Article

Brønsted Acid-Catalyzed Functionalization of Aromatic Alcohols through Nucleophilic Substitution of Hydroxyl Group

Abhishek Kumar Mishra, and Srijit Biswas

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.5b02849 • Publication Date (Web): 02 Feb 2016

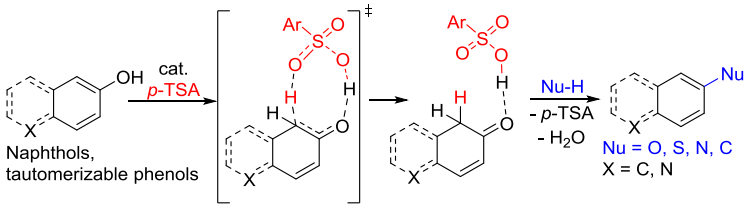
Brønsted Acid-Catalyzed Functionalization of Aromatic Alcohols through Nucleophilic Substitution of Hydroxyl Group

Abhishek Kumar Mishra and Srijit Biswas*

Division of Molecular Synthesis and Drug Discovery, Centre of Bio-Medical Research, SGPGIMS Campus, Raebareli Road, Lucknow 226014, India

Email: srijit.biswas@cbmr.res.in

Table of content graphic:



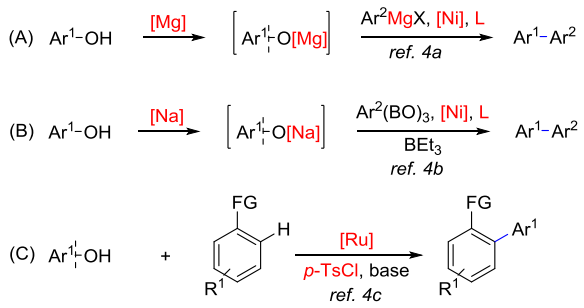
Abstract

The hydroxyl groups of naphthol and tautomerizable phenol derivatives have been substituted by *O*-, *S*-, *N*-, and *C*-centered nucleophiles in a solvent free reaction condition. The products are generated in good to excellent yields. *para*-Toluenesulfonic acid exhibits the best catalytic activity compared to other Brønsted acids. Experimental observations suggest that the reaction proceeds through the intermediacy of the keto tautomer of naphthol. Nucleophilic addition to the carbonyl group followed by elimination of water generates the desired product. The present methodology provides access to substituted naphtho[2,1-*b*]furan derivatives. The products generated using *N*-centered nucleophiles can be further transformed to important classes of organic molecules such as benzocarbazole and imidazole derivatives.

Introduction

Nucleophilic aromatic substitution (S_NAr) and cross-coupling reactions are useful for functionalizing many aromatic compounds.[1] Most of these reactions use aryl halides that give salt by-products, a source of atom inefficiency.[2] Recent improvements of these reactions still have drawbacks such as costly reagents and catalysts, atom inefficiency, and low reactivity with many nucleophiles.[3] Our research is devoted to finding efficient means of functionalizing phenols through aryl C–OH bond cleavage, which is difficult because of the stability of carbon-oxygen bond.[4a]

Scheme 1: Recent Reports of Biaryl Formations Through Aryl C-OH Bond Cleavage

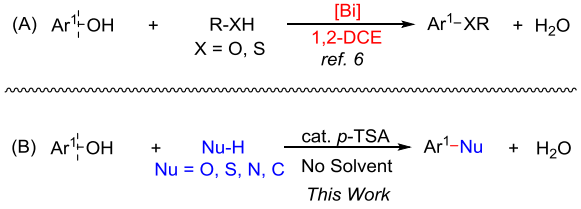


In recent times, cross-coupling methods have been developed where phenols are functionalized through the cleavages of aryl C–OH bonds (Scheme 1A–C).[4] These methods generally require *in situ* functional group interconversion (FGI) of the aryl C–OH functionality and are applicable only for biaryl synthesis. A general method to functionalize aryl C–OH bonds by nucleophilic substitution would be desirable because the transformation would not require prefunctionalization of the hydroxyl group, and water would be generated as the only by-product. Also, access to variety of functional derivatives could be achieved employing different types of nucleophiles.

