butyl-substituted NH-sulfoximine **8e** in 74% overall yield (Scheme 5).

Table 1 Syntheses of *S*-Arylethyl-*S*-methyl Sulfoximines **8a–d**



Entry	14	R^2	15	Yield (%)[a]	8	Yield (%)[a]
1	**a**	H	**a**	70	**a**	79
2	**b**	Me	**b** + **b′**[b]	39 (17)[c]	**b** + **b′**	86 (91)[c]
3	**c**	H	**c**	72	**c**	87
4	**d**	H	**d**	61[d]	**d**	79

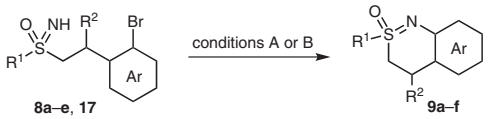
[a] Yield after column chromatography.
[b] A 2:1 mixture of diastereoisomers (**b** and **b′**) was obtained.
[c] Yield of the minor isomer in brackets.
[d] Instead of *n*-BuLi, lithium (*S*,*S*)-bis(α-methylbenzyl)amide was used as the base.



Scheme 5 Syntheses of NH-sulfoximines **17** and **8e**

Next, the conditions for the metal-catalyzed cyclizations of **8a–e** and **17** to give compounds **9a–f** were studied (Table 2). Following our previously published protocol for N-arylations of sulfoximines by palladium catalysis using palladium(II) acetate [$Pd(OAc)_2$] (10 mol%), BINAP (15 mol%) and potassium carbonate in toluene,[19] *S*-phenyl sulfoximine **17** reacted well affording heterocyclic sulfoximine **9f** in 98% yield (Table 2, entry 1). However, when these conditions were applied to the corresponding *S*-methyl sulfoximine **8a** no clean product was obtained (Table 2, entry 3). Consequently, the approach was modified and a copper-catalyzed cyclization was attempted. As in the intermolecular N-arylation,[20] copper(I) iodide (10 mol%) in combination with *N*,*N′*-dimethylethylenediamine (DMEDA) (20 mol%) and potassium carbonate in toluene were applied. Both *S*-phenyl and *S*-methyl sulfoximines **17** and **8a** reacted well providing the corresponding 3,4-dihydro 2,1-benzothiazines **9f** and **9a** in yields of 97% and 89%, respectively (Table 2, entries 2 and 4). Encouraged by these results, the behavior of the other substrates was studied and the results are shown in Table 2. High yields (92%) were observed in cyclizations of diastereomeric *S*-methyl sulfoximines **8b** and **8b′**, which both have a methyl substituent at the benzylic position to give products **9b** and **9b′**, respectively (Table 2, entry 5).[21] In contrast, sulfoximines **8c** and **8d** with a *p*-methoxy-substituted bromoarene and a 3-pyridinyl group gave **9c** and **9d** in only moderate to good yields (66% and 81%, respectively, Table 2, entries 6 and 7). Finally, *S*-*tert*-butyl sulfoximine **8e** afforded the cyclization product **9e** in 63% yield (Table 2, entry 8), which compares well to the other cyclization results considering the increased buttressing effect of the *tert*-butyl group at the sulfur atom.

Table 2 Syntheses of 3,4-Dihydro 2,1-Benzothiazines **9**[a]

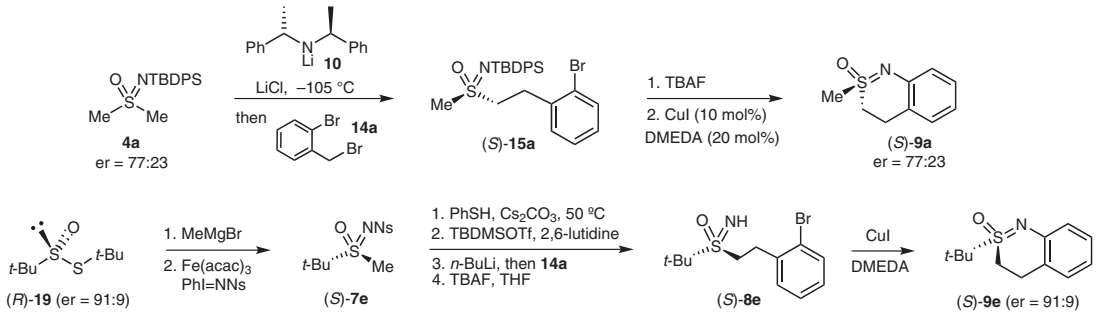


Entry	R^1	Substrate	R^2	Conditions	Product	Yield (%)[b]
1	Ph	**17**	H	A	**9f**	98
2	Ph	**17**	H	B	**9f**	97
3	Me	**8a**	H	A	**9a**	–[c]
4	Me	**8a**	H	B	**9a**	89
5[d]	Me	**8b**/**8b′**	Me	B	**9b**/**9b′**	92 (92)
6	Me	**8c**	H	B	**9c**	66
7	Me	**8d**	H	B	**9d**	81
8	*t*-Bu	**8e**	H	B	**9e**	63

[a] Conditions A: $Pd(OAc)_2$, BINAP; conditions B: CuI, DMEDA. For details see the experimental section.
[b] Yield after column chromatography.
[c] A complex reaction mixture was obtained.
[d] Cyclization yield of the minor diastereoisomer in brackets.

To demonstrate the applicability of the devised protocols for the preparation of enantiomerically enriched 2-oxa-2-alkyl 3,4-dihydro 2,1-benzothiazines, two approaches were followed (Scheme 6). The first made use of optically active *S*-arylethyl *S*-methyl sulfoximine **15a**. This intermediate was obtained by asymmetric deprotonation of N-silylated dimethyl sulfoximine **4a** with lithium (*S*,*S*)-bis(α-methylbenzyl)amide (**10**) in the presence of lithium chloride at –105 °C[9] and trapping of the resulting anion with 1-bromo-2-(bromomethyl)benzene (**14a**). After aqueous work-up, N-protected sulfoximine (*S*)-**15a** was obtained with an enantiomeric ratio of 77:23 in 70% yield. Subsequent cleavage of the silyl group with tetrabutylammonium fluoride to give (*S*)-**8a** followed by copper-catalyzed cyclization under standard conditions afforded 2-oxa-2-methyl 3,4-dihydro 2,1-benzothiazine [(*S*)-**9a**] in 70% yield over two steps. Analysis of the enantiomeric ratio by HPLC using a chiral stationary phase revealed the stereospecificity of the reaction sequence (er = 77:23).

The potential of this cyclization strategy for the synthesis of an enantiomerically enriched 2-oxa-2-alkyl 3,4-dihydro 2,1-benzothiazine was further illustrated for *S*-*tert*-butyl-substituted **9e**, an example of a substrate with a



Scheme 6 Syntheses of enantiomerically enriched 2-oxa-2-alkyl 3,4-dihydro 2,1-benzothiazines **9a** and **9e**

sterically hindered *S*-alkyl group. Here, (*R*)-*tert*-butyl thiosulfinate [(*R*)-**19**][22] served as an intermediate. Treatment of (*R*)-**19** (having an enantiomeric ratio of 91:9)[23] with methylmagnesium bromide[22c] followed by imination of the resulting sulfoxide under iron-catalysis (10 mol% of iron(III) acetylacetonate [$Fe(acac)_3$] as catalyst and a mixture of iodosobenzene and *p*-nitrobenzenesulfonamide (PhI=O/$NsNH_2$) or [*N*-(*p*-nosylsulfonyl)imino]phenyliodinane (PhI=NNs) as nitrene sources in acetonitrile at room temperature)[24] gave *N*-nosyl protected sulfoximine (*S*)-**7e** in 80% yield (over two steps).[25] In order to introduce the 2-bromoaryl group required for the copper-catalyzed cyclization, the N-substituent had to be changed from nosyl to *tert*-butyldimethylsilyl. This was achieved in 75% yield (over two steps) by treatment of (*S*)-**7e** with thiophenol in the presence of cesium carbonate[16] and subsequent silylation of the intermediate NH-sulfoximine with *tert*-butyldimethylsilyl triflate to give (*S*)-**7f**. Alkylation under standard conditions [*n*-butyllithium, 1-bromo-2-(bromomethyl)benzene (**14a**); 88% yield] followed by desilylation with tetrabutylammonium fluoride afforded sulfoximine (*S*)-**8e** (67% yield). Finally, applying the aforementioned copper catalysis to this optically active substrate gave (*S*)-2-oxa-2-*tert*-butyl 3,4-dihydro 2,1-benzothiazine [(*S*)-**9e**] in 72% yield. HPLC analysis of (*S*)-**9e** using a chiral stationary phase revealed an enantiomeric ratio of 91:9 confirming the expected stereospecificity of the overall reaction sequence.

In conclusion, we have demonstrated the synthesis of a sulfoximine-based myristic acid analogue in enantiomerically enriched form through a desymmetrization strategy using lithium (*S*,*S*)-bis(α-methylbenzyl)amide as the chiral base. Moreover, a range of 2-oxa-2-alkyl 3,4-dihydro 2,1-benzothiazines has been prepared by copper-catalyzed intramolecular N-arylation. Finally, the possibility of synthesizing optically active dialkyl sulfoximines from sulfoxides was also investigated.

