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Cyano Sacrificial (Arylthio)-arylamination of Quinoline and Isoquinoline *N*-Oxides using *N*-(2-(Arylthio)aryl)cyanamides

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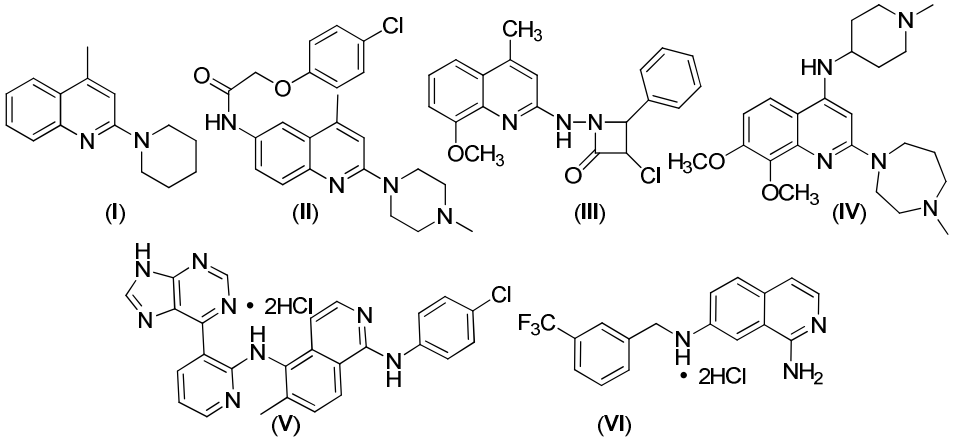
ABSTRACT: A copper(I) catalyzed regioselective arylthio-arylamination of quinoline and isoquinoline *N*-oxides have been achieved at the expense of a cyano (-CN) group from *N*-(2-(arylthio)aryl)cyanamides. This reductive amination proceeds in one pot at 80 ^{o}C in the absence of any additives. This is a unique illustration of aryl cyanamides serving as arylaminating agents on quinoline/isoquinoline *N*-oxides with concurrent auto-reduction of *N*-oxide.

INTRODUCTION

Recent advances in transition-metal catalysis have led to the development of effective methods for regioselective C−C and C−heteroatom bond formations.[1,2] The construction of C−N bonds has attracted considerable attention since nitrogen containing motifs have found significant applications in biological and medicinal chemistry.[1a,3] Among various nitrogen bearing scaffolds, functionalized quinolines are reported to have antimalarial, antibacterial, antifungal and antimicrobial activities (Figure 1).[4] Representative examples of 2-aminoquinoline moieties exhibiting various biologically activities are shown in Figure 1. Compound (**I**) is a potent antagonist that selectively modulates native TRPC4/C5 ion channels and has been used in physiological and pathophysiological studies.[4c] Quinoline derivative (**II**) is an antagonist of the MCH-1R for the treatment of obesity.[4d] The potential activity of compound (**II**) demonstrated an

IC_{50} value of 55 nM in a primary screening and exhibited antagonist properties in a functional cellular assay measuring Ca^{2+} release. Compound (**III**) exhibits antibacterial activity against gram-positive bacteria.[4e] 2-Aminiquinoline (**IV**) display an IC_{50} value of 1.2 μM against EZH2, decreased global H3K27me3 level in cells and also showed good anti-viability activities against tumor cell lines.[4f]

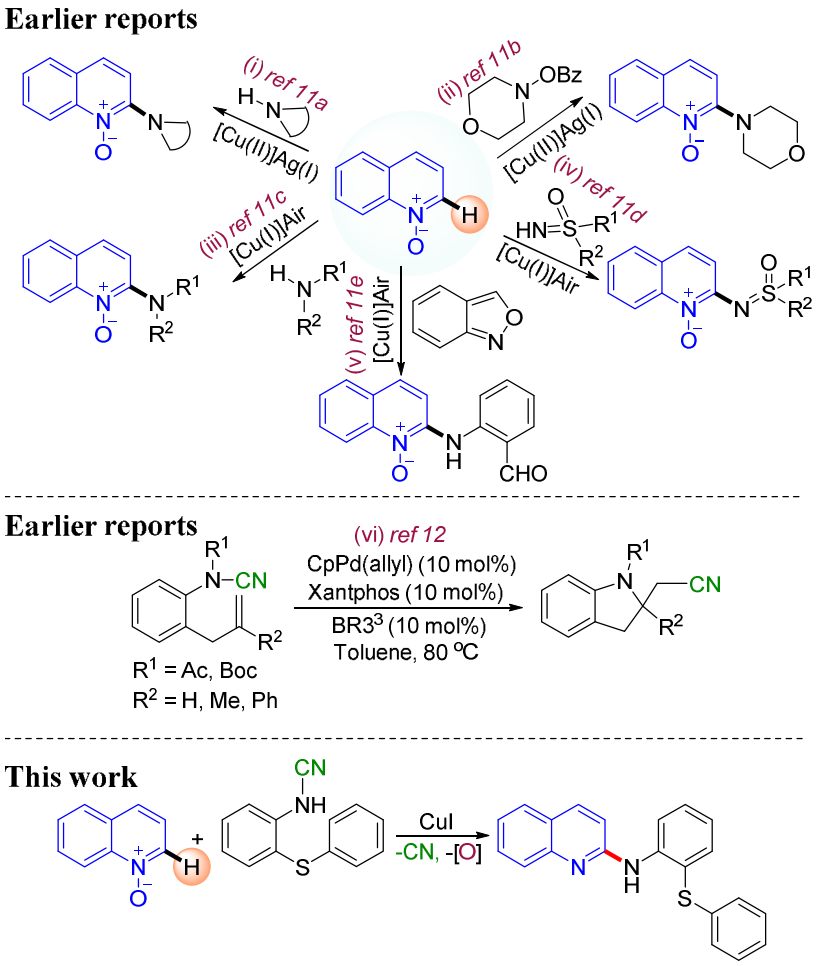
Figure 1. Representative Biologically Active 2-Aminoquinolines.



Various transition metal catalyzed C2 selective functionalizations such as arylation,[5] heteroarylation,[6] alkylation,[7] alkenylation[8] and C−O or C−S bond formations[9,10] on quinoline *N*-oxide moiety have been successfully accomplished. Undoubtedly, the regioselective C−N bond formation of these heterocyclic *N*-oxides have emerged as powerful tools in organic synthesis. Nevertheless few specialized synthetic methods are available to achieve this in a step-economic way (Scheme 1).[11] A copper(II)-catalyzed C2 amination of quinoline *N*-oxides using lactams, cyclamines, or *O*-benzoyl hydroxylamines have been reported by Li *et.al.* [Scheme 1, (i) and (ii)].[11a,b] Wu and Cui's group have utilized aliphatic secondary amines as the aminyl sources for the same in the presence of CuI [Scheme 1, (iii)].[11c] Bolm and co-workers described a CuI-catalyzed sulfoximinations of quinoline *N*-oxides at its C2 position [Scheme 1, (iv)].[11d] Recently, Samanta group demonstrated a Cu(I) catalyzed regioselective arylamination using anthranils as

the arylaminating source [Scheme 1, (v)].[11e] While the methods described in Scheme 1 (i-iii) are applicable for secondary aliphatic aminations, the use of anthranil is the sole example of an arylamination of quinoline *N*-oxides. The last three methods in Scheme 1 use air as the oxidant but in the first two protocols, sub-stoichiometric amounts of silver salt are essential. Very recently Zhao group has reported a reductive amination of quinoline *N*-oxides using ammonia, primary and secondary amines. However, the method requires stoichiometric amount of reducing agent such as H-phosphonate in the presence of potassium carbonate.[11f]

Scheme 1. Differential Reactivity of Quinoline *N*-oxides



A Pd/xantphos catalyzed intramolecular regioselective aminocyanation of alkene has been achieved via the cleavage of N-CN bond by Nakao group [Scheme 1, (vi)].[12a] Here,

simultaneous installation of a cyano (-CN) group and tetra or tri substituted carbon afforded various indolines and pyrrolidines. An organic cyanamide possesses a nucleophilic N-H site, an electrophilic cyanamide carbon[12b-e] and a fragile N-CN bond. On the other hand, because of the nucleophilic nature of quinoline *N*-oxide (**1**) and the presence of an electrophilic C-2 site, we envisaged that the *N*-(2-(arylthio)aryl)cyanamide (**a**) might serve as an C2-arylthio-arylaminating agent on (**1**). This may be accomplished by the initial nucleophilic attack of the quinoline *N*-oxide (**1**) onto the electrophilic carbon of cyanamide (**a**) followed by an intramolecular nucleophilic attack at the C-2 position of (**1**). Here, the sulfur atom of *S*-phenyl ring may further facilitate the reactivity of the cyanamide via co-ordination with a Cu-salt. The above anticipated reaction was initially executed using a *N*-(2-(phenylthio)phenyl)cyanamide (**a**) (0.25 mmol), quinoline *N*-oxide (**1**) (0.25 mmol) and CuI (20 mol%) in 1,4-dioxane (2 mL) at 110 ^{o}C. Formation of a new product (**1a**) (43%) was observed along with the isolation of quinoline (23%) and unreacted quinoline *N*-oxide (15%). Spectroscopic analysis of the isolated product revealed its structure to be *N*-(2-(phenylthio)phenyl)quinolin-2-amine (**1a**) (Scheme 1). Here, formation of a C2 selective product (**1a**) using cyanamide (**a**) is associated with the concurrent reduction of quinoline *N*-oxide (**1**) and loss of a cyano (-CN) group. To the best of our knowledge, such arylamination of quinoline *N*-oxide using arylcyanamide as the arylaminating agent is unprecedented in the literature.

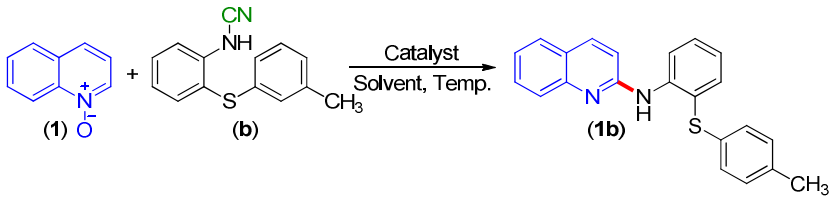
RESULTS AND DISCUSSION

Encouraged by this C2 selective cyano sacrificial arylthio-arylamination, various other reaction parameters were further evaluated to achieve better yield of the product. The initial investigation

was commenced by taking *N*-(2-(*p*-tolylthio)phenyl)cyanamide (**b**) and quinoline *N*-oxide (**1**) as the reacting partner (Table 1, entry 1). Since substantial amount of quinoline by product was observed, this may be originating from the *N*-oxide (**1**) via a reductive path, thereby decreasing the net yield of (**1a**). Gratifyingly, an improved yield (65%) of the product (**1b**) was found when a reaction was carried out using 2 equivalents of (**1**) (Table 1, entry 2). As solvent systems play a pivotal role in any organic transformations, we screened few solvents for the present C-2 amination process. Among various solvents *viz.* chlorobenzene (39%), *p*-xylene (27%), CH_3CN (79%), DMSO (45%) and methanol (51%) surveyed (Table 1, entries 3–7), CH_3CN turned out to be the best (Table 1, entry5). The yield of the product remained unaltered (78%) even when the reaction was performed at 80 ^oC (Table 1, entry 8). The reaction took longer time giving lower yield of the product when carried out below 80 ^oC. Using CH_3CN as the solvent at 80 ^oC, the efficacy of other copper I and II salts such as CuCl, CuBr and $Cu(OAc)_2$ were screened (Table 1, entries 9–11). All were turned out to be inferior to initially used CuI (Table 1, entry 8). The superiority of CuI towards C2 selective amination of quinoline *N*-oxides compared to other Cu salts have been well established [Scheme 1 (iii-iv)].[11c-e] The product (**1b**) yield (76%) remain unchanged even by performing the reaction with 15 mol% of the catalyst loading (Table 1 and entry 13). However, a 12% reduction in the yield (i.e. 68%) was noticed by further lowering the catalyst loading to 10 mol% (Table 1 and entry 14). Interestingly, the same reaction in the absence of any catalyst also gave a decent yield (22%) of the product (**1b**) (Table 1, entry 15). Nevertheless, CuI is found to be essential for obtaining better yield, as it enhances the electrophilicity of the cyanamide and brings the quinolone *N*-oxide (**1**) and cyanamide (**b**) to its proximity via coordination. Thus, the ideal optimized condition for this arylamination is the use

of *N*-(2-(*p*-tolylthio)phenyl)cyanamide (**b**) (0.25 mmol), quinoline *N*-oxide (**1**) (0.5 mmol) and CuI (15 mol%) in CH_3CN (2 mL) at 80 ^oC for 18 h (Table 1, entry 13).

Table 1. Optimization of the Arylthio-amination of Quinoline *N*-oxide[a]



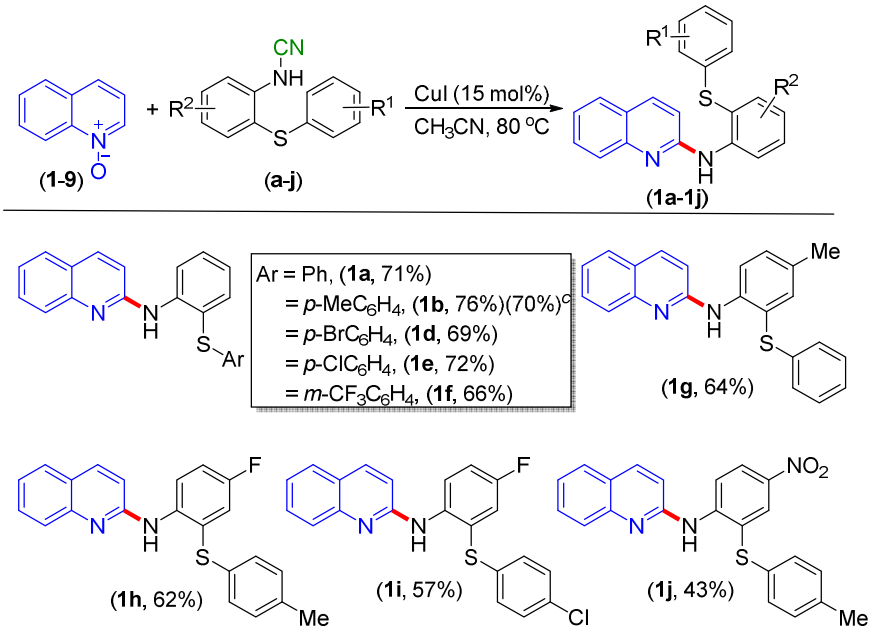
Entry	Catalyst (mol %)	Solvent	Temp ^oC	Yield (%)
1	CuI (20)	Dioxane	110	49[c]
2	CuI (20)	Dioxane	110	65
3	CuI (20)	PhCl	110	39
4	CuI (20)	*p*-Xylene	110	27
5	CuI (20)	CH_3CN	110	79
6	CuI (20)	DMSO	110	45
7	CuI (20)	MeOH	110	51
8	CuI (20)	CH_3CN	80	78
9	CuCl (20)	CH_3CN	80	72
10	CuBr (20)	CH_3CN	80	53
11	$Cu(OAc)_2$(20)	CH_3CN	80	51
12	**CuI (15)**	**CH_3CN**	**80**	**76**
13	CuI (10)	CH_3CN	80	68
14	-	CH_3CN	80	22

[a]Reaction conditions: *N*-(2-(*p*-tolylthio)phenyl)cyanamide(**b**) (0.25 mmol), quinoline*N*-Oxide (**1**) (0.5 mmol), solvent (2 mL).[b]Isolated yield.[c]1 equiv. of quinoline *N*-oxide (**b**).

After establishing the above cyanamide mediatory unprecedented arylamination, the feasibility of the strategy was surveyed with a variety of substituted *N*-(2-(arylthio)aryl)cyanamides (**a-f**) having electron-donating and electron-withdrawing groups (R^1) on the *S*-phenyl ring with quinoline *N*-oxide (**1**) (Scheme 2). The *N*-(2-(phenylthio)phenyl)cyanamide (**a**) reacted

efficiently with (**1**) giving C-2 aminated product (**1a**) in 71% yield. Presence of moderately *p*-Br (**d**), *p*-Cl (**e**) and strongly *m*-CF_3 (**f**) electro-withdrawing groups (R^1) on the *S*-phenyl ring of aryl cyanamides, underwent C-2 amination with quinoline *N*-oxide (**1**) affording arylaminated products (**1d**), (**1e**) and (**1f**) in 69%, 72% and 66% yields respectively (Scheme 2). The structure of product (**1e**) has been reconfirmed by X-ray crystallographic analysis (Figure S1, see Supporting Information). Subsequently, the variation of substituents (R^1 and R^2) on both the aryl rings of arylcyanamides were explored (Scheme 1). When the substituent cyanamide possessing an electron-donating group such as 4-Me (**g**) was treated with quinoline *N*-oxide (**1**), a moderate yield (64%) of the C2 aminated product (**1g**) was obtained. Further, the cyanamide bearing ring is substituted with electron-withdrawing (-F/-NO_2) and the *S*-phenyl ring with either electron-donating (-Me/-OMe) or electron-withdrawing (-Cl) groups were tested. Various combinations of substituents (R^1 and R^2) such as *p*-Me/4-F (**h**), *p*-Cl/4-F (**i**), and *p*-OMe/4-NO_2 (**j**) all provided their respective aryl aminated products (**1h**, 62%), (**1i**, 57%) and (**1j**, 43%) in modest yields (Scheme 2). To demonstrate the scalability of the present methodology, a reaction of *N*-(2-(*p*-tolylthio)phenyl)cyanamide (**b**) (1 mmol) and quinoline *N*-oxide (2 mmol), under the standard optimized reaction condition give 70% yield of the product (**1b**) [Scheme 2, (**1b**)^c].

Scheme 2. Demonstration of C2 Arylamination using Arylthiophenyl Cyanamides[a,b]

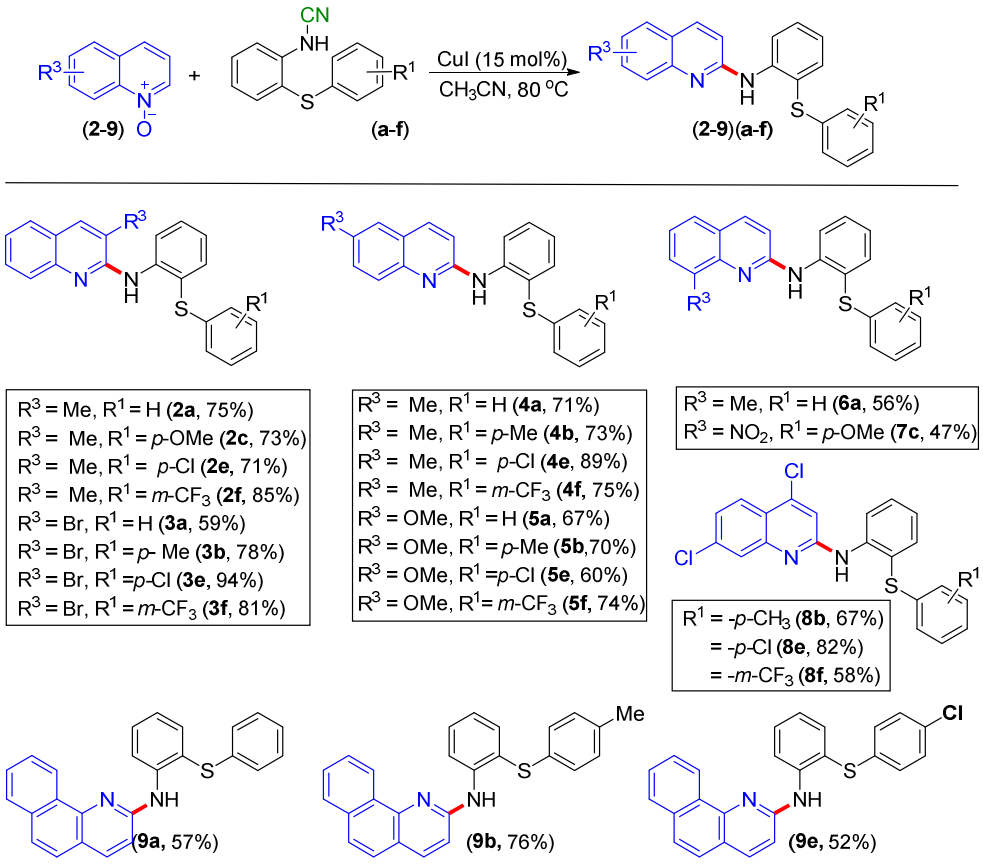


[a]Reaction conditions: *N*-(2-(phenylthio)phenyl)cyanamide (**a-j**) (0.25 mmol), quinoline *N*-oxide (0.5 mmol) (**1**), CuI (15 mol%), CH_3CN (2 mL), time (20 h) at 80 °C. [b]Yields of isolated pure products. [c]1 mmol scale

After successfully demonstrating the C2 selective arylthio-arylamination of quinoline *N*-oxide (**1**), the scope and versatility of the process was assessed with other substituted (R^3) quinoline *N*-oxides (Scheme 3). We were delighted to observe that the developed protocol displayed a broad scope across various sterically and electronically distinct quinoline *N*-oxides (**2-9**). Both electron donating 3-Me (**2**) and electron-withdrawing 3-Br (**3**) groups on the quinoline *N*-oxide at its C3-position did not suffer any significant steric effect. 3-Methyl quinoline *N*-oxide (**2**) reacted smoothly with cyanamides having a variety of substituents (R^1). The electron-neutral (**a**), electron-donating *p*-OMe (**b**) and electro-withdrawing *p*-Cl (**c**) and *m*-CF_3 (**d**) all afforded their corresponding products (**2a**, 75%), (**2c**, 73%), (**2e**, 71%) and (**2f**, 85%) respectively (Scheme 3). The presence of a C3-Br group (**3**) in lieu of a C3-Me (**2**) at the C-3 position of quinoline *N*-oxide was equally successful with a similar set of substituted arylcyanamides (**a-f**) providing their arylaminated products (**3a**, 59%), (**3b**, 78%), (**3e**, 94%) and (**3f**, 81%) respectively (Scheme

3). The cyano sacrificial C-2 amination strategy was equally effective with quinoline *N*-oxides substituted with electron-donating groups such as 6-Me (**4**) and 6-OMe (**5**) when reacted with a set of cyanamides (**a-f**) as shown in Scheme 3. Their C-2 aminated products (**4a-5f**) were isolated in the range of 60-89% and product yields are summarized in Scheme 3. It was not possible to correlate the actual yield of product obtained with the electronic and steric effects of the substituents present in quinoline *N*-oxides or cynamides. This strategy was feasible when electron-donating 8-Me (**6**) and electron-withdrawing 8-NO_2 (**7**) substituents (R^2) are present at the C-8 position of quinoline *N*-oxide. Inspite of the anticipated steric crowding due to (R^3) when *N*-oxide (**6**) was reacted with cyanamide (**a**) and *N*-oxide (**8**) with cyanamide (**c**) decent yields of the C-2 aminated products (**6a**, 56%) and (**7c**, 47%) were obtained. In addition to this, mono substituted quinoline *N*-oxides (**1-7**), 4,7-dichloro-quinoline *N*-oxide (**8**) underwent C-2 amination with *N*-(2-(phenylthio)phenyl)cyanamides bearing *p*-Me (**b**), *p*-Cl (**e**) and *m*-CF_3 (**f**) substituents on the *S*-phenyl ring, providing their corresponding products (**8b**, 67%), (**8e**, 82%) and (**8f**, 52%) respectively. Besides quinoline *N*-oxides (Schemes 2 and 3), a benzo-fused analogue, benzo[*h*]quinoline *N*-oxide (**9**) (Scheme 3) underwent effective C2-amination with a variety of cyanamides such as H (**a**), *p*-Me (**b**) and *p*-Cl (**e**), all providing their respective C-2 arylaminated products (**9a**), (**9b**) and (**9e**) in 57%, 76% and 52% yields. Surprisingly, this arylamination strategy, using pyridine *N*-oxide and quinoxaline *N*-oxides as the C-2 aminating sites failed to react with *N*-(2-(phenylthio)phenyl)cyanamide (**a**).

Scheme 3. Demonstration of C2 Arylamination using Various Quinoline*N*-oxides[a,b]



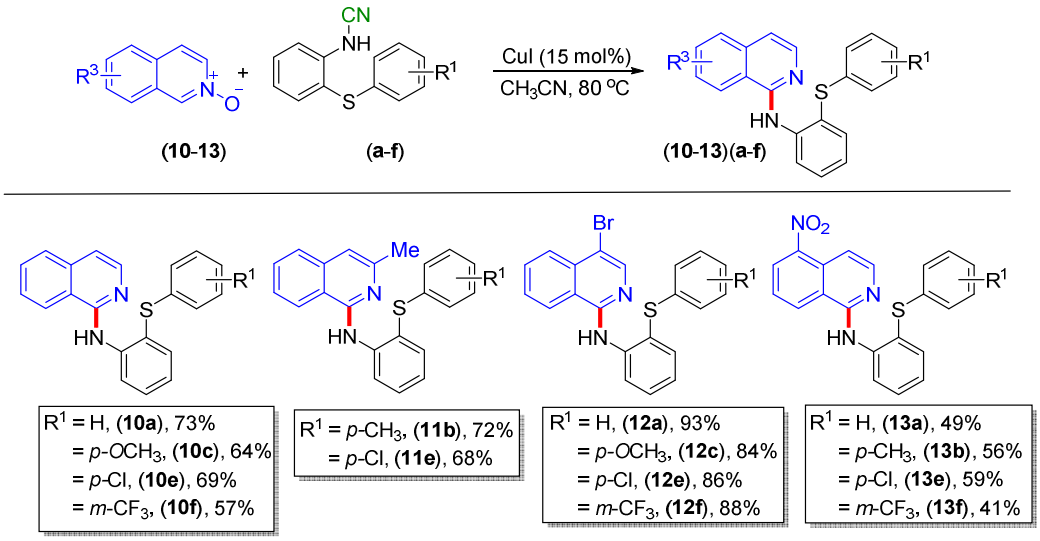
[a]Reaction conditions: *N*-(2-(phenylthio)phenyl)cyanamide (**a–f**) (0.25 mmol), quinoline *N*-oxides (**2-9**) (0.5 mmol), CuI (15 mol%), CH_3CN (2 mL), time (20 h) at 80 °C. [b]Yields of isolated pure products.

We are inquisitive to see whether the present C-2 arylamination strategy of quinoline *N*-oxide (**1**) will be applicable to isoquinoline *N*-oxide (**10**) as well to provide analogous C-1 arylamination? To our delight, the reaction of isoquinoline *N*-oxide (**10**) with *N*-(2-(phenylthio)phenyl)cyanamide (**a**), resulted in the formation of an exclusive C1 arylaminated product (**10a**) in 73% yield (Scheme 4). This result is significant, because 1-aminoisoquinolines are found to have interesting biological activities (Figure 1). The amino isoquinoline core in compound (**V**) is reported to have potent antitumor activity in xenograft models.[13a] The compound (**VI**) possess antimalarial activity and found to be submicromolar inhibitors *in vitro*

towards drug-resistant plasmodium falciparum and the best possessing activity comparable to chloroquine.[13b]

Encouraged by this positive outcome, the scope of this protocol was then extended to other substituted cyanamides (**c-f**) and isoquinoline *N*-oxides (**10-13**). Initially, the electronic effect of the substituent R^1 present on the *N*-(2-(phenylthio)phenyl)cyanamides (**c-f**) was investigated (Scheme 4). *N*-(2-(Phenylthio)phenyl)cyanamides containing electron-donating [*p*-OMe (**c**)] or electro-withdrawing [*p*-Cl (**e**) and *m*-CF_3 (**f**)] substituents, all underwent effective C1-amination with isoquinoline *N*-oxides (**10**) giving products [(**10b**, 64%), (**10e**, 69%) and (**10f**, 57%)] as shown in Scheme 4. Next, the effect of the substituents (R^3) present on the isoquinoline *N*-oxides (**11-13**) were examined with (R^1)-substituted cyanamides (**b-f**). Isoquinoline *N*-oxides bearing an electron-donating group such as 3-Me (**11**) reacted smoothly with (R^1) substituted cyanamides *p*-Me (**b)** and *p*-Cl (**e**), furnishing their corresponding C1 arylaminated products (**11b**, 86%) and (**11e**, 83%). Similarly, 4-bromo isoquinoline *N*-oxide (**12**) reacted with differentially (R^1) substituted *N*-(2-(arylthio)phenyl)cyanamides (**a-f**) and yielded their C1 aminated products (**12a-12e**) in a range of 84-93% (Scheme 4). Moderate to lower yields of C1 aminated products (**13a-13f**) were obtained via the coupling of 5–NO_2 isoquinoline *N*-oxide (**13**) with (R^1) substituted cyanamides (**a-f**) (Scheme 4).

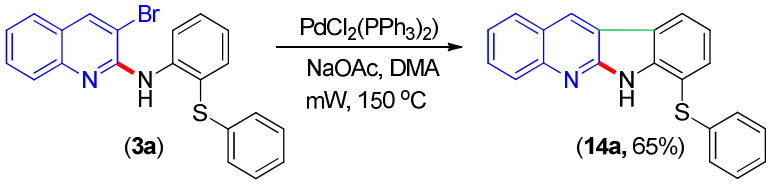
Scheme 4. Demonstration of C1 Arylamination with Isoquinoline *N*-oxide[a,b]



[a]Reaction conditions: *N*-(2-(phenylthio)phenyl)cyanamide (**a-f**) (0.25 mmol), isoquinoline*N*-oxides (**10-13**) (0.5 mmol), CuI (15 mol%), CH_3CN (2 mL), time (20 h) at 80 °C. [b]Yields of isolated pure products.

To demonstrate the applicability of our protocol, biologically active indoloquinoline moiety (**14a**) was synthesized in good yield (65%) utilizing product (**3a**) (in Scheme 3) via an intramolecular Heck coupling (Scheme 5).[14]

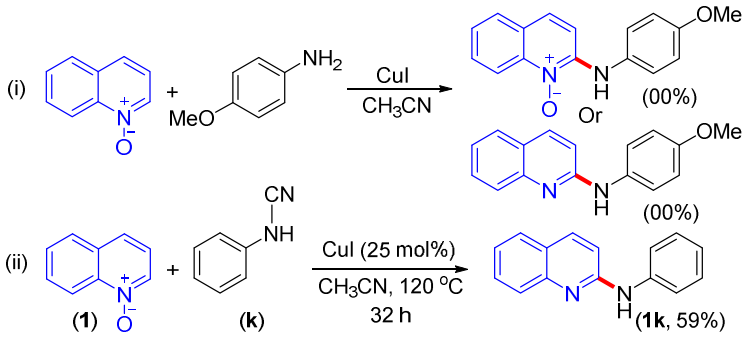
Scheme 5. Post Synthetic Modifications



To understand the mechanistic aspect for this cyano sacrificial regioselective arylthio-arylamination of quinoline and isoquinoline *N*-oxides, some experiments were carried out (Scheme 6). Most of the C-2 amination protocols of quinoline *N*-oxides uses secondary amines directly or indirectly as the aminating source. In this strategy as well arylamine might be generating from arylcyanamide which could be the actual aminating source. To ascertain this, when a reaction was executed using *p*-anisidine in lieu of (**a**) under otherwise identical condition,

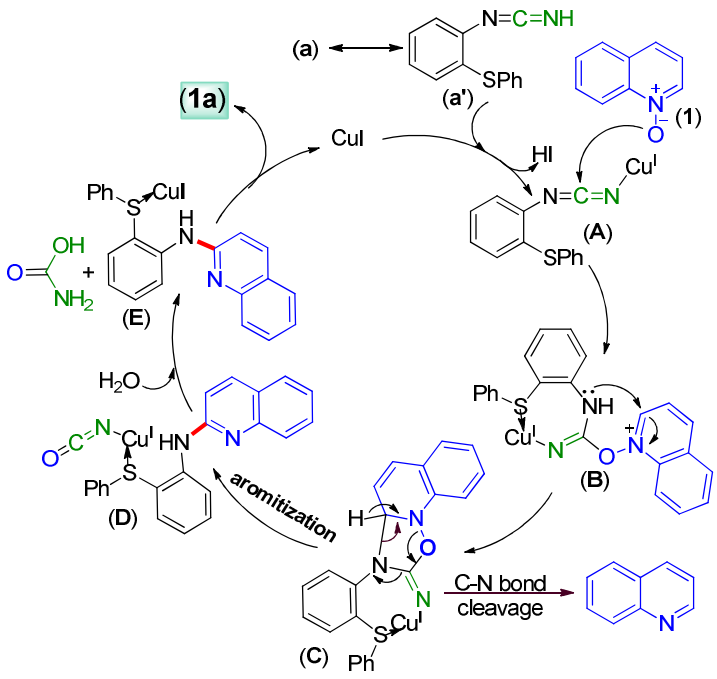
failed to give any product which rules out arylamine to be the possible aminating source [Scheme 6, (i)]

Scheme 6. Control Experiments



Now a query arises whether S atom of the (arylthio)aryl)cyanamides play any specific role in achieving the C2-amination, or other simple arylcyanamides may also serve as the possible aminating source towards quinoline/isoquinoline *N*-oxides? When phenyl cyanamide (**k**) was employed for the C2 amination of quinoline *N*-oxide (**1**) under the present reaction condition, a trace amount of C-2 aminated product (<10%) was observed. However, after further optimization an acceptable yield (59%) could be achieved using 25 mol% of catalyst (CuI), at 120 ^{o}C for 32 h [Scheme 6, (ii)]. This observation suggests that the S atom in (arylthio)aryl)cyanamides is playing an active role via chelating with the metal. However, other aryl cyanamides can serve as the alternative amine source only at high temperature, high catalyst loading at longer reaction time.

Scheme 7. Plausible Mechanism



Based on the control experiments and the literature reports[11c,12] a possible mechanism for this regioselective arylthio-arylamination is depicted in Scheme 7. The imidic form (**a'**) of cyanamide co-ordinates with Cu(I) forming a reactive intermediate (**A**). The quinoline *N*-oxide (**1**) attacks at the electrophilic carbon of (**A**) to form a new Cu intermediate (**B**) by bringing both the reacting partners to the proximity which is facilitated by the S atom of cyanamide (**a**). An intramolecular nucleophilic attack of the amine on to the metal bound C-2 site of quinoline *N*-oxide generates intermediate (**C**). Rearomatization of quinoline part of the (**C**) with transfer of *N*-oxide oxygen forms species (**D**). The unstable N-C=O bound Cu moiety is hydrolyzed to amine carbonate (which is decomposed to CO_2 and ammonia) releasing the metallated product (**E**). Finally, the C2 aminated product (**1a**) is released from intermediate (**E**) with regeneration of the CuI for the subsequent catalytic cycle. An unfavourable reversible cleavage of N-C bond (C2 carbon of quinoline *N*-oxide) of intermediate (**C**) leads to the formation of by product quinoline. A similar mechanism can be proposed for the C-1 amination of isoquinoline *N*-oxide.

In conclusion, for the first time we have utilized arylcyanamides as an aminating agent towards regioselective C2-arylamination and C-1-arylamination of quinoline and isoquinoline respectively. In many amination of quinoline and isoquinoline *N*-oxides, the *N*-oxide moiety remained intact there by requiring additional reduction step, however here it is removed *in situ via* an auto-reduction process. The present arylthio-arylamination of quinoline and isoquinoline using *N*-(2-(phenylthio)phenyl)cyanamide as an aminating agent works best. Nevertheless, there is avenues to develop other aryl and alkyl cyanamides as aminating agents for various heterocyclic *N*-oxides.

EXPERIMENTAL SECTION

General information:

All the reagents were of commercial grade and purified according to the established procedures. Organic extracts were dried over anhydrous sodium sulphate. Solvents were removed in a rotary evaporator under reduced pressure. Silica gel (60–120 mesh size) was used for the column chromatography. Reactions were monitored by TLC on silica gel 60 F_{254} (0.25 mm). NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard for ^1H NMR (400 MHz and 600 MHz) $CDCl_3$ solvent as the internal standard for ^{13}C NMR (100 MHz and 150 MHz). Mass spectra were recorded using ESI mode and APCI mode (Q-TOF MS analyzer). IR spectra were recorded in KBr or neat.

General Procedure for the Formation of *N*-(2-(Phenylthio)phenyl)quinolin-2-amine (1a).

An oven-dried round bottom flask was charged with *N*-(2-(phenylthio)phenyl)cyanamide (**a**) (56.5 mg, 0.25 mmol), quinoline *N*-oxide (**1**) (72.5 mg, 0.5 mmol), CuI (15 mol%, 7 mg), CH_3CN (2 mL). The flask was fitted with a condenser and the resultant reaction mixture was stirred in a pre-heated oil bath maintained at 80 ^oC. The reaction progress was monitored by

TLC. After 18 h, the reaction mixture was cooled to room temperature. The reaction mixture was evaporated under reduced pressure to remove CH_3CN. Then it was admixed with ethyl acetate (25 mL) and washed with saturated brine solution (5 mL). The ethyl acetate layer was dried over anhydrous Na_2SO_4. The solvent was then evaporated under reduced pressure and the residue was purified by column chromatography with an eluent hexane / ethylacetate (98 / 02) to afford the desired product (**1a**) in an isolated yield of 71% (58 mg).

General Procedure for the Synthesis of 7-(Phenylthio)-6*H*-indolo[2,3-b]quinoline (14a): A 5 mL microwave vial was charged with bis(-triphenylphosphine)palladium(II) dichloride (14 mg, 0.02 mmol), 3-bromo-*N*-(2-(phenylthio)phenyl)quinolin-2-amine (**3a**) (0.2 mmol, 81 mg) and sodium acetate (65 mg, 0.8 mmol) followed by *N*,*N*-dimethylacetamide (3 mL) and flushed with argon. The reaction was irradiated at 150 ^oC for 120 min. After completion of the reaction the reaction was cooled to room temperature. Then it was admixed with ethyl acetate (25 mL) and washed with ice-cooled water (3 x 5 mL). The ethyl acetate layer was dried over anhydrous Na_2SO_4. The solvent was then evaporated under reduced pressure and the residue was purified by column chromatography with an eluent hexane / ethylacetate (93 / 07) to afford 7-(Phenylthio)-6*H*-indolo[2,3-b]quinoline (**14a**) in an isolated yield of 65% (42 mg).

General Procedure for Control Experiments:

General Procedure for the Synthesis of *N*-Phenylquinolin-2-amine (1k).

N-Phenylcyanamide (**k**) (29 mg, 0.25 mmol), quinoline *N*-oxide (**1**) (72.5 mg, 0.5 mmol), CuI (25 mol%, 11 mg), CH_3CN (2 mL) were taken in a round bottom flask. Then it was fitted with a condenser and the resultant reaction mixture was stirred in a pre-heated oil bath maintained at 120 ^oC. The reaction progress was monitored by TLC. After 32 h, the reaction mixture was cooled to room temperature. The reaction mixture was evaporated under reduced pressure to

remove CH_3CN. Then it was admixed with ethyl acetate (25 mL) and washed with brine solution (2 x 5 mL). The ethyl acetate layer was dried over anhydrous Na_2SO_4. The solvent was then evaporated under reduced pressure and the residue was purified by column chromatography with an eluent hexane / ethylacetate (97 / 03) to afford the desired product (**1k**) in an isolated yield of 59% (32 mg).

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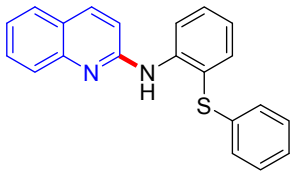
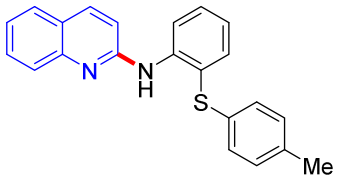
*N-(2-(Phenylthio)phenyl)quinolin-2-amine (**1a**):*



Yield 71% (58 mg) as a brownish solid; mp 97–99 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.79 (d, 1H, J = 8.8 Hz), 7.03–7.17 (m, 4H), 7.17–7.24 (m, 3H), 7.32 (t, 1H, J = 7.6 Hz), 7.45–7.53 (m, 1H), 7.59–7.64 (m, 3H), 7.87 (t, 2H, J = 8.4 Hz), 8.94 (d, 1H, J = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 113.6, 115.5, 118.9, 119.5, 122.5, 123.7, 124.4, 126.2, 126.6, 127.2, 127.4, 127.5, 129.2, 129.4, 130.0, 131.1, 136.3, 136.9, 137.8, 142.4, 147.3, 153.5; IR (KBr): 3449, 2927, 2856, 1625, 1587, 1523, 1437, 1317, 810, 754cm^{-1}; HRMS (ESI): calcd. for $C_{21}H_{17}N_2S$ $[M+H]^+$ 329.1107; found 329.1117.

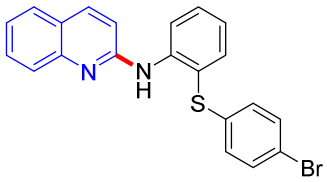
*N-(2-(p-Tolylthio)phenyl)quinolin-2-amine (**1b**):*



Yield 76% (65 mg) as a light yellowish solid; mp 84–86 ^oC; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm); 2.25 (s, 3H), 6.79 (d, 1H, J = 9.0 Hz), 7.03 (d, 3H, J = 8.4 Hz), 7.10 (d, 2H, J = 7.8 Hz), 7.30–7.33 (m, 1H), 7.45–7.48 (m, 1H), 7.55 (d, 1H, J = 7.2 Hz), 7.59–7.61 (m, 1H), 7.63 (d, 1H, J = 7.8 Hz), 7.85 (d, 1H, J = 8.4 Hz), 7.89 (d, 1H, J = 8.4 Hz), 8.86 (d, 1H, J = 8.4 Hz);^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 21.1, 113.6, 119.7, 122.6, 123.7, 124.4, 127.2, 127.5, 128.3, 129.9, 130.2, 130.6, 132.5, 136.3, 136.5, 137.7, 142.0, 147.4, 153.6; IR (KBr): 3448, 2925, 2855, 1623,

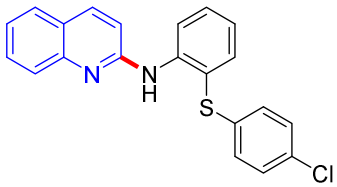
1586, 1524, 1438, 1316, 806, 753 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{19}N_2S$ $[M+H]^+$ 343.1263; found 343.1269.

*N-(2-((4-Bromophenyl)thio)phenyl)quinolin-2-amine (**1d**):*



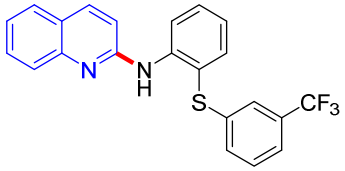
Yield 69% (70 mg) as a brownish solid; mp 101–103 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.80 (d, 1H, J = 8.8 Hz), 7.0 (d, 2H, J = 8.4 Hz), 7.05 (t, 1H, J = 7.2 Hz), 7.33 (t, 3H, J = 8.0 Hz), 7.52 (t, 1H, J = 8.0 Hz), 7.57–7.66 (m, 3H), 7.76 (s, 1H), 7.88 (dd, 2H, J = 17.6, 8.8 Hz), 8.94 (d, 1H, J = 8.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 113.5, 118.8, 119.6, 119.9, 122.6, 123.8, 124.5, 127.3, 127.6, 128.8, 130.0, 131.4, 132.4, 135.8, 136.9, 137.8, 142.6, 147.4, 153.4; IR (KBr): 3367, 2964, 2928, 2854, 1630, 1582, 1524, 1438, 1260, 1091, 1012, 814, 750, 630 cm^{-1}; HRMS (ESI): calcd. for $C_{21}H_{16}BrN_2S$ $[M+H]^+$ 407.0212; found 407.0233.

*N-(2-((4-Chlorophenyl)thio)phenyl)quinolin-2-amine (**1e**):*



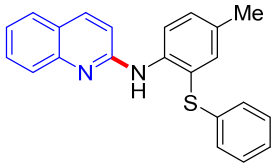
Yield 72% (65 mg) as a brownish solid; mp 102–104 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.80 (d, 1H, J = 8.8 Hz), 7.03–7.09 (m, 3H), 7.18 (d, 2H, J = 7.4 Hz), 7.33 (t, 1H, J = 7.2 Hz), 7.50–7.54 (m, 1H), 7.57–7.65 (m, 3H), 7.76 (s, 1H), 7.88 (dd, 2H, J = 17.2, 8.8 Hz), 8.93 (d, 1H, J = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 113.5, 119.0, 119.6, 122.6, 123.8, 124.5, 127.3, 127.6, 128.6, 129.5, 130.0, 131.4, 132.1, 135.0, 136.9, 137.8, 142.6, 147.4, 153.4; IR (KBr): 3369, 2963, 2929, 2853, 1631, 1585, 1525, 1439, 1262, 1092, 1010, 813, 752, 576 cm^{-1}; HRMS (ESI): calcd. for $C_{21}H_{16}ClN_2S$ $[M+H]^+$ 363.0717; found 363.0718.

*N-(2-((3-(Trifluoromethyl)phenyl)thio)phenyl)quinolin-2-amine (**1f**)***:**



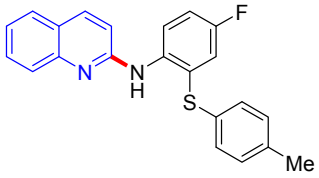
Yield 66% (65 mg) as a light brownish gummy; ^{1}H NMR (400 MHz, $CDCl_3$):δ(ppm) 6.82 (d, J = 8.8 Hz, 1H), 7.08 (t, 1H, J = 7.6 Hz), 7.20 (d, 1H, J = 8.0 Hz), 7.28–7.35 (m, 3H), 7.45 (s, 1H), 7.55 (t, 1H, J = 7.6 Hz), 7.59–7.65 (m, 3H), 7.73 (s, 1H), 7.85 (d, 1H, J = 8.4 Hz), 7.90 (d, 1H, J = 8.8 Hz), 8.91 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ(ppm) 113.4, 118.0, 119.8, 122.7, 122.8 (q, J = 3.6 Hz), 123.7 (q, J= 3.8 Hz), 123.9, 124.5, 127.4, 127.6, 129.8, 129.9, 130.0, 131.8, 137.2, 137.9, 138.3, 142.9, 147.5, 153.4; ^{19}F NMR ($CDCl_3$ + Hexafluorobenzene): δ -66.0 (s); IR (KBr): 3448, 2921, 2851, 1626, 1587, 1523, 1321, 1127, 1073, 749, 697 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{16}F_3N_2S$ $[M+H]^+$ 397.0981; found 397.0994.

*N-(4-Methyl-2-(phenylthio)phenyl)quinolin-2-amine (**1g**):*



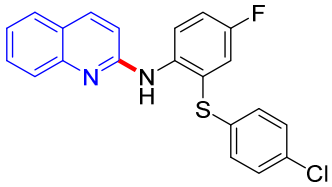
Yield 64% (55 mg) as a brownish gummy; ^{1}H NMR (600 MHz, $CDCl_3$):δ(ppm) 2.34 (s, 3H), 6.76 (d, 1H, J = 9.0 Hz), 7.12 (t, 1H, J = 7.2 Hz), 7.16 (d, 2H, J = 8.4 Hz), 7.21 (t, 2H, J = 7.2 Hz), 7.29–7.32 (m, 2H), 7.42 (s, 1H), 7.58–7.63 (m, 2H), 7.69 (s, 1H), 7.85 (t, 2H, J = 8.4 Hz), 8.76 (d, 1H, J = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ(ppm) 20.8, 113.4, 119.8, 123.5, 124.3, 126.1, 127.2, 127.4, 127.5, 129.4, 129.8, 131.6, 132.2, 136.5, 137.0, 137.6, 140.0, 147.5, 153.7; IR (KBr): 3435, 2923, 2853, 1620, 1599, 1520, 1395, 1313, 814, 740, 690 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{19}N_2S$ $[M+H]^+$343.1263; found 343.1275.

*N-(4-Fluoro-2-(p-tolylthio)phenyl)quinolin-2-amine (**1h**):*



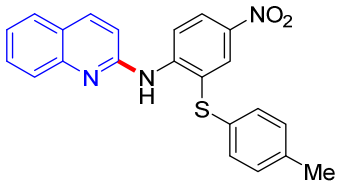
Yield 62% (56 mg) as a brownish gummy; ^{1}H NMR (600 MHz, $CDCl_3$):δ(ppm) 2.29 (s, 3H), 6.75 (d, 1H, J = 8.4 Hz), 7.07–7.10 (m, 3H), 7.11–7.14 (m, 2H), 7.17 (d, 2H, J = 8.4 Hz), 7.31 (t, 1H, J = 7.8 Hz), 7.60 (t, 1H, J = 7.2 Hz), 7.64 (d, 1H, J = 8.4 Hz), 7.81 (d, 1H, J = 8.4 Hz), 7.89 (d, 1H, J = 9.0 Hz), 8.67 (dd, 1H, J = 9.0, 5.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ(ppm) 21.2, 113.0, 116.4 (d, J = 21.6 Hz), 120.6 (d, J = 23.2 Hz), 122.0 (q, J = 7.4 Hz), 123.6, 124.4, 125.4 (d, J = 7.3 Hz), 127.1, 127.6, 128.2, 129.9, 130.0, 130.2, 130.5, 130.7, 137.1, 137.6, 137.9, 147.4, 153.9, 158.0 (d, J = 242.7 Hz); ^{19}F NMR ($CDCl_3$ + Hexafluorobenzene): δ -122.8 (s); IR (KBr): 3361, 2924, 2854, 1619, 1526, 1396, 1314, 1256, 1119, 901, 811, 754 cm^{-1}; HRMS (ESI): calcd. For $C_{22}H_{18}FN_2S$ $[M+H]^+$ 361.1169; found 361.1179.

*N-(2-((4-Chlorophenyl)thio)-4-fluorophenyl)quinolin-2-amine (**1i**):*



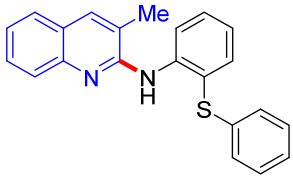
Yield 57% (54 mg) as a brownish gummy; ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 6.74 (d, 1H, J = 8.8 Hz), 7.13–7.17 (m, 2H), 7.18–7.23 (m, 4H), 7.30–7.34 (m, 1H), 7.58–7.65 (m, 2H), 7.82 (d, 1H, J = 8.4 Hz), 7.90 (d, 1H, J = 8.8 Hz), 8.78 (dd, 1H, J = 8.8, 5.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ(ppm) 113.0, 117.4 (d, J = 21.6 Hz), 121.5, 121.7, 122.0 (d, J = 7.4 Hz), 123.8, 124.5, 127.2, 127.6, 129.8, 129.9, 130.1, 133.1, 133.5, 138.0, 147.3, 153.6, 157.8 (d, J = 243.2 Hz); ^{19}F NMR ($CDCl_3$ + Hexafluorobenzene): δ -122.7 (s); IR (KBr): 3445, 2924, 1620, 1525, 1476, 1395, 1188, 1091, 1011, 813, 753 cm^{-1};HRMS (ESI): calcd. For $C_{21}H_{15}ClFN_2S$ $[M+H]^+$ 381.0623; found 381.0632.

*N-(4-Nitro-2-(p-tolylthio)phenyl)quinolin-2-amine (**1j**):*



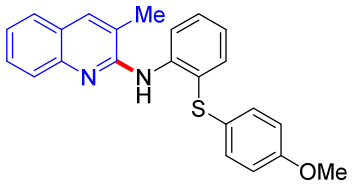
Yield 43% (42 mg) as a yellowish solid; mp 156–158 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.29 (s, 3H), 6.84 (d, 1H, J = 8.8 Hz), 7.09 (d, 2H, J = 8.0 Hz), 7.16 (d, 2H, J = 8.0 Hz), 7.41 (t, 1H, J= 8.0 Hz), 7.65–7.71 (m, 2H), 7.93 (d, 1H, J = 8.4 Hz), 8.01 (d, 1H, J = 8.4 Hz), 8.30 (s, 1H), 8.35 (dd, 1H, J = 9.6, 2.8 Hz), 8.51 (d, 1H, J = 2.8 Hz), 9.36 (d, 1H, J = 9.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 114.1, 117.5, 120.4, 124.9, 125.0, 126.7, 127.7, 127.8, 128.9, 130.4, 130.5, 130.7, 132.0, 137.8, 138.4, 140.9, 147.0, 147.7, 152.1; IR (KBr): 3447, 2921, 2853, 1630, 1584, 1504, 1321, 1266, 1121, 745 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{18}N_3O_2S$ $[M+H]^+$ 388.1114; found 388.1139.

*3-Methyl-N-(2-(phenylthio)phenyl)quinolin-2-amine (**2a**):*



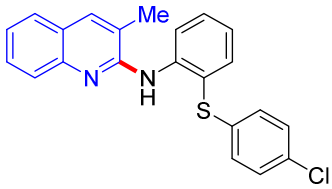
Yield 75% (64 mg) as a brownish solid; mp 97–99 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 2.17 (s, 3H), 7.06 (t, 1H, J = 7.2 Hz), 7.10–7.15 (m, 3H), 7.21 (t, 2H, J = 7.8 Hz), 7.30 (t, 1H, J = 7.2 Hz), 7.54–7.59 (m, 3H), 7.67–7.68 (m, 2H), 7.89 (d, 1H, J = 8.4 Hz), 8.06 (s, 1H), 9.40 (d, 1H, J = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 17.4, 118.0, 119.2, 121.3, 121.9, 123.6, 124.7, 126.0, 126.6, 126.7, 127.0, 128.2, 128.8, 129.4, 129.7, 131.6, 136.1, 136.5, 137.3, 142.7, 146.2, 152.5; IR (KBr): 3345, 2940, 2841, 1634, 1586, 1527, 1438, 1416, 1249, 1170, 1012, 830, 754, 708, 619 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{19}N_2S$ $[M+H]^+$ 343.1263; found 343.1289.

*N-(2-((4-Methoxyphenyl)thio)phenyl)-3-methylquinolin-2-amine (**2c**):*



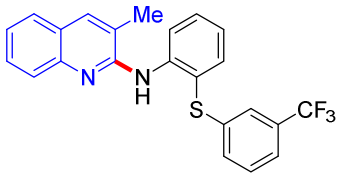
Yield 73% (68 mg) as a brownish solid; mp 74–76 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.27 (s, 3H), 3.72 (s, 3H), 6.79 (d, 2H, J = 8.8 Hz), 7.04 (t, 1H, J = 7.6 Hz), 7.15 (d, 2H, J = 8.8 Hz), 7.30 (t, 1H, J = 6.8 Hz), 7.52–7.59 (m, 3H), 7.64 (d, 1H, J = 7.6 Hz), 7.70 (s, 1H), 7.89 (d, 1H, J = 8.4 Hz), 8.08 (s, 1H), 9.34 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 17.6, 55.5, 115.1, 119.3, 120.1, 121.2, 121.9, 123.5, 124.7, 126.4, 126.7, 127.0, 128.8, 129.3, 130.9, 136.4, 136.5, 142.2, 146.3, 152.6, 158.6; IR (KBr): 3344, 2938, 2842, 1632, 1587, 1526, 1436, 1417, 1248, 1172, 1011, 829, 753, 709, 617 cm^{-1}; HRMS (ESI): calcd. for $C_{23}H_{21}N_2OS$ $[M+H]^+$ 373.1369; found 373.1379.

*N-(2-((4-Chlorophenyl)thio)phenyl)-3-methylquinolin-2-amine (**2e**):*



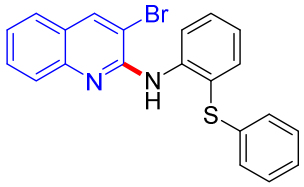
Yield 71% (67 mg) as a white solid; mp 139–141 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.20 (s, 3H), 7.05–7.09 (m, 3H), 7.18 (d, 2H, J = 8.4 Hz), 7.31 (t, 1H, J = 6.8 Hz), 7.58 (q, 3H, J = 8.4 Hz), 7.65 (d, 1H, J = 7.6 Hz), 7.69 (s, 1H), 7.89 (d, 1H, J = 8.4 Hz), 8.01 (s, 1H), 9.41 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 17.4, 117.5, 119.3, 121.1, 122.0, 123.7, 124.7, 126.7, 127.1, 127.8, 128.9, 129.5, 131.8, 131.9, 134.9, 136.6, 137.3, 142.7, 146.2, 152.4; IR (KBr): 3370, 2920, 2859, 1637, 1587, 1522, 1438, 1304, 1152, 1088, 1007, 900, 808, 757, 710 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{18}ClN_2S$ $[M+H]^+$ 377.0874; found 377.0875.

*3-Methyl-N-(2-((3-(trifluoromethyl)phenyl)thio)phenyl)quinolin-2-amine (**2f**):*



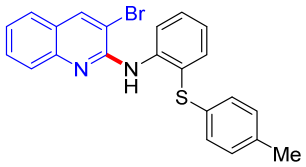
Yield 85% (87 mg) as a light brownish solid; mp 123–125 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.15 (s, 3H), 7.06 (t, 1H, J = 7.6 Hz), 7.16 (d, 1H, J = 7.6 Hz), 7.27 (dd, 2H, J = 17.6, 8.4 Hz), 7.34 (d, 1H, J = 8.0 Hz), 7.48 (s, 1H), 7.52–7.61 (m, 3H), 7.65 (d, 2H, J = 9.6 Hz), 7.87 (d, 1H, J = 8.4 Hz), 7.94 (s, 1H), 9.38 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 17.3, 116.8, 119.5, 121.0, 122.8 (q, J = 3.7 Hz), 123.3 (q, J = 3.8 Hz), 123.7, 124.8, 126.7, 127.1, 128.9, 129.5, 129.9, 132.1, 136.6, 137.4, 138.1, 142.9, 146.2, 152.4; ^{19}F NMR ($CDCl_3$ + Hexafluorobenzene): δ -66.0 (s); IR (KBr): 3379, 2923, 2856, 1632, 1586, 1526, 1417, 1319, 1166, 1120, 1071, 893, 795, 760, 699 cm^{-1}; HRMS (ESI): calcd. for $C_{23}H_{18}F_3N_2S$ $[M+H]^+$ 411.1173; found 411.1178.

*3-Bromo-N-(2-(phenylthio)phenyl)quinolin-2-amine (**3a**):*



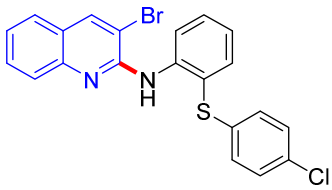
Yield 59% (60 mg) as a light brownish solid; mp 116–118 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.10 (dd, 2H, J = 13.6, 8.0 Hz), 7.16–7.22 (m, 4H), 7.32 (t, 1H, J = 7.2 Hz), 7.56 (t, 2H, J = 8.0 Hz), 7.61 (t, 1H, J = 8.4 Hz), 7.86 (d, 1H, J = 8.4 Hz), 8.16 (s, 1H), 8.85 (s, 1H), 9.25 (d, 1H, J= 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 109.2, 119.2, 119.6, 122.7, 124.2, 125.1, 126.1, 126.6, 127.2, 127.3, 129.3, 130.2, 131.2, 136.2, 137.3, 139.5, 142.3, 146.0, 149.1; IR (KBr): 3432, 2924, 2855, 1602, 1527, 1474, 1401, 1318, 1227, 1089, 10007, 895, 813, 747 cm^{-1}; HRMS (ESI): calcd. for $C_{21}H_{16}BrN_2S$ $[M+H]^+$ 407.0212; found 407.0216.

*3-Bromo-N-(2-(p-tolylthio)phenyl)quinolin-2-amine (**3b**)*:



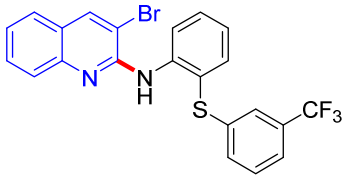
Yield 78% (82 mg) as a light brownish solid; mp 104–106 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 2.26 (s, 3H), 7.04 (d, 2H, J = 7.8 Hz), 7.01 (t, 1H, J = 7.2 Hz), 7.13 (d, 2H, J= 8.4 Hz), 7.31 (t, 1H, J = 7.8 Hz), 7.54 (d, 2H, J = 7.2 Hz), 7.60–7.62 (m, 1H), 7.68 (d, 1H, J = 7.8 Hz), 7.86 (d, 1H, J= 8.4 Hz), 8.14 (s, 1H), 8.91 (s, 1H), 9.25 (d, 1H, J= 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.1, 109.2, 119.2, 120.6, 122.6, 124.2, 125.1, 126.6, 127.2, 128.0, 130.0, 130.1, 130.8, 132.5, 136.2, 137.0, 139.5, 142.0, 146.0, 149.0; IR (KBr): 3299, 2922, 2854, 1581, 1528, 1438, 1402, 1301, 1204, 1158, 1004, 907, 800, 755, 612 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{18}BrN_2S$ $[M+H]^+$ 421.0369; found 421.0343.

*3-Bromo-N-(2-((4-chlorophenyl)thio)phenyl)quinolin-2-amine (**3e**):*



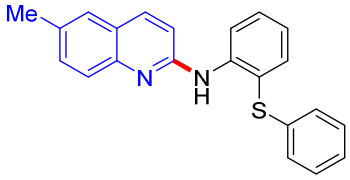
Yield 94% (103 mg) as a brownish solid; mp 141–143 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.10 (t, 3H, J= 8.4 Hz), 7.17 (d, 2H, J = 8.8 Hz), 7.32 (t, 1H, J = 7.6 Hz), 7.56 (d, 2H, J = 9.8 Hz), 7.61 (d, 1H, J = 8.0 Hz), 7.66 (t, 1H, J = 8.0 Hz), 7.86 (d, 1H, J = 8.4 Hz), 8.15 (s, 1H), 8.80 (s, 1H), 9.26 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 109.1, 119.1, 119.3, 122.8, 124.3, 125.2, 126.6, 127.2, 128.5, 129.4, 130.2, 131.5, 132.0, 134.9, 137.3, 139.6, 142.2, 145.9, 148.9; IR (KBr): 3321, 3053, 2922, 1581, 1526, 1441, 1315, 1160, 1117, 1070, 1002, 851, 793, 746, 693 cm^{-1}; HRMS (ESI): calcd. for $C_{21}H_{15}BrClN_2S$ $[M+H]^+$ 440.9822; found 440.9831.

*3-Bromo-N-(2-((3-(trifluoromethyl)phenyl)thio)phenyl)quinolin-2-amine (**3f**):*



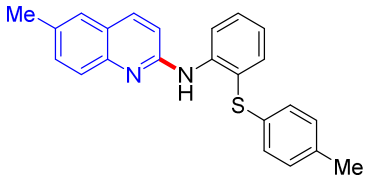
Yield 81% (96 mg) as a light yellowish solid; mp 155–157 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.11 (t, 1H, J = 7.6 Hz), 7.20–7.35 (m, 4H), 7.50–7.62 (m, 4H), 7.68 (d, 1H, J = 7.6 Hz), 7.84 (d, 1H, J = 8.0 Hz), 8.14 (s, 1H), 8.73 (s, 1H), 9.26 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 109.0, 118.2, 119.6, 122.9 (t, J= 3.2 Hz), 124.0 (q, J = 3.8 Hz), 124.4, 125.2, 126.6, 127.3, 129.7, 130.0, 130.2, 131.4, 131.8, 137.5, 138.0, 139.6, 142.3, 145.9, 148.9; ^{19}F NMR ($CDCl_3$ + Hexafluorobenzene): δ -66.0 (s); IR (KBr) 3327, 3059, 2924, 1583, 1528, 1443, 1318, 1165, 1120, 1071, 1003, 854, 794, 750, 695 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{15}BrF_3N_2S$ $[M+H]^+$ 475.0086; found 475.0088.

*6-Methyl-N-(2-(phenylthio)phenyl)quinolin-2-amine (**4a**):*



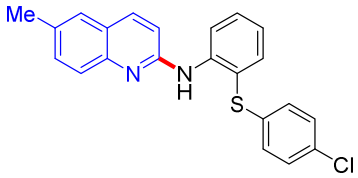
Yield 71% (61 mg) as a light brownish solid; mp 122–124 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.48 (s, 3H), 6.76 (d, 1H, J = 8.8 Hz), 7.04 (t, 1H, J = 7.6 Hz), 7.13 (t, 1H, J = 7.2 Hz), 7.18 (d, 2H, J = 7.2 Hz), 7.20–7.25 (m, 2H), 7.41 (s, 1H), 7.45 (d, 1H, J = 8.8 Hz), 7.51 (t, 1H, J = 8.4 Hz), 7.62 (d, 1H, J = 7.6 Hz), 7.79 (t, 3H, J = 8.4 Hz), 8.95 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.4, 113.6, 119.16, 119.2, 122.2, 124.4, 126.2, 126.7, 127.1, 127.4, 129.2, 129.4, 131.1, 131.9, 133.3, 136.5, 136.9, 137.1, 142.7, 145.7, 153.0; IR (KBr) 3362, 3054, 2960, 2922, 1611, 1587, 1521, 1435, 1314, 1127, 1023, 808, 755, 738, 688 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{19}N_2S$ $[M+H]^+$ 343.1263; found 343.1266.

*6-Methyl-N-(2-(p-tolylthio)phenyl)quinolin-2-amine (**4b**):*



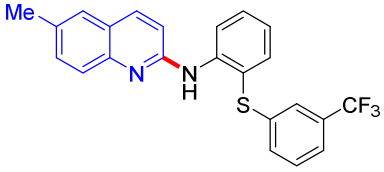
Yield 73% (65 mg) as a brownish solid; mp 150–152 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.26 (s, 3H), 2.47 (s, 3H), 6.77 (d, 1H, J = 8.8 Hz), 6.99–7.04 (m, 3H), 7.09 (d, 2H, J = 8.4 Hz), 7.41–7.48 (m, 3H), 7.55 (d, 1H, J = 7.6 Hz), 7.78 (dd, 3H, J = 21.6, 8.8 Hz), 8.87 (d, 1H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.1, 21.5, 113.6, 119.3, 120.4, 122.2, 124.4, 126.7, 127.1, 128.1, 130.2, 130.7, 131.9, 132.6, 133.3, 136.4, 137.1, 142.4, 145.8, 153.1; IR (KBr) 3361, 3052, 2958, 2921, 1610, 1585, 1518, 1434, 1315, 1125, 1020, 810, 754, 687 cm^{-1};HRMS (ESI): calcd. for $C_{23}H_{21}N_2S$ $[M+H]^+$ 357.1420; found 357.1428.

*N-(2-((4-Chlorophenyl)thio)phenyl)-6-methylquinolin-2-amine (**4e**):*



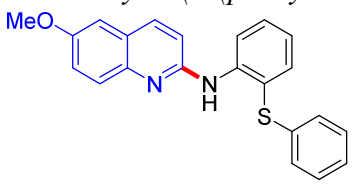
Yield 89% (84 mg) as a white solid; mp 158–160 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.48 (s, 3H), 6.77 (d, 1H, J = 8.8 Hz), 7.01–7.08 (m, 3H), 7.17 (d, 2H, J = 8.8 Hz), 7.42–7.46 (m, 2H), 7.51 (t, 1H, J = 8.4 Hz), 7.58 (d, 1H, J = 7.6 Hz), 7.71 (s, 1H), 7.76 (d, 1H, J = 8.4 Hz), 7.82 (d, 1H, J = 8.8 Hz), 8.91 (d, 1H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.5, 113.5. 118.7, 119.3, 122.3, 124.5, 126.7, 127.1, 128.5, 129.5, 131.4, 132.0, 132.1, 133.5, 135.1, 136.9, 137.3, 142.8, 145.7, 152.9; IR (KBr) 3365, 3059, 2961, 2924, 1614, 1590, 1523, 1431, 1315, 1128, 1025, 809, 759, 740, 697 cm^{-1};HRMS (ESI): calcd. for $C_{22}H_{18}ClN_2S$ $[M+H]^+$ 377.0874; found 377.0882.

*6-Methyl-N-(2-((3-(trifluoromethyl)phenyl)thio)phenyl)quinolin-2-amine (**4f**):*



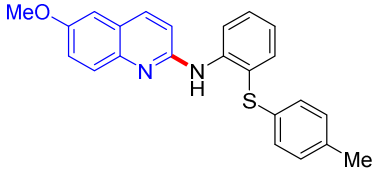
Yield 75% (77 mg) as a brownish solid; mp 89–91 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.47 (s, 3H), 6.80 (d, 1H, J = 8.8 Hz), 7.06 (t, 1H, J = 7.6 Hz), 7.19 (d, 1H, J = 7.6 Hz), 7.28 (d, 1H, J = 8.0 Hz), 7.34 (d, 1H, J = 7.6 Hz), 7.42 (s, 1H), 7.43 (d, 2H, J = 8.8 Hz), 7.53 (t, 1H, J = 7.8 Hz), 7.60 (d, 1H, J = 7.6 Hz), 7.69 (s, 1H), 7.75 (d, 1H, J = 8.4 Hz), 7.83 (d, 1H, J = 8.8 Hz), 8.88 (d, 1H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.5, 113.4, 117.4, 119.5, 122.5, 122.8 (q, J = 3.7 Hz), 123.7 (q, J = 3.7 Hz), 124.5, 125.2, 126.7, 127.1, 129.8, 129.9, 131.5, 131.8, 131.9, 132.1, 133.5, 137.3, 137.4, 138.4, 143.0, 145.7, 152.8; ^{19}F NMR ($CDCl_3$ + Hexafluorobenzene): δ -66.0 (s); IR (KBr) 3386, 2924, 2857, 1635, 1589, 1527, 1419, 1320, 1167, 1124, 1077, 895, 797, 761, 703 cm^{-1}; HRMS (ESI): calcd. for $C_{23}H_{18}F_3N_2S$ $[M+H]^+$ 411.1137; found 411.1142.

*6-Methoxy-N-(2-(phenylthio)phenyl)quinolin-2-amine (**5a**):*



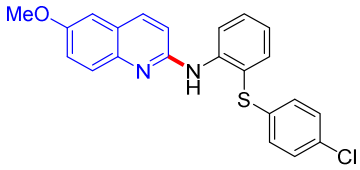
Yield 67% (60 mg) as a brownish solid; mp 93–95 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.89 (s, 3H), 6.78 (d, 1H, J = 8.8 Hz), 6.98–7.03 (m, 2H), 7.11–7.17 (m, 3H), 7.21 (t, 2H, J = 8.0 Hz), 7.26–7.29 (m, 1H), 7.49 (t, 1H, J = 8.8 Hz), 7.59 (d, 1H, J = 7.6 Hz), 7.75 (s, 1H), 7.79 (dd, 2H, J = 11.6, 9.2 Hz), 8.88 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 55.7, 106.4, 113.9, 118.9, 121.5, 122.0, 125.0, 126.2, 127.3, 128.8, 129.4, 131.1, 136.5, 136.7, 137.0, 142.9, 152.1, 156.1; IR (KBr) 3426, 2923, 2855, 1611, 1585, 1520, 1451, 1364, 1229, 1090, 1032, 813, 750 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{19}N_2OS$ $[M+H]^+$359.1213; found 359.1237.

*6-Methoxy-N-(2-(p-tolylthio)phenyl)quinolin-2-amine (**5b**):*



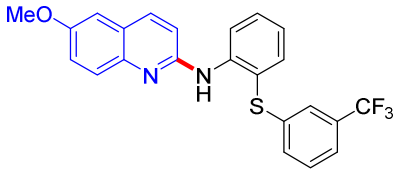
Yield 70% (65 mg) as a brownish solid; mp 123–125 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.15 (s, 3H), 3.78 (s, 3H), 6.68 (d, 1H, J = 8.8 Hz), 6.87–6.94 (m, 4H), 7.00 (d, 2H, J = 8.4 Hz), 7.17 (dd, 1H, J = 8.8, 2.8 Hz), 7.36 (t, 1H, J = 8.8 Hz), 7.46 (d, 1H, J = 7.6 Hz), 7.64 (s, 1H), 7.69 (dd, 2H, J = 8.8, 5.6 Hz), 8.75 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 21.1, 55.7, 106.3, 113.9, 118.9, 120.1, 121.4, 122.0, 124.9, 128.0, 128.7, 130.2, 130.7, 132.6, 136.3, 136.4, 136.6, 142.5, 142.9, 152.1, 156.0; IR (KBr) 3420, 2921, 2852, 1610, 1583, 1520, 1449, 1362, 1227, 1085, 1031, 808, 746 cm^{-1}; HRMS (ESI): calcd. for $C_{23}H_{21}N_2OS$ $[M+H]^+$ 373.1369; found 373.1375.

*N-(2-((4-Chlorophenyl)thio)phenyl)-6-methoxyquinolin-2-amine (**5e**):*



Yield 60% (59 mg) as a brownish solid; mp 122–124 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.89 (s, 3H), 6.80 (d, 1H, J = 8.8 Hz), 6.98–7.04 (m, 2H), 7.06 (d, 2H, J = 8.8 Hz), 7.17 (d, 2H, J = 8.8 Hz), 7.27–7.30 (m, 1H), 7.50 (t, 1H, J = 7.6 Hz), 7.57 (d, 1H, J= 7.6 Hz), 7.68 (s, 1H), 7.80 (dd, 2H, J = 18.8, 9.2 Hz), 8.86 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 55.7, 106.4, 113.8, 118.4, 119.0, 121.6, 122.2, 125.0, 128.5, 128.7, 129.5, 131.4, 132.0, 135.2, 136.8, 137.0, 142.9, 142.94, 152.0, 156.1; IR (KBr) 3438, 2926, 2857, 1613, 1587, 1521, 1452, 1363, 1230, 1091, 1034, 811, 753 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{18}ClN_2OS$ $[M+H]^+$ 393.0823; found 393.0831.

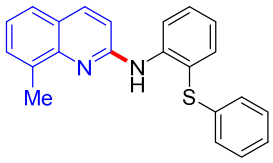
*6-Methoxy-N-(2-((3-(trifluoromethyl)phenyl)thio)phenyl)quinolin-2-amine (**5f**):*



Yield 74% (79 mg) as a brownish solid; mp 108–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.88 (s, 3H), 6.81 (d, 1H, J = 8.8 Hz), 6.97 (d, 1H, J = 2.8 Hz), 7.04 (t, 1H, J= 7.6 Hz), 7.18 (d, 1H, J = 7.6 Hz), 7.25–7.29 (m, 2H), 7.33 (d, 1H, J = 8.0 Hz), 7.44 (s, 1H), 7.52 (t, 1H, J = 8.0 Hz), 7.59 (d, 1H, J = 7.6 Hz), 7.65 (s, 1H), 7.77 (d, 1H, J = 9.2 Hz), 7.82 (d, 1H, J = 8.8 Hz), 8.84 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 55.7, 106.3, 113.7, 117.4, 119.2,

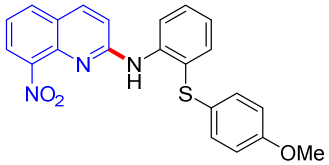
121.7, 122.3, 122.5, 122.7 (q, J = 3.7 Hz), 123.6 (q, J = 3.9 Hz), 125.1, 125.2, 128.8, 129.8, 129.9, 131.5, 131.8, 136.9, 137.3, 138.4, 142.9, 143.2, 151.9, 156.2; ^{19}F NMR ($CDCl_3$ + Hexafluorobenzene): δ -66.0 (s); IR (KBr): 3369, 2945, 2849, 1613, 1589, 1520, 1450, 1365, 1319, 1245, 1162, 1122, 1072, 906, 833, 751, 693 cm^{-1}; HRMS (ESI): calcd. for $C_{23}H_{18}F_3N_2OS$ $[M+H]^+$ 427.1036; found 427.1039.

*8-Methyl-N-(2-(phenylthio)phenyl)quinolin-2-amine (**6a**):*



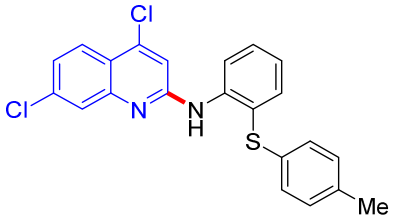
Yield 56% (47 mg) as a yellowish gummy; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.75 (s, 3H), 6.68 (d, 1H, J= 8.8 Hz), 7.01 (t, 1H, J= 7.2 Hz), 7.09 (t, 1H, J = 7.2 Hz), 7.13–7.21 (m, 5H), 7.45 (d, 2H, J = 8.4 Hz), 7.51 (t, 1H, J = 8.8 Hz), 7.61 (d, 1H, J = 8.0 Hz), 7.81 (d, 1H, J = 8.8 Hz), 7.94 (s, 1H), 9.23 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 18.6, 113.5, 118.4, 119.1, 121.9, 123.4, 124.1, 125.4, 126.1, 127.2, 129.4, 130.1, 131.2, 135.2, 136.6, 137.1, 137.8, 142.9, 146.3, 152.4; IR (KBr) 3357, 3053, 2919, 1619, 1589, 1524, 1433, 1342, 1312, 1142, 1025, 822, 741, 690 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{19}N_2S$ $[M+H]^+$ 343.1263; found 343.1290.

*N-(2-((4-Methoxyphenyl)thio)phenyl)-8-nitroquinolin-2-amine (**7c**):*



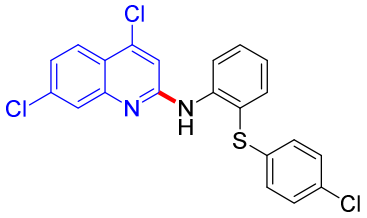
Yield 47% (47 mg) as a yellowish gummy; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.75 (s, 3H), 6.82 (d, 2H, J = 8.8 Hz), 7.12–7.16 (m, 3H), 7.38 (t, 1H, J = 8.0 Hz), 7.43–7.51 (m, 2H), 7.57–7.60 (m, 2H), 7.64 (t, 1H, J = 2.0 Hz), 8.56 (d, 1H, J = 8.4 Hz), 8.95 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 55.6, 115.5, 121.0, 122.8, 124.9, 125.3, 125.4, 127.5, 130.3, 130.4, 130.7, 132.1, 135.2, 135.8, 136.8, 139.1, 159.2, 164.1; IR (KBr) 3430, 2923, 2853, 1624, 1592, 1519, 1449, 1313, 1262, 1085, 1017, 756 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{18}N_3O_3S$ $[M+H]^+$ 404.1063; found 404.1069.

*4,7-Dichloro-N-(2-(p-tolylthio)phenyl)quinolin-2-amine (**8b**):*



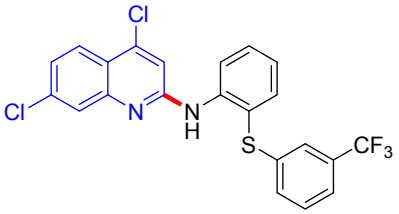
Yield 67% (69 mg) as a brownish solid; mp 80–82 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 2.26 (s, 3H), 6.83 (s, 1H), 7.04 (d, 2H, J = 7.8 Hz), 7.07–7.10 (m, 3H), 7.29–7.31 (m, 1H), 7.47 (t, 1H, J= 6.6 Hz), 7.56 (d, 1H, J = 7.8 Hz), 7.78 (s, 1H), 7.82 (d, 1H, J = 1.8 Hz), 7.92 (d, 1H, J = 8.4 Hz), 8.72 (d, 1H, J = 8.4 Hz);^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 21.1, 113.0, 120.5, 121.1, 122.0, 123.4, 125.0, 125.4, 126.6, 128.4, 130.3, 130.5, 132.1, 136.1, 136.7, 136.8, 141.1, 142.9, 148.8, 154.0; IR (KBr): 3436, 2924, 2859, 1606, 1564, 1493, 1428, 1353, 1272, 1177, 1078, 959, 810, 749, 659 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{17}Cl_2N_2S$ $[M+H]^+$ 411.0484; found 411.0479.

*4,7-Dichloro-N-(2-((4-chlorophenyl)thio)phenyl)quinolin-2-amine (**8e**):*



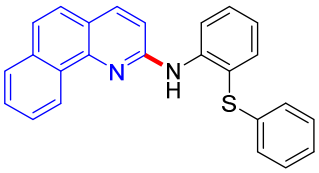
Yield 82% (88 mg) as a brownish gummy; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 6.88 (s, 1H), 7.05 (d, 2H, J = 8.4 Hz), 7.10 (t, 1H, J = 7.8 Hz), 7.18 (d, 2H, J = 8.4 Hz), 7.33 (dd, 1H, J = 9.0, 2.4 Hz), 7.52 (t, 1H, J = 9.0 Hz), 7.58 (d, 1H, J = 7.8 Hz), 7.74 (s, 1H), 7.84 (d, 1H, J = 2.4 Hz), 7.95 (d, 1H, J = 9.0 Hz), 8.78 (d, 1H, J = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 113.0, 120.1, 120.4, 121.2, 123.5, 125.2, 125.5, 126.6, 128.7, 129.6, 131.3, 132.4, 134.6, 136.8, 137.0, 141.6, 143.1, 148.7, 153.8; IR (KBr) 3437, 2927, 2863, 1609, 1561, 1494, 1429, 1352, 1271, 1179, 1079, 961, 812, 748, 667 cm^{-1}; HRMS (ESI): calcd. for $C_{21}H_{14}Cl_3N_2S$ $[M+H]^+$ 430.9938; found 430.9941.

*4,7-Dichloro-N-(2-((3-(trifluoromethyl)phenyl)thio)phenyl)quinolin-2-amine (**8f**):*



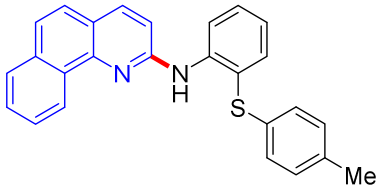
Yield 58% (67 mg) as a white solid; mp 121–123 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.79 (s, 1H), 7.04 (t, 1H, J = 7.2 Hz), 7.10 (d, 1H, J = 7.6 Hz), 7.17–7.28 (m, 3H), 7.35 (s, 1H), 7.46 (t, 1H, J = 8.4 Hz), 7.52 (d, 1H, J = 7.6 Hz), 7.63 (s, 1H), 7.74 (d, 1H, J = 2.0 Hz), 7.84 (d, 1H, J = 8.8 Hz), 8.70 (d, 1H, J = 8.4 Hz): ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 112.9, 119.0, 120.6, 121.3, 122.5, 123.0 (q, J = 3.7 Hz), 123.7, 123.8 (q, J = 3.8 Hz), 125.3, 125.4, 126.7, 129.9, 130.1, 131.7, 132.0, 137.0, 137.1, 138.0, 141.9, 143.2, 148.7, 153.7; ^{19}F NMR ($CDCl_3$ + Hexafluorobenzene): δ -66.1 (s); IR (KBr) 3436, 3340, 2923, 2853, 1618, 1579, 1528, 1452, 1321, 1164, 1121, 1073, 963, 791, 758, 695 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{14}Cl_2F_3N_2S$ $[M+H]^+$ 465.0201; found 465.0200.

*N-(2-(Phenylthio)phenyl)benzo[h]quinolin-2-amine (**9a**):*



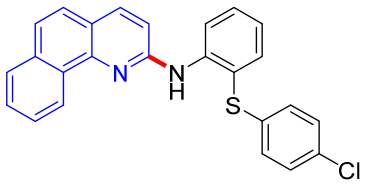
Yield 57% (54 mg) as a brownish solid; mp 122–124 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.88 (d, 1H, J = 8.4 Hz), 7.06–7.14 (m, 2H), 7.20 (dd, 4H, J = 12.0, 6.8 Hz), 7.57 (d, 1H, J = 8.8 Hz), 7.64 (q, 4H, J = 7.0 Hz), 7.71 (t, 1H, J = 6.8 Hz), 7.88 (d, 1H, J = 8.0 Hz), 7.95 (d, 2H, J = 8.4 Hz), 9.11 (d, 1H, J = 8.4 Hz), 9.16 (d, 1H, J= 8.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 112.8, 119.0, 119.1, 121.4, 122.2, 124.5, 124.8, 125.3, 126.2, 126.6, 127.3, 127.9, 129.4, 131.0, 131.1, 134.4, 136.5, 137.1, 137.7, 142.8, 145.5, 153.2; IR (KBr) 3357, 2928, 2857, 1624, 1585, 1529, 1455, 1359, 1315, 1243, 1087, 828, 809, 758, 652 cm^{-1}; HRMS (ESI): calcd. for $C_{25}H_{19}N_2S$ $[M+H]^+$ 379.1263; found 379.1273.

*N-(2-(p-Tolylthio)phenyl)benzo[h]quinolin-2-amine (**9b**):*



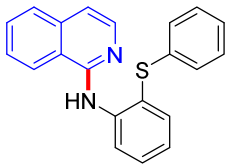
Yield 76% (74 mg) as a white solid; mp 110–112 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 2.27 (s, 3H), 6.88 (d, 1H, J = 8.4 Hz), 7.08 (dd, 3H, J = 16.2, 7.8 Hz), 7.16 (d, 2H, J = 7.8 Hz), 7.57 (d, 1H, J = 9.0 Hz), 7.59–7.69 (m, 4H), 7.73 (t, 1H, J = 7.2 Hz), 7.89 (d, 1H, J = 7.8 Hz), 7.93 (d, 1H, J = 9.0 Hz), 7.95 (s, 1H), 9.09 (d, 1H, J = 8.4 Hz), 9.19 (d, 1H, J = 7.8 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 21.1, 112.7, 119.2, 120.3, 121.3, 122.1, 124.4, 124.8, 125.3, 126.5, 127.8, 127.9, 128.1, 130.2, 130.7, 131.0, 132.6, 134.4, 136.4, 136.5, 137.6, 142.4, 145.5, 153.2; IR (KBr) 3349, 2921, 2854, 1621, 1584, 1528, 1452, 1357, 1310, 1240, 1081, 826, 800, 746, 649 cm^{-1}; HRMS (ESI): calcd. For $C_{26}H_{21}N_2S$ $[M+H]^+$ 393.1420; found 393.1422.

*N-(2-((4-Chlorophenyl)thio)phenyl)benzo[h]quinolin-2-amine (**9e**):*



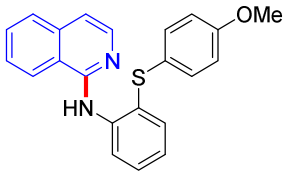
Yield 52% (53 mg) as a light yellowish solid; mp 121–123 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.89 (d, 1H, J = 8.4 Hz), 7.10 (d, 3H, J = 8.0 Hz), 7.19 (d, 2H, J = 8.0 Hz), 7.57–7.74 (m, 6H), 7.92 (dd, 3H, J = 27.2, 8.4 Hz), 9.14 (dd, 2H, J = 19.2, 8.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 112.7, 118.6, 119.4, 121.5, 122.3, 124.6, 124.7, 125.3, 126.6, 128.0, 128.5, 129.5, 131.0, 131.4, 132.1, 134.4, 135.2, 137.0, 137.8, 142.8, 145.5, 153.1; IR (KBr) 3433, 3349, 2924, 2854, 1584, 1528, 1356, 1136, 1087, 1007, 828, 752, 649 cm^{-1}; HRMS (ESI): calcd. for $C_{25}H_{18}ClN_2S$ $[M+H]^+$ 413.0874; found 413.0883.

*N-(2-(Phenylthio)phenyl)isoquinolin-1-amine (**10a**):*



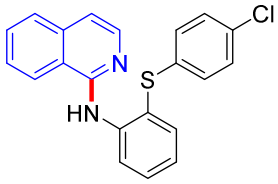
Yield 73% (60 mg) as a brownish gummy; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.04 (t, 1H, J = 7.2 Hz), 7.10–7.15 (m, 2H), 7.21–7.24 (m, 4H), 7.44 (t, 1H, J = 8.0 Hz), 7.52 (t, 1H, J = 7.2 Hz), 7.61 (dd, 2H, J = 18.0, 8.4 Hz), 7.69 (dd, 2H, J = 16.4, 8.0 Hz), 8.13 (d, 1H, J = 6.0 Hz), 8.58 (s, 1H), 8.91 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 114.1, 118.8, 119.3, 119.7, 121.5, 122.1, 126.2, 126.9, 127.1, 127.5, 129.5, 130.1, 131.4, 136.4, 137.2, 137.5, 140.8, 142.7, 151.7; IR (KBr) 3372, 3056, 2924, 2852, 1627, 1589, 1565, 1526, 1438, 1398, 1322, 1024, 806, 740, 689 cm^{-1}; HRMS (ESI): calcd. for $C_{21}H_{17}N_2S$ $[M+H]^+$ 329.1107; found 329.1095.

*N-(2-((4-Methoxyphenyl)thio)phenyl)isoquinolin-1-amine (**10c**):*



Yield 64% (57 mg) as a brownish solid; mp 80–82 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.72 (s, 3H), 6.78 (d, 2H, J = 8.8 Hz), 7.02 (t, 1H, J = 7.6 Hz), 7.14 (d, 1H, J = 6.0 Hz), 7.22 (d, 2H, J = 8.8 Hz), 7.44–7.51 (m, 2H), 7.60–7.64 (m, 2H), 7.75 (dd, 2H, J = 17.6, 8.4 Hz), 8.13 (d, 1H, J = 5.6 Hz), 8.59 (s, 1H), 8.84 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 55.5, 113.9, 115.0, 115.2, 119.6 (d, J = 8.5 Hz), 121.3, 121.6, 122.2, 126.5, 126.9, 127.5, 129.9, 130.1 (d, J = 10.0 Hz), 130.6, 136.2, 137.5, 140.8, 142.0, 151.9, 158.9; IR (KBr) 3364, 2925, 2841, 1624, 1590, 1563, 1530, 1493, 1436, 1400, 1323, 1248, 1207, 1027, 827, 800, 753, 581 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{19}N_2OS$ $[M+H]^+$ 359.1213; found 359.1235.

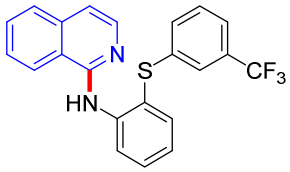
*N-(2-((4-Chlorophenyl)thio)phenyl)isoquinolin-1-amine (**10e**):*



Yield 69% (62 mg) as a brownish solid; mp 73–75 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.05 (t, 1H, J = 7.2 Hz), 7.10 (d, 2H, J = 9.0 Hz), 7.16 (d, 3H, J = 8.4 Hz), 7.49 (t, 1H, J = 7.2 Hz), 7.53 (t, 1H, J = 7.2 Hz), 7.61–7.65 (m, 2H), 7.68 (d, 1H, J = 8.4 Hz), 7.73 (d, 1H, J = 7.8 Hz), 8.13 (d, 1H, J = 5.4 Hz), 8.52 (s, 1H), 8.88 (d, 1H, J = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 114.3, 118.4, 119.6, 119.7, 121.4, 122.3, 127.1, 127.7, 128.3, 129.6, 130.2,

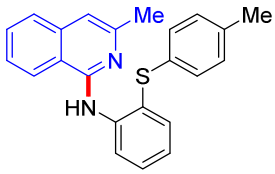
131.7, 132.1, 135.0, 137.2, 137.6, 140.8, 142.7, 151.7; IR (KBr): 3376, 2921, 2850, 1624, 1578, 1563, 1534, 1401, 1115, 1064, 805, 739, 692 cm^{-1}; HRMS (ESI): calcd. for $C_{21}H_{16}ClN_2S$ $[M+H]^+$ 363.0717; found 363.0688.

*N-(2-((3-(Trifluoromethyl)phenyl)thio)phenyl)isoquinolin-1-amine (**10f**):*



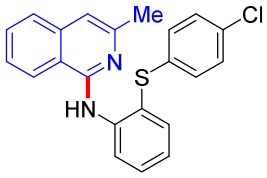
Yield 57% (56 mg) as a brownish solid; mp 123–125 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.06 (t, 1H, J = 7.2 Hz), 7.15 (d, 1H, J = 6.0 Hz), 7.21 (d, 1H, J = 8.0 Hz), 7.26 (t, 1H, J = 7.6 Hz), 7.33 (d, 1H, J = 7.6 Hz), 7.45 (t, 1H, J = 7.6 Hz), 7.52–7.56 (m, 2H), 7.58–7.67 (m, 3H), 7.71 (d, 1H, J = 8.0 Hz), 8.12 (d, 1H, J = 5.6 Hz), 8.46 (s, 1H), 8.89 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 114.4, 117.5, 119.6, 119.8, 121.3, 122.4, 122.9 (q, J = 3.7 Hz), 123.6 (q, J = 3.8 Hz), 127.1, 127.6, 129.8 (d, J = 1.1 Hz), 129.9, 130.2, 132.0, 137.3, 137.5, 138.2, 140.7, 142.8, 151.6; ^{19}F NMR ($CDCl_3$ + Hexafluorobenzene): δ -66.0 (s); IR (KBr): 3382, 2923, 2853, 1626, 1582, 1567, 1535, 1402, 1119, 1070, 806, 742, 697, cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{16}F_3N_2S$ $[M+H]^+$ 397.0981; found 397.0989.

*3-Methyl-N-(2-(p-tolylthio)phenyl)isoquinolin-1-amine (**11b**):*



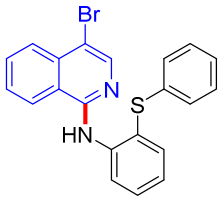
Yield 72% (64 mg) as a red gummy; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 2.25 (s, 3H), 2.59 (s, 3H), 6.98 (s, 1H), 7.02 (t, 1H, J = 7.2 Hz), 7.04 (d, 2H, J = 7.8 Hz), 7.14 (d, 2H, J= 7.8 Hz), 7.36 (t, 1H, J = 7.2 Hz), 7.50 (t, 1H, J = 7.2 Hz), 7.55 (t, 1H, J = 7.8 Hz), 7.61 (t, 2H, J = 7.2 Hz), 7.65 (d, 1H, J = 7.8 Hz), 8.71 (s, 1H), 9.09 (d, 1H, J = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 21.1, 24.5, 117.7, 117.9, 118.6, 119.1, 121.5, 121.7, 125.8, 126.9, 127.5, 129.9, 130.2, 131.1, 132.7, 136.2, 137.0, 138.3, 142.7, 149.7, 151.1; IR (KBr) 3367, 2926, 2845, 1627, 1591, 1564, 1535, 1492, 1437, 1404, 1322, 1249, 1208, 1026, 829, 801, 754, 582 cm^{-1}; HRMS (ESI): calcd. for $C_{23}H_{21}N_2S$ $[M+H]^+$ 357.1420; found 357.1435.

*N-(2-((4-Chlorophenyl)thio)phenyl)-3-methylisoquinolin-1-amine (**11e**):*



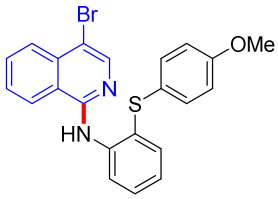
Yield 68% (64 mg) as a brownish gummy; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 2.61 (s, 3H), 7.00 (s, 1H), 7.04 (t, 1H, J = 7.8 Hz), 7.13 (d, 2H, J = 9.0 Hz), 7.19 (d, 2H, J = 9.0 Hz), 7.39 (t, 1H, J = 7.2 Hz), 7.52–7.57 (m, 2H), 7.61–7.66 (m, 3H), 8.64 (s, 1H), 9.12 (d, 1H, J = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 24.5, 112.0, 117.7, 117.8, 118.8, 121.2, 121.8, 126.0, 127.0, 128.2, 129.5, 130.0, 131.7, 132.0, 135.0, 137.2, 138.3, 142.9, 149.6, 150.9; IR (KBr) 3370, 2928, 2847, 1629, 1592, 1567, 1537, 1493, 1438, 1405, 1321, 1253, 1209, 1027, 830, 802, 755, 583 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{18}ClN_2S$ $[M+H]^+$ 377.0874; found 377.0897.

*4-Bromo-N-(2-(phenylthio)phenyl)isoquinolin-1-amine (**12a**):*



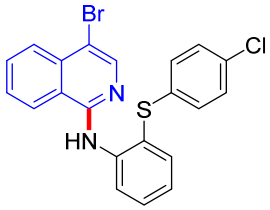
Yield 93% (94 mg) as a light brownish solid; mp 113–115 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.92–7.00 (m, 2H), 7.06–7.11 (m, 4H), 7.34 (t, 1H, J = 8.0 Hz), 7.39 (t, 1H, J = 7.2 Hz), 7.45 (d, 1H, J = 8.4 Hz), 7.54 (t, 2H, J = 7.6 Hz), 7.91 (d, 1H, J = 8.4 Hz), 8.15 (s, 1H), 8.46 (s, 1H), 8.71 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$):δ (ppm) 110.3, 119.2, 119.5, 120.9, 121.7, 122.5, 126.3, 126.9, 127.1, 127.7, 129.5, 131.1, 131.3, 135.6, 136.2, 137.1, 140.1, 142.1, 151.1; IR (KBr): 3447, 3378, 3051, 2924, 1620, 1590, 1527, 1438, 1403, 1312, 1180, 1070, 901, 748, 689 cm^{-1}; HRMS (ESI): calcd. for $C_{21}H_{16}BrN_2S$ $[M+H]^+$ 407.0212; found 407.0220.

*4-Bromo-N-(2-((4-methoxyphenyl)thio)phenyl)isoquinolin-1-amine (**12c**):*



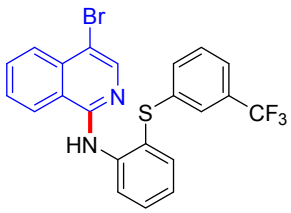
Yield 84% (92 mg) as a light brownish solid; mp 124–126 °C;^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.71 (s, 3H), 6.77 (d, 2H, J = 8.8 Hz), 7.04 (t, 1H, J = 7.6 Hz), 7.21 (d, 2H, J = 8.4 Hz), 7.46 (t, 1H, J = 8.0 Hz), 7.54 (t, 1H, J = 8.0 Hz), 7.61 (d, 1H, J = 8.0 Hz), 7.69–7.74 (m, 2H), 8.07 (d, 1H, J = 8.4 Hz), 8.28 (s, 1H), 8.58 (s, 1H), 8.74 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 55.5, 110.2, 115.2, 119.9, 120.1, 121.7, 121.9, 122.6, 126.2, 127.0, 127.7, 130.2, 130.6, 131.1, 135.7, 136.1, 141.4, 142.2, 151.3, 158.9; IR (KBr): 3357, 2924, 2837, 1618, 1587, 1529, 1493, 1436, 1404, 1313, 1248, 1175, 1028, 944, 827, 754, 664 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{18}BrN_2SO$ $[M+H]^+$ 437.0318; found 437.0319.

*4-Bromo-N-(2-((4-chlorophenyl)thio)phenyl)isoquinolin-1-amine (**12e**):*



Yield 86% (95 mg) as a brownish solid; mp 102–104 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.05–7.10 (m, 3H), 7.17 (d, 2H, J = 8.8 Hz), 7.53 (dd, 2H, J = 13.6, 6.8 Hz), 7.65 (t, 2H, J = 8.4 Hz), 7.72 (t, 1H, J = 8.0 Hz), 8.09 (d, 1H, J = 8.4 Hz), 8.29 (s, 1H), 8.52 (s, 1H), 8.80 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 110.6, 118.9, 119.8, 120.9, 121.6, 122.7, 127.1, 127.9, 138.3, 129.6, 131.2, 131.6, 132.3, 134.8, 135.8, 137.1, 142.2, 151.1; IR (KBr): 3367, 3040, 2916, 1614, 1587, 1521, 1435, 1392, 1312, 1158, 1123, 1069, 939, 745, 687cm^{-1}; HRMS (ESI): calcd. for $C_{21}H_{15}BrClN_2S$ $[M+H]^+$ 440.9822; found 440.9823.

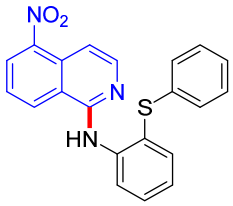
*4-Bromo-N-(2-((3-(trifluoromethyl)phenyl)thio)phenyl)isoquinolin-1-amine (**12f**):*



Yield 88% (104 mg) as a light yellowish solid; mp 120–122 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.07 (t, 1H, J = 7.6 Hz), 7.18 (d, 1H, J = 8.0 Hz), 7.24 (t, 1H, J = 7.6 Hz), 7.32 (d, 1H, J = 7.6 Hz), 7.46–7.55 (m, 3H), 7.58 (d, 1H, J = 8.4 Hz), 7.66 (dd, 2H, J = 14.8, 7.2 Hz), 8.03 (d, 1H, J = 8.4 Hz), 8.25 (s, 1H), 8.44 (s, 1H), 8.80 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz,

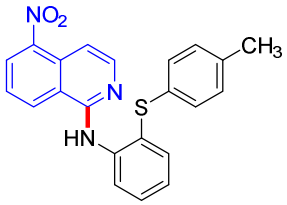
$CDCl_3$): δ (ppm) 110.6, 117.9, 120.0, 120.8, 121.5, 122.8, 123.0 (q, J = 3.7 Hz), 123.6 (q, J = 3.8 Hz), 127.1, 127.9, 129.8, 130.0, 131.2, 131.6, 131.9, 135.7, 137.3, 138.0, 142.1, 142.3, 151.0; ^{19}F NMR ($CDCl_3$ + Hexafluorobenzene): δ -66.1 (d, J = 7.8 Hz); IR (KBr): 3375, 3044, 2921, 1619, 1588, 1525, 1439, 1399, 1317, 1159, 1124, 1070, 940, 748, 692, 662 cm^{-1}; HRMS (ESI): calcd. For $C_{22}H_{15}BrF_3N_2S$ $[M+H]^+$ 475.0086; found 475.0095.

*5-Nitro-N-(2-(phenylthio)phenyl)isoquinolin-1-amine (**13a**):*



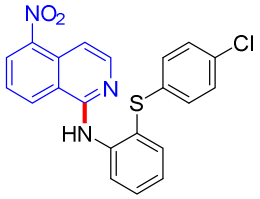
Yield 49% (46 mg) as a orange solid; mp 150–152 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.11–7.22 (m, 6H), 7.48–7.56 (m, 2H), 7.68 (d, 1H, J = 7.6 Hz), 7.81 (d, 1H, J = 6.0 Hz), 7.89 (d, 1H, J = 8.4 Hz), 8.32 (dd, 2H, J = 19.6, 8.0 Hz), 8.59 (s, 1H), 8.81 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 108.3, 119.7, 120.1, 120.6, 123.2, 125.1, 126.5, 127.1, 127.6, 128.0, 129.4, 129.6, 130.4, 131.4, 136.0, 137.1, 141.8, 144.8, 145.9, 152.0; IR (KBr): 3337, 2923, 2851, 1623, 1590, 1516, 1433, 1315, 1089, 1009, 869, 801, 755, 592 cm^{-1}; HRMS (ESI): calcd. for $C_{21}H_{16}N_3O_2S$ $[M+H]^+$ 374.0958; found 374.0952.

*5-Nitro-N-(2-(p-tolylthio)phenyl)isoquinolin-1-amine (**13b**):*



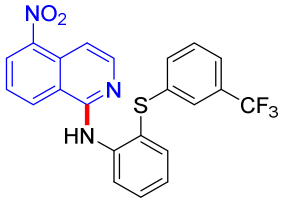
Yield 56% (54 mg) as a reddish solid; mp 93–95 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 2.24 (s, 3H), 7.03 (d, 2H, J = 7.8 Hz), 7.08–7.10 (m, 3H), 7.51 (t, 2H, J = 7.8 Hz), 7.66 (d, 1H, J = 7.8 Hz), 7.81 (d, 1H, J = 6.0 Hz), 7.94 (d, 1H, J = 8.4 Hz), 8.30 (d, 1H, J = 6.0 Hz), 8.36 (d, 1H, J = 7.8 Hz), 8.60 (s, 1H), 8.78 (d, 1H, J = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 21.1, 108.2, 120.1, 120.6, 123.1, 125.1, 127.6, 127.7, 127.8, 128.1, 130.2, 130.3, 130.4, 130.5, 131.0, 132.2, 136.6, 136.8, 141.5, 144.8, 145.8, 152.1; IR (KBr) 3332, 2921, 2850, 1621, 1585, 1517, 1431, 1313, 1081, 1002, 862, 799, 753, 585 cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{18}N_3O_2S$ $[M+H]^+$ 388.1114; found 388.1093.

*N-(2-((4-Chlorophenyl)thio)phenyl)-5-nitroisoquinolin-1-amine (**13e**):*



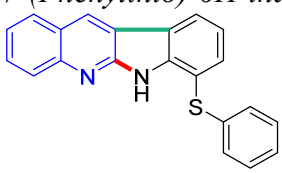
Yield 59% (60 mg) as a orange solid; mp 113–115 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.07–7.10 (m, 3H), 7.16–7.18 (m, 2H), 7.53–7.57 (m, 2H), 7.66 (d, 1H, J = 7.8 Hz), 7.84 (d, 1H, J = 6.6 Hz), 7.98 (d, 1H, J = 8.4 Hz), 8.31 (d, 1H, J = 6.0 Hz), 8.38 (d, 1H, J = 7.2 Hz), 8.54 (s, 1H), 8.79 (d, 1H, J = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 108.5, 119.4, 120.3, 120.6, 123.3, 125.2 127.7, 127.8, 128.3, 129.5, 129.7, 130.4, 131.6, 132.4, 134.6, 137.1, 141.8, 144.8, 146.0, 152.0; IR (KBr) 3340, 2924, 2853, 1626, 1591, 1519, 1434, 1316, 1091, 1010, 871, 802, 758, 597 cm^{-1}; HRMS (ESI): calcd. for $C_{21}H_{15}ClN_3O_2S$ $[M+H]^+$ 408.0568; found 408.0575.

*5-Nitro-N-(2-((3-(trifluoromethyl)phenyl)thio)phenyl)isoquinolin-1-amine (**13f**):*



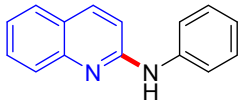
Yield 41% (45 mg) as a yellowish gummy; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.14 (t, 1H, J = 7.6 Hz), 7.20 (d, 1H, J = 8.0 Hz), 7.34 (t, 2H, J = 7.6 Hz), 7.52–7.58 (m, 3H), 7.69 (d, 1H, J = 7.6 Hz), 7.84 (d, 1H, J = 6.4 Hz), 7.95 (d, 1H, J = 8.4 Hz), 8.30 (d, 1H, J = 6.4 Hz), 8.37 (d, 1H, J = 7.6 Hz), 8.48 (s, 1H), 8.79 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 108.6, 115.7, 118.6, 120.5, 120.7, 123.1 (q, J = 3.4 Hz), 123.5, 123.7 (q, J = 3.8 Hz), 125.3, 127.7, 127.74, 129.9, 130.1, 130.4, 132.0, 137.3, 137.9, 138.0, 142.0, 144.7, 151.9; ^{19}F NMR ($CDCl_3$ + Hexafluorobenzene): δ -66.1 (s); IR (KBr) 3345, 2929, 2854, 1627, 1593, 1522, 1434, 1317, 1094, 1012, 877, 806, 759, 599cm^{-1}; HRMS (ESI): calcd. for $C_{22}H_{15}F_3N_3O_2S$ $[M+H]^+$ 442.0832; found 442.0835.

*7-(Phenylthio)-6H-indolo[2,3-b]quinoline (**14a**):*



Yield 65% (42 mg) as a brownish solid; mp 110–112 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.96 (t, 2H, J = 8.4 Hz), 7.08 (d, 2H, J = 7.6 Hz), 7.33 (t, 1H, J = 8.0 Hz), 7.50 (t, 1H, J = 8.0 Hz), 7.70–7.75 (m, 2H), 8.04 (dd, 2H, J = 14.0, 8.4 Hz), 8.19 (d, 1H, J = 8.0 Hz), 8.76 (s, 1H), 9.10 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 113.4, 118.7, 121.3, 122.1, 123.0, 123.9, 124.7, 127.7, 128.6, 128.7, 128.74, 129.4, 129.6, 132.2, 134.5, 134.9, 143.0, 147.0, 152.5; IR (KBr) 3441, 2918, 2851, 1635, 1603, 1475, 1400, 1224, 1090, 1011, 814, 748, 477 cm^{-1}; HRMS (ESI): calcd. for $C_{21}H_{15}N_2S$ $[M+H]^+$ 327.0950; found 327.0964.

*N-phenylquinolin-2-amine (**1k**)*[11f]*:*



Yield 59% (32 mg) as a yellowish gummy; ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 6.92 (s, 1H), 7.00 (d, 1H, J = 8.4 Hz), 7.10 (t, 1H, J = 7.2 Hz), 7.30 (t, 1H, J = 8.4 Hz), 7.37 (t, 2H, J = 7.2 Hz), 7.56–7.60 (m, 3H), 7.65 (d, 1H, J = 8.4 Hz), 7.79 (d, 1H, J = 8.4 Hz), 7.92 (d, 1H, J = 8.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 111.8, 119.2, 120.7, 123.3, 124.3, 126.8, 127.6, 129.4, 130.0, 138.0, 140.3, 147.8, 154.5; IR (KBr) 3406, 2924, 1618, 1597, 1532, 1500, 1442, 1324, 1248, 1148, 817, 754, 693, 496 cm^{-1}; HRMS (ESI): calcd. for $C_{15}H_{12}N_2$ $[M+H]^+$ 221.1073; found 221.1081.

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Notes

The authors declare no competing financial interest.

Supporting Information Available

The Supporting Information is available free of charge on the ACS Publications website at http://pubs.acs.org

Spectra of all compounds and X-ray data for **3a** (CIF)

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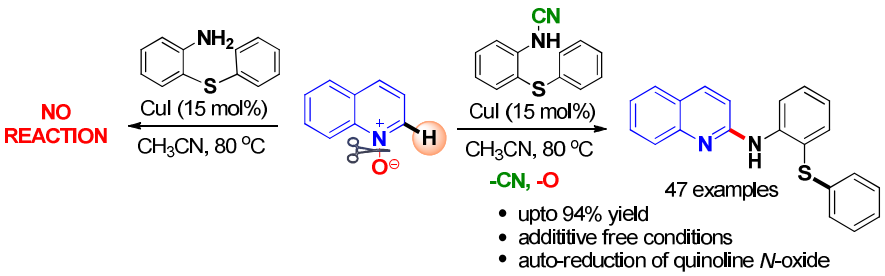
NO REACTION
CuI (15 mol%)
CH3CN, 80 °C
CuI (15 mol%)
CH3CN, 80 °C
-CN, -O
47 examples
• upto 94% yield
• addititive free conditions
• auto-reduction of quinoline N-oxide