Acid-mediated thiolation of naphthols and aryl diols through nucleophilic substitution of the aryl C–OH bond have been previously reported.[5] Hardy and co-workers developed a novel

method in which the hydroxyl group of 2-naphthol was replaced by thioglycolic acid and other *S*- centered nucleophiles.[5a] Large amounts of catalyst (30–60 mol%) were required to achieve high yields of the desired products. Thongpanchang and co-workers subsequently developed a protocol to synthesize bisthioalkylarenes from aryl diols and thiols using 50 mol% catalyst and a large excess of thiol.[5b] Nakazawa and co-workers also demonstrated a reaction of naphthols with alkyl and arylthiols employing 2 equivalents of triflic acid to synthesize naphthyl thioethers.[5c] These methods[5] are limited to the synthesis of aryl thioethers. Very recently, Takai and co-workers developed a method where bismuth triflate was successfully employed in nucleophilic substitution of aryl C–OH bonds by *O*- and *S*-centered nucleophiles (Scheme 2A).[6] There remain some limitations such as use of heavy metal catalysts and applicability only for *O*- and *S*- centered nucleophiles. Moreover, secondary alcohols did not work as nucleophiles in the desired reaction.

Scheme 2: Catalytic Nucleophilic Substitution of Aryl C-OH Bond

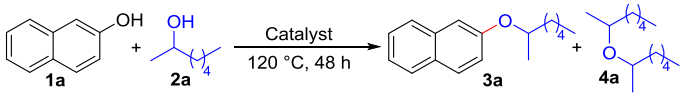


We report herein a straightforward method of nucleophilic substitution of aryl C–OH bonds by a variety of *O*-, *S*-, *N*-, and *C*-centered uncharged nucleophiles (Scheme 2B). Catalytic amounts of *para*-toluenesulfonic acid (*p*-TSA) were found to be suitable for this transformation. Best results were observed by executing the reaction in solvent free reaction conditions. Importantly, the present protocol allows direct access to substituted naphtha[2,1-*b*]furan derivatives and precursors of valuable target molecules such as benzocarbazole and imidazole derivatives.

Results and Discussion

We first sought to make alkyl-naphthyl ethers *via* nucleophilic substitution of the naphthyl C–OH bond by aliphatic alcohols (dehydrative etherification). We chose 2-naphthol (**1a**) as the electrophile and a secondary alcohol, 2-heptanol (**2a**), as the nucleophile. Aryl ethers derived from secondary alcohols cannot be prepared by traditional Williamson synthesis because of low reactivity and undesired side reactions.[7] Moreover, a secondary alcohol was reported not to take part in the bismuth-catalyzed naphthyl-alkyl ether formation reaction[6] and in a stoichiometric version of the etherification reaction.[8] Several Brønsted acids

Table 1. Optimization of Reaction Conditions[a]



entry	catalyst (mol%)	solvent	yield (%)[b]	
			3a	**4a**
1	*p*-TSA·H_2O (10)	toluene	53	10
2	CH_3SO_3H (10)	toluene	18[c]	12
3	$Bi(OTf)_3$ (10)	toluene	0[c]	0
4	***p*-TSA·H_2O (10)**	**neat**	**76 (72)[d]**	**8**
5	CH_3SO_3H (10)	neat	22[c]	10