All reactions were carried out under an atmosphere of N_2 or Ar using oven-dried glassware. Et_2O and THF were freshly distilled from benzophenone ketyl. All other reagents were purchased from commercial suppliers and used without further purification. Flash column chromatography was carried out using Silica gel 60 (Merck). TLC was carried out using Merck F254 alumina-backed silica plates. Melting points were determined in open-end capillary tubes on a Buchi B-540 melting point apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer PE-241 instrument. IR spectra were obtained using a Perkin-Elmer FT/IR 1760 and were recorded as KBr pellets, as neat liquids or in $CHCl_3$ soln. ^1H and ^{13}C NMR spectra were recorded on Varian Innova 400 (400 and 100 MHz) or Mercury 300 (300 and 75 MHz) instruments. Chemical shifts are given in ppm and spin-spin coupling constants, *J*, are given in Hz. Mass spectra were acquired on a Varian MAT 212 spectrometer (CI, 100 eV and EI, 70 eV) and HRMS were recorded on a Finnegan MAT 95 spectrometer. Microanalyses were obtained with a Vario EL element analyzer. HPLC was performed on a Gynkotek M480 instrument or on a Merck Hitachi instrument with a D7000 interface, L7100 pump and L7400 UV detector with Daicel Chiralcel AD-H, OB-H, OD-H, OJ and Daicel Chiralpack AS columns.

Chiral Base-Promoted Reactions; General Procedure A

To a suspension of (*S*,*S*)-bis(α-methylbenzyl)amine hydrochloride (1.5 equiv) in THF (0.3 M) was added *n*-BuLi (2.7 equiv, 1.4–1.6 M in hexanes) at –105 °C and the resulting soln was allowed to warm to r.t. over 30 min before being re-cooled to –105 °C. A soln of sulfoximine (1.0 equiv) in THF (0.2 M) was added and the mixture was stirred for a further 1 h at –105 °C. A soln/suspension of the electrophile in THF (0.2 M) was added and the mixture was stirred at –105 °C and then at r.t. for the indicated period of time. The reaction was quenched by addition of 5% H_3PO_4 (aq) and the mixture extracted with Et_2O. The combined aq layers were washed with 5% H_3PO_4 (aq) and $NaHCO_3$ (aq) and dried over $MgSO_4$. Concentration under reduced pressure afforded the product, which was purified by flash chromatography.

Lithiation–Electrophilic Trapping; General Procedure B

To a soln of sulfoximine (1 equiv) in THF (0.1 M) at –78 °C was added *n*-BuLi (1.1 equiv, 1.4–1.6 M in hexanes) and the soln was stirred at this temperature for 20 min. A soln of the electrophile (2 equiv) in THF (0.5 M) was added and the resulting soln was allowed to warm to r.t. The mixture was quenched with H_2O or H_3PO_4 and the aq layer was extracted with Et_2O or CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, concentrated and the residue purified by flash chromatography.

***tert*-Butyldiphenylsilyl Deprotection; General Procedure C**

Silyl protected sulfoximine (1 equiv) was dissolved in THF (0.04–0.06 M) and a 1 M soln of TBAF in THF (3 equiv) was added. The resulting soln was stirred at r.t. until TLC indicated complete consumption of the starting material. The soln was concentrated and the residue was subjected to flash chromatography to afford the desired product.

Copper-Catalyzed Cyclization; General Procedure D

Under Ar, DMEDA (20 mol%) was added to a suspension of K_2CO_3 (4 equiv), sulfoximine (1 equiv) and CuI (10 mol%) in toluene

(0.07–0.25 M) and the resulting soln heated in a sealed tube at 140 °C for 8–20 h. The reaction mixture was cooled to r.t. and then subjected to purification by flash chromatography to afford the cyclized product.

Palladium-Catalyzed Cyclization; General Procedure E

Under Ar, a mixture of sulfoximine (1 equiv), BINAP (20 mol%), K_2CO_3 (5 equiv) and $Pd(OAc)_2$ (10 mol%) in toluene (0.1 M) was heated in a sealed tube at 140–160 °C for 1 h. The mixture was cooled to r.t. and then subjected to purification by flash chromatography to afford the cyclized product.

(*S*)-*N*-*tert*-Butyldiphenylsilyl Methyl Trimethylsilylmethyl Sulfoximine [(*S*)-7b]

Using general procedure A, reaction of **4a** (668 mg, 2.02 mmol), (*S*,*S*)-bis(α-methylbenzyl)amine hydrochloride (792 mg, 3.03 mmol), *n*-BuLi (3.6 mL, 1.5 M, 5.45 mmol) and TMSCl (0.76 mL, 3.03 mmol) in THF (22 mL) gave the crude product. Purification by flash chromatography (pentane–EtOAc, 11:1) gave the title compound as a white solid (659 mg, 81%, er = 79:21). Spectroscopic data were consistent with the literature.[9]

HPLC: Chiralcel OD-H, heptane–*i*-PrOH, 99:1, 0.5 mL·min^{-1}; 210 nm; t_{R1} = 18 min, t_{R2} = 29 min.

(*S*)-*N*-*tert*-Butyldiphenylsilyl Methyl *n*-Tridecyl Sulfoximine [(*S*)-7a]

To a soln of sulfoximine (*S*)-**7b** (179.0 mg, 0.444 mmol) in THF (4 mL) at –78 °C was added *n*-BuLi (0.33 mL, 1.5 M in hexanes, 0.489 mmol) and the mixture was stirred at –78 °C for 20 min. A soln of dodecanal (185.0 mg, 1 mmol) in THF (2 mL) was added and the resulting soln allowed to warm to r.t. overnight. 5% H_3PO_4 (aq) (10 mL) was added and the aq layer was extracted with CH_2Cl_2 (3 × 20 mL).The combined organic layers were dried over $MgSO_4$ and concentrated and the residue filtered through a plug of silica. The resulting oil was dissolved in EtOAc (20 mL), 10% Pd/C (69.0 mg) was added and the suspension was stirred under an atm of H_2 for 12 h. The suspension was filtered through Celite, the filter cake washed with EtOAc (30 mL) and the filtrate concentrated. Flash chromatography (5% EtOAc–pentane) afforded the title compound as an oil (81.0 mg, 37%, er = 79:21).

$[\alpha]_D$ –7.9 (*c* 0.7, $CHCl_3$).

IR (capillary): 2926, 2855, 1464, 1327, 1299, 1154, 1108, 704 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69–7.62 (m, 4 H), 7.34–7.24 (m, 6 H), 2.82–2.72 (m, 2 H), 2.58 (s, 3 H, CH_3S), 1.73–1.63 (m, 2 H, CH_2), 1.25–1.12 (m, 20 H, CH_2), 0.99 (s, 9 H, *t*-Bu), 0.81 (t, *J* = 6.5 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.6 (C), 136.5 (C), 135.6 (CH), 135.5 (CH), 129.0 (CH), 127.4 (CH), 59.0 (CH_2), 44.4 (CH_3), 32.1 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.2 (CH_2), 28.5 (CH_2), 27.3 (CH_3), 23.5 (CH_2), 22.8 (CH_2), 19.4 (CH_2), 14.3 (CH_3).

MS (EI): *m*/*z* (%) = 470 (1) [M – Et]$^+$, 444 (21), 443 (65), 442 (100) [M – *t*-Bu]$^+$, 260 (1), 244 (10), 212 (22), 199 (4), 197 (6), 183 (4), 57 (12).

HRMS: *m*/*z* [M – C_4H_9]$^+$ calcd for $C_{26}H_{40}NOSSi$: 442.2600; found: 442.2615.

HPLC: Daicel Chiralcel OD-H, heptane–*i*-PrOH, 99:1, 0.5 mL·min^{-1}; 210 nm; t_{R1} = 19.0 min, t_{R2} = 22.0 min.

(*S*)-*NH*-Methyl *n*-Tridecyl Sulfoximine [(*S*)-2][7]

According to general procedure C, sulfoximine (*S*)-**7a** (60.0 mg, 0.12 mmol) and TBAF (0.48 mL, 1 M in THF, 0.48 mmol) were reacted together in THF (3 mL) to give a crude product. Flash chromatography (50% EtOAc–pentane then 10% EtOH–EtOAc) gave the title compound as a white solid (10.2 mg, 53%). For analytical data, see the description of (*R*)-**2**.

$[\alpha]_D$ +1.7 (*c* 0.20, $CHCl_3$).

(*S*)-4-Bromophenyl Methyl Sulfoxide [(*S*)-6][10]

In a flask containing (–)-(*S*,*S*)-DET (1.22 g, 5.91 mmol) dissolved in anhyd CH_2Cl_2 (10 mL) a soln of Ti(O*i*-Pr)$_4$ (840 mg, 2.95 mmol) dissolved in anhyd CH_2Cl_2 (6 mL) was added and the mixture stirred vigorously for 2 min, after which distilled H_2O (16 μL) was added. This mixture was stirred for 20 min at r.t. and then cooled to –20 °C. *p*-Bromophenyl methyl sulfide (**11**) (600 mg, 2.95 mmol) in anhyd CH_2Cl_2 (6 mL) and cumene hydroperoxide (3.25 mmol) were then added to the cooled mixture. The mixture was stirred at –20 °C for 3 h after which the reaction was allowed to warm to r.t. The reaction was quenched by addition of a sat. soln of NH_4Cl (25 mL). The reaction mixture was filtered over Celite and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The organic layers were collected, washed with H_2O (2 × 50 mL) and then dried over anhyd $MgSO_4$. The solvent was evaporated in vacuo and the residue purified by column chromatography (pentane–EtOAc, 3:7) to give (*S*)-**6** as a white solid [501.0 mg, 77%, er = 99.7:0.3 (after recrystallization from hexane)].

