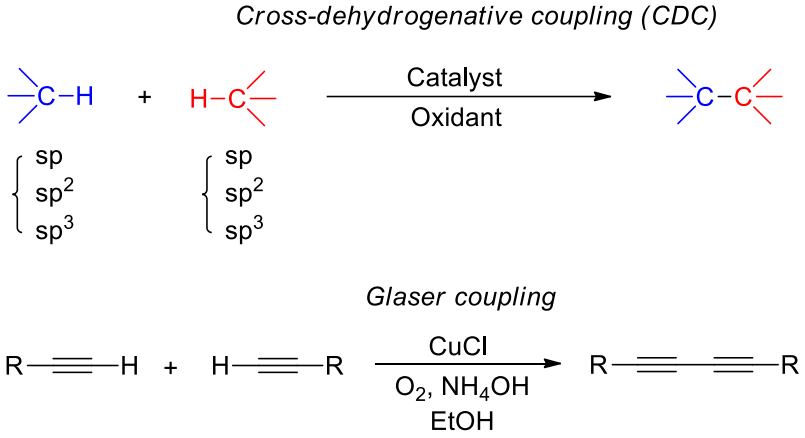
Chapter I

Section B

Graphene Oxide (GO) Promoted Direct C–H Sulfenylation of Aromatic Compounds

I.B.1 Introduction

Cross-dehydrogenative coupling (CDC) has emerged as a breakthrough synthetic strategy for the formation of C–C bonds.[1] It involves direct coupling of two different C–H bonds under oxidative conditions, hence the name cross-dehydrogenative coupling. The C–H bonds could be part of sp^3-C, sp^2-C and sp-C, for either of the partners (Scheme I.B.1). For example, Glaser coupling which is a coupling between two C(sp)–H bonds has been documented long before the concept of CDC has emerged.[2] Apart from C–C bond formation, C–X bonds are also generated via cross-dehydrogenative coupling between C–H and X–H (X = N, O, S, P, etc) bonds. This technique has been pioneered by Chao-Jun Li and co-workers in 2004 while working with the synthesis of propargylamines.[3] They successfully constructed C–C bond via C(sp^3)–H and C(sp)–H bond activation.

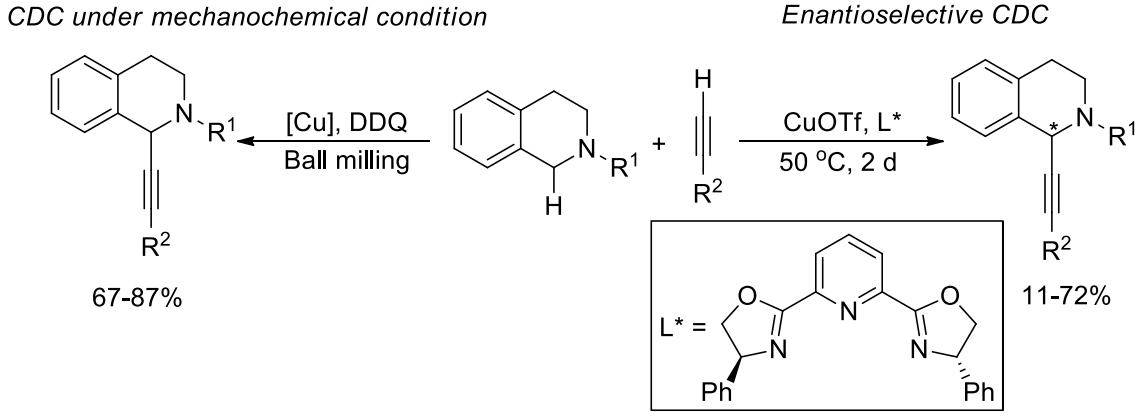


Scheme I.B.1 Cross-dehydrogenative coupling (CDC).

The classical method for the formation of C–C bond has been based on the nucleophile-electrophile approach. However, such transformation requires pre-functionalization of either of the reacting species. The methodology took a huge leap after the development of transition-metal catalyzed cross-coupling reactions[4] and metathesis reactions.[5] Although transition-metal catalyzed cross-coupling reactions sufficed the gaps to a great extent, the problem of pre-functionalization of the starting materials remained as a challenge. For instance, the presence of a leaving group is essential for one of the coupling partners. Besides, the use of expensive metal catalysts, harsh reaction conditions and lack of atom-economy are others limitations of transition-metal catalyzed coupling reactions. Hence, CDC has become an elegant strategy for direct access to C–C or C–X bonds.[6,7] Since the formation of C–C bond via CDC occurs at the expense of two C–H bonds, it is also known as dual C–H activation. In such transformation there is a loss of hydrogen, which is thermodynamically

unfavourable, hence an oxidant is used which acts as sink for excess electrons and make the overall process feasible.[8] Commonly used oxidants are hydrogen peroxide, *tert*-butylhydroperoxide (TBHP),[9-11] di-*tert*-butyl peroxide (DTBP),[12] molecular oxygen (O_2),[13,14] molecular iodine (I_2),[15] hypervalent iodine,[16,17] 2,3-dichloro-2,6-dicyanobenzoquinone (DDQ),[18] potassium perdisulfate ($K_2S_2O_8$).[19]

Ever since the origin of CDC, several different research groups have focussed their attention towards the development of this novel synthetic methodology.[20] Although transition-metal catalyzed CDC is well known; metal-free protocols are also gaining popularity due to environmental considerations. In this context, molecular iodine (I_2) has been recognized as an inexpensive and benign catalyst for CDC.[15] Numerous catalytic systems have been developed for the formation of C–C,[13,17,21,22] C–N,[23] C–O,[23,24] C–S,[14,25] and C–Se,[26,27] bonds via CDC. Furthermore, enantioselective CDC is also possible and has been reported for the alkynylation of tetrahydroisoquinolines.[28,29] Moreover, tetrahydroisoquinolines have also been alkynylated under mechanochemical conditions using ball milling technique in presence of DDQ as oxidant (Scheme I.B.2).[30]



Scheme I.B.2 Cross-dehydrogenative coupling between C(sp^3)–H and C(sp)–H bond.

Organosulfur compounds are endowed with a wide range of potential biological activities.[31] The synthesis of heterocyclic scaffolds bearing sulfur unit has been the topic of immense research. For instance, functionalized indoles are prevalent in myriads of natural products possessing medicinal properties.[32-34] Among the various indole derivatives, 3-sulfenylindoles have received enormous attention because of their potential uses in the treatment of cancer,[35] heart diseases,[35] allergies,[36] HIV,[37] obesity, Alzheimer's disease,[35] and bacterial infections.[38] Moreover, indolylarylsulfones acts as HIV-1 non-nucleoside reverse transcriptase inhibitors.[39] The 3-sylfenylindoles are also found to be effective against tubulin polymerization,[40] and COX-2 inhibition.[41] Furthermore, aryl sulphides are essential building

blocks for several active pharmaceutical ingredients (APIs).[35] Few representative bioactive molecules with sulfur functionalized indole skeleton are shown in Figure I.B.1.

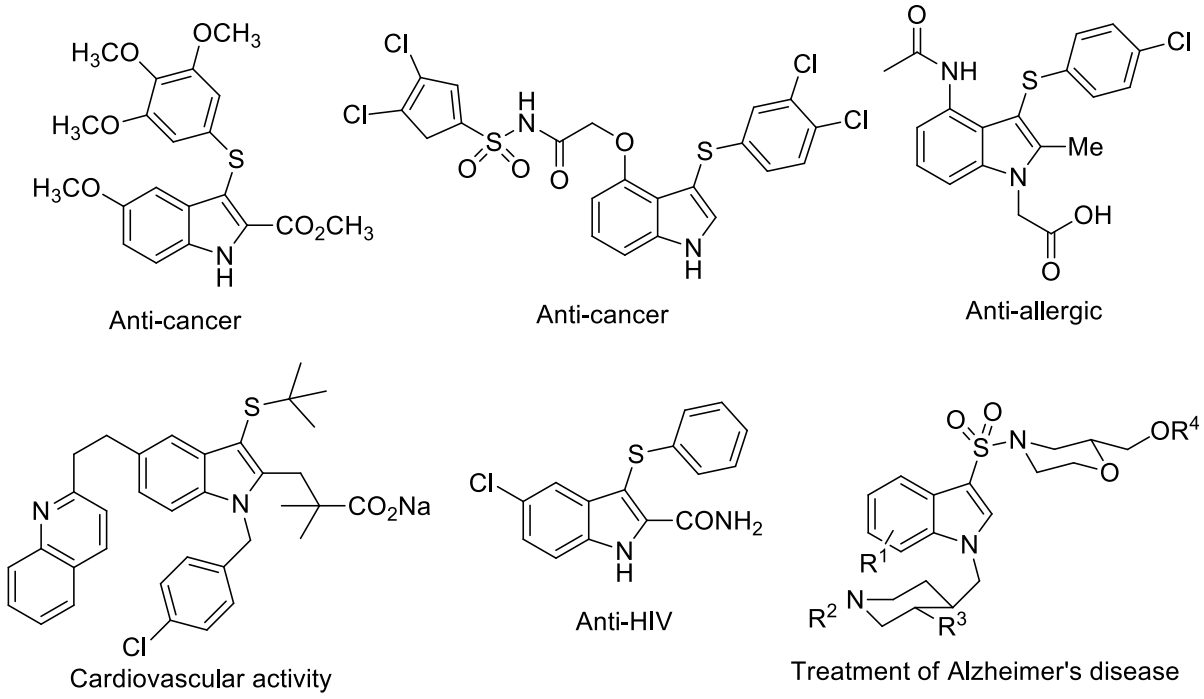
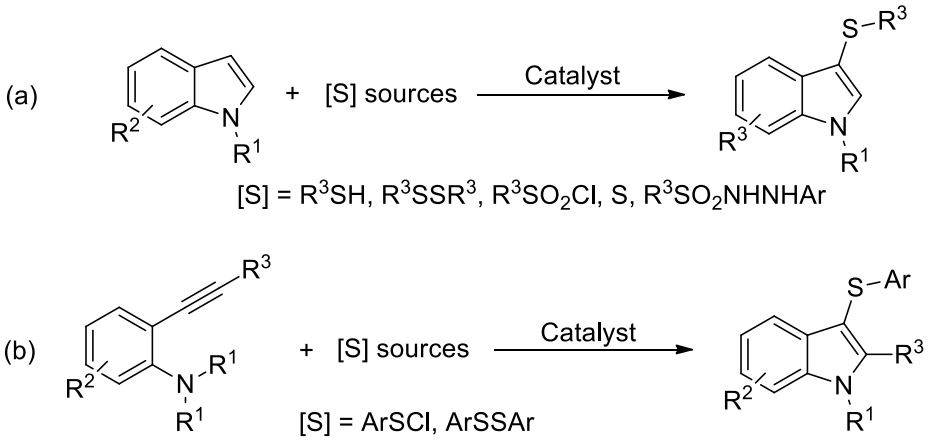


Figure I.B.1 Bioactive sulfur functionalized indoles.

Owing to their prevalence in numerous bioactive molecules, natural products and APIs the synthesis of 3-sulfenylindoles has attracted widespread attention. The two most common ways for the synthesis of 3-sulfenylindoles are: (a) the direct sulfenylation of indole ring and (b) the cyclization reactions of 2-alkynylanilines,[42,43] or N,N-dialkyl-2-iodoanilines (Scheme I.B.3).[44,45] The direct sulfenylation of indole ring has been carried out using diverse sulfenylating reagents like thiols,[46-51] disulfides,[52,53] sulfenyl halides,[54] sulfinates,[37,55] sulfonyl hydrazides,[56] sulfonyl chlorides[57,58] and N-thioimides.[59,60] In addition, the sulfenylation of indoles has been accomplished by using elemental sulfur as the sulfenylating reagent, avoiding the use of any organic sulfenylating reagents.[60]

Carbonaceous nanomaterials like graphenes and chemically modified graphenes (CMGs) have been used as catalyst for synthetic organic transformations since the first seminal paper by Bielawaski in 2010.[61] Ever since the concepts of green chemistry became customary in organic synthesis, the use of carbon based heterogeneous nanomaterials has become more popular.[62] Apart from its versatile catalytic activity, such catalysts can be re-used for several catalytic cycles without its activity getting diminished.



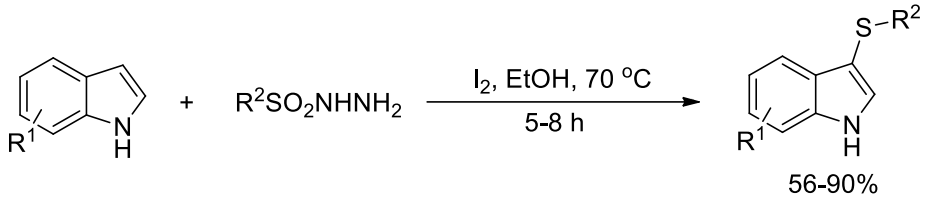
Scheme I.B.3 Common strategies for the synthesis of 3-sulfenylindoles.

I.B.2 Background and objectives

The fascinating biological profile of sulfenylated indoles intrigued researchers to develop numerous synthetic methods for its synthesis. Among the various known protocols, transition metal catalyzed regioselective sulfenylation of indole has been reported with various metals like Cu, Fe, Mg, Ce, V, Ru, etc.[58,59,63-67] The direct C–H sulfenylation of aromatic compounds have been reported either using peroxides or transition metal catalysts in combination with DMSO as oxidant.[68-71] Considering the toxicity as well as expensive nature of various transition metal based catalysts, metal-free methods have been developed. The most common approach has been the use molecular iodine in the presence of various sulfenylating reagents like thiols, disulfides, etc. However, most of these conditions using thiols as the sulfenylating reagent, required the presence of *tert*-butyl hydroperoxide (TBHP),[46] hydrogen peroxide (H_2O_2),[47] or DMSO as oxidant.[48-51] Moreover, the use of sulfenylating reagents other than thiols generated by-products thereby lowering atom economy of the reaction.[52,53,56,57] Although, the use of thiols in the regioselective sulfenylation, appears to be atom-economic, the presence of strong oxidants could lead to unwanted side reactions.[46-51] In another report, bovine serum albumin has been used as catalyst in combination with iodine for the regioselective sulfenylation of aromatic C(sp^2)–H using thiol.[72] Furthermore, the reaction has also been successful in the absence of any metal catalysts or iodine but required a strong base like NaOH.[73,74] A few examples citing recent developments in catalytic systems towards sulfenylation are presented below.

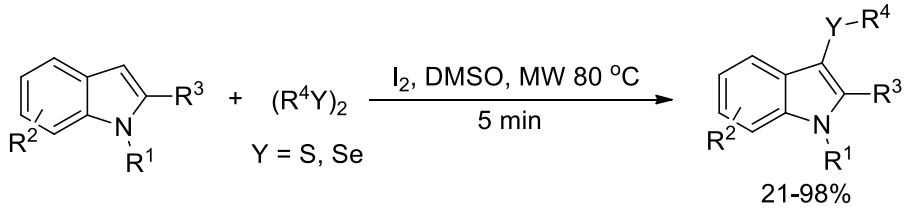
Iodine catalyzed regioselective sulfenylation of have been reported by using sulfonyl hydrazides as the sulfenylation reagent (Scheme I.B.4). The investigators presumed that the –$NHNH_2$ group of sulfonyl hydrazide removes the two oxygen atoms of the sulfonyl group

and serves as an effective sulfenylating agent. The sulfenyl group has been introduced selectively at the 3 position 1*H*-indole. However, when the 3 position of 1*H*-indole has been occupied the sulfenylation took place at the 2 position.[56]



Scheme 1.B.4 Iodine catalyzed regioselective sulfenylation of 1*H*-indoles.

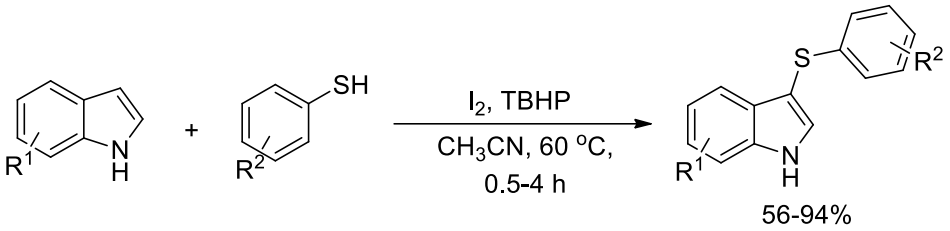
Microwave (MW) assisted synthesis of 3-sulfenyl and 3-selenylindoles have been achieved by using molecular iodine as catalyst.[53] The reaction took place in presence of DMSO as oxidant under MW irradiation (Scheme I.B.5). The authors suggested that iodine reacted with disulfide/diselenide and resulted in the formation of an electrophilic species RYI (Y = S/Se). The electrophilic species then reacted with indole leading to the formation of the desired product along with the concomitant release of HI.



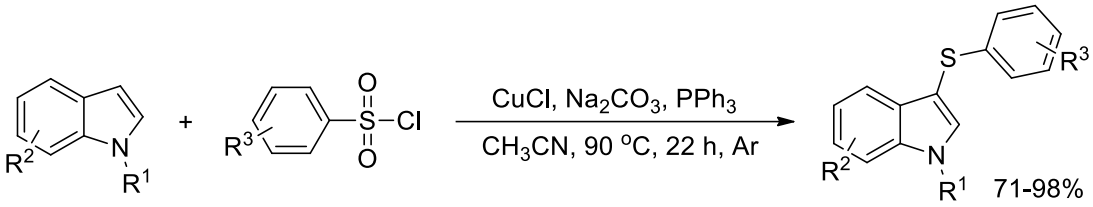
Scheme I.B.5 MW assisted and iodine catalyzed synthesis of 3-sulfenyl and 3-selenylindoles.

A facile method for the synthesis of 3-sulfenylindoles under mild conditions has been reported by using iodine as catalyst and TBHP as oxidant (Scheme I.B.6). A series of thiophenols and mercaptobenzoic acids have been used as the sulfenylation reagent furnishing the desired products in good to excellent yields. However, in the case of 3-substituted indoles, sulfenylation took place regioselectively at the 2 position. In addition 2,3-bis-sulfenylindoles has also been synthesized by following the same protocol. Moreover, the authors also carried out gram scale synthesis which afforded the desired product in 86% yield.[46]

An expedient synthesis of 3-sulfenylindoles has been reported by using cuprous chloride in presence of PPh_3 as reductant (Scheme I.B.7). The reaction conditions involve sulfonyl chloride as the sulfenylation reagent and the desired products have been obtained in 71-98%. Moreover, the investigators proposed a plausible mechanism.[58]

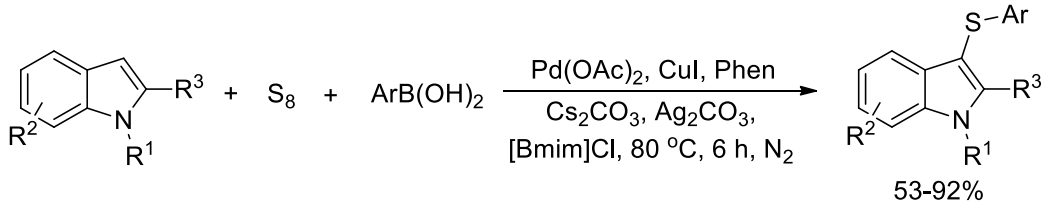


Scheme I.B.6 Molecular iodine catalyzed sulfenylation of indoles using thiophenols.



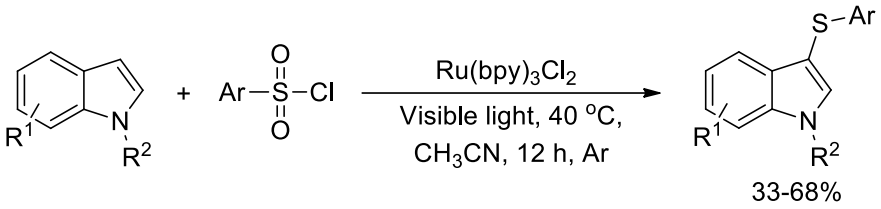
Scheme I.B.7 Copper catalyzed 3-sulfenylation of indoles.

Palladium catalyzed and ionic liquid mediated regioselective sulfenylation of indoles has been accomplished by using elemental sulfur as the sylfenylating reagent. The reaction conditions involve three-component strategy involving indoles, arylboronic acids and sulfur in the presence of copper iodide (Scheme I.B.8). Both 1*H*-indoles as well as N-substituted indoles reacted efficiently during the course of the reaction. Moreover, the protocol has been further extended towards the sulfenylation of 1*H*,1′*H*-2,2′-bisindole, pyrrole, furan, benzofuran and imidazo[1,2-*a*]pyridines. The investigators also suggested a plausible mechanism on the basis of some control experiments.[60]



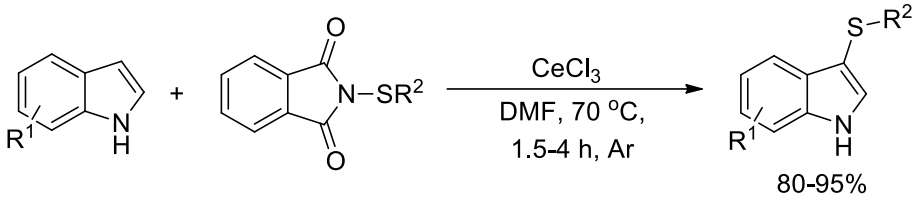
Scheme I.B.8 Palladium catalyzed regioslective sulfenylation of heteroarenes.

The regioselective sulfenylation of N-methylindoles has been developed under photoredox catalysis (Scheme I.B.9). The investigators have used $Ru(bpy)_3Cl_2$ as photoredox catalyst and arylsulfonyl chlorides as the sulfenylation reagent. The mechanism of the reaction involved a single electron transfer (SET) process generating radical intermediates.[63] A 23 W compact fluorescent lamp (CFL) has been used as the source of visible light.



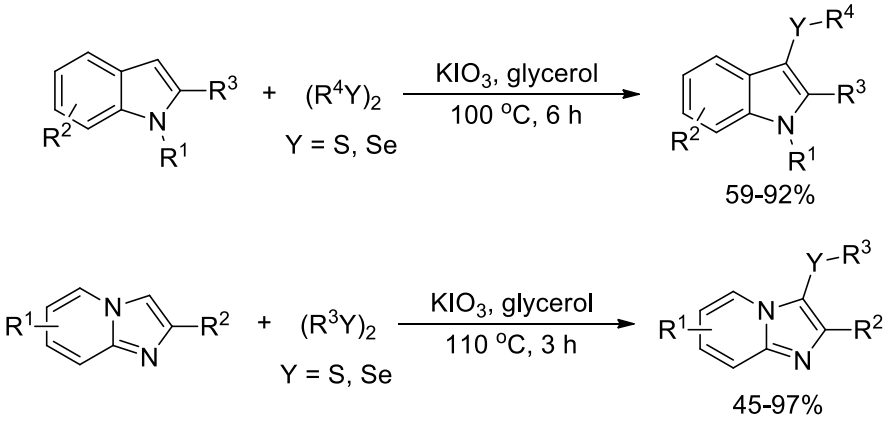
Scheme I.B.9 Visible light induced photocatalytic synthesis of 3-sulfenylindoles.

An efficient synthesis of 3-sulfenylindoles has been developed by using anhydrous $CeCl_3$ as catalyst.[59] N-(alkylthio) and N-(arylthio)phthalimides have been used as the sulfenylation reagent (Scheme I.B.10). The reaction conditions are facile and the desired products have been obtained in 80-95%.



Scheme I.B.10 $CeCl_3$ catalyzed synthesis of 3-sulfenylindoles.

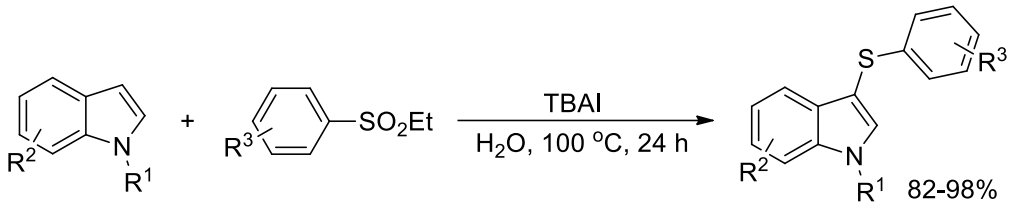
Potassium iodate (KIO_3) has been used as an oxidant for the metal-free chalcogenation of indoles and imidazopyridines (Scheme I.B.11). The authors carried out the synthesis using disulfides/diselenides and glycerol as a benign additive.[27] Moreover several control experiments have been performed to get insights into the mechanistic pathway for the reaction.



Scheme I.B.11 KIO_3 catalyzed chalcogenation of indoles and imidazopyridines.

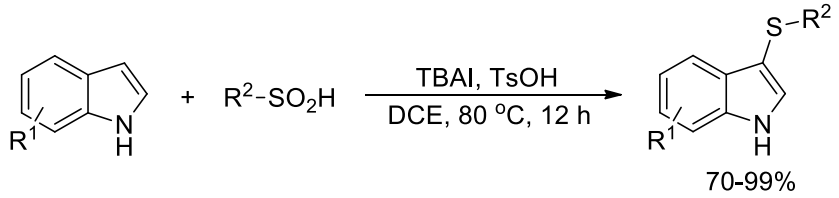
A tetrabutylammonium iodide (TBAI) mediated and on-water sulfenylation of aromatic compounds has been developed.[25] Diverse aryl sulfides have been synthesized by using ethyl

arylsulfinates as the sulfenylation reagent (Scheme I.B.12). Moreover, bisthioethers of pyrroles through double sulfenylation has been carried out by employing the same protocol. The investigators also performed end product functionalization via Suzuki and Sonogashira coupling reaction.



Scheme I.B.12 TBAI mediated and on-water sulfenylation of indoles.

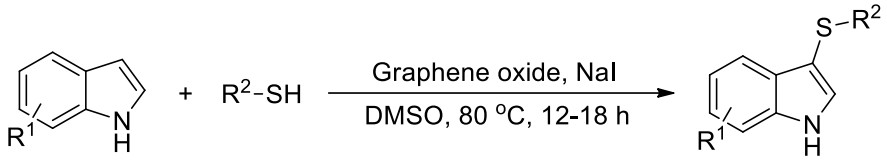
In another report, Liu and co-workers,[75] have developed TBAI mediated synthesis of diverse 3-sulfenylindoles by using sulfinic acids as the sulfenylation reagent (Scheme I.B.13). The mechanism of the reaction involved the formation of disulfide intermediate along with in situ liberation of iodine from TBAI, in the presence of TsOH. A library of 3-sulfenylindoles has been synthesized in 70-99% yield.



Scheme I.B.13 TBAI mediated synthesis of diverse 3-sulfenylindoles.

I.B.3 Present work: Results and discussions

Organic transformations that are greener and atom-economic have been of great interest recently. In this context, graphene oxide (GO) has emerged as an efficient cabocatalyst. GO could be obtained easily from graphite powder by oxidation and subsequent exfoliation.[76] Its mild acidic nature (pH 4.5 at 0.1 mg/ml),[77] and oxidising properties have been exploited in various organic transformations.[62] We have developed a new metal-free protocol for the regioselective sulfenylation of indole using thiols using catalytic graphene oxide (GO) and NaI as an additive (Scheme I.B.14).

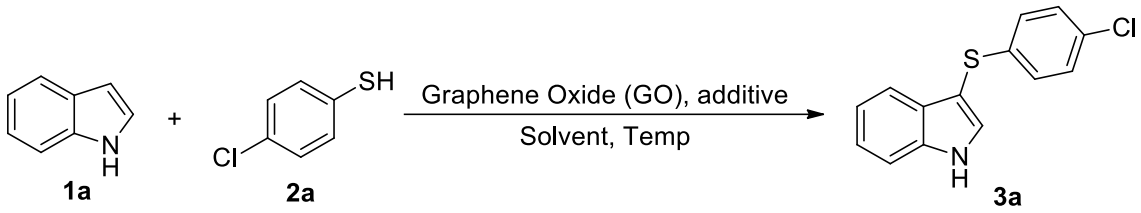


Scheme I.B.14 Graphene oxide catalyzed synthesis of 3-sulfenylindoles.

I.B.3.1 Optimization of reaction conditions

We began our preliminary investigations by using 1*H*-indole and 4-chlorothiophenol as model substrates for the reaction using GO and NaI under different conditions (Table I.B.1). Initially, we used GO (50 mg) and NaI (10 mol%) in toluene at 80 °C for 24 h. The reaction proceeded with isolation of the desired product **3a** in 68% yield (entry 1). The formation of the desired product 3-(4-chlorophenylthio)-1*H*-indole (**3a**) was confirmed by ^{1}H and ^{13}C NMR spectroscopy and by comparing its melting point with previously reported literature reports.[52] In the ^{13}C NMR spectrum, the peak at 102.4 ppm corresponds to C-3 of indole moiety which has been sulfenylated. After the confirmation of the desired product we continued further optimization of the reaction conditions. We then reduced the amount of GO to 25 mg which resulted in similar conversion (entry 2, 70%). While changing the solvent to polar aprotic (CH_3CN) or protic (MeOH) resulted in lower yield of the sulfenylated products (entries 4 and 5), the reaction in DMSO gave excellent conversion (entry 6, 97%). This was due to the oxidative nature of DMSO. There were reports suggesting the liberation of HI during the course of the reaction.[52] We assumed that the presence of DMSO along with GO oxidizes the HI back to I_2, which then continues the catalytic cycle. The absence of any of the components like GO, NaI or DMSO did exhibit considerable effect in the course of the reaction and in terms of yield of the product. For example, a neat mixture of reactants, GO and NaI afforded the product in lower yield (entry 7, 55%), while there was meagre conversion without using GO or NaI (entries 8 and 9). However, in the absence of GO and NaI, we did not observe any conversion (entry 10). Altering NaI with KI, KBr or NaCl lowered the yield of the product **3a** significantly (entries 11-13). Although the use of KI resulted in good yield of the desired product, its expensive nature prevented its further use in our catalytic system. The use of I_2 also afforded the desired product but in lower yield (entry 14, 64%). We presumed that that the freshly generated iodine via in situ oxidation of NaI was more active than commercially available molecular iodine. To check the viability of the catalytic system for industrial applications, we carried out gram scale synthesis of **3a** by employing the optimized reaction conditions. The reaction resulted in excellent conversion and the desired product **3a** was isolated in 94% yield (entry 15).

Table I.B.1 Optimization of reaction conditions[a]



Entry	GO (mg)	Additive (10 mol%)	Solvent	Temp (°C) / time (h)	Yield (%)[b]
1	50	NaI	Toluene	80 / 24	68
2	25	NaI	Toluene	80 / 24	70
3	10	NaI	Toluene	100 / 24	43
4	25	NaI	CH_3CN	80 / 24	10
5	25	NaI	MeOH	80 / 24	12
6	**25**	**NaI**	**DMSO**	**80 / 12**	**97**
7	25	NaI	–	80 / 24	55
8	25	–	DMSO	80 / 24	Trace
9	–	NaI	DMSO	80 / 24	Trace
10	–	–	DMSO	80 / 24	–
11	25	KI	DMSO	80 / 12	72
12	25	KBr	DMSO	80 / 12	20
13	25	NaCl	DMSO	80 / 12	24
14	25	I_2	DMSO	80 / 12	64
15	60	NaI	DMSO	80 / 12	94[c]

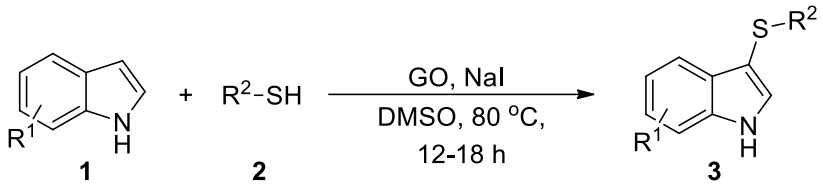
[a]Reaction conditions: 1*H*-indole (1 mmol), 4-chlorothiophenol (1.5 mmol), additive (10 mol%), solvent (2 mL). [b]Isolated yield. [c]Reaction was performed in 10 mmol scale.

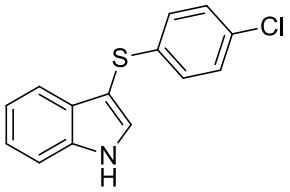
I.B.3.2 Synthesis of 3-sulfenylindoles

After optimization of the reaction conditions, various 1*H*-indoles and thiols were employed for the synthesis of 3-sulfenylindoles, as listed in Table I.B.2. Arylthiols containing chloro, methyl, amino group or 2-naphthylthiol worked efficiently leading to the exclusive formation of corresponding 3-sulfenylated products (**3a-d**). Further attempt with aliphatic thiols like cyclohexylthiol, *n*-pentylthiol or *n*-heptylthiol also worked fairly efficiently affording the desired products in 81-89% yields (**3e-g**). On the part of the indole moiety, we tried with an electron withdrawing group at C-6 position of indole and that too gave excellent conversions, exhibiting similar reactivity, selectivity and yield of products (**3h-j**). We then checked the presence of substituents in the N-containing five-membered ring of the indole moiety. Whereas 3-substituted indole underwent sulfenylation selectively at C-2 position (**3k**), the 2-substituted indole gave the corresponding 3-sulfenylated product in 95% yield (**3l**). Furthermore, heterocyclic thiols like 2-thiazoline-2-thiol and pyridine-2-thiol also worked efficiently furnishing the desired products in 81% and 89% yield respectively (**3m** and **3n**).

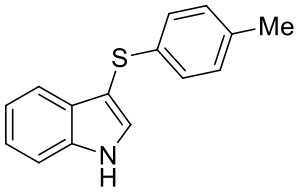
The formation of the desired products was confirmed by ^{1}H and ^{13}C NMR spectroscopy and by HRMS. For instance in case of **3b**, the ^{1}H NMR peak at δ 2.24 and 8.37 ppm corresponds to that of the CH_3 group of the thiol moiety and indole NH respectively. Similarly, the ^{13}C NMR peak at δ 20.9 ppm represents the CH_3 group of the thiol moiety. In case of **3f** the triplet centred at δ 2.68 ppm was due to the SCH_2 moiety of *n*-pentylthiol. The compound **3f** was subjected to ESI-HRMS analysis and the (*m/z*) for $C_{13}H_{17}NS$ $[M + H]^+$ was calculated at 220.1160 and found at 220.1156, which confirmed the formation of **3f**. The formation of **3h** was confirmed by the peak at 3.94 ppm due to the ester CH_3 group. Moreover, the doublet of doublet at δ 7.85 ppm (J = 1.5 and 8.4 Hz) was due to the H-5 of indole moiety. In case of ^{13}C NMR the peak at δ 137.9 ppm was due to the ester C=O group of indole.

Table I.B.2 Sulfenylation of indoles[a]

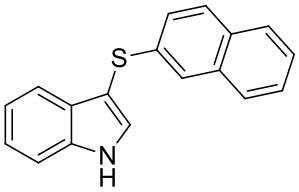




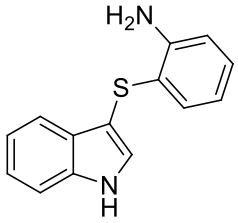
3a, 97%, 12 h



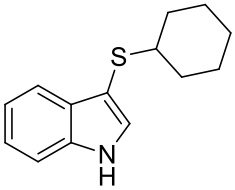
3b, 94, 12 h



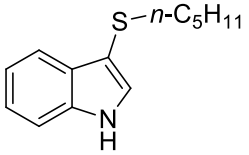
3c, 81%, 12 h



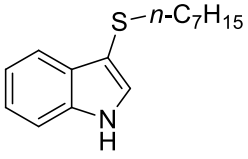
3d, 85%, 12 h



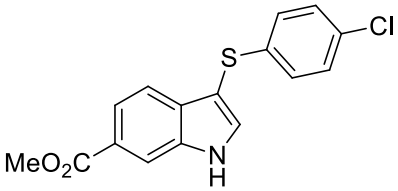
3e, 81%, 18 h



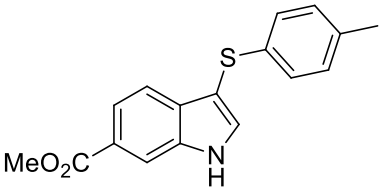
3f, 89%, 14 h



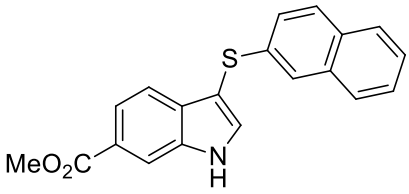
3g, 86%, 14 h



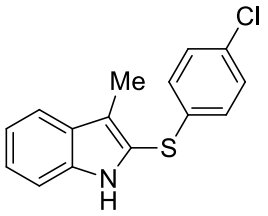
3h, 91%, 12 h



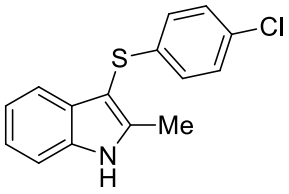
3i, 90%, 12 h



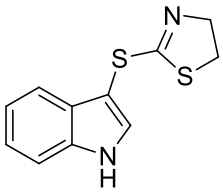
3j, 81%, 18 h



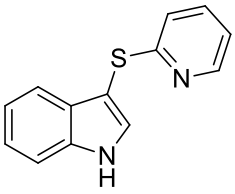
3k, 85%, 12 h



3l, 95%, 12 h



3m, 81%, 18 h



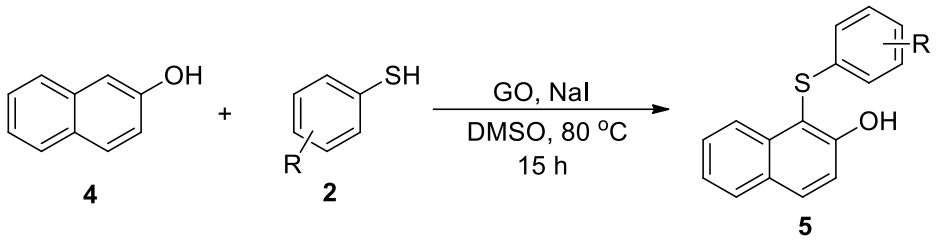
3n, 89%, 12 h

[a]Reaction conditions: **1** (1 mmol), **2** (1.5 mmol), NaI (10 mol%), GO (25 mg) and DMSO (2 mL) were stirred at 80 °C for 12-18 h.

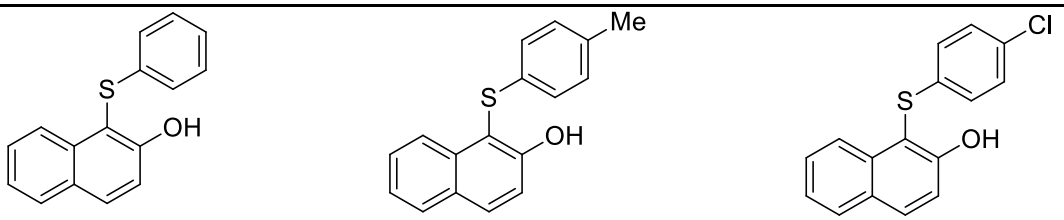
I.B.3.3 Sulfenylation of 2-naphthol, resorcinol and 2-naphthylamine

We then extended the scope of the protocol towards the sulfenylation of other aromatic systems like 2-naphthol, resorcinol and 2-naphthylamine.[78,79] Gratifyingly, in all cases, the reaction worked successfully as well as selectively affording the desired sulfenylated products in good to excellent yields. The results are presented in Table I.B.3, I.B.4 and I.B.5. While 2-naphthol and 2-naphthylamine afforded exclusive formation of C-1 sulfenylated products, sulfenylation of resorcinol took place regioselectively at the C-4 position. Aromatic thiols with different substitutions and aliphatic thiols reacted in the same manner without any significant variations in terms of reactivity. The products were characterized by ^{1}H and ^{13}C NMR spectroscopy. In case of the compound **5e** the ^{1}H NMR peaks at δ 1.98 and 2.53 ppm were due to the two methyl groups of the thiol moiety. The same peaks appeared at δ 19.6 and 21.0 ppm in the ^{13}C NMR spectrum. The compound **7c** showed two triplets at δ 0.83 (J = 7.2 Hz) and 2.58 (J = 7.5 Hz) ppm due to the terminal CH_3 and SCH_2 moieties respectively of *n*-pentylthiol. In the ^{13}C NMR spectrum those peaks appeared at δ 13.9 and 37.1 ppm. In the ^{13}C NMR spectrum of **7d**, heteronuclear coupling between ^{13}C and ^{19}F was observed. The peak centred at δ 130.35 ppm showed J value of 189 Hz which was due to one-bond coupling between ^{13}C and ^{19}F. Similarly, the peaks at δ 116.46 (J = 87 Hz) and δ 128.80 (J = 30 Hz) ppm were respectively due to two-bond and three-bond coupling between ^{13}C and ^{19}F.

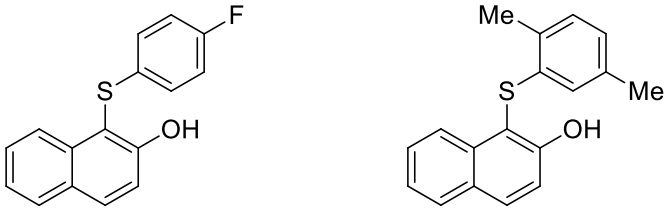
Table I.B.3 Sulfenylation of 2-naphthol[a]



4 2 5



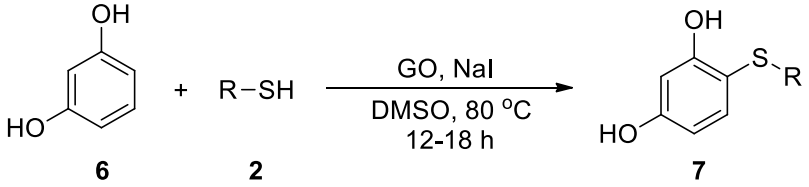
5a, 85% **5b**, 87% **5c**, 89%



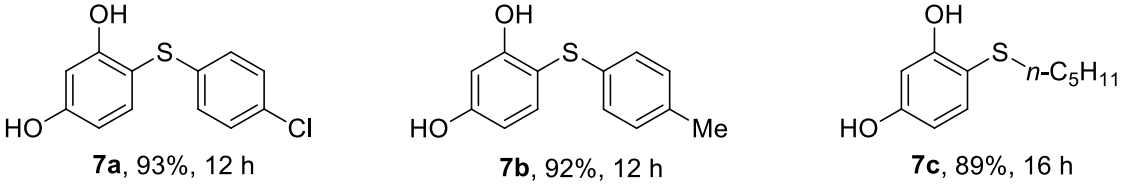
5d, 90% **5e**, 84%

[a]Reaction conditions: **4** (1 mmol), **2** (1.5 mmol), NaI (10 mol%), GO (25 mg) and DMSO (2 mL) were stirred at 80 °C for 15 h.

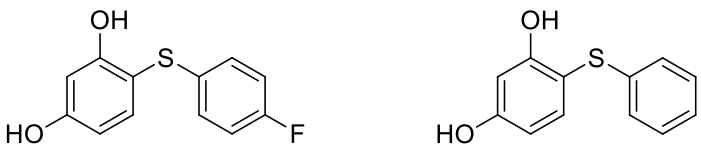
Table I.B.4 Sulfenylation of resorcinol[a]



6 2 7



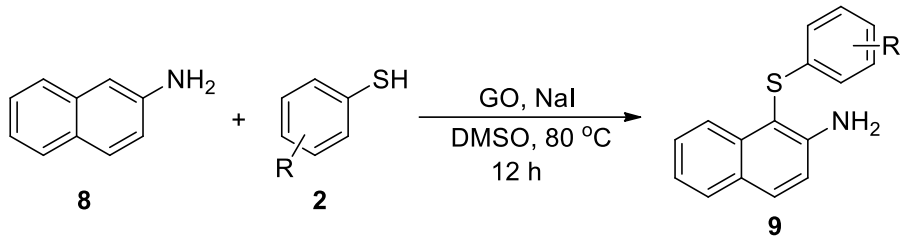
7a, 93%, 12 h **7b**, 92%, 12 h **7c**, 89%, 16 h



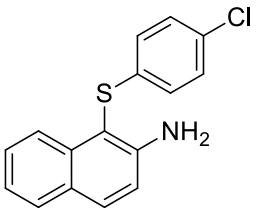
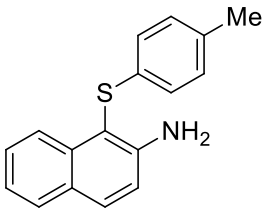
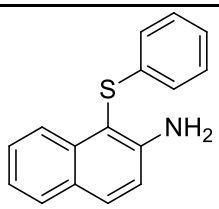
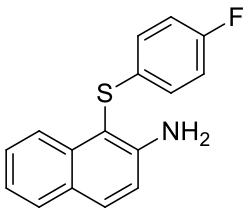
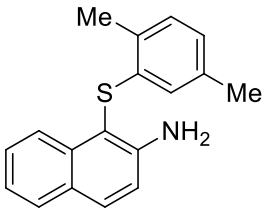
7d, 91%, 12 h **7e**, 84%, 18 h

[a]Reaction conditions: **6** (1 mmol), **2** (1.5 mmol), NaI (10 mol%), GO (25 mg) and DMSO (2 mL) were stirred at 80 °C for 12-18 h.

Table I.B.5 Sulfenylation of 2-naphthylamine[a]



8 + **2** → **9**

 **9a**, 85%	 **9b**, 82%	 **9c**, 79%
 **9d**, 85%	 **9e**, 91%	

[a]Reaction conditions: **8** (1 mmol), **2** (1.5 mmol), NaI (10 mol%), GO (25 mg) and DMSO (2 mL) were stirred at 80 °C for 12 h.

I.B.3.4 Recyclability of graphene oxide

The reusability of the catalyst (GO) was evaluated in the sulfenylation of indole for the synthesis of **3a**. After the first run conducted in 2 mmol scale using GO (50 mg), the reaction mixture was partitioned between ethyl acetate and water and centrifuged at 5000 rpm. The supernatant was decanted and the process was repeated twice. The residual solid material was dried under vacuum to obtain free flowing GO powder. The recovery was however ~10% less than the used quantity. The recovered catalyst was then used for second run (1 mmol scale) using GO (25 mg) with almost equal efficiency. From the third run, there was a decreasing trend in its performance and after the fourth run, the isolated yield was significantly low (Figure I.B.2). The FT-IR spectrum of the recovered GO after first, second and fourth run was recorded (Figure I.B.3). The IR absorption after fourth run indicated partial loss of oxygenated functional groups which might be due to the repeated use of the recovered catalyst under the reaction condition.

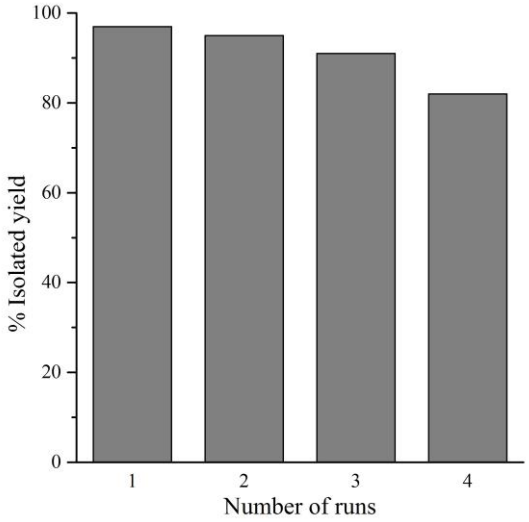


Figure I.B.2 Recyclability of GO for the sulfenylation of indole.

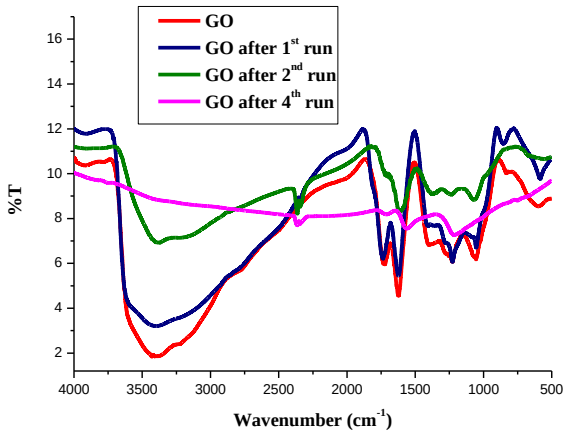


Figure I.B.3 FT-IR spectra of GO before and after first, second and fourth run.

The catalyst was then characterized by powder X-ray diffraction (XRD) for both fresh and recovered (after the first run) and found to be consistent with literature reports.[62,76] The XRD pattern of fresh GO was observed at 2θ = 9.5° and the recovered GO showed an additional peak at 2θ = 24.9° indicating partial reduction of GO (Figure I.B.4(a)). Thereafter, both the fresh as well as recovered catalyst were subjected to Raman analysis (Figure I.B.4(b)). The Raman spectra of GO clearly showed the D- and G-bands respectively at 1359 cm^{-1} and 1596 cm^{-1}. Similarly, the Raman spectra of recovered GO (after the first run) showed both the bands at 1360 cm^{-1} and 1591 cm^{-1}. Since the Raman spectra for both fresh and recovered catalyst were fairly similar, hence no conclusive information could be drawn. Furthermore, we quantified the amount of acidic functionalities on GO (both fresh and after the first run)

using pH titration (Figure I.B.5). The pH potentiometric acid-base titration of the fresh GO (50 mg) with 0.1 M NaOH aqueous solution using 50 mL of 0.5 M NaCl aqueous solution as back electrolyte was performed and calculated an approximate value of 1.68 mmol g^{-1} for the presence of carboxylic and hydroxyl groups.[77] In the case of using recovered GO (after the first run), the calculated value was 1.60 mmol g^{-1}. The results obtained thus confirmed that the acidic property of GO remained almost same even after the reaction.

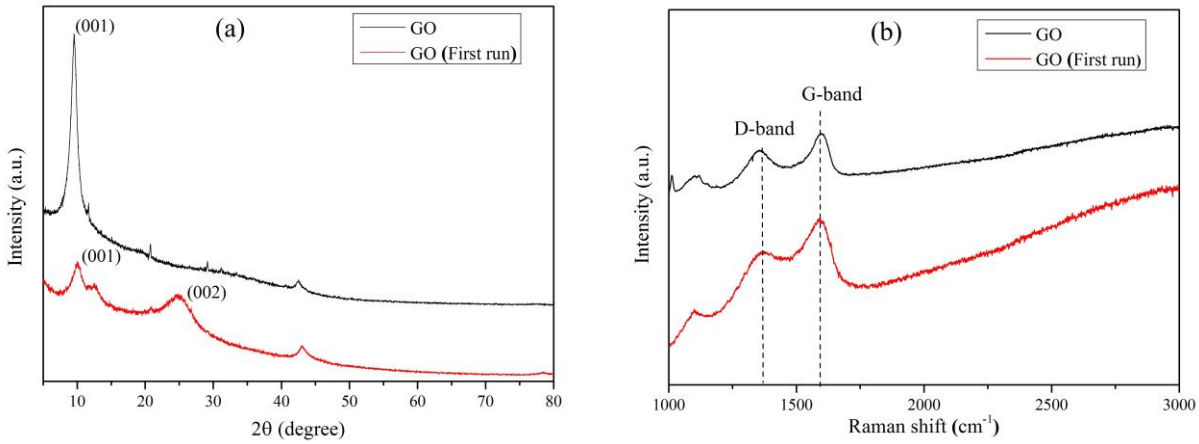


Figure I.B.4 (a) XRD patterns and (b) Raman spectra of GO fresh and after the first run.

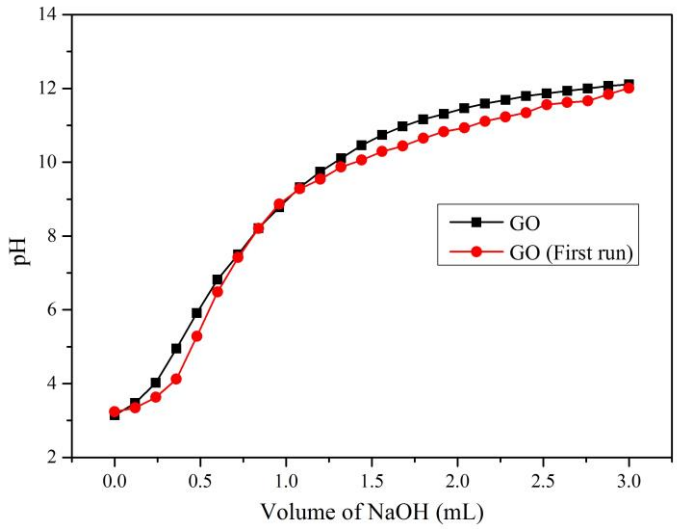
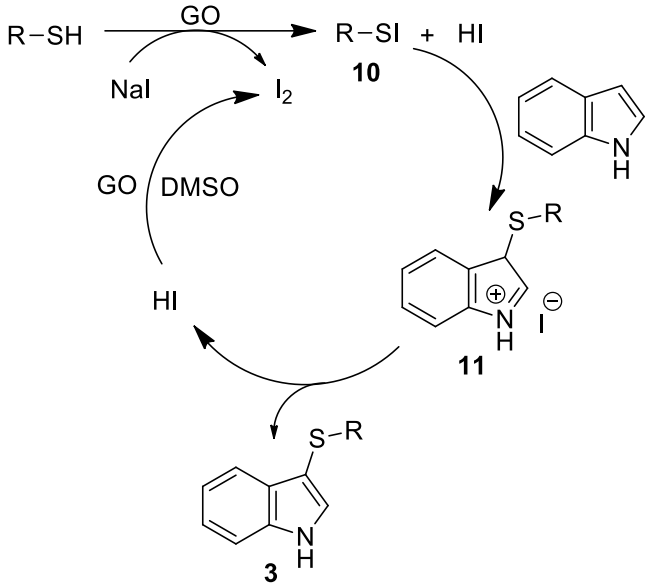


Figure I.B.5 The pH potentiometric titration curve of GO fresh and after the first run.

I.B.3.5 Plausible mechanism for the sulfenylation of indoles

Similar reactions with thiol mediated by molecular iodine (I_2) are believed to occur via disulfide formation, which subsequently produces an electrophilic species **10**.[52] We set up one reaction between 1*H*-indole and bis(4-chlorophenyl) disulfide which did not give the desired product (**3a**). This suggests that a strong oxidizing agent is essential for the reaction.

Moreover, GO catalyzed sulfenylation in the presence of molecular iodine (I_2) resulted in poor conversion (Table I.B.1, entry 14). Although we do not have clear explanation but we presumed that the freshly generated I_2 from the oxidation of NaI in the presence of GO could be more reactive towards thiol to form the electrophilic species **10**, which subsequently reacted with 1*H*-indole to form **11.** Finally, the intermediate 11 led to the formation of the desired product along with the liberation of HI. Thereafter HI underwent oxidation in the presence of GO in DMSO to form I_2 for the next catalytic cycle (Scheme I.B.15).



Scheme I.B.15 Proposed mechanism for the sulfenylation of 1*H*-indoles.

I.B.4 Conclusion

In summary, we have developed a metal-free, facile and atom-economic protocol for the site-selective C–H sulfenylation of various aromatic compounds using catalytic graphene oxide (GO). We believed that the freshly generated iodine in presence of GO could be highly reactive towards the formation of the electrophilic species that adds to indole to afford the desired thioethers. The reaction shows good tolerance towards several substituted aromatic systems. The present protocol is likely to attract the interest of synthetic chemists because of simple and greener aspects, devoid of strong oxidants, reusability of catalyst and broader applicability.

I.B.5 Experimental Section

I.B.5.1 General Information

All reagents were purchased from Sigma Aldrich and TCI, and used directly without further purification. The solvents were purchased from commercial suppliers and used after distillation. All the products were purified by column chromatography on 60-120 mesh silica gel (SRL, India). For TLC, Merck plates coated with silica gel 60, F_{254} were used. FT-IR spectra were recorded in FT-IR 8300 SHIMADZU spectrophotometer. The ^{1}H and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz respectively on Bruker AV 300 spectrometer in $CDCl_3$ and DMSO-d_6. Splitting patterns of protons were described as s (singlet), d (doublet), t (triplet), dd (doublet of doublet), m (multiplet) and br (broad). Chemical shifts (δ) were reported in parts per million (ppm) relative to TMS as internal standard. *J* values (coupling constant) were reported in Hz (Hertz). ^{13}C NMR spectra were recorded with complete proton decoupling ($CDCl_3$: δ 77.0 ppm and DMSO-d_6: 39.5 ppm). Centrifugation was done in REMI R-8C DX centrifuge at 5250 rpm. The X-ray diffraction studies were done using the Rigaku SmartLab (9 kW) diffractometer using CuKα radiation. Raman spectra were performed on ENSpectr R532 Raman microscope using 532 nm laser. The pH potentiometric titration was done by using Digital pH meter, Systronics, India.

I.B.5.2 Preparation of graphene oxide (GO)

Graphene oxide was prepared by following Tour's method.[76] In this method a 9:1 (v/v) mixture of H_2SO_4 / H_3PO_4 (180:20 mL) was added to a mixture of graphite powder (1.5 g) and $KMnO_4$ (9.0 g). The mixture was then stirred at 50 °C for 12 h. After cooling the mixture to room temperature, it was gradually poured into crushed ice (200 g), which was followed by the slow addition of H_2O_2 (30%, 1.5 mL). The solution was then centrifuged (5000 rpm) and the supernatant was discarded. The residual solid material was successively washed with deionised water (100 mL) and then with 30% HCl (100 mL). The solid material was then repeatedly washed with water and centrifuged. Finally, the solid brown material was collected and dried at 60 °C under vacuum to obtain solid graphene oxide.

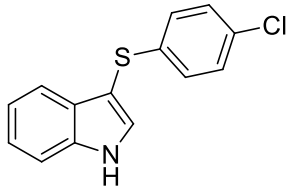
I.B.5.3 General procedure for the sulfenylation of aromatic compounds

In a screw-capped sealed tube equipped with a magnetic stir bar, aromatic compounds (1 mmol), thiols (1.5 mmol), NaI (10 mol%) and GO (25 mg) were added to 2 mL of freshly distilled DMSO. The resulting reaction mixture was stirred at 80 °C for 12-18 h. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature. The catalyst was then recovered through simple filtration. The reaction mixture was diluted with water and extracted by ethyl acetate (3 x 5 mL). Finally, the combined organic layer was dried over anhydrous Na_2SO_4 and concentrated. The residue was then further purified by column chromatography on silica gel using the light petroleum ether and

ethyl acetate as eluent to afford the desired products. All products were characterized by ^{1}H, ^{13}C NMR spectroscopy and compared with the reported melting points for known solid compounds.

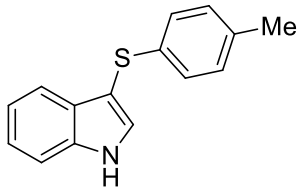
I.B.5.4 Characterization data of compounds listed in Table I.B.2-I.B.5

3-(4-Chlorophenylthio)-1*H*-indole (3a)[52]



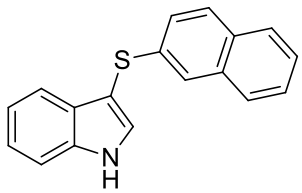
White solid; m.p.: 126–127 °C (Lit. m.p.: 127.5–128.3 °C); **^{1}H NMR ($CDCl_3$, 300 MHz):** δ 7.00–6.98 (m, 2H, ArH), 7.02–7.01 (m, 2H, ArH), 7.19–7.08 (m, 1H, ArH), 7.29–7.23 (m, 1H, ArH), 7.46–7.41 (m, 2H, ArH), 7.56 (d, *J* = 7.8 Hz, 1H, ArH), 8.41 (s, br, 1H, NH); **^{13}C NMR ($CDCl_3$, 75 MHz):** δ 102.4, 111.7, 119.5, 121.0, 123.2, 127.1, 128.7, 128.8, 130.5, 130.7, 136.5, 137.8.

3-(*p*-Tolylthio)-1*H*-indole (3b)[52]



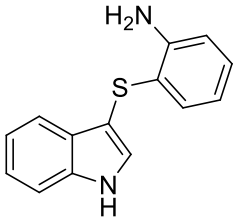
White solid; m.p.: 125–126 °C (Lit. m.p.: 125–126 °C); **^{1}H NMR ($CDCl_3$, 300 MHz):** δ 2.24 (s, 3H, CH_3), 7.03–6.95 (m, 4H, ArH), 7.28–7.12 (m, 2H, ArH), 7.45–7.40 (m, 2H, ArH), 7.61 (d, *J* = 7.2 Hz, 1H, ArH), 8.37 (s, br, 1H, NH); **^{13}C NMR ($CDCl_3$, 300 MHz):** δ 21.0, 103.3, 111.5, 119.7, 120.8, 123.0, 126.2, 129.1, 129.5, 130.5, 134.6, 135.4, 136.4.

3-(Naphthalen-2-ylthio)-1*H*-indole (3c)[56]



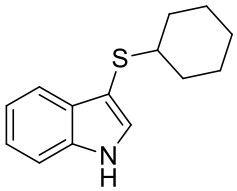
Off white solid; m.p.: 174–175 °C (Lit. m.p.: 141–143 °C); **^{1}H NMR ($CDCl_3$, 300 MHz):** δ 7.16–7.14 (m, 3H, ArH), 7.28–7.24 (m, 2H, ArH), 7.36–7.34 (m, 2H, ArH), 7.48–7.45 (m, 2H, ArH), 7.55–7.54 (m, 2H, ArH), 7.70–7.65 (m, 1H, ArH), 8.45 (s, br, 1H, NH); **^{13}C NMR ($CDCl_3$, 75 MHz):** δ 102.9, 111.6, 119.7, 120.9, 123.1, 123.5, 124.8, 125.0, 127.0, 127.6, 128.2, 130.6, 131.3, 133.7, 136.5, 136.7, 137.0, 139.9.

3-(2-Aminophenylthio)1*H*-indole (3d)[52]



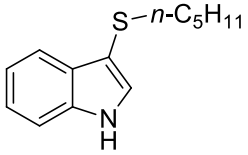
Brown solid; m.p.: 89–90 °C (Lit. m.p.: 93–95 °C); **^{1}H NMR ($CDCl_3$, 300 MHz):** δ 3.22 (d, *J* = 2.7, 2H, NH_2), 6.69–6.57 (m, 2H, ArH), 7.02–6.97 (m, 1H, ArH), 7.26–7.11 (m, 3H, ArH), 7.37–7.34 (m, 2H, ArH), 7.66 (d, *J* = 8.1 Hz, 1H, ArH), 8.36 (s, br, 1H, NH); **^{13}C NMR ($CDCl_3$, 75 MHz):** δ 111.5, 115.3, 119.0, 119.4, 120.6, 120.7, 122.8, 128.0, 128.7, 129.0, 132.0, 136.3, 145.6.

3-(Cyclohexylthio)-1*H*-indole (3e)[67]



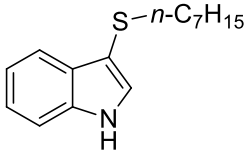
Light brown solid; m.p.: 96–97 °C (Lit. m.p.: 91–93.1 °C); **^{1}H NMR ($CDCl_3$, 300 MHz):** δ 1.42–1.16 (m, 5H, CH_2), 1.57–1.52 (m, 1H, CH_2), 1.65–1.61 (m, 1H, CH_2), 1.75–1.71 (m, 2H, CH_2), 1.96–1.92 (m, 2H, CH_2), 2.82–2.74 (m, 1H, CH), 7.26–7.17 (m, 2H, ArH), 7.30 (d, *J* = 2.4 Hz, 1H, ArH), 7.41–7.35 (m, 1H, ArH), 7.80–7.76 (m, 1H, ArH), 8.27 (s, br, 1H, NH); **^{13}C NMR ($CDCl_3$, 75 MHz):** δ 25.7, 26.2, 33.7, 47.5, 104.7, 111.3, 119.7, 120.4, 122.5, 130.2, 130.3, 136.2.

3-(Pentylthio)-1*H*-indole (3f)



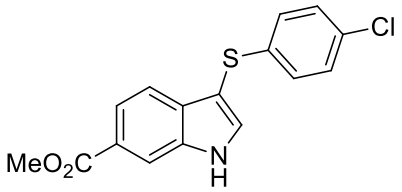
Colourless liquid; **^{1}H NMR ($CDCl_3$, 300 MHz):** δ 0.85 (t, *J* = 7.2 Hz, 3H, CH_3), 1.39–1.20 (m, 4H, CH_2), 1.65–1.49 (m, 2H, CH_2), 2.68 (t, *J* = 7.2 Hz, 2H, CH_2), 7.23–7.16 (m, 2H, ArH), 7.25–7.28 (m, 1H, ArH), 7.36–7.33 (m, 1H, ArH), 7.79–7.74 (m, 1H, ArH), 8.21 (s, br, 1H, NH); **^{13}C NMR ($CDCl_3$, 75 MHz):** δ 14.0, 22.3, 29.6, 30.7, 36.4, 106.2, 111.4, 119.4, 120.3, 122.6, 129.2, 129.5, 136.3; HRMS–ESI (*m/z*) calcd for $C_{13}H_{17}NS$ $[M + H]^+$ 220.1160 found 220.1156.

3-(Heptylthio)-1*H*-indole (3g)



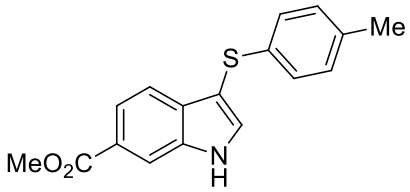
Colourless liquid; **^{1}H NMR (CDCl$_3$, 300 MHz):** δ 0.87–0.83 (m, 3H, CH_3), 1.30–1.23 (m, 7H, CH_2), 1.65–1.49 (m, 3H, CH_2), 2.68 (t, *J* = 7.2 Hz, 2H, CH_2), 7.23–7.17 (m, 3H, ArH), 7.36–7.32 (m, 1H, ArH), 7.79–7.77 (m, 1H, ArH), 8.19 (s, br, 1H, NH); **^{13}C NMR (CDCl$_3$, 75 MHz):** δ 14.1, 22.6, 28.5, 28.9, 30.0, 31.8, 36.4, 106.2, 11.5, 119.4, 120.4, 122.6, 129.2, 129.5, 136.3; HRMS–ESI (*m/z*) calcd for $C_{15}H_{21}NS$ $[M + H]^+$ 248.1473 found 248.1492.

Methyl 3-(4-chlorophenylthio)-1*H*-indole-6-carboxylate (3h)



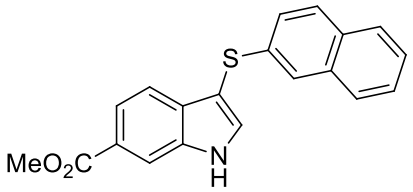
White solid; m.p.: 162–163 °C; **^{1}H NMR (CDCl$_3$, 300 MHz);** δ 3.94 (s, 3H, OCH_3), 7.13–6.98 (m, 4H, ArH), 7.64–7.57 (m, 2H, ArH), 7.85 (dd, *J* = 1.5, 8.4 Hz, 1H, ArH), 8.23 (s, 1H, ArH), 9.06 (s, br, 1H, NH); **^{13}C NMR (CDCl$_3$, 75 MHz):** δ 52.1, 103.1, 114.1, 119.1, 121.9, 124.9, 127.2, 128.8, 130.8, 132.5, 133.8, 135.9, 137.2, 167.9.

Methyl 3-(*p*-tolylthio)-1*H*-indole-6-carboxylate (3i)



White solid; m.p.: 155–157 °C; **^{1}H NMR (CDCl$_3$, 300 MHz):** δ 2.24 (s, 3H, CH_3), 3.93 (s, 3H, OCH_3), 7.00–6.98 (m, 4H, ArH), 7.64–7.60 (m, 2H, ArH), 7.83 (dd, *J* = 1.5, 8.4 Hz, 1H, ArH), 8.20 (s, 1H, ArH), 8.91 (s, br, 1H, NH); **^{13}C NMR (CDCl$_3$, 75 MHz):** δ 20.8, 52.1, 104.3, 114.0, 119.4, 121.7, 124.7, 126.4, 129.6, 132.8, 133.5, 134.9, 135.0, 135.9, 168.0.

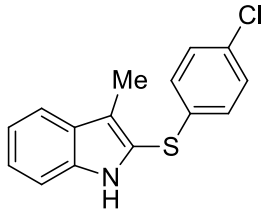
Methyl 3-(naphthalen-2-ylthio)-1*H*-indole-6-carboxylate (3j)



White solid; m.p.: 185–186 °C; **^{1}H NMR (DMSO-d$_6$, 300 MHz):** δ 3.91 (s, 3H, OCH_3), 7.27 (dd, *J* = 1.8, 8.7 Hz, 1H, ArH), 7.48–7.44 (m, 2H, ArH), 7.56–7.54 (m, 2H, ArH), 7.74–7.70

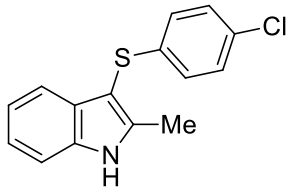
(m, 2H, ArH), 7.87–7.81 (m, 2H, ArH), 8.15 (d, *J* = 2.7 Hz, 1H, ArH), 8.22 (s, 1H, ArH); **^{13}C NMR (DMSO-d$_6$, 75 MHz):** δ 52.3, 100.7, 114.8, 118.7, 121.2, 123.5, 124.9, 125.8, 127.1, 127.2, 128.0, 128.9, 131.4, 132.8, 132.8, 133.7, 136.5, 136.6, 167.4.

2-(4-Chlorophenylthio)-3-methyl-1*H*-indole (3k)[80]



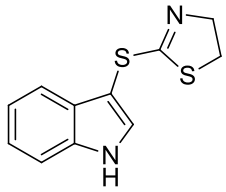
White solid; m.p.: 124–126 °C (Lit. m.p.: 126–127 °C); **^{1}H NMR (CDCl$_3$, 300 MHz):** δ 2.27–2.22 (s, 3H, CH_3), 6.84–6.81 (m, 2H, ArH), 7.05–7.02 (m, 3H, ArH), 7.15–7.06 (m, 2H, ArH), 7.50 (d, *J* = 8.1 Hz, 1H, ArH), 7.79 (s, br, 1H, NH); **^{13}C NMR (CDCl$_3$, 75 MHz):** δ 9.4, 111.0, 119.6, 119.8, 120.2, 120.9, 123.8, 127.7, 128.4, 129.2, 131.6, 135.8, 136.9.

3-(4-Chlorophenylthio)-2-methyl-1*H*-indole (3l)[81]



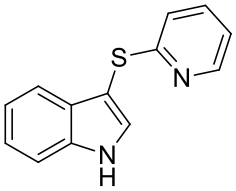
Light pink solid; m.p.: 97–99 °C (Lit. m.p.: 102–104 °C); **^{1}H NMR (CDCl$_3$, 300 MHz)**: δ 2.44–2.32 (m, 3H, CH_3), 6.95–6.94 (m, 2H, ArH), 7.20–7.06 (m, 4H, ArH), 7.28 (d, *J* = 7.8 Hz, 1H, ArH), 7.50 (d, *J* = 7.5 Hz, 1H, ArH), 8.15 (s, br, 1H, NH); **^{13}C NMR (CDCl$_3$, 75 MHz):** δ 12.1, 98.9, 110.8, 118.8, 120.9, 122.4, 126.8, 128.8, 130.0, 130.3, 135.5, 138.0, 141.3.

3-(4,5-Dihydrothiazol-2-ylthio)-1*H*-indole (3m)



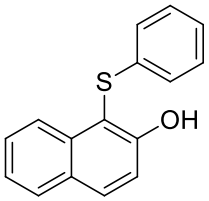
Off white solid; m.p.: 62 °C; **^{1}H NMR (CDCl$_3$, 300 MHz)**: δ 2.89 (t, *J* = 6.6 Hz, 2H, CH_2), 3.51 (t, *J* = 6.6 Hz, 2H, CH_2), 7.29–7.20 (m, 2H, ArH), 7.41–7.36 (m, 2H, ArH), 7.75–7.72 (m, 1H, ArH), 8.35 (s, br, 1H, NH); **^{13}C NMR (CDCl$_3$, 75 MHz):** δ 35.7, 44.5, 103.2, 111.7, 119.0, 120.9, 123.1, 129.1, 130.5, 131.7, 136.3.

3-(Pyridin-2-ylthio)-1*H*-indole (3n)[67]



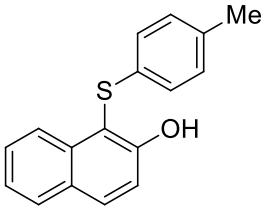
White solid; m.p.: 136 °C (Lit. m.p.: 137.2–138 °C); **^{1}H NMR (CDCl$_3$, 300 MHz):** δ 6.93–6.80 (m, 1H, ArH), 6.97–6.95 (m, 1H, ArH), 7.44–7.07 (m, 5H, ArH), 7.62 (d, *J* = 7.8 Hz, 1H, ArH), 8.40–8.38 (m, 1H, ArH), 9.52 (s, br, 1H, NH); **^{13}C NMR (CDCl$_3$, 75 MHz):** δ 100.6, 112.3, 119.6, 119.7, 120.4, 121.2, 123.3, 129.1, 131.9, 137.1, 149.2, 163.1.

1-(Phenylthio)naphthalen-2-ol (5a)[82]



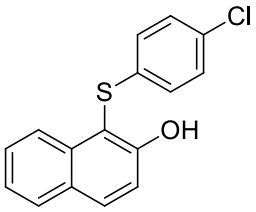
Off white solid; m.p.: 65–67 °C (Lit. m.p.: 66–67 °C); **^{1}H NMR (CDCl$_3$, 300 MHz):** δ 7.00–7.10 (m, 2H, ArH), 7.27–7.10 (m, 4H ArH), 7.39–7.31 (m, 2H, ArH), 7.51–7.45 (m, 1H, ArH), 7.80 (d, *J* = 8.1 Hz, 1H, ArH), 7.89 (dd, *J* = 3.6, 9 Hz, 1H, ArH), 8.21 (d, *J* = 7.8 Hz, 1H, ArH); **^{13}C NMR (CDCl$_3$, 75 MHz):** δ 108.0, 116.9, 123.9, 124.7, 125.9, 126.4, 128.0, 128.6, 129.2, 129.5, 132.8, 135.4, 135.4.

1-(*p*-Tolylthio)naphthalen-2-ol (5b)[82]



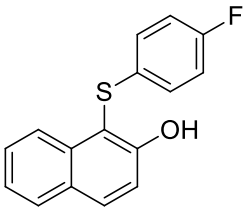
White solid; m.p.: 76–77 °C (Lit. m.p.: 78–79 °C); **^{1}H NMR (CDCl$_3$, 300 MHz):** δ 2.22 (s, 3H, CH_3), 6.99–6.91(m, 4H, ArH),7.50–7.21 (m, 4H, ArH), 7.87 (d, *J* = 8.7 Hz, 1H, ArH), 7.79 (d, *J* = 7.8 Hz, 1H, ArH) 8.22 (d, *J* = 8.4 Hz, 1H, ArH); **^{13}C NMR (CDCl$_3$, 75 MHz):** δ 20.8, 108.7, 116.8, 123.7, 124.7, 126.6, 127.8, 128.5, 129.4, 129.9, 131.7, 132.6, 135.4, 135.8, 156.8.

1-(4-Chlorophenylthio)naphthalen-2-ol (5c)[82]



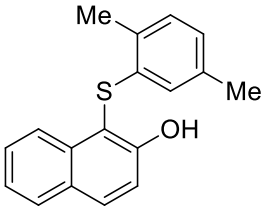
White solid; m.p.: 84–85 °C (Lit. m.p.: 84–85 °C); **^{1}H NMR ($CDCl_3$, 300 MHz):** δ 6.95–6.90 (m, 2H, ArH), 7.13–7.09 (m, 3H, ArH), 7.39–7.31 (m, 2H, ArH), 7.51–7.46 (m, 1H, ArH), 7.80 (d, *J* = 7.8 Hz, 1H, ArH), 7.89 (d, *J* = 9 Hz, 1H, ArH), 8.15 (d, *J* = 8.4 Hz, 1H, ArH); **^{13}C NMR ($CDCl_3$, 75 MHz):** δ 107.6, 116.9, 124.0, 124.4, 127.6, 128.1, 128.7, 129.3, 129.5, 131.9, 133.1, 133.9, 135.2, 157.0.

1-(4-Fluorophenylthio)naphthalen-2-ol (5d)[83]



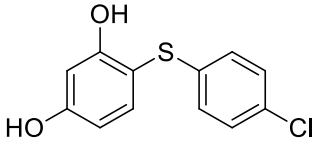
White solid; m.p.: 116–117 °C (Lit. m.p.: 116–119 °C); **^{1}H NMR ($CDCl_3$, 300 MHz):** δ 6.90–6.84 (m, 2H, ArH), 7.03–6.97 (m, 2H, ArH), 7.18 (s, 1H, ArH), 7.40–7.31 (m, 2H, ArH), 7.52–7.47 (m, 1H, ArH), 7.81 (d, *J* = 8.1 Hz, 1H, ArH), 7.90 (d, *J* = 8.7 Hz, 1H, ArH), 8.20 (d, *J* = 8.4 Hz, 1H, ArH); **^{13}C NMR ($CDCl_3$, 75 MHz)**: δ 108.4, 116.1, 116.4, 116.8, 123.9, 124.4, 128.0, 128.2, 128.3, 128.6, 129.5, 130.3, 132.9, 135.2, 156.8, 159.7, 163.0.

1-(2,5-Dimethylphenylthio)naphthalen-2-ol (5e)[84]



Yellow solid; m.p.: 57–58 °C (Lit. m.p.: 58–60 °C); **^{1}H NMR ($CDCl_3$, 300 MHz):** δ 1.98 (s, 3H, CH_3), 2.53 (s, 3H, CH_3), 6.20 (s, 1H, ArH), 6.82 (d, *J* = 7.5 Hz, 1H, ArH), 7.06 (d, *J* = 7.5 Hz, 2H, ArH), 7.48–7.33 (m, 3H, ArH), 7.82 (d, *J* = 8.1 Hz, 1H, ArH), 7.92 (d, *J* = 9.0 Hz, 1H, ArH), 8.14 (d, *J* = 8.4 Hz, 1H, ArH); **^{13}C NMR ($CDCl_3$, 75 MHz)**: δ 19.6, 21.0, 107.5, 116.8, 123.8, 124.7, 125.2, 126.4, 127.8, 128.5, 129.5, 130.2, 132.1, 132.7, 133.9, 135.5, 136.4, 157.1.

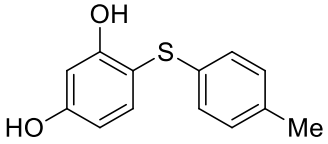
4-(4-Chlorophenylthio)benzene-1,3-diol (7a)[82]



White solid; m.p.: 102–103 °C (Lit. m.p.: 99–100 °C); **^{1}H NMR ($CDCl_3$, 300 MHz):** δ 2.24 (s, br, 1H, OH), 6.09 (s, br, 1H, OH), 6.57–6.46 (m, 2H, ArH), 6.95 (d, *J* = 8.4

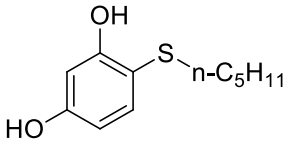
Hz, 2H, ArH), 7.17 (d, *J* = 8.1 Hz, 2H, ArH), 7.33 (d, *J* = 9 Hz, 1H, ArH); **^{13}C NMR ($CDCl_3$, 75 MHz):** δ 102.6, 106.8, 109.5, 127.5, 129.2, 131.8, 135.2, 138.2, 158.4, 159.6.

4-(*p*-Tolylthio)benzene-1,3-diol (7b)[82]



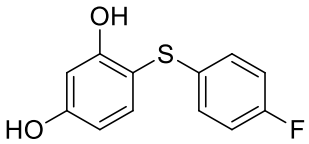
Pale brown solid; m.p.: 88–89 °C (Lit. m.p.: 77–78 °C); **^{1}H NMR ($CDCl_3$, 300 MHz):** δ 2.27 (s, 3H, CH_3), 5.72 (s, br, 1H, OH), 6.46 (dd, *J* = 3, 8.4 Hz, 1H, ArH), 6.61–6.55 (m, 2H, ArH), 7.05–6.95 (m, 4H, ArH), 7.38 (d, *J* = 8.4 Hz, 1H, ArH); **^{13}C NMR ($CDCl_3$, 75 MHz):** δ 20.9, 102.4, 108.0, 109.1, 126.7, 129.9, 133.0, 135.9, 138.0, 158.4, 159.2.

4-(Pentylthio)benzene-1,3-diol (7c)



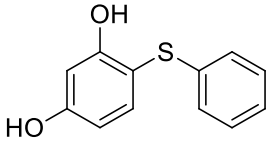
Pale yellow liquid; **^{1}H NMR ($CDCl_3$, 300 MHz):** δ 0.86 (t, *J* = 7.2 Hz, 3H, CH_3), 1.37–1.22 (m, 4H, CH_2), 1.67–1.47 (m, 2H, CH_2), 1.76–1.67 (m, 2H, CH_2), 2.26 (s, br, 1H, OH), 2.58 (t, *J* = 7.5 Hz, 2H, ArH), 6.21 (s, br, 1H, OH), 6.43–6.37 (m, 1H, ArH), 6.50 (d, *J* = 2.4 Hz, 1H, ArH), 6.96–6.88 (m, 1H, ArH), 7.32–7.26 (m, 1H, ArH); **^{13}C NMR ($CDCl_3$, 75 MHz)**: δ 13.9, 22.2, 29.2, 30.7, 37.8, 101.7, 108.5, 110.2, 137.2, 158.0, 158.4.

4-(4-Fluorophenylthio)benzene-1,3-diol (7d)



White solid; m.p.: 104–105 °C; **^{1}H NMR ($CDCl_3$, 300 MHz):** δ 6.47–6.43 (m, 2H, ArH), 6.70–6.55 (m, 5H, ArH), 6.87–6.78 (m, 4H, ArH), 7.78–7.77 (m, 1H, ArH); **^{13}C NMR ($CDCl_3$, 75 MHz):** δ 102.4, 109.7, 116.3, 116.6, 128.7, 128.8, 130.9, 144.9, 160.0, 160.6, 163.3.

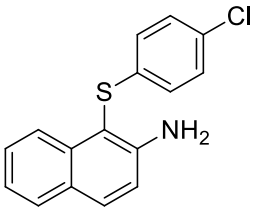
4-(Phenylthio)benzene-1,3-diol (7e)[82]



Brown solid; m.p.: 110–111 °C (Lit. m.p.: 111–112 °C); **^{1}H NMR ($CDCl_3$, 300 MHz)**: δ 1.90 (s, br, 1H, OH), 5.61 (s, br, 1H, OH), 6.60–6.45 (m, 3H, ArH), 7.25–7.02 (m, 5H,

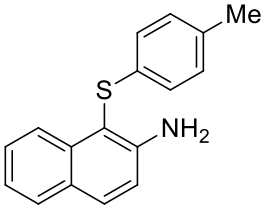
ArH), 7.39 (d, *J* = 8.4 Hz, 1H); **^{13}C NMR ($CDCl_3$, 75 MHz)**: δ 102.4, 107.2, 109.2, 125.8, 126.1, 129.1, 136.6, 138.2, 158.5, 159.3.

1-(4-Chlorophenylthio)naphthalen-2-amine (9a)[84]



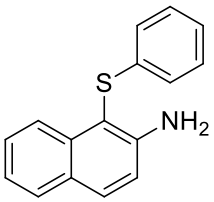
Deep brown solid; m.p.: 123–124 °C (Lit. m.p.: 123–125 °C); **^{1}H NMR ($CDCl_3$, 300 MHz):** δ 4.66 (s, br, 2H, NH_2), 6.95–6.86 (m, 2H, ArH), 7.00 (d, *J* = 9 Hz, 1H, ArH), 7.11–7.06 (m, 2H, ArH), 7.27–7.21 (m, 1H, ArH), 7.45–7.39 (m, 1H, ArH), 7.71 (t, *J* = 9 Hz, 2H, ArH), 8.20 (d, *J* = 8.4 Hz, 1H, ArH); **^{13}C NMR ($CDCl_3$, 75 MHz):** δ 104.1, 117.6, 122.7, 124.0, 127.1, 128.0, 128.4, 128.5, 129.1, 130.8, 132.1, 135.4, 136.4, 148.5.

1-(*p*-Tolylthio)naphthalen-2-amine (9b)[84]



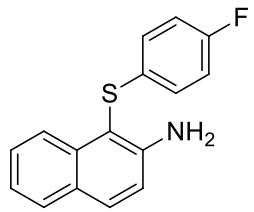
Deep brown solid; m.p.: 111–112 °C (Lit. m.p.: 113–115 °C); **^{1}H NMR ($CDCl_3$, 300 MHz):** δ 2.20 (s, 3H, CH_3), 4.43 (s, br, 2H, NH_2), 6.98–6.89 (m, 5H, ArH), 7.25–7.16 (m, 1H, ArH), 7.43–7.37 (m, 1H, ArH), 7.71–7.66 (m, 2H, ArH), 8.2 (d, *J* = 8.4 Hz, 1H, ArH); **^{13}C NMR ($CDCl_3$, 75 MHz):** δ 21.0, 105.2, 117.7, 122.6, 124.3, 126.1, 127.8, 128.4, 129.8, 131.7, 133.2, 134.9, 136.7, 148.4.

1-(Phenylthio)naphthalen-2-amine (9c)[84]



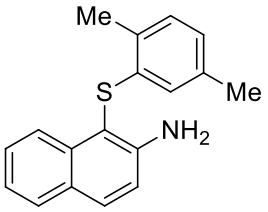
Deep brown solid; m.p.: 98–99 °C (Lit. m.p.: 99–101 °C); **^{1}H NMR ($CDCl_3$, 300 MHz):** δ 4.40 (s, br, 2H, NH_2), 7.03–6.87 (m, 4H, ArH), 7.05–7.04 (m, 1H, ArH), 7.15–7.09 (m, 1H, ArH), 7.26–7.17 (m, 1H, ArH), 7.46–7.37 (m, 1H, ArH), 7.73–7.67 (m, 2H, ArH), 8.26 (d, *J* = 8.1 Hz, 1H, ArH); **^{13}C NMR ($CDCl_3$, 75 MHz):** δ 104.5, 117.7, 122.7, 124.3, 125.1, 125.8, 127.9, 128.0, 128.4, 129.0, 132.0, 136.7, 137.0, 148.6.

1-(4-Fluorophenylthio)naphthalen-2-amine (9d)



Brown solid; m.p.: 65–66 °C; **^{1}H NMR (CDCl$_3$, 300 MHz):** δ 4.66 (s, br, 2H, NH_2), 6.85–6.81 (m, 2H, ArH), 6.97–6.93 (m, 3H, ArH), 7.23 (t, *J* = 7 Hz, 1H, ArH), 7.41 (t, *J* = 7.5 Hz, 1H, ArH), 7.70–7.66 (m, 2H, ArH), 8.24 (d, *J* = 8.4, 1H, ArH); **^{13}C NMR (CDCl$_3$, 75 MHz):** δ 105.0, 116.0, 116.3, 117.8, 122.7, 124.1, 127.7, 127.8, 128.0, 128.5, 131.8, 131.9, 132.0, 136.6, 148.5, 159.4, 162.6.

1-(2,5-Dimethylphenylthio)naphthalen-2-amine (9e)[84]



Light pink solid; m.p.: 60–61 °C (Lit. m.p.: 60–62 °C); **^{1}H NMR (CDCl$_3$, 300 MHz)**: δ 1.96 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 4.26 (s, br, 2H, NH_2), 6.25 (s, 1H, ArH), 6.76 (d, *J* = 7.5 Hz, 1H, ArH), 7.04–6.97 (m, 2H, ArH), 7.25–7.20 (m, 1H, ArH), 7.41–7.36 (m, 1H, ArH), 7.72–7.67 (m, 2H, ArH), 8.20 (d, *J* = 8.4 Hz, 1H, ArH); **^{13}C NMR (CDCl$_3$, 75 MHz)**: δ 19.5, 21.0, 104.0, 117.5, 122.4, 124.2, 124.5, 125.5, 127.6, 128.2, 128.4, 130.0, 131.5, 131.8, 135.0, 136.0, 136.7, 148.4.

I.B.5.5 Scanned copies of ^{1}H, ^{13}C NMR and HRMS spectra of 3-(pentylthio)-1*H*-indole (3f)

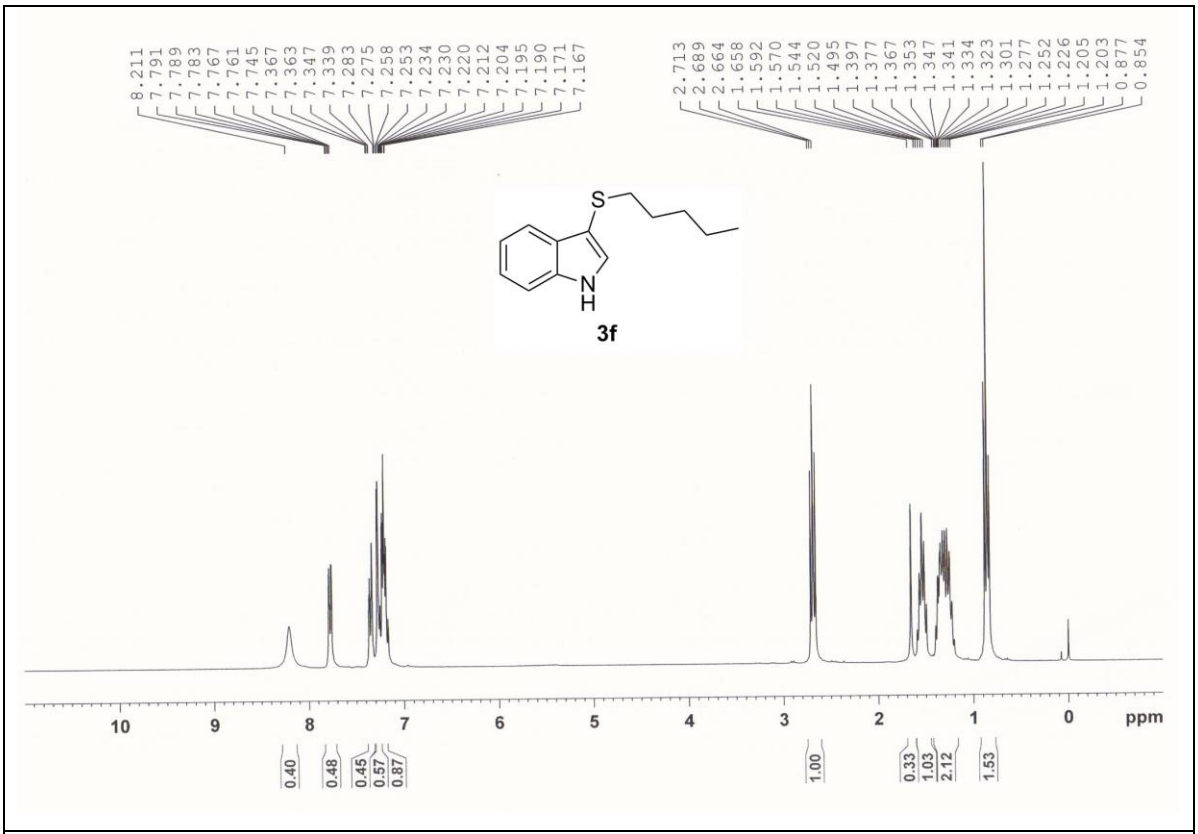


Figure I.B.6 Scanned copy of ^{1}H NMR spectrum of 3-(pentylthio)-1*H*-indole **(3f)**

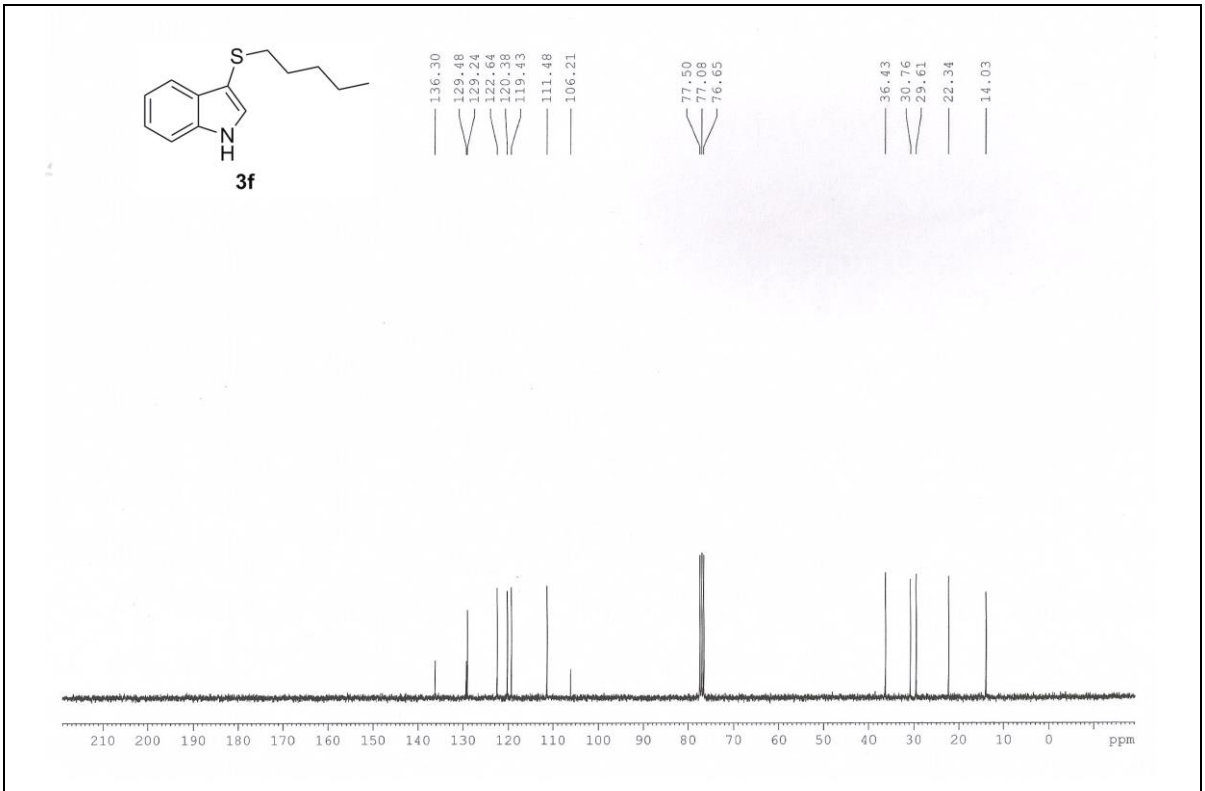


Figure I.B.7 Scanned copy of ^{13}C NMR spectrum of 3-(pentylthio)-1*H*-indole **(3f)**

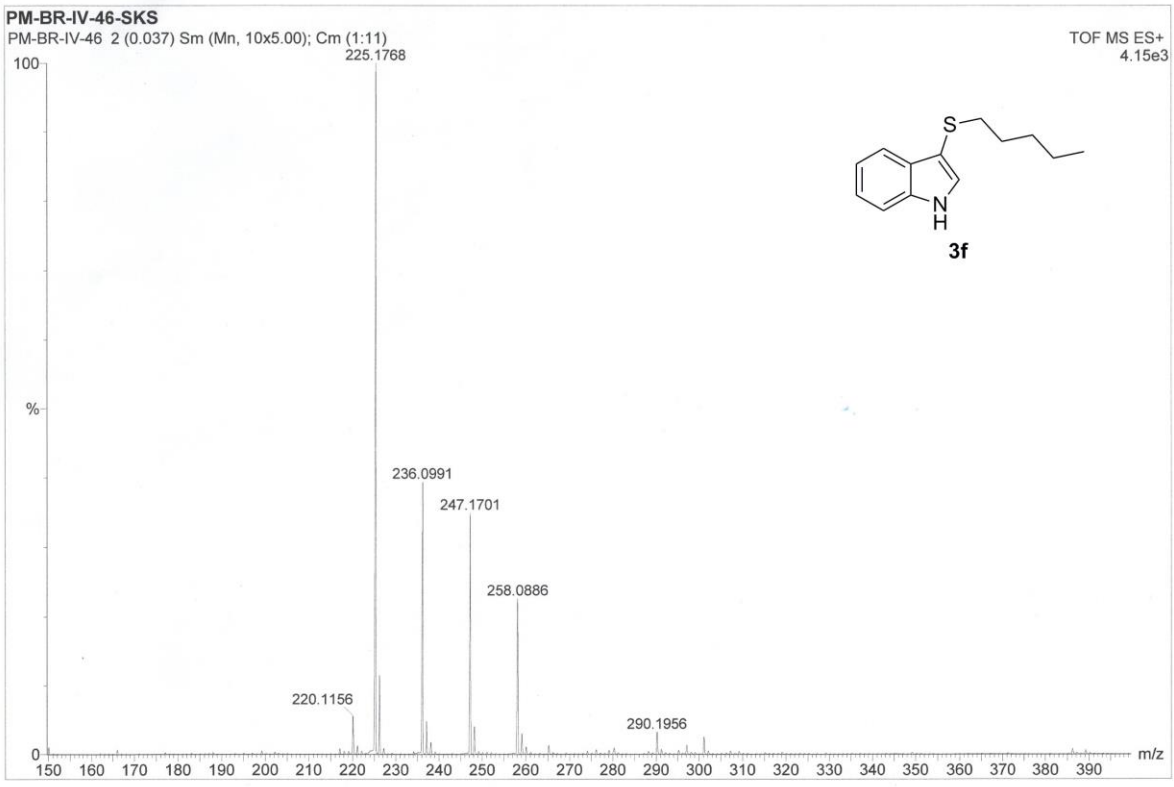


Figure I.B.8 Scanned copy of HRMS spectrum 3-(pentylthio)-1*H*-indole **(3f)**

I.B.6 References

References are given in BIBLIOGRAPHY under Chapter I, Section B.