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ortho-Lithiation of *S*-*tert*-butyl-*S*-phenylsulfoximines. New route to enantiopure sulfinamides via a de-*tert*-butylation reaction

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Abstract—The sulfoximine group proved to be an excellent *ortho*-directing group in lithiation reactions. Several electrophiles were used to afford the corresponding *ortho*-functionalized aryl sulfoximines in good yields. The use of prochiral electrophiles lead to modest to good diastereoselectivities up to 95%. During this study, we observed a side reaction due to a *S*-de-*tert*-butylation. After optimization of this *S*-de-*tert*-butylation reaction, the corresponding enantiopure sulfinamides could be obtained in good yields.

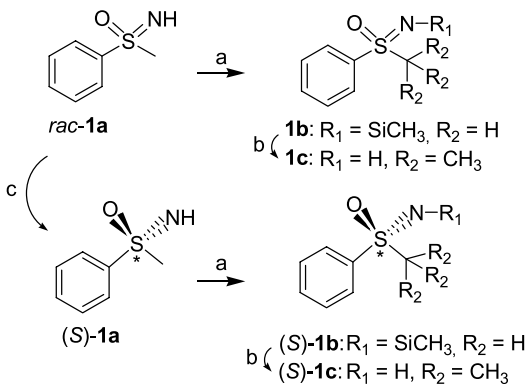
1. Introduction

The directed *ortho*-lithiation reaction is a very powerful method for the functionalization of aromatic compounds and synthesis of polysubstituted homoaromatic and heteroaromatic compounds.[1] In a previous paper,[2] we reported our first results concerning the sulfoximine[3a] group as an *ortho*-directing group[3b] for the lithiation reaction of homoaromatic systems. The reaction with *n*-butyllithium in THF at −78 °C afforded the corresponding *ortho*-lithiated species, which could be trapped with different electrophiles in good yields. Addition of benzaldehyde proceeded with modest diastereoselectivity (de=52%). The aim of this paper is to provide full details concerning the scope and limitations of this new *ortho*-directing group and to improve the stereoselectivity in the case of prochiral electrophiles. During the course of this study, we observed a troubleshooting de-*tert*-butylation side-reaction leading to sulfinamides or in some cases to cyclic sulfinic esters. We found it interesting to define optimal conditions leading to enantiopure *ortho*-substituted sulfinamides.

2. Results and discussion

2.1. Synthesis of *N*-substituted sulfoximines 1a–i

Racemic sulfoximine **1c** has been prepared as described in our previous paper.[2] The starting material for the synthesis was *rac*-**1a**, which was converted quantitatively into **1b** (Scheme 1). Repeated lateral lithiation of **1b** followed by quenching with CH_3I afforded **1c** in 86% yield. We also turned our interest in the stereoselective preparation of sulfoximine (*S*)-**1c** by using the same procedure. For that purpose, (*S*)-*S*-phenyl-*S*-methylsulfoximine ((*S*)-**1a**) was prepared in 80% optical purity by resolution of the racemic (±)-**1a** according to a published procedure.[4] In order to study the influence of the *N*-substituent sulfoximine on the *ortho*-lithiation properties, we first prepared a series of *N*-functionalized sulfoximines **1d–i** (Table 1). *N*-silylation could be achieved by reacting **1c**[2] with HMDS leading to compound **1d** in a quantitative yield (Table 1, entry 1). First attempts to alkylate sulfoximine **1c** in the presence of



Scheme 1. (a) HMDS (5 equiv), 85 °C, 40 min (100%); (b) *n*-BuLi, THF, 0 °C then CH_3I, 30 min, 20 °C repeated twice (86%); (c) (1*S*)-(+)-camphorsulfonic acid, acetone.[4]

Keywords: Sulfoximine; Lithiation; Sulfinamide; Asymmetric synthesis.
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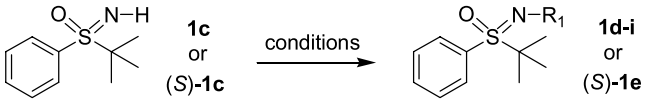
Table 1. *N*-functionalization of sulfoximine **1c** and (*S*)-**1c**



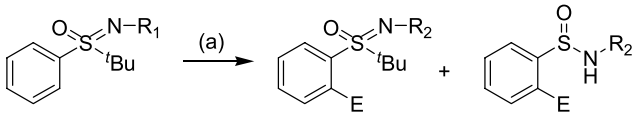
Entry	Conditions	Product	R_1	Yield%
1	HMDS (5 equiv), 85 °C, 40 min (100%)	**1d**	$Si(CH_3)_3$	100
2	KH (1 equiv), DME, 20 °C, 1 h then CH_3I, PTC, 20 °C, 12 h	**1e**	CH_3	86
3	KH (1 equiv), DME, 20 °C, 1 h then CH_3I, PTC, 20 °C, 12 h	(*S*)-**1e**	CH_3	86
4	KH (1 equiv), DME, 20 °C, 1 h then Br-$(CH_2)_2OCH_3$, PTC, 20 °C, 12 h	**1f**	$(CH_2)_2OCH_3$	92
5	KH (1 equiv), DME, 20 °C, 1 h then Br–CH_2–CH=CH_2, PTC, 20 °C, 12 h	**1g**	CH_2–CH=CH_2	95
6	KH (1 equiv), DME, 20 °C, 1 h then Boc_2O, PTC, 20 °C, 12 h	**1h**	COO^tBu	63
7	$(CH_3)_3COCl$, Na_2CO_3, CH_2Cl_2, 20 °C, 2 h	**1i**	CO^tBu	44

sodium hydride afforded low yields, most likely due to steric hindrance of the *tert*-butyl group and the poor nucleophilicity of the sulfoximine nitrogen. Finally, sulfoximine **1c** could be alkylated with success according to a literature procedure by deprotonation with potassium hydride in DME[5] in the presence of tetrabutylammonium bromide and quenching with various electrophiles to afford the *N*-substituted sulfoximines **1e–h** in good yields (Table 1, entries 2, 4–6). *tert*-Butylsulfoximine[2] (*S*)-**1e** (Table 1, entry 3) was obtained without erosion of the optical purity (ee = 80%) by using this procedure. Treatment of sulfoximine **1c** with pivaloyl chloride and sodium carbonate in a biphasic mixture of water and dichloromethane afforded, in a moderate yield, the instable[6] crude *N*-pivaloyl sulfoximine **1i** (Table 1, entry 7).

2.2. Metalation reaction of sulfoximines 1c–g

Preliminary experiments using various conditions have been described before by us.[2] We summarize here the main results. With the *N*-unprotected sulfoximine **1c**, 2 equiv of *n*-BuLi followed by quenching with methyl iodide or methanol-*d* afforded, respectively, products **2a** and **2b** in low yields (Table 2, entries 1 and 2). To examine the scope of this reaction with several other electrophiles, we then studied the *ortho*-functionalization of the *N*-protected sulfoximines **1d–g** (Table 2, entries 3–18). *ortho*-Lithiation of the *N*-trimethylsilyl sulfoximine **1d** with *n*-BuLi at −78 °C is very fast and, the intermediate lithio species was quenched after 10 min with methanol-*d* to afford compound **2f** in 95% yield (Table 2, entry 7). However, a small amount

Table 2. Metalation reaction of sulfoximines **1c–g** and quenching with electrophiles