$[\alpha]_D$ –106.2 (*c* 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66–7.63 (m, 2 H), 7.51–7.48 (m, 2 H), 2.69 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.0 (C), 132.7 (CH), 125.6 (C), 125.3(CH), 44.3 (CH_3).

HPLC: Daicel Chiralcel OB-H column, *n*-heptane–*i*-PrOH, 70:30, 0.7 mL·min^{-1}; 254 nm; t_{R1} = 10.3 min (major), t_{R2} = 13.4 min (minor).

(*R*)-Methyl *n*-Tridecyl Sulfoxide [(*R*)-12][10b]

A soln of (*S*)-**6** (150 mg, 0.68 mmol) in THF (5 mL) was cooled to 0 °C under an Ar atm. A 0.1 M soln of *n*-tridecylmagnesium bromide (295.4 mg, 1.03 mmol) in THF was added dropwise to the above cooled soln over a period of 30 min. After addition, the mixture was stirred at 0 °C for 1.5 h, after which it was allowed to warm to r.t. and then quenched with a sat. soln of NH_4Cl (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 12 mL), washed with H_2O (1 × 25 mL), dried over $MgSO_4$ and the solvent removed in vacuo. Purification by column chromatography (EtOAc) gave (*R*)-**12** as a white solid [155.0 mg, 92%, er >99.7:0.3 (after recrystallization from a minimum amount of hexane)].

$[\alpha]_D$ –15.2 (*c* 0.7, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.74–2.58 (m, 2 H), 2.53 (s, 3 H), 1.76–1.68 (m, 2 H), 1.48–1.37 (m, 2 H), 1.35–1.22 (m, 18 H), 0.85 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.1 (CH_2), 38.9 (CH_3), 32.2 (CH_2), 29.9 (CH_2), 29.83 (CH_2), 29.81 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 28.7 (CH_2), 23.0 (CH_2), 22.9 (CH_2), 14.4 (CH_3).

HPLC: Daicel Chiralcel OB-H column, *n*-heptane–*i*-PrOH, 99:1, 0.5 mL·min^{-1}; 230 nm; t_{R1} = 22.9 min (minor), t_{R2} = 25.5 min (major).

(*R*)-*N*-(4-Nitrobenzenesulfonyl Methyl *n*-Tridecyl) Sulfoximine [(*R*)-7c]

A mixture of sulfoxide (*R*)-**12** (70 mg, 0.28 mmol), $Fe(OTf)_2$ (5 mol%), powdered 4 Å MS (0.5 g/mmol), and PhI=NNs[15] (125.8 mg, 0.37 mmol) in MeCN (3 mL) was stirred at r.t. for 1.5 h. The solvent was evaporated in vacuo and the residue purified by column chromatography (EtOAc–pentane, 1:1) to afford (*R*)-**7c** as a white solid (82.0 mg, 65%, er >99.5:0.5).

Mp 100–101 °C; $[\alpha]_D$ –4.4 (*c* 1.0, $CHCl_3$).

IR (KBr): 3117, 3026, 2916, 2849, 1606, 1526, 1466, 1417, 1399, 1351, 1298, 1223, 1164, 1073, 967, 854, 733, 681 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.32–8.29 (m, 2 H), 8.15–8.11 (m, 2 H), 3.43–3.35 (m, 2 H), 3.34 (s, 3 H), 1.94–1.77 (m, 2 H), 1.47–1.39 (m, 2 H), 1.31–1.23 (m, 18 H), 0.86 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.2 (C), 141.1 (C), 128.2 (CH), 124.2 (CH), 56.7 (CH_2), 41.9 (CH_3), 32.2 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.2 (CH_2), 22.9 (CH_2), 22.7 (CH_2), 14.3 (CH_3).

MS (CI): *m*/*z* (%) = 447 (100) $[M]^+$, 262 (25), 247 (24), 215 (8), 173 (28), 156 (17), 107 (15), 97 (73).

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{35}N_2O_5S_2$: 447.1982; found: 447.1982.

HPLC: Daicel Chiralcel AD-H column, *n*-heptane–*i*-PrOH, 9:1, 0.6 mL·min^{-1}; 210 nm; t_{R1} = 45.6 min (minor), t_{R2} = 49.5 min (major).

(*R*)-*NH*-Methyl *n*-Tridecyl Sulfoximine [(*R*)-2][7]

A mixture of sulfoximine (*R*)-**7c** (90 mg, 0.20 mmol), PhSH (32.9 μL, 0.32 mmol) and Cs_2CO_3 (118.2 mg, 0.36 mmol) in MeCN (3 mL) was stirred at 30 °C for 9 h. H_2O (10 mL) was then added and the mixture was extracted with CH_2Cl_2 (3 × 7 mL), dried over $MgSO_4$ and the solvent removed in vacuo. The residue was purified by column chromatography (EtOAc–acetone, 1:0.2) to give (*R*)-**2** as a white solid (51.0 mg, 97%).

Mp 62.5–64.8 °C; $[\alpha]_D$ –2.2 (*c* 1.05, $CHCl_3$).

IR (KBr): 3289, 3008, 2914, 2848, 1650, 1548, 1466, 1375, 1313, 1188, 1100, 1011, 982, 936, 764, 722, 663 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.70 (br s, 1 H), 3.07–3.03 (m, 2 H), 2.95 (s, 3 H), 1.86–1.77 (m, 2 H), 1.45–1.38 (m, 2 H), 1.35–1.23 (m, 18 H), 0.85 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 57.4 (CH_2), 43.1 (CH_3), 32.1 (CH_2), 29.81 (CH_2), 29.79 (CH_2), 29.76 (CH_2), 29.7 (CH_2), 29.51 (CH_2), 29.46 (CH_2), 29.3 (CH_2), 28.6 (CH_2), 23.3 (CH_2), 22.9 (CH_2), 14.3 (CH_3).

MS (CI): *m*/*z* (%) = 262 (100) $[M]^+$, 247 (8), 83 (7).

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{32}NOS$: 262.2199; found: 262.2197.

(*S*)-*N*-(*tert*-Butyldiphenylsilyl) (2-Bromophenyl)ethyl Methyl Sulfoximine [(*S*)-15a]

Using general procedure A, reaction of *n*-BuLi (1.2 mL, 1.43 M in hexanes, 1.74 mmol), (*S*,*S*)-(1-phenylethyl)amine hydrochloride (253 mg, 0.97 mmol), sulfoximine **4a** (213.0 mg, 0.645 mmol), and 1-bromo-2-(bromomethyl)benzene (**14a**) (400.0 mg, 1.84 mmol) gave the crude product. Purification by flash chromatography (10% then 20% EtOAc–pentane) gave the title compound as a colorless oil (223.0 mg, 70%, er = 77:23).

$[\alpha]_D$ –7.7 (*c* 1.7, $CHCl_3$).

IR ($CHCl_3$): 3067, 3014, 2931, 2890, 2855, 1472, 1427, 1299, 1158, 1107, 1025, 941, 822, 753, 704, 640, 600, 503 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.80–7.76 (m, 4 H), 7.53 (dd, *J* = 8.0, 1.0 Hz, 1 H), 7.40–7.37 (m, 7 H), 7.25–7.21 (m, 1 H), 7.11 (t, *J* = 7.0 Hz, 1 H), 3.22–3.14 (m, 4 H), 2.73 (s, 3 H), 1.11 (s, 9 H, *t*-Bu).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.4 (C), 136.4 (C), 136.2 (C), 135.5 (CH), 135.4 (CH), 132.9 (CH), 130.6 (CH), 129.0 (CH), 128.5 (CH), 127.8 (CH), 127.4 (CH), 124.2 (C), 58.1 (CH_2), 44.6 (CH_3), 30.7 (CH_2), 27.2 (CH_3), 19.3 (C).

MS (EI): *m*/*z* (%) = 444 (100) $[M - t\text{-Bu } (^{81}Br)]^+$, 442 (96) $[M - t\text{-Bu } (^{79}Br)]^+$, 366 (18), 364 (15), 212 (8), 199 (23), 104 (9).

HRMS: *m*/*z* $[M - t\text{-Bu}]^+$ calcd for $C_{21}H_{21}NO^{79}BrSSi$: 442.0297; found: 442.0297.

HPLC: Daicel Chiralcel OD-H, heptane–*i*-PrOH, 99:1, 0.5 mL·min^{-1}; 230 nm; t_{R1} = 51 min, t_{R2} = 92 min.

