JOC The Journal of Organic Chemistry

Direct Ortho-Selective Amination of 2-Naphthol and Its Analogues with Hydrazines

lei jia, Qiang Tang, Meiming Luo, and Xiaoming Zeng

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.8b00421 • Publication Date (Web): 12 Apr 2018

Just Accepted

ACS Publications

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Direct *Ortho*-Selective Amination of 2-Naphthol and Its Analogues with Hydrazines

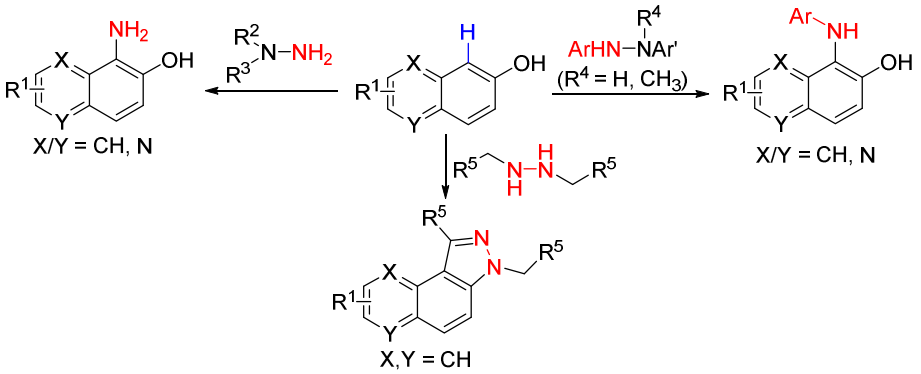
Lei Jia[†], Qiang Tang[†,‡], Meiming Luo*[†] and Xiaoming Zeng*[†]

[†]Key Laboratory of Green Chemistry and Technology of Ministry of Education, College of Chemistry, Sichuan University, Chengdu 610064, P. R. China

[‡]College of Pharmacy, Chongqing Medical University, Chongqing 400016, P. R. China

Email: luomm@scu.edu.cn; zengxiaoming@scu.edu.cn

TOC Graphic



Abstract:

Described herein is a regioselective *ortho*-amination of 2-naphthol and its analogues with substituted hydrazines. It provides a direct methodology for the synthesis of *N*-arylaminated naphthol derivatives without the formation of related 1,1'-biaryl-2,2'-diamine or carbazole byproducts. Specifically, using *N,N*-disubstituted hydrazine precursors, *N*-unsubstituted *ortho*-aminated derivatives and related

secondary amines can be formed in ethylene glycol in moderate to excellent yields. Variation of substrates to *N,N′*-diarylhydrazines and *N*-methyl-*N,N′*-diarylhydrazines led to *N*-aryl-1-amino-2-naphthol compounds. It is noted that biologically interesting indazole motifs can be facilely created by the reaction of *N,N′*-dialkylhydrazines with 2-naphthols. These *ortho*-amination reactions have the advantage of one-pot operation without the use of transition metal catalysts.

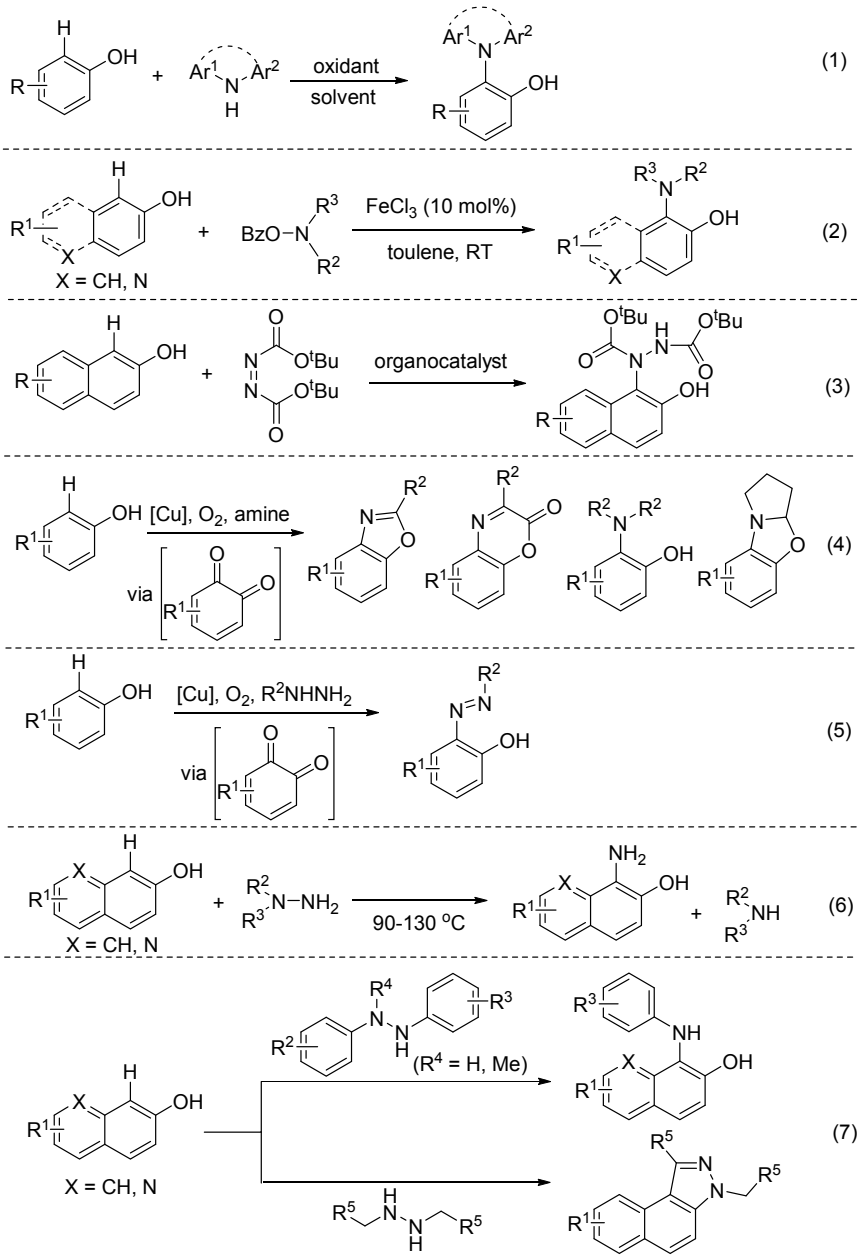
Introduction

Aromatic amines are found in a wide range of materials, natural products and biologically active compounds, which usually serve as fundamental units for the buildup of pharmaceuticals.[1] Various methods for the creation of arylamine motifs have been developed, typically mediated by traditional transition metal-catalyzed carbon-nitrogen cross-coupling reactions with aromatic electrophiles such as aryl halides and triflates.[1c, 2] The direct amination of aromatic hydrocarbons provides a valuable alternative to these traditional strategies and recently has attracted great attention,[3-5] which is typically effected by oxidative C-H/N-H coupling,[3] by electrophilic attack,[4] or through nitrogen radical intermediates.[5] These reactions generally do not need to pre-functionalize aromatics and enable the formation of C–N bonds by a single operation step.

Aminophenols occur in many dyes,[6] pharmaceuticals,[7] and biological compounds.[8] These compounds are commonly formed by multi-step reactions such as nitration/reduction, *N*-alkylation and/or *N*-arylation in low overall yields.[9] When compared with other aromatics, naturally abundant phenols have rarely been utilized

as precursors for direct amination reactions, which often suffer from a prominent selectivity issue because of the existence of multiple reactive sites of phenols and ease of concomitant homocoupling.[10] Recently, Li and co-workers reported the amination of phenols by *ipso*-substitution to produce arylamine.[11] The groups of Patureau and Xia independently reported the cross-dehydrogenative coupling (CDC) amination of phenols with phenothiazines, phenoxazines and acyclic diarylamines in the presence of oxidants (Eq 1, Scheme 1).[12] We recently showed that the use of *O*-benzoyl-*N*-alkylhydroxylamines and benzoyl aldehyde oximes as aminating agents allowed realizing the iron-catalyzed synthesis of alkylaminophenols and benzoxazoles (Eq 2, Scheme 1).[13a,b] Bella and Jørgenson disclosed an organocatalytic amination of 2-naphthols using diazodicarboxylate as aminating reagent in the formation of substituted hydrazines (Eq 3, Scheme 1).[13d] Phenols were reported to react with amines via cyclohexa-3,5-diene-1,2-dione intermediates in the presence of copper catalyst and oxidants to form various *ortho*-aminated products such as benzoxazole, benzoxazinone, aminophenol and *N*-arylpyrrolidine (Eq 4, Scheme 1).[14a-f] Moreover, Lumb and co-workers also found when the amines were replaced with hydrazine or hydrazide, *ortho*-azophenols were produced (Eq 5, Scheme 1).[14g] With *N,N*-disubstituted hydrazines, we found that the reaction of 2-naphthols formed aminonaphthols under neat conditions (Eq 6, Scheme 1).[15a,b] However, only *N*-unsubstituted products containing NH_2 moiety can be accessed by this protocol. The use of other types of substituted hydrazines as precursors to react with naphthols has not been explored yet. Herein, we demonstrate a detail study on the direct

ortho-selective arylamination and cyclization of 2-naphthol and its analogues with respect to the reaction scope and limitation by the use of different types of substituted hydrazines. It provides a new strategy for the synthesis of *N*-aryl-substituted 1-amino-2-naphthols and indazole compounds (Eq 7, Scheme 1).



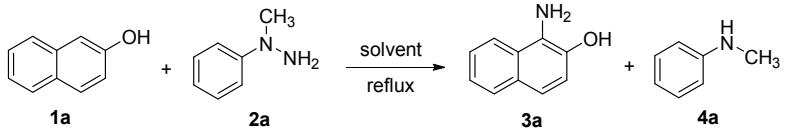
Scheme 1. Direct *ortho*-amination reactions of phenols

Results and Discussion

Ortho-amination of 2-naphthol and its analogues with *N*,*N*-disubstituted hydrazines

In our preliminary study, the reaction of 2-naphthol and its analogues with *N*,*N*-disubstituted hydrazines was performed under solvent-free conditions.[15a] However, the amination suffered from harsh conditions and must be conducted at high temperature for some substrates, which facilitated the melt of reactants and resulted in a homogeneous reaction. We questioned whether it's possible to carry out the *ortho*-amination at lower temperature in organic solvent. We then sought to study the effect of solvents on the transformation. As shown in Table 1, the use of THF, $CHCl_3$, EtOAc, MeOH and EtOH as solvents did not largely promote the *ortho*-amination reaction (entries 1–6). By contrast, the formation of the 1-amino-2-naphthol (**3a**) in preparatively useful yield was observed when performing the amination in ethylene glycol at 80 ^{o}C. Ethylene glycol as a highly polar solvent could be in favor of the dissociation of 2-naphthol to form naphthalen-2-olate anion and protonated hydrazine, so that facilitated the reaction, which was in accordance with the reaction mechanism proposed by using the density functional theory.[15b]

Table 1. Studying the effect of solvent on the *ortho*-amination of 2-naphthol with *N*-methyl-*N*-phenylhydrazine[a]

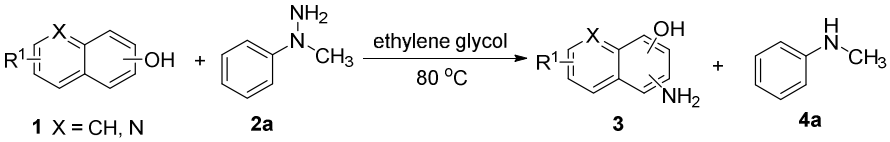


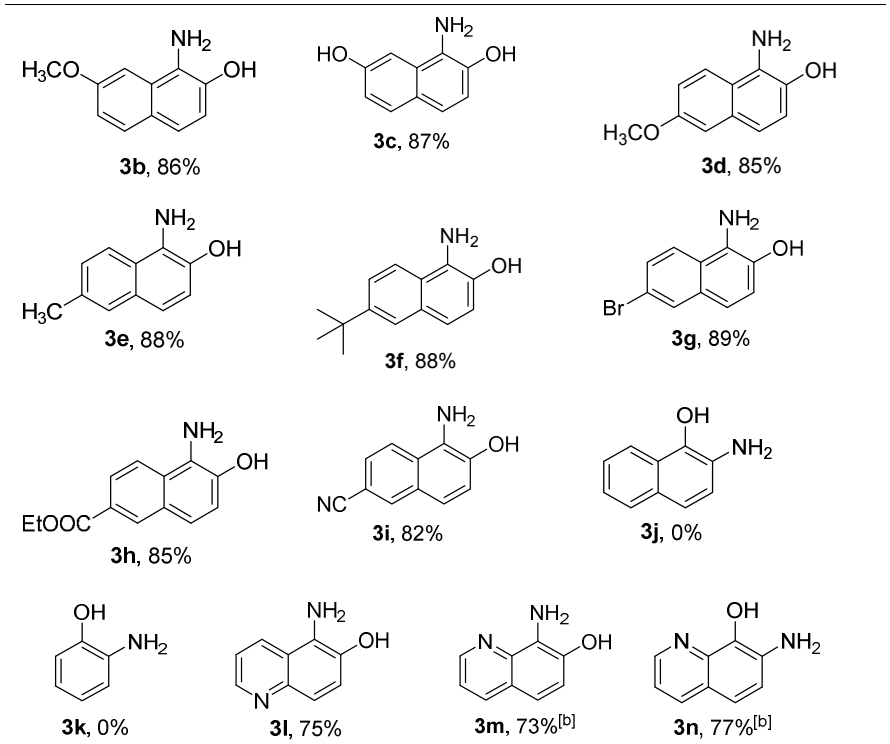
Entry	Solvent	Time / h	Yield of **3a**[b]
1	THF	17	41
2	chloroform	15	36
3	EtOAc	19	27
4[c]	methanol	15	35
5	methanol	10	47
6	ethanol	10	53
7[d]	ethylene glycol	4	88

[a]Reaction conditions: 2-naphthol (**1a**, 2 mmol), *N*-methyl-*N*-phenylhydrazine (**2a**, 2 mmol), argon atmosphere, solvent (1 mL), monitored by TLC. [b]Isolated yields. [c]25 °C. [d]80 °C.

The substrate scope of 2-naphthol derivatives (**1**) was next explored by the treatment with *N*-methyl-*N*-phenylhydrazine (**2a**) (Table 2). 2-Naphthols containing electron-donating groups such as methoxy, methyl, *tert*-butyl and hydroxyl reacted with *N*-methyl-*N*-phenylhydrazine smoothly in ethylene glycol to form the *ortho*-aminated products in excellent yields (**3b**–**3f**). Functionalities of bromide, ester and cyano were tolerated by the reaction system, and the related products **3g**, **3h** and **3i** can be facilely prepared by this method. Whereas 1-naphthol and phenol did not react with **2a**. It was noteworthy that the amination with 6-, 7-, or 8-hydroxyquinoline in ethylene glycol proceeded fast to give the corresponding *ortho*-aminated hydroxyquinolines (**3l**, **3m** and **3n**) in better yields than that under solvent-free conditions at high temperature.[15a]

Table 2. Regioselective *ortho*-amination of 2-naphthol and its analogues with *N*-methyl-*N*-phenylhydrazine[a]



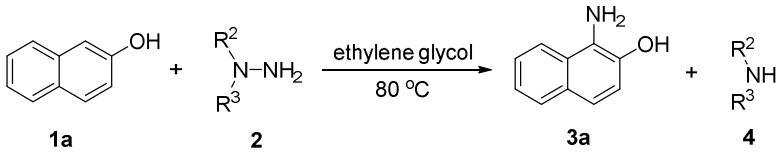


[a]Reaction conditions: naphthol (**1**, 5 mmol), *N*-methyl-*N*-phenylhydrazine (**2a**, 5 mmol), argon atmosphere, ethylene glycol (2.5 mL). [b]2 equivalents of hydrazine were used.

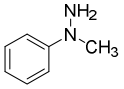
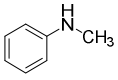
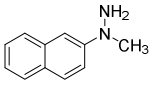
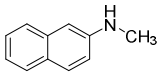
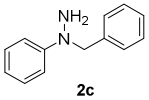
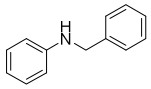
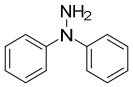
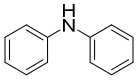
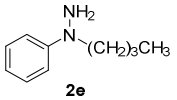
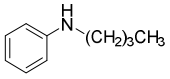
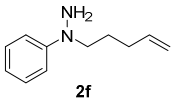
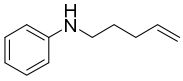
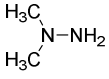
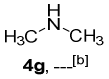
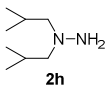
The scope of *N*,*N*-disubstituted hydrazines (**2**) was then probed through the reactions with 2-naphthol (**1a**) (Table 3). 1-Amino-2-naphthol (**3a**) and the corresponding amines were obtained in moderate to excellent yields in ethylene glycol. It was noted that in ethylene glycol at 80 °C, the reaction of *N*-benzyl-*N*-phenylhydrazine (**2c**) and *N*,*N*-diphenylhydrazine (**2d**) with 2-naphthol furnished 1-amino-2-naphthol (**3a**) in 85% and 86% yield, respectively (entry 3 and 4).

Under neat conditions, however, the amination reaction did not occur at a temperature lower than 100 °C.[15a]

Table 3. Regioselective *ortho*-amination of 2-naphthol and its analogues with *N*,*N*-disubstituted hydrazines [a]



1a **2** **3a** **4**

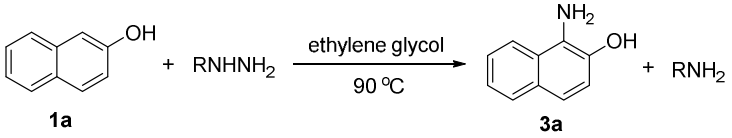
Entry	Hydrazine **2**	Yield of **3a**	Yield of **4**
1	 **2a**	88%	 **4b**, 94%
2	 **2b**	87%	 **4b**, 92%
3	 **2c**	85%	 **4c**, 90%
4	 **2d**	86%	 **4d**, 90%
5	 **2e**	89%	 **4e**, 93%
6	 **2f**	86%	 **4f**, 91%
7	 **2g**	91%	 **4g**, ---[b]
8	 **2h**	73%	 **4h**, 78%

[a]Reaction conditions: 2-naphthol (**1a**, 5 mmol), *N*,*N*-disubstituted hydrazine (**2**, 5 mmol), argon atmosphere, ethylene glycol (2.5 mL). [b]The yield was not measured.

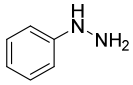
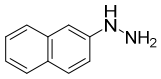
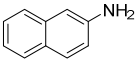
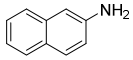
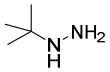
The reaction of *N*-monosubstituted hydrazines and hydrazine hydrate with 2-naphthol

The reactions between *N*-monosubstituted hydrazines and hydrazine hydrate with 2-naphthol usually resulted in the substitution of the phenolic hydroxyl group of 2-naphthol by hydrazine residue, and then followed by benzidine rearrangement to produce the corresponding 1,1'-biaryl-2,2'-diamines or carbazoles in the case of *N*-arylhydrazines.[16] In contrast to those results, we found that in ethylene glycol, the reaction of 2-naphthol with *N*-phenylhydrazine and *N*-(2-napththyl)hydrazine led to the *ortho*-aminated product of 1-amino-2-naphthol (**3a**) in good yield without the formation of related 1,1'-biaryl-2,2'-diamine or carbazole compounds (Table 4, entries 1 and 2). Interestingly, the reaction of hydrazine hydrate with 2-naphthol in ethylene glycol also furnished 1-amino-2-naphthol (**3a**) in 42% yield along with 45% of 2-napththylamine (Table 4, entry 3). 1,1'-Binaphthyl-2,2'-diamine was not detected. In the process, the reaction of hydrazine hydrate with 2-naphthol firstly produced 2-naphthylhydrazine[16] which could be detected from TLC analysis and isolated, and then the resulting 2-naphthylhydrazine reacted with the residual 2-naphthol as shown in entry 2 to give **3a** and 2-naphthylamine. Notably, the reaction of *tert*-butylhydrazine with 2-naphthol did not form the *ortho*-aminated compound **3a**, but 1-(*tert*-butyl)-2-(naphthalen-2-yl)diazene was obtained in 41% yield. The azo compound might be formed by air oxidation of 1-(*tert*-butyl)-2-(naphthalene-2-yl)hydrazine which was derived from the substitution of the phenolic hydroxyl group of 2-naphthol with hydrazine residue.[16]

Table 4. *Ortho*-amination of 2-naphthol with mono-substituted hydrazine and hydrazine in ethylene glycol[a]



1a 3a

Entry	Hydrazine	Yield of **3a**	RNH_2
1		72%	 81%
2		66%	 72%
3	H_2N-NH_2	42%	 45%
4		0%[b]	0%

[a]Reaction conditions: 2-naphthol (**1a**, 5 mmol), hydrazine (5 mmol), argon atmosphere, ethylene glycol, (2.5 mL). [b]1-(*Tert*-butyl)-2-(naphthalen-2-yl)diazene was obtained in 41% yield.

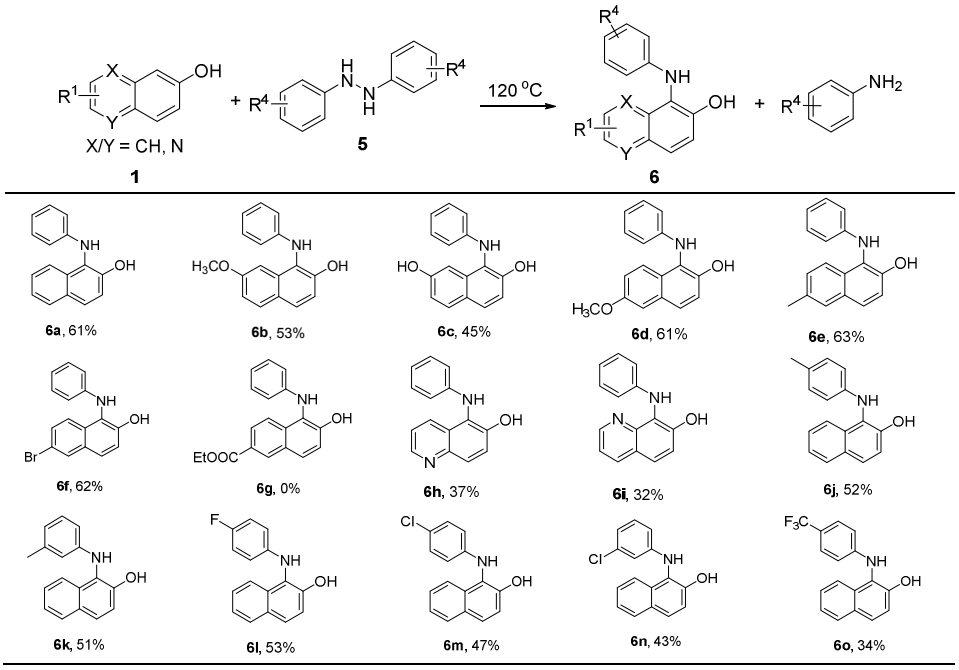
The reaction of *N,N′*-disubstituted hydrazines with 2-naphthol and its analogues

N,N′-Diarylhydrazines are appealing substrates for the *ortho*-amination with 2-naphthol, which may provide a new entry to the synthesis of arylamino-containing derivatives. However, because of the ease of benzidine rearrangement and dismutation into anilines and azobenzenes under thermal conditions, especially in hydroxylic solvents,[17] the *ortho*-amination by the use of *N,N′*-diarylhydrazines remains a great challenge. By the treatment of *N,N′*-diphenylhydrazine with **1a**, we found that the related anilines and azobenzenes were produced as major compounds through dismutation reaction. Then, we turned our attention to explore the reaction of

N,N′-diphenylhydrazine (**5a**) with 2-naphthol (**1a**) under neat conditions. When performing the reaction at 120 °C, we were pleased to find that 1-phenylamino-2-naphthol (**6a**) was formed in 61% yield (Table 5). *This finding provides an unprecedent and effective method for direct introduction of an arylamino group to the α-position of 2-naphthol.* The substrate scope of 2-naphthol derivatives was examined by treating with *N,N′*-diphenylhydrazine. 2-Naphthols bearing electron-donating groups such as methoxy, hydroxyl and methyl were amenable to the transformation, giving the 1-phenylamino-2-naphthol products **6b**–**6e** in moderate yields. Importantly, sensitive functionality of bromide was well retained in the reaction to give the product **6f** in 62% yield. Whereas the arylamination of ethyl 6-hydroxy-2-naphthoate with **5a** did not occur. The phenylaminated hydroxyquinolines (**6h** and **6i**) were prepared from the reaction of *N,N′*-diphenylhydrazine with 6- and 7-hydroxyquinoline in 37% and 32% yield, respectively.

The arylamination of 2-naphthol with diverse substituted *N,N′*-diarylhydrazines was conducted. As expected, diarylhydrazines bearing both electron-donating and electron-withdrawing groups reacted with **1a** smoothly to form the desired products **6j**-**6o**. The retained substituents of chloride and fluoride in the products may open upon an opportunity for late-stage functionalization. Only moderate yields were obtained, which was largely due to the incomplete conversion of phenols and some dismutation of *N,N′*-diarylhydrazine. The structure of product **6m** was further verified by X-ray single-crystal diffraction analysis (see the Supporting Information).

Table 5. *Ortho*-arylamination of *N,N′*-diarylhydrazines with 2-naphthol and its analogues[a]

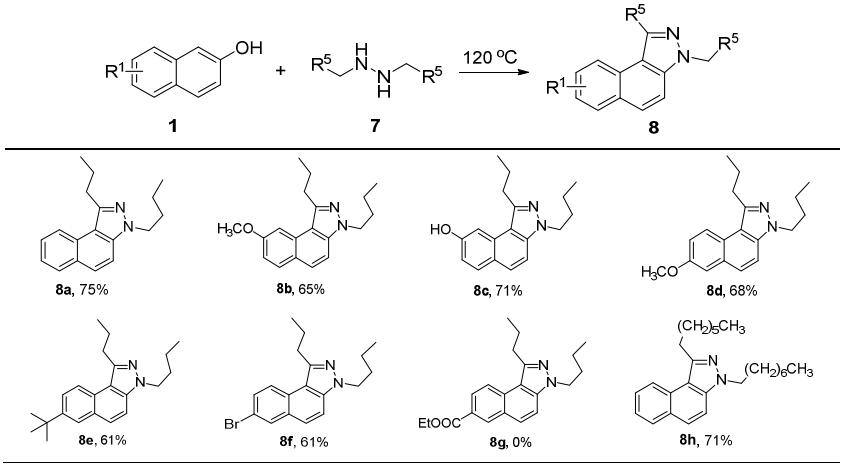


[a]Reaction conditions: naphthol (**1**, 5 mmol), *N,N′*-diarylhydrazines (**5**, 7.5 mmol), argon atmosphere.

Inspired by the results of *ortho*-arylamination of 2-naphthols, we next probed the possibility of incorporation of an alkylamino group onto the α-position of 2-naphthols by using *N,N′*-dialkylhydrazine. Our initial efforts focused on studying the reaction of 2-naphthol (**1a**) with *N,N′*-dibutylhydrazine (**7a**). Surprisingly, performing the reaction at 120 °C under neat conditions, we found that **1a** was completely consumed and an unexpected cyclization product 3-butyl-1-propyl-3*H*-benzo[e]indazole (**8a**) was formed in 75% yield instead of the anticipatory α-aminated product (Table 6). *It was worthy to note that this demonstrated the first example of the synthesis of biologically interesting indazole compounds*[18] *by the reaction of hydrazines with 2-naphthols*.

Subsequently, we examined the scope of 2-naphthols by the treatment with *N,N′*-dibutylhydrazine (**7a**) for the preparation of functionalized indazole motifs. The incorporation of electron-donating groups such as methoxy, hydroxyl and *tert*-butyl into the backbones of 2-naphthols had no effect on the transformation, forming the desired 3-butyl-1-propyl-3*H*-benzo[e]indazoles (**8b**-**8e**) in good yields. The cyclization reaction tolerated bromide function (**8f**). In addition, octyl-substituted indazole **8h** could also be prepared by this protocol. The reactivity of *N*-alkyl-*N′*-arylhydrazine in the cyclization was examined, whereas the *ortho*-aminated compound or indazole was not detected in this case.

Table 6. Cyclization for the synthesis of functionalized indazole motifs[a]

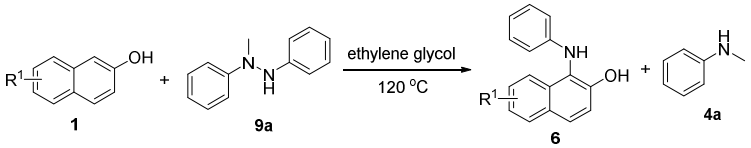


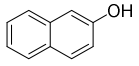
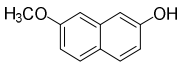
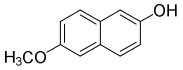
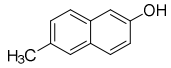
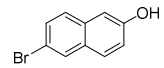
[a]Reaction conditions: 2-naphthol (**1**, 2 mmol), *N,N′*-dialkylhydrazine (**7**, 6 mmol), argon atmosphere, 120 °C.

***Ortho*-arylamination of 2-naphthol and its analogues by the reaction with trisubstituted hydrazines**

After the realization of the *ortho*-arylamination of 2-naphthols with *N,N′*-disubstituted hydrazines, the use of trisubstituted hydrazines as reactants for the transformation was investigated. As shown in Table 7, the reaction between *N*-methyl-*N,N′*-diphenylhydrazine with 2-naphthol (**1a**) occurred in high selectivity, giving the *N*-phenyl-1-amino-2-naphthol **6a** as the sole aminated product in good yield both in ethylene glycol and neat system (entry 1). Notably, the *N*-methyl-*N*-phenyl-1-amino-2-naphthol was not formed in the reaction. We also noticed that the arylamination proceeded faster in ethylene glycol than in solvent-free system. 2-Naphthols bearing methoxy, methyl and bromide function were suitable substrates, providing related 1-phenylamino-2-naphthol products (**6b-e**) in good yields.

Table 7. *Ortho*-arylamination by the use of *N*-methyl-*N,N′*-diphenylhydrazine[a]

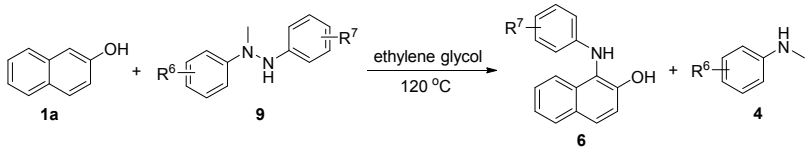


Entry	Naphthol **1**	Amination product **6**
1		**6a**, 89% (85%)[b]
2		**6b**, 83%
3		**6d**, 82%
4		**6e**, 83%
5		**6f**, 81%

[a]Reaction conditions: 2-naphthol (**1**, 5 mmol), *N*-methyl-*N,N′*-diaryhydrazine (**9a**, 5 mmol), argon atmosphere, ethylene glycol (2.5 mL). [b]No solvent.

Variation of the aryl groups in trisubstituted hydrazines allowed the synthesis of diverse substituted arylaminated products. The preparation of methyl, fluoro and chloro-containing 1-phenylamino-2-naphthols (**6j-n**) by this method was successful (Table 8, entries 1-5). When 2-naphthol (**1a**) was treated with *N*-methyl-*N*-phenyl-*N*′-arylhydrazines which have two different aryl groups, the related aryl group rather than phenyl was incorporated into the scaffold of aminonaphthols to form methyl-, fluoro- and chloro-containing products in over 80% yield (entries 6-10). Unsurprisingly, by the treatment of *N*-methyl-*N*-aryl-*N*′-phenylhydrazine with 2-naphthol (**1a**), 1-phenylamino-2-naphthol (**6a**) was produced in good yield (entries 11-15). However, the reactions of 2-naphthol (**1a**) with other types of tri- or tetra-substituted hydrazines such as *N,N*′-dibutyl-*N*-methylhydrazine, *N,N*′-dibutyl-*N*-phenylhydrazine, *N*-anilino-piperidine and *N,N*′-dimethyl-*N,N*′-diphenylhydrazine did not give the aminated products.

Table 8. *Ortho*-amination of 2-naphthol with *N*-methyl-*N,N*′-diarylhydrazine[a]



Entry	Hydrazine **9**	Product **6**
1	**9b**, $R^6 = R^7 = 4$-Me	**6j**, 84%
2	**9c**, $R^6 = R^7 = 3$-Me	**6k**, 83%
3	**9d**, $R^6 = R^7 = 4$-F	**6l**, 82%

4	**9e**, $R^6 = R^7 = 4$-Cl	**6m**, 79%
5	**9f**, $R^6 = R^7 = 3$-Cl	**6n**, 74%
6	**9g**, $R^6 = H$, $R^7 = 4$-Me	**6j**, 84%
7	**9h**, $R^6 = H$, $R^7 = 3$-Me	**6k**, 85%
8	**9i**, $R^6 = H$, $R^7 = 4$-F	**6l**, 85%
9	**9j**, $R^6 = H$, $R^7 = 4$-Cl	**6m**, 81%
10	**9k**, $R^6 = H$, $R^7 = 3$-Cl	**6n**, 89%
11	**9l**, $R^6 = 4$-Me, $R^7 = H$	**6a**, 83%
12	**9m**, $R^6 = 3$-Me, $R^7 = H$	**6a**, 85%
13	**9n**, $R^6 = 4$-F, $R^7 = H$	**6a**, 86%
14	**9o**, $R^6 = 4$-Cl, $R^7 = H$	**6a**, 82%
15	**9p**, $R^6 = 3$-Cl, $R^7 = H$	**6a**, 81%

[a]Reaction conditions: 2-naphthol (**1**, 5 mmol), *N*-methyl-*N,N'*-diaryhydrazine (**9**, 5 mmol), argon atmosphere, ethylene glycol (2.5 mL).

Conclusion

In summary, we have developed the direct *ortho*-arylamination and cyclization of 2-naphthol and its analogues by the use of aryl- or alkyl-substituted hydrazines as amino sources. This transition metal-free protocol can be used to introduce arylamino scaffolds onto the ortho position of 2-naphthols, thus providing a novel entry to the synthesis of *ortho*-arylaminated products that usually can not be directly prepared by previous methodology. In particular, biologically appealing indazole compounds can

be facilely prepared by the reaction of 2-naphthols with *N,N′*-dialkylhydrazines, which do not form the related *ortho*-amination compounds. The advantages of simple operation, transition metal-free conditions of the present protocol make it attractive for future applications in organic synthesis.

Experimental Section

General methods

NMR spectra were obtained on a Bruker 400 (400 MHz for ^{1}H NMR; 100 MHz for ^{13}C NMR). ^{1}H NMR chemical shifts are reported in parts per million (ppm) relative to TMS, with the residual solvent peak used as an internal reference. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), triplet (t), triplet of doublets (td), quartet (q), multiplet (m), and broad resonance (br). HRMS analyses were made on a Bruker Daltonics Bio TOF-Q Mass Spectrometer using ESI or MALDI-TOF ionization. Column chromatography was performed with silica gel (200-300 mesh). Thin layer chromatography was carried out using Merck silica gel GF254 plates. Commercially available reagents were used without further purification.

6-*Tert*-butyl-2-naphthol, 7-methoxy-2-naphthol, 6-methyl-2-naphthol and ethyl 6-hydroxy-2-naphthoate were prepared following the procedures previously reported.[19] *N*-Alkyl-arylhydrazines were prepared from the corresponding arylhydrazines, while *N,N*-diarylhydrazines and *N,N*-dialkylhydrazines were prepared from the appropriate secondary amines.[20] *N,N′*-diarylhydrazines were prepared from

reduction of the corresponding azo compounds.[21] *N,N′*-dialkylhydrazines and monoalkylhydrazines were prepared from the alkylation of di-*tert*-butylhydrazine-1,2-dicarboxylate followed by hydrolysis.[22] *N*-Methyl-*N,N′*-diarylhydrazines were prepared from the methylation of *N,N′*-diarylhydrazines or the reaction of *N*-hydroxyl-*N*-arylacetamide with *N*-methyl-arylamine.[23]

General procedure for the reaction of *N,N*-disubstituted hydrazines with 2-naphthol and its analogues in ethylene glycol

Under argon atmosphere, *N*-methyl-*N*-arylhydrazine (**2**, 5 mmol) was added to a mixture of 2-naphthols (**1**, 5 mmol) and ethylene glycol (2.5 mL). The mixture was heated in an oil bath at 80 °C for 4-10 h (tracked by TLC). After cooled down, water (20 mL) was introduced and the residue was extracted with ethyl acetate. The combined extracts were washed with saturated brine and dried with anhydrous sodium sulfate. The solvent was removed in vacuum and the residue was purified by flash column chromatography on silica gel (gradient elution: hexane to hexane/ethyl acetate (1:1)) to afford products **3** and **4**.

1-Amino-2-naphthol (3a): Yield: 88% (0.70 g); gray solid; m.p.> 142 °C (decomp.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.15 (br s, 1H), 7.93 (d, J = 8.5 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 7.0 Hz, 1H), 7.20 (t, J = 7.1 Hz, 1H), 7.07 (s, 2H), 4.96 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 139.4, 129.3, 129.0, 128.3, 124.22, 124.18,

122.7, 121.9, 118.0, 116.5; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{10}H_{10}NO$ 160.0757; Found 160.0742.

7-Methoxy-1-amino-2-naphthol (3b): Yield: 86% (0.82 g); white solid; m.p. 120~121 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.13 (br s, 1H), 7.56 (d, J = 9.2 Hz, 1H), 7.28 (d, J = 1.6 Hz, 1H), 7.00 (d, J = 8.8 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 6.86 (dd, J = 8.8 Hz, 2.0 Hz, 1H), 4.82 (br s, 2H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 156.7, 140.0, 129.8, 128.4, 125.2, 124.4, 116.6, 115.5, 115.2, 100.8, 55.4; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{11}H_{12}NO_2$ 190.0863; Found 190.0859.

1-Amino-2,7-naphthalenediol (3c): Yield: 87% (0.76 g); gray solid; m.p.> 200 °C (decomp.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.36 (s, 1H), 9.07 (br s. 1H), 7.51 (d, J = 8.8 Hz, 1H), 7.10 (s, 1H), 6.98 (d, J = 8.8 Hz, 1H), 6.86 (d, J = 8.8 Hz, 1H), 6.82 (d, J = 8.8 Hz, 1H), 4.45 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 154.6, 139.9, 129.8, 127.3, 126.2, 123.8, 117.2, 115.5, 115.0, 103.6; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{10}H_{10}NO_2$ 176.0706; Found 176.0711.

1-Amino-6-methoxy-2-naphthol (3d): Yield: 85% (0.80 g); gray solid; m.p. 123~125 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.89 (br s, 1H), 7.86 (d, J = 9.2 Hz, 1H), 6.94-7.06 (m, 4H), 4.91 (br s, 2H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 155.2, 137.9, 130.0, 129.8, 123.6, 119.6, 118.5, 116.6, 115.1, 106.4, 55.3; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{11}H_{12}NO_2$ 190.0863; Found 190.0868.

1-Amino-6-methyl-2-naphthol (3e): Yield: 88% (0.76 g); gray solid; m.p. 144~146 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.01 (br s, 1H), 7.84 (d, J = 8.6 Hz, 1H), 7.41 (s, 1H), 7.13 (dd, J = 8.6 Hz, 1.2 Hz, 1H), 7.02 (d, J = 8.6 Hz, 1H), 6.95 (d, J = 8.6 Hz, 1H), 4.88 (br s, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 138.8, 131.4, 129.3, 129.2, 127.1, 126.4, 122.5, 121.9, 118.1, 115.7, 21.4; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{11}H_{12}NO$ 174.0913; Found 174.0919.

6-(*Tert*-butyl)-1-amino-2-naphthol (3f): Yield: 88% (0.95 g); white solid; m.p. 154~156 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.87 (br s. 1H), 7.85 (d, J = 8.8 Hz, 1H), 7.56 (s, 1H), 7.38 (d, J = 8.8 Hz, 1H), 7.04 (s, 2H), 4.85 (br s. 2H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 144.6, 138.9, 129.1, 128.9, 123.0, 122.9, 122.5, 121.8, 118.0, 116.5, 34.7, 31.6; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{18}NO$ 216.1383; Found 216.1381.

6-Bromo-1-amino-2-naphthol (3g): Yield: 89% (1.05 g); gray solid; m.p.> 162 °C (decomp.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.35 (br s, 1H), 7.93 (d, J = 9.2 Hz, 1H), 7.90 (d, J = 2.0 Hz, 1H), 7.38 (dd, J = 8.8 Hz, 2.0 Hz, 1H), 7.11 (d, J = 8.4 Hz, 1H), 7.05 (d, J = 8.4 Hz, 1H), 5.08 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 139.9, 130.2, 130.0, 129.9, 126.8, 124.6, 122.4, 119.0, 115.8, 115.6; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{10}H_9BrNO$ 237.9862; Found 237.9857.

Ethyl 5-amino-6-hydroxy-2-naphthoate (3h): Yield: 85% (0.98 g); gray solid; m.p. 131~133 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.58 (br s. 1H), 8.40 (d, J = 1.6 Hz, 1H), 8.07 (d, J = 8.8 Hz, 1H), 7.78 (dd, J = 9.2 Hz, 2.0 Hz, 1H), 7.31 (d, J = 8.4 Hz, 1H), 7.20 (d, J = 8.4 Hz, 1H), 5.12 (br s. 2H), 4.35 (q, J = 7.2 Hz, 2H), 1.36 (t, J = 7.2

Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.7, 142.0, 131.4, 129.7, 127.7, 125.7, 123.9, 122.9, 122.5, 118.7, 118.5, 60.9, 14.8; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{14}NO_3$ 232.0968; Found 232.0973.

5-Amino-6-hydroxy-2-naphthonitrile (3i): Yield: 82% (0.75 g); gray solid; m.p.> 156 °C (decomp.); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.79 (br s, 1H), 8.29 (d, J = 1.4 Hz, 1H), 8.12 (d, J = 8.9 Hz, 1H), 7.51 (dd, J = 8.8 Hz, 1.6 Hz, 1H), 7.23 (s, 2H), 5.22 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 142.4, 135.0, 130.1, 127.6, 124.6, 124.0, 123.6, 120.4, 119.2, 117.5, 104.7; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{11}H_9N_2O$ 185.0709; Found 185.0705.

5-Amino-6-hydroxylquinoline (3l): Yield: 75% (0.60 g); gray solid; m.p. 165-168°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.41 (br s, 1H), 8.60 (dd, J = 4.0 Hz, 1.2 Hz, 1H), 8.43 (d, J = 8.0 Hz, 1H), 7.31-7.27 (m, 2H), 7.20 (d, J = 8.8 Hz, 1H), 5.15 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.2, 143.8, 139.4, 130.4, 129.6, 120.9, 119.1, 118.8, 117.1; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_9H_9N_2O$ 161.0709; Found 161.0711.

8-Amino-7-hydroxylquinoline (3m): Yield: 73% (0.58 g); gray solid; m.p. 168-170 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.42 (br s, 1H), 8.68 (dd, J = 4.0 Hz, 1.6 Hz, 1H), 8.11 (dd, J = 8.4 Hz, 1.6 Hz,1H), 7.26 (q, J = 4.0 Hz, 1H), 7.17 (d, J = 8.4 Hz, 1H), 7.07 (d, J = 8.8 Hz, 1H), 5.06 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.9, 141.7, 138.5, 136.2, 130.3, 123.2, 118.8, 118.7, 114.8; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_9H_9N_2O$ 161.0709; Found 161.0707.

7-Amino-8-hydroxyquinoline (3n): Yield: 77% (0.62 g); colourless oil; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.08 (br s, 1H), 8.66 (dd, J = 4.0 Hz, 1.2 Hz, 1H), 8.08 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.23 (d, J = 8.8 Hz, 1H), 7.16 (q, J = 4.0 Hz, 1H), 7.12 (d, J = 8.8 Hz, 1H), 5.09 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 148.5, 138.9, 136.2, 135.8, 134.8, 121.4, 119.3, 118.4, 117.3; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_9H_9N_2O$ 161.0709; Found 161.0713.

General procedure for the reaction of hydrazine hydrate and mono-substituted hydrazine with 2-naphthol in ethylene glycol

Under argon atmosphere, hydrazine hydrate or mono-substituted hydrazine (5 mmol) was added to a mixture of 2-naphthol (**1a**, 5 mmol) and ethylene glycol (2.5 mL). The mixture was heated in an oil bath at 90 °C for 15~21 h (tracked by TLC). After cooled down, water (20 mL) was introduced and the residue was extracted with ethyl acetate. The combined extracts were washed with saturated brine and dried with anhydrous sodium sulfate. The solvent was removed in vacuum and the residue was purified by flash column chromatography on silica gel (gradient elution: hexane to hexane/ethyl acetate (1:1)) to provide 1-amino-2-naphthol (**3a**) and mono-substituted amine.

General procedure for the reaction of *N,N′*-diarylhydrazines with 2-naphthol and its analogues

Under argon atmosphere, a mixture of 2-naphthol (**1**, 5.0 mmol) and *N,N′*-diarylhydrazine (**5**, 7.5 mmol) was heated in an oil bath at 120 °C for 5~10 h (tracked by TLC). After cooled down, dichloromethane (50 mL) was introduced and the residue was decolorized by activated carbon. After filtration, the solvent was

removed in vacuum and the residue was purified by flash column chromatography on silica gel (gradient elution: hexane to hexane/ethyl acetate (10:1)) to provide arylamine and 1-arylamino-2-naphthol (**6**).

1-Phenylamino-2-naphthol (6a): Yield: 61% (0.72 g); gray solid; m.p. 155-156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.1 Hz, 1H), 7.78 (d, *J* = 8.9 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 1H), 7.38 (td, *J* = 6.8 Hz, 1.2 Hz, 1H), 7.30-7.34 (m, 2H), 7.18 (t, *J* = 7.5 Hz, 2H), 6.83 (t, *J* = 7.4 Hz, 1H), 6.65 (d, *J* = 7.9 Hz, 2H), 6.54 (br s, 1H), 5.27 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 146.7, 132.1, 129.6, 129.1, 128.7, 127.0, 123.5, 121.5, 119.8, 118.6, 116.9, 114.2; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{14}NO$ 236.1070; Found 236.1075.

7-Methoxy-1-phenylamino-2-naphthol (6b): Yield: 53% (0.70 g); gray solid; m.p. 128-130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.72 (m, 2H), 7.14-7.20 (m, 3H), 6.92-6.98 (m, 2H), 6.83 (t, *J* = 7.3 Hz, 1H), 6.67 (d, *J* = 7.6 Hz, 2H), 6.56 (br s, 1H), 5.17 (br s, 1H), 3.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 152.7, 146.5, 133.4, 130.3, 129.6, 128.8, 124.9, 119.8, 118.0, 115.5, 114.3, 114.2, 100.7, 55.2; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{16}NO_2$ 266.1176; Found 266.1179.

1-Phenylamino-2,7-naphthalendiol (6c): Yield: 45% (0.57 g); gray solid; m.p. 167-169 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (t, *J* = 7.8 Hz, 2H), 7.14-7.20 (m, 3H), 6.90-6.93 (m, 2H), 6.84 (t, *J* = 7.4 Hz, 1H), 6.64 (d, *J* = 7.6 Hz, 2H), 6.55 (br s, 1H), 5.11 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 155.7, 151.4, 148.1, 134.2, 129.7, 128.6, 126.6, 123.2, 118.6, 116.4, 115.2, 115.1, 113.2, 104.2; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{14}NO_2$ 252.1019; Found 252.1021.

6-Methoxy-1-phenylamino-2-naphthol (6d): Yield: 61% (0.81 g); gray solid; m.p. 132-134 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.17 (s, 1H), 7.58-7.63 (m, 2H), 7.34 (s, 1H), 7.20-7.24 (m, 2H), 7.01-7.05 (m, 3H), 6.58 (t, J = 7.1 Hz, 1H), 6.47 (d, J = 7.7 Hz, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 150.4, 146.7, 130.5, 129.6, 127.7, 127.3, 123.1, 119.7, 119.5, 118.9, 117.4, 114.2, 107.0, 55.4; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{16}NO_2$ 266.1176; Found 266.1178.

6-Methyl-1-phenylamino-2-naphthol (6e): Yield: 63% (0.79 g); gray solid; m.p. 142-144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.8 Hz, 1H), 7.56-7.59 (m, 2H), 7.16-7.29 (m, 4H), 6.83 (t, J = 7.3 Hz, 1H), 6.65 (d, J = 8.0 Hz, 2H), 6.44 (br s, 1H), 5.23 (br s, 1H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 150.0, 147.9, 131.5, 130.3, 128.8, 128.6, 128.0, 126.9, 125.7, 122.5, 120.1, 118.7, 116.6, 113.4, 20.8; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{16}NO$ 250.1226; Found 250.1229.

6-Bromo-1-phenylamino-2-naphthol (6f): Yield: 62% (0.97 g); gray solid; m.p. 134-136 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.69 (s, 1H), 8.10 (d, J = 2.0 Hz, 1H), 7.69 (d, J = 8.9 Hz, 1H), 7.65 (d, J = 9.0 Hz, 1H), 7.45-7.49 (m, 2H), 7.31 (d, J = 8.8 Hz, 1H), 7.04 (t, J = 7.5Hz, 2H), 6.60 (t, J = 7.2 Hz, 1H), 6.46 (d, J = 7.7 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 151.2, 147.6, 130.7, 129.7, 128.70, 128.66, 125.7, 125.0, 120.5, 120.1, 116.9, 115.6, 113.4; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}BrNO$ 314.0175; Found 314.0172.

5-Phenylamino-6-hydroxyquinoline (6h): Yield: 37% (0.44 g); gray solid; m.p. 230-232 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.78 (s, 1H), 8.67 (dd, J = 4.0 Hz,

1.4Hz, 1H), 8.08 (d, J = 8.4Hz, 1H), 7.81 (d, J = 9.1 Hz, 1H), 7.49-7.51 (m, 2H), 7.38 (dd, J = 8.5 Hz, 4.1 Hz, 1H), 7.07 (t, J = 8.2 Hz, 2H), 6.61 (t, J = 7.3 Hz, 1H), 6.48 (d, J = 7.7 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 150.8, 147.6, 147.0, 143.6, 130.7, 128.7, 127.4, 127.0, 122.0, 120.9, 119.8, 117.0, 113.4; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{13}N_2O$ 237.1022; Found 237.1025.

8-Phenylamino-7-hydroxyquinoline (6i): Yield: 32% (0.38 g); gray solid; m.p. 227-229 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.84 (s, 1H), 8.72 (dd, J = 4.2 Hz, 1.6 Hz, 1H), 8.22 (dd, J = 8.2 Hz, 1.5 Hz, 1H), 7.59-7.61 (m, 2H), 7.29-7.32 (m, 2H), 7.06 (t, J = 8.2 Hz, 2H), 6.61-6.68 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 150.9, 149.6, 146.4, 144.6, 136.5, 128.6, 123.9, 123.3, 122.7, 120.0, 119.1, 118.1, 115.7; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{13}N_2O$ 237.1022; found 237.1024.

1-(*p*-Tolylamino)-2-naphthol (6j): Yield: 52% (0.65 g); gray solid; m.p. 134-136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 8.9 Hz, 1H), 7.66 (d, J = 8.3 Hz, 1H), 7.37 (t, J = 7.2 Hz, 1H), 7.29-7.32 (m, 2H), 6.98 (d, J = 8.2 Hz, 2H), 6.55-6.58 (m, 3H), 5.15 (br s, 1H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 150.5, 145.5, 132.0, 129.0, 128.6, 128.0, 126.2, 125.7, 125.2, 122.6, 120.6, 118.7, 113.6, 20.1; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{16}NO$ 250.1226; Found 250.1229.

1-(*m*-Tolylamino)-2-naphthol (6k): Yield: 51% (0.63 g); gray solid, m.p. 100-101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75-7.81 (m, 2H), 7.65 (d, J = 8.3 Hz, 1H), 7.35-7.39 (m, 1H), 7.29-7.33 (m, 2H), 7.05 (t, J = 8.1 Hz, 1H), 6.64 (d, J = 7.5 Hz, 1H), 6.54 (s, 1H), 6.42-6.44 (m, 2H), 5.12 (br s, 1H), 2.21 (s, 3H); ^{13}C NMR (100

MHz, DMSO-d_6) δ 150.8, 147.9, 137.6, 132.2, 128.54, 128.49, 128.0, 126.5, 125.8, 122.7, 122.5, 120.2, 118.7, 117.6, 114.0, 110.7, 21.3; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{16}NO$ 250.1226; Found 250.1228.

1-(4-Fluorophenylamino)-2-naphthol (6l): Yield: 53% (0.67 g); gray solid, m.p. 132-134 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76-7.82 (m, 2H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.38 (t, *J* = 7.1 Hz, 1H), 7.31 (t, *J* = 8.1 Hz, 2H), 6.84-6.88 (m, 2H), 6.54-6.57 (m, 3H), 5.13 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 150.6, 144.4, 132.0, 128.6, 128.0, 126.5, 125.9, 122.7, 122.3, 120.4, 118.7, 115.1, 114.9, 114.2, 114.1; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}FNO$ 254.0976; Found: 254.0978.

1-(4-Chlorophenylamino)-2-naphthol (6m): Yield: 47% (0.63 g); gray solid, m.p. 100-102 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.77-7.83 (m, 2H), 7.61 (d, *J* = 8.3 Hz, 1H), 7.40 (t, *J* = 7.1 Hz, 1H), 7.29-7.35 (m, 2H), 7.12 (d, *J* = 8.7 Hz, 2H), 6.57 (d, *J* = 8.7 Hz, 2H), 6.44 (br s, 1H), 5.23 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 145.3, 131.8,129.9, 129.6, 129.5, 129.4, 128.7, 127.2, 123.6, 121.3, 118.2, 117.8, 116.9, 115.4; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}ClNO$ 270.0680; Found 270.0683.

1-(3-Chlorophenylamino)-2-naphthol (6n): Yield: 43% (0.58 g); gray solid, m.p. 99-101 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.77-7.82 (m, 2H), 7.60 (d, *J* = 8.3 Hz, 1H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.29-7.35 (m, 2H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.78 (dd, *J* = 7.9 Hz, 1.0 Hz, 1H), 6.59 (t, *J* = 1.8 Hz, 1H), 6.48 (dd, *J* = 8.1 Hz, 1.8 Hz, 1H), 6.41 (s, 1H), 5.22 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 148.0, 135.4, 131.8, 130.6,

129.6, 129.5, 128.7, 127.2, 123.7, 121.2, 119.9, 117.8, 117.0, 114.2, 112.4; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}ClNO$ 270.0680; Found 270.0682.

1-(4-(Trifluoromethyl)phenylamino)-2-naphthol (6o): Yield: 34% (0.52 g); gray solid, m.p. 110-112 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (t, *J* = 8.1 Hz, 2H), 7.61 (d, *J* = 8.3 Hz, 1H), 7.40-7.43 (m, 3H), 7.31-7.37 (m, 2H), 6.68 (d, *J* = 8.4 Hz, 2H), 6.27 (s, 1H), 5.49 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 149.5, 131.8, 129.72, 129.66, 128.8, 127.3, 127.0 (q, *J* = 3.8 Hz), 123.8, 121.2, 117.4, 117.1, 113.7; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{13}F_3NO$ 304.0944; Found 304.0947.

General procedure for the reaction of *N,N′*-dialkylhydrazines with 2-naphthol and its analogues

Under an argon atmosphere, a mixture of 2-naphthol (**1**, 2 mmol) and *N,N′*-dialkylhydrazine (**7**, 6 mmol) was heated in an oil bath at 120 °C for 20~24 h (tracked by TLC). After cooled down, dichloromethane (50 mL) was introduced and the residue was decolorized by activated carbon. After filtration, the solvent was removed in vacuum and the residue was purified by flash column chromatography on silica gel (gradient elution: hexane to hexane/ethyl acetate (10:1)) to afford product **8**.

3-Butyl-1-propyl-3*H*-benzo[e]indazole (8a): Yield: 75% (0.40 g); colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.2 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.69 (d, *J* = 9.0 Hz, 1H), 7.63 (t, *J* = 7.8 Hz, 1H), 7.46 (m, 2H), 4.39 (t, *J* = 7.1 Hz, 2H), 3.24 (t, *J* = 7.6 Hz, 2H), 1.97 (m, 4H), 1.38 (m, 2H), 1.10 (t, *J* = 7.3 Hz, 3H), 0.93 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.3, 138.9, 129.4, 129.0, 128.5, 128.0,

127.3, 123.7, 122.9, 115.9, 110.4, 48.6, 32.4, 31.6, 22.1, 20.1, 14.2, 13.8; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{23}N_2$ 267.1856; Found 267.1861.

3-Butyl-8-methoxy-1-propyl-3*H*-benzo[e]indazole (8b): Yield: 65% (0.39 g); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.8 Hz, 1H), 7.66 (d, *J* = 2.4 Hz, 1H), 7.62 (d, *J* = 9.0 Hz, 1H), 7.28 (d, *J* = 9,0 Hz, 1H), 7.09 (dd, *J* = 8.8 Hz, 2.5 Hz, 1H), 4.37 (t, *J* = 7.1 Hz, 2H), 3.98 (s, 3H), 3.23 (t, *J* = 7.6 Hz, 2H), 1.87-1.98 (m, 4H), 1.30-1.39 (m, 2H), 1.11 (t, *J* = 7.4 Hz, 3H), 0.93 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 146.2, 139.3, 130.4, 129.8, 127.8, 124.1, 115.7, 114.0, 107.8, 104.0, 55.3, 48.6, 32.3, 31.6, 22.3, 20.1, 14.2, 13.7; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{25}N_2O$ 297.1961; Found 297.1965.

3-Butyl-1-propyl-3*H*-benzo[e]indazol-8-ol (8c): Yield: 71% (0.40 g); gray solid; m.p. 144-146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.7 Hz, 1H), 7.65 (d, *J* = 8.8 Hz, 2H), 7.26-7.28 (m, 1H), 7.04 (d, *J* = 8.8 Hz, 1H), 5.68 (br s, 1H), 4.41 (t, *J* = 7.0 Hz, 2H), 3.21 (t, *J* = 7.4 Hz, 2H), 1.89-1.94 (m, 4H), 1.29-1.39 (m, 2H), 1.07 (t, *J* = 7.4 Hz, 3H), 0.93 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 156.8, 145.1, 139.0, 130.5, 129.3, 127.5, 122.8, 114.44, 114.38, 107.4, 105.9, 47.5, 31.8, 30.7, 21.5, 19.3, 13.9, 13.5; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{23}N_2O$ 283.1805; Found 283.1808.

3-Butyl-7-methoxy-1-propyl-3*H*-benzo[e]indazole (8d): Yield: 68% (0.40 g); gray solid; m.p. 67-69 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.6 Hz, 1H), 7.63 (d, *J* = 9.0 Hz, 1H), 7.43 (d, *J* = 9.0 Hz, 1H), 7.28-7.31 (m, 2H), 4.39 (t, *J* = 7.1 Hz, 2H), 3.94 (s, 3H), 3.22 (t, *J* = 7.6 Hz, 2H), 1.87-1.94 (m, 4H), 1.30-1.39 (m, 2H), 1.09 (t, *J*

= 7.3 Hz, 3H), 0.93 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 145.6, 138.1, 130.6, 127.2, 124.2, 123.0, 118.0, 116.1, 110.8, 109.1, 55.4, 48.6, 32.4, 31.5, 22.1, 20.1, 14.2, 13.8; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{25}N_2O$ 297.1961; Found 297.1964.

7-(*tert*-Butyl)-3-butyl-1-propyl-3*H*-benzo[e]indazole (8e): Yield: 61% (0.39 g); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.7 Hz, 1H), 7.87 (d, *J* = 2.0 Hz, 1H), 7.72 (dd, *J* = 8.6 Hz, 2.1 Hz, 1H), 7.68 (d, *J* = 9.1 Hz, 1H), 7.42 (d, *J* = 9.0 Hz, 1H), 4.39 (t, *J* = 7.1 Hz, 2H), 3.23 (t, *J* = 7.6 Hz, 2H), 1.87-1.97 (m, 4H), 1.30-1.47 (m, 11H), 1.09 (t, *J* = 7.3 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.5, 146.1, 138.8, 129.3, 128.4, 126.3, 125.7, 124.6, 122.6, 115.8, 110.2, 48.6, 34.6, 32.4, 31.5, 22.2, 20.1, 14.1, 13.7; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{31}N_2$ 323.2482; Found: 323.2486.

7-Bromo-3-butyl-1-propyl-3*H*-benzo[e]indazole (8f): Yield: 61% (0.42 g); white solid; m.p. 45-46 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.8 Hz, 1H), 8.05 (d, *J* = 1.7 Hz, 1H), 7.70 (dd, *J* = 8.8 Hz, 1.9 Hz, 1H), 7.59 (d, *J* = 9.0 Hz, 1H), 7.47 (d, *J* = 9.0 Hz, 1H), 4.39 (t, *J* = 7.2 Hz, 2H), 3.20 (t, *J* = 7.6 Hz, 2H), 1.85-1.95 (m, 4H), 1.30-1.39 (m, 2H), 1.09 (t, *J* = 7.4 Hz, 3H), 0.94 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.2, 138.8, 131.0, 130.8, 130.3, 127.0, 126.9, 124.5, 117.0, 115.7, 111.5, 48.7, 32.4, 31.5, 22.0, 20.1, 14.1, 13.7; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{22}BrN_2$ 345.0961; Found 345.0965.

1-Heptyl-3-octyl-3*H*-benzo[e]indazole (8h): Yield: 71% (0.54 g); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.2 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.70 (d,

J = 9.0 Hz, 1H), 7.63 (t, *J* = 8.1 Hz, 1H), 7.43-7.47 (m, 2H), 4.39 (t, *J* = 7.1 Hz, 2H), 3.26 (t, *J* = 7.7 Hz, 2H), 1.85-1.94 (m, 4H), 1.47-1.53 (m, 2H), 1.35-1.42 (m, 2H), 1.23-1.30 (m, 14H), 0.83-0.89 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.5, 138.9, 129.4, 129.0, 128.5, 128.0, 127.3, 123.7, 122.9, 115.9, 110.4, 48.9, 31.9, 31.8, 30.4, 29.7, 29.6, 29.23, 29.17, 28.9, 26.9, 22.7, 22.6, 14.13, 14.08; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd for $C_{26}H_{39}N_2$ 379.3108; Found 379.3111.

General procedure for the reaction of *N*-methyl-*N,N′*-diarylhydrazines with 2-naphthol and its analogues in ethylene glycol

Under argon atmosphere, *N*-methyl-*N,N′*-diarylhydrazine (**9**, 5 mmol) was added to a mixture of 2-naphthol (**1**, 5mmol) and ethylene glycol (2.5 mL). The mixture was heated in an oil bath at 120 °C for 8~15 h (tracked by TLC). After cooled down, water (20 mL) was introduced and the residue was extracted with ethyl acetate. The combined extracts were washed with saturated brine and dried with anhydrous sodium sulfate. The solvent was removed in vacuum and the residue was purified by flash column chromatography on silica gel (gradient elution: hexane to hexane/ethyl acetate (10:1)) to afford products **4** and **6**.

Acknowledgements

We gratefully acknowledge the National Natural Science Foundation of China (21321061, 21072134 and J1103315/J0104) for financial support, and the Comprehensive Training Platform of Specialized Laboratory, College of Chemistry, Sichuan University for NMR and MS measurements.

Supporting Information

Characterization data (including ^{1}H and ^{13}C NMR spectra) of products **3**, **6** and **8**, single crystal data of product **6m**. This material is available free of charge via the internet at http://pubs.acs.org.

References

(1) (a) Inaf, S. S.; Witiak, D. T. Facile Non-Racemizing Route for the N-Alkylation of Hindered Secondary Amines. *Synthesis* **1999**, 435-440. (b) Salvatore, R. N.; Yoon, C. H.; Jung, K. W. Synthesis of Secondary Amines. *Tetrahedron* **2001**, *57*, 7785-7811. (c) Kienle, M.; Dubbaka, S. R.; Brade, K.; Knochel, P. Modern Amination Reactions. *Eur. J. Org. Chem.* **2007**, 4166-4176. (d) Bergeron, R.; Feng, Y.; Weimer, W.; McManis, J.; Dimova, H.; Porter, C.; Raisler, B.; Phanstiel, O. A Comparison of Structure−Activity Relationships between Spermidine and Spermine Analogue Antineoplastics. *J. Med. Chem.* **1997**, *40*, 1475-1494.

(2) (a) Ricci, A. Ed. *Modern Amination Methods*; Wiley-VCH: Weinheim, 2000. (b) Ricci, A. Ed. *Amino Group Chemistry, From Synthesis to the Life Sciences*; Wiley-VCH: Weinheim, 2007.

(3) (a) Chen, X.; Hao, X.-S.; Goodhue, C. E.; Yu, J.-Q. Cu(II)-Catalyzed Functionalizations of Aryl C−H Bonds Using O_2 as an Oxidant. *J. Am. Chem. Soc.* **2006**, *128*, 6790-6791. (b) Jordan-Hore, A. A.; Johansson, C. C. C.; Gulias, M.; Beck, E. M.; Gaunt, M. J. Oxidative Pd(II)-Catalyzed C−H Bond Amination to Carbazole at Ambient Temperature. *J. Am. Chem. Soc.* **2008**, *130*, 16184-16186. (c) Armstrong, A.; Collins, J. C. Direct Azole Amination: C-H Functionalization

as a New Approach to Biologically Important Heterocycles. *Angew. Chem. Int. Ed.* **2010**, *49*, 2282-2285. (d) Kim, J. Y.; Cho,S. H.; Joseph, J.; Chang, S. Cobalt□ and Manganese□Catalyzed Direct Amination of Azoles under Mild Reaction Conditions and the Mechanistic Details. *Angew. Chem. Int. Ed.* **2010**, *49*, 9899-9903. (e) Xiao, B.; Gong, T. J.; Xu, J.; Liu, Z. J.; Liu, L. Palladium-Catalyzed Intermolecular Directed C−H Amidation of Aromatic Ketones. *J. Am. Chem. Soc.* **2011**, *133*, 1466-1474.

(4) (a) Tan, Y.; Hartwig, J. F. Palladium-Catalyzed Amination of Aromatic C−H Bonds with Oxime Esters. *J. Am. Chem. Soc.* **2010**, *132*, 3676-3677. (b) Yoo, E. J.; Ma, S.; Mei, T. -S.; Chan, K. S. L.; Yu, J.-Q. Pd-Catalyzed Intermolecular C–H Amination with Alkylamines. *J. Am. Chem. Soc.* **2011**, *133*, 7652-7655. (c) Grohmann, C.; Wang, H.; Glorius, F. Rh[III]-Catalyzed Direct C–H Amination Using N-Chloroamines at Room Temperature. *Org. Lett.* **2012**, *14*, 656-659.

(5) (a) Foo, K.; Sella, E.; Thomé, I.; Eastgate, M. D.; Baran, P. S. A Mild, Ferrocene-Catalyzed C–H Imidation of (Hetero)Arenes. *J. Am. Chem. Soc.* **2014**, *136*, 5279-5282. (b) Allen, L. J.; Cabrera, P. J.; Lee, M.; Sanford, M. S. *N*-Acyloxyphthalimides as Nitrogen Radical Precursors in the Visible Light Photocatalyzed Room Temperature C–H Amination of Arenes and Heteroarenes. *J. Am. Chem. Soc.* **2014**, *136*, 5607-5610.

(6) Fabian, J.; Nakazumi, H.; Matsuoka, M. Near-Infrared Absorbing Dyes. *Chem. Rew.* **1992**, *92*, 1197-1226.

(7) (a) Musser, J. H.; Jones, H.; Sciortino, S.; Bailey, K.; Coutts, S. M.; Khandwala, A.; Sonnino, G. P.; Leibowitz, M.; Wolf, P.; Neiss, E. S. Synthesis and Antiallergic Activities of 1,3-Oxazolo[4,5-h]quinolines. *J. Med. Chem.* **1985**, *28*, 1255-1259. (b) Sleath, P. R.; Noar, J. B.; Eberlein, G. A.; Bruice, T. C. Synthesis of 7,9-Didecarboxymethoxatin (4,5-Dihydro-4,5-dioxo-1H-pyrrolo[2,3-f] quinoline-2-carboxylic Acid) and Comparison of its Chemical Properties with those of Methoxatin and Analogous *o*-Quinones. Model Studies Directed toward the Action of PQQ Requiring Bacterial Oxidoreductases and Mammalian Plasma Amine Oxidase. *J. Am. Chem. Soc.* **1985**, *107*, 3328. (c) Maryanoff, B. E.; Nortey, S. O.; McNally, J. J.; Sanfilippo, P. J.; McComsey, D. F.; Dubinsky, B.; Shank, R. P.; Reitz, A. B. Potential Anxiolytic Agents. 3. Novel A-ring Modified Pyrido[1,2-a]benzimidazoles. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1547-1552.

(8) (a) Kadlubar, F. F.; Unruh, L. E.; Flammang, T. J.; Sparks, D.; Mitchum, R. K.; Mulder, G. J. Alteration of Urinary Levels of the Carcinogen, *N*-Hydroxy-2-naphthylamine, and its *N*-Glucuronide in the Rat by Control of Urinary pH, Inhibition of Metabolic Sulfation, and Changes in Biliary Excretion. *Chem-Biol Interact.* **1981**, *33*, 129-147. (b) Glennon, R. A.; Naiman, N. A.; Pierson, M. E.; Smith, J. D.; Ismaiel, A. M.; Titeler, M.; Lyon, R. A. *N*-(Phthalimidoalkyl) Derivatives of Serotonergic Agents: a Common Interaction at 5-HT_{1A} Serotonin Binding Sites. *J. Med. Chem.* **1989**, *32*, 1921-1926. (c) Dukat, M.; Smith, C.; Herrick-Davis, K.; Teitler, M.; Glennon, R. A. Binding of Tryptamine Analogs at *h*5-HT_{1E} Receptors: A Structure–Affinity Investigation.

Bioorg. Med. Chem. **2004**, *12*, 2545-2552. (d) Kling, A.; Lange, E. W.; Mack, H.; Bakker, H. M.; Drescher, K. U.; Hornberger, W.; Hutchins, C. W.; Möller, A.; Müller, R.; Schmidt, M.; Unger, L.; Wicke, K.; Schellhaas, K.; Steiner, G. Synthesis and SAR of Highly Potent Dual 5-HT_{1A} and 5-HT_{1B} Antagonists as Potential Antidepressant Drugs. *Bioorg. Med. Chem.* **2005**, *15*, 5567-5573.

(9) (a) Bosco, M.; Forlani, L.; Todesco, P. E. The Reactivity of the Halogenonaphthols towards Nucleophiles. Part II. The Kinetics and Mechanisms of the Reactions of 1-Halogeno-2-naphthols with Anilines. *J. Chem. Soc. B* **1970**, 1742-1746. (b) Didenko, V.; Labeish, V.; Trukhin, V.; Petrov, L. Facile Replacement of the Halogen Atom in 4-Amino-1-chloronaphthalen-2-ols by S- and N-Centered Nucleophiles. *Russ. J. Org. Chem.* **2007**, *43*, 1092-1095. (c) Emerson, S.; Reed, K.; Merner, R. Secondary and Tertiary Amines from Azo Compounds. *J. Am. Chem. Soc.* **1941**, *63*, 751-752. (d) Behrman, E. The Persulfate Oxidation of Phenols and Arylanmines (The Elbs and the Boyland-Sims Oxidations). *J. Org. React.* **1988**, 422-504.

(10) (a) Tyman, J. H. *Synthetic and natural phenols*, Elsevier, New York, 1996. (b) Rappoport, Z. *The Chemistry of Phenols*, Wiley, Chichester, 2003. (c) Weber, M.; Kleine-Boymann, M. *"Phenol" in Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, 2004. (d) Huang, Z. L.; Jin, L. Q.; Feng, Y.; Peng, P.; Yi, H.; Lei, A. W. Iron-Catalyzed Oxidative Radical Cross-Coupling/Cyclization between Phenols and Olefins. *Angew. Chem. Int. Ed.* **2013**, *52*, 7151-7155.

(11) Chen, Z.-W.; Zeng, H.-Y.; Girard, S. A.; Wang, F.; Chen, N.; Li, C.-J. Formal Direct Cross-Coupling of Phenols with Amines. *Angew. Chem. Int. Ed.* **2015**, *54*, 14487-14491.

(12) (a) L.-Habermeyer, M.-L.; Jin, R.; Patureau, F. W. O_2-Mediated Dehydrogenative Amination of Phenols. *Angew. Chem. Int. Ed.* **2015**, *54*, 4102-4104. (b) Jin, R; Patureau, F. W. Mild, Periodate-Mediated, Dehydrogenative C–N Bond Formation with Phenothiazines and Phenols. *Org. Lett.* **2016**, *18*, 4491-4493. (c) Zhao, Y.-T.; Huang, B.-B.; Yang, C.; Xia, W.-J. Visible-Light-Promoted Direct Amination of Phenols via Oxidative Cross-Dehydrogenative Coupling Reaction. *Org. Lett.* **2016**, *18*, 3326-3329. (d) Zhao, Y.-T.; Huang, B.-B.; Yang, C.; Li, B.; Gou, B.-Q.; Xia, W.-J. Photocatalytic Cross-Dehydrogenative Amination Reactions between Phenols and Diarylamines. *ACS Catal.* **2017**, *7*, 2446-2451.

(13) (a) Jia, L.; Gao, S.; Xie, J.; Luo, M. Iron-Catalyzed Direct Alkylamination of Phenols with *O*-Benzoyl-*N*-alkylhydroxylamines under Mild Conditions. *Adv. Synth. Catal*. **2016**, *358*, 3840-3846. (b) Gao, S.; Gao, L; Meng, H.; Luo, M.; Zeng, X. Iron-catalyzed Synthesis of Benzoxazoles by Oxidative Coupling/cyclization of Phenol Derivatives with Benzoyl Aldehyde Oximes. *Chem. Commun*. **2017**, *53*, 9886-9889. (c) Brandes, S.; Bella, M.; Kjæsgaard, A.; Jørgenson, K. A. Chirally Aminated 2-Naphthols—Organocatalytic Synthesis of Non-Biaryl Atropisomers by Asymmetric Friedel–Crafts Amination. *Angew. Chem. Int. Ed.* **2006**, *45*, 1147-1151. (d) Wang, S.-G.; Yin, Q.; Zhuo, C.-X.; You, S.-L. Asymmetric Dearomatization of β-Naphthols through an Amination

Reaction Catalyzed by a Chiral Phosphoric Acid. *Angew. Chem. Int. Ed.* **2015**, *54*, 647-650.

(14) (a) Esguerra, K. V. N.; Xu, W.-B.; Lumb, J.-P. Unified Synthesis of 1,2-Oxy-aminoarenes via a Bio-inspired Phenol-Amine Coupling. *Chem.* **2017**, *2*, 533-549. (b) Qin, Y.; Luo, S. Nature Inspires an Aerobic Coupling of Phenol and Amine. *Chem*. **2017**, *2*, 461-462. (c) Esguerra, K. V. N.; Lumb, J.-P. A Bioinspired Catalytic Aerobic Functionalization of Phenols: Regioselective Construction of Aromatic C−N and C−O Bonds. *ACS Catal.* **2017**, *7*, 3477-3482. (d) Cheng Y.-F.; Rong, H.-J.; Yi, C.-B.; Yao, J.-J.; Qu, J. Redox-Triggered α-C–H Functionalization of Pyrrolidines: Synthesis of Unsymmetrically 2,5-Disubstituted Pyrrolidines. *Org. Lett.* **2015**, *17*, 4758-4761. (e) Liu, L.; Qian, L.-W.; Wu, S.-F.; Dong, J.-Y.; Xu, Q.; Zhou, Y.-B.; Yin, S.-F. Selective Aerobic C–H Amination of Phenols with Primary Amines over Copper toward Benzoxazoles. *Org. Lett.* **2017**, *19*, 2849-2852. (f) Rong, H.-J.; Cheng, Y.-F.; Liu, F.-F.; Ren, S.-J.; Qu, J. Synthesis of γ-Lactams by Mild, o-Benzoquinone-Induced Oxidation of Pyrrolidines Containing Oxidation-Sensitive Functional Groups. *J. Org. Chem.* **2017**, *82*, 532-540. (g) Esguerra, K. V. N.; Lumb, J.-P. Synthesis of ortho-Azophenols by Formal Dehydrogenative Coupling of Phenols and Hydrazines or Hydrazides. *Chem. Eur. J.* **2017**, *23*, 8596-8600.

(15) (a) Tang, Q.; Zhang, C.; Luo, M. A New Method for N−N Bond Cleavage of *N*,*N*-Disubstituted Hydrazines to Secondary Amines and Direct Ortho Amination

of Naphthol and Its Analogues. *J. Am. Chem. Soc.* **2008**, *130*, 5840-5841. (b) Gao, J. Y.; Zhang, C. H.; Luo, M.; Kim, C. K.; Chu, W.; Xue, Y. Mechanism for the Reaction of 2-Naphthol with *N*-Methyl-*N*-phenyl-hydrazine Suggested by the Density Functional Theory Investigations. *J. Comput. Chem.* **2012**, *33*, 220-230.

(16) (a) Japp, F. R.; Maitland, W. J. Formation of Carbazoles by the Interaction of Phenols, in the Ortho-Ketonic Form, with Arylhydrazines. *J. Chem. Soc. Trans.* **1903**, *83*, 267-276. (b) Seeboth, H. H. The Bucherer Reaction and the Preparative Use of Its Intermediate Products. *Angew. Chem. Int. Ed.* **1967**, *6*, 307-317. (c) Jia, L.; Tang, Q.; Luo, M.; Zeng, X. One-Step Synthesis of Unsymmetric 1,1'-Biaryl-2,2'-diamines by the Reaction of 2-Naphthols with Aryl Hydrazines. *Chin. J. Org. Chem.* **2018**, *38*, 443-450.

(17) (a) Patai, S. *The Chemistry of the Hydrazo, Azo and Azoxy Groups*, Vol. 1, John Wiley & Sons, Ltd., New York, **1975**, pp. 776-806. (b) Smith, P. A. S. *Derivatives of hydrazine and other hydronitrogens having N-N bonds*, Benjamin/Cummings Pub. Co., Advanced Book Program, **1983**, pp. 1-42.

(18) (a) Frost, J. M.; DeGoey, D. A.; Shi, L.; Gum, R. J.; Fricano, M. M.; Lundgaard, G. L.; Elkouhen, O. F.; Hsieh, G. C.; Neelands, T.; Matulenko, M. A. Substituted Indazoles as Nav1.7 Blockers for the Treatment of Pain. *J. Med. Chem.* **2016**, *59*, 3373-3391. (b) Yan, W.; Wang, X.; Dai, Y.; Zhao, B.; Yang, X.; Fan, J.; Gao, Y.; Meng, F.; Wang, Y.; Luo, C. Discovery of 3-(5′-Substituted)-Benzimidazole-5-(1-(3,5-dichloropyridin-4-yl)ethoxy)-1H-indazoles as Potent Fibroblast Growth

Factor Receptor Inhibitors: Design, Synthesis, and Biological Evaluation. *J. Med. Chem.* **2016**, *59*, 6690-6708. (c) Wada, Y.; Nakano, S.; Morimoto, A.; Kasahara, K.; Hayashi, T.; Takada, Y.; Suzuki, H.; Niwa-Sakai, M.; Ohashi, S.; Mori, M. Discovery of Novel Indazole Derivatives as Orally Available β3-Adrenergic Receptor Agonists Lacking Off-Target-Based Cardiovascular Side Effects. *J. Med. Chem.* **2017**, *60*, 3252-3265. (d) Taneja, G.; Gupta, C.; Mishra, S.; Srivastava, R.; Rahuja, N.; Rawat, A.; Pandey, J.; Gupta, P.; Jaiswal, N.; Gayen, J. R. Synthesis of Substituted 2H-Benzo[e]indazole-9-carboxylate as a Potent Antihyperglycemic Agent that May Act through IRS-1, Akt and GSK-3β Pathways. *Med. Chem. Comm.* **2017**, *8*, 329-337.

(19) (a) Brown, G. R.; Foubister, A. J. Direct Transformation of Cyano into Methyl Groups under Mild Conditions. *Synthesis* **1982,** 1036-1037. (b) Lockhart, J. C.; McDonnell, M. B.; Clegg, W.; Hill, M. N. S. Structure and Dynamics of Crowns Containing the Phenyldinaphthylmethane Subunit (a three-bladed propeller): Observations of Correlated Rotation of the Propeller Blades and Certain Ether Segments. *J. Chem. Soc. Perkin Trans. 2* **1987**, 639-649. (c) Bell, K.; Mccaffery, L. Regioselective Monomethylation of Unsymmetrical Naphthalenediols With Methanolic HCl. *Aust. J. Chem.* **1993**, *46*, 731-737. (d) Kumar, R.; Ramachandran, U.; Srinivasan, K.; Ramarao, P.; Raichur, S.; Chakrabarti, R. Design, Synthesis and Evaluation of Carbazole Derivatives as PPARα/γ Dual Agonists and Antioxidants. *Bioorg. Med. Chem.* **2005**, *13*, 4279-4290.

(20) (a) Entwistle, I. D.; Johnstone, R. A. W.; Wilby, A. H. Metal-Assisted Reactions—Part 11: Rapid Reduction of N-Nitrosoamines to *N,N*-Disubstituted Hydrazines; the Utility of Some Low-valent Titanium Reagents. *Tetrahedron* **1982**, *38*, 419-423. (b) Lerch, U.; König, J. Selective Alkylation of Phenylhydrazine: A Facile and Efficient Synthesis of 1-Alkyl-1-phenylhydrazines. *Synthesis* **1983**, 157-158. (c) Lunn, G.; Sansone, E. B.; Keefer, L. K. Reduction of Nitrosamines with Aqueous Titanium Trichloride: Convenient Preparation of Aliphatic Hydrazines. *J. Org. Chem.* **1984**, *49*, 3470-3473. (d) Bredihhin, A.; Mäeorg, U. Effective Strategy for the Systematic Synthesis of Hydrazine Derivatives. *Tetrahedron* **2008**, *64*, 6788-6793.

(21) Zhang, Y.; Tang, Q.; Luo, M. *Org.* Reduction of Hydrazines to Amines with Aqueous Solution of Titanium(III) Trichloride. *Org. Biomol. Chem.* **2011**, *9*, 4977-4982.

(22) Rasmussen, L. K. Facile Synthesis of Mono-, Di-, and Trisubstituted Alpha-Unbranched Hydrazines. *J. Org. Chem.* **2006**, *71*, 3627-3629.

(23) (a) Boche, G.; Bosold, F.; Schröder, S. *N*-Aryl-*O*-acylhydroxylamines: Preparation by O-Acylation or N → O Transacylation and Reaction with Amines; Model Reactions for Key Steps Connected with the Carcinogenicity of Aromatic Amines. *Angew. Chem. Int. Ed.* **1988**, *27*, 973-974. (b) Corminboeuf, O.; Renaud, P. Enantioselective Diels−Alder Reactions with *N*-Hydroxy-*N*-phenylacrylamide. *Org. Lett.* **2002**, *4*, 1731-1733.