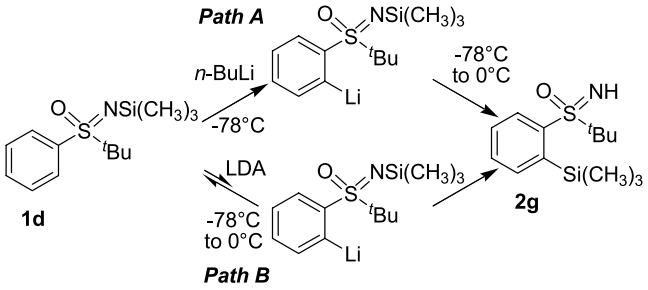


Entry	Sulfoximine	R_1	Electrophile	E	R_2	Product	Yield%
1	**1c**	H	CH_3I	CH_3	H	**2a**	50
2	**1c**	H	CH_3OD	D	H	**2b**	60
3	**1d**	$Si(CH_3)_3$	CH_3I	CH_3	H	**2a**	90
4	**1d**	$Si(CH_3)_3$	$(CH_3)_2S_2$	SCH_3	H	**2c**	95
5	**1d**	$Si(CH_3)_3$	I_2	I	H	**2d**	75
6	**1d**	$Si(CH_3)_3$	C_2Cl_6	Cl	H	**2e**	76
7	**1d**	$Si(CH_3)_3$	CH_3OD	D	$Si(CH_3)_3$	**2f**	95[a]
8	**1d**	$Si(CH_3)_3$	—	$Si(CH_3)_3$	H	**2g**	95
9	**1e**	CH_3	CH_3I	CH_3	CH_3	**2h**	95
10	**1e**	CH_3	$(CH_3)_2S_2$	SCH_3	CH_3	**2i**	78
11	**1e**	CH_3	I_2	I	CH_3	**2j**+**3a**[b]	—
12	**1e**	CH_3	C_2Cl_6	Cl	CH_3	**2k**+**3b**[b]	—
13	**1e**	CH_3	CH_3OD	D	CH_3	**2l**	92[a]
14	**1f**	$(CH_2)OCH_3$	CH_3I	CH_3	$(CH_2)OCH_3$	**2m**	55
15	**1f**	$(CH_2)OCH_3$	$(CH_3)_2S_2$	SCH_3	$(CH_2)OCH_3$	**2n**	65
16	**1g**	$CH_2CH=CH_2$	CH_3I	CH_3	$CH_2CH=CH_2$	**2o**	96
17	**1g**	$CH_2CH=CH_2$	$(CH_3)_2S_2$	SCH_3	$CH_2CH=CH_2$	**2p**	90
18	**1g**	$CH_2CH=CH_2$	CH_3OD	D	$CH_2CH=CH_2$	**2q**	95[a]

(a) Reaction performed with *n*-BuLi (1.2 equiv), THF, −78 °C (2 equiv of *n*-BuLi with **1c** to obtain **2a**, **2b**; 0 °C with **1d** to obtain **2g**), 10 min then electrophile, 2 h (1 h for **1d**), −78 °C.
[a] Conversion determined by ^1H NMR.
[b] Conversion into the sulfinamide occured during the purification.

of compound **2g** corresponding to the migration of the trimethylsilyl group could be isolated. When the *ortho*-lithiated species was allowed to reach 0 °C, compound **2g** was obtained in 95% yield (Table 2, entry 8).

It is interesting to note that this migration also occurred when LDA is used as lithiating agent. When a lithium amide is employed, the formation of **2g** probably proceeded via an equilibrium between the starting sulfoximine **1d** and the *ortho*-lithiated sulfoximine, which is trapped by the trimethylsilyl group shifting the equilibrium to the formation of **2g** (Scheme 2).



Scheme 2. Lithiation of *N*-trimethylsilysulfoximine **1d**: Path A: Non-reversible conditions (*n*-BuLi). Path B: Reversible conditions (LDA).

Trapping of the intermediate lithio species obtained from **1d–g** with methyl iodide and dimethyl disulfide, afforded the corresponding *ortho*-substituted sulfoximines in good yields (Table 2, respectively, entries 3, 9, 14, and 16 and entries 4, 10, 15, and 17). These last results clearly show that *N*-protected sulfoximines **1d–g** are superior to the *N*-unprotected sulfoximine **1c** to provide satisfactory yields. Use of iodine or hexachloroethane as electrophiles proceeded smoothly with the *N*-silylated sulfoximine **1d** (Table 2, entries 5 and 6). With sulfoximine **1e**, an unseparable mixture of *ortho*-substituted sulfoximines **2j**,**k** and their corresponding sulfinamides **3a**,**b** was observed (Table 2, entries 11 and 12). Optimization of this reaction giving rise to the exclusive formation of sulfinamides will be further described in this paper.

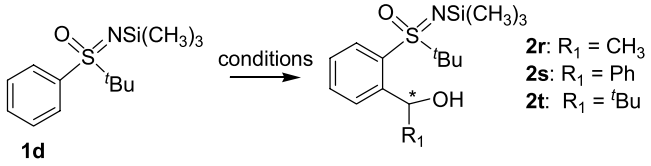
2.3. Quenching with prochiral electrophiles

In order to investigate the potential of the chiral sulfoximine *ortho*-directing group as a new synthetic tool for asymmetric induction, we decided to test various prochiral electrophiles. The first experiments were carried out with sulfoximine **1d** in THF and various aldehydes (Table 3). Acetaldehyde and pivaldehyde (Table 3, entries 1 and 7) gave satisfactory yields and medium stereocontrol, while no stereocontrol was obtained with benzaldehyde (Table 3, entry 2). Decreasing the solvent polarity by means of toluene in the presence of *sec*-BuLi/TMEDA allowed us to improve somewhat the level of stereocontrol (de=50%) with benzaldehyde (Table 3, entry 6). Under the same conditions, *N*-methylsulfoximine **1e** afforded along with the desired *ortho*-functionalized sulfoximines **2u**,**v**, sulfinic esters **4a–c** (Table 4). These by-products result from a de-*tert*-butylation reaction followed by an intramolecular cyclisation of the resultant sulfinamide with the hydroxy group. With acetaldehyde, the sulfinic ester **4a** is the sole product observed with modest diastereoselectivity (Table 4, entry 1). In the case of benzaldehyde, alcohol **2u** was recovered quantitatively in the crude reaction mixture, but flash chromatography led to the sulfinic ester **4b** in a quantitative yield and once again with a modest diastereoisomeric excess (Table 4, entry 2). Pivaldehyde gave a 1/1 mixture of *ortho*-substituted sulfoximine **2v** and sulfinic ester **4c** in moderate yields and excellent stereocontrol in both cases (Table 4, entry 3). It is interesting to point out that this de-*tert*-butylation reaction seems to be easier with *ortho*-substituted sulfoximines. Indeed, no de-*tert*-butylation reaction is detected during flash chromatography of the starting material **1e**. In spite of these interesting results in terms of stereocontrol, the de-*tert*-butylation reaction limits the yields and the reproducibility of this *ortho*-functionalization of aryl-sulfoximines. Since we could not get away from this side reaction, we optimized the conditions to obtain a clean stereoselective de-*tert*-butylation reaction to improve the overall yield of this process. Given the impressive applications of chiral sulfinamides reported these last years in literature,[7] efficient stereoselective routes to new *ortho*-substituted sulfinamides may be highly desirable.

2.4. Optimization of the de-*tert*-butylation reaction

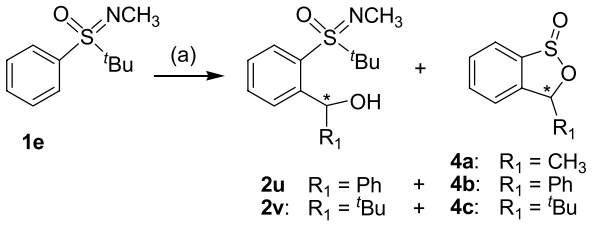
Many papers[8–11] report the conversion of sulfoximines into sulfinamides. These include the preparation of epoxides and cyclopropanes from β-hydrosulfoximines[10] and γ-ketosulfoximines,[8b] respectively, which is accompanied in both cases by the formation of sulfinamides (Scheme 3a

Table 3. Metalation reaction of sulfoximine **1d** followed by trapping with prochiral electrophiles



Entry	Conditions	Product	Yield%	de%
1	*n*-BuLi (1.2 equiv), THF, −78 °C, 10 min then CH_3CHO, −78 °C, 1 h	**2r**	76	50
2	*n*-BuLi (1.2 equiv), THF, −78 °C, 10 min then PhCHO, −78 °C, 1 h	**2s**	60	0
3	*n*-BuLi (1.2 equiv), TMEDA, THF, −78 °C, 10 min then PhCHO, −78 °C, 1 h	**2s**	60	25
4	*n*-BuLi (1.2 equiv), TMEDA, ether, −78 °C, 10 min then PhCHO, −78 °C, 1 h	**2s**	60	40
5	*n*-BuLi (1.2 equiv), TMEDA, toluene, −78 °C, 10 min then PhCHO, −78 °C, 1 h	**2s**	60	40
6	*sec*-BuLi (1.2 equiv), TMEDA, toluene, −78 °C, 10 min then PhCHO, −78 °C, 1 h	**2s**	60	50
7	*n*-BuLi (1.2 equiv), THF, −78 °C, 10 min then ^{t}BuCHO, −78 °C, 1 h	**2t**	71	67

Table 4. Quenching of the *ortho*-lithiated *N*-methylsulfoximine **1e** with prochiral electrophiles