(*S*)-(2-Bromophenyl)ethyl Methyl Sulfoximine [(*S*)-8a]

According to general procedure C, sulfoximine (*S*)-**15a** (173.0 mg, 0.35 mmol) and TBAF (0.69 mL, 1 M in THF, 0.69 mmol) were reacted together to give the crude product. Purification by flash chromatography (50% EtOAc–PE then 10% MeOH–EtOAc) gave the title compound as an oil (72.0 mg, 79%).

$[\alpha]_D$ +6.8 (*c* 0.25, $CHCl_3$).

IR ($CHCl_3$): 3335, 2969, 1465, 1217, 1025, 949, 758 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.55 (dd, *J* = 8.0, 0.8 Hz, 1 H, CH), 7.32–7.25 (m, 2 H, ArH), 7.13 (td, *J* = 8.0, 2.0 Hz, 1 H, CH), 3.39–3.35 (m, 2 H, CH_2), 3.28–3.24 (m, 2 H, CH_2), 2.98 (s, 3 H, CH_3), 2.43 (br s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.9 (C), 133.2 (CH), 130.9 (CH), 128.6 (CH), 128.0 (CH), 124.2 (C), 56.6 (CH_2), 43.0 (CH_3), 30.7 (CH_2).

MS (EI): *m*/*z* (%) = 263 (1) $[M\ (^{81}Br)]^+$, 261 (1) $[M\ (^{79}Br)]^+$, 184 (26), 183 (23), 181 (100).

HRMS: *m*/*z* $[M - Br]^+$ calcd for $C_9H_{12}NOS$: 182.0640; found: 182.0636.

2λ4-2,1-Benzothiazine-3,4-dihydro-2-methyl-2-oxide [(*S*)-9a]

Following general procedure D, sulfoximine (*S*)-**8a** (105.0 mg, 0.40 mmol), CuI (7.6 mg, 0.04 mmol), DMEDA (7.0 mg, 0.08 mmol) and K_2CO_3 (225.0 mg, 1.6 mmol) were reacted together in toluene (2 mL). The residue was subjected to flash chromatography (EtOAc then 10% MeOH–EtOAc) to give the title compound as a white solid (65.0 mg, 89%, er = 77:23).

Mp 153–154 °C; $[\alpha]_D$ +46.0 (*c* 0.4, $CHCl_3$).

IR (KBr): 2971, 1596, 1567, 1480, 1452, 1265, 1189, 1048, 1018, 753 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.16 (td, *J* = 8.0, 1.0 Hz, 1 H), 7.02 (br d, *J* = 6.5 Hz, 1 H), 6.89 (dd, *J* = 8.0, 1.0 Hz, 1 H), 6.84 (td, *J* = 6.5, 1.0 Hz, 1 H), 3.42–3.06 (m, 4 H), 3.21 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.2 (C), 128.7 (CH), 128.4 (CH), 122.9 (CH), 120.4 (CH), 44.5 (CH_2), 42.5 (CH_3), 24.0 (CH_2).

MS (EI): *m*/*z* (%) = 182 (11) $[M + H]^+$, 181 (100) $[M]^+$, 138 (24), 118 (35), 117 (40), 91 (25).

Anal. Calcd for $C_9H_{11}NOS$: C, 59.64; H, 6.12; N, 7.73. Found: C, 59.24; H, 6.30; N, 7.86.

HPLC: Daicel Chiralcel OD-H, heptane–*i*-PrOH, 75:25, 0.6 mL·min^{-1}, 230 nm; t_{R1} = 23.4 min, t_{R2} = 37.7 min.

N-(*tert*-Butyldiphenylsilyl) 2-(2-Bromophenyl)propyl Methyl Sulfoximines [(*R**,*R**)-15b] and [(*R**,*S**)-15b′][21]

Following general procedure B, sulfoximine **4a** (86.1 mg, 0.26 mmol), *n*-BuLi (200 μL, 1.6 M in hexanes, 0.32 mmol) and 1-bromo-2-(1-bromoethyl)benzene (**14b**) (84.0 mg, 0.32 mmol) were reacted together in THF. Purification by flash chromatography (10% then 20% EtOAc–pentane) gave a 2:1 mixture of diastereoisomers **15b**/**15b′** as colorless oils (52.0 mg, 39% major isomer **15b**; 22.5 mg, 17% minor isomer **15b′**).

Major Isomer (*R**,*R**)-15b

IR (capillary): 3067, 2932, 2856, 1471, 1429, 1297, 1151, 1107, 704 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.69–7.61 (m, 4 H), 7.60 (dd, *J* = 7.9, 1.5 Hz, 1 H), 7.31–7.25 (m, 6 H), 7.18 (td, *J* = 7.7, 1.5 Hz,

1 H), 7.10 (td, *J* = 7.9, 1.7 Hz, 1 H), 6.85 (ddd, *J* = 7.9, 7.2, 1.7 Hz, 1 H), 3.89–3.75 (m, 1 H), 3.25 (dd, *J* = 14.6, 5.2 Hz, 1 H), 2.92 (ddd, *J* = 14.6, 7.9, 0.7 Hz, 1 H), 2.47 (s, 3 H), 1.32 (d, *J* = 6.9 Hz, 3 H), 0.98 (s, 9 H, *t*-Bu).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.4 (C), 136.5 (C), 136.4 (C), 135.7 (CH), 135.6 (CH), 133.4 (CH), 129.1 (CH), 128.4 (CH), 128.1 (CH), 127.9 (CH), 127.5 (CH), 123.8 (C), 65.3 (CH_2), 45.2 (CH_3), 35.1 (CH), 27.2 (CH_3), 21.1 (CH_3), 19.2 (C).

MS (EI): *m*/*z* (%) = 458 (100) [M – *t*-Bu (^{81}Br)]$^+$, 456 (95) [M – *t*-Bu (^{79}Br)]$^+$, 199 (26).

HRMS: *m*/*z* [M – *t*-Bu]$^+$ calcd for $C_{22}H_{23}NOSiSBr$: 457.0531; found: 457.0531.

Minor Isomer (*R,*S**)-15b′**

IR ($CHCl_3$): 3064, 2932, 2856, 1471, 1297, 1149, 1107, 757, 703 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.74–7.62 (m, 4 H), 7.47 (dd, *J* = 7.9, 1.2 Hz, 1 H), 7.32–7.21 (m, 6 H), 7.18 (dd, *J* = 7.4, 1.2 Hz, 1 H), 7.11 (dd, *J* = 7.7, 1.7 Hz, 1 H), 7.00 (ddd, *J* = 7.9, 7.2, 1.7 Hz, 1 H), 4.03–3.90 (m, 1 H), 3.31 (dd, *J* = 13.6, 5.2 Hz, 1 H), 2.99 (dd, *J* = 13.6, 7.9 Hz, 1 H), 2.40 (s, 3 H), 1.33 (d, *J* = 6.9 Hz, 3 H), 1.02 (s, 9 H, *t*-Bu).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.5 (C), 136.5 (C), 136.3 (C), 135.8 (CH), 135.7 (CH), 133.4 (CH), 129.1 (CH), 129.0 (CH), 128.3 (CH), 128.0 (CH), 127.5 (CH), 123.8 (C), 64.2 (CH_2), 45.9 (CH_3), 34.5 (CH), 27.2 (CH_3), 21.1 (CH_3), 19.3 (C).

MS (EI): *m*/*z* (%) = 458 (100) [M – *t*-Bu (^{81}Br)]$^+$, 456 (91) [M – *t*-Bu (^{79}Br)]$^+$, 199 (29).

HRMS: *m*/*z* [M – *t*-Bu]$^+$ calcd for $C_{22}H_{23}NOSiSBr$: 456.0453; found: 456.0454.

(*R,*R**)-2-(2-Bromophenyl)propyl Methyl Sulfoximine [(*R**,*R**)-8b]**

According to general procedure C, (*R**,*R**)-**15b** (155.0 mg, 0.30 mmol) and TBAF (0.9 mL, 1 M in THF, 0.90 mmol) were reacted together to give the crude product. Purification by flash chromatography (50% EtOAc–pentane to EtOAc, then acetone) gave the title compound as a white solid (71.3 mg, 86%).

Mp 90–91 °C.

IR (KBr): 3282, 2984, 1474, 1415, 1208, 1030, 757 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57 (dd, *J* = 7.9, 1.2 Hz, 1 H), 7.36–7.25 (m, 2 H), 7.11 (ddd, *J* = 8.9, 7.9, 2.2 Hz, 1 H), 3.95 (sext, *J* = 6.9 Hz, 1 H), 3.55 (dd, *J* = 14.3, 6.4 Hz, 1 H), 3.25 (ddd, *J* = 14.3, 7.2, 0.7 Hz, 1 H), 2.84 (s, 3 H), 2.65 (br s, 1 H), 1.47 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.7 (C), 133.5 (CH), 128.6 (CH), 128.2 (CH), 127.9 (CH), 123.9 (C), 63.5 (CH_2), 43.7 (CH_3), 34.9 (CH), 21.2 (CH_3).

MS (EI): *m*/*z* (%) = 196 (100) [M – Br]$^+$, 171 (52), 169 (51), 117 (45), 115 (38).