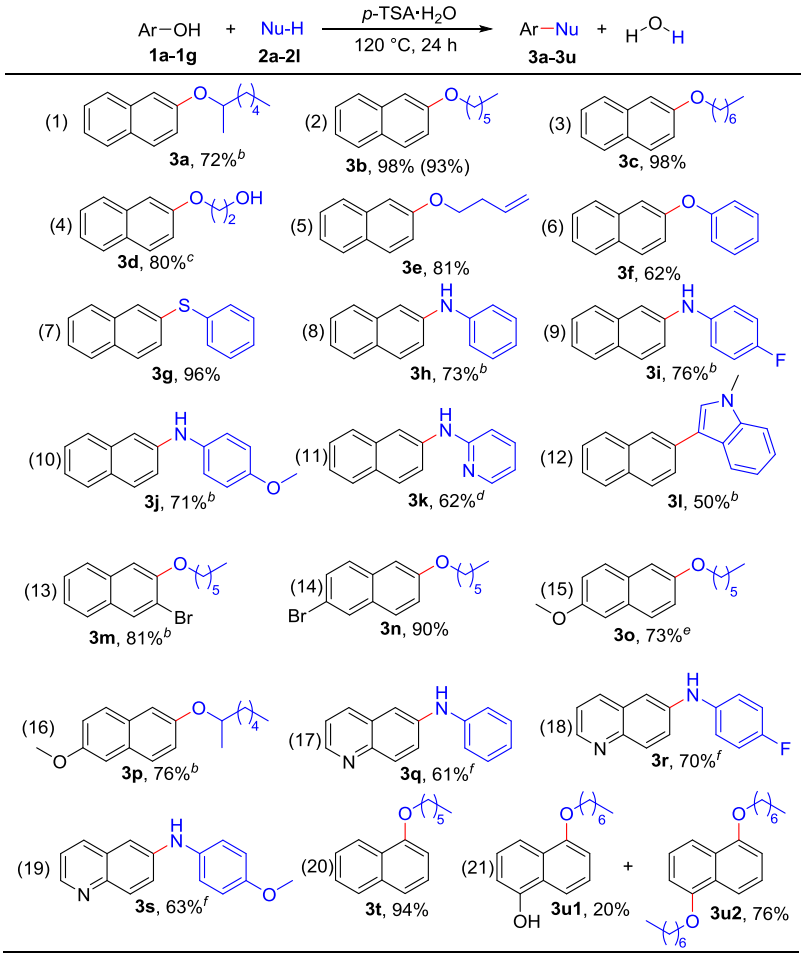
[a]Reaction conditions: **1a** (1.0 mmol), **2a** (3.0 mmol) and catalyst was taken in 1.5 mL solvent. The reaction mixture was purged with nitrogen and stirred at 120 °C for 48 hours in a closed 5 mL reaction vial. The residue was used directly for purification and GCMS analysis. [b]GC conversion, calculated with respect to **1a**. [c]Formation of complex mixture with full consumption of starting materials. [d]Isolated yield within the parenthesis.

such as, *para*-toluenesulfonic acid (*p*-TSA), methanesulfonic acid (CH_3SO_3H), phosphinic acid (H_3PO_2), acetic acid (AcOH), sulfanilic acid ($H_2NC_6H_4SO_3H$), triflic acid (CF_3SO_3H) and trifluoroacetic acid (CF_3CO_2H) were tested and *p*-TSA was found to give 53% of the desired ether **3a** in toluene (Table 1, entry 1). Methanesulfonic acid generated a small amount of the desired product under the same reaction conditions (Table 1, entry 2). All other Brønsted acid catalysts and bismuth triflate (Table 1, entry 3)[6] did not generate the desired product (see SI for a detailed optimization table including solvent screening and amounts of

nucleophile). Symmetrical ether **4a**, resulting from dehydration of **2a** was formed as by-product in different conditions (Table 1). The best result was observed by running the reaction using 3 equiv. of **2a** at 120 °C for 48 h without using any solvent, which generated the desired product **3a** in 72% isolated yield (Table 1, entry 4). Other Brønsted acid catalysts that were inactive in toluene did not give better results in solvent free reaction conditions (see SI for details), but a marginal improvement of the conversion was observed for methanesulfonic acid (Table 1, entry 5).

