CHAPTER-2

Copper Catalyzed *N*-Arylation of Sulfoximines with Aryldiazonium Salts in the Presence of DABCO Under Mild Conditions

2.1 Introduction

Sulfoximines are aza-analogues of sulfones that have been considered as an important pharmacophore in drug discovery (Figure **2.1**) [1-5]. Currently, few sulfoximine compounds are in the different phases of clinical trials for the treatment of different diseases including cancer [7]. On the other hand, sulfoximines were also explored as building blocks, chiral ligands and auxiliaries, organocatalysts, directing groups for *CH*-activation, etc. in organic synthesis [6-15].

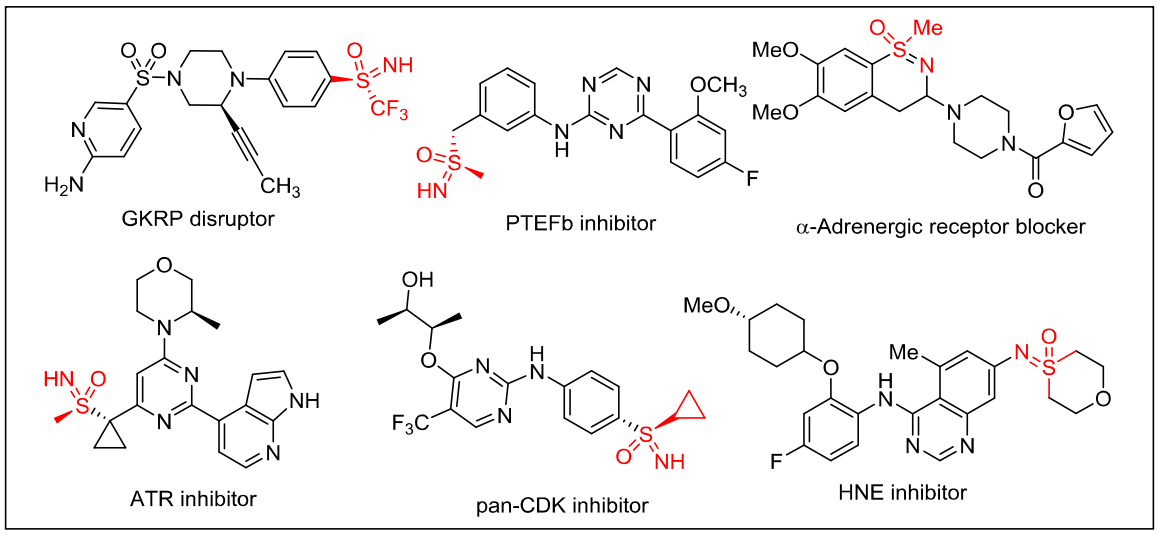
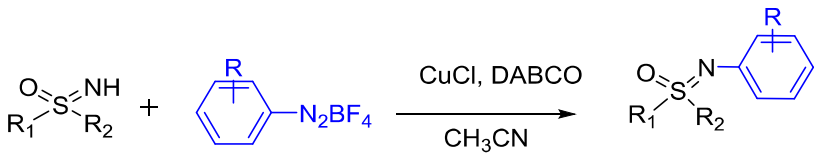


Figure 2.1: Structures of some biologically important sulfoximines.

From synthetic as well as biological perspectives, *N*-functionalization of sulfoximine received significant interest over the decades [1-16]. In this context, *N*-arylation of sulfoximine has been reported with aryl halides, arylboronic acids, diaryliodonium salts, aryl sulfonates, aryl siloxanes, etc., in the presence of metal catalysts [17-31]. However, most of these developed methods require harsh reaction conditions, expensive ligands, longer reaction time, etc. Our group also recently reported a copper catalyzed *N*-arylation of sulfoximimes with different arylboronic acids [32]. This method provides clean access to

various *N*-aryl sulfoximines, including sterically hindered *N*-aryl sulfoximines as well as biologically relevant *N*-aryl L-methionine sulfoximines, in good to excellent yields. However, arylboronic acids are relatively expensive, hence the development of alternative and complementary method, is of great interest. Aryldiazonium salts are highly useful aryl donors that have been utilized extensively in many palladium catalyzed cross-coupling reactions in the place of aryl halides and arylboronic acids [33-35]. In this context, our group recently reported a palladium catalyzed aryldizonium salts mediated stereo-controlled synthesis of *C*-aryl glycosides from glycals at room temperature [37]. Besides C-C coupling reactions, aryldizonium salts were also explored in many C-S bond forming reactions [38-42]. In contrast, their applications in C-N bond forming reactions are underexplored [43-45]. In this context, here we investigated a copper catalyzed *N*-arylation of sulfoximines using aryldiazonium salts under mild conditions (Scheme **2.1**).



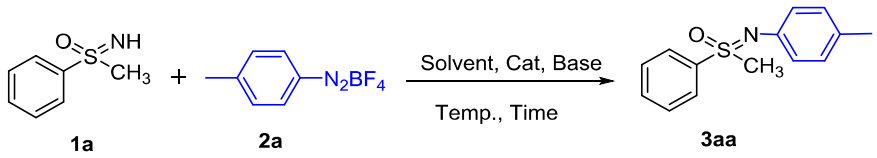
Scheme 2.1: *N*-Arylation of sulfoximines using aryldiazonium tetrafluoroborates.

2.2 Results and Discussion

At the outset, the optimization of the reaction condition was investigated using *(S,S)*-methylphenyl sulfoximine (**1a**) and 4-methylbenzenediazonium tetrafluoroborate (**2a**) as model substrates. Initially, the reaction was tested in different solvents including methanol, dimethyl sulfoxide (DMSO) and acetonitrile (ACN) at 30 °C for 10 hours in the absence of any catalyst or additives (Table **2.1,** entry **1**). However, no reaction was observed. Hence, the optimization was performed with various copper (I) and copper (II) catalysts in acetonitrile

(Table **2.1,** entries **2-7**). Among them, CuCl showed better activity by providing the desired product **3aa** in 36% yield.

Table 2.1: Optimization of the reaction conditions for *N*-arylation of sulfoximine.[a,b]



1a 2a 3aa

Entry	Solvent	Catalyst (10 mol%)	Base (1.0 eq.)	Temp. (°C)	Time (h)	Yield[b] (%)
1	MeOH/ DMSO/ ACN	-	-	30	10	ND
2	Acetonitrile	CuOAc	-	30	10	13
3	Acetonitrile	CuBr	-	30	10	10
4	Acetonitrile	CuCl	-	30	10	36
5	Acetonitrile	CuI	-	30	10	17
6	Acetonitrile	$CuCl_2$	-	30	10	~10
7	Acetonitrile	$Cu(OAc)_2$	-	30	10	~10
8	Acetonitrile	CuCl	K_2CO_3	30	10	40
9	Acetonitrile	CuCl	Cs_2CO_3	30	10	47
10	Acetonitrile	CuCl	Pyridine	30	10	41
11	Acetonitrile	CuCl	DMAP	30	10	45
12	Acetonitrile	CuCl	Et_3N	30	10	43
13	Acetonitrile	CuCl	DBU	30	10	40
14	Acetonitrile	CuCl	DABCO	30	10	51
15	Acetonitrile	CuCl	DABCO	45	6	63
16	**Acetonitrile**	**CuCl**	**DABCO**	**60**	**6**	**88**
17	Acetonitrile	CuCl	DABCO	75	6	81
18	Water	CuCl	DABCO	60	6	ND
19	MeOH	CuCl	DABCO	60	6	30
20	DMSO	CuCl	DABCO	60	6	69
21	Dioxane	CuCl	DABCO	60	6	72
22	Acetonitrile	$Ni(OAc)_2$/$Pd(OAc)_2$ / $PdCl_2$	DABCO	60	6	ND

[a]*S,S*-methylphenyl sulfoximine (50 mg, 0.32 mmol), 4-methylbenzenediazonium tetrafluoroborate (99 mg, 0.48 mmol) and solvent (2 mL). [b]Isolated yield.

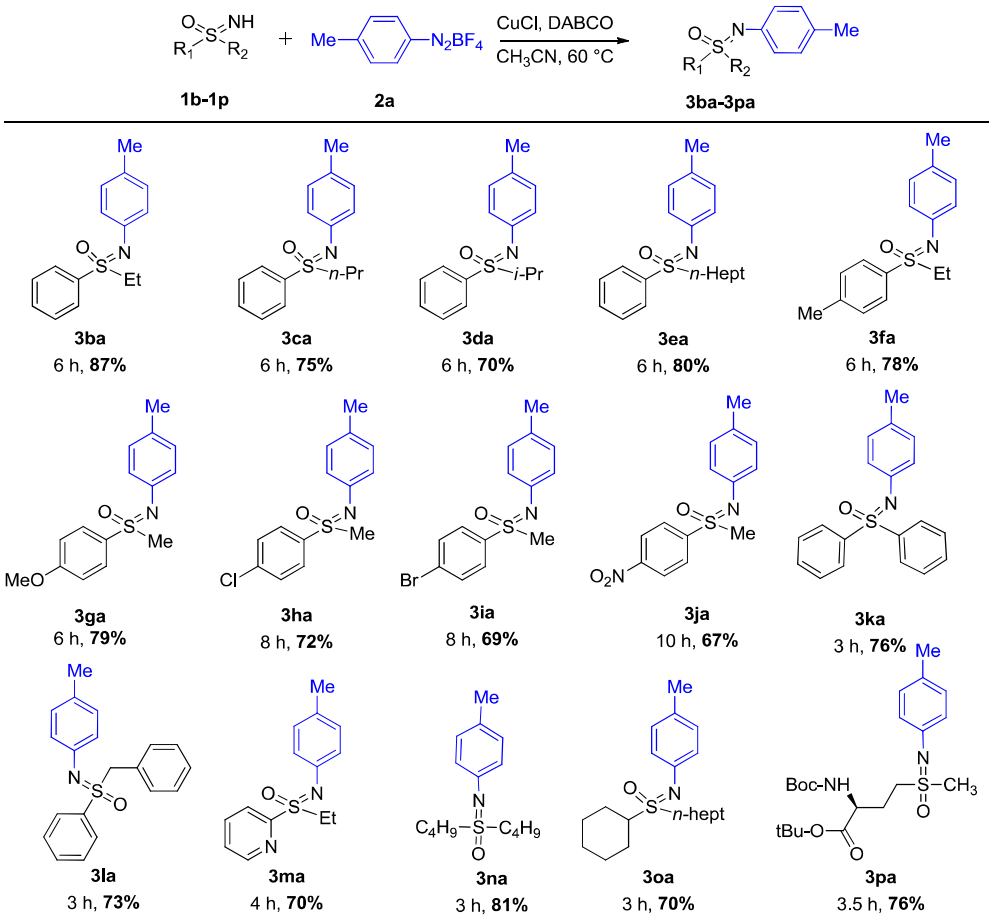
Further, the reaction was carried out with different bases including potassium carbonate, cesium carbonate, pyridine, *N,N*-dimethylaminopyridine (DMAP), triethylamine, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and 1,4-diazabicyclo[2.2.2]octane (DABCO) in the presence of 10 mol% CuCl (Table **2.1,** entries **8 to 14**). Among these bases, DABCO was found to be superior that provided **3aa** in 51% yield in 10 hours. Further, the reaction was performed at elevated temperatures, i.e. 45-75 °C in acetonitrile in the presence of CuCl and DABCO (Table **2.1,** entries **15 to 17**). To our delight, the desired product **3aa** was obtained in 88% yield at 60 °C within 6 hours. Relatively, low yields of **3aa** were observed at 45 °C and 75 °C. Furthermore, the optimization of the reaction condition was investigated in different solvents in the presence of 10 mol% CuCl and DABCO. However, acetonitrile remained the best out of the solvents used in this study. Moreover, other metal catalysts including $Ni(OAc)_2$, $Pd(OAc)_2$ and $PdCl_2$ were failed to yield the desired product (Table **2.1,** entry **22**). Overall, the optimization study indicated that *N*-arylation of sulfoximine with aryl diazonium salts can be achieved efficiently using 10% CuCl in the presence of DABCO in acetonitrile at 60 °C.

2.3 Substrates Scope

Having developed optimized condition, we have investigated the scope of different sulfoximines in C-N bond forming reactions with 4-methylbenzenediazonium tetrafluoroborate (**2a**) and summarized in Table **2.2**. (*S*,*S*)-alkyl-phenyl sulfoximines bearing different length of side alkyl chains, including sterically hindered *iso*-propyl, provided the corresponding *N*-arylated products in good yields under optimized condition (Table **2.2, 3ba–3ea**). On the other hand, (*S*,*S*)-alkyl-phenyl sulfoximines bearing different electron donating and withdrawing substituents on the aryl ring underwent *N*-arylation with 67–79%

yields (Table **2.2, 3fa–3ja**). It was noted that the electron withdrawing group functionalized phenyl sulfoximines (e.g. *p*-NO_2, *p*-Br, *p*-Cl, etc.) required slightly longer time for the *N*-arylation when compared with electron donating group substituted sulfoximines (e.g. *p*-Me and *p*-OMe). Likewise (*S,S*)-aryl-aryl, aryl-benzyl and heteroaryl-alkyl sulfoximines were successfully arylated with 70-76% yields (Table **2.2, 3ka–3ma**). Furthermore, to our delight, *N*-arylation of (*S,S*)-dialkyl sulfoximines as well as biologically relevant L-methionine sulfoximine were also successfully accomplished in 70-81% yields, which demonstrates the broad applicability of the present method (Table **2.2, 3na–3pa**).

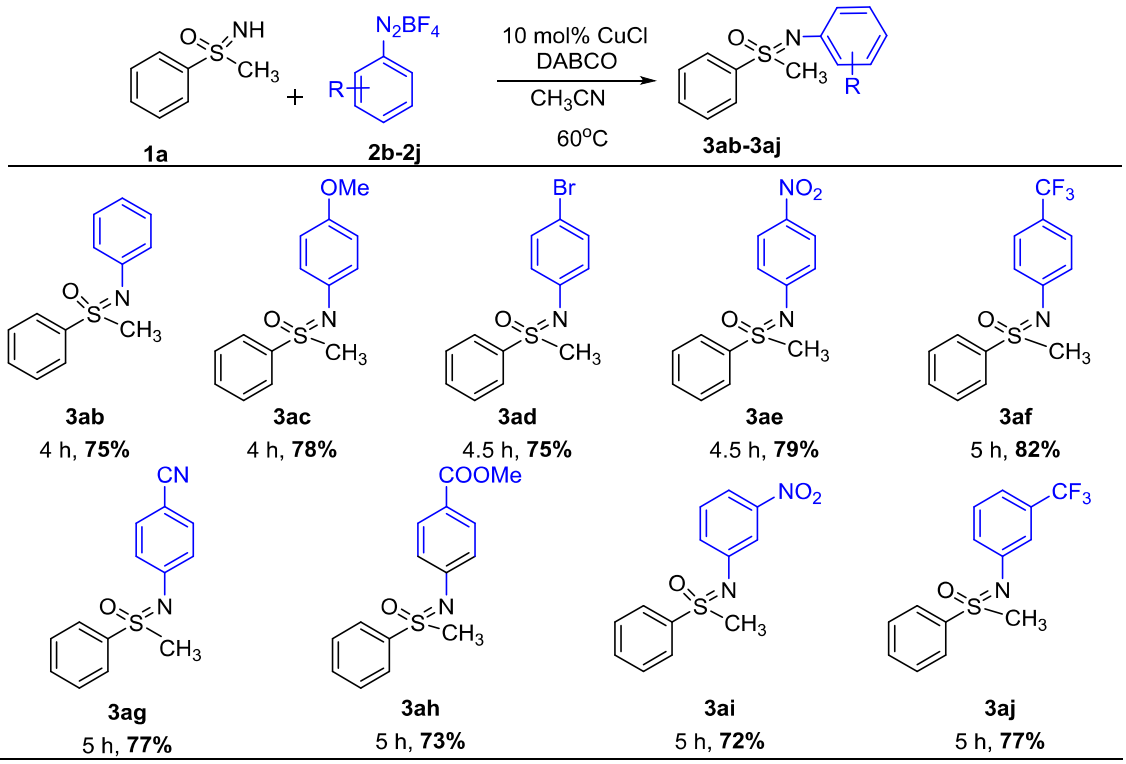
Table 2.2: *N*-Arylation of various sulfoximines with 4-methylbenzenediazonium tetrafluoroborate.[a,b]



[a]Sulfoximine (0.5 mmol), 4-methylbenzenediazonium tetrafluoroborate (1.5 eq.), DABCO (1 eq.) and acetonitrile (5 mL). [b]Isolated yield.

Encouraged, we further investigated the scope of different readily accessible aryldiazonium tetrafloroborate salts in the arylation reaction with *S,S*-methylphenyl sulfoximine (**1a**) and summarized in Table **2.3**. To our delight, aryl diazonium salts bearing electron donating and withdrawing groups participated efficiently in the C-N forming reactions and provided the desired *N*-arylated sulfoximines in 72-82% yields (Table **2.3, 3ab-3aj**).

Table 2.3: *N*-Arylation of (*S,S*)- methylphenyl sulfoximine with various diazonium salts.[a,b]

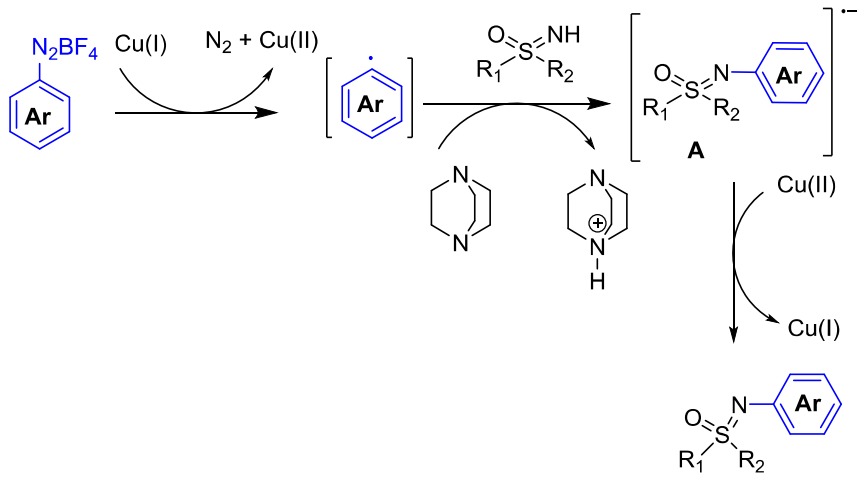


[a](*S,S*)-methylphenyl sulfoximine (0.5 mmol, 1eq), aryldiazonium tetrafloroborate (1.5 eq.) DABCO (1 eq.) and acetonitrile (5 mL). [b]Isolated yield.

2.4 Plausible Reaction Mechanism

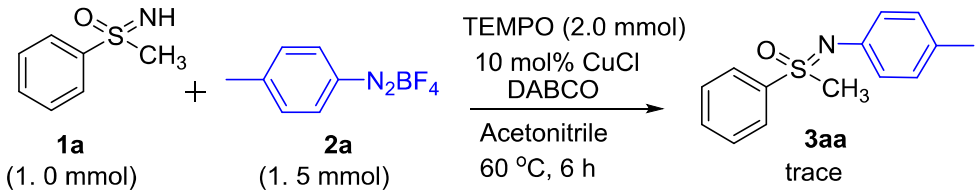
A plausible mechanism for the imino-arylation of sulfoximine is shown in Scheme **2.2** [43-45]. In the first step, aryl radical is generated from arenediazonium salt in the presence of Cu(I) *via* single electron transfer. During this process, Cu(I) turns into Cu(II).

Simultaneously, sulfoximine reacts with aryl radical in the presence of DABCO and generates radical anion intermediate **A**. The intermediate **A** is converted into product in the presence of copper (II).



Scheme 2.2: Plausible mechanism for the *N*-arylation of sulfoximines.

During this process, Cu (I) is regenerated to resume the catalytic cycle. To strengthen the proposed mechanism, the *N*-arylation reaction was performed in the presence of radical scavenger TEMPO (2,2,6,6-tetramethylpiperidine-1-yl)oxyl. The desired product was obtained only in trace amount, suggesting that the reaction proceeds through a radical mechanism.



Scheme 2.3: Control experiment with TEMPO.

2.5 Conclusion

In conclusion, a simple and efficient method for the *N*-arylation of sulfoximines is demonstrated using arenediazonium salts in the presence of a copper catalyst and DABCO. Wide range of aryl and alkyl sufoximines, including a biologically relevant L-methionine sulfoximine have participated in the coupling reaction with different aryldiazonim salts bearing electron donating and withdrawing groups. The desired products i.e. *N*-aryl sulfoximines were obtained in good to excellent yields. Controlled experiment suggests that the reaction proceeds through a radical mechanism. The present methodology appears to be more general, hence expected to find promising applications in organic synthesis.

2.6 Experimental Section

2.6.1 Experimental procedure for the optimization table

S,S-Methylphenylsulfoximine (50 mg, 0.32 mmol), tolyl diazoniumtetrafloroborate (99 mg, 0.48 mmol), and solvent (2 mL) were taken in a round bottom flask [with or without base (1 equivalent to sulfoximine) and catalyst (0.1 equivalent to sulfoximine)] and stirred at appropriate temperature. The progress of the reactions was monitored by thin-layer chromatography. After completion of the reaction (or appropriate time), the reaction mixture was diluted with ethyl acetate and washed with water and brine solution. The organic layer was dried over anhydrous sodium sulfate and evaporated to dryness. The crude product was purified on silica-gel (100-200 mesh) column chromatography using a mixture ethyl acetate/hexane as eluent to obtain 3aa. [R_f: 0.48 with 40 % EA/hexane].

2.6.2 Experimental procedure for the arylation of sulfoximines

Sulfoximines (0.5 mmol), aryldiazonium tetrafloroborate (1.5 eq.), DABCO (1 eq.) and acetonitrile (5 mL) were added into 50 mL round bottom vessel and heated at 60 °C on oil

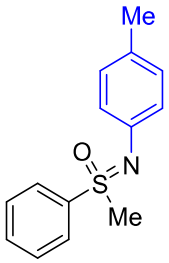
bath with magnetic stirrer for appropriate time. The progress of the reactions was monitored by thin-layer chromatography using 40% ethyl acetate (EA) and hexane (hex) as eluent. After completion of the reaction, the reaction mixture was diluted with ethyl acetate and washed with water and brine solution. The organic layer was dried over anhydrous sodium sulfate and evaporated to dryness. The crude product was further purified on silica-gel (100–200 mesh) column chromatography using a mixture of ethyl acetate/hexane as eluent.

2.6.3 Experimental procedure for the control experiment

S,S-Methylphenylsulfoximine (155 mg, 1 mmol), tolyl diazoniumtetrafloroborate (310 mg, 1.5 mmol), DABCO (112 mg, 1 mmol), TEMPO (468 mg, 3 mmol) and acetonitrile (8 mL) were added into 50 mL round bottom vessel and heated at 60 °C on oil bath with magnetic stirrer for 8 hour. The progress of the reactions was monitored by thin-layer chromatography using 40% ethyl acetate (EA) and hexane (hex) as eluent. Only a trace amount of formation of product was observed in TLC, hence not isolated.

2.7 Analytical data for *N*-aryl sulfoximines

2.7.1: ***N*-(4-methylphenyl)-*S,S*-methylphenylsulfoximine (3aa):**

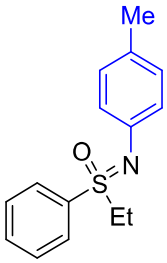


3aa

Sulfoximine was taken 0.32 mmol (50 mg) and the titled compound was obtained as white solid (Yield = 69 mg, 88%). Melting point: 112-113 °C. The product was isolated by silica-gel Column Chromatography using 30% ethyl acetate:hexane as eluent. R_f = 0.52. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.97 (d, J = 7.8 Hz, 2H), 7.60–7.55 (m, 1H), 7.52 (t, J = 7.5 Hz, 2H), 6.92 (s, 4H), 3.22 (s, 3H), 2.20 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 142.1, 139.5, 133.1,

131.0, 129.5, 128.6, 123.2, 45.8, 20.6.

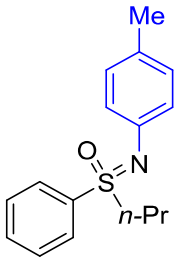
2.7.2: ***N*-(4-methylphenyl)-*S*,*S*-ethylphenylsulfoximine (3ba):**



3ba

Sulfoximine was taken 0.5 mmol (85 mg) and the titled compound was obtained as brown solid (Yield = 112 mg, 87%). Melting point: 85-88 °C. The product was isolated by silica-gel Column Chromatography using 30% ethyl acetate:hexane as eluent. R_f = 0.24. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.89 (d, J = 7.9 Hz, 2H), 7.60–7.54 (m, 1H), 7.50 (dd, J = 10.3, 4.6 Hz, 2H), 6.92 (s, 4H), 3.39–3.26 (m, 2H), 2.20 (s, 3H), 1.29 (t, J = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 142.4, 137.6, 133.1, 130.8, 129.6, 129.6, 129.4, 123.2, 51.9, 20.7, 7.7.

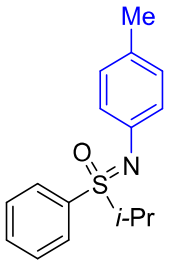
2.7.3: ***N*-(4-methylphenyl)-*S*,*S*-phenylpropylsulfoximine (3ca):**



3ca

Sulfoximine was taken 0.5 mmol (92 mg) and the titled compound was obtained as white solid (Yield = 102 mg, 75%). Melting point: 108 °C. The product was isolated by silica-gel Column Chromatography using 30% ethyl acetate:hexane as eluent. R_f = 0.61. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.95–7.89 (m, 2H), 7.55 (dd, J = 5.0, 3.7 Hz, 1H), 7.53–7.47 (m, 2H), 6.91 (s, 4H), 3.34–3.19 (m, 2H), 2.20 (s, 3H), 1.89–1.72 (m, 2H), 0.97 (t, J = 7.5 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 142.5, 140.6, 138.3, 133.1, 130.8, 129.6, 129.4, 123.3, 59.2, 20.7, 16.7, 12.8.

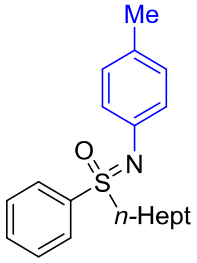
2.7.4: ***N*-(4-methylphenyl)-*S*,*S*-*iso*-propylphenylsulfoximine (3da):**



3da

Sulfoximine was taken 0.5 mmol (92 mg) and the titled compound was obtained as pale yellow oil (Yield = 96 mg, 70%). The product was isolated by silica-gel Column Chromatography using 20% ethyl acetate: hexane as eluent. R_f = 0.58. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.84 (d, J = 7.5 Hz, 2H), 7.54 (t, J = 7.2 Hz, 1H), 7.47 (t, J = 7.4 Hz, 2H), 6.89 (s, 4H), 3.39 (m, 1H), 2.17 (s, 3H), 1.40 (d, J = 6.6 Hz, 3H), 1.26 (d, J = 6.6 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 142.8, 136.2, 133.0, 130.4, 129.6, 129.2, 123.2, 57.0, 20.7, 16.4, 15.8.

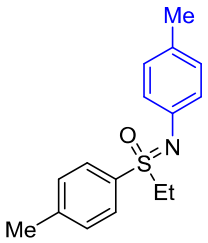
2.7.5: ***N*-(4-methylphenyl)-*S*,*S*-*n*-heptylphenylsulfoximine (3ea):**



3ea

Sulfoximine was taken 0.5 mmol (120 mg) and the titled compound was obtained as white solid (Yield = 132 mg, 80%). Melting point: 76 °C. The product was isolated by silica-gel Column Chromatography using 10% ethyl acetate:hexane as eluent. R_f = 0.80. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.90 (d, J = 7.1 Hz, 2H), 7.54–7.46 (m, 3H), 6.90 (s, 4H), 3.34–3.28 (m, 1H), 3.24–3.18 (m, 1H), 2.17 (s, 3H), 1.79–1.78 (m, 1H), 1.67-1.65 (m, 1H), 1.33–1.15 (m, 8H), 0.83 (t, J = 6.8 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 142.5, 138.3, 133.1, 130.8, 130.1, 129.6, 129.52, 129.50, 123.3, 115.4, 57.5, 31.5, 28.8, 28.2, 22.8, 22.6, 20.7, 14.1.

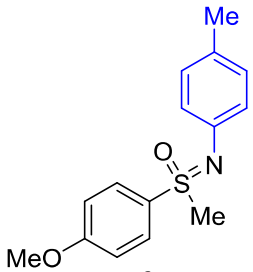
2.7.6: ***N*-(4-methylphenyl)-*S*,*S*-ethyl-(4-methylphenyl)sulfoximine (3fa):**



3fa

Sulfoximine was taken 0.5 mmol (92 mg) and the titled compound was obtained as white solid (Yield = 106 mg, 78%). Melting point: 76 °C. The product was isolated by silica-gel Column Chromatography using 10% ethyl acetate:hexane as eluent. R_f = 0.48. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.80 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 6.94 (s, 4H), 3.33 (ddt, J = 17.9, 14.1, 7.1 Hz, 2H), 2.42 (s, 3H), 2.22 (s, 3H), 1.30 (d, J = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 144.0, 142.6, 134.4, 130.7, 130.1, 129.6, 129.6, 123.2, 51.9, 21.6, 20.7, 7.7.

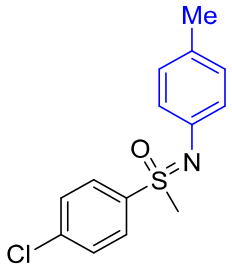
2.7.7: ***N*-(4-methylphenyl)-*S*,*S*-(4-methoxyphenyl)methylsulfoximine (3ga):**



3ga

Sulfoximine was taken 0.5 mmol (93 mg) the titled compound was obtained as white solid (Yield = 108 mg, 79%). Melting point: 76 °C. The product was isolated by silica-gel Column Chromatography using 10% ethyl acetate:hexane as eluent. R_f = 0.55. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.91–7.85 (m, 2H), 6.98–6.95 (m, 2H), 6.92 (d, J = 10.0 Hz, 4H), 3.83 (s, 3H), 3.20 (s, 3H), 2.20 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 163.4, 142.5, 130.9, 130.8, 130.7, 129.6, 123.2, 114.8, 55.7, 46.3, 20.7.

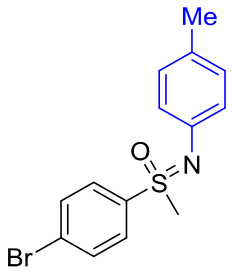
2.7.8: ***N*-(4-methylphenyl)-*S*,*S*-(4-chlorophenyl)methylsulfoximine (3ha):**



3ha

Sulfoximine was taken 0.5 mmol (95 mg) the titled compound was obtained as white solid (Yield = 101 mg, 72%). Melting point: 112-113 °C. The product was isolated by silica-gel Column Chromatography using 30% ethyl acetate:hexane as eluent. R_f = 0.45. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.94–7.82 (m, 2H), 7.52–7.45 (m, 2H), 6.91 (dd, J = 21.6, 8.4 Hz, 4H), 3.22 (s, 3H), 2.21 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 141.9, 140.0, 138.1, 131.5, 130.3, 129.9 129.8, 123.3, 46.0, 20.8.

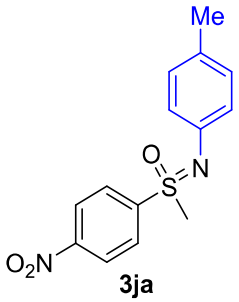
2.7.9: ***N*-(4-methylphenyl)-*S*,*S*-(4-bromophenyl)methylsulfoximine (3ia):**



3ia

Sulfoximine was taken 0.5 mmol (117 mg) the titled compound was obtained as white solid (Yield = 110 mg, 69%). Melting point: 150 °C. The product was isolated by silica-gel Column Chromatography using 30% ethyl acetate:hexane as eluent. R_f = 0.48. **^{1}H NMR** (500 MHz, CDCl3) δ 7.85–7.78 (m, 2H), 7.69–7.61 (m, 2H), 6.93 (d, J = 8.2 Hz, 2H), 6.91–6.84 (m, 2H), 3.22 (s, 3H), 2.21 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 141.8, 138.6, 132.9, 131.5, 130.4, 129.8, 128.5, 123.2, 46.0, 20.8.

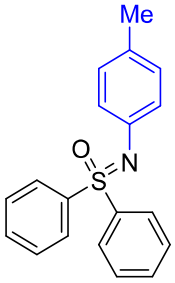
2.7.10: ***N*-(4-methylphenyl)-*S*,*S*-methyl-(4-nitrophenyl)sulfoximine (3ja):**



3ja

Sulfoximine was taken 0.5 mmol (100 mg) the titled compound was obtained as yellow solid (Yield = 98 mg, 67%). Melting point: 85 °C. The product was isolated by silica-gel Column Chromatography using 20% ethyl acetate:hexane as eluent. R_f = 0.40. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.34 (d, J = 8.8 Hz, 2H), 8.15 (d, J = 8.9 Hz, 2H), 6.93 (d, J = 8.3 Hz, 2H), 6.86 (d, J = 8.0 Hz, 2H), 3.28 (s, 3H), 2.20 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 150.7, 145.8, 141.2, 132.0, 130.2, 129.9, 124.7, 123.3, 45.7, 20.7.

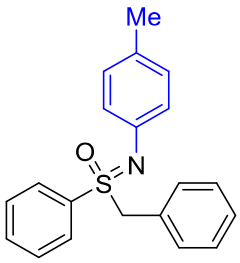
2.7.11: ***N*-(4-methylphenyl)-*S*,*S*-diphenylsulfoximine (3ka):**



3ka

Sulfoximine was taken 0.5 mmol (109 mg) the titled compound was obtained as white solid (Yield = 116 mg, 76%). Melting point: 171 °C. The product was isolated by silica-gel Column Chromatography using 20% ethyl acetate:hexane as eluent. R_f = 0.72. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.04 (d, J = 7.6 Hz, 4H), 7.50–7.41 (m, 6H), 7.04 (d, J = 8.0 Hz, 2H), 6.93 (d, J = 7.9 Hz, 2H), 2.19 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 141.9, 141.1, 132.6, 131.1, 129.7, 129.3, 128.7, 123.7, 20.8.

2.7.12: ***N*-(4-methylphenyl)-*S*,*S*-benzylphenylsulfoximine (3la):**

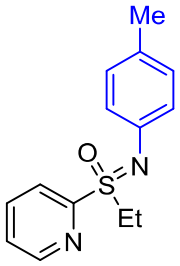


3la

Sulfoximine was taken 0.5 mmol (116 mg) the titled compound was obtained as pale yellow solid (Yield = 117 mg, 73%). Melting point: 148-149 °C. The product was isolated by silica-gel Column Chromatography using 20% ethyl acetate:hexane as eluent. R_f = 0.70. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67–7.60 (m, 2H), 7.51 (t, J =

7.4 Hz, 1H), 7.37 (t, J = 7.8 Hz, 2H), 7.29 (d, J = 7.6 Hz, 1H), 7.20 (t, J = 7.6 Hz, 2H), 7.06–6.88 (m, 6H), 4.53 (q, J = 13.7 Hz, 2H), 2.22 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 142.4, 136.8, 133.2, 131.4, 131.0, 129.9, 129.7, 129.0, 128.7, 128.4, 123.4, 63.3, 20.8.

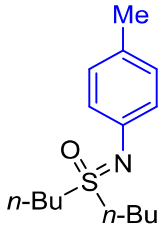
2.7.13: ***N*-(4-methylphenyl)-*S*,*S*-ethyl-(2-pyridyl)sulfoximine (3ma):**



3ma

Sulfoximine was taken 0.5 mmol (85 mg) the titled compound was obtained as pale yellow solid (Yield = 91 mg, 70%). Melting point: 165 °C. The product was isolated by silica-gel Column Chromatography using 20-30% ethyl acetate:hexane as eluent. R_f = 0.28. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.71 (d, J = 4.1 Hz, 1H), 8.09 (d, J = 7.8 Hz, 1H), 7.85 (td, J = 7.7, 1.6 Hz, 1H), 7.43 (ddd, J = 7.6, 4.7, 0.8 Hz, 1H), 7.00–6.84 (m, 4H), 3.68–3.53 (m, 2H), 2.19 (s, 3H), 1.30 (t, J = 7.4 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 156.6, 150.5, 142.0, 137.8, 131.2, 129.5, 126.6, 124.4, 123.5, 47.8, 20.7, 7.1.

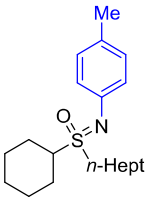
2.7.14. ***N*-(4-methylphenyl)-*S*,*S*-dibutylsulfoximine (3na):**



3na

Sulfoximine was taken 0.5 mmol (89 mg) the titled compound was obtained as transparent oil (Yield = 108 mg, 81%). The product was isolated by silica-gel Column Chromatography using 10% ethyl acetate:hexane as eluent. R_f = 0.70 (20% EA/Hex). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.05–6.91 (m, 4H), 3.22–3.03 (m, 4H), 2.27 (s, 3H), 1.86–1.76 (m, 4H), 1.50–1.37 (m, 4H), 0.94 (t, J = 7.4 Hz, 6H).**^{13}C NMR** (125 MHz, $CDCl_3$) δ 142.8, 131.2, 129.8, 123.5, 51.6, 25.2, 21.8, 20.8, 13.7.

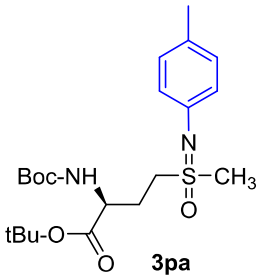
2.7.15. ***N*-(4-methylphenyl)-*S*,*S*-cyclohexylheptylsulfoximine (3oa):**



3oa

Sulfoximine was taken 0.5 mmol (73 mg) the titled compound was obtained as yellow oil (Yield = 83 mg, 70%). The product was isolated by silica-gel Column Chromatography using 15 % ethyl acetate:hexane as eluent. R_f = 0.24. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.99 (s, 4H), 3.09 (ddd, J = 11.6, 9.2, 3.7 Hz, 2H), 3.04–2.97 (m, 1H), 2.26 (s, 3H), 1.95–1.89 (m, 2H), 1.80 (dd, J = 15.9, 8.1 Hz, 2H), 1.68 (dd, J = 28.2, 8.0 Hz, 2H), 1.64–1.53 (m, 2H), 1.35 (dd, J = 7.6, 4.7 Hz, 2H), 1.30–1.19 (m, 10H), 0.86 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 143.3, 130.8, 129.7, 123.5, 61.6, 48.7, 31.5, 28.8, 28.6, 26.3, 25.9, 25.6, 25.6, 25.3, 22.8, 22.6, 20.8, 14.1.

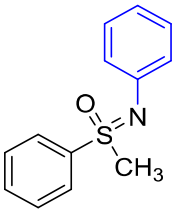
2.7.16. ***tert*-butyl (2S)-4-(*N*-(4-tolyl)-*S*-methylsulfonimidoyl)-2-((*tert*-butoxy carbonyl) amino)butanoate (3pa):**



3pa

Sulfoximine was taken 0.5 mmol (168 mg) the titled compound was obtained as white solid (Yield = 161 mg, 76%). Melting point: 112-113 °C. The product was isolated by silica-gel Column Chromatography using 30% ethyl acetate:hexane as eluent. R_f = 0.18. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.02 (dd, J = 8.3, 2.9 Hz, 2H), 6.96 (ddd, J = 8.3, 5.2, 2.0 Hz, 2H), 5.28 (s, 1H), 4.24 (s, 1H), 3.39–3.14 (m, 2H), 3.03 (s, 3H), 2.45–2.37 (m, 1H), 2.27 (s, 3H), 2.21–2.12 (m, 1H), 1.43 (dd, J = 8.8, 6.0 Hz, 17H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.4, 142.1, 131.8, 129.9, 129.9, 123.5, 123.5, 83.1, 83.1 80.3, 52.6, 50.6, 39.6, 29.8, 28.4, 28.0, 28.0, 27.0, 20.8.

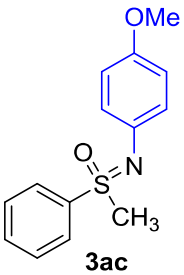
2.7.17: ***N*-phenyl-*S*,*S*-methylphenylsulfoximine (3ab):**



3ab

Sulfoximine was taken 0.5 mmol (78 mg) and the titled compound was obtained as white solid (Yield = 86.5 mg, 75%). The product was isolated by silica-gel Column Chromatography using 30% ethyl acetate:hexane as eluent. Melting point: 100-101 °C. R_f = 0.43. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.94–7.88 (m, 2H), 7.48 (m, 3H), 7.05 (t, J = 7.8 Hz, 2H), 6.94 (d, J = 7.5 Hz, 2H), 6.80 (t, J = 7.3 Hz, 1H), 3.17 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 145.1, 139.7, 133.4, 129.7, 129.2, 128.8, 123.5, 121.9, 46.2.

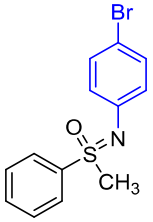
2.7.18: ***N*-(4-methoxyphenyl)-*S*,*S*-methylphenylsulfoximine (3ac):**



3ac

Sulfoximine was taken 0.5 mmol (78 mg) and the titled compound was obtained as white solid (Yield = 102 mg, 78%). Melting point: 102-104 °C. The product was isolated by silica-gel Column Chromatography using 40% ethyl acetate:hexane as eluent. R_f = 0.42. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99–7.90 (m, 2H), 7.58–7.47 (m, 3H), 6.93 (d, J = 9.0 Hz, 2H), 6.66 (d, J = 9.0 Hz, 2H), 3.67 (s, 3H), 3.19 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.0, 139.7, 138.1, 133.3, 129.6, 128.9, 124.5, 114.5, 55.5, 45.8.

2.7.19: ***N*-(4-bromophenyl)-*S*,*S*-methylphenylsulfoximine (3ad):**

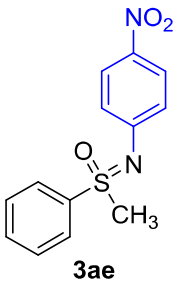


3ad

Sulfoximine was taken 0.5 mmol (78 mg) and the titled compound was obtained as white solid (Yield = 116 mg, 75%). Melting point: 110-111 °C. The product was isolated by silica-gel Column Chromatography using 30% ethyl acetate:hexane as eluent. R_f =

0.44. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.91 (d, J = 7.9 Hz, 2H), 7.53 (m, 3H), 7.17 (d, J = 8.2 Hz, 2H), 6.85 (d, J = 8.2 Hz, 2H), 3.21 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 144.4, 138.9, 133.6, 132.0, 129.7, 128.7, 124.9, 114.4, 46.2.

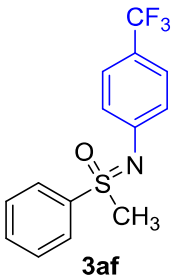
2.7.20: ***N*-(4-nitrophenyl)-*S*,*S*-methylphenylsulfoximine (3ae):**



3ae

Sulfoximine was taken 0.5 mmol (78 mg) and the titled compound was obtained as yellow solid (Yield = 110 mg, 79%). Melting point: 150-152 °C. The product was isolated by silica-gel Column Chromatography using 40% ethyl acetate:hexane as eluent. R_f = 0.22. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.95 (d, J = 8.7 Hz, 2H), 7.91 (d, J = 7.9 Hz, 2H), 7.61 (t, J = 7.3 Hz, 1H), 7.53 (t, J = 7.6 Hz, 2H), 6.97 (d, J = 8.7 Hz, 2H), 3.29 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 162.3, 152.8, 141.7, 138.2, 134.1, 130.0, 128.5, 126.3, 125.3, 122.5, 115.8, 46.6.

2.7.21: ***N*-(4-trifluoromethylphenyl)-*S*,*S*-methylphenylsulfoximine (3af):**

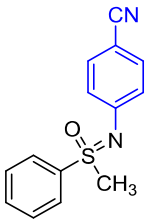


3af

Sulfoximine was taken 0.5 mmol (78 mg) and the titled compound was obtained as white solid (Yield = 123 mg, 82%). Melting point: 112-113 °C. The product was isolated by silica-gel Column Chromatography using 30% ethyl acetate:hexane as eluent. R_f = 0.55. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.00–7.91 (m, 2H), 7.62 (d, J = 7.4 Hz, 1H), 7.58–7.52 (m, 2H), 7.35 (d, J = 8.4 Hz, 2H), 7.05 (d, J = 8.3 Hz, 2H), 3.27 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 148.78 (q, $J_{C\text{-}F}$ = 1.4 Hz), 139.0, 133.7, 129.8, 128.6, 128.1 (q, $J_{C\text{-}F}$ = 272

Hz), 126.31 (q, $J_{C\text{-}F}$ = 3.7 Hz), 123.46 (q, $J_{C\text{-}F}$ = 32.7 Hz), 122.9, 46.4.

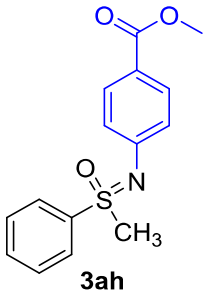
2.7.22: ***N*-(4-cyanophenyl)-*S*,*S*-methylphenylsulfoximine (3ag):**



3ag

Sulfoximine was taken 0.5 mmol (78 mg) and the titled compound was obtained as pale yellow oil (Yield = 98 mg, 77%). The product was isolated by silica-gel Column Chromatography using 40% ethyl acetate:hexane as eluent. R_f = 0.35. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.91 (d, J = 7.9 Hz, 2H), 7.62 (t, J = 7.4 Hz, 1H), 7.55 (d, J = 7.6 Hz, 2H), 7.35 (d, J = 8.3 Hz, 2H), 6.98 (d, J = 8.3 Hz, 2H), 3.27 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 150.2, 134.0, 133.9, 133.3, 130.0, 128.6, 123.3, 117.9, 104.1, 46.7.

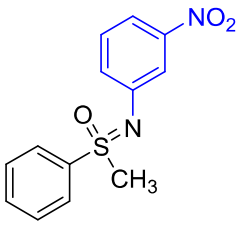
2.7.23: ***N*-(4-methylbenzoate)-*S*,*S*-methylphenylsulfoximine (3ah):**



3ah

Sulfoximine was taken 0.5 mmol (78 mg) and the titled compound was obtained as pale yellow oil (Yield = 110 mg, 73%). The product was isolated by silica-gel Column Chromatography using 40% ethyl acetate:hexane as eluent. R_f = 0.42. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.96–7.94 (m, 2H), 7.80–7.79 (m, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.54 (t, J = 7.6 Hz, 2H), 7.04–6.96 (m, 2H), 3.82 (s, 3H), 3.28 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.2, 150.3, 138.9, 133.7, 130.9, 129.8, 128.6, 123.1, 122.6, 51.8, 46.5.

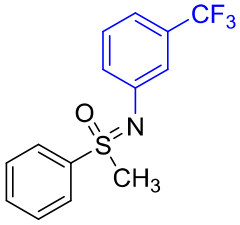
2.7.24: ***N*-(3-nitrophenyl)-*S*,*S*-methylphenylsulfoximine (3ai):**



3ak

Sulfoximine was taken 0.5 mmol (78 mg) and the titled compound was obtained as white solid (Yield = 100 mg, 72%). Melting point: 112-113 °C. The product was isolated by silica-gel Column Chromatography using 30% ethyl acetate:hexane as eluent. R_f = 0.42. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99–7.93 (m, 2H), 7.81 (t, J = 2.1 Hz, 1H), 7.73–7.59 (m, 4H), 7.56 (dd, J = 10.4, 4.8 Hz, 2H), 3.29 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 149.0, 146.7, 138.6, 133.9, 129.9, 129.5, 129.1, 128.6, 117.9, 116.4, 46.4.

2.7.25: ***N*-(3-trifluoromethylphenyl)-*S*,*S*-methylphenylsulfoximine (3aj):**



3al

Sulfoximine was taken 0.5 mmol (78 mg) and the titled compound was obtained as pale yellow oil (Yield = 115 mg, 77%). The product was isolated by silica-gel Column Chromatography using 30% ethyl acetate:hexane. R_f = 0.28. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.97 (d, J = 7.8 Hz, 2H), 7.62 (t, J = 7.3 Hz, 1H), 7.54 (t, J = 7.5 Hz, 2H), 7.28 (d, J = 2.9 Hz, 1H), 7.24–7.09 (m, 3H), 3.27 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 145.8, 138.9, 133.6, 131.3 (q, $J_{C\text{-}F}$ = 32 Hz), 129.8, 129.4, 128.6, 126.0, 124.2 (q, $J_{C\text{-}F}$ =272.5 Hz), 120.2 (q, J = 3.7 Hz), 118.3 (q, J = 3.9 Hz), 462.

2.8 Spectral Data of Selected Product

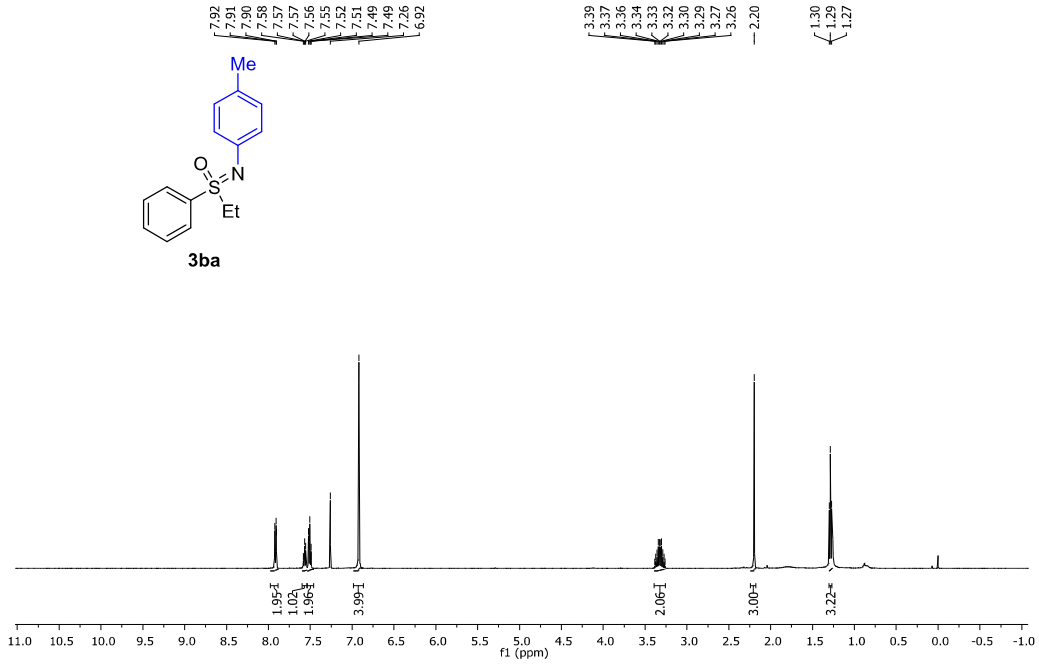


Figure 2.2: ^{1}H NMR for 3ba

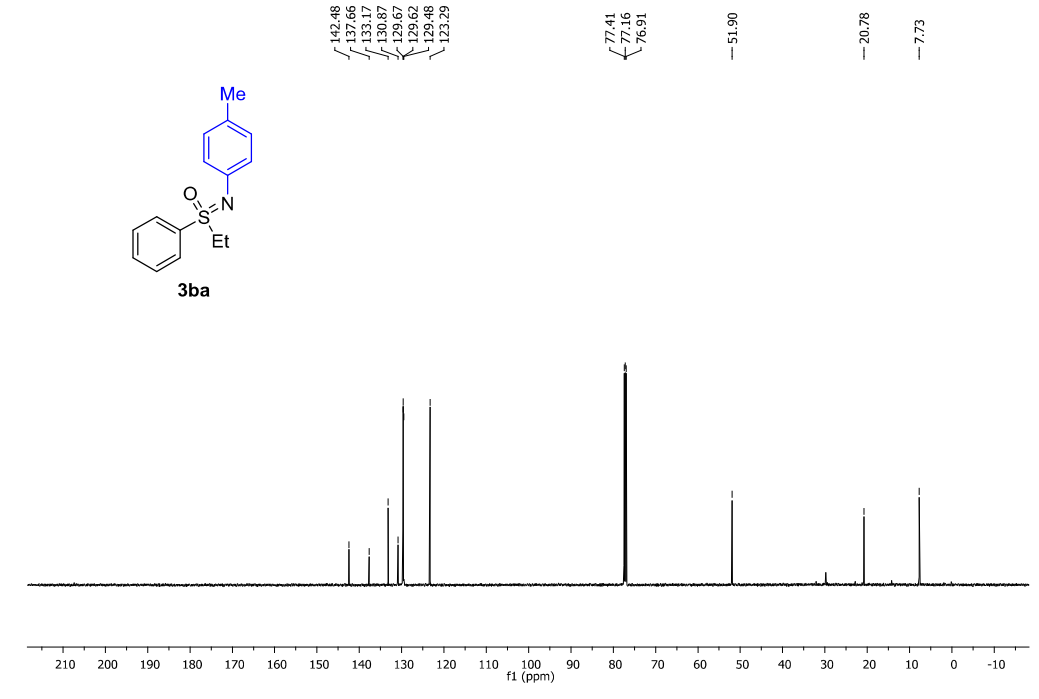


Figure 2.3: ^{13}C NMR for 3ba

2.9 References

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