HRMS: *m*/*z* [M – Br]$^+$ calcd for $C_{10}H_{14}NOS$: 196.0796; found: 196.0797.

(*R,*S**)-2-(2-Bromophenyl)propyl Methyl Sulfoximine [(*R**,*S**)-8b′]**

According to general procedure C, (*R**,*S**)-**15b′** (75.5 mg, 0.15 mmol) and TBAF (428 μL, 1 M in THF, 0.43 mmol) were reacted together to give the crude product. Purification by flash chromatography (gradient 50% EtOAc–pentane to EtOAc, then acetone) gave the title compound as a white solid (37.0 mg, 91%).

Mp 75–76 °C.

IR (KBr): 3323, 2987, 2916, 1472, 1422, 1202, 1159, 1034, 759 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 8.0 Hz, 1 H), 7.29–7.19 (m, 2 H), 7.08–7.02 (m, 1 H), 3.92 (sext, *J* = 6.9 Hz, 1 H), 3.46 (dd, *J* = 13.7, 6.0 Hz, 1 H), 3.21 (dd, *J* = 13.7, 7.4 Hz, 1 H), 2.78 (s, 3 H), 2.40 (br s, 1 H), 1.43 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.6 (C), 133.5 (CH), 128.6 (CH), 128.1 (CH), 127.9 (CH), 123.8 (C), 63.1 (CH_2), 44.0 (CH_3), 34.7 (CH), 21.2 (CH_3).

MS (EI): *m*/*z* (%) = 196 (100) [M – Br]$^+$, 171 (44), 169 (45), 133 (26), 117 (45), 115 (37).

HRMS: *m*/*z* [M – Br]$^+$ calcd for $C_{10}H_{14}NOS$: 196.0796; found: 196.0797.

(*R,*R**)-(*R*$_S$,*R*)-2λ4–2,1-Benzothiazine-3,4-dihydro-2,4-dimethyl-2-oxide [(*R**,*R**)-9b][21]**

Following general procedure D, (*R**,*R**)-**8b** (65.0 mg, 0.236 mmol), CuI (4.5 mg, 0.024 mmol), DMEDA (4.2 mg, 0.048 mmol) and K_2CO_3 (130.3 mg, 0.944 mmol) were reacted together in toluene (1 mL). The residue was subjected to flash chromatography (50% EtOAc–pentane then EtOAc) to give the title compound as a colorless oil (42.5 mg, 92%).

IR ($CHCl_3$): 2971, 2926, 1598, 1476, 1447, 1268, 1208, 1038, 757 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.10 (ddd, *J* = 8.4, 7.7, 1.5 Hz, 1 H), 7.03 (d, *J* = 7.4 Hz, 1 H), 6.90–6.79 (m, 2 H), 3.38 (dd, *J* = 13.0, 4.9 Hz, 1 H), 3.33–3.19 (m, 1 H), 3.12 (s, 3 H), 3.07 (dd, *J* = 13.1, 8.2 Hz, 1 H), 1.44 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.9 (C), 128.4 (CH), 126.9 (C), 126.4 (CH), 123.3 (CH), 121.0 (CH), 52.1 (CH_2), 43.6 (CH_2), 31.3 (CH), 19.5 (CH_3).

MS (EI): *m*/*z* (%) = 195 (100) [M]$^+$, 180 (9), 132 (36), 130 (52), 117 (63).

HRMS: *m*/*z* [M]$^+$ calcd for $C_{10}H_{13}NOS$: 195.0718; found: 195.0719.

(*R,*S**)-2λ4–2,1-Benzothiazine-3,4-dihydro-2,4-dimethyl-2-oxide [(*R**,*S**)-9b′][21]**

Following general procedure D, (*R**,*S**)-**8b′** (34.0 mg, 0.123 mmol), CuI (2.3 mg, 0.012 mmol), DMEDA (2.2 mg, 0.024 mmol) and K_2CO_3 (68.0 mg, 0.493 mmol) were reacted together in toluene (1 mL). The residue was subjected to flash chromatography (50% EtOAc–pentane then EtOAc) to give the title compound as a white solid (42.5 mg, 92%).

Mp 123–125 °C.

IR (KBr): 2979, 2923, 1597, 1474, 1441, 1295, 1261, 1200, 1025, 753 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.14 (d, *J* = 7.9 Hz, 1 H), 7.08 (d, *J* = 7.7 Hz, 1 H), 6.84 (d, *J* = 7.7 Hz, 2 H), 3.48–3.33 (m, 1 H), 3.30 (dd, *J* = 12.4, 4.2 Hz, 1 H), 3.11 (s, 3 H), 2.81 (t, *J* = 12.4 Hz, 1 H), 1.50 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.1 (C), 128.3 (CH), 126.3 (C), 125.3 (CH), 122.6 (CH), 120.6 (CH), 51.4 (CH_2), 43.2 (CH_2), 27.6 (CH), 18.4 (CH_3).

MS (EI): *m*/*z* (%) = 195 (100) [M]$^+$, 180 (6), 132 (28), 130 (71), 117 (55).

HRMS: *m*/*z* [M]$^+$ calcd for $C_{10}H_{13}NOS$: 195.0718; found: 195.0721.

***N*-(*tert*-Butyldiphenylsilyl) 2-Bromo-5-methoxyphenyl)ethyl Methyl Sulfoximine (15c)**

Following general procedure B, sulfoximine **4a** (324.4 mg, 0.98 mmol), *n*-BuLi (730 μL, 1.6 M in hexanes, 1.17 mmol) and 2-bromo-1-(bromomethyl)-4-methoxybenzene (302.4 mg, 1.08 mmol)

were reacted together in THF. Purification by flash chromatography (10% then 20% EtOAc–pentane) gave **15c** as an oil (374.6 mg, 72%).

IR ($CHCl_3$): 3068, 2933, 2855, 1473, 1330, 1154, 1108, 1018, 703 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.86–7.78 (m, 4 H), 7.45–7.37 (m, 7 H), 6.71–6.65 (m, 2 H), 3.77 (s, 3 H, CH_3), 3.32–3.10 (m, 4 H), 1.68 (s, 3 H, CH_3), 1.14 (s, 9 H, *t*-Bu).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3 (C), 138.5 (C), 136.5 (C), 136.3 (C), 135.7 (CH), 135.6 (CH), 133.6 (CH), 129.2 (CH), 127.6 (CH), 114.6 (C), 114.5 (CH), 58.1 (CH_2), 55.5 (CH_3), 44.6 (CH_3), 30.9 (CH_2), 27.2 (CH_3), 19.3 (C).

MS (EI): *m*/*z* (%) = 474 (100) [M – *t*-Bu (^{81}Br)]$^+$, 472 (100) [M – *t*-Bu (^{79}Br)]$^+$, 396 (12), 394 (11), 199 (36).

HRMS: *m*/*z* [M – *t*-Bu]$^+$ calcd for $C_{22}H_{23}BrNO_2SSi$: 474.0384; found: 474.0374.

(2-Bromo-5-methoxyphenyl)ethyl Methyl Sulfoximine (8c)

According to general procedure C, sulfoximine **15c** (175.0 mg, 0.33 mmol) and TBAF (1.0 mL, 1 M in THF, 1.00 mmol) were reacted together to give the crude product. Purification by flash chromatography (50% EtOAc–pentane to EtOAc, then acetone) gave the title compound as a white solid (84.0 mg, 87%).

IR ($CHCl_3$): 3276, 2933, 1593, 1576, 1475, 1414, 1243, 1211, 1018, 755 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 8.8 Hz, 1 H), 6.82 (d, *J* = 3.0 Hz, 1 H), 6.66 (dd, *J* = 8.8, 3.0 Hz, 1 H), 3.74 (s, 3 H), 3.36–3.28 (m, 2 H), 3.21–3.12 (m, 2 H), 2.96 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.2 (C), 137.8 (C), 133.7 (CH), 116.4 (CH), 114.6 (CH), 114.4 (C), 56.5 (CH_2), 55.6 (CH_3), 43.0 (CH_3), 30.9 (CH_2).

MS (EI): *m*/*z* (%) = 214 (25), 212 (56) [M – Br]$^+$, 149 (100), 134 (29), 132 (27).

HRMS: *m*/*z* [M – Br]$^+$ calcd for $C_{10}H_{14}NO_2S$: 212.0745; found: 212.0736.

2λ4-2,1-Benzothiazine-3,4-dihydro-2-methyl-6-methoxy-2-oxide (9c)

Following general procedure D, **8c** (72.0 mg, 0.246 mmol), CuI (4.7 mg, 0.025 mmol), DMEDA (4.3 mg, 0.049 mmol) and K_2CO_3 (135.8 mg, 0.984 mmol) were reacted together in toluene (1 mL). The residue was subjected to flash chromatography (50% EtOAc–pentane then EtOAc) to give the title compound as a white solid (34.0 mg, 66%).

Mp 169–170 °C.