The optimized reaction conditions were applied to a variety of electrophiles and nucleophiles to synthesize the products through nucleophilic substitution of naphthyl C–OH bonds (Table 2). Primary alcohols, such as 1-hexanol (**2b**) and 1-heptanol (**2c**) reacted smoothly with 2-naphthol (**1a**) and generated the substitution products, **3b** and **3c**, respectively, in nearly quantitative yields (Table 2, entries 2–3). Importantly, only 5 mol% catalyst and 24 h reaction time was sufficient for complete conversion. A gram scale reaction employing **1a** and **2b** was also carried out using 2 g of **1a**, which generated the product **3b** in 93% yield under the same reaction conditions (see experimental section for details). Selective mono-naphthylation was observed using ethane-1,2-diol (**2d**) as nucleophile to generate the product **3d** in 80% yield (Table 2, entry 4). Homo-allylic alcohol (**2e**) also reacted with 2-naphthol (**1a**) to furnish the product **3e** in 81% yield (Table 2, entry 5). Phenol (**2f**) also served as nucleophile under the optimized reaction conditions and reacted with **1a** to generate the product **3f** in 62% yield (Table 2, entry 6). The protocol was also found to be general with respect to various *S*-, *C*-, and *N*-centered nucleophiles. Thiophenol (**2g**) reacted with **1a** and generated the corresponding thioether **3g** in 96% yield in the presence of 5 mol% *p*-TSA (Table 2, entry 7).[5] The *N*-centered nucleophile, such as aniline (**2h**), also worked well to produce the secondary amine

Table 2. Substrate Scope in Catalytic Nucleophilic Substitution of Naphthyl C–OH Bonds[a]



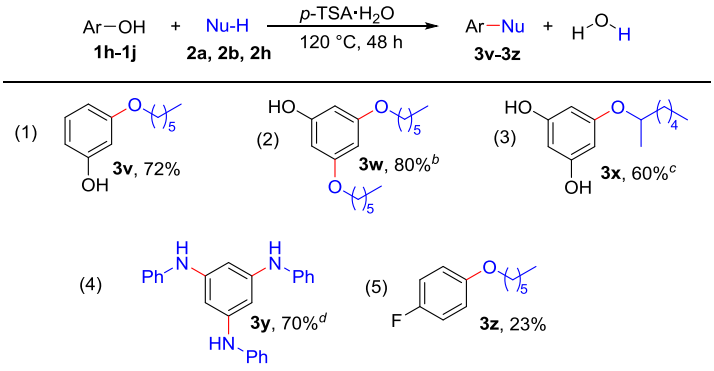
[a]Reaction conditions: Unless otherwise mentioned, **1** (1.0 mmol), **2** (3.0 mmol) and catalyst (0.05 mmol) were purged with nitrogen and stirred at 120 °C for 24 h in a closed 5 mL reaction vial. The residue was used directly for purification and GCMS analysis. Yields are optimized and refer to pure and isolated products, calculated with respect to **1**. Yield of gram scale reaction is given within the parenthesis (see experimental section for details). [b]0.1 mmol catalyst, 48 h. [c]0.1 mmol catalyst, 6 mmol nucleophile, 48 h. [d]0.2 mmol catalyst, 200 °C, 48 h. [e]80 °C, 48 h. [f]0.1 mmol catalyst, 160 °C, 48 h.

3h in 73% yield (Table 2, entry 8). 4-Substituted aniline derivatives such as 4-fluoroaniline (**2i**) and *p*-anisidine (**2j**) also reacted smoothly with **1a** to generate the products **3i** and **3j** in 76% and 71% yields, respectively (Table 2, entry 9–10). 2-Aminopyridine (**2k**) also reacted with 2-naphthol (**1a**) at elevated reaction temperature to furnish the product **3k** in 62% yield (Table 2, entry 11). *N*-Methylindole (**2l**) served as a *C*-centered nucleophile to generate 3-substituted indole derivative **3l** in 50% yield (Table 2, entry 12). The generality of the present methodology was investigated using a variety of substituted naphthol derivatives. 3-Bromo-