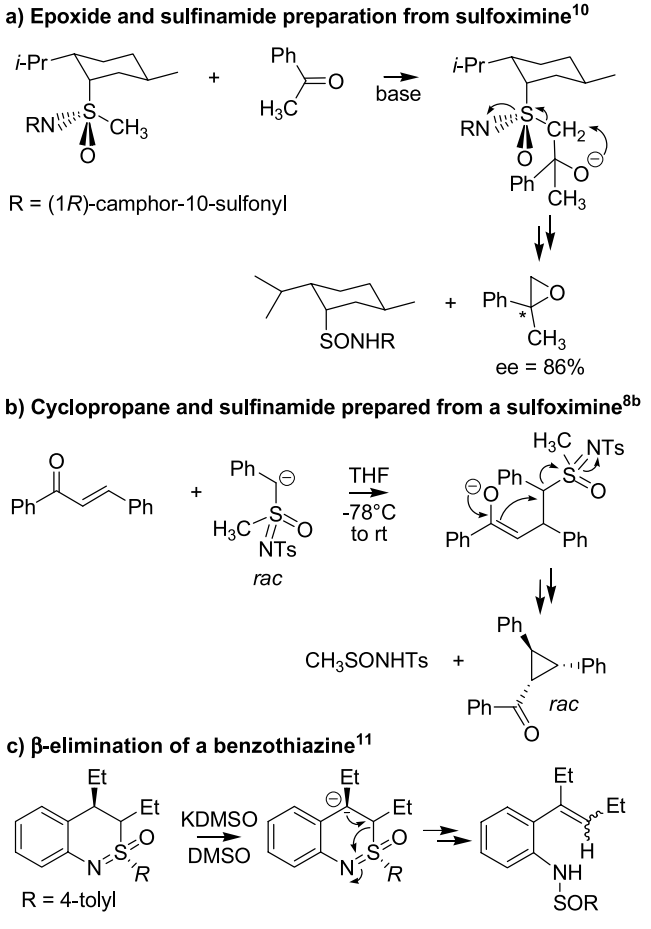
Entry	Electrophile	Product	Yield%	de%[a]	Product	Yield%	de%[b]
1	CH_3CHO	—	—	—	**4a**	100	13
2	PhCHO	**2u**	100[c]	10	**4b**	100[c]	10
3	^{t}BuCHO	**2v**	25	95	**4c**	25	95

(a) Reaction performed with *n*-BuLi (1.2 equiv), THF, −78 °C, 10 min, then electrophile, −78 °C, 2 h.
[a] Determined by ^{1}H NMR from the crude product.
[b] After purification on silica gel.
[c] Before purification.

and b). More closely related to our case, is the β-elimination of benzothiazines reported by Harmata[11] in the presence of KDMSO (Scheme 3c). The driving force of this rearrangement seems to be the apparition of an anion at the β- or γ-position related to the sulphur atom generated by the use of a base. A second driving force might also appear after complexation of the lone pair of the nitrogen atom by an electron poor species (proton or Lewis acid).[12] This fact would explain the observed instability of **1i** bearing an electron withdrawing group on the nitrogen atom.[6] Sulfoximine **1e** was first subjected to Harmata conditions[10] using KDMSO at 50 °C. The racemic sulfinamide **3c** was obtained in 70% yield (Table 5, entry 1). A weaker base such as potassium *tert*-butoxide yielded the starting sulfoximine **1e** besides traces of the desired sulfinamide **3c**. During the course of our study, Bolm et al.[13] described the conversion of C_2 symmetric bis(sulfoximines) into bis(sulfinamides) by using diborane. These results prompted us to test these new conditions with the sulfoximine **1e** (Table 5, entry 2). A clean de-*tert*-butylation reaction was achieved with 2 equiv of BH_3 affording sulfinamide **3c** in 76% yield. The formation of sulfinamide **3c** could be explained by both the Lewis acid property and the hydride donor ability of diborane.

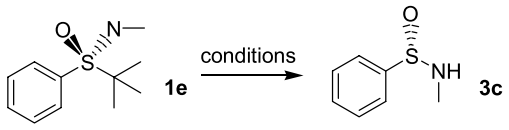
We also tried other hydride donors such as lithium tetrahydruroaluminate or sodium cyanoborohydride (Table 5, entries 3–7). The best result was obtained with 3 equiv of lithium tetrahydruroaluminate in THF affording **3c** in 60% yield (Table 5, entry 7) whereas other reducing agents gave only poor yields. Finally, the de-*tert*-butylation reaction was studied in the presence of Brönsted or Lewis acids. Strong Brönsted acids (2 M hydrochloric acid or Amberlyst® 15) gave rise to degradation products. Similarly, zinc or magnesium bromides and copper(II) chloride (Table 5, entries 8–10) afforded sulfinamide **3c** in a poor yield together with degradation products while magnesium perchlorate in THF gave sulfinamide **3c** in 76% yield (Table 5, entry 12).

Having at hand good conditions (BH_3 or $Mg(ClO_4)_2$) to convert *tert*-butyl-arylsulfoximines to racemic arylsulfinamides, we focused then our attention on the stereoselectivity of this de-*tert*-butylation reaction. The sulfinamide (*S*)-**3c** was obtained using diborane or magnesium perchlorate in 76% yield, and this, without detectable loss in optical purity (ee = 80%). Comparison of the optical rotation with literature data[14] allowed us to assign the *S*-absolute configuration showing that the de-*tert*-butylation reaction proceeded with complete retention of configuration.



Scheme 3. Conversion of sulfoximines into sulfinamides. (a) Epoxide and sulfinamide preparation from sulfoximine;[10] (b) Cyclopropane and sulfinamide prepared from a sulfoximine;[8b] (c) β-elimination of a benzothiazine.[11]

Table 5. Study of the de-*tert*-butylation reaction of **1e** to obtain sulfinamide **3c**

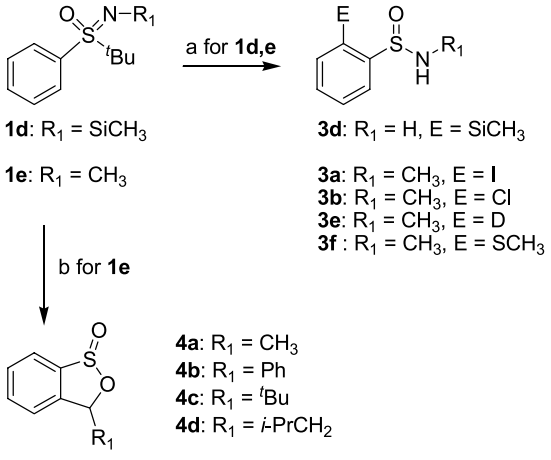


Entry	Conditions	Solvent	Yield%
1	KDMSO (2 equiv), 30 min, 50 °C	DMSO	70[a]
2	BH_3 (2 equiv), 12 h, 20 °C	THF	76[a]
3	$NaBH_4$ (1 equiv), 5 days, 20 °C	$CDCl_3$	5[b]
4	$NaBH_3CN$ (1 equiv), 5 days, 20 °C	$CDCl_3$	5[b]
5	$LiAlH_4$ (1 equiv), 5 days, 20 °C	$CDCl_3$	10[b]
6	$LiAlH_4$ (1 equiv), 24 h, 20 °C	THF	20[b]
7	$LiAlH_4$ (3 equiv), 24 h, 20 °C	THF	60[b]
8	$ZnBr_2$ (1 equiv), 5 days, 20 °C	$CDCl_3$	35[b,c]
9	$MgBr_2$ (1 equiv), 5 days, 20 °C	$CDCl_3$	43[b,c]
10	$CuCl_2$ (1 equiv), 5 days, 20 °C	$CDCl_3$	—[c]
11	$Mg(ClO_4)_2$ (1 equiv), 24 h, 20 °C	$CDCl_3$	—[c]
12	$Mg(ClO_4)_2$ (1 equiv), 24 h, 20 °C	THF	84[b] (76[a])

[a] Isolated yield.
[b] Determined by ^1H NMR.
[c] Degradation.

2.5. Optimization of the *ortho*-functionalization/de-*tert*-butylation sequence

We next examined various conditions in order to develop a procedure affording the *ortho*-substituted sulfinamides from sulfoximines **1d**,**e**. The best results were obtained by treating the residue of the *ortho*-lithiation step in THF with magnesium perchlorate (Scheme 4). According to this procedure, the sulfinamides **3a**,**b**,**d**–**f** were obtained in fair to good yields (Table 6). In the case of prochiral electrophiles, the sulfinic esters **4a** and **4c**,**d** were obtained in moderate yields and 28–95% diastereoisomeric excess (Scheme 4, Table 7). At this stage of the study, it seems difficult to provide additional information on the origin of the stereoselectivity. Curiously, no stereocontrol was observed with benzaldehyde (Table 7, entry 2).



Scheme 4. (a) *n*-BuLi (1.5 equiv), THF, −78 °C, 10 min then electrophile (Table 6), 2 h, 0 °C and quenching with NH_4Cl, extraction, evaporation then $Mg(ClO_4)_2$ (1 equiv), THF, 24 h (66 to 95%); (b) *n*-BuLi (1.5 equiv), THF, −78 °C, 10 min then aldehyde (Table 7), 2 h, −78 °C and quenching with NH_4Cl, extraction, evaporation then $Mg(ClO_4)_2$ (1 equiv), THF followed for **4b**–**d** by $MgBr_2$ (1 equiv) in $CHCl_3$ (35 to 58%).

3. Conclusion

The sulfoximine group has shown to be an excellent *ortho*-directing group in lithiation reactions. Several electrophiles were used to afford the corresponding *ortho*-functionalized arylsulfoximines in good yields. We had better to use *N*-substituted sulfoximines. The use of prochiral electrophiles afford modest to good diastereoselectivities up to 95%. During this study, we observed a side reaction due to a *S*-de-*tert*-butylation. This side *S*-de-*tert*-butylation reaction has been optimized and allowed us to open a new route to *ortho*-substituted enantiopure sulfinamides and sulfinic esters.

Table 6. *ortho*-Functionalization/de-*tert*-butylation sequence

Entry	Sulfoximine	Electrophile	Product	Yield%
1	**1d**	—[a]	**3d**	71
2	**1e**	I_2	**3a**	80
3	**1e**	C_2Cl_6	**3b**	82
4	**1e**	CH_3OD	**3e**	95[b]
5	**1e**	$(CH_3)_2S_2$	**3f**	66

[a] The electrophile is sulfoximine **1d** itself.
[b] Conversion determined by ^1H NMR

Table 7. Synthesis of sulfinic esters **4a**–**d**

Entry	Electrophile	Product	Yield%	de%
1	CH_3CHO	**4a**	58	28
2	PhCHO	**4b**	45	0
3	^{t}BuCHO	**4c**	40	>95
4	*i*-$PrCH_2CHO$	**4d**	35	48

4. Experimental

4.1. General details

Infrared spectra were recorded on a Beckmann IR 4250 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a

200 or 300 MHz Bruker apparatus and calibrated with the residual undeuterated solvent. Spectra were recorded in deuteriochloroform. Chemicals were purchased from Aldrich Co. and Janssen Co. and, unless otherwise stated, were used without further purification. Tetrahydrofuran was distilled from sodium–benzophenone ketyl. Flash chromatography was performed with silica gel 60 (70–230 mesh from Merck) and monitored by thin layer chromatography (TLC) with silica plates (Merck, Kieselgel 60 F254).

4.1.1. *S*-Methyl-*S*-phenylsulfoximine (1a). In a 500 mL round-bottomed flask were introduced NaN_3 (4.8 g, 73.7 mmol), $CHCl_3$ (20 mL) and methyl-phenylsulfoxide[15] (9.4 g, 67 mmol) previously dissolved in $CHCl_3$ (60 mL). The mixture was cooled at 0 °C and concentrated H_2SO_4 (17.5 mL) was added dropwise. The solution was stirred and heated at 45 °C for 5 h. After cooling at 0 °C, 150 mL of water were added and stirring was continued until dissolution is complete. The aqueous layer was extracted three times with CH_2Cl_2 (100 mL). The combined organic layers were dried on $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (AcOEt) to yield 8.1 g (78%) of **1a** as a yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.70 (br s, 1H), 3.10 (s, 3H), 7.60 (m, 3H), 8.06 (d, J= 8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 46.5, 128.0, 129.7, 133.5, 143.7. IR (cm^{-1}, KBr): ν=3269, 1645, 1445, 1221, 1099. Anal. Calcd for C_7H_9NOS: C, 54.17; H, 5.84; N, 9.02; S, 20.66. Found: C, 54.40; H, 5.72; N, 9.02; S, 20.31. Conditions for the separation of the two enantiomers: CHIRALCEL OJ. Eluent: heptane/isopropanol 90:10. Temperature: 18 °C. λ=230 nm, flow rate: 1 mL min^{-1}. Retention times: 24 min (*R*) and 30 min (*S*).

4.1.2. *N*-Trimethylsilyl-*S*-methyl-*S*-phenylsulfoximine (1b). In a 250 mL round-bottomed flask were introduced the sulfoximine **1a** (3.4 g, 22.0 mmol) and HMDS (23.3 mL, 110 mmol). The mixture was heated at 85 °C for 40 min under a vigorous stirring. The solvent was removed under reduced pressure. The compound **1b** was obtained as a yellow oil in a quantitative yield. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.10 (s, 9H), 3.00 (s, 3H), 7.50 (m, 3H), 8.00 (d, J=8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 2.7, 49.7, 127.4, 129.3, 132.7, 145.2. IR (cm^{-1}, KBr): ν= 3270, 2955, 1446, 1320, 1285, 1247, 1228, 1151, 1089. Anal. Calcd for $C_{10}H_{17}NOSSi$: C, 52.82; H, 7.54; N, 6.16; S, 14.10. Found: C, 52.83; H, 7.26; N, 5.98; S, 14.16.

4.1.3. *S-tert*-Butyl-*S*-phenylsulfoximine (1c). To a solution of sulfoximine **1b** (4.98 g, 21.9 mmol) in anhydrous THF (50 mL) under a nitrogen atmosphere at −0 °C, a 2.5 M solution of *n*-BuLi in hexanes (8.76 mL, 21.9 mmol) was slowly added. Then, methyl iodide (1.36 mL, 21.9 mmol) was added and the mixture was stirred for 30 min at 20 °C. The solution was cooled at 0 °C and the same procedure was repeated two more times. Hydrolysis was carried out with MeOH (20 mL) and stirred for an additional 30 min. So, a saturated aqueous solution of NH_4Cl (20 mL) and water (20 mL) were added. The mixture was extracted with CH_2Cl_2 (3×100 mL). The collected organic layers were dried ($MgSO_4$) and concentrated under reduced pressure to give a yellow oil. The residue was purified by flash chromatography on silica gel (AcOEt/cyclohexane 1:1). The sulfoximine **1c** was obtained as a yellow oil (3.72 g, 86%). ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.34 (s, 9H), 2.50 (br s, 1H), 7.54 (m, 3H), 7.94 (d, J=8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.4, 60.7, 128.9, 131.1, 133.3, 138.2. IR (cm^{-1}, KBr): ν=3256, 2975, 1476, 1448, 1366, 1210, 1107, 1075. MS (IC$^+$, isobutane, *m/z*): M+H$^+$=198. Conditions for the separation of the two enantiomers: CHIRALCEL OJ. Eluent: heptane/isopropanol 90:10. Temperature: 19 °C. λ=220 nm, flow rate: 1 mL min^{-1}. Retention times: 13 and 16 min.

4.1.4. *S-tert*-Butyl-*N*-trimethylsilyl-*S*-phenylsulfoximine (1d). As described for **1b** starting from sulfoximine **1c** (2.0 g, 10.1 mmol) and HMDS (10.7 mL, 50.5 mmol). The compound **1d** was obtained as a yellow oil in a quantitative yield. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.08 (s, 9H), 1.25 (s, 9H), 7.51 (m, 3H), 7.85 (d, J=6 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 2.6, 23.8, 60.9, 128.2, 130.4, 132.1, 140.1. IR (cm^{-1}, KBr): ν=3066, 2955, 2897, 1445, 1286, 1137, 1083, 837, 756, 694, 633. Anal. Calcd for $C_{13}H_{23}NOSSi$: C, 57.94; H, 8.60; N, 5.20; S, 11.90. Found: C, 58.19; H, 8.31; N, 5.07; S, 12.27.

4.1.5. *S-tert*-Butyl-*N*-methyl-*S*-phenylsulfoximine (1e). In a 250 mL round-bottomed flask were introduced DME (40 mL) and sodium hydride (30% dispersion in mineral oil, 2.04 g, 15.2 mmol). A solution of *S*-phenyl-*S-tert*-butylsulfoximine (**1c**) (3.0 g, 15.2 mmol) in DME (20 mL) was then added dropwise in the sodium hydride solution. The mixture was stirred for 1 h at 20 °C. Methyl iodide (4.7 mL, 76 mmol) was added and the solution stirred for 12 h at 20 °C. The mixture was quenched with a saturated aqueous solution of NH_4Cl (100 mL), and extracted with CH_2Cl_2 (3×100 mL). The collected organic layers were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The product was purified by flash chromatography on silica gel (AcOEt/cyclohexane 1:1). The sulfoximine **1e** was obtained as a white solid (2.76 g, 86%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.64 (s, 3H), 7.55 (m, 3H), 7.75 (d, J=8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.4, 30.2, 60.3, 129.2, 132.1, 133.0, 134.3. IR (cm^{-1}, KBr): ν=1446, 1232, 1130, 1101, 1068. Anal. Calcd for $C_{11}H_{17}NOS$: C, 62.52; H, 8.05; N, 6.63; S, 15.17. Found: C, 62.46; H, 7.98; N, 6.72; S, 15.10. Conditions for the separation of the two enantiomers: CHIRALCEL OJ. Eluent: heptane/isopropanol 95:5. Temperature: 19 °C. λ=220 nm, flow rate: 1 mL min^{-1}. Retention times: 6 and 9 min.

4.1.6. *S-tert*-Butyl-*N*-2-methoxyethyl-*S*-phenylsulfoximine (1f). In a 250 mL round-bottomed flask were introduced DME (30 mL) and potassium hydride (30% dispersion in mineral oil, 1.35 g, 10.1 mmol). A solution of *S*-phenyl-*S-tert*-butylsulfoximine (**1c**) (2.0 g, 10.1 mmol) in DME (15 mL) was then added dropwise in the potassium hydride solution. The mixture was stirred for 1 h at 20 °C. Tetrabutylammonium bromide (150 mg, 0.5 mmol) and 2-bromoethylmethylether (1.9 mL, 20.2 mmol) were then added and the resulting mixture was stirred for 12 h. The mixture was hydrolyzed with a saturated aqueous solution of NH_4Cl (100 mL) and extracted with CH_2Cl_2 (3×100 mL). The work-up was the same as above. The product was purified by flash chromatography on silica gel (AcOEt/

cyclohexane 1:2). Product **1f** was obtained as a colorless oil (2.37 g, 92%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (s, 9H), 3.12 (m, 2H), 3.31 (s, 3H), 3.49 (m, 2H), 7.50 (m, 3H), 7.80 (d, $J=8.0$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.4, 43.8, 59.2, 60.4, 75.0, 129.1, 132.1, 133.0, 135.1. IR (cm^{-1}, KBr): 3220, 2927, 1444, 1123, 1087, 1055. Anal. Calcd for $C_{13}H_{21}NO_2S$: C, 61.14; H, 8.29; N, 5.48; S, 12.56. Found: C, 60.86; H, 8.34; N, 5.68; S, 12.46.

4.1.7. *N*-Allyl-*S*-*tert*-butyl-*S*-phenylsulfoximine (1g). As above reaction of *S*-phenyl-*S*-*tert*-butylsulfoximine (**1c**) (2 g, 10.1 mmol) in DME (20 mL), potassium hydride (30% dispersion in mineral oil, 1.35 g, 10.1 mmol) in DME (30 mL), tetrabutylammonium bromide (150 mg, 0.5 mmol) and allyl bromide (1.7 mL, 20.2 mmol) afforded after flash chromatography on silica gel (AcOEt/cyclohexane 1:2) product **1g** as a colorless oil (2.27 g, 95%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (s, 9H), 3.45 (ddt, $J=16$, 5, 2 Hz, 1H), 3.64 (ddt, $J=16$, 5, 2 Hz, 1H), 5.05 (dq, $J=10$, 2 Hz, 1H), 5.25 (dq, $J=17$, 2 Hz, 1H), 5.96 (dq, $J=17$, 5 Hz, 1H), 7.55 (m, 3H), 7.76 (d, $J=8$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.4, 46.3, 60.6, 114.0, 129.1, 132.0, 133.0, 135.0, 138.9. IR (cm^{-1}, KBr): 2976, 1444, 1266, 1214, 1133, 1083. Anal. Calcd for $C_{13}H_{19}NOS$: C, 65.78; H, 8.01; N, 5.90; S, 13.51. Found: C, 65.93; H, 8.40; N, 6.07; S, 13.57.

4.1.8. *S*-*tert*-Butyl-*N*-*tert*-butyloxycarbonyl-*S*-phenylsulfoximine (1h). As above, reaction of *S*-phenyl-*S*-*tert*-butylsulfoximine (**1c**) (1.0 g, 5 mmol) in DME (10 mL), potassium hydride (30% dispersion in mineral oil, 0.70 g, 5.2 mmol) in DME (20 mL), tetrabutylammonium bromide (75 mg, 0.25 mmol) and di-*tert*-butyl dicarbonate (2.18 g, 10 mmol) afforded, after purification by chromatography on silica gel (AcOEt/petroleum ether 1:2), the product **1h** as a sticky colorless oil (0.95 g, 63%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.23 (s, 9H), 1.37 (s, 9H), 7.56 (m, 3H), 7.83 (d, $J=8$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.7, 28.3, 61.6, 80.4, 129.3, 130.6, 133.7, 134.7, 158.4. IR (cm^{-1}, KBr): 2977, 1693, 1668, 1274, 1154. Anal. Calcd for $C_{15}H_{23}NO_3S$: C, 60.58; H, 7.74; N, 4.71; S, 10.78. Found: C, 60.56; H, 7.34; N, 4.68; S, 10.46.

4.2. General procedure A for the metalation reaction of compounds 1d–g

To a cooled (−78 °C) solution of the corresponding *N*-protected-*S*-phenyl-*S*-*tert*-butylsulfoximine **1d–g** (0.71 mmol) in anhydrous THF (10 mL) under a nitrogen atmosphere was added a 2.5 M solution in hexanes of *n*-BuLi (0.34 mL, 0.85 mmol) while maintaining the temperature at −78 °C. The mixture was stirred for 10 min at this temperature before addition of the appropriate electrophile. The resulting solution was then stirred for 1 h at −78 °C with **1d** and 2 h with **1e–g**. The reaction was quenched with a saturated aqueous solution of NH_4Cl (10 mL) and extracted with dichloromethane (3×10 mL). The organic layers were dried on $MgSO_4$ and the solvent was removed under reduced pressure. The residues obtained from **1e–g** were purified by flash chromatography on silica gel (AcOEt/cyclohexane) whereas the oil obtained from **1d** was dissolved in methanol and stirred for 1 h at 20 °C. Methanol was removed under reduced pressure and the product was purified by flash chromatography on silica gel (AcOEt).

4.2.1. *S*-*tert*-Butyl-*S*-(2-tolyl)sulfoximine (2a). According to the general procedure A from **1d**, the electrophile was MeI (0.22 mL, 3.55 mmol). The yield was 0.135 g (90%) of an oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.33 (s, 9H), 2.74 (s, 3H), 7.30–7.48 (m, 3H), 8.00 (d, $J=11$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.3, 24.4, 62.1, 126.4, 133.3, 133.6, 134.0, 136.8, 141.0. IR (cm^{-1}, KBr): $\nu=3200$, 2974, 2931, 1478, 1459, 1221, 1189, 1065, 976, 775. Anal. Calcd for $C_{11}H_{17}NOS$: C, 62.52; H, 8.11; N, 6.63; S, 13.51. Found: C, 62.15; H, 8.10; N, 6.67; S, 13.37.

4.2.2. *S*-*tert*-Butyl-*S*-(2-methylthiophenyl)sulfoximine (2c). According to the general procedure A from **1d**, the electrophile was Me_2S_2 (0.32 mL, 3.55 mmol). The yield was 0.164 g (95%) of an oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.42 (s, 9H), 2.43 (s, 3H), 7.25 (m, 2H), 7.50 (t, $J=11$ Hz, 1H), 8.00 (d, $J=11$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.9, 24.2, 62.8, 123.6, 125.1, 133.0, 134.4, 134.5, 143.2. IR (cm^{-1}, KBr): $\nu=3273$, 2968, 2919, 1447, 1432, 1217, 1072, 971, 774. HRMS (IE, *m*/*z*): calcd for $C_{11}H_{17}NOS_2$: 243.0752. Found: 243.0748.

4.2.3. *S*-*tert*-Butyl-*S*-(2-iodophenyl)sulfoximine (2d). According to the general procedure A from **1d**, the electrophile was I_2 (0.432 g, 1.7 mmol). The yield was 0.172 g (75%) of a white solid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.44 (s, 9H), 7.16 (t, $J=11$ Hz, 1H), 7.51 (t, $J=11$ Hz, 1H), 8.17 (d, $J=11$ Hz, 1H), 8.25 (d, $J=11$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.0, 54.9, 93.9, 125.7, 129.0, 132.5, 140.1, 147.1. HRMS (IE, *m*/*z*): calcd for $C_{10}H_{14}INOS$: 322.9841. Found: 322.9842.

4.2.4. *S*-*tert*-Butyl-*S*-(2-chlorophenyl)sulfoximine (2e). According to the general procedure A from **1d**, the electrophile was C_2Cl_6 (0.113 mL, 0.99 mmol). Yield 0.125 g (76%) of a white solid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.39 (s, 9H), 7.40 (m, 3H), 8.13 (d, $J=11$ Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 24.1, 62.5, 126.7, 132.7, 133.9, 134.7, 135.2, 136.0. HRMS (IE, *m*/*z*): calcd for $C_{10}H_{14}ClNOS$: 231.0485. Found: 231.0480.

4.2.5. *S*-*tert*-Butyl-*N*-trimethylsilyl-*S*-(2-^{2}*H*-phenyl)sulfoximine (2f) According to the general procedure A from **1d**, the electrophile was MeOD (0.144 mL, 3.55 mmol). No methanolysis at the end of the reaction. The yield was 95% determined by ^{1}H NMR. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.11 (s, 9H), 1.28 (s, 9H), 7.52 (m, 3H), 7.90 (d, $J=8$ Hz, 1H).

4.2.6. *S*-*tert*-Butyl-*S*-(2-trimethylsilylphenyl)-sulfoximine (2g). In a round-bottomed flask flushed with nitrogen, a solution of *N*-trimethylsilyl-*S*-phenyl-*S*-*tert*-butylsulfoximine (**1d**) (0.2 g, 0.74 mmol) in THF (5 mL) was cooled at −78 °C. A 2.5 M solution in hexanes of *n*-BuLi (0.35 mL, 0.87 mmol) was then added. The mixture was allowed to warm to 0 °C and stirred for 1 h. Hydrolysis was carried out with a saturated aqueous solution of NH_4Cl (5 mL) and the aqueous layer was extracted with dichloromethane (3× 5 mL). The yield was 0.19 g (95%) of **2g** as a yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.41 (s, 9H), 1.35 (s, 9H), 7.54 (m, 2H), 7.85 (d, $J=9$ Hz, 1H), 8.01 (d, $J=9$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 2.5, 24.7, 61.5, 129.0, 131.8, 131.9, 136.9, 143.0, 143.7. IR (cm^{-1}, KBr): $\nu=3333$, 3256, 2955, 1245, 1214, 1109, 966, 846, 760. Anal. Calcd for

$C_{13}H_{23}NOSSi$: C, 57.94; H, 8.60; N, 5.20; S, 11.90. Found: C, 58.03; H, 8.40; N, 5.07; S, 12.37.

4.2.7. *S*-*tert*-Butyl-*N*-methyl-*S*-(2-tolyl)sulfoximine (2h). According to the general procedure A from **1e**, the electrophile was MeI (88 μL, 1.42 mmol). The yield was 0.152 g (95%) of a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 9H), 2.65 (s, 3H), 2.69 (s, 3H) 7.29 (m, 2H), 7.42 (t, J=8 Hz, 1H), 7.76 (d, J=8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.3, 30.0, 60.3, 61.7, 126.3, 128.7, 132.6, 134.0, 134.6, 142.0. Anal. Calcd for $C_{12}H_{19}NOS$: C, 63.96; H, 8.50; N, 6.22; S, 14.23. Found: C, 63.93; H, 8.39; N, 6.07; S, 14.57.

4.2.8. *S*-*tert*-Butyl-*N*-methyl-*S*-(2-methylthiophenyl)sulfoximine (2i). According to the general procedure A from **1e**, the electrophile was Me_2S_2 (0.32 mL, 3.55 mmol). The yield was 0.142 g (78%) of a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 9H), 2.40 (s,3H), 2.68 (s, 3H), 7.18 (t, J=7 Hz, 1H), 7.26 (d, J=8 Hz, 1H), 7.47 (t, J=7 Hz, 1H), 7.75 (d, J=8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.8, 24.3, 29.9, 62.7, 123.5, 125.3, 130.9, 132.8, 135.2, 144.4. HRMS (IE, *m*/*z*): calcd for $C_{12}H_{19}NOS_2$: 257.0908. Found: 257.0904.

4.2.9. *S*-*tert*-Butyl-*N*-(2-methoxyethyl)-*S*-(2-tolyl)sulfoximine (2m). According to the general procedure A from **1f**, the electrophile was MeI (88 μL, 1.42 mmol). The yield was 0.105 g (55%) of an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 9H), 2.69 (s, 3H), 3.00–3.20 (m, 2H), 3.32 (s, 3H), 3.49 (m, 2H), 7.28 (m, 1H), 7.41 (t, J=7 Hz, 1H), 7.54 (m, 1H), 7.78 (d, J=7 Hz, 1H). IR (cm^{-1}, KBr): ν=2974, 2928, 1455, 1245, 1191, 1124, 763. ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5, 24.0, 43.4, 58.8, 61.5, 74.6, 125.9, 132.6, 133.2, 133.5, 134.2, 141.7. Anal. Calcd for $C_{14}H_{23}NO_2S$: C, 62.42; H, 8.61; N, 5.20; S, 11.90. Found: C, 62.59; H, 8.41; N, 5.07; S, 12.27.

4.2.10. *S*-*tert*-Butyl-*N*-(2-methoxyethyl)-*S*-(2-methylthiophenyl)sulfoximine (2n). According to the general procedure A from **1f**, the electrophile was Me_2S_2 (0.32 mL, 3.55 mmol). The yield was 0.14 g (65%) of an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 9H), 2.39 (s, 3H), 3.04–3.16 (m, 2H), 3.32 (s, 3H), 3.50 (m, 2H), 7.22 (m, 1H), 7.41 (m, 2H), 7.81 (d, J=7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.7, 24.1, 43.4, 58.8, 62.7, 74.4, 123.4, 125.2, 131.4, 132.7, 134.9, 144.3. IR (cm^{-1}, KBr): ν=2923, 2872, 1436, 1246, 1120, 768. HRMS (IE, *m*/*z*): calcd for $C_{14}H_{23}NO_2S_2$: 301.1170. Found: 301.1166.

4.2.11. *N*-Allyl-*S*-(2-tolyl)-*S*-*tert*-butylsulfoximine (2o). According to the general procedure A from **1g**, the electrophile was MeI (88 μL, 1.42 mmol). The yield was 0.171 g (96%) of a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 9H), 2.69 (s, 3H), 3.45 (m, 1H), 3.65 (m, 1H), 5.04 (d, J=10 Hz, 1H), 5.34 (d, J=17 Hz, 1H), 5.97 (m, 1H), 7.29 (m, 2H), 7.42 (t, J=7 Hz, 1H), 7.78 (d, J=7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.6, 24.1, 46.0, 61.8, 113.7, 126.0, 132.7, 133.1, 133.6, 134.1, 138.7, 141.9. IR (cm^{-1}, KBr): ν=3057, 2976, 2930, 1455, 1270, 1216, 1118, 762. Anal. Calcd for $C_{14}H_{21}NOS$: C, 66.89; H, 8.42; N, 5.57; S, 12.76. Found: C, 66.59; H, 8.53; N, 5.57; S, 13.17.

4.2.12. *N*-Allyl-*S*-*tert*-butyl-*S*-(2-methylthiophenyl)sulfoximine (2p). According to the general procedure A from **1g**, the electrophile was Me_2S_2 (0.32 mL, 3.55 mmol). The yield was 0.151 g (90%) of a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (s, 9H), 2.39 (s, 3H), 3.46 (m, 1H), 3.67 (m, 1H), 5.02 (d, J=11 Hz, 1H), 5.33 (d, J=17 Hz, 1H), 5.95 (m, 1H), 7.14 (t, J=7.9 Hz, 1H), 7.26 (d, J=7.9 Hz, 1H), 7.44 (t, J=7.8 Hz, 1H), 7.74 (d, J=7.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.1, 24.6, 46.3, 63.3, 114.1, 123.7, 125.6, 129.1, 131.8, 133.1, 135.1, 144.9. Anal. Calcd for $C_{14}H_{21}NOS_2$: C, 59.32; H, 7.47; N, 4.94; S, 22.62. Found: C, 59.52; H, 7.63; N, 5.07; S, 22.97.

4.2.13. *S*-*tert*-Butyl-*S*-[2-(1-hydroxyethyl)phenyl]-sulfoximine (2r). According to the general procedure A from **1d**, the electrophile was CH_3CHO (large excess). The yield was 0.13 g (76%) of an oil consisting in an unseparable mixture of two diastereoisomers, de=50%. Minor diastereoisomer: ^{1}H NMR (200 MHz, $CDCl_3$): 1.35 (s, 9H), 1.52 (d, J=7 Hz, 3H), 5.80 (q, J=7 Hz, 1H), 7.35 (t, J=8 Hz, 1H), 7.56 (t, J=8 Hz, 1H), 7.69 (d, J=8 Hz, 1H), 7.97 (d, J=7.7 Hz, 1H). Major diastereoisomer: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.31 (s, 9H), 1.52 (d, J=7 Hz, 3H), 5.69 (q, J=7 Hz, 1H), 7.38 (t, J=8 Hz, 1H), 7.57 (t, J=8 Hz, 1H), 7.72 (d, J=8 Hz, 1H), 7.98 (d, J=7.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.4, 136.0, 133.8 (3), 133.7, 133.3, 127.8, 127.6, 127.5, 127.4, 65.3, 65.1, 62.9, 61.7, 24.2, 22.8. IR (cm^{-1}, KBr): ν=3459, 3310, 2974, 2931, 1466, 1206, 1184, 979, 782, 770. HRMS (IE, *m*/*z*): calcd for $C_{12}H_{19}NO_2S$: 241.1136. Found: 241.1134.

4.2.14. *S*-*tert*-Butyl-*S*-[2-(1-hydroxybenzyl)phenyl]-sulfoximine (2s). According to the general procedure A from **1d**, the solvent was toluene and TMEDA (129 μL, 0.85 mmol) was added. *sec*-BuLi was used instead of *n*-BuLi. The electrophile was benzaldehyde (0.172 mL, 1.7 mmol). The yield was 0.13 g (60%) of an oil consisting in a mixture of two diastereoisomers (de=50%). ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.49 (s, 9H), 6.75 (s, 1H), 7.12 (d, J=13 Hz, 1H), 7.43 (m, 7H), 8.10 (d, J=13 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7, 141.8, 133.9, 133.8, 133.3, 130.8, 128.3, 127.7, 127.3, 126.8, 71.2, 63.9, 24.4. IR (cm^{-1}, KBr): ν=3273, 2972, 1451, 1205, 1176, 986, 755, 707. HRMS (IE, *m*/*z*): calcd for $C_{17}H_{21}NO_2S$: 303.1293. Found: 303.1298 and ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.52 (s, 9H), 4.03 (m, 1H), 6.84 (s, 1H), 7.17 (d, J=13 Hz, 1H), 7.36 (m, 7H), 8.07 (d, J=13 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7, 141.9, 134.0, 133.7, 133.1, 130.9, 128.4, 128.0, 127.5, 126.9, 71.3, 61.9, 24.3. IR (cm^{-1}, KBr): ν=3271, 2972, 1447, 1206, 980, 759, 707. HRMS (IE, *m*/*z*): calcd for $C_{17}H_{21}NO_2S$: 303.1293. Found: 303.1289.

4.2.15. *S*-*tert*-Butyl-*S*-[2-(1-hydroxy-2,2-dimethyl-propyl)phenyl]sulfoximine (2t). According to the general procedure A from **1d**, the electrophile was pivaldehyde (0.19 mL, 1.7 mmol). The yield was 0.143 g (71%) of an oil consisting in a mixture of two diastereoisomers (de=67%). ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.99 (s, 9H), 1.32 (s, 9H), 6.02 (s, 1H), 7.42 (t, J=11 Hz, 1H), 7.53 (t, J=11 Hz, 1H), 7.78 (d, J=11 Hz, 1H), 8.10 (d, J=11 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.1, 26.4, 27.0, 36.7, 62.1, 127.1, 129.9, 132.5, 133.5, 135.7, 144.7. IR (cm^{-1}, KBr): ν=3413, 3140, 2955, 1480, 1202, 1180, 1100, 976, 736. HRMS (IE, *m*/*z*):

calcd for $C_{15}H_{25}NO_2S$: 283.1606. Found: 283.1606. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.97 (s, 9H), 1.33 (s, 9H), 5.86 (s, 1H), 7.43 (t, J=11 Hz, 1H), 7.61 (t, J=11 Hz, 1H), 7.79 (d, J=11 Hz, 1H), 8.11 (d, J=11 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.1, 26.5, 27.0, 36.6, 61.6, 127.0, 129.6, 132.5, 133.3, 135.9, 145.3. IR (cm^{-1}, KBr): ν=3333, 2955, 2871, 1480, 1364, 1211, 1183, 1097, 978, 760. HRMS (IE, *m/z*): calcd for $C_{15}H_{25}NO_2S$: 283.1606. Found: 283.1605.

4.3. De-*tert*-butylation reaction

4.3.1. *N*-Methylbenzenesulfinamide ((*S*)-3c). To a solution of sodium borohydride (0.225 g, 5.94 mmol) in anhydrous THF (5 mL) was added at 0 °C a solution of iodine[16] (0.603 g, 2.36 mmol) in anhydrous THF (10 mL). The sulfoximine (*S*)-**1e** (0.25 g, 1.18 mmol) was dissolved in anhydrous THF (5 mL) and the previously prepared BH_3 solution was added. The mixture was stirred for 1 h at 0 and 20 °C overnight. The excess of BH_3 was cautiously destroyed with MeOH (10 mL). After 30 min, a 20% aqueous solution of potassium hydroxide (10 mL) was added and the mixture was stirred for 4 h. The product was extracted with CH_2Cl_2 (3×10 mL) and the organic layers were dried on $MgSO_4$. After removing of the solvents under reduced pressure, the residue was purified on silica gel (AcOEt/cyclohexane 1:1). The yield was 0.14 g (76%). RMN ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.53 (d, J=6 Hz, 3H), 4.07 (q, J=6 Hz, 1H), 7.47 (m, 3H), 7.67 (d, J=9 Hz, 2H). IR (cm^{-1}, KBr): 3224, 1444, 1086, 1051. MS (IC$^+$, isobutane, *m/z*): M+H$^+$=156. HRMS (IE, *m/z*): calcd for C_7H_9NOS: 155.0405. Found: 155.0405. Separation of the enantiomers was achieved on a CHIRALPAK AD. Eluent: heptane/isopropanol: 95:5. Temperature: 18 °C. λ=230 nm, flow rate: 1 mL min^{-1}. Retention times: 10.6 and 12 min. Enantiomeric excess=80%.

4.3.2. *N*-*tert*-Butylcarbonylbenzenesulfinamide (3g). To a solution of *S*-phenyl-*S*-*tert*-butylsulfoximine (**1c**) (2.0 g, 10.1 mmol) in CH_2Cl_2 (20 mL) was added a solution of Na_2CO_3 (0.53 g, 5.0 mmol) in water (15 mL). The mixture was cooled at 10 °C and pivaloyl chloride (1.25 mL, 10.1 mmol) was added. The mixture was stirred for 2 h at 20 °C. The organic layer was dried on $MgSO_4$, filtered and the solvent was removed under reduced pressure. Flash chromatography on silica gel (AcOEt/ cyclohexane 1:2) afforded **3g** as a white solid (1.0 g, 45%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (s, 9H), 7.52 (m, 3H), 7.65 (m, 2H), 7.90 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.4, 40.1, 125.1, 129.8, 132.2, 144.4, 179.2. IR (cm^{-1}, KBr): 3205, 1686. MS (IC$^+$, isobutane, *m/z*): M+H$^+$=226. Anal. Calcd for $C_{11}H_{15}NO_2S$: C, 58.64; H, 6.71; N, 6.22; S, 14.23. Found: C, 58.59; H, 6.51; N, 6.15; S, 14.28.

4.4. General procedure B for the sequence metalation/de-*tert*-butylation of sulfoximines 1d,e

To a solution of the corresponding sulfoximine **1d**,**e** (0.95 mmol) in anhydrous THF (10 mL) under a nitrogen atmosphere at −78 °C, a 2.5 M solution of *n*-BuLi in hexanes (0.57 mL, 1.42 mmol) was slowly added. The mixture was stirred for 10 min and the electrophile was added. The solution was stirred for a further 2 h at 0 °C or at −78 °C for aldehydes. Hydrolysis was carried out with a saturated aqueous solution of NH_4Cl (10 mL) and the mixture was extracted with CH_2Cl_2 (3×10 mL). The collected organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was dissolved in anhydrous THF (10 mL) under a nitrogen atmosphere. Magnesium perchlorate (0.212 g, 0.95 mmol) was then added and the solution was stirred for 24 h. Hydrolysis was again achieved with a saturated aqueous solution of NH_4Cl (10 mL) and the mixture was extracted with CH_2Cl_2 (3×10 mL). The organic layers were dried ($MgSO_4$), concentrated and the residue was purified by flash chromatography on silica gel.

4.4.1. *S*-(2-Iodophenyl)-*N*-methylbenzenesulfinamide (3a). The starting sulfoximine was **1e**. According to the general procedure B, the electrophile was I_2 (0.96 g, 3.78 mmol). Hydrolysis was carried out with an aqueous saturated solution of $Na_2S_2O_3$. The eluent for purification was AcOEt/cyclohexane 1:1. The yield was 0.213 g (80%) of an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.50 (d, J=5.3 Hz, 3H), 4.14 (br s, 1H), 7.14 (m, 1H), 7.84 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.5, 94.4, 127.6, 128.7, 132.7, 140.5, 145.0. IR (cm^{-1}, KBr): 3228, 1443, 1088, 1059. HRMS (IE, *m/z*): calcd for C_7H_8INOS: 281.9450. Found: 281.9453.

4.4.2. *S*-(2-Chlorophenyl)-*N*-methylbenzenesulfinamide (3b). The starting sulfoximine was **1e**. According to the general procedure B, the electrophile was C_2Cl_6 (0.43 mL, 3.8 mmol). Eluent: AcOEt/cyclohexane 1:1. The yield was 0.147 g (82%) of an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.50 (d, J=5.6 Hz, 3H), 4.17 (br s, 1H), 7.38 (m, 3H), 7.92 (d, J=6.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.3, 127.4, 127.5, 130.7, 132.3, 132.7, 140.9. IR (cm^{-1}, KBr): 3229, 2925, 1450, 1066, 1029. HRMS (IE, *m/z*): calcd for C_7H_8ClNOS: 189.0015. Found: 189.0020.

4.4.3. *S*-(2-Trimethylsilylphenyl)benzenesulfinamide (3d). According to the general procedure B, the starting sulfoximine was **1d**. Migration of the trimethylsilyl group occurred while stirring the solution at 0 °C. Eluent for purification: AcOEt. The yield was 0.143 g (71%) of a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.36 (s, 9H), 4.16 (br s, 2H), 7.50 (m, 3H), 8.11 (d, J=7.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.0, 121.0, 128.9, 129.2, 134.1, 137.3, 152.4. IR (cm^{-1}, KBr): 2954, 1474, 1250, 1108, 1051.

4.4.4. *N*-Methyl-*S*-(2-methylthiophenyl)benzenesulfinamide (3f). The starting sulfoximine was **1e**. According to the general procedure B, the electrophile was Me_2S_2 (0.34 mL, 3.78 mmol). Eluent for purification: AcOEt/cyclohexane 1:1. The yield was 0.125 g (66%) of an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.42 (s, 3H), 2.48 (d, J=5.3 Hz, 3H), 4.15 (d, J=4.9 Hz, 1H), 7.25 (m, 3H), 7.83 (d, J=7.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.9, 26.4, 125.5, 127.3, 129.2, 131.7, 137.8, 141.3. IR (cm^{-1}, KBr): 3226, 1434, 1097, 1066, 1032. HRMS (IE, *m/z*): calcd for $C_8H_{11}NOS_2$: 201.0282. Found: 201.0280.

4.4.5. 3-Methyl-3*H*-2,1-benzoxathiol-1-oxide (4a). The starting sulfoximine was **1e**. According to the general procedure B, the electrophile was acetaldehyde (0.265 mL, 4.74 mmol). Eluent for purification: AcOEt/CH_2Cl_2 1:1. The yield was 0.092 g (58%) of an oil consisting in a

mixture of two diastereoisomers (de=13%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.65 (d, J=6.4 Hz, 1.8H), 1.81 (d, J=6.4 Hz, 1.2H), 5.80 (q, J=6.6 Hz, 0.4H), 6.23 (q, J=6.6 Hz, 0.6H), 7.36 (t, J=7.5 Hz, 1H), 7.55 (m, 2H), 7.72 (d, J=7.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.7, 24.0, 87.1, 90.1, 122.5, 122.6, 123.7, 124.0, 129.7, 129.8, 132.6, 132.7, 142.6, 143.0, 146.6, 147.4. IR (cm^{-1}, KBr): 2972, 2926, 1734, 1083, 1044. HRMS (IE, *m/z*): calcd for $C_8H_8O_2S$: 168.0245. Found: 168.0241.

4.4.6. 3-Phenyl-3*H*-2,1-benzoxathiol-1-oxide (4b). The starting sulfoximine was **1e**. According to the general procedure B, the electrophile was benzaldehyde (0.192 mL, 1.89 mmol). The Lewis acid was $Mg(ClO_4)_2$ followed by $MgBr_2$ (0.175 g, 0.95 mmol) in $CHCl_3$. Eluent for purification: cyclohexane/CH_2Cl_2 1:1. The yield was 0.098 g (45%) of an oil containing a mixture of two diastereoisomers. 1st diastereoisomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01 (s, 1H), 7.09 (m, 1H), 7.21 (m, 2H), 7.32 (m, 3H), 7.46 (m, 2H), 7.73 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 95.7, 123.9, 124.0, 128.4, 129.3, 129.5, 130.0, 133.0, 138.4, 141.6, 146.6. 2nd diastereoisomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.54 (s, 1H), 7.24 (m, 1H), 7.26 (m, 2H), 7.30 (m, 3H), 7.45 (m, 2H), 7.71 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 92.7, 95.8, 123.7, 123.9, 128.5, 129.4, 132.9, 136.9, 141.6, 147.9. IR (cm^{-1}, KBr): 1456, 1116. HRMS (IE, *m/z*): calcd for $C_{13}H_{10}O_2S$: 230.0402. Found: 230.0400.

4.4.7. 3-*tert*-Butyl-3*H*-2,1-benzoxathiol-1-oxide (4c). The starting sulfoximine was **1e**. According to the general procedure B, the electrophile was pivaldehyde (0.233 mL, 1.89 mmol). The Lewis acid was $Mg(ClO_4)_2$ followed by $MgBr_2$ (0.175 g, 0.95 mmol) in $CHCl_3$. The eluent for purification on silica gel was cyclohexane/CH_2Cl_2 1:1. An other flash chromatography was performed on basic alumina with cyclohexane/CH_2Cl_2 gradient from 3:1 to 1:3. The yield was 0.079 g (40%, de>95%) of a yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.08 (s, 9H), 5.41 (s, 1H), 7.51 (d, J=7.5 Hz, 3H), 7.72 (d, J=6.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.6, 36.1, 102.2, 124.4, 129.7, 132.0, 139.8, 146.9. IR (cm^{-1}, KBr): 2958, 1468, 1109. HRMS (IC^+, isobutane, *m/z*): calcd for $C_{11}H_{14}O_2S$: 211.0793. Found: 211.0789.

4.4.8. 3-Isobutyl-3*H*-2,1-benzoxathiol-1-oxide (4d). The starting sulfoximine was **1e**. According to the general procedure B, the electrophile was 3-methylbutyraldehyde (0.204 mL, 1.89 mmol). The Lewis acid was $Mg(ClO_4)_2$ followed by $MgBr_2$ (0.175 g, 0.95 mmol) in $CHCl_3$. The eluent for purification was cyclohexane/CH_2Cl_2 1:1. The yield was 0.069 g (35%) of an oil consisting in a mixture of two diastereoisomers (de=48%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89 (m, 6H), 1.50–2.10 (m, 3H), 5.66 (d, J=10.2 Hz, 0.4H), 6.12 (d, J=9.8 Hz, 0.6H), 7.29 (m, 1H), 7.40 (m, 2H), 7.64 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.1, 22.2, 23.9, 24.1, 25.7, 25.8, 38.3, 49.1, 89.4, 92.4, 122.6, 122.8, 124.0, 123.8, 130.5, 132.5, 142.1, 142.6, 146.9, 147.4. IR (cm^{-1}, KBr): 2958, 1467, 1126. HRMS (IE, *m/z*): calcd for $C_{11}H_{14}O_2S$: 210.0715. Found: 210.0721.

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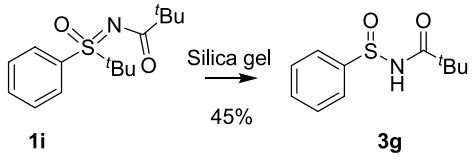

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