IR (KBr): 2923, 1609, 1489, 1422, 1266, 1232, 1187, 1020, 819 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.84 (d, *J* = 8.7 Hz, 1 H), 6.75 (dd, *J* = 8.7, 3.0 Hz, 1 H), 6.61 (d, *J* = 3.0 Hz, 1 H), 3.76 (s, 3 H), 3.44–3.29 (m, 2 H), 3.23–3.08 (m, 2 H), 3.20 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.7 (C), 137.5 (C), 123.5 (CH), 121.4 (C), 114.2 (CH), 113.8 (CH), 55.6 (CH_3), 44.6 (CH_2), 42.4 (CH_3), 24.3 (CH_2).

MS (EI): *m*/*z* (%) = 211 (100) [M]$^+$, 196 (37), 168 (29), 132 (26).

HRMS: *m*/*z* [M]$^+$ calcd for $C_{10}H_{13}NO_2S$: 211.0667; found: 211.0670.

Anal. Calcd for $C_{10}H_{13}NO_2S \cdot 1/5H_2O$: C, 55.89; H, 6.29; N, 6.52. Found: C, 55.95; H, 6.21; N, 6.54.

N-(*tert*-Butyldiphenylsilyl) (2-Bromo-3-pyridyl)ethyl Methyl Sulfoximine (15d)

Following general procedure A, reaction of sulfoximine **4a** (292.0 mg, 0.88 mmol), *n*-BuLi (1.6 mL, 1.5 M in hexanes, 2.40 mmol), (*S*,*S*)-bis(α-methylbenzyl)amine hydrochloride (346.0 mg, 1.32 mmol) and 2-bromo(3-bromomethyl)pyridine (**14d**) (442.0 mg, 1.76 mmol) in THF (22 mL) gave the crude product. Purification by flash chromatography (20% then 40% EtOAc–pentane) gave the title compound as a colorless oil (272.0 mg, 61%).

IR ($CHCl_3$): 3051, 3013, 2930, 2891, 2855, 1560, 1405, 1303, 1158, 1108, 1053, 745, 703 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.14 (dd, *J* = 4.0, 2.0 Hz, 1 H), 7.72–7.64 (m, 4 H), 7.35–7.22 (m, 7 H), 7.07 (dd, *J* = 6.0, 4.0 Hz, 1 H), 3.16–3.04 (m, 4 H), 2.67 (s, 3 H, CH_3), 1.01 (s, 9 H, *t*-Bu).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.6 (CH), 144.0 (C), 138.9 (CH), 136.3 (C), 136.1 (C), 135.6 (CH), 135.5 (CH), 135.1 (C), 129.2 (CH), 127.6 (CH), 123.1 (CH), 57.4 (CH_3), 44.9 (CH_2), 29.7 (CH_2), 27.2 (CH_3), 19.4 (C).

MS (EI): *m*/*z* (%) = 445 (100) [M – *t*-Bu (^{81}Br)]$^+$, 443 (95) [M – *t*-Bu (^{79}Br)]$^+$, 263 (15), 261 (15), 199 (9), 197 (7), 128 (10), 104 (9).

HRMS: *m*/*z* [M – *t*-Bu]$^+$ calcd for $C_{20}H_{20}BrN_2OSSi$: 445.0230; found: 445.0244.

(2-Bromo-3-pyridyl)ethyl Methyl Sulfoximine (8d)

Following general procedure C, reaction of sulfoximine **15d** (270.0 mg, 0.54 mmol) and TBAF (1.6 mL, 1 M in THF, 1.60 mmol) gave the crude product. Purification by flash chromatography (50% EtOAc–pentane to EtOAc, then acetone) gave the title compound as a colorless oil (111.0 mg, 79%).

IR ($CHCl_3$): 3245, 3007, 2925, 1561, 1407, 1210, 1114, 1048, 804, 751, 664 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.25 (dd, *J* = 4.5, 2.0 Hz, 1 H), 7.60 (ddd, *J* = 7.5, 5.0, 2.0 Hz, 1 H), 7.17 (dd, *J* = 7.5, 5.0 Hz, 1 H), 4.1 (br s, 1 H), 3.40–3.25 (m, 2 H), 3.25–3.15 (m, 2 H), 2.92 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.9 (CH), 144.0 (C), 139.2 (CH), 134.6 (C), 123.3 (CH), 55.8 (CH_2), 43.3 (CH_3), 29.7 (CH_2).

MS (EI): *m*/*z* (%) = 183 (100) [M – Br]$^+$, 119 (20), 104 (82), 78 (20), 77 (36), 51 (25).

HRMS: *m*/*z* [M – Br]$^+$ calcd for $C_8H_{11}BrN_2OS$: 183.0598; found: 183.0595.

2λ4-Pyrido[2,3-*c*][1,2]thiazine-3,4-dihydro-2-methyl-2-oxide (9d)

Following general procedure D, sulfoximine **8d** (72.5 mg, 0.276 mmol), CuI (5.2 mg, 0.027 mmol), DMEDA (4.8 mg, 0.054 mmol) and K_2CO_3 (152.0 mg, 1.10 mmol) were reacted together in THF–toluene (1:1, 4 mL) to give the crude product. Purification by flash chromatography (50% EtOAc–pentane then EtOAc) gave the title compound as a white solid (40.5 mg, 81%).

Mp 174–175 °C.

IR (KBr): 2986, 2909, 1586, 1561, 1434, 1291, 1200, 1028, 788 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.20 (d, *J* = 4.0 Hz, 1 H), 7.31 (d, *J* = 7.0 Hz, 1 H), 6.77 (dd, *J* = 7.0, 4.0 Hz, 1 H), 3.45–3.00 (m, 4 H), 3.27 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.5 (C), 148.2 (CH), 136.8 (CH), 116.2 (CH), 115.3 (C), 43.7 (CH_2), 42.7 (CH_3), 23.1 (CH_2).

MS (EI): *m*/*z* (%) = 182 (100) [M]$^+$, 167 (9), 120 (9), 119 (65), 92 (21).

HRMS: *m*/*z* [M]$^+$ calcd for $C_8H_{10}N_2OS$: 182.0514; found: 182.0512.

***N*-(*tert*-Butyldiphenylsilyl) Methyl Phenyl Sulfoximine (16)[17]**

TBDPSCl (425 μL, 2.43 mmol) was added dropwise to a soln of methyl phenyl sulfoximine (300.0 mg, 1.94 mmol) and imidazole (263.8 mg, 3.88 mmol) in DMF (4 mL) at 0 °C under Ar. The resulting soln was heated at 60 °C for 48 h, poured into H_2O (6 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined CH_2Cl_2 layers were dried over $MgSO_4$ and concentrated to afford the crude product. Purification by flash chromatography (4% then 10% EtOAc–pentane) gave **16** as an oil (700.0 mg, 92%).

IR (capillary): 3062, 2936, 2858, 1428, 1331, 1164, 1105, 703 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 8.2 Hz, 2 H), 7.57 (d, *J* = 8.2 Hz, 2 H), 7.47 (d, *J* = 8.2 Hz, 2 H), 7.58–7.28 (m, 9 H), 2.88 (s, 3 H), 1.12 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.5 (C), 136.6 (C), 136.4 (C), 135.7 (CH), 135.6 (CH), 132.2 (CH), 129.1 (CH), 129.0 (CH), 128.9 (CH), 127.4 (CH), 127.3 (CH), 127.0 (CH), 49.0 (CH_2), 27.2 (CH_3), 19.4 (C).

MS (EI): *m*/*z* (%) = 336 (100) $[M - t\text{-Bu}]^+$.

(2-Bromophenyl)ethyl Phenyl Sulfoximine (17)

Step 1: *N*-(*tert*-Butyldiphenylsilyl) (2-Bromophenyl)ethyl Phenyl Sulfoximine

According to general procedure B, sulfoximine **16** (400.0 mg, 1.02 mmol), *n*-BuLi, (762 μL, 1.6 M in hexanes, 1.22 mmol) and 1-bromo-2-(bromomethyl)benzene (**14a**) (305.0 mg, 1.22 mmol) were reacted together. Purification by flash chromatography (10% then 20% EtOAc–pentane) gave the corresponding *N*-TBDPS protected sulfoximine as a colorless oil (400.0 mg, 70%).

IR (capillary): 3062, 2934, 1440, 1382, 1155, 1104, 703 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 7.4 Hz, 2 H), 7.71 (dd, *J* = 7.2, 1.7 Hz, 2 H), 7.66 (dd, *J* = 7.7, 1.7 Hz, 2 H), 7.46–7.18 (m, 10 H), 7.04 (td, *J* = 7.4, 1.4 Hz, 1 H), 6.92 (td, *J* = 7.7, 1.7 Hz, 1 H), 6.81 (dd, *J* = 7.7, 1.7 Hz, 1 H), 3.20 (ddd, *J* = 13.5, 9.9, 7.2 Hz, 1 H), 3.08 (ddd, *J* = 13.5, 10.4, 6.4 Hz, 1 H), 2.95–2.79 (m, 2 H), 1.04 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.3 (C), 137.6 (C), 136.4 (C), 136.3 (C), 135.7 (CH), 135.6 (CH), 132.9 (CH), 132.3 (CH), 130.5 (CH), 129.0 (CH), 128.9 (CH), 128.8 (CH), 128.4 (CH), 127.9 (CH), 127.7 (CH), 127.4 (CH), 127.3 (CH), 124.2 (C), 59.4 (CH_2), 30.6 (CH_2), 27.2 (CH_3), 19.5 (C).

MS (EI): *m*/*z* (%) = 506 (93) $[M - t\text{-Bu } (^{81}Br)]^+$, 504 (100) $[M - t\text{-Bu } (^{79}Br)]^+$, 426 (15), 199 (29).

HRMS: *m*/*z* $[M - t\text{-Bu } (^{81}Br)]^+$ calcd for $C_{26}H_{23}NO^{79}BrSSi$: 504.0453; found: 504.0453.

Step 2: Desilylation

Following general procedure C, reaction of the *N*-TBDPS protected sulfoximine (175.0 mg, 0.31 mmol), prepared via step 1, and TBAF (930 μL, 1 M in THF, 0.93 mmol) gave the crude product. Purification by flash chromatography (50% EtOAc–pentane to EtOAc, then acetone) gave compound **17** as a colorless oil (88.7 mg, 88%).

IR (capillary): 3269, 3062, 1444, 1221, 1112, 988, 755 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.96 (dd, *J* = 8.0, 1.5 Hz, 2 H), 7.59–7.53 (m, 1 H), 7.49 (t, *J* = 8.0 Hz, 2 H), 7.39 (d, *J* = 7.5 Hz, 1 H), 7.17–7.10 (m, 2 H), 7.00 (ddd, *J* = 7.0, 6.5, 3.0 Hz, 1 H), 3.34 (dd, *J* = 9.1, 7.7 Hz, 2 H), 3.12–2.97 (m, 2 H), 2.71 (br s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.5 (C), 137.0 (C), 133.1 (CH), 133.0 (CH), 130.7 (CH), 129.2 (CH), 128.7 (CH), 128.5 (CH), 127.8 (CH), 124.2 (CH), 56.7 (CH_2), 30.4 (CH_2).

MS (EI): *m*/*z* (%) = 326 [17, M $(^{81}Br)]^+$, 324 [15, M $(^{79}Br)]^+$, 244 [100, M – Br]$^+$.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{14}H_{15}NO^{79}BrS$: 324.0058; found: 324.0052.

2λ4-2,1-Benzothiazine-3,4-dihydro-2-phenyl-2-oxide (9f)

Following general procedure D, sulfoximine **17** (46.9 mg, 0.145 mmol), CuI (2.8 mg, 0.015), DMEDA (2.6 mg, 0.029 mmol) and K_2CO_3 (60.0 mg, 0.43 mmol) were reacted together in toluene (1 mL) to afford the crude product. Purification by flash chromatography (30% EtOAc–pentane then EtOAc) gave the title compound as a pale-yellow solid (34.0 mg, 97%).

Following general procedure E, sulfoximine **17** (64.0 mg, 0.198 mmol), $Pd(OAc)_2$ (4.4 mg, 0.0198 mmol), BINAP (18.4 mg, 0.0295 mmol) and K_2CO_3 (137.0 mg, 0.99 mmol) were dissolved in toluene (2 mL) and the resulting soln was degassed. The reaction mixture was heated in a sealed tube at 160 °C for 1 h and then cooled to r.t. Purification by flash chromatography (30% EtOAc–pentane) gave the title compound as a pale-yellow solid (48.0 mg, 98%).

Mp >100 °C (dec.).

IR (KBr): 1594, 1565, 1475, 1447, 1263, 1195, 1110, 1002, 750 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.06 (dt, *J* = 5.0, 1.5 Hz, 2 H), 7.69 (tt, *J* = 8.0, 2.0 Hz, 1 H), 7.64–7.56 (m, 2 H), 7.21 (td, *J* = 7.5, 1.5 Hz, 1 H), 7.15–7.08 (m, 2 H), 6.89 (td, *J* = 7.0, 1.0 Hz, 1 H), 3.48–3.03 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.9 (C), 138.4 (C), 133.9 (CH), 129.4 (CH), 129.0 (CH), 128.6 (CH), 128.4 (CH), 123.5 (CH), 120.9 (C), 120.5 (CH), 47.3 (CH_2), 24.8 (CH_2).

MS (EI): *m*/*z* (%) = 244 (36) $[M + H]^+$, 243 (100) $[M]^+$.

HRMS: *m*/*z* $[M]^+$ calcd for $C_{14}H_{13}NOS$: 243.0718; found: 243.0721.

***N*-Cyano *tert*-Butyl Methyl Sulfoximine (7d)**

The title product was prepared according to literature procedures.[14]

Mp 56–58 °C.

IR (KBr): 2996, 2924, 2192, 1471, 1236, 1162, 969, 836 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.15 (s, 3 H), 1.56 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 111.6 (CN), 63.3 (C), 34.4 (CH_3), 23.4 (CH_3).

MS (EI): *m*/*z* (%) = 161 (25) $[M + H]^+$, 145 (11) $[M - Me]^+$, 105 (34), 57 (100).

Anal. Calcd for $C_6H_{12}N_2OS$: C, 44.97; H, 7.55; N, 17.48. Found: C, 45.03; H, 7.48; N, 17.47.

***tert*-Butyl (2-Bromophenyl)ethyl Sulfoximine (8e)**

Step 1: *N*-Cyano *tert*-Butyl (2-Bromophenyl)ethyl Sulfoximine (18)

Following general procedure B, sulfoximine **7d** (248.0 mg, 1.55 mmol), *n*-BuLi (1.1 mL, 1.6 M in hexanes, 1.70 mmol) and 1-bromo-2-(bromomethyl)benzene (**14a**) (775.0 mg, 3.10 mmol) were reacted together in THF. Purification by flash chromatography (20% EtOAc–pentane) gave the desired *N*-cyano sulfoximine as an oil (383.0 mg, 75%).

IR ($CHCl_3$): 2990, 2196, 1465, 1370, 1263, 1204, 1156, 1023, 845, 811, 767, 659 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.56 (dd, *J* = 7.5, 1.5 Hz, 1 H), 7.37 (dd, *J* = 7.5, 2.0 Hz, 1 H), 7.31 (td, *J* = 7.5, 1.5 Hz, 1 H), 7.17 (td, *J* = 7.5, 2.0 Hz, 1 H), 3.52–3.37 (m, 4 H), 1.58 (s, 9 H, *t*-Bu).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.9 (C), 133.1 (CH), 131.1 (CH), 129.3 (CH), 128.1 (CH), 124.0 (C), 113.0 (CN), 65.3 (C), 46.8 (CH_2), 28.3 (CH_2), 23.5 (CH_3).

MS (EI): *m*/*z* (%) = 331 (1) $[M + H\ (^{81}Br)]^+$, 329 (1) $[M + H\ (^{79}Br)]^+$, 193 (23), 185 (43), 183 (43), 104 (28), 103 (15), 77 (17), 57 (100).

Anal. Calcd for $C_{13}H_{17}N_2OSBr$: C, 47.42; H, 5.20; N, 8.51. Found: C, 47.24; H, 5.40; N, 8.37.

Step 2: Cyano Group Cleavage

TFAA (376 μL, 2.66 mmol) was added to a soln of *N*-cyano sulfoximine **18** (309.0 mg, 0.94 mmol), prepared via step 1, at 0 °C and the resulting soln was stirred until TLC indicated complete consumption of the starting material. The soln was concentrated and then K_2CO_3 (684.0 mg, 4.96 mmol) and MeOH (10 mL) were added and the soln stirred overnight at r.t. Purification by flash chromatography gave **8e** as a colorless oil (286.0 mg, 99%).

(*S*)-*N*-(*p*-Nitrobenzenesulfonyl) *tert*-Butyl Methyl Sulfoximine [(*S*)-7e]; Asymmetric Synthesis

Step 1: (*S*)-*tert*-Butyl Methyl Sulfoxide[22c]

To a soln of (*R*)-*tert*-butyl *tert*-butanethiosulfinate [(*R*)-**19**] (1.5 g, 7.73 mmol, er = 91:9), obtained at r.t. by the asymmetric vanadium oxidation procedure reported by Ellman,[22] in THF at –78 °C was added slowly a 1 M soln of MeMgBr in Et_2O (23.2 mL, 23.2 mmol). The temperature was allowed to reach –20 °C, and the mixture was stirred at this temperature until the starting material was consumed. The reaction was quenched with an aq sat. soln of NH_4Cl (20 mL) and the mixture extracted with EtOAc (3 × 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. The product was purified by flash chromatography (50% EtOAc–pentane then EtOAc) to afford (*S*)-(+)-*tert*-butyl methyl sulfoxide (649.3 mg, 70%).

$[\alpha]_D$ +6.4 (*c* 0.88, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.21 (s, 3 H), 1.87 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.3 (C), 31.4 (CH_3), 22.2 (CH_3).

Step 2: Imination[14]

(*S*)-*tert*-Butyl methyl sulfoxide (600.0 mg, 5.0 mmol), prepared via step 1, was reacted with PhI=NNs[15] (2.6 g, 6.4 mmol) in the presence of $Fe(acac)_3$ (176.5 mg, 0.5 mmol) in MeCN (45 mL) at r.t. The reaction mixture was concentrated and subjected to column chromatography (CH_2Cl_2) to give sulfoximine (*S*)-**7e** as a white solid (1.28 g, 80%).

Mp 155–156 °C (dec.); $[\alpha]_D$ –103.0 (*c* 0.66, acetone).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (d, *J* = 9.1 Hz, 2 H), 8.08 (d, *J* = 9.1 Hz, 2 H), 3.33 (s, 3 H), 1.40 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.6 (C), 149.4 (C), 127.8 (CH), 123.9 (CH), 62.5 (C), 35.5 (CH_3), 22.8 (CH_3).

(*S*)-*tert*-Butyl (2-Bromophenyl)ethyl Sulfoximine [(*S*)-8e]

Step 1: (*S*)-*tert*-Butyl Methyl Sulfoximine[14]

A mixture of (*S*)-**7e** (640.0 mg, 2.0 mmol), Cs_2CO_3 (1.17 g, 3.6 mmol) and PhSH (328 μL, 3.2 mmol) in MeCN (20 mL) was stirred at 50 °C overnight. H_2O (15 mL) was added to the reaction mixture and the product was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. Purification by flash column chromatography (EtOAc then acetone) gave the corresponding NH-sulfoximine as a white solid (270.0 mg, >99%).

Mp 100–103 °C; $[\alpha]_D$ +6.0 (*c* 0.5, acetone).

IR (KBr): 3446, 3298, 2984, 1467, 1197, 1086, 1002, 935, 748 cm^{-1}.

^{1}H NMR (400 MHz, acetone-d_6): δ = 2.78 (s, 3 H), 1.36 (s, 9 H).

^{13}C NMR (100 MHz, acetone-d_6): δ = 58.9 (C), 36.0 (CH_3), 23.2 (CH_3).

MS (EI): *m*/*z* (%) = 120 (13) $[M - 15]^+$, 85 (55), 83 (85), 57 (100).

Step 2: (*S*)-*N*-(*tert*-butyldimethylsilyl) *tert*-Butyl Methyl Sulfoximine (7f)

To a soln of the NH-sulfoximine (150.0 mg, 1.10 mmol), prepared via step 1, and 2,6-lutidine (140.0 μL, 1.20 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added dropwise TBDMSOTf (380 μL, 1.65 mmol). The resulting soln was stirred at 0 °C for 1 h and then concentrated under vacuum to afford the crude product. Purification by flash chromatography (4% then 10% EtOAc–pentane) gave the *N*-TBDMS protected sulfoximine as a colorless oil (206.0 mg, 75%).

$[\alpha]_D$ –10.0 (*c* 1.0, $CHCl_3$).

IR (capillary): 2950, 1296, 1136, 831 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.66 (s, 3 H), 1.28 (s, 9 H), 0.81 (s, 9 H), 0.00 (s, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 59.9 (C), 38.7 (CH_3), 26.0 (CH_3), 23.7 (CH_3), 18.0 (C), –2.3 (CH_3), –2.4 (CH_3).

MS (EI): *m*/*z* (%) = 192 (34) $[M - t\text{-Bu}]^+$, 136 (100), 85 (31), 83 (41), 57 (46).

HRMS: *m*/*z* $[M - t\text{-Bu}]^+$ calcd for $C_7H_{18}NOSSi$: 192.0878; found: 192.0871.

Step 3: (*S*)-*N*-(*tert*-butyldimethylsilyl) *tert*-Butyl (2-Bromophenyl)ethyl Sulfoximine

According to general procedure B, to the *N*-TBDMS protected sulfoximine (176.0 mg, 0.71 mmol), prepared via step 2, *n*-BuLi, (530 μL, 1.6 M in hexanes, 0.85 mmol) and 1-bromo-2-(bromomethyl)benzene (**14a**) (212.0 mg, 0.85 mmol) were reacted together at –78 °C. Purification by flash chromatography (4% then 20% EtOAc–pentane) gave the corresponding *N*-TBDMS protected sulfoximine as a colorless oil (259.3 mg, 88%).

$[\alpha]_D$ –33.4 (*c* 0.32, $CHCl_3$).

IR (capillary): 2953, 2854, 1470, 1295, 1129, 832, 770 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42 (d, *J* = 7.9 Hz, 1 H), 7.17–7.12 (m, 2 H), 6.98 (ddd, *J* = 7.9, 5.7, 3.2 Hz, 1 H), 3.20–2.90 (m, 4 H), 1.25 (s, 9 H), 0.81 (s, 9 H), 0.04 (s, 3 H), 0.00 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.9 (C), 133.1 (CH), 130.7 (CH), 128.4 (CH), 127.9 (CH), 124.5 (C), 61.0 (C), 49.2 (CH_2), 28.7 (CH_2), 26.2 (CH_3), 24.0 (CH_3), 18.3 (C), –1.7 (CH_3), –1.9 (CH_3).

MS (EI): *m*/*z* (%) = 362 (44) $[M + H - t\text{-Bu}\ (^{81}Br)]^+$, 360 (41) $[M + H - t\text{-Bu}\ (^{79}Br)]^+$, 306 (100) $[M + H - 2t\text{-Bu}\ (^{81}Br)]^+$, 304 (93) $[M + H - 2t\text{-Bu}\ (^{79}Br)]^+$, 225 (17).

HRMS: *m*/*z* $[M - t\text{-Bu}]^+$ calcd for $C_{14}H_{24}BrNOSSi$: 360.0453; found: 360.0457.

Step 4: Desilylation

Following general procedure C, reaction of the sulfoximine (205.0 mg, 0.49 mmol), prepared via step 3, and TBAF (1.5 mL, 1 M in THF, 1.50 mmol) gave the crude product. Purification by flash chromatography (50% EtOAc–pentane to EtOAc, then acetone) gave compound (*S*)-**8e** as a colorless oil (100.0 mg, 67%).

$[\alpha]_D$ –12.0 (*c* 0.25, $CHCl_3$).

IR ($CHCl_3$): 3332, 3279, 2971, 2874, 1683, 1366, 1203, 1092, 1023, 989, 957, 756, 662, 637 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 (dd, *J* = 8.0, 1.0 Hz, 1 H), 7.34 (dd, *J* = 7.5, 2.0 Hz, 1 H), 7.27 (td, *J* = 7.5, 1.5 Hz, 1 H), 7.13 (td, *J* = 8.0, 2.0 Hz, 1 H), 3.37–3.21 (m, 4 H), 2.27 (br s, 1 H, NH), 1.46 (s, 9 H, *t*-Bu).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.9 (C), 133.0 (CH), 130.9 (CH), 128.6 (CH), 127.9 (CH), 124.3 (C), 60.8 (C), 46.8 (CH_2), 28.5 (CH_2), 23.9 (CH_3).

MS (EI): *m*/*z* (%) = 249 (1) [M – *t*-Bu + H (^{81}Br)]$^+$, 247 (1) [M – *t*-Bu + H (^{79}Br)]$^+$, 185 (17), 182 (23), 168 (44), 104 (25), 77 (20), 57 (100).

HRMS: *m*/*z* [M – Br]$^+$ calcd for $C_{12}H_{18}NOS$: 224.1109; found: 224.1110.

(*S*)-2λ4-2,1-Benzothiazine-3,4-dihydro-2-*tert*-butyl-2-oxide [(*S*)-9e]

Following general procedure D, sulfoximine (*S*)-**8e** (50.0 mg, 0.16 mmol), CuI (3.1 mg, 0.016 mmol), DMEDA (2.9 mg, 0.032 mmol), K_2CO_3 (68 mg, 0.49 mmol) and toluene (1.0 mL) were reacted together at 140 °C for 20 h to afford the crude product. Purification by flash chromatography (50% EtOAc–pentane) afforded the title compound as a colorless oil (25.7 mg, 72%).

$[\alpha]_D$ +94.5 (*c* 0.33, $CHCl_3$).

IR ($CHCl_3$): 2984, 2936, 1599, 1568, 1479, 1454, 1270, 1207, 1161, 1105, 1044, 1013, 816, 755, 490, 459 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.13 (t, *J* = 7.6 Hz, 1 H), 7.00 (d, *J* = 7.5 Hz, 1 H), 6.93 (dd, *J* = 8.0, 1.0 Hz, 1 H), 6.79 (td, *J* = 7.5, 1.5 Hz, 1 H), 3.45–3.33 (m, 1 H), 3.19–3.12 (m, 2 H), 3.01–2.91 (m, 1 H), 1.51 (s, 9 H, *t*-Bu).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.4 (C), 128.3 (CH), 128.1 (CH), 122.8 (CH), 121.1 (C), 119.5 (CH), 59.8 (C), 37.0 (CH_2), 23.5 (CH_2), 23.5 (CH_3).

MS (EI): *m*/*z* (%) = 224 (11) [M + H]$^+$, 223 (63) [M]$^+$, 168 (12), 167 (63), 150 (39), 119 (100), 118 (67), 117 (29), 91 (29), 57 (49).

HRMS: *m*/*z* [M]$^+$ calcd for $C_{12}H_{17}NOS$: 223.1031; found: 223.1036.

HPLC: Chiralcel OJ, heptane–*i*-PrOH, 75:25, 0.6 mL·min^{-1}, 230 nm, t_{R1} = 14.4 min, t_{R2} = 19.2 min.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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