2-naphthol (**1b**) and 6-bromo-2-naphthol (**1c**) reacted with **2b** to afford the desired ethers **3m** and **3n** in 81% and 90% yields, respectively (Table 2, entries 13–14). The reaction was selective towards the naphthyl C–OH functionality and substitution of naphthyl C–Br bonds was not observed at C3 or C6 positions of **1b** and **1c**, respectively. 6-Methoxy-2-naphthol (**1d**) reacted with primary alcohol **2b** as well as hindered secondary alcohol **2a** and produced the desired products **3o** and **3p** in 73% and 76% yields, respectively, *via* selective nucleophilic substitution of the naphthyl C–OH bond (Table 2, entries 15–16). The heterocyclic naphthol derivative, quinolin-6-ol (**1e**), was less reactive and did not react with primary alcohols. However, **1e** reacted with aniline (**2h**) at elevated reaction temperature to generate the product **3q** in 61% yield (Table 2, entry 17). Under the same reaction conditions, 4-fluoroaniline (**2i**) and *p*-anisidine (**2j**) also reacted with **1e** to generate the heterocyclic products **3r** and **3s** in 70% and 63% yields, respectively (Table 2, entry 18–19). 1-Naphthol (**1f**) was found to be an equally efficient electrophile in the present reaction. Thus, 94% formation of **3t** was observed by the reaction between **1f** and 1-hexanol (**2b**) (Table 2, entry 20). A mixture of mono- and di-etherification was observed when naphthalene-1,5-diol (**1g**) was employed as electrophile to generate **3u1** and **3u2** in 20% and 76% yields, respectively (Table 2, entry 21).

To further extend the substrate scope, phenol derivatives were employed as electrophile in the present nucleophilic substitution reaction (Table 3). Unfortunately, unsubstituted phenol did not produce any desired product, but led to a complex mixture of Friedel-Crafts alkylation products. Gratifyingly, the two poly-phenols, resorcinol (**1h**) and phloroglucinol (**1i**), smoothly underwent the reaction. Steric effect of the nucleophile had a pivotal role. Thus, selective mono-ether formation was observed when resorcinol (**1h**) was subjected to reaction with 1-hexanol (**2b**) producing **3v** in 72% yield (Table 3, entry 1). Di-ether **3w** was formed by the reaction between phloroglucinol (**1i**) and 1-hexanol (**2b**) in 80% yield (Table 3, entry

Table 3. Substrate Scope in Catalytic Nucleophilic Substitution of Phenyl C–OH Bonds[a]



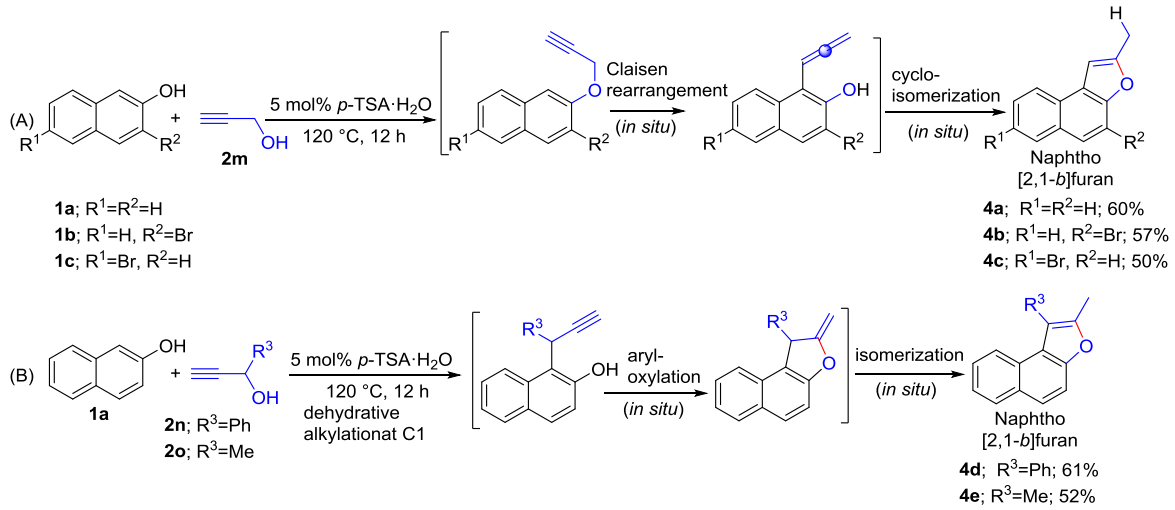
[a]Reaction conditions: Unless otherwise mentioned, **1** (1.0 mmol), **2** (3.0 mmol) and catalyst (0.1 mmol) were purged with nitrogen and stirred at 120 °C for 48 h in a closed 5 mL reaction vial. The residue was used directly use for purification and GCMS analysis. Yields are optimized and refer to pure and isolated products, calculated with respect to **1**. [b]6.0 mmol nucleophile. [c]0.2 mmol catalyst, 10 mmol nucleophile, 1.5 mL toluene as solvent. [d]0.2 mmol catalyst, 6 mmol nucleophile.

