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ARTICLE

Palladium-Catalyzed Direct Coupling of 2-Vinylanilines and Isocyanides: An Efficient Synthesis of 2-Aminoquinolines

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Palladium-catalyzed oxidative coupling of 2-vinylanilines and isocyanides constitutes a direct, facile, and efficient approach to 2-aminoquinolines. The procedure, employing palladium acetate and silver carbonate, is attractive in terms of assembly efficiency, functional group tolerance, and operational simplicity. A variety of 2-aminoquinolines were prepared in good to excellent yields.

Introduction

The2-Aminoquinoline derivatives represent an important class of heterocyclic motifs exhibiting a broad spectrum of biological and medicinal activities. For instance, Imiquimod (1-isobutyl-1*H*-imidazo[4,5-c]quinolin-4-amine) is marketed under the trade name Aldara to treat genital warts, actinic keratosis and superficial skin cancers.[1] Recently, 2-aminoquinoline scaffolds have been developed to be adenosine A2A receptor antagonists,[2] *β*-secretase (BACE) inhibitor,[3] and melanin-concentrating hormone (MCH) antagonist.[4] They are also frequently employed in molecular recognition processes as the core structure.[5] Thus, intensive research efforts have been devoted to the preparation of 2-aminoquinolines, and several synthetic routes are known: (i) direct *α*-amination of quinolines with sodium or potassium amide, named commonly as the Chichibabin reaction;[6] (ii) substitution of 2-haloquinolines with ammonia or amines under high temperature and pressure[7] or *via* transition-metal-catalyzed cross-coupling amination;[8] (iii) activation of quinolines to the corresponding N-oxides, followed by either displacement of nucleophiles[9] or transition-metal-catalyzed dehydrogenative amination;[10] (iv) condensation of 2-aminobenzaldehyde or analogoues with appropriate nitrile derivatives[11] and (V) direct cyclization of 2-vinylphenyl (thio)ureas or 2-vinylphenylcarbodiimides.[12] Many of these procedures suffer from harsh reaction conditions, poor regioselectivities, limited functional group tolerance, and low yields. Hence, exploring new approaches to 2-aminoquinolines is still a highly desirable goal.

Isocyanide is isoelectronic with carbon monoxide, and thus it can be considered to have similar reactivity toward transition-metal catalysts and undergo analogous fundamental transformations (e.g., insertion into M-C bond).[13] However, compared to carbonylation reactions, which have been well established for generating carbonyl-containing compounds,[14] transition-metal-catalyzed reactions using isocyanides as C1 building blocks are much less explored. Recently, they have begun to emerge as practical and powerful tools to construct nitrogen- (or carbonyl-) containing compounds, carrying several distinct advantages over reactions with carbon monoxide, such as operational simplicity, non-toxicity, and the ability to employ the isocyanide reagent stoichiometrically.[15] So far, isocyanides are predominantly employed in the synthesis of amidines and imidates.[16] Inspired by Alper's work,[17] we herein disclose a straightforward and efficient strategy to synthesize 2-aminoquinolines *via* palladium-catalyzed direct coupling of 2-vinylanilines and isocyanides.

Results and discussion

We initially subjected 2-(1-phenyl-vinyl)aniline (**1a**) and *tert*-butyl isocyanide (**2a**) to a set of conditions commonly used for oxidative couplings, $Pd(OAc)_2/Cu(OAc)_2$ in toluene at 110 °C, and were delighted to obtain the anticipated aminoquinoline **3aa** in 48% isolated yield (Table1, entry 1). Addition of CF_3CO_2H as a promoter increased the yield only slightly (55%). The success of this transformation did depend significantly, however, on the nature of the oxidant, and reaction with the best performer, Ag_2CO_3, furnished quinoline **3aa** in 90% yield (entries 3-7). The choice of solvent also had a dramatic impact on reactivity, and dioxane proved to be the optimal choice, generating **3aa** in 92% yield (entries 7 and 10-13). Unfortunately, the catalyst loading could not be decreased (from 10 mol %) without observing significant sacrifice to yield. Running the reaction at a lower loading of palladium precursor, for instance 7 mol % and 5 mol %, hampered the reaction efficiency (table 1 entries 8, 9 and 14). Various other combinations of palladium precursor and oxidant were tested

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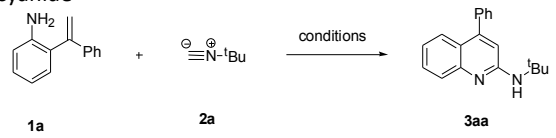
(Table 1, entries 15-19). However, none offered results superior to $Pd(OAc)_2/Ag_2CO_3$ (Table 1, entry 13). It is noteworthy that the rhodium complex $[Cp^*RhCl_2]_2$ showed acceptable catalytic activity in this transformation.

Table 1. Optimization of Reaction Conditions Using the Reaction of 2-(1-Phenyl-vinyl)aniline with *tert*-Butyl Isocyanide[a]



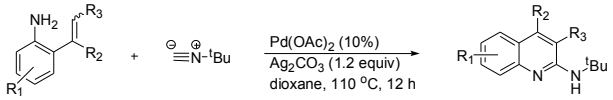
1a 2a 3aa

entry	catalyst (mol %)	oxidant	solvent	yield (%)[b]
1	$Pd(OAc)_2$ (10)	$Cu(OAc)_2$	PhMe	48
2[c]	$Pd(OAc)_2$ (10)	$Cu(OAc)_2$	PhMe	55
3[d]	$Pd(OAc)_2$ (10)	$Cu(OAc)_2/O_2$	PhMe	44
4[e]	$Pd(OAc)_2$ (10)	$Cu(OAc)_2/O_2$	PhMe	73
5[f]	$Pd(OAc)_2$ (10)	BQ	PhMe	38
6	$Pd(OAc)_2$ (10)	AgOAc	PhMe	0
7	$Pd(OAc)_2$ (10)	Ag_2CO_3	PhMe	90
8	$Pd(OAc)_2$ (5)	Ag_2CO_3	PhMe	63
9	$Pd(OAc)_2$ (7)	Ag_2CO_3	PhMe	80
10	$Pd(OAc)_2$ (10)	Ag_2CO_3	CH_3CN	55
11	$Pd(OAc)_2$ (10)	Ag_2CO_3	DCE[g]	60
12	$Pd(OAc)_2$ (10)	Ag_2CO_3	DME[h]	86
13	$Pd(OAc)_2$ (10)	Ag_2CO_3	dioxane	92
14	$Pd(OAc)_2$ (5)	Ag_2CO_3	dioxane	62
15	$Pd(TFA)_2$ (10)	Ag_2CO_3	dioxane	71
16	$Pd(Cl)_2$ (10)	Ag_2CO_3	dioxane	66
17	$Pd(OAc)_2$ (10)	Ag_2O	dioxane	88
18	$Pd(OAc)_2$ (10)	$PhI(OAc)_2$	dioxane	0
19	[Ru] (5)[i]	Ag_2CO_3	PhMe	0
20	$[Cp^*RhCl_2]_2$ (5)	Ag_2CO_3	PhMe	39

[a] All reactions were carried with 0.5 mmol **1a**, 1.0 mmol of **2a**, 10 mol% of $Pd(OAc)_2$, 2.4 equiv of $[Ag^+]$ or $[Cu^{2+}]$, 5 mL of solvent, sealed flask, 110 °C, 12 h. [b] isolated yield. [c] 0.5 equiv of CF_3COOH. [d] 1.0 equiv of $[Cu^{2+}]$, 1.0 atm of O_2. [e] 2.0 equiv of $[Cu^{2+}]$, 1.0 atm of O_2. [f] 2.4 equiv of BQ. [g] DCE = dichloroethane. [h] DME = dimethoxyethane. [i] [Ru] = $[Ru(p\text{-cymene})Cl_2]_2$.

With the optimal reaction conditions established, the generality of this reaction was explored by the reaction of *tert*-butyl isocyanide with a variety of 2-vinylanilinic substrates. The results are summarized in Table 2. Both electron-donating and -withdrawing groups, *e.g.*, methyl (**1b**), methoxy (**1c**), chloro (**1d**), and bromo (**1e**), *para* to the nitrogen were well tolerated. The tolerance of halogen is especially interesting because the halogen atom offers a further avenue for structural elaboration. Steric crowding, by introduction of a substituent, such as Me and Cl, *ortho* to the amino group of the aniline, depressed the yields of **3fa** and **3ga**.The properties of R_2 have a significant effect on the efficiency of this reaction. When R_2 were *p*-Cl-phenyl, phenyl, and *p*-Me-phenyl, the corresponding products **3ha**, **3ba**, and **3ia** were obtained in 72%, 80%, and 94% yields, respectively, indicating that direct correlation exists between the yields and the electron density of the phenyl group. Using methyl group instead of aromatic groups decreased the yields slightly (**3ja-3ma**). The substrate without substitution on the vinyl group only formed the desired product **3na** in 48% yield. This was not due to its susceptibility to polymerization at elevated temperatures, because most of unreacted starting material was recovered. Gratifyingly, the transformation tolerates substituents on the other side of the double bond. When R_3 was Me instead of H (Table 2, entry 15; E/Z = 1:1), the product **3oa** was isolated in 76% with only trace amount of **1o** left. The substrates with endocyclic C=C bonds **1p** and **1q** also gave the desire products **3pa** and **3qa** in moderate yields (Table 2, entries 16 and 17). The substrate **1r** with strongly electron- withdrawing group NO_2 also produced the target product **3ra** in acceptable yield (entry 18). It is noteworthy that 2-(2-propen-1-yl)aniline (**1s**) only provided 20% of the anticipated product **3sa**, demonstrating that the conjugation of the vinyl group to the aryl moiety plays a key role in this transformation.[18]

Table 2. Synthesis of 2-*tert*-Butylaminoquinolines Using *tert*-Butyl Isocyanide[a]



1 2a 3

entry	1	R_1	R_2	R_3	product	yield (%)[b]
1	**1a**	H	Ph	H	**3aa**	92
2	**1b**	4-Me	Ph	H	**3ba**	80
3	**1c**	4-MeO	Ph	H	**3ca**	72
4	**1d**	4-Cl	Ph	H	**3da**	87
5	**1e**	4-Br	Ph	H	**3ea**	65
6	**1f**	6-Me	Ph	H	**3fa**	58
7	**1g**	6-Cl	Ph	H	**3ga**	37[c]
8	**1h**	4-Me	p-Cl-Ph	H	**3ha**	72
9	**1i**	4-Me	p-tolyl	H	**3ia**	94
10	**1j**	H	Me	H	**3ja**	73
11	**1k**	5-Cl	Me	H	**3ka**	63
12	**1l**	5-F	Me	H	**3la**	61
13	**1m**	4-Me	Me	H	**3ma**	73
14	**1n**	H	H	H	**3na**	48
15	**1o**	H	Ph	Me	**3oa**	76
16	**1p**	4-Me	$-(CH_2)_3-$		**3pa**	58
17	**1q**	4-Me	$-(CH_2)_4-$		**3qa**	60
18	**1r**	4-NO_2	Ph	H	**3ra**	32

[a] All reactions were carried with 0.5 mmol of **1**, 1.0 mmol of **2a**, 10 mol % of $Pd(OAc)_2$, 1.2 equiv of Ag_2CO_3, 5 mL of dioxane, sealed flask, 110 °C, 12 h. [b] isolated yield. [c] determined by 1H NMR spectroscopy.

The scope of isocyanides was further investigated by the reaction of several isocyanides with 2-(1-phenyl-vinyl)aniline (Scheme 1). The results demonstrate that the substitution of isocyanide plays a key role in this transformation and the *tert*-butyl group is certainly the best of all functional groups tested. The secondary aliphatic group, *iso*-propyl, gave the anticipated products **3ab** in moderate yield (48%). The primary aliphatic group, *n*-Hexyl, gave a rather poor yield of product **3ac** (24%). Phenyl group only gave a trace amount of product **3ad**. It was very interesting that 2,6-diisopropylphenyl provided single-insertion product **3ae** and 2,4,6-trimethylphenyl offered the double-insertion product **3af**, albeit both in low yields.

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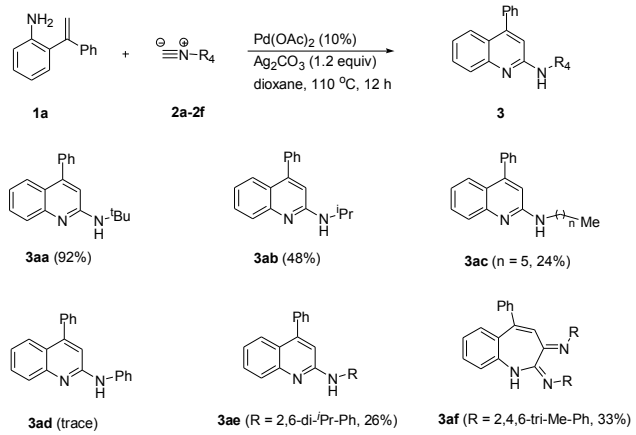
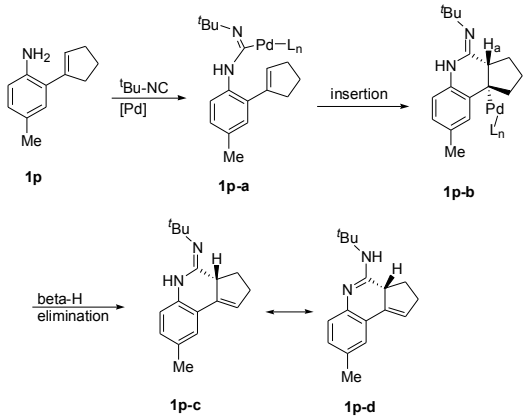
There are three possible pathways for this ring-closing process: (i) oxidative heck-reaction pathway;[17] (ii) direct C-H bond activation (concerted metalation-deprotonation pathway) (Scheme 3, **8'**); and (iii) intramolecular nucleophilic attack of the conjugated alkene on the electrophilic palladium(II), followed by deprotonation process (Scheme 3, **8** and **9**). The *E*/*Z* isomer of 2-(1-phenylprop-1-en-1-yl)aniline (**1o**, *E*/*Z* = 1:1) gave the product **3oa** in 76% isolated yield with only a trace amount of **1o** left under the standard conditions, which favors the pathway (iii) (Table 1, entry 15). The substrate **1p** and **1q** offered the product **3pa** and **3qa** in 58% and 60% isolated yield, respectively, which eliminates the heck-reaction pathway. If via heck-reaction pathway, cis-insertion step only gives the intermediate **1p-b**, with H_a opposite to the palladium atom (Scheme 2). The following cis-elimination step provides the product **1p-c** or **1p-d** instead of **3pa**. Neither**1p-c** or **1p-d** was observed by NMR spectroscopy.

Scheme 1. Insertion of Isocyanides to vinylaniline **1a**[a]



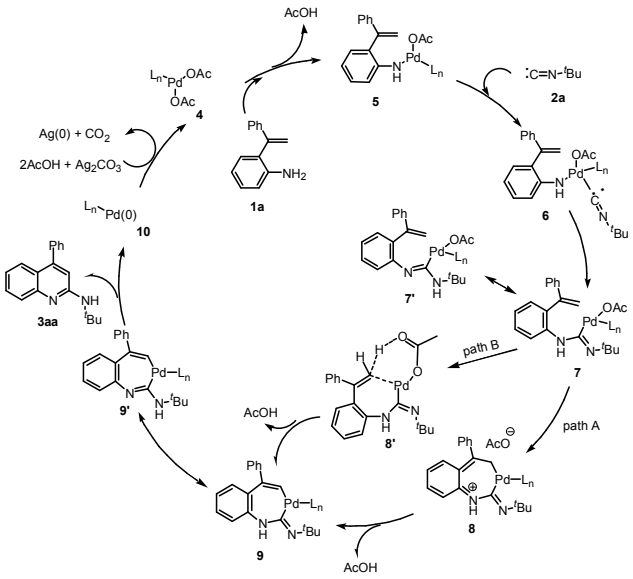
[a] All reactions were carried with 0.5 mmol of **1a**, 1.0 mmol of **2**, 10 mol% of $Pd(OAc)_2$, 1.2 equiv of Ag_2CO_3, 5 mL of dioxane, sealed flask, 110 °C, 12 h. [b] isolated yield.

Scheme 2.



Based on the preliminary results, a possible mechanism for the formation of 2-aminoquinoline **3** is depicted in Scheme 3 with **1a** and **2a** as the model substrates. Initially, the nitrogen atom of aniline **1a** adds to Pd(II) species **4** to give palladium complex **5**, with elimination of acetic acid. Isocyanide **2a** coordinates to the palladium centre of **5**, and then inserts to Pd-N bond leading to imidoyl-palladium complex **7**, which is converted to intermediate **9** by an intramolecular nucleophilic attack of the conjugated alkene on the electrophilic palladium(II) followed by deprotonation process (path A, Scheme 3, **8** and **9**; it is a *N*-assisted dearomatization-rearomatization process; If the C=C bond is not conjugated with anillinic moiety, the efficiency of this transformation is rather poor[18]) or by a carboxylate-assisted direct $C(sp^2)$-H bond activation pathway (Scheme 3, **8'**)[19] (path B). Reductive elimination produces **3aa**, along with palladium(0) species **10**. Complex **10** may then be re-oxidized by an oxidant to the palladium(II) species **4**.

Scheme 3. Possible Reaction Mechanism



Conclusions

A new strategy for the synthesis of 2-aminoquinoline derivatives has been developed based on the palladium-catalyzed direct coupling of 2-vinylanilines and isocyanides. This procedure constitutes a straightforward, efficient and practical access to a synthetically interesting and biologically active class of products. To our knowledge, it is the first oxidative coupling of anilines and terminal alkenes involving isocyanides, and thus expands the methodological scope of palladium-catalyzed migratory insertion of isocyanides.

Experimental section

General procedures for the Pd-catalyzed synthesis of 2-aminoquinoline 3

A mixture of $Pd(OAc)_2$ (0.05 mmol), Ag_2CO_3 (0.6 mmol), **1** (0.5 mmol), **2** (1.0 mmol), and 1,4-dioxane (5 mL) were added sequentially to a heavy glass flask. The resulting mixture was stired and heated at 110 °C for 12 h. After cooling to room temperature, the solvent was removed under reduced pressure, and then the residue was purified by flash

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chromatography with a gradient of hexane to ethyl acetate/hexane (solvent ratios varied with product polarities) as the eluant to afford the products.

N-*tert*-butyl-4-phenyl-2-aminoquinoline, **3aa**: yellow solid, m.p. = 125.7-127.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.75 (d, J = 8.4 Hz, 1 H), 7.61 (d, J = 8 Hz, 1 H), 7.44-7.54 (m, 6 H), 7.14 (t, J = 6.8 Hz, 1 H), 6.55 (s, 1 H), 4.68 (s, 1 H), 1.57 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 156.2, 148.9, 148.7, 138.8, 129.4, 129.3, 128.5, 128.1, 127.1, 125.7, 122.0, 121.9, 113.0, 51.6, 29.6. HRMS (ESI) m/z calcd for $C_{19}H_{20}N_2$ $(M+H)^+$ 277.1700, found 277.1694.

N-*tert*-butyl-6-methyl-4-phenyl-2-aminoquinoline, **3ba**: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.66 (d, J = 8.8 Hz, 1 H), 7.46-7.49 (m, 5 H), 7.35-7.37 (m, 2 H), 6.52 (s, 1 H), 4.62 (br s, 1 H), 2.36 (s, 3 H), 1.56 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 155.8, 148.5, 147.0, 139.0, 131.4, 131.2, 129.5, 128.5, 128.1, 126.8, 124.7, 121.9, 113.0, 51.5, 29.7, 21.5. HRMS (ESI) m/z calcd for $C_{20}H_{22}N_2$ $(M+H)^+$ 291.1856, found 291.1854.

N-*tert*-butyl-6-methoxy-4-phenyl-2-aminoquinoline, **3ca**: pale yellow solid, m.p. = 85.1-86.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.93 (d, J = 8.8 Hz, 1 H), 7.73 (s, 6 H), 7.45-7.51 (m, 1 H), 6.79 (s, 1 H), 4.79 (s, 1 H), 3.98 (s, 3 H), 1.80 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 155.2, 154.8, 148.1, 144.3, 138.9, 129.3, 128.6, 128.4, 128.1, 122.2, 120.2, 113.3, 105.4, 55.6, 51.5, 29.7. HRMS (ESI) m/z calcd for $C_{20}H_{22}N_2O$ $(M+H)^+$ 307.1805, found 307.1805.

N-*tert*-butyl-6-chloro-4-phenyl-2-aminoquinoline, **3da**: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.67 (d, J = 8.8 Hz, 1 H), 7.56 (d, J = 2.4 Hz, 1 H), 7.42-7.53 (m, 6 H), 6.52 (s, 1 H), 4.66 (br s, 1 H), 1.56 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 156.2, 148.1, 147.2, 138.1, 129.8, 129.3, 128.7, 128.6, 128.4, 127.1, 124.5, 122.7, 113.9, 51.7, 29.5. HRMS (ESI) m/z calcd for $C_{19}H_{19}ClN_2$ $(M+H)^+$ 311.1310, found 311.1309.

N-*tert*-butyl-6-bromo-4-phenyl-2-aminoquinoline, **3ea**: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.71 (d, J = 2.0 Hz, 1 H), 7.55-7.62 (m, 2 H), 7.47-7.53 (m, 3 H), 7.42-7.45 (m, 2 H), 6.51 (s, 1 H), 4.67 (br s, 1 H), 1.56 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 156.3, 148.1, 147.5, 138.0, 132.4, 129.3, 128.9, 128.7, 128.4, 127.7, 123.4, 114.9, 113.8, 51.8, 29.5. HRMS (ESI) m/z calcd for $C_{19}H_{19}BrN_2$ $(M+H)^+$ 355.0805, found 355.0809.

N-*tert*-butyl-8-methyl-4-phenyl-2-aminoquinoline, 3fa: yellow solid, m.p. = 84.1-85.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.40-7.49 (m, 7 H), 7.01-7.05 (m, 1 H), 6.44 (s, 1 H), 4.51 (br s, 1 H), 2.72 (s, 3 H), 1.61 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 154.9, 149.2, 147.5, 139.2, 134.8, 129.5, 128.4, 128.0, 123.6, 121.6, 121.4, 113.1, 51.7, 29.1, 19.0. HRMS (ESI) m/z calcd for $C_{20}H_{22}N_2$ $(M+H)^+$ 291.1856, found 291.1858.

N-*tert*-butyl-8-chloro-4-phenyl-2-aminoquinoline, 3ga: white solid, m.p. = 83.5-84.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.65 (d, J = 8.0 Hz, 1 H), 7.42-7.51 (m, 6 H), 7.01 (t, J = 8.0 Hz, 1 H), 6.51 (s, 1 H), 4.76 (br s, 1 H), 1.64 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 155.9, 149.3, 144.9, 138.4, 131.1, 129.3, 128.5, 128.3, 124.7, 123.3, 121.3, 113.8, 51.9, 29.1; HRMS (ESI) m/z calcd for $C_{19}H_{19}ClN_2$ $(M+H)^+$ 311.1310, found 311.1311.

N-*tert*-butyl-4-(4-chlorophenyl)-6-methyl-2-aminoquinoline, 3ha: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.65 (d, J = 8.4 Hz, 1 H), 7.30-7.48 (m, 6 H), 6.47 (s, 1 H), 4.60 (br s, 1 H), 2.36 (s, 3 H), 1.55 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 155.7, 147.2, 147.0, 137.4, 134.1, 131.5, 131.4, 130.7, 128.8, 127.0, 124.4, 121.6, 112.9, 51.6, 29.6, 21.5. HRMS (ESI) m/z calcd for $C_{20}H_{21}ClN_2$ $(M+H)^+$ 325.1467, found 325.1466.

N-*tert*-butyl-6-methyl-4-(4-methylphenyl)-2-aminoquinoline, 3ia: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.65 (d, J = 8.4 Hz, 1 H), 7.30-7.40 (m, 6 H), 6.53 (s, 1 H), 4.70 (br s, 1 H), 2.47 (s, 3 H), 2.36 (s, 3 H), 1.55 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 155.9, 148.5, 147.0, 137.9, 136.1, 131.3, 131.2, 129.3, 129.2, 126.8, 124.8, 122.0, 112.8, 51.5, 29.7, 21.5, 21.4. HRMS (ESI) m/z calcd for $C_{21}H_{24}N_2$ $(M+H)^+$ 305.2013, found 305.2016.

N-*tert*-butyl-4-methyl-2-aminoquinoline, 3ja: white solid, m.p. = 83.5-84.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.73 (d, J = 8.4 Hz, 1 H), 7.67 (d, J = 8.4 Hz, 1 H), 7.50 (t, J = 7.2 Hz, 1 H), 7.20 (t, J = 7.2 Hz, 1 H), 6.46 (s, 1 H), 4.55 (br s, 1 H), 2.53 (s, 3 H), 1.53 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 156.5, 148.1, 144.2, 129.1, 127.0, 123.5, 123.4, 121.7, 113.1, 51.4, 29.7, 18.9. HRMS (ESI) m/z calcd for $C_{14}H_{18}N_2$ $(M+H)^+$ 215.1543, found 215.1543.

N-*tert*-butyl-7-chloro-4-methyl-2-aminoquinoline, 3ka: yellow solid, m.p. = 80.3-81.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.61-7.67 (m, 2 H), 7.13 (d, J = 8.8 Hz, 1 H), 6.38 (s, 1 H), 4.57 (br s, 1 H), 2.48 (s, 3 H), 1.52 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 157.0, 149.0, 143.8, 134.7, 126.1, 124.8, 122.1, 121.8, 113.4, 51.6, 29.5, 18.8. HRMS (ESI) m/z calcd for $C_{14}H_{17}ClN_2$ $(M+H)^+$ 249.1154, found 249.1151.

N-*tert*-butyl-7-fluoro-4-methyl-2-aminoquinoline, 3la: pale yellow solid, m.p. = 62.0-63.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.66-7.70 (m, 1 H), 7.29 (dd, J = 11.0 Hz, 2.4 Hz, 1 H), 6.92-6.97 (m, 1 H), 6.37 (s, 1 H), 4.58 (br s, 1 H), 2.50 (s, 3 H), 1.52 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 163.5 (d, J = 244 Hz), 157.2, 149.7 (d, J = 13 Hz), 143.9, 125.3 (d, J = 10.4 Hz), 120.3, 112.4 (d, J = 2.1 Hz), 111.0 (d, J = 43.1 Hz), 110.9 (d, J = 1.5 Hz), 51.6, 29.6, 18.9. HRMS (ESI) m/z calcd for $C_{14}H_{17}FN_2$ $(M+H)^+$ 233.1449, found 233.1448.

N-*tert*-butyl-4,6-dimethyl-2-aminoquinoline, 3ma: yellow solid, m.p. = 108.7-109.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.58 (d, J = 8.4 Hz, 1 H), 7.51 (s, 1 H), 7.34 (dd, J = 8.4 Hz, 1.6 Hz, 1 H), 6.46 (s, 1 H), 4.53 (br s, 1 H), 2.52 (s, 3 H), 2.46 (s, 3 H), 1.52 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 156.1, 146.3, 143.7, 131.0, 130.9, 126.8, 123.3, 122.9, 113.0, 51.3, 29.8, 21.6, 18.9. HRMS (ESI) m/z calcd for $C_{15}H_{20}N_2$ $(M+H)^+$ 229.1700, found 229.1698.

N-*tert*-butyl-2-aminoquinoline, 3na: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.51 (d, J = 8 Hz, 1 H), 7.07-7.23 (m, 4 H), 5.72 (d, J = 17.6 Hz, 1 H), 5.29 (d, J = 11.2 Hz, 1 H), 1.41 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 138.5, 135.5, 132.8, 131.7, 128.7, 126.1, 124.8, 124.0, 115.0, 57.5, 31.8. HRMS (ESI) m/z calcd for $C_{13}H_{16}N_2$ $(M+H)^+$ 201.1387, found 201.1389.

N-*tert*-butyl-3-methyl-4-phenyl-2-aminoquinoline, 3oa: yellow solid, m.p. = 93.5-95.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.76-7.78 (d, J = 8.4 Hz, 1 H), 7.46-7.53 (m, 5 H), 7.24 (s, 1 H), 7.04-7.13 (m, 2 H), 4.54 (br s, 1 H), 1.96 (s, 3 H), 1.66 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 155.2, 146.4, 145.9, 138.4, 129.6, 128.5, 128.1, 127.5, 126.7, 126.2, 123.2, 121.5, 117.2, 51.9, 29.5, 14.9. HRMS (ESI) m/z calcd for $C_{20}H_{22}N_2$ $(M+H)^+$ 291.1856, found 291.1850.

N-*tert*-butyl-2,3-dihydro-5-methyl-1H-cyclopenta[c]-9-aminoquinoline, 3pa: yellow solid, m.p. = 108.1-109.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.66-7.68 (d, J = 8.4 Hz, 1 H), 7.30-7.34 (m, 2 H), 4.14 (br s, 1 H), 3.15 (t, J = 15.2 Hz, 7.6 Hz, 2 H), 2.76 (t, J = 14.8 Hz, 7.2 Hz, 2 H), 2.47 (s, 3 H), 2.23-2.29 (m, 2 H), 1.60(s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 153.6, 148.3, 146.1, 130.8, 129.9, 126.9, 125.5, 123.2, 121.7, 51.7, 31.4, 30.5, 29.6, 23.7, 21.5; HRMS (ESI) m/z calcd for $C_{17}H_{22}N_2$ $(M+H)^+$ 255.1856, found 255.1873.

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N-*tert*-butyl-5-methyl-7,8,9,10-tetrahydro-9-aminophenanthridine, 3qa: yellow solid, m.p. = 97.7-98.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.61-7.63 (d, J = 8.4 Hz, 1 H), 7.51 (s, 1 H), 7.30-7.32 (d, J = 8.0 Hz, 1 H), 4.32 (br s, 1 H), 2.98 (s, 2 H), 2.47 (s, 3 H), 2.42 (s, 2 H), 1.89 (s, 4 H), 1.59 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 154.5, 144.1, 139.7, 130.6, 129.6, 127.0, 122.7, 121.7, 118.5, 51.6, 29.5, 25.5, 24.5, 22.5, 22.1, 21.7; HRMS (ESI) m/z calcd for $C_{18}H_{24}N_2$ $(M+H)^+$ 269.2012, found 269.2007.

N-*tert*-butyl-6-nitro-4-phenyl-2-aminoquinoline, 3ra: yellow solid, m.p. = 217.6-219.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.54 (s, 1 H), 8.28 (d, J = 8.8 Hz, 1 H), 7.72 (d, J = 9.2 Hz, 1 H), 7.42-7.51 (m, 5 H), 6.58 (s, 1 H), 5.01 (s, 1 H), 1.59 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 157.9, 152.5, 150.2, 141.9, 137.1, 129.2, 129.9, 127.8, 123.4, 123.1, 120.7, 114.8, 52.4, 29.3. HRMS (ESI) m/z calcd for $C_{19}H_{19}N_3O_2$ $(M+H)^+$ 322.1550, found 322.1556.

N-*tert*-butyl-3,4-dihydro-3-methylene-2-aminoquinoline, 3sa: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.16-7.17 (d, J = 4.4 Hz, 3 H), 7.05-7.07 (m, 1 H), 5.94-6.04 (m, 1 H), 5.02-5.06 (m, 2 H), 3.43-3.45 (d, J = 6.4 Hz, 2 H), 1.40 (s, 9 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 139.1, 137.0, 135.9, 133.9, 130.1, 127.3, 124.8, 123.7, 115.7, 57.3, 36.0, 31.7; HRMS (ESI) m/z calcd for $C_{14}H_{18}N_2$ $(M+H)^+$ 215.1543, found 215.1548.

N-isopropyl-4-phenyl-2-aminoquinoline, 3ab: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.73 (d, J = 8.4 Hz, 1 H), 7.62 (d, J = 8 Hz, 1 H), 7.47-7.55 (m, 6 H), 7.12-7.16 (m, 1 H), 6.56 (s, 1 H), 4.67 (d, J = 7.2 Hz, 1 H), 4.20-4.25 (m, 1 H), 1.30 (d, J = 6.4 Hz, 6 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 156.1, 149.38, 148.9, 138.7, 129.6, 129.4, 128.5, 128.2, 126.5, 125.8, 122.4, 122.0, 111.2, 43.0, 23.3. HRMS (ESI) m/z calcd for $C_{18}H_{18}N_2$ $(M+H)^+$ 263.1543, found 263.1538.

N-*n*-hexyl-4-phenyl-2-aminoquinoline, 3ac: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.74 (d, J = 8.4 Hz, 1 H), 7.62 (d, J = 8.0 Hz, 1 H), 7.47-7.53 (m, 6 H), 7.12-7.16 (m, 1 H), 6.58 (s, 1 H), 4.81 (br s, 1 H), 3.46-3.51 (m, 2 H), 1.64-1.71 (m, 2 H), 1.42-1.46 (m, 2 H), 1.32-1.35 (m, 4 H), 0.89-0.92 (m, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 156.8, 149.8, 148.8, 138.7, 129.6, 129.4, 128.5, 128.3, 126.5, 125.9, 122.5, 122.0, 111.0, 42.1, 31.7, 29.9, 26.9, 22.7, 14.2. HRMS (ESI) m/z calcd for $C_{21}H_{24}N_2$ $(M+H)^+$ 305.2013, found 305.2005.

N-(2,6-diisopropylphenyl)-4-phenyl-2-aminoquinoline, 3ae: pink solid, m.p. = 227.2-228.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.60 (d, J = 8.4 Hz, 1 H), 7.43-7.52 (m, 2 H), 7.23-7.34 (m, 6 H), 7.14-7.16 (m, 2 H), 7.08 (t, J = 7.2 Hz, 1 H), 6.90 (br s, 1 H), 6.17 (s, 1 H), 3.22-3.29 (m, 2 H), 1.07 (d, J = 5.2 Hz, 12 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 157.5, 150.7, 148.6, 148.2, 138.6, 133.0, 129.9, 129.3, 128.5, 128.4, 128.2, 126.2, 126.1, 124.2, 122.8, 122.3, 108.9, 31.1, 28.6. HRMS (ESI) m/z calcd for $C_{27}H_{28}N_2$ $(M+H)^+$ 381.2326, found 381.2319.

5-phenyl-2,3-di-(2,4,6-trimethylphenylimino)-1H-benzo[b]azepine, 3af: pink solid, m.p. = 192.5-193.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.59 (s, 1 H), 7.89 (d, J = 8.4 Hz, 1 H), 7.73 (d, J = 8.4 Hz, 1 H), 7.63-7.67 (m, 1H), 7.46-7.48 (m, 3 H), 7.31-7.38 (m, 3 H), 7.06 (s, 2 H), 6.87 (s, 2 H), 6.39 (s, 1 H), 2.34 (s, 3 H), 2.28 (s, 3 H), 2.27 (s, 6 H), 2.19 (s, 6 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 152.9, 151.2, 149.8, 147.9, 147.7, 138.5, 138.2, 136.7, 133.6, 132.0, 130.1, 129.6, 128.8, 128.7, 128.6, 128.5, 128.3, 125.8, 124.3, 124.2, 110.5, 31.1, 21.4, 20.8, 19.1, 18.8, 18.1. HRMS (ESI) m/z calcd for $C_{34}H_{33}N_3$ $(M+H)^+$ 484.2748, found 484.2768.

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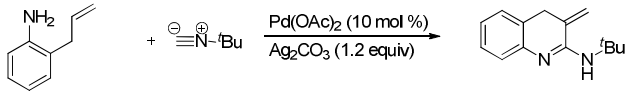

1s **2a** **3sa** (20%)

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