CHAPTER-3

COPPER- PROMOTED *N*-ALKYLATION OF SULFOXIMINES WITH ALKYLBORONIC ACID UNDER MILD CONDITION

CHAPTER-3

COPPER-PROMOTED *N*-ALKYLATION OF SULFOXIMINES WITH ALKYLBORONIC ACID UNDER MILD CONDITION

3.1 INTRODUCTION

In synthetic organic chemistry, sulfoximines have been explored as building blocks, chiral auxiliaries, organocatalysts, fluorophores, trifluoromethylating agents as well as directing groups for *C-H* activation reactions (Figure **3.1**) [1]. On the other hand, sulfoximine derivatives have also been identified as drugs and insecticides (Figure **3.1**) [2-3]. In particular, *N*-methylated sulfoximine motifs were found in many bioactive compounds [4].

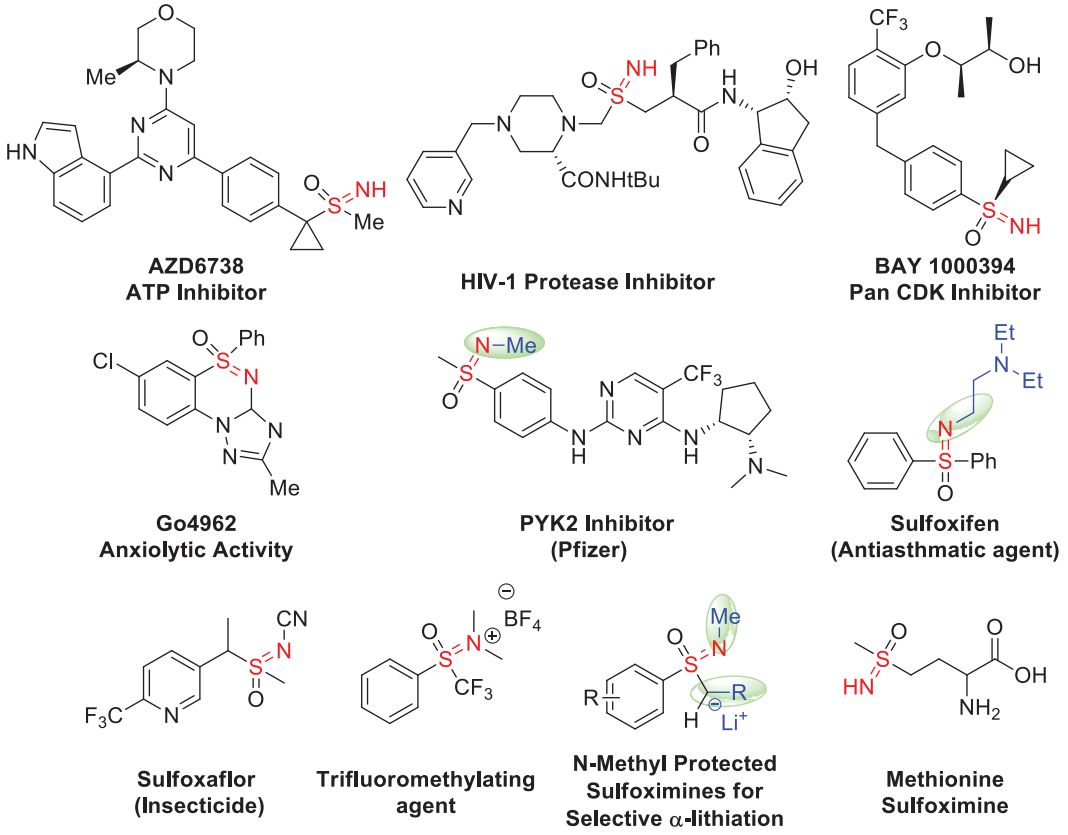
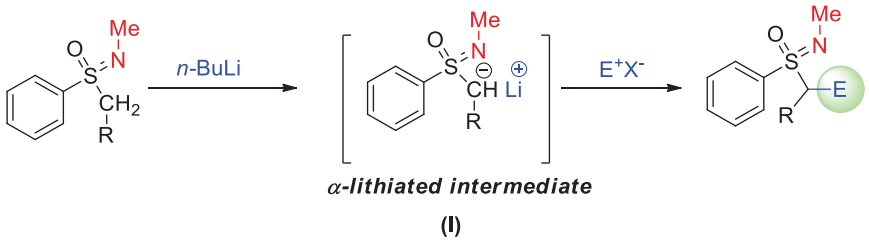


Figure 3.1 Biologically and chemically relevant sulfoximines.

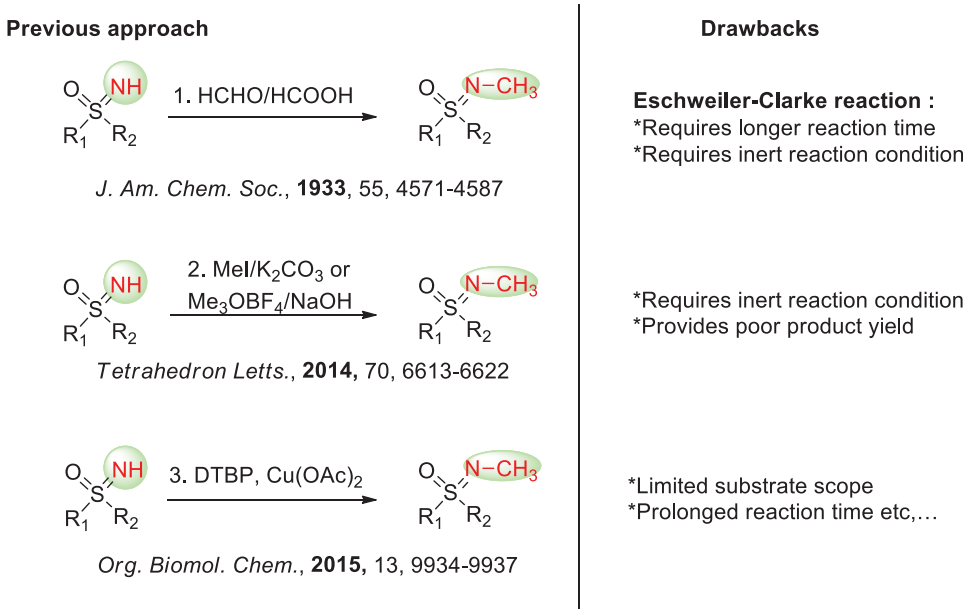
From a synthetic perspective, *N*-methylated sulfoximines are considered as stable *N*-protected sulfoximines in which a selective functionalization at the α-carbon *via* lithiation can be performed [5]. Such lithiated sulfoximines (I) are extensively used as precursors for the asymmetric synthesis of various bioactive compounds (**Scheme 3.1**) [5a].



Scheme 3.1. A selective α-carbon functionalization of *N*-methylsulfoximine *via* lithiation.

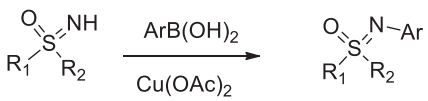
N-Methylation of sulfoximines was typically achieved using the *Eschweiler-Clarke* reaction (*i.e.* formaldehyde/formic acid under reflux condition) which required longer reaction time [4c, 5b]. In lieu of this, methyl iodide/K_2CO_3[4a] or Me_3OBF_4/NaOH [6] was also occasionally used for the *N*-methylation of sulfoximines.

However, these methods provided low yields owing to poor nucleophilicity of the nitrogen atom present in sulfoximines [7]. Recently, *N*-methylation of sulfoximines using di-*tert.*-butyl peroxide was demonstrated in the presence of copper (II) acetate (**Scheme 3.2**) [8]. Nevertheless, requirement of inert reaction condition, prolonged reaction time and moderate yield limit the extensive use of this protocol for *N*-methylation reaction. Therefore, development of an amenable route for the synthesis of *N*-methylsulfoximines is an important task.



Scheme 3.2. Representative methods for *N*-methylation of sulfoximines and their drawbacks.

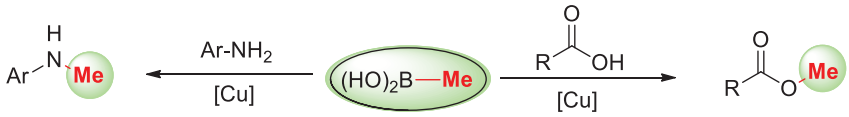
In the series of organoboron compounds, boronic acids have received significant attention in synthetic organic chemistry [9]. These compounds are known to be non-toxic and stable, enabling ease of handling and storage. Copper-mediated *C-N* bond formation reactions with arylboronic acids have emerged as a powerful tool for the synthesis of various bioactive compounds and natural products [9]. In this context, *N*-arylation of sulfoximines with arylboronic acid was demonstrated by Bolm research group (**Scheme 3.3**) [3a].



Bolm *et al*., *Org. Lett*., **2005**, *7*, 2667-2669

Scheme 3.3. Copper-mediated *N*-arylation of sulfoximine using arylboronic acid.

In contrast, the application of alkylboronic acids as *N*-alkylating agents was less explored [9a]. Recently, few reports have demonstrated a copper-mediated *Chan-Lam* type *N*- and *O*-alkylation of organic compounds with different alkylboronic acids [10]. Notably, the reaction conditions used for *N*-alkylation with alkylboronic acids are quite different from the *N*-arylation reactions carried out with arylboronic acids [11]. Methylboronic acid has been used as a reagent for mono-methylation of anilines and esterification of carboxylic acids with different copper salts (**Scheme 3.4**) [10a, 10b].



Org. Lett., **2009**, *11*, 1677-1680 *J. Org. Chem.*, **2015**, *80*, 7305-7310

Scheme 3.4. Methylboronic acid used as methylating reagent.

To the best of our knowledge, *N*-methylation or alkylation of sulfoximines with respective alkylboronic acid is not explored. Nevertheless, development of such protocol would provide not only an alternative route, but also conceptually different approach for the efficient preparation of *N*-alkylsulfoximines under mild condition (**Scheme 3.5**). For instance, previous methods proceed through simple substitution reaction between a nucleophile (sulfoximine) and an electrophile (alkyl halide) while this approach discloses a reaction in which two nucleophiles (*i.e.* sulfoximine and alkylboronic acid) undergo coupling in the presence of Cu (II) species.

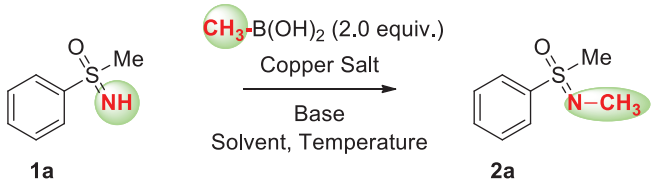
Scheme 3.5. *N*-alkylation of sulfoximine with alkylboronic acid.

3.2 RESULTS AND DISCUSSION

3.2.1 Optimization of reaction condition

To execute the challenge, *N*-methylation of *S*-methyl-*S*-phenylsulfoximine (**1a**) was studied with methylboronic acid in the presence of copper salts in various solvents (**Table 3**). Initially, the reaction was performed with 0.1 equiv. copper (II) acetate in methanol using 2.0 equiv. of methylboronic acid at room temperature (**Table 3.1**, **entry 1**). In fact, this is the condition employed for the *N*-arylation of sulfoximines with arylboronic acids by Bolm *et al*., (**Scheme 3.3**) [3a]. However, no reaction was detected under this condition after 12h. In addition, no reaction takes place with an equimolar amount of copper (II) acetate with or without base (*i.e.* pyridine, 2.4 equiv.) at room temperature as well as under reflux condition (*i.e.* 80 °C) in methanol (**Table 3.1**, **entries 2** and **3**). Thus, the reactions were carried out in different aprotic solvents such as THF, acetonitrile, dichloroethane and 1,4-dioxane with one equivalent of copper (II) acetate and pyridine at 80 °C (**Table 3.1**, **entries 4-7**). We were pleased to see a significant conversion of sulfoximine **1a** to the desired *N*-methylated sulfoximine **2a** (*i.e.* 86%) in 1,4-dioxane (**Table 3.1**, **entry 7**), while low yields were obtained with other solvents after 12h. Encouraged, we further modified the reaction condition where the reaction was carried out with 1.5 equiv. of copper (II) acetate at 100 °C in 1,4-dioxane (**Table 3.1**, **entry 8**).To our delight, under this condition, *N*-methyl *S*-methyl-*S*-phenyl sulfoximine (**2a**) was obtained in 94% yield within 30 mins. Further, the optimization of reaction condition was continued with different copper (I) and copper (II) salts in the presence of pyridine in 1,4-dioxane at 100 °C (**Table 3.1**, **entries 9-14**).

Table 3.1. Optimization of reaction condition for *N*-methylation of sulfoximine using methylboronic acid.[a,b]



1a 2a

Entry	Solvent	Metal salt (equiv.)	Base	Temperature (°C)	Time (h)	Yield (%)[b]
1	MeOH	$Cu(OAc)_2$ (0.1)	-	rt	12 h	NR[c]
2	MeOH	$Cu(OAc)_2$ (1.0)	-	rt (or) 80	12 h	NR
3	MeOH	$Cu(OAc)_2$ (1.0)	Py	rt (or) 80	12 h	NR
4	THF	$Cu(OAc)_2$ (1.0)	Py	80	12 h	33
5	AcCN	$Cu(OAc)_2$ (1.0)	Py	80	12 h	17
6	DCE	$Cu(OAc)_2$ (1.0)	Py	80	12 h	10
7	1,4-Dioxane	$Cu(OAc)_2$ (1.0)	Py	80	12 h	86
8	**1,4-Dioxane**	**$Cu(OAc)_2$ (1.5)**	**Py**	**100**	**30 min**	**94**
9	1,4-Dioxane	$CuSO_4$ (1.5)	Py	100	30 min	18
10	1,4-Dioxane	$CuCl_2$ (1.5)	Py	100	30 min	23
11	1,4-Dioxane	$CuBr_2$ (1.5)	Py	100	30 min	27
12	1,4-Dioxane	CuOAc (1.5)	Py	100	30 min	87
13	1,4-Dioxane	CuCl (1.5)	Py	100	30 min	14
14	1,4-Dioxane	Cu_2O (1.5)	Py	100	30 min	<5
15	1,4-Dioxane	$Cu(OAc)_2$ (1.5)	Et_3N	100	30 min	80
16	1,4-Dioxane	$Cu(OAc)_2$ (1.5)	DMAP	100	30 min	92
17	1,4-Dioxane	$Cu(OAc)_2$ (1.5)	K_2CO_3	100	30 min	<5
18	1,4-Dioxane	$Cu(OAc)_2$ (1.5)	NaOH	100	30 min	NR

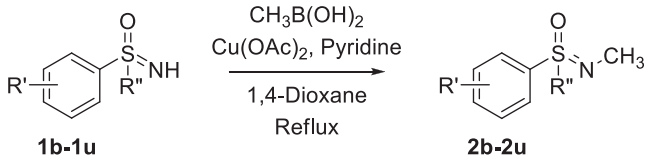
[a]**Reaction Condition:** Sulfoximine (1.0 mmol), methylboronic acid (2.0 equiv.), base (2.4 equiv.), and copper salt were stirred in different solvents (8 mL) at appropriate temperature. [b]Isolated Yield. [c]Condition used for the *N*-arylation of sulfoximine by Bolm *e.al.*(see ref 3).

Surprisingly, most of the copper salts failed to provide significant amount of desired product while copper (I) acetate showed a comparable reactivity to that of copper (II) acetate (**Table 3.1**, **entry 12**). Furthermore, the reactions were carried out with different organic and inorganic bases in the presence of copper (II) acetate (**Table 3.1**, **entries 15-18**). The reactions with Et_3N and 4-DMAP provided good yields whereas negligible yield was observed in the case of K_2CO_3 and NaOH. In fact, 4-DMAP showed an equal reactivity to that of pyridine in the *N*-methylation reaction (**Table 3.1**, **entry 16**).

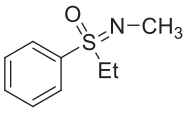
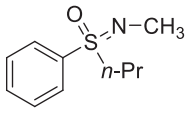
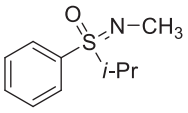
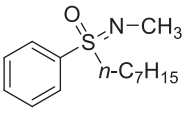
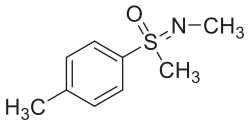
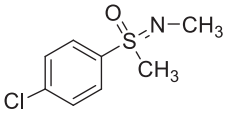
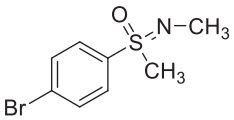
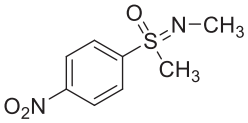
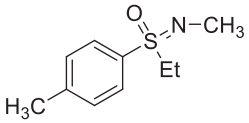
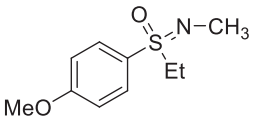
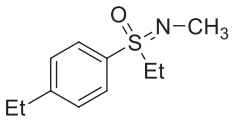
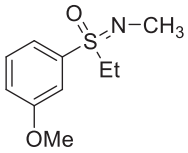
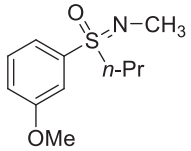
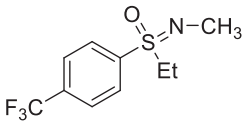
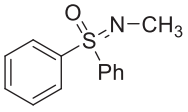
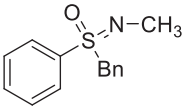
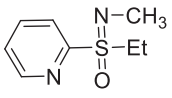
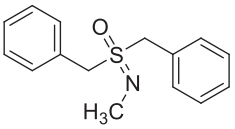
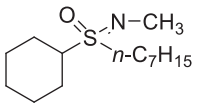
3.2.2 Substrates scope

With optimized condition in hand, *N*-methylation of various sulfoximines was performed using methylboronic acid in the presence of copper (II) acetate and the results were summarized in **Table 3.2**. *S*-alkyl-*S*-phenylsulfoximines bearing linear or branched alkyl chains were *N*-methylated successfully in excellent yields under the optimized condition (**Table 3.2**, **2b-2e**). It is noteworthy that the sterically hindered *S*-phenyl-*S*-*iso*-propylsulfoximine was also methylated in 91% yield within 60 mins (**Table 3.2**, **2d**). In the case of *S*-heptyl-*S*-phenylsulfoximine, a long alkyl substituent led to slightly longer reaction time to yield *N*-methylated sulfoximine **2e** in 82% yield. The substrates with electron donating or withdrawing substituents on the phenyl ring also underwent *N*-methylation in 89-94% yields (**Table 3.2**, **2f-2i**). In general, we observed that the electron withdrawing group substituted phenylsulfoximines (e.g. *p*-NO_2, *p*-Br, *p*-Cl) required slightly longer time for *N*-methylation when compared with electron donating group substituted sulfoximines (e.g. *p*-Me).

Table 3.2. *N*-Methylation of various sulfoximines with methylboronic acid under optimized conditions.[a,b]



1b-1u → **2b-2u**

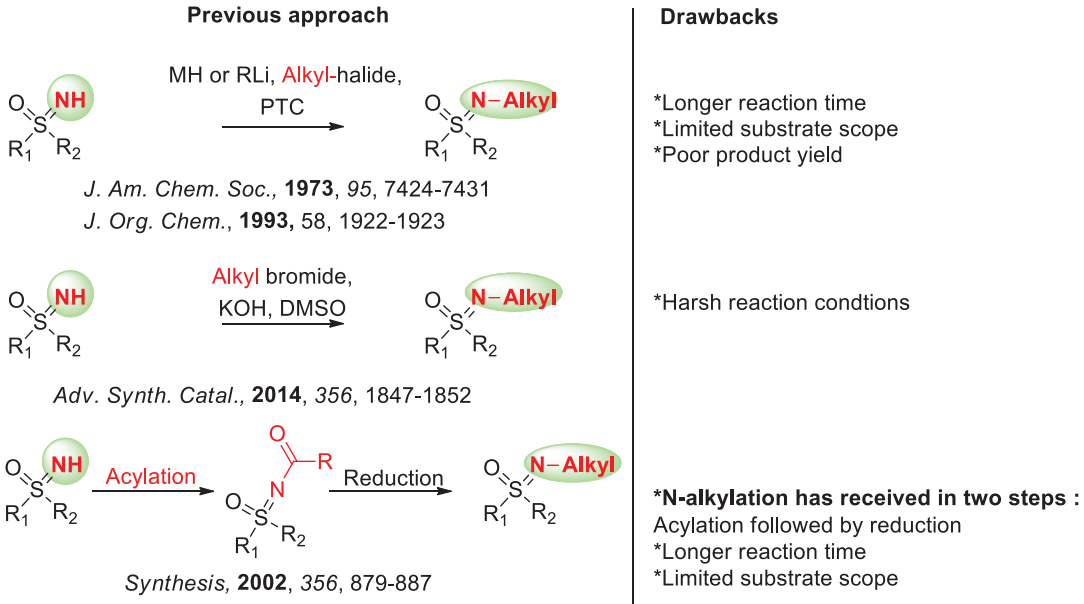
 **2b** (45 mins, **93%**)	 **2c** (60 mins, **95%**)	 **2d** (60 mins, **91%**)	 **2e** (120 mins, **82%**)
 **2f** (30 mins, **94%**)	 **2g** (120 mins, **89%**)	 **2h** (120 mins, **93%**)	 **2i** (180 mins, **91%**)
 **2j** (30 mins, **92%**)	 **2k** (30 mins, **91%**)	 **2l** (30 mins, **93%**)	 **2m** (60 mins, **93%**)
 **2n** (60 mins, **92%**)	 **2o** (90 mins, **82%**)	 **2p** (90 mins, **90%**)	 **2q** (180 mins, **87%**)
 **2r** (90 mins, **86%**)	 **2s** (90 mins, **87%**)	 **2t** (45 mins, **82%**)	

[a]**Reaction Condition:** Sulfoximine (1 mmol), alkylboronic acid (2.0 equiv.), $Cu(OAc)_2$ (1.5 equiv.), and Pyridine (2.4 equiv.) was refluxed in 1,4-dioxane (8 mL) at 100 °C in a pressure tube. [b]Isolated yield.

In order to demonstrate the versatility of the current methodology, *N*-methylation of various functionalized *S*-aryl-*S*-alkyl, *S*-aryl-*S*-benzyl and *S,S*-diarylsulfoximines were performed under optimized condition (**Table 3.2**, **2j-2q**). All these substrates were successfully *N*-methylated in 82-95% yield with methylboronic acid in a short span of time. Further, *N*-methylation of heterocylic sulfoximine (*i.e.S*-ethyl-*S*-pyridylsulfoximine) was also accomplished in excellent yield in 90 mins (**Table 3.2**, **2r**). Similar to arylsulfoximines, *S,S*-dibenzyl and *S,S*-dialkylsulfoximines underwent *N*-methylation in high yields (**Table 3.2**, **2s** and **2t**), which shows the great versatility and broad scope of the current methodology.

Similar to *N*-methylated sulfoximines, other *N*-alkylated sulfoximines also play an important role in chemistry and biology [4]. However, only limited methods are available for the introduction of alkyl groups in sulfoximines [7,12]. Due to poor nucleophilicity of sulfoximines, *N*-alkylation requires strong bases like alkali metal hydrides or *n*-butyllithium [7, 12a, 12b]. Alternatively, a two-step protocol is required, *i.e. N*-acylation followed by reduction, to achieve *N*-alkylated sulfoximines [12c]. Recently, Bolm *et al.,*have successfully demonstrated *N*-alkylation of various sulfoximines using alkyl halides with KOH in DMSO (**Scheme 3.6**) [12d].

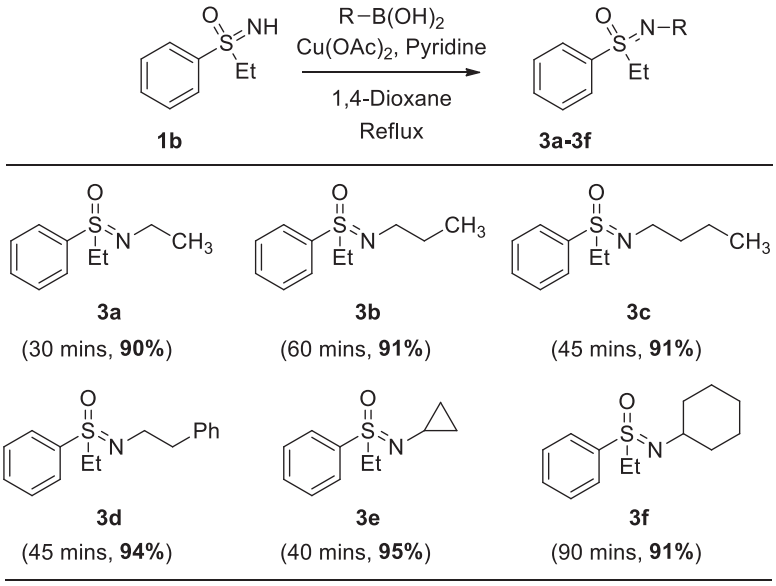
Favorable results in *N*-methylation of sulfoximines with methylboronic acid have spurred us to further explore the *N*-alkylation of sulfoximines with different alkylboronic acids. Initially, *N*-ethylation of *S*-ethyl-*S*-phenylsulfoximine (**1b**) with ethylboronic acid was examined under optimized condition. To our surprise, the reaction proceeds smoothly with similar efficiency to that of *N*-methylation and gave the desired product **3a** in 90% yield.



Scheme 3.6. Representative methods for *N*-alkylation of sulfoximines and their drawbacks.

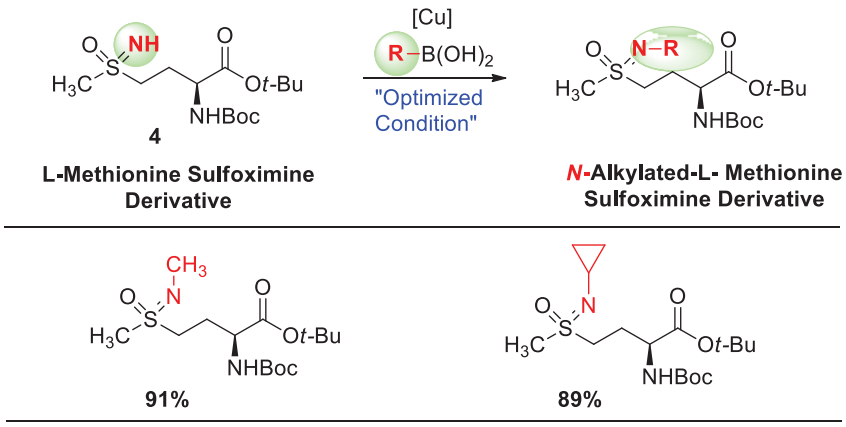
Encouraged, we further tested *N*-propylation, butylation and phenethylation of sulfoximine **1b** with respective boronic acids. These reactions gave the desired *N*-alkylated products in excellent yields (**Table 3.3**, **3b-3d**) within 60 mins. Since, the cyclopropyl group, which appears frequently in preclinical and clinical drug molecules, has received significant attention in medicinal chemistry due to its unique structural properties [13]. Thus, we have examined the *N*-cyclopropylation of sulfoximine **1b** with cyclopropylboronic acid under optimized condition. Interestingly, the reaction provides the *N*-cyclopropyl-*S*-ethyl-*S*-phenylsulfoximine (**3e**) in 95% yield within 45 mins. Similarly, *N*-cyclohexylsulfoximine **3f** was obtained in 91% yield.

Table 3.3. *N*-Alkylation of *S*-ethyl-*S*-phenylsulfoximine (**1b)** with different alkylboronic acids.[a,b]



[a]**Reaction Condition:** Sulfoximine (1 mmol), alkylboronic acid (2.0 equiv.), $Cu(OAc)_2$ (1.5 equiv.), and Pyridine (2.4 equiv.) was refluxed in 1,4-dioxane (8 mL) at 100 °C. [b]Isolated yield.

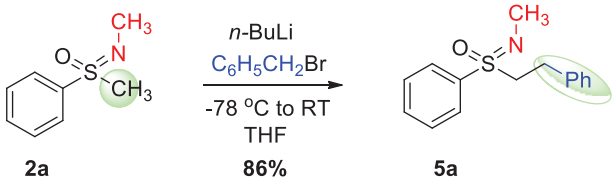
L-Methionine sulfoximine is a bioactive molecule which inhibits glutamine synthetase and ɤ-glutamylcysteine synthetase [14]. In this respect, L-methionine sulfoximine shows considerable therapeutic applications in animal models for many human diseases [14a]. To expand the scope of our methodology, *N*-methylation and cyclopropylation of bioactive L-methionine sulfoximine derivative **4** was tested with corresponding alkylboronic acids. To our delight, the optimized reaction condition was well suited to the task and gave *N*-methylated and cyclopropylated L-methionine sulfoximine derivatives in 89-91% yield. It is remarkable that *Boc*-protected primary amine was found to be intact during the *N*-methylation of L-methionine sulfoximine with methylboronic acid (**Scheme 3.7**).



Scheme 3.7. *N*-Alkylation of L-methionine sulfoximine derivative under optimized reaction condition.

Finally, a synthetic application of *N*-methyl sulfoximine was demonstrated as shown in **Scheme 3.8**. Selective lithiation of *S*-methyl group in *N,S*-dimethyl-*S*-phenylsulfoximine (**2a**) was performed using *n*-butyllithium in dry THF, which was subsequently reacted with benzyl bromide to obtain *N*-methyl-*S*-phenyl-*S*-(2-phenylethyl)sulfoximine **(5a)** in 86% yield.

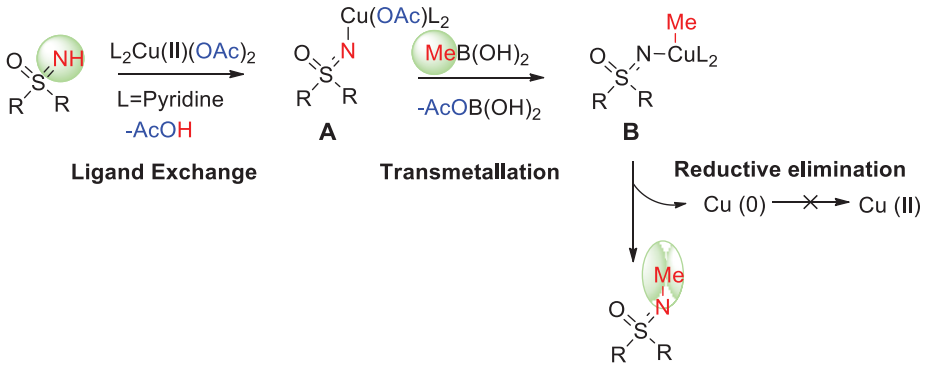
Finally, a synthetic application of *N*-methylsulfoximine was demonstrated as shown in **Scheme 3.8**. Selective lithiation of *S*-methyl group in *N,S*-dimethyl-*S*-phenylsulfoximine (**2a**) was performed using *n*-butyllithium in dry THF, which was subsequently reacted with benzyl bromide to obtain *N*-methyl-*S*-phenyl-*S*-(2-phenylethyl)sulfoximine **(5a)** in 86% yield.



Scheme 3.8. An example of selective functionalization of *N*-methylsulfoximine *via* lithiation.

3.3 PLAUSIBLE REACTION MECHANISM

A proposed mechanism for the *N*-methylation of sulfoximine was shown in **Scheme 3.9** [9]. In the first step, sulfoximine undergoes ligand exchange reaction with copper (II) acetate to form intermediate **A**. Further, methylboronic acid undergoes *trans*-metallation with intermediate **A** to form intermediate **B,** which subsequently undergoes reductive elimination to yield the desired products. During the reductive elimination process, Cu (II) species is converted to Cu (0) which is basically inactive for the coupling reaction, hence stoichiometric amount of $Cu(OAc)_2$ is required for completion of the reaction. Requirement of equivalent of $Cu(OAc)_2$ indicates that transmetalation of alkylboronic acid is very difficult when compared with aryl boronic acids.



Scheme 3.9. Proposed mechanism for *N*-methylation reaction.

3.4 CONCLUSION

In conclusion, we have established a copper mediated *N*-methylation of sulfoximines using methylboronic acid under mild condition. The reaction proceeds smoothly to provide the desired products in excellent yields in a short span of time. In addition to *N*-methylation, *N*-alkylation of sulfoximine with different alkylboronic acids was also demonstrated. Under optimized condition, *N*-methylation and cyclopropylation of bioactive L-methionine sulfoximine derivative was achieved in high yields. Further, a

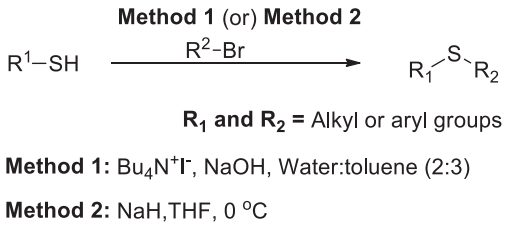
selective functionalization of *N*-methylsulfoximine was also successfully demonstrated *via* lithiation method which shows a broad scope in synthetic organic chemistry.

3.5 EXPERIMENTAL SECTION

All the reactions were performed in round bottom flask or pressure tube as described below. The ^{1}H NMR and ^{13}C NMRs of the known sulfoximines were compared with literature reports. For unknown compounds, physical appearance, R_f value, IR, ^{1}H, ^{13}C NMR, HRMS and melting point is provided.

3.5.1 Experimental procedure for the synthesis of sulfides

Two methods, method **1** and method **2** have been used for the preparation of different sulfides. The method **1** is used for the preparation of aryl-alkyl and alkyl-alkyl sulfides while aryl-benzyl and benzyl-benzyl sulfides were obtained using method 2.

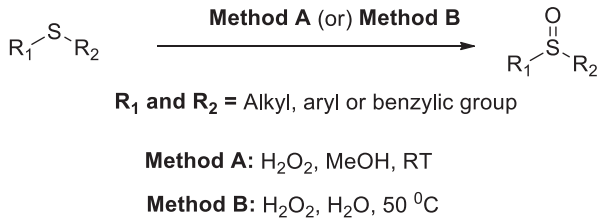


Method 1: In a mixture of water and toluene (2:3), *tetra*-butylammonium iodide (0.14 equiv.), NaOH (1.1 equiv.) and alkyl bromide (1.1 equiv.) was added successively. Reaction mixture was stirred vigorously at room temperature to which alkyl or aryl thiol (1 equiv.) was added dropwise. The progress of reaction was monitored on thin layer chromatography. After completion of reaction, reaction mixture was diluted with ethyl acetate (2×50 mL) and washed with 10% NaOH and H_2O (2×50 mL). The organic layer

was dried over anhydrous sodium sulfate and filtered. The filtrate was evaporated under reduced pressure in rota-evaporator. The compound purified in silica-gel column chromatography (*60-120 mesh*) using ethyl acetate:hexane as eluent. Yield of the products were between 75-85%. **Method 2:** Thiophenol or benzyl mercaptan (1.1 equiv.) was taken in dry THF and cooled to 0 ºC and after which NaH (1.1 equiv.) was added portion wise. After 5 minutes, benzyl bromide (1 equiv.) was added dropwise and allowed to stir until the completion of reaction. After completion, the reaction was quenched with 5 ml of water and stirred for 10 minutes. This reaction mixture was diluted with ethyl acetate, and washed with water, and brine. The organic layer was dried over anhydrous sodium sulfate and concentrated. The residue was purified in column chromatography on silica-gel (*60-120 mesh*) using ethyl acetate:hexane as eluent. Yield of the products were between 70-80%.

3.5.2 Experimental procedure for the synthesis of sulfoxides

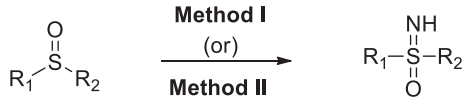
Two methods, method **A** and method **B** have been used for the preparation of different sulfides. The method **A** is used for the oxidation of aryl-alkyl and alkyl-alkyl sulfides while aryl-benzyl and benzyl-benzyl sulfides were obtained using method **B**.



Method A: Sulfide (5 gm, 1 equiv.), aqueous H_2O_2 (35%, 2 equiv.) was stirred in methanol (25 mL) at room temperature for overnight. After that methanol was evaporated, diluted with ethyl acetate and washed with distilled water and brine solution.

The organic layer was dried over anhydrous sodium sulfate, filtered and evaporated. The corresponding sulfoxide was isolated by silica-gel column chromatography using ethyl acetate/hexane as eluent. Yield of the products were between 75-80%. **Method B:** Sulfide (10 mmol) and H_2O_2 (35 % in water, 1.2 equiv.) were stirred in H_2O (3 mL) at 50 °C for 3 h. After the completion, the mixture was cooled to room temperature and extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4, concentrated and purified in column chromatography on silica gel using EtOAc as eluent. Yield of the products were between 65-75%.

3.5.3 Experimental procedure for the synthesis of *NH*-Sulfoximines



Method I: NaN_3, H_2SO_4, $CHCl_3$, 0 °C-45 °C

Method II: $H_2NCOONH_4$, $PhI(OAc)_2$, MeOH, 25 °C

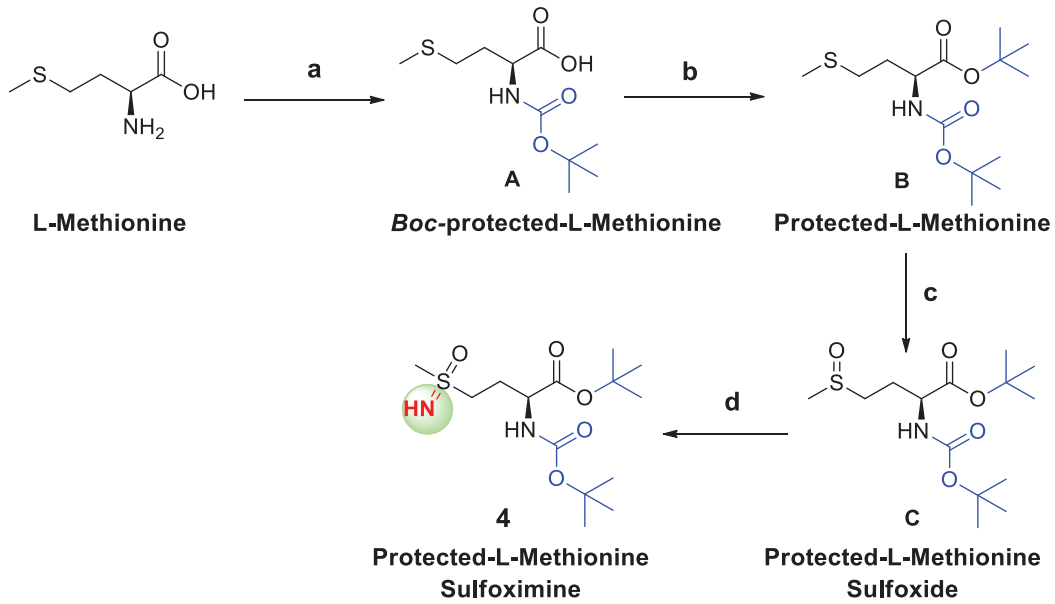
Sulfoximines **1a-h, 1j-p** and **1t** have been prepared using method A while Sulfoximines **1i**, **1q-s**, **1u** and **4** were prepared using literature method B.

Method A: Sulfoxide (4.0 mmol) and sodium azide (1.2 equiv) was stirred in $CHCl_3$ (15 mL) at 0 °C for 10 mins. Then, conc. H_2SO_4 (approx. 2.0 mL for 1 g of sulfoxide) was added dropwise over 10 min at 0 °C. After that the reaction mixture was heated to 45 °C for overnight and cooled to room temperature. The reaction mixture was quenched by ice-cooled water (10 mL) and $CHCl_3$ layer was separated. The aqueous layer of the reaction mixture was neutralized using 20% NaOH solution and re-extracted with $CHCl_3$ (3×100 mL). The combined organic extracts were washed with brine, dried over anhyd. Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified using column

chromatography on silica-gel (ethyl acetate/hexane) to obtain the sulfoximines **1a-h, 1j-p** and **1t** in >70 yields.

Method B: Sulfoxide (4.0 mmol), $PhI(OAc)_2$ (3.0 equiv.) and ammonium carbamate (4.0 equiv.) were added to a 50 mL round bottom flask containing MeOH (10.0 mL). The reaction mixture was stirred for 30 min at 25 °C in an open flask. The progress of reaction was analyzed by TLC. After completion, methanol was removed under *vacuo* and the crude residue was purified by silica-gel column chromatography using ethyl acetate/ hexane as eluent to obtain the sulfoximines **1i**, **1q-s**, **1u** and **4** in > 65% yields.

3.5.4 Experimental procedure for the synthesis of protected L-methionine sulfoximine (4)



a) $(Boc)_2O$, Et_3N, MeOH; **b)** *t*-BuOH, DCC, 4-DMAP, DCM; **c)** m-CPBA, DCM; **d)** $PhI(OAc)_2$, NH_2COONH_4, MeOH

(a) Experimental procedure for the synthesis of protected L-methionine sulfide A:

L-Methionine (3 g, 20.1 mmol) was dissolved in methanol (30 mL) and stirred. The $(Boc)_2O$ (5.28 g, 24 mmol) and triethylamine (16.8 mL, 120.6 mmol) were added to the reaction mixture and allowed to stir overnight at room temperature. The reaction was monitored using thin layer chromatography (80% Ethyl acetate/hexane solvent, *Ninhydrin* stain). After completion, methanol was evaporated and the residue was dissolved in 1N HCl and extracted with ethyl acetate (3×50 mL). The organic layer was dried over anhydrous sodium sulfate, filtered and evaporated to obtain crude *N-Boc*-protected methionine **A** in 70%, 3.51 g.

(b) Experimental procedure for the synthesis of protected L-methionine sulfide B:

To a cooled solution of crude *Boc*-L-methionine **A** (2 g, 8 mmol) in dry CH_2Cl_2 (20 mL), 4-DMAP (0.08 g, 0.67 mmol) and *tert.*-butanol (0.71 g, 9.6 mmol) was added. After 10 mins, *N,N*-dicyclohexylcarbodiimide (DCC) (2.15 g, 10.4 mmol) was added at 0 °C and stirred for 12 h. The reaction was monitored using thin layer chromatography (15% ethyl acetate/hexane solvent, *Ninhydrin* stain). The resulted dicyclohexylurea (DCU) precipitate was filtered off and washed with DCM (2×10 mL). The collected filtrate was washed with 1M HCl (2×5 mL), saturated $NaHCO_3$ (2×10 mL) and water (2×5mL) and dried over anhydrous sodium sulfate. Then, the solvent was evaporated in *vacuo,* and the crude product was purified by column chromatography (SiO_2, 5-20% ethyl acetate:hexane) to give desired product **B** in 80 %, 1.96 g.

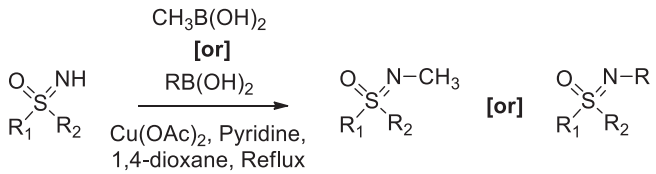
(c) Experimental procedure for protected L-methionine sulfoxide C:

To a cooled solution of protected L-methionine **B** (1 g, 3.28 mmol) in DCM (5 mL) at 0 °C, *m*-CPBA (1.5 equiv.) was added portion wise. After 30 mins, the reaction mixture was allowed to stir at room temperature till the completion of reaction (TLC analysis, 20% MeOH: $CHCl_3$, *Ninhydrin* stain). The reaction mixture was neutralized with saturated $NaHCO_3$ and extracted with DCM. The organic layer was washed with brine, dried over anhydrous sodium sulfate and evaporated. The crude residue was purified through silica-gel column chromatography using ethyl acetate/ hexane as eluent to obtain the title compound in 89%, 0.936 g as viscous liquid.

(d) Experimental procedure for protected L-methionine sulfoximine 4:

The sulfoxide (2.0 mmol, 0.672 g), $PhI(OAc)_2$ (3.0 equiv., 1.932 g) and ammonium carbamate (4.0 equiv., 0.624 g) were added to a 50 mL round bottom flask containing MeOH (5.0 mL). The reaction mixture was stirred for 30 min at 25 °C in an open flask. The progress of reaction was analyzed by TLC (20% MeOH/$CHCl_3$ as eluent, *Ninhydrin* stain). After completion, methanol was removed under *vacuo* and the crude residue was purified by silica-gel column chromatography using 40% ethyl acetate/ hexane as eluent to obtain the sulfoximine **4** in 79% , 0.556 g.

3.5.5 Experimental procedure for the *N*-methylation/alkylation of sulfoximines using methyl/alkylboronic acid



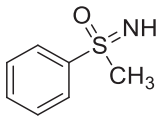
Sulfoximine (1 mmol), copper (II) acetate (1.5 equiv.), pyridine (2.4 equiv.) and 1,4-dioxane (8 mL) was taken in a pressure tube (50 mL) under open air condition and stirred for 5 mins at room temperature to which methylboronic acid (2.0 equiv.) was added. The pressure tube was closed with Teflon cap and refluxed in a pre-heated oil bath at 100 °C until the starting material (sulfoximine) was consumed (as per the time given in manuscript). After that the reaction mixture was cooled to room temperature, diluted with ethyl acetate and washed with distilled water and brine solution. The ethyl acetate layer was dried over anhydrous sodium sulfate, evaporated and purified in silica-gel column chromatography using ethyl acetate/hexane as eluent to obtain the *N*-methylated or alkylated sulfoximines.

3.5.6 Experimental procedure for the synthesis of *N*-methyl-*S*-phenyl-*S*-(2-phenylethyl)sulfoximine (5a):

N,S-Dimethyl-*S*-phenylsulfoximine(169 mg, 1.0 mmol)was stirredin dry THF (3 mL) at –78 °C to which *n*-butyllithium (1.6 m in hexane, 1.05 equiv.) was added slowly over a period of 10 min. The reaction temperature was further increased to -26 °C in a period of 30 mins to which benzyl bromide (0.36 mL, 1.05 equiv.) was added slowly. After the addition of benzyl bromide, the reaction mixture was allowed to stir at room temperature for overnight. After completion, the reaction mixture was quenched by adding water and extracted with dichloromethane. The organic layer was dried with anhydrous sodium sulphate, concentrated and subjected for column chromatography purification with hexane: ethyl acetate to obtain the title compound in 86% (222 mg).

3.6 ANALYTICAL DATA FOR SULFOXIMINES

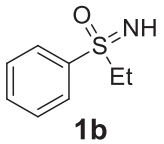
3.6.1 *S*-Methyl-*S*-phenylsulfoximine (1a)



1a

The titled compound was obtained as pale yellow oil. The crude product was purified by silica-gel column chromatography (40% EtOAc/Hexane); R_f = 0.30. **IR** (neat, cm^{-1}):3263, 1219, 1089, 1017, 984, 725, 679. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.08–7.95 (m, 2H), 7.64–7.60 (m, 1H), 7.55 (t, *J* = 7.6 Hz, 2H), 3.10 (s, 3H), 2.68 (brs, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 143.7, 133.2, 129.4, 127.8, 46.3. **HRMS:** Calc. for C_7H_9NOSNa $[M+Na]^+$: 178.0303, Obser. 178.0297.

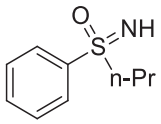
3.6.2 *S*-Ethyl-*S*-phenylsulfoximine (1b)



1b

The titled compound was obtained as yellow oil. The crude product was purified by silica-gel column chromatography (40% EtOAc/Hexane); R_f = 0.28. **IR** (neat, cm^{-1}): 3256, 1456, 1213, 1088, 959, 762, 719, 691. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.01–7.91 (m, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 2H), 3.17 (q, *J* = 7.4 Hz, 2H), 2.90 (brs, 1H), 1.25 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 141.6, 133.2, 129.3, 128.7, 52.0, 8.0. **HRMS:** Calc. for $C_8H_{12}NOS$ $[M+H]^+$: 170.0640, Obser. 170.0638.

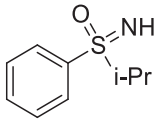
3.6.3 *S*-Phenyl-*S*-propylsulfoximine (1c)



1c

The titled compound was obtained as pale yellow oil. The crude product was purified by silica-gel column chromatography (30% EtOAc/Hexane); R_f = 0.31. **IR** (neat, cm^{-1}): 3281, 1449, 1233, 1074, 966, 759, 711, 687. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.95–7.91 (m, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 2H), 3.10-3.06 (m, 2H), 2.59 (brs, 1H), 1.74-1.65 (m, 2H), 0.92 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 142.1, 133.0, 129.2, 128.5, 59.3, 17.0, 12.9. **HRMS:** Calc. for $C_9H_{14}NOS$ $[M+H]^+$: 184.0796, Obser. 184.0781.

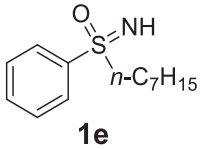
3.6.4 *S-iso*-Propyl-*S*-phenylsulfoximine (1d)



1d

The titled compound was obtained as light yellow oil. The crude product was purified by silica-gel column chromatography (50% EtOAc/Hexane); R_f = 0.29. **IR** (neat, cm^{-1}): 3279, 1464, 1252, 1099, 981, 770, 729, 693. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.94-7.92 (m, 2H), 7.64–7.56 (m, 1H), 7.53-7.51 (m, 2H), 3.22 (hept, *J* = 6.8 Hz, 1H), 2.49 (brs, 1H), 1.30 (d, *J* = 6.8 Hz, 3H), 1.25 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 139.9, 133.1, 129.5, 129.0, 56.6, 16.5, 16.1. **HRMS:** Calc. for $C_9H_{14}NOS$ $[M+H]^+$: 184.0796, Obser. 184.0782.

3.6.5 *S*-Heptyl-*S*-phenylsulfoximine (1e)

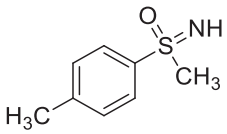


1e

The titled compound was obtained as pale yellow liquid. The crude product was purified by silica-gel column chromatography (80%

EtOAc/Hexane); R_f= 0.30.**IR** (neat, cm^{-1}): 3270, 2929, 1441, 1223, 1111, 991, 752, 679. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.96–7.92 (m, 2H), 7.60–7.56 (m, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 3.15–3.04 (m, 2H), 2.52 (brs, 1H), 1.76–1.59 (m, 2H), 1.31–1.17 (m, 8H), 0.81 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 142.2, 133.0, 129.2, 128.5, 57.6, 31.5, 28.8, 28.2, 23.1, 22.6, 14.1. **HRMS:** Calc. for $C_{13}H_{21}NOSNa$ $[M+Na]^+$: 262.1242, Obser. 262.1230.

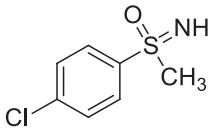
3.6.6 *S*-Methyl *S*-*p*-tolylsulfoximine (1f)



1f

The titled compound was obtained as pale yellow oil. The crude product was purified by silica-gel column chromatography (30% EtOAc/Hexane); R_f= 0.34. **IR** (neat, cm^{-1}): 3281, 3192, 2923, 2734, 2217, 1990, 1818, 1733, 1590, 1489, 1403, 1379, 1202, 1097, 954, 813, 739. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.86 (d, *J* = 7.0 Hz, 2H), 7.32 (d, *J* = 7.8 Hz, 2H), 3.06 (s, 3H), 2.65 (brs, 1H), 2.42 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 144.0, 140.6, 130.0, 127.8, 46.4, 21.6. **HRMS:** Calc. for $C_8H_{12}NOS$ $[M+H]^+$: 170.064, Obser. 170.0635.

3.6.7 *S*-(4-Chlorophenyl)-*S*-methylsulfoximine (1g)

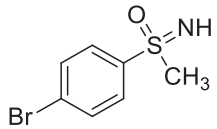


1g

The titled compound was obtained as transparent colorless oil. The crude product was purified by silica-gel column chromatography (40% EtOAc/Hexane); R_f = 0.31. **IR** (neat, cm^{-1}): 3269, 1211, 1086, 993, 828, 754. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.94 (d,

J = 8.6 Hz, 2H), 7.51 (d, *J* = 8.6 Hz, 2H), 3.09 (s, 3H), 2.71 (brs, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 142.3, 139.9, 129.7, 129.4, 46.4. **HRMS:** Calc. for C_7H_9ClNOS $[M+H]^+$: 190.0093, Obser. 190.008.

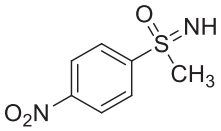
3.6.8 *S*-(4-Bromophenyl)-*S*-methylsulfoximine (1h)



1h

The titled compound was obtained as white solid. The crude product was purified by silica-gel column chromatography (50% EtOAc/Hexane); R_f = 0.30. Melting point: 105-106 °C. **IR** (KBr, cm^{-1}):3428, 3309, 3081, 2914, 2851, 2639, 2381, 2109, 1983, 1886, 1794, 1648, 1569, 1461, 1384, 1326, 1264, 1187, 1030, 948, 819, 755, 713. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 8.6 Hz, 2H), 7.65 (d, *J* = 8.6 Hz, 2H), 3.06 (s, 3H), 2.64 (brs, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 142.7, 132.6, 129.4, 128.3, 46.2. **HRMS:** Calc. for C_7H_9BrNOS $[M+H]^+$: 233.9588, Obser. 235.9573.

3.6.9 *S*-Methyl-*S*-(4-nitrophenyl)sulfoximine (1i)

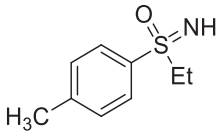


1i

The titled compound was obtained as yellow solid. The crude product was purified by silica-gel column chromatography (40% EtOAc/Hexane); R_f = 0.32. Melting point: 103-105 °C. **IR** (KBr, cm^{-1}): 3096, 1538, 1355, 1231, 994, 946, 859, 731. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.40–8.33 (m, 2H), 8.23–8.16 (m, 2H), 3.14 (s, 3H), 2.91 (brs, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ

150.6, 149.5, 129.3, 124.6, 46.1. **HRMS:** Calc. for $C_7H_9N_2O_3S$ $[M+H]^+$: 201.0334, Obser. 201.0337.

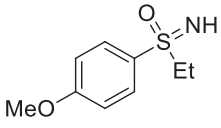
3.6.10 *S*-Ethyl-*S*-(4-methylphenyl)sulfoximine (1j)



1j

The titled compound was obtained as pale yellow oil. The crude product was purified by silica-gel column chromatography (50% EtOAc/Hexane); R_f= 0.28. **IR** (neat, cm^{-1}): 3273, 3058, 2966, 2936, 2874, 1647, 1595, 1453, 1408, 1207, 1085, 1051, 965, 819, 713. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.92–7.61 (m, 2H), 7.26 (d, *J* = 5.9 Hz, 2H), 3.22–2.97 (m, 2H), 2.65 (brs, 1H), 2.36 (s, 3H), 1.35–0.95 (m, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 143.8, 138.2, 129.7, 128.5, 51.8, 21.4, 7.8. **HRMS:** Calc. for $C_9H_{13}NOSNa$ $[M+Na]^+$: 206.0616, Obser. 206.0617.

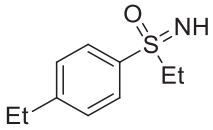
3.6.11 *S*-Ethyl-*S*-(4-methoxyphenyl)sulfoximine (1k)



1k

The titled compound was obtained as brown oil. The crude product was purified by silica-gel column chromatography (70% EtOAc/Hexane); R_f= 0.22. **IR** (neat, cm^{-1}): 3273, 3064, 3027, 2927, 1530, 1451, 1409, 1220, 1097, 799, 754, 625, 527. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.84 (d, *J* = 8.6 Hz, 2H), 6.97 (d, *J* = 8.6 Hz, 2H), 3.85 (s, 3H), 3.12 (q, *J* = 7.3 Hz, 2H), 2.59 (brs, 1H), 1.21 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 163.4, 132.8, 130.8, 114.4, 55.8, 52.2, 8.1. **HRMS:** Calc. for $C_9H_{14}NO_2S$ $[M+H]^+$: 200.0745, Obser. 200.0746.

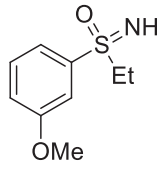
3.6.12 *S*-Ethyl-*S*-(4-ethylphenyl)sulfoximine (1l)



1l

The titled compound was obtained as yellow liquid. The crude product was purified by silica-gel column chromatography (80% EtOAc/Hexane); R_f= 0.24. **IR** (neat, cm^{-1}): 3273, 3057, 2970, 2938, 2873, 1644, 1596, 1454, 1409, 1209, 1096, 1053, 969, 817, 716. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.86 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.5 Hz, 2H), 3.15 (q, *J* = 7.4 Hz, 2H), 2.73 (q, *J* = 7.6 Hz, 2H), 2.63 (brs, 1H), 1.28-1.24 (m, 6H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 150.2, 138.7, 128.9, 128.8, 52.1, 29.0, 15.3, 8.1. **HRMS:** Calc. for $C_{10}H_{16}NOS$ $[M+H]^+$: 198.0953, Obser. 198.0954.

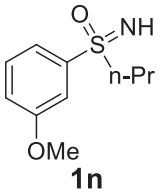
3.6.13 *S*-Ethyl-*S*-(3-methoxyphenyl)sulfoximine (1m)



1m

The titled compound was obtained as brown liquid. The crude product was purified by silica-gel column chromatography (70% EtOAc/Hexane); R_f= 0.22. **IR** (neat, cm-1): 3279, 3062, 3023, 2926, 1599, 1474, 1411, 1321, 1227, 1094, 1019, 993, 792, 751, 680. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.47-7.45 (m, 1H), 7.41–7.35 (m, 2H), 7.10–7.03 (m, 1H), 3.80 (s, 3H), 3.14–3.04 (m, 2H), 2.64 (brs, 1H), 1.21-1.17 (m, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 160.0, 142.7, 130.1, 120.7, 119.4, 113.1, 55.7, 51.7, 7.9. **HRMS:** Calc. for $C_9H_{13}NO_2SNa$ $[M+Na]^+$: 222.0565, Obser. 222.0554.

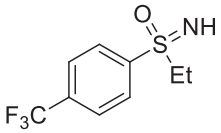
3.6.14 *S*-(3-Methoxyphenyl)-*S*-propylsulfoximine (1n)



1n

The titled compound was obtainedas brown liquid. The crude product was purified by silica-gel column chromatography (70% EtOAc/Hexane); R_f= 0.22.**IR** (neat, cm^{-1}): 3297, 3064, 3013, 2920, 1599, 1478, 1411, 1321, 1227, 1094, 1019, 993, 794, 756, 670. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.52 (d, *J* = 7.7 Hz, 1H), 7.49–7.38 (m, 2H), 7.11 (dd, *J* = 8.2, 2.4 Hz, 1H), 3.85 (s, 3H), 3.15–3.04 (m, 2H), 2.51 (brs, 1H), 1.80-1.65 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 160.2, 143.5, 130.3, 120.7, 119.6, 113.0, 59.3, 55.8, 17.0, 13.0. **HRMS:** Calc. for $C_{10}H_{16}NO_2S$ $[M+H]^+$: 214.0902, Obser. 214.0887.

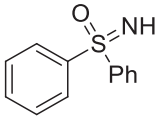
3.6.15 *S*-Ethyl-*S*-(4-trifluoromethylphenyl)sulfoximine (1o)



1o

The titled compound was obtained as transparent oil. The crude product was purified by silica-gel column chromatography(70% EtOAc/Hexane); R_f= 0.24. **IR** (neat, cm-1): 3270, 3092, 2911, 1900, 1607, 1318, 1127, 1097, 1059, 998, 947, 835, 789, 749, 691. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 8.2 Hz, 2H), 7.82 (d, *J* = 8.2 Hz, 2H), 3.22–3.16 (m, 2H), 2.32 (brs, 1H), 1.27 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 145.4, 134.9 (q, *J* = 33 Hz), 129.3, 126.5 (q, *J* = 3.7 Hz), 123.4 (q, *J* = 272.9 Hz), 51.9, 7.9. **HRMS:** Calc. for $C_9H_{11}F_3NOS$ $[M+H]^+$: 238.0513, Obser. 238.0497.

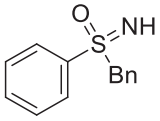
3.6.16 *S*,*S*-Diphenylsulfoximine (1p)



1p

The titled compound was obtained as White solid. The crude product was purified by silica-gel column chromatography (50% EtOAc/Hexane); R_f = 0.36. Melting point: 101 °C. **IR** (KBr, cm^{-1}): 3244, 1446, 1216, 1133, 1074, 953, 723, 681. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.12–7.96 (m, 4H), 7.54–7.44 (m, 6H), 3.06 (brs, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 143.5, 132.7, 129.3, 128.0. **HRMS:** Calc. for $C_{12}H_{12}NOS$ $[M+H]^+$: 218.064, Obser. 218.0642.

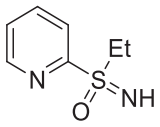
3.6.17 *S*-Phenyl-*S*-(phenylmethyl)sulfoximine (1q)



1q

The titled compound was obtained as pale yellow solid. The crude product was purified by silica-gel column chromatography (60% EtOAc/Hexane); R_f = 0.31.Melting point: 108 °C. **IR** (KBr, cm^{-1}): 3444, 1438, 1218, 1123, 986, 706. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.75-7.73 (m, 2H), 7.59–7.53 (m, 1H), 7.46–7.40 (m, 2H), 7.32–7.28 (m, 1H), 7.27–7.22 (m, 2H), 7.11–7.07 (m, 2H), 4.37 (d, *J* = 13.4 Hz, 1H), 4.29 (d, *J* = 13.4 Hz, 1H), 2.83 (brs, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 140.4, 133.2, 131.1, 128.9, 128.8, 128.7, 128.6, 64.7. **HRMS:** Calc. for $C_{13}H_{14}NOS$ $[M+H]^+$: 232.0796, Obser. 232.0792.

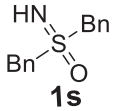
3.6.18 *S*-Ethyl-*S*-(2-pyridyl)sulfoximine (1r)



1r

The titled compound was obtained as yellow oil. The crude product was purified by silica-gel column chromatography (100% EtOAc); R_f= 0.28. **IR** (neat, cm^{-1}): 3261, 3010, 2920, 2851, 1659, 1579, 1411, 1317, 1223, 1068, 1014, 990, 784, 750, 512. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.73 (d, *J* = 4.7 Hz, 1H), 8.12 (d, *J* = 7.8 Hz, 1H), 7.94-7.91 (m, 1H), 7.50-7.48 (m, 1H), 3.52–3.44 (m, 1H), 3.40–3.32 (m, 1H), 2.81 (brs, 1H), 1.26 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 159.3, 150.3, 138.2, 126.8, 122.5, 48.4, 7.4. **HRMS:** Calc. for $C_7H_{14}N_2OS$ $[M+H]^+$: 171.0592, Obser. 171.0576.

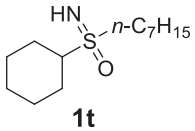
3.6.19 *S*,*S*-Dibenzylsulfoximine (1s)



1s

The titled compound was obtainedas white solid. The crude product was purified by silica-gel column chromatography (50% EtOAc/Hexane); R_f= 0.26. Melting point: 173°C. **IR** (KBr, cm^{-1}): 3245, 3067, 3033, 2974, 2918, 1494, 1451, 1416, 1255, 1149, 1079, 1014, 752, 698. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.41 (s, 10H), 4.29 (d, *J* = 13.1 Hz, 2H), 4.17 (d, *J* = 13.1 Hz, 2H), 2.60 (brs, 1H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 131.3, 129.2, 129.1, 128.0, 60.7. **HRMS:** Calc. for $C_{14}H_{16}NOS$ $[M+H]^+$: 246.0953, Obser. 246.0951.

3.6.20 *S*-Cyclohexyl-*S*-heptylsulfoximine (1t)

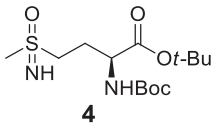


1t

The titled compound was obtained as yellow viscous liquid. The crude

product was purified by silica-gel column chromatography (50% EtOAc/Hexane); R_f= 0.48. **IR** (neat, cm^{-1}): 3510, 2920, 2875, 2814, 2313, 1981, 1644, 1450, 1129, 958, 849, 770, 691. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 2.95–2.88 (m, 2H), 2.83 (tt, *J* = 12.2, 3.5 Hz, 1H), 2.67 (brs, 1H), 2.17-2.11 (m, 2H), 1.93–1.89 (m, 2H), 1.84–1.77 (m, 2H), 1.73–1.67 (m, 1H), 1.52-1.44 (m, 2H), 1.42–1.35 (m, 2H), 1.33–1.21 (m, 9H), 0.85 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 62.5, 51.2, 31.6, 28.9, 28.7, 25.7, 25.4, 25.2, 22.6, 21.8, 14.1. **HRMS:** Calc. for $C_{13}H_{28}NOS$ $[M+H]^+$: 246.1892, Obser. 246.1888.

3.6.22 L-Methionine SulfoximineDerivative (4)

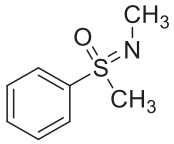


4

The titled compound was obtained as transparent viscous liquid. The crude product was purified by silica-gel column chromatography (40% EtOAc/Hexane); R_f= 0.38. **IR** (neat, cm^{-1}):3418, 2984, 2526, 1678, 1453, 1204, 1154, 1045, 981. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 5.34 (d, *J* = 6.3 Hz, 1H), 4.24 (s, 1H), 3.22–3.04 (m, 2H), 2.96 (s, 3H), 2.85–2.60 (m, 1H), 2.37-2.32 (m, 1H), 2.13-2.05 (m, 1H), 1.44 (s, 9H), 1.40 (s, 9H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 170.5, 155.6, 83.0, 80.3, 53.5, 52.7, 43.1, 28.4, 28.1, 26.7. **HRMS:** Calc. for $C_{14}H_{29}N_2O_5S$ $[M+H]^+$: 337.4555, Obser. 337.1820.

3.7 ANALYTICAL DATA FOR *N*-ALKYLSULFOXIMINE

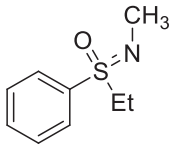
3.7.1 *N,S*-Dimethyl-*S*-phenylsulfoximine (2a)



2a

The titled compound was obtained as yellow liquid. Yield= 158 mg, 94%. The crude product was purified by silica-gel column chromatography (80% EtOAc/Hexane); R_f= 0.20. **IR** (neat, cm^{-1}):3874, 3188, 3056, 2316, 2074, 1987, 1913, 1659, 1487, 1303, 1218, 1104, 965, 844, 759, 689. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.96–7.81 (m, 2H), 7.64–7.52 (m, 3H), 3.06 (s, 3H), 2.63 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 138.9, 133.0, 129.6, 128.9, 45.1, 29.7. **HRMS:** Calc. for $C_8H_{12}NOS$ $[M+H]^+$: 170.064, Obser. 170.0632

4.7.2 *N*-Methyl-*S*-ethyl-*S*-phenylsulfoximine (2b)

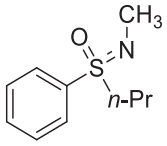


2b

The titled compound was obtained as pale yellow liquid (Yield= 170 mg, 93%). The crude product was purified by silica-gel column chromatography (80% EtOAc/Hexane); R_f= 0.24. **IR** (neat, cm^{-1}): 3824, 3406, 3041, 2924, 2827, 2669, 2323, 2098, 1927, 1744, 1673, 1445, 1234, 980, 925, 854, 773, 721, 688. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.84 (d, *J* = 7.3 Hz, 2H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.55 (t, *J* = 7.3 Hz, 2H), 3.24-3.11 (m, 2H), 2.65 (s, 3H), 1.21 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 136.9, 133.0, 129.7, 129.6, 50.7, 29.5, 7.4. **HRMS:** Calc. for $C_9H_{14}NOS$ $[M+H]^+$: 184.0796, Obser.

184.0787.

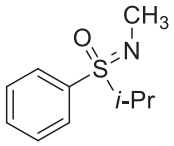
3.7.3 *N*-Methyl-*S*-phenyl-*S*-propylsulfoximine (2c)



2c

The titled compound was obtained as pale yellow liquid (Yield= 187 mg, 95%).The crude product was purified by silica-gel column chromatography (80% EtOAc/Hexane); R_f= 0.30. **IR** (neat, cm^{-1}): 3071, 2983, 2928, 2869, 2811, 1640, 1454, 1241, 1140. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.89–7.75 (m, 2H), 7.60–7.51 (m, 3H), 3.15–3.01 (m, 2H), 2.64 (s, 3H), 1.79–1.60 (m, 2H), 0.92 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 137.7, 132.9, 129.5, 128.5, 58.3, 29.5, 16.6, 13.0. **HRMS:** Calc. for $C_{10}H_{16}NOS$ $[M+H]^+$: 198.0953, Obser. 198.0937.

3.7.4 *N*-Methyl-*S*-*iso*-propyl-*S*-phenylsulfoximine (2d)

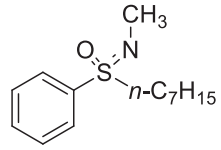


2d

The titled compound was obtained as transparent liquid (Yield= 179 mg, 91%).The crude product was purified by silica-gel column chromatography (60% EtOAc/Hexane); R_f= 0.28. **IR** (neat, cm^{-1}): 3067, 2980, 2919, 2870, 2811, 1640, 1454, 1245, 1144. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.84–7.77 (m, 2H), 7.62–7.58 (m, 1H), 7.57–7.53 (m, 2H), 3.26-3.21 (m, 1H), 2.67 (s, 3H), 1.35 (d, *J* = 6.8 Hz, 3H), 1.19 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 135.7, 132.9, 130.5, 129.4, 55.9, 29.7, 16.6, 15.7. **HRMS:** Calc. for $C_{10}H_{16}NOS$ $[M+H]^+$:

198.0953, Obser. 198.0937.

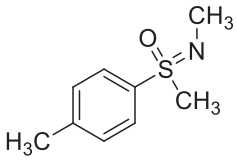
3.7.5 *N*-Methyl-*S*-heptyl-*S*-phenylsulfoximine (2e)



2e

The titled compound was obtained as transparent oil (Yield= 207 mg, 82%).The crude product was purified by silica-gel column chromatography (80% EtOAc/Hexane); R_f= 0.32. **IR** (neat, cm^{-1}): 3274, 2930, 1664, 1441, 1223, 1122, 991, 752, 679. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.82-7.80 (m, 2H), 7.60–7.49 (m, 3H), 3.15-3.00 (m, 2H), 2.63 (s, 3H), 1.75–1.55 (m, 2H), 1.25–1.11 (m, 8H), 0.84–0.77 (m, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 137.8, 132.9, 129.5, 128.5, 56.7, 31.5, 29.6, 28.8, 28.3, 22.7, 22.6, 14.1. **HRMS:** Calc. for $C_{14}H_{24}NOS$ $[M+H]^+$: 254.1579, Obser. 254.1567.

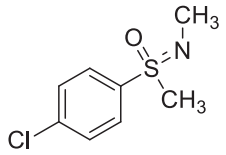
3.7.6 *N*-Methyl-*S*-methyl-*S*-(4-methylphenyl)sulfoximine (2f)



2f

The titled compound was obtained as pale yellow liquid. Yield= 172 mg, 94%. The crude product was purified by silica-gel column chromatography (60% EtOAc/Hexane); R_f= 0.22. **IR** (neat, cm^{-1}): 3386, 2904, 2359, 1975, 1671, 1583, 1426, 1311, 1246, 1103, 980, 813, 766**. ^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 7.9 Hz, 2H), 3.04 (s, 3H), 2.61 (s, 3H), 2.43 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 143.9, 135.7, 130.3, 128.9, 45.2, 29.6, 21.6. **HRMS:** Calc. for $C_9H_{14}NOS$ $[M+H]^+$: 184.0796, Obser. 184.0795.

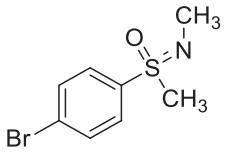
3.7.7 *N*-Methyl-*S*-(4-chlorophenyl)-*S*-methylsulfoximine (2g)



2g

The titled compound was obtained as white solid (Yield= 181 mg, 89%). The crude product was purified by silica-gel column chromatography (80% EtOAc/Hexane); R_f= 0.28.Melting point: 51 °C. **IR** (KBr, cm^{-1}):3564, 3243, 2908, 2801, 2294, 2093, 1914, 1672, 1572, 1474, 1394, 1318, 1246, 1077, 984, 829, 769. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.82–7.78 (m, 2H), 7.53–7.49 (m, 2H), 3.04 (s, 3H), 2.60 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 139.7, 137.5, 130.4, 129.9, 45.1, 29.6. **HRMS:** Calc. for $C_8H_{11}ClNOS$ $[M+H]^+$: 204.025, Obser. 204.0236.

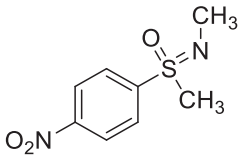
3.7.8 *N*-Methyl-*S*-(4-bromophenyl)-*S*-methylsulfoximine (2h)



2h

The titled compound was obtained as white solid (Yield= 231 mg, 93%). The crude product was purified by silica-gel column chromatography (80% EtOAc/Hexane); R_f= 0.20. Melting point: 58 °C. **IR** (KBr, cm^{-1}): 3191, 2814, 2271, 2083, 1674, 1568, 1462, 1381, 1254, 1198, 1013, 961, 823, 759. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.77–7.72 (m, 2H), 7.72–7.67 (m, 2H), 3.06 (s, 3H), 2.62 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 138.0, 133.0, 130.6, 128.3, 45.1, 29.7. **HRMS:** Calc. for $C_8H_{11}BrNOS$ $[M+H]^+$: 247.9745, Obser. 249.9717.

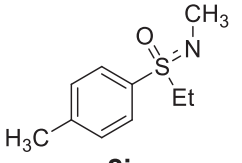
3.7.9 *N*-Methyl-*S*-methyl-*S*-(4-nitrophenyl)sulfoximine (2i)



2i

The titled compound was obtained as yellow solid (Yield= 195 mg, 91%).The crude product was purified by silica-gel column chromatography (80% EtOAc/Hexane); R_f= 0.36. Melting point: 128 °C. **IR** (KBr, cm^{-1}): 3113, 3043, 2908, 2798, 2450, 2087, 2214, 2141, 2081, 2013, 1921, 1819, 1703, 1604, 1516, 1466, 1401, 1343, 1229, 1146, 1081, 996, 854, 771, 682. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.40 (d, *J* = 8.9 Hz, 2H), 8.09 (d, *J* = 8.9 Hz, 2H), 3.12 (s, 3H), 2.65 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 150.7, 145.6, 130.3, 124.8, 44.9, 29.6. **HRMS:** Calc. for $C_8H_{11}N_2O_3S$ $[M+H]^+$: 215.049, Obser. 215.0496.

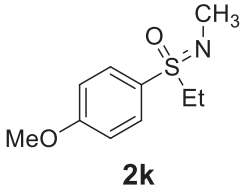
3.7.10 *N*-Methyl-*S*-ethyl-*S*-(4-methylphenyl)sulfoximine (2j)



2j

The titled compound was obtained as transparent liquid. Yield= 181 mg, 92%. The crude product was purified by silica-gel column chromatography (80% EtOAc/Hexane); R_f= 0.24. **IR** (neat, cm-1): 3370, 2919, 2811, 2361, 2089, 1660, 1595, 1408, 1234, 1144, 971, 815, 759. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 7.9 Hz, 2H), 3.17-3.08 (m, 2H), 2.63 (s, 3H), 2.42 (s, 3H), 1.19 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 143.8, 133.7, 130.2, 129.7, 50.9, 29.5, 21.6, 7.5. **HRMS:** Calc. for $C_{10}H_{16}NOS$ $[M+H]^+$: 198.0953, Obser. 198.0949.

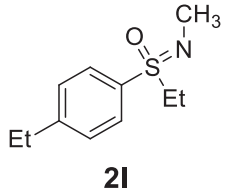
3.7.11 *N*-Methyl-*S*-ethyl-*S*-(4-methoxyphenyl)sulfoximine (2k)



2k

The titled compound was obtained as yellow liquid (Yield= 194 mg, 91%). The crude product was purified by silica-gel column chromatography (100% EtOAc); R_f= 0.28. **IR** (neat, cm^{-1}): 3557, 2929, 2572, 2302, 2084, 1906, 1737, 1589, 1479, 1139, 1098, 1020, 974, 836, 767. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 8.9 Hz, 2H), 7.01 (d, *J* = 8.9 Hz, 2H), 3.86 (s, 3H), 3.18–3.09 (m, 2H), 2.64 (s, 3H), 1.20 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 163.4, 131.8, 127.9, 114.8, 55.7, 51.0, 29.5, 7.6. **HRMS:** Calc. for $C_{10}H_{16}NO_2S$ $[M+H]^+$: 214.0902, Obser. 214.0901.

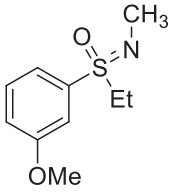
3.7.12 *N*-Methyl-*S*-ethyl-*S*-(4-ethylphenyl)sulfoximine (2l)



2l

The titled compound was obtained as yellow viscous liquid(Yield= 196 mg, 93%).The crude product was purified by silica-gel column chromatography(100% EtOAc); R_f= 0.24. **IR** (neat, cm^{-1}): 3508, 3062, 2932, 2804, 2321, 2099, 1920, 1741, 1646, 1580, 1447, 927, 859, 728, 689. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 3.20-3.11 (m, 2H), 2.74 (q, *J* = 7.6 Hz, 2H), 2.67 (s, 3H), 1.28 (t, *J* = 7.6 Hz, 3H), 1.22 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 150.0, 134.1, 129.9, 129.1, 51.0, 29.6, 29.0, 15.3, 7.6. **HRMS:** Calc. for $C_{11}H_{18}NOS$ $[M+H]^+$: 212.1109, Obser. 212.1097.

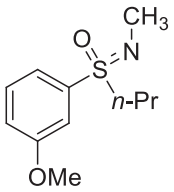
3.7.13 *N*-Methyl-*S*-ethyl-*S*-(3-methoxyphenyl)sulfoximine (2m)



2m

The titled compound was obtained as brown liquid (Yield= 198 mg, 93%). The crude product was purified by silica-gel column chromatography (60% EtOAc/Hexane); R_f= 0.18. **IR** (neat, cm^{-1}): 3547, 2921, 2572, 2302, 2054, 1916, 1737, 1589, 1479, 1139, 1098, 1020, 993, 794, 756, 670. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.47–7.42 (m, 1H), 7.41–7.36 (m, 1H), 7.36–7.32 (m, 1H), 7.13-7.10 (m, 1H), 3.85 (s, 3H), 3.20-3.10 (m, 2H), 2.67 (s, 3H), 1.22 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 160.5, 138.5, 130.5, 121.7, 119.4, 114.1, 55.8, 51.0, 29.6, 7.5. **HRMS:** Calc. for $C_{10}H_{16}NO_2S$ $[M+H]^+$: 214.0902, Obser. 214.0887.

3.7.14 *N*-Methyl-*S*-(3-methoxyphenyl)-*S*-propylsulfoximine (2n)

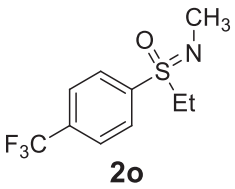


2n

The titled compound was obtained as brown liquid (Yield= 209 mg, 92%). The crude product was purified by silica-gel column chromatography (60% EtOAc/Hexane); R_f= 0.20. **IR** (neat, cm^{-1}): 3347, 2919, 2570, 2302, 1917, 1737, 1640, 1479, 1139, 1098, 1020, 993, 795, 756, 671. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.45 (t, *J* = 7.9 Hz, 1H), 7.42–7.38 (m, 1H), 7.37–7.33 (m, 1H), 7.13-7.10 (m, 1H), 3.86 (s, 3H), 3.15–3.02 (m, 2H), 2.66 (s, 3H), 1.83–1.74 (m, 1H), 1.70-1.62 (m, 1H), 0.94 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 160.5, 139.1, 130.5, 121.6, 119.4, 114.0, 58.4, 55.8, 29.6, 16.6,

13.0. **HRMS:** Calc. for $C_{11}H_{18}NO_2S$ $[M+H]^+$: 228.1058, Obser. 228.1045.

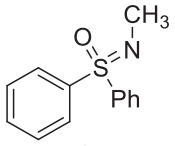
3.7.15 *N*-Methyl-*S*-ethyl-*S*-(4-trifluoromethylphenyl)sulfoximine (2o)



2o

The titled compound was obtained as yellow liquid (Yield= 205 mg, 82%). The crude product was purified by silica-gel column chromatography (60% EtOAc/Hexane); R_f= 0.24. **IR** (neat, cm^{-1}): 2919, 2807, 2300, 2099, 1817, 1611, 1401, 1318, 1241, 1130, 970, 844, 769. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.98 (d, *J* = 8.3 Hz, 2H), 7.83 (d, *J* = 8.3 Hz, 2H), 3.25–3.11 (m, 2H), 2.67 (s, 3H), 1.25 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 141.3, 134.9 (q, *J* = 32.8 Hz), 130.3, 126.7 (q, *J* = 3.2 Hz), 123.5 (q, *J* = 272.8 Hz), 50.9, 29.6, 7.5. **HRMS:** Calc. for $C_{10}H_{13}F_3NOS$ $[M+H]^+$: 252.067, Obser. 252.0653.

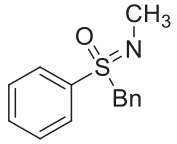
3.7.16 *N*-Methyl-*S*,*S*-diphenylsulfoximine (2p)



2p

The titled compound was obtained as white solid (Yield= 208 mg, 90%). The crude product was purified by silica-gel column chromatography (50% EtOAc/Hexane); R_f= 0.40. Melting point: 89 ºC. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.96-7.94 (m, 4H), 7.51–7.43 (m, 6H), 2.81 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 140.5, 132.5, 129.3, 128.6, 29.7. **HRMS:** Calc. for $C_{13}H_{14}NOS$ $[M+H]^+$: 232.0796, Obser. 232.0794.

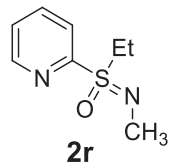
3.7.17 *N*-Methyl-*S*,*S*-dibenzylsulfoximine (2q)



2q

The titled compound was obtained as white solid (Yield= 213 mg, 87%).The crude product was purified by silica-gel column chromatography (60% EtOAc/Hexane); R_f= 0.44. Melting point: 105-108 °C**. IR** (KBr, cm^{-1}) 3067, 2927, 2852, 2359, 2330, 1448, 1246, 1240, 1145, 1100, 1080. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.58-7.54 (m, 3H), 7.44-7.40 (m, 2H), 7.26–7.16 (m, 3H), 7.00 (d, *J* = 7.5 Hz, 2H), 4.37 (s, 2H), 2.73 (s, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 136.4, 133.0, 131.3, 130.0, 129.1, 128.7, 128.4, 126.5, 62.9, 29.9. **HRMS:** Calc. for $C_{14}H_{16}NOS$ $[M+H]^+$: 246.0953, Obser. 246.0949.

3.7.18 *N*-Methyl-*S*-ethyl-*S*-(2-pyridyl)sulfoximine (2r)

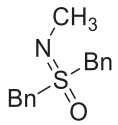


2r

The titled compound was obtained as white solid (Yield= 158 mg, 86%). The crude product was purified by silica-gel column chromatography (100% EtOAc); R_f= 0.34.Melting point: 56 °C. **IR** (KBr, cm^{-1}): 3260, 3014, 2930, 2871, 1662, 1580, 1411, 1319, 1223, 1068, 1014, 990, 784, 754, 512. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.76 (d, *J* = 4.0 Hz, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.95-7.91 (m, 1H), 7.49-7.47 (m, 1H), 3.51 (dq, *J* = 14.8, 7.4 Hz, 1H), 3.34 (dq, *J* = 15.0, 7.5 Hz, 1H), 2.67 (s, 3H), 1.24 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 156.3, 150.7, 137.9, 126.5,

124.8, 47.2, 29.8, 7.1. **HRMS:** Calc. for $C_8H_{13}N_2OS$ $[M+H]^+$: 185.0749, Obser. 185.0733.

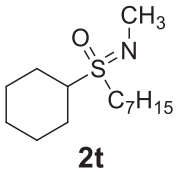
3.7.19 *N*-Methyl-*S*,*S*-dibenzylsulfoximine (2s)



2s

The titled compound was obtained as white solid (Yield= 225 mg, 87%). The crude product was purified by silica-gel column chromatography (60% EtOAc/Hexane); R_f= 0.32.Melting point: 96-98 °C. **IR** (KBr, cm^{-1}): 3275, 3100, 3062, 3010, 2996, 2908, 1497,1440, 1416, 1246, 1136, 1053, 1037, 760, 698, 580. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.39–7.34 (m, *J* = 4.9, 4.2 Hz, 10H), 4.21–4.11 (m, 4H), 2.76 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 131.1, 128.9, 128.9, 128.8, 57.9, 29.7. **HRMS:** Calc. for $C_{15}H_{18}NOS$ $[M+H]^+$: 260.1109, Obser. 260.1114.

3.7.20 *N*-Methyl-*S*-cyclohexyl-*S*-heptylsulfoximine (2t)

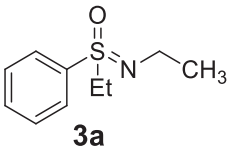


2t

The titled compound was obtained as yellow viscous liquid. (Yield= 212 mg, 82%). The crude product was purified by silica-gel column chromatography (40% EtOAc/Hexane); R_f= 0.44. **IR** (neat, cm^{-1}): 3530, 2924, 2875, 2811, 2313, 1981, 1640, 1450, 1133, 958, 860, 770, 670. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 2.99–2.84 (m, 3H), 2.78 (s, 3H), 1.90 (d, *J* = 11.6 Hz, 2H), 1.77-1.69 (m, 3H), 1.54-1.45 (m, 3H), 1.41–1.21 (m, 12H), 0.86 (t, *J* = 6.7 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 61.1, 48.4, 31.6, 28.9, 28.9, 26.4,

26.2, 25.8, 25.7, 25.4, 22.8, 22.6. **HRMS:** Calc. for $C_{14}H_{30}NOS$ $[M+H]^+$: 260.2048, Obser. 260.2045.

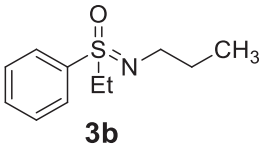
3.7.21 *N*-Ethyl-*S*-ethyl-*S*-phenylsulfoximine (3a)



3a

The titled compound was obtained as transparent oil (Yield= 177 mg, 90%). The crude product was purified by silica-gel column chromatography(40% EtOAc/Hexane); R_f= 0.30. **IR** (neat, cm^{-1}): 3061, 2975, 2930, 2873, 2818, 1644, 1445, 1249, 1151. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.95–7.75 (m, 2H), 7.64–7.57 (m, 1H), 7.57–7.49 (m, 2H), 3.23–3.10 (m, 2H), 3.03 (dq, *J* = 12.3, 7.2 Hz, 1H), 2.87 (dq, *J* = 12.3, 7.2 Hz, 1H), 1.18 (dt, *J* = 14.4, 7.3 Hz, 6H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 137.9, 132.9, 129.6, 129.4, 51.0, 38.6, 18.5, 7.6. **HRMS:** Calc. for $C_{10}H_{15}NOS$ $[M+H]^+$: 198.0953, Obser. 198.0926.

3.7.22 *N*-Propyl-*S*-ethyl-*S*-phenylsulfoximine (3b)

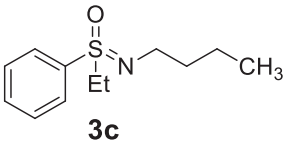


3b

The titled compound was obtained as transparent oil (Yield= 192 mg, 91%). The crude product was purified by silica-gel column chromatography (40% EtOAc/Hexane); R_f= 0.34. **IR** (neat, cm^{-1}): 3073, 2995, 2934, 2870, 2820, 1640, 1445, 1249, 1140. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 7.0 Hz, 2H), 7.57 (dd, *J* = 8.4, 6.2 Hz, 1H), 7.52 (t, *J* = 7.3 Hz, 2H), 3.21–3.08 (m, 2H), 2.91 (dt, *J* = 12.1, 7.2 Hz, 1H), 2.74 (dt, *J* = 12.1, 7.2 Hz, 1H), 1.54 (h, *J* = 7.3 Hz, 2H), 1.18

(t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 137.9, 132.8, 129.6, 129.4, 50.9, 45.7, 26.2, 11.9, 7.6. **HRMS:** Calc. for $C_{11}H_{17}NOS$ $[M+H]^+$: 212.1109, Obser. 212.1081.

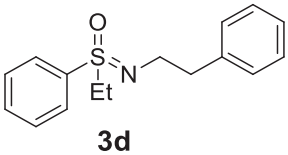
3.7.23 *N*-Butyl-*S*-ethyl-*S*-phenylsulfoximine (3c)



3c

The titled compound was obtained as pale yellow oil (Yield= 205 mg, 91%). The crude product was purified by silica-gel column chromatography(50% EtOAc/Hexane); R_f= 0.26. **IR** (neat, cm-1): 3831, 3404, 2928, 2674, 2097, 1658, 1581, 1531, 1447, 1368, 1085. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.84 (d, *J* = 7.4 Hz, 2H), 7.66–7.46 (m, 3H), 3.16 (m, 2H), 2.96 (dt, *J* = 12.3, 7.2 Hz, 1H), 2.79 (dt, *J* = 12.2, 7.2 Hz, 1H), 1.56-1.50 (m, 2H), 1.33 (h, *J* = 7.3 Hz, 2H), 1.19 (t, *J* = 7.4 Hz, 3H), 0.85 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 138.0, 132.8, 129.6, 129.4, 51.0, 43.6, 35.2, 20.5, 14.0, 7.6. **HRMS:** Calc. for $C_{12}H_{20}NOS$ $[M+H]^+$: 226.1266, Obser. 226.1273.

3.7.24 *N*-Ethylphenyl-*S*-ethyl-*S*-phenylsulfoximine (3d)

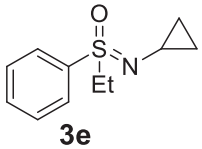


3d

The titled compound was obtained as pale yellow viscous liquid (Yield= 256 mg, 94%). The crude product was purified by silica-gel column chromatography (60% EtOAc/Hexane); R_f= 0.32. **IR** (neat, cm-1): 3631, 3444, 2928, 2676, 2087, 1658, 1581, 1521, 1447, 1368, 1085 976,

863, 782, 742, 688. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.71 (d, *J* = 7.2 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.26–7.22 (m, 2H), 7.18 (d, *J* = 7.1 Hz, 3H), 3.26 (dt, *J* = 12.0, 7.9 Hz, 1H), 3.20-3.11 (m, 2H), 3.02 (dt, *J* = 12.0, 7.9 Hz, 1H), 2.93–2.83 (m, 2H), 1.20 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 140.7, 137.7, 132.9, 129.7, 129.4, 129.2, 128.3, 126.1, 51.1, 45.8, 39.8, 7.7. **HRMS:** Calc. for $C_{16}H_{20}NOS$ $[M+H]^+$: 274.1266, Obser. 274.1263.

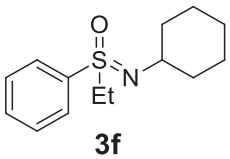
3.7.25 *N*-Cylcopropyl-*S*-ethyl-*S*-phenylsulfoximine (3e)



3e

The titled compound was obtained as transparent viscous liquid (Yield= 198 mg, 95%). The crude product was purified by silica-gel column chromatography (60% EtOAc/Hexane); R_f= 0.42. **IR** (neat, cm^{-1}): 3577, 3391, 3054, 3017, 2905, 2870, 2814, 2673, 1990, 1730, 1640, 863, 793, 742, 690. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.90 (d, *J* = 7.8 Hz, 2H), 7.63–7.59 (m, 1H), 7.56 (t, *J* = 7.4 Hz, 2H), 3.25-3.11 (m, 2H), 2.38 (tt, *J* = 7.4, 4.0 Hz, 1H), 1.19 (t, *J* = 7.4 Hz, 3H), 0.61-0.56 (m, 1H), 0.51–0.43 (m, 1H), 0.42–0.35 (m, 2H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 138.2, 133.0, 129.5, 129.4, 50.7, 26.2, 7.4, 7.2, 6.4. **HRMS:** Calc. for $C_{11}H_{16}NOS$ $[M+H]^+$: 210.0953, Obser. 210.0946.

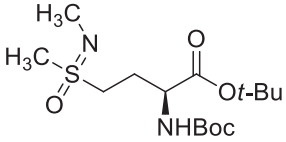
3.7.26 *N*-Cylcohexyl-*S*-ethyl-*S*-phenylsulfoximine (3f)



3f

The titled compound was obtained as transparent liquid (Yield= 228 mg, 91%). The crude product was purified by silica-gel column chromatography (40% EtOAc/Hexane); R_f= 0.38. **IR** (neat, cm^{-1}): 3059, 2940, 2852, 2359, 2331, 1448, 1247, 1130. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.86 (d, *J* = 7.4 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 2H), 3.18-3.06 (m, 2H), 2.91-2.85 (m, 1H), 1.88-1.86 (m, 1H), 1.70–1.63 (m, 3H), 1.46–1.21 (m, 3H), 1.17-1.14 (m, 4H), 1.12–1.05 (m, 2H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 139.2, 132.7, 129.5, 129.2, 54.0, 51.2, 37.9, 36.7, 25.8, 25.6, 25.4, 7.6. **HRMS:** Calc. for $C_{14}H_{22}NOS$ $[M+H]^+$: 252.1422, Obser. 252.1419.

3.7.27 L-Methionine sulfoximine derivative (4a)

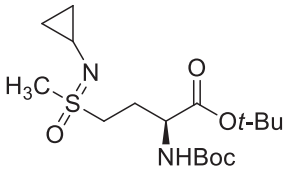


4a

The titled compound was obtained as white semi-solid (Yield= 319 mg, 91%). The crude product was purified by silica-gel column chromatography (20% MeOH/$CHCl_3$); R_f= 0.48. **IR** (neat, cm^{-1}): 3845, 3322, 2941, 2817, 2641, 2320, 2082, 1717, 1529, 1446, 1223, 1148, 1047, 853, 744. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 5.31 (m, 1H), 4.28–4.20 (m, 1H), 3.26–3.00 (m, 2H), 2.90 (s, 3H), 2.77 (d, *J* = 3.4 Hz, 3H), 2.37-2.28 (m, 1H), 2.14–2.04 (m, 1H), 1.47 (s, 9H), 1.43 (s, 9H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 170.6,

155.6, 83.1, 83.1, 80.4, 52.8, 50.0, 39.0, 39.0, 29.2, 29.2, 28.4, 28.1, 27.0. **HRMS:** Calc. for $C_{15}H_{31}N_2O_5S$ $[M+H]^+$: 351.1954, Obser. 351.1964.

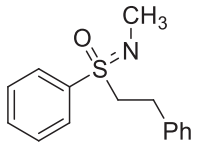
3.7.28 L-Methionine sulfoximine derivative (4b)



4b

The titled compound was obtained as white semi-solid (Yield= 334 mg, 89%).The crude product was purified by silica-gel column chromatography (20% MeOH/$CHCl_3$); R_f= 0.44. **IR** (neat, cm^{-1}): 3885, 3342, 2949, 2661, 2320, 2082, 1719, 1530, 1440, 1223, 1148, 1047, 844, 746. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 5.38 (dd, *J* = 42.7, 6.7 Hz, 1H), 4.23 (s, 1H), 3.32–3.02 (m, 2H), 2.94 (d, *J* = 7.8 Hz, 3H), 2.57–2.49 (m, 1H), 2.40-2.33 (m, 1H), 2.15-2.06 (m, 1H), 1.89 (s, 1H), 1.46 (s, 9H), 1.43 (s, 9H), 0.55 (dt, *J* = 7.4, 4.2 Hz, 2H), 0.46 (dt, *J* = 6.2, 3.2 Hz, 2H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 170.4, 155.4, 82.9, 80.1, 52.7, 50.4, 50.2, 39.3, 29.6, 28.4, 28.2, 27.9, 25.6, 6.7. **HRMS:** Calc. for $C_{17}H_{33}N_2O_5S$ $[M+H]^+$: 377.2110, Obser. 377.2138.

3.7.29 *N*-Methyl-*S*-phenyl-*S*-(2-phenylethyl) sulfoximine (5a)



5a

The titled compound was obtained as transparent oil (Yield= 222 mg, 86%).The crude product was purified by silica-gel column chromatography (40% EtOAc/Hexane); R_f= 0.28. **IR** (neat, cm^{-1}): 3033, 2942, 2813, 2318, 2106, 1743, 1597, 1449, 1224, 1151, 971, 843, 746, 691. **^{1}H NMR** (500 MHz,

Chloroform-*d*) δ 7.97–7.90 (m, 2H), 7.70–7.59 (m, 3H), 7.32–7.21 (m, 3H), 7.18–7.12 (m, 2H), 3.50 (m, 1H), 3.38 (m, 1H), 3.17 (m, 1H), 3.01 (m, 1H), 2.76 (s, 3H). **^{13}C NMR** (125 MHz, Chloroform-*d*) δ 137.9, 137.6, 133.1, 129.6, 129.5, 128.9, 128.5, 126.9, 57.8, 29.6, 28.9. **HRMS:**Calc. for $C_{17}H_{33}N_2O_5S$ $[M+H]^+$: 260.1104, Obser. 260.1106.

3.8 SPECTRAL DATA FOR FEW PRODUCTS

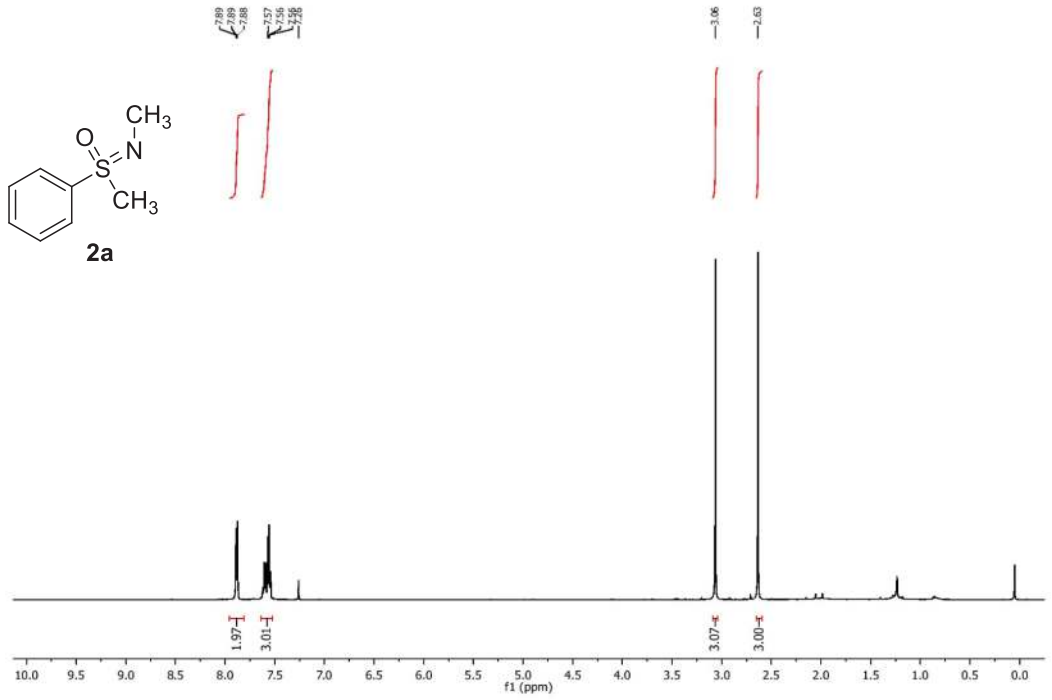


Figure 3.2 ^{1}H NMR of *N,S*-dimethyl-*S*-phenylsulfoximine (**2a**)

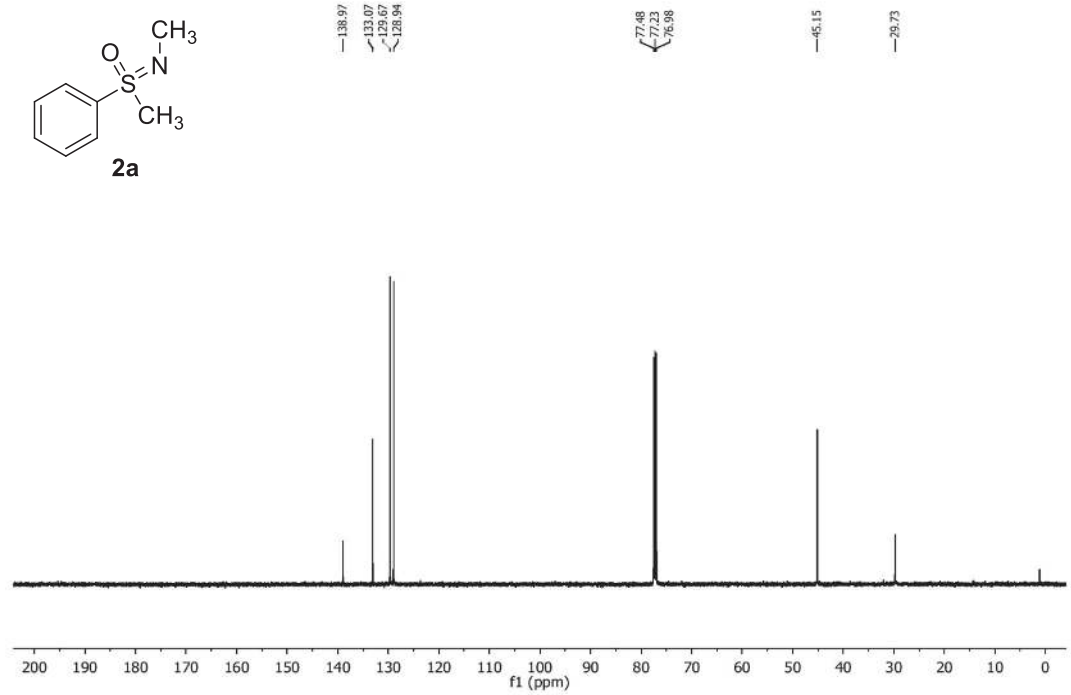


Figure 3.3 ^{13}C NMR of *N,S*-dimethyl-*S*-phenylsulfoximine (**2a**)

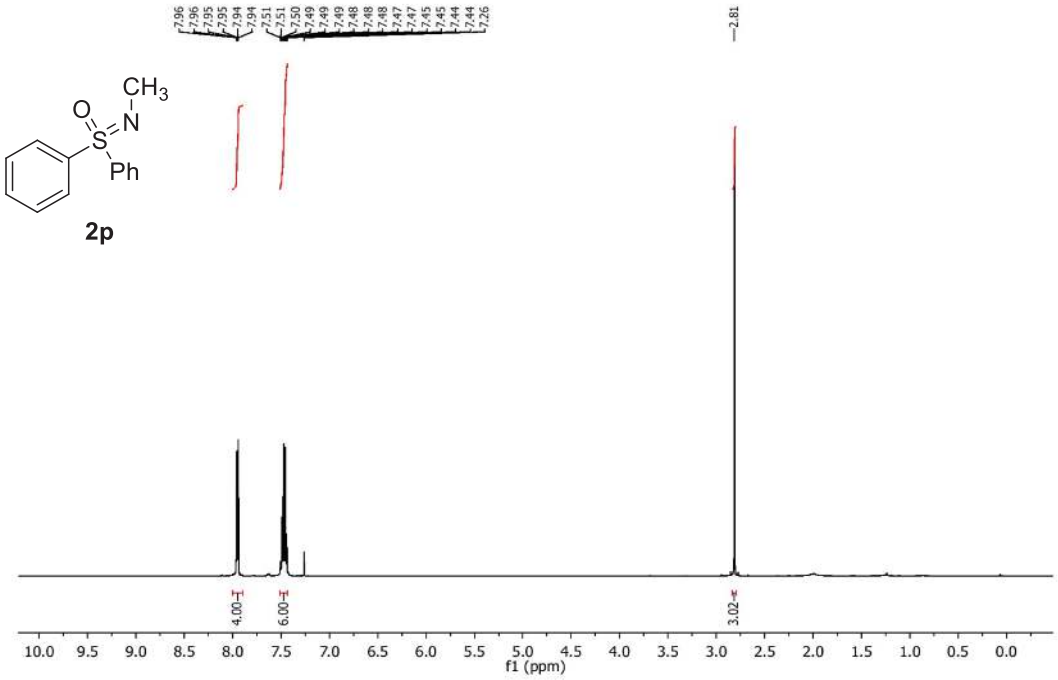


Figure 3.4 ^{1}H NMR of *N*-methyl-*S,S*-diphenylsulfoximine (**2p**)

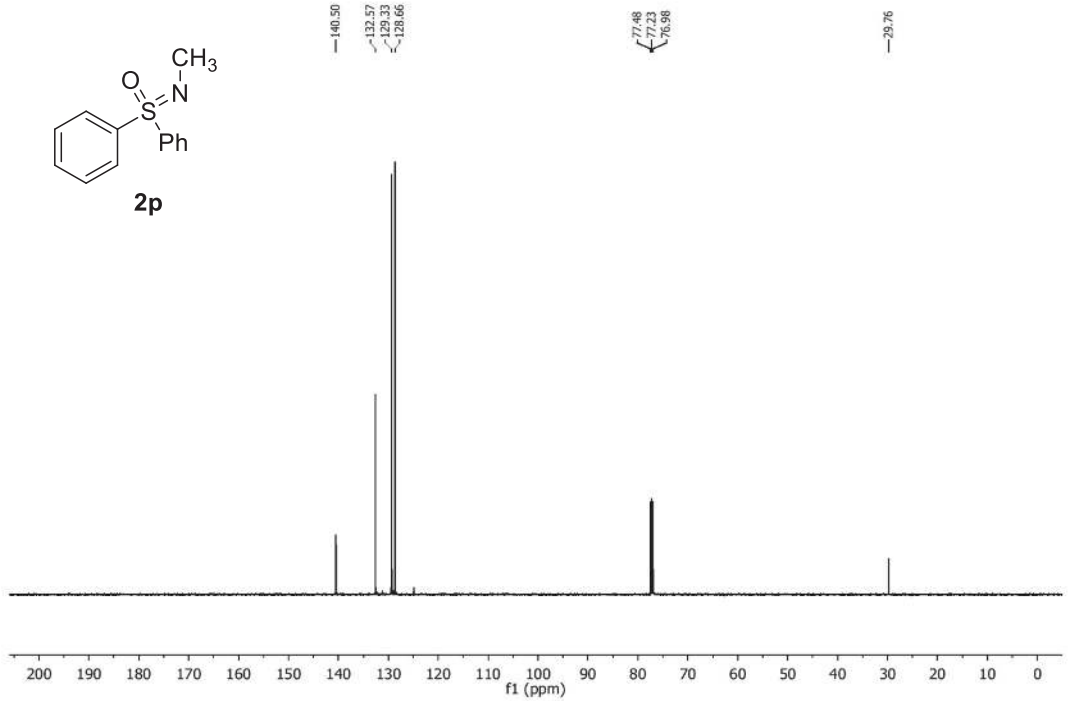


Figure 3.5 ^{13}C NMR of *N*-methyl-*S,S*-diphenylsulfoximine (**2p**)

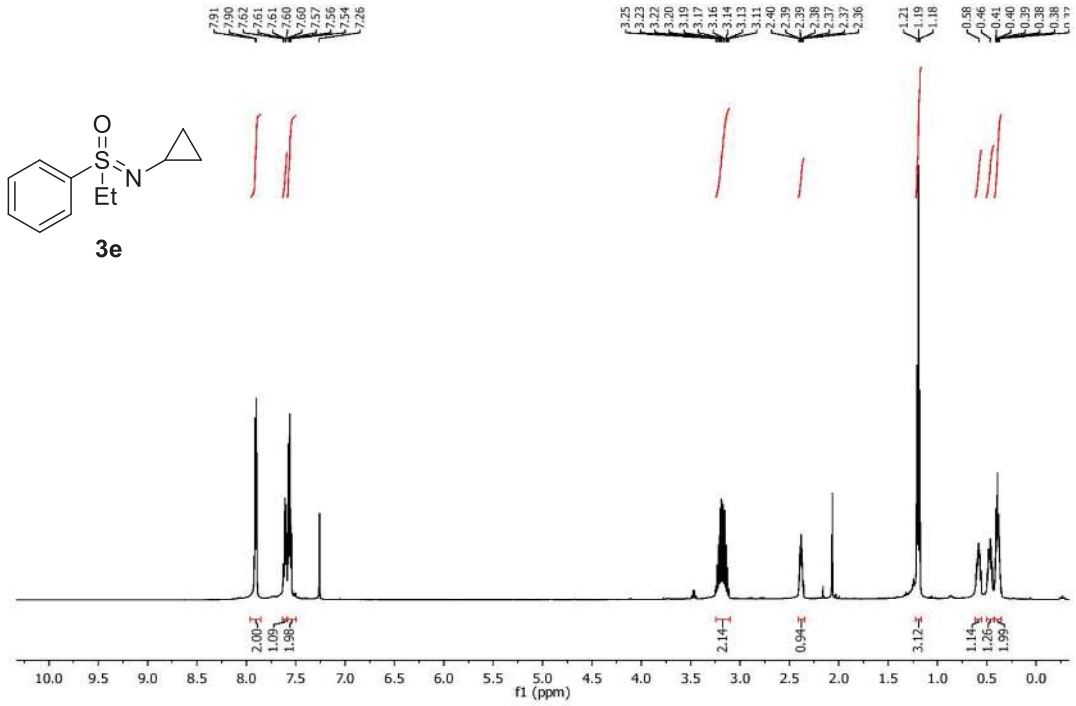


Figure 3.6 ^{1}H NMR of *N*-cylcopropyl-*S*-ethyl-*S*-phenylsulfoximine (**3e**)

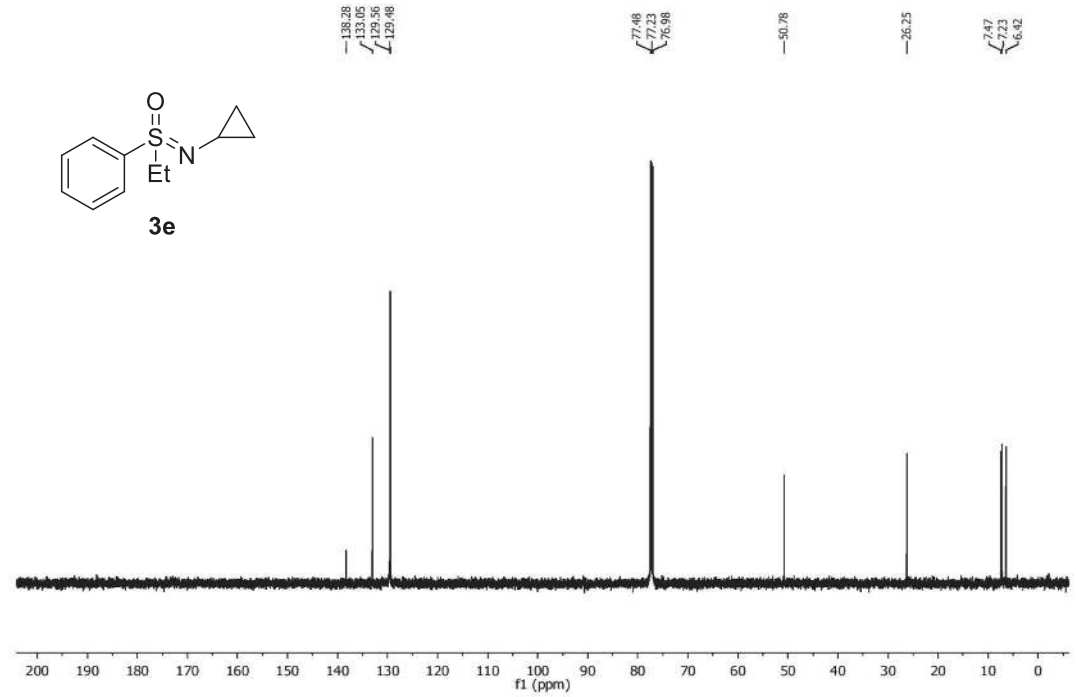


Figure 3.7 ^{13}C NMR of *N*-cylcopropyl-*S*-ethyl-*S*-phenylsulfoximine (**3e**)

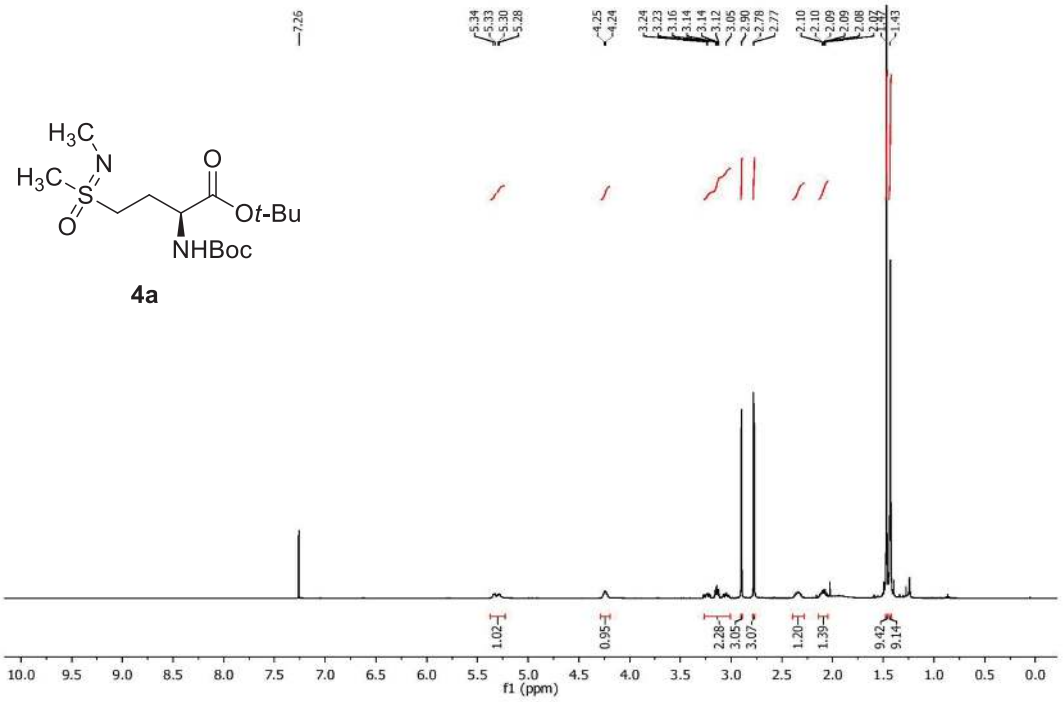


Figure 3.8 ^{1}H NMR of L-Methionine sulfoximine derivative (**4a**)

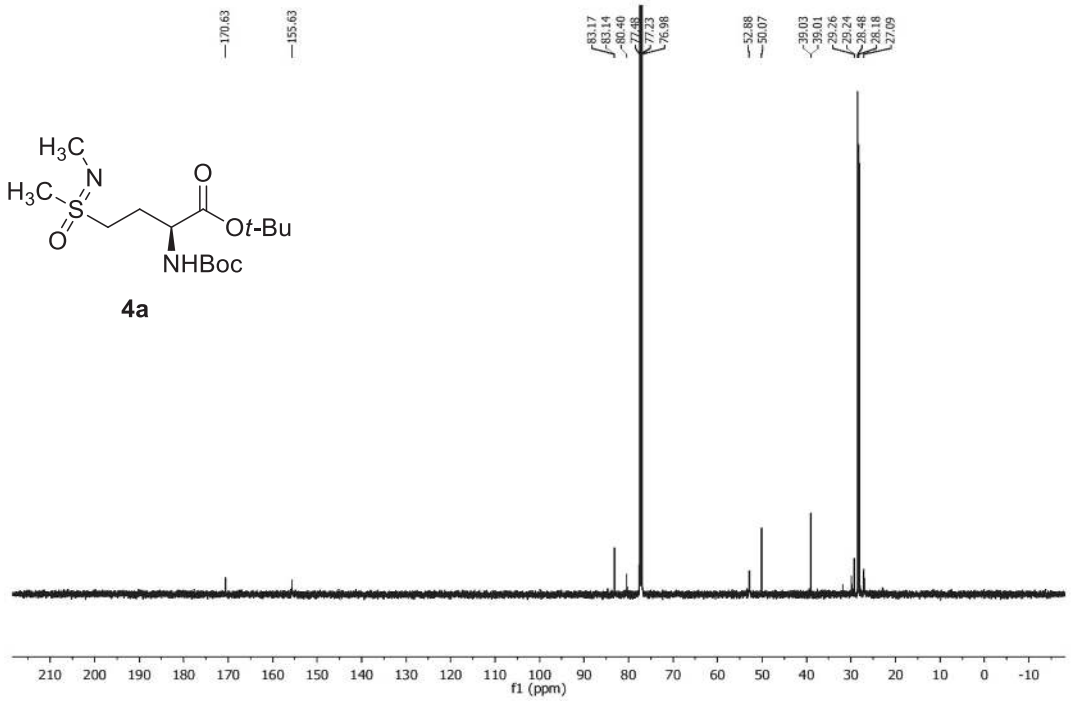


Figure 3.9 ^{13}C NMR of L-Methionine sulfoximine derivative (**4a**)

3.9 REFERENCES

[1] (a) M. Reggelin, and C. Zur, "Sulfoximines: structures, properties and synthetic applications," *Synthesis*, **1**(2000) 1-64. (b) W. R. Dong, K. Parthasarathy, Y. Cheng, F. F. Pan, and C. Bolm, "Hydroarylations of heterobicyclic alkenes through rhodium catalyzed directed C-H functionalizations of *S*-aryl sulfoximines," *Chemistry: A European Journal*, **20**(2014) 15732-15736. (c) K. Ghosh, R. K. Rit, E. Ramesh, and A. K. Sahoo, "Ruthenium-catalyzed hydroarylation and one-pot two fold unsymmetrical C-H functionalization of arenes," *Angewandte Chemie International Edition*, **55**(2016) 7821-7825. (d) K. Raghuvanshi, D. Zell, and L. Ackermann, "Ruthenium(II)-catalyzed C-H oxygenations of reusable sulfoximine benzamides," *Organic Letters*, **19**(2017) 1278-1281. (e) V. Bizet, R. Kowalczyk, and C. Bolm, "Fluorinated sulfoximines: syntheses, properties and applications," *Chemical Society Reviews*, **43**(2014) 2426-2438. (f) M. Frings, I. Thome, and C. Bolm, "Synthesis of chiral sulfoximine-based thioureas and their application in asymmetric organocatalysis," *Beilstein Journal of Organic Chemistry*, **8**(2012) 1443-1451. (g) C. Bolm, Asymmetric synthesis with chemical and biological methods, WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim, 2007. (h) S. Noritake, N. Shibata, S. Nakamura, T. Toru, and M. Shiro, "Fluorinated johnson reagent for transfer-trifluoromethylation to carbon nucleophiles," *European Journal of Organic Chemistry*, (2008) 3465–3468.

[2] U. Lucking, "Sulfoximines: A neglected opportunity in medicinal chemistry," *Angewandte Chemie International Edition*, **52**(2013) 9399-9408.

[3] (a) C. Moessner, and C. Bolm, "$Cu(OAc)_2$-catalyzed *N*-arylations of sulfoximines with aryl boronic acids", *Organic Letters*, **7**(2005) 2667-2669. (b) C. A. Dannenberg, L. Fritze, F. Krauskopf, and C. Bolm, "Access to *N*-cyanosulfoximines by transition metal-free iminations of sulfoxides," *Organic Biomolecular Chemistry*, **15**(2017) 1086-1090. (c) F. Teng, J. Cheng, and C. Bolm, "Silver-mediated *N*-trifluoromethylation of sulfoximines," *Organic Letters*, **17**(2015) 3166-3169. (d) L. Wang, H. Huang, D. L. Priebbenow, F.-F. Pan, and C. Bolm, "Copper-catalyzed oxidative cross-coupling of sulfoximines and alkynes," *Angewandte Chemie International Edition*, **52**(2013) 3478-3480. (e) F. Teng, J. T. Yu, Y. Jiang, H. T. Yang, and J. Cheng, "A copper-mediated oxidative *N*-cyanation reaction," *Chemical Communications*, **50**(2014) 8412-8415. (f) P. J. Harvison, and T. I. Kalman, "Synthesis and biological activity of novel folic acid analogues: pteroyl-*S*-alkylhomocysteine sulfoximines", *Journal Medicinal Chemistry*, **35**(1992) 1227-1233. (g) H. Zhu, J. T. Yu, and J. Cheng, "Copper-catalyzed *N*-thioetherification of sulfoximines using disulfides", *Chemical Communications*, **52**(2016) 11908-11911. (h) C. Pimpasri, L. Sumunnee, and S. Yotphan, "Copper-catalyzed oxidative decarboxylative coupling of α-keto acids and sulfoximines,"*Organic and Biomolecular Chemistry*, **15**(2017) 4320-4327. (i) F. Teng, S. Sun, Y. Jiang, J. T. Yu, and J. Cheng, "Copper-catalyzed oxidative $C(sp^3)$-H/N-H coupling of sulfoximines and amides with simple alkanes *via* radical process", *Chemical Communications*, **51**(2015) 5902-5905.

[4] (a) F. W. Goldberg, J. G. Kettle, J. Xiong, and D. G. Lin, "General synthetic strategies towards *N*-alkyl sulfoximine building blocks for medicinal chemistry and the use of dimethylsulfoximine as a versatile precursor," *Tetrahedron*, **70**(2014) 6613-6622. (b) D. P. Walker, M. P. Zawistoski, M. A. McGlynn, J. C. Li, D. W. Kung, P. C. Bonnette, A. Baumann, L. Buckbinder, J. A. Houser, J. Boer, A. Mistry, S. Han, L. Xing, and A. G. -Perez, "Sulfoximine-substituted trifluoromethylpyrimidine analogs as inhibitors of proline-rich tyrosine kinase 2 (PYK2) show reduced hERG activity," *Bioorganic and Medicinal Chemistry Letters*, **19**(2009) 3253-3258. (c) M. Frings, C. Bolm, A. Blum, and C. Gnamm, "Sulfoximines from a medicinal chemist's perspective: physicochemical and *in vitro* parameters relevant for drug discovery," *European Journal of Medicinal Chemistry*, **126**(2017) 225-245.

[5] (a) H. -J. Gais, Asymmetric synthesis with chemical and biological methods, WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim, 2007. (b) F. Lemasson, H. J. Gais, J. Runsink, and G. Raabe, "Synthesis of phosphanylsulfoximines through phospha-michael reaction of alkenylsulfoximines and their evaluation as chiral bidentate 1,5-*N*,*P* ligands for palladium in asymmetric allylic alkylation," *European Journal of Organic Chemistry*, (2010) 2157-2175. (c) P. Lamers, D. L. Priebbenow, and C. Bolm, "Iron-catalyzed acylative dealkylation of *N*-alkylsulfoximines," *European Journal of Organic Chemistry*, (2015) 5594-5602.

[6] (a) M. L.Boys, E. W. Collington, H. Finch, S. Swanson, and J. F. Whitehead, "α-Fluoromethyl-*N*-methyl-phenylsulphoximine: A new fluoromethylenation reagent," *Tetrahedron Letters*, **29**(1988) 3365-3368. (b) G. K. S. Prakash, Z. Zhang, F. Wang, C. F. Ni, and G. A. Olah, "*N,N*-Dimethyl-*S*-difluoromethyl-*S*-phenylsulfoximinium tetrafluoroborate: A versatile electrophilic difluoromethylating reagent," *Journal of Fluorine Chemistry*, **132**(2011) 792-798.

[7] C. R. Johnson, C. W. Schroeck, and J. R. Shanklin, "The mechanism of nucleophilic alkylidene transfer by sulfonium and oxo sulfonium ylides," *Journal of American Chemical Society*, **95**(1973) 7424-7431.

[8] F. Teng, J. Cheng, and J. T. Yu, "Copper-catalyzed *N*-methylation/ethylation of sulfoximines," *Organic and Biomolecular Chemistry*, **13**(2015) 9934-9937.

[9] (a) D. G. Hall, Boronic acids: Preparation and applications in organic synthesis, medicine and materials Wiley-VCH Verlag GmbH & Co. KGaA, 2011. (b) E. Fernandez, and A. Whiting, Synthesis and application of organoboron compounds, Springer, New York, 2015.

[10] (a) I. Gonzalez, J. Mosquera, C. Guerrero, R. Rodriguez, and J. Cruces, "Selective mono-methylation of anilines by $Cu(OAc)_2$-promoted cross-coupling with $MeB(OH)_2$," *Organic Letters*, **11**(2009) 1677-1680. (b) C. E. Jacobson, N. M. -Munoz, and D. J. Gorin, "Aerobic copper-catalyzed *O*-methylation with methylboronic acid,"*Journal of Organic Chemistry*, **80**(2015) 7305-7310. (c) R. Yamashita, A. Sakakura, and K. Ishihara, "Primary alkylboronic acids as highly active catalysts for the dehydrative amide condensation of α-hydroxycarboxylic acids," *Organic Letters*, **15**(2013) 3654-3657. (d) S. Benard, L. Neuville, and J. P. Zhu, "Copper-promoted *N*-cyclopropylation of anilines and amines by cyclopropylboronic acid," *Chemical Communications*, **46**(2010) 3393-3395. (e) L.

M. M. -Quiroz, K. W. Shimkin, S. Rezazadeh, R. A. Kozlowski, and D. A. Watson, "Copper-catalyzed amidation of primary and secondary alkyl boronic esters," *Chemistry: A European Journal*, **22**(2016) 15654-15658. (f) S. A. Rossi, K. W. Shimkin, Q. Xu, L. M. M. -Quiroz, and D. A. Watson, "Selective formation of secondary amides *via* the copper-catalyzed cross-coupling of alkylboronic acids with primary amides," *Organic Letters*, **15**(2013) 2314-2317. (g) T. Tsuritani, N. A. Strotman, Y. Yaimamoto, M. Kawasaki, N. Yasuda, and T. Maset, "*N*-cyclopropylation of indoles and cyclic amides with copper (II) reagent," *Organic Letters*, **10**(2008) 1653-1655. (h) M. Larrosa, C. Guerrero, R. Rodriguez, and J. Cruces, "Selective copper-promoted cross-coupling of aromatic amines with alkylboronic acids," *Synlett*, (2010) 2101-2105. (i) S. Sueki, and Y. Kuninobu, "Copper-catalyzed *N*- and *O*-alkylation of amines and phenols using alkylborane reagents," *Organic Letters*, **15**(2013) 1544-1547.

[11] In general, *N*-arylation reactions with arylboronic acid require catalytic amount of copper salts in the absence of any base. Reaction also proceeds at room temperature in methanol (See ref 3a). On the other hand, *N*-alkylation reaction with alkylboronic acid requires equivalent amount of copper salts with base or ligands (see ref. 10a). Reaction proceeds only in aprotic solvents at high temperature.

[12] (a) C. R. Johnson, and O. M. Lavergne, "Alkylation of sulfoximines and related compounds at the imino nitrogen under phase-transfer conditions," *Journal of Organic Chemistry*, **58**(1993) 1922-1923. (b) T. R. Williams, and D. J. Cram, "Stereochemistry of sulfur compounds. IV. New ring systems of carbon, nitrogen, and chiral sulfur," *Journal of Organic Chemistry*, **38**(1973) 20-26. (c) C. Bolm, C. P. R. Hackenberger, O. Simic, M. Verrucci, D. Muller, and F. Bienewald, "A mild synthetic procedure for the preparation of *N*-alkylated sulfoximines," *Synthesis*, (2002) 879-887. (d) C. M. M. Hendriks, R. A. Bohmann, M. Bohlem, and C. Bolm, "*N*-Alkylations of *NH*-sulfoximines and *NH*-sulfondiimines with alkyl halides mediated by potassium hydroxide in dimethyl sulfoxide," *Advanced Synthesis and Catalysis*, **356**(2014) 1847-1852.

[13] T. T. Talele, "The "Cyclopropyl fragment" is a versatile player that frequently appears in preclinical/clinical drug molecules," *Journal of Medicinal Chemistry*, **59**(2016) 8712-8756.

[14] (a) W. S. A. Brusilow, and T. J. Peters, "Therapeutic effects of methionine sulfoximine in multiple diseases include and extend beyond inhibition of glutamine synthetase," *Expert Opinion on Therapeutic Targets*, **21**(2017) 461-469. (b) L. Buglioni, V. Bizet, and C. Bolm, "Methionine and buthionine sulfoximines: Syntheses under mild and safe imidation/oxidation conditions," *Advanced Synthesis and Catalysis*, **356**(2014) 2209-2213.