2). Under similar reaction conditions, phloroglucinol (**1i**) reacted with 2-heptanol (**2a**), which is a hindered secondary alcohol, to generate the ether **3x** in 60% yield through selective mono-etherification of the substrate (Table 3, entry 3). All the three hydroxyl groups of phloroglucinol (**1i**) were substituted by aniline (**2h**) to generate the product N^1,N^3,N^5-triphenylbenzene-1,3,5-triamine (**3y**) in 70% yield (Table 3, entry 4). 4-Fluorophenol (**1j**) was a less reactive substrate and only 23% of the product **3z** was formed when **1j** was subjected to reaction with 1-hexanol **2b** (Table 3, entry 5).

The present methodology served for the synthesis of naphtho[2,1-*b*]furan derivatives in one step (Scheme 3). Naphthofuran derivatives are found in a large number of biologically important natural products.[9] Under the optimized reaction conditions, naphtho[2,1-*b*]furan **4a** was formed in 60% yield by the reaction between propargyl alcohol **2m** and 2-naphthol **1a** (Scheme 3A). The reaction took place through nucleophilic substitution of the naphthyl C–OH bond followed by *in situ* Claisen rearrangement and cyclo-isomerization. 2-Naphthol derivatives having bromo-substituents at two different positions also reacted at the hydroxyl

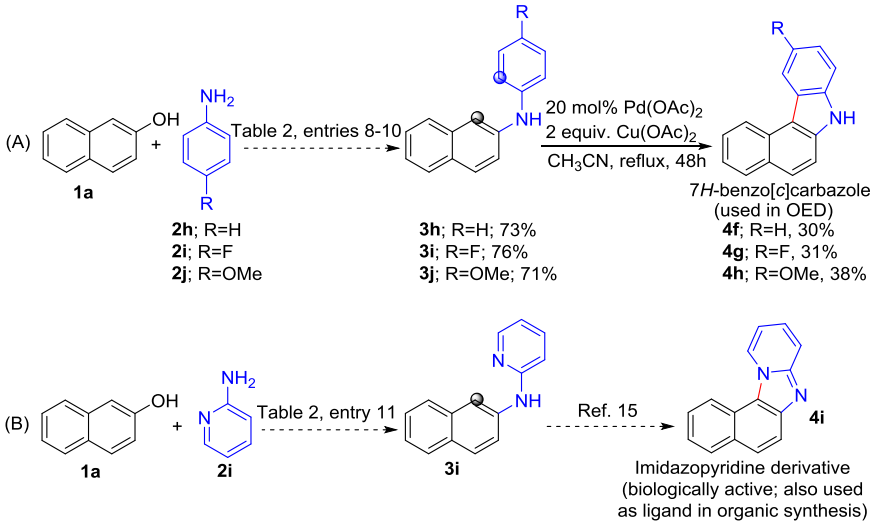
function under the present reaction conditions. Thus, 3- bromo- and 6-bromo-2-naphthols (**1b** and **1c** respectively) reacted with

Scheme 3: Synthesis of Naphtho[2,1-*b*]furan Derivatives



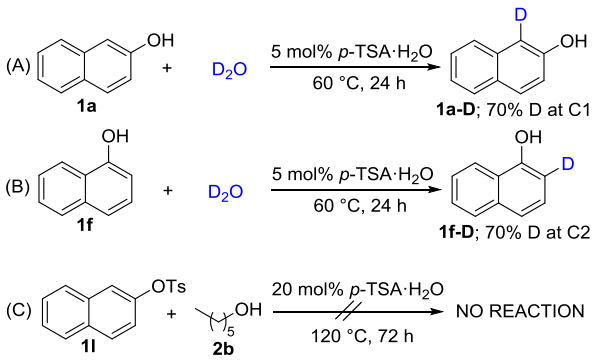
propargyl alcohol **2m** to afford the bromo-substituted naphtha[2,1-*b*]furan derivatives **4b** and **4c** in 57% and 50% yields, respectively (Scheme 3A). For further applications, the aryl C–Br bonds of the products **4b** and **4c** enable transformation to functionalized derivatives.[10] A different mechanism was found to operate when phenyl substituted secondary propargylic alcohol **2n** was employed instead of primary propargyl alcohol **2m** (Scheme 3B). Due to the stabilization of the benzylic carbocation,[11] **2n** formed the carbocation, which alkylated the C1 position of **1a**.[12] *In situ* aryl-oxylation followed by isomerisation generated the phenyl substituted naphtho[2,1-*b*]furan derivative **4d** in 61% yield (Scheme 3B). Similar reactivity was observed when methyl substituted secondary propargylic alcohol **2o** was used instead of **2n**. Thus, **4e** was generated in 52% yield when subjected to reaction with **1a** through a similar alkylation and *in situ* aryl-oxylation / isomerisation mechanism (Scheme 3B). This observation indicated that the reaction reported in scheme 3B occurred with both benzylic and secondary alkyl carbocations.

Scheme 4: Synthesis of Benzocarbazole and Imidazopyridine Derivative



The present protocol also provides useful precursors for synthesizing benzocarbazoles and imidazopyridines (Scheme 4). Benzocarbazole derivatives are used in material science, including the construction of organic electro-emission diodes (OED).[13] The product **3h** obtained *via* nucleophilic substitution of hydroxyl group of ß-naphthol (**1a**) by aniline (**2h**) (Table 2, entry 8) was converted to *7H*-benzo[*c*]carbazole **3y** in 30% yield when treated with 20 mol% $Pd(OAc)_2$ and 2 equivalents of $Cu(OAc)_2$ through a dehydrogenative C–C coupling reaction (Scheme 4A). The reaction also occurred when electron withdrawing 4-fluoro and electron donating 4-methoxy substituents were present in the phenyl ring (**3i** and **3j** respectively). Thus, compound **3i** and **3j** obtained by the reaction of 2-naphthol (**1a**) with 4-fluoroaniline (**2i**) and *p*-anisidine (**2j**), respectively (Table 2, entries 9–10), underwent dehydrogenative coupling reactions under same reaction conditions to generate the fluoro- and methoxy- substituted *7H*-benzo[*c*]carbazole derivatives **4g** and **4h** in 31% and 38% yields, respectively (Scheme 4B). In a similar way, product **3i** obtained by the reaction between 2-naphthol (**1a**) by 2-aminopyridine (**2k**) could be transformed to the synthetically and pharmaceutically relevant imidazopyridine[14] derivative (**4i**) by a reported method (Scheme 4B).[15]

Scheme 5: Mechanistic Investigations

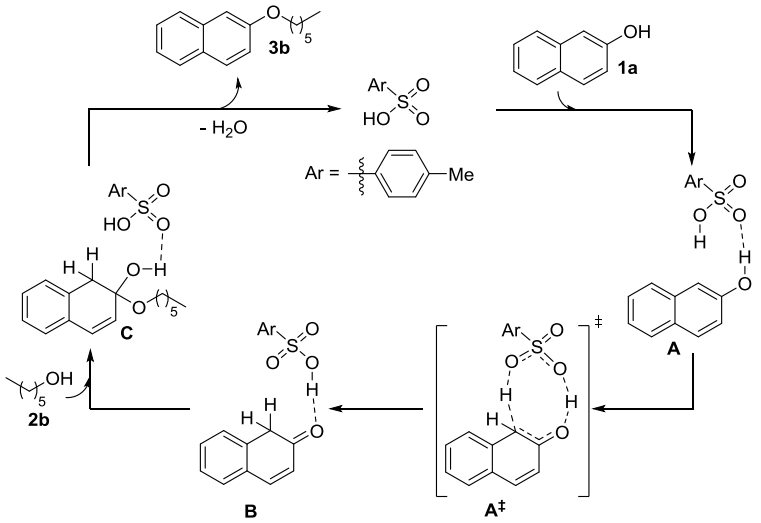


Experiments outlined in Scheme 5 were performed in order to probe the reaction mechanism. 2-Naphthol (**1a**) was treated with 3 equiv. of 99.8% D_2O in the presence of 5 mol% *p*-TSA catalyst at 60 °C for 24 h in dry 1,2-dichloroethane solvent. Selective deuterium incorporation (70%) was observed exclusively at the C1-position of **1a** to produce **1a-D** (Scheme 5A). Similarly, selective deuterium incorporation (70%) at C2-position was observed when 1-naphthol (**1f**) was subjected to reaction with D_2O under the same reaction conditions to generate **1f-D** (Scheme 5B).[16] These experimental outcomes imply keto-enol tautomerization of the naphthols during the course of the reaction. To exclude the possibility of *in situ* formation of tosylate (OTs), substrate **1k** was prepared and isolated in a separate step. When **1k** was subjected to react with **2b** under identical reaction conditions, no reaction occurred and unreacted **1k** was recovered quantitavely even after 72 h (Scheme 5C). This experiment ruled out the possibility of *in situ* functionalization group interconversion of aryl C–OH to aryl C–OTs followed by *ipso* substitution. All the experimental observations are in line if the keto-tautomer of the electrophile would have formed during the course of the reaction.

Based on the experimental outcomes and taking into account the theoretical work reported by Ellervik and co-workers,[17a] a plausible mechanism is proposed considering the etherification

reaction between 2-naphthol **1a** and 1-hexanol **2b** (Scheme 6). The first step is the tautomerization of 2-naphthol **1a** to the keto form **B** through formation of a complex (**A**).

Scheme 6: Plausible Mechanism



Complex **A** is roughly thermo-neutral as calculated in Ellervik's report with a relative energy of ΔH (ΔG) = 1 (15) kJ mol^{-1}.[17a] From **A**, a concerted mechanism proposed by Ellervik would operate. Thus, in complex **A**, the acidic proton of the catalyst protonates the C1 centre of **1a** whereas, one of the oxo groups of the catalyst abstracts the proton from the hydroxyl group[18] to form the keto tautomer **B**[17b] through a cyclic transition state **A**‡. The relative energy of the transition state **A**‡ is reported as $\Delta H^{\ddagger}_{calcd}$ ($\Delta G^{\ddagger}_{calcd}$) = 42 (64) kJ mol^{-1}.[17a] Nucleophile **2b** attacks the electrophilic carbonyl carbon of **B** to produce the addition product **C**, which upon elimination of water and regeneration of the catalyst produces the desired substitution product **3b**. Overall, the reaction undergoes *via* an addition-elimination mechanism, rather than the traditional S_NAr mechanism.

Conclusion: We report a simple strategy for catalytic nucleophilic substitution of the hydroxyl groups of aryl alcohols by *O*-, *S*-, *N*-, and *C*-centered uncharged nucleophiles. Pre-activation or pre-functionalization of the hydroxyl group is not required and catalytic amount

of *para*-toluenesulfonic acid (*p*-TSA) is sufficient to selectively activate the aryl C–OH bond. Experimental studies and previously reported theoretical work suggests that formation of the keto-tautomer of the aryl alcohol occurs in the first step. Nucleophilic addition to the carbonyl group of the keto-tautomer followed by water elimination generates the substitution products, mostly in high yields. The reaction does not require any organic reaction medium and water is formed as the only by-product. As application, the present protocol allows a direct access to substituted naphtha[2,1-*b*]furan derivatives and benzocarbazole and imidazole derivatives.

Experimental Section:

General Considerations: ^{1}H and ^{13}C NMR spectra were recorded with a 400 MHz spectrometer as solutions in $CDCl_3$. Chemical shifts are expressed in parts per million (ppm, δ) and are referenced to $CHCl_3$ (δ = 7.28 ppm) as an internal standard. All coupling constants are absolute values and are expressed in Hz. The description of the signals include: s = singlet, d = doublet, t = triplet, q = quadrate, sxt = sextet, m = multiplet, dd = doublet of doublets, dq = doublet of quadrate, ddd = doublet of doublet of doublets, ddt = doublet of doublet of triplates, td = triplet of doublet, and br. s. = broad singlet. ^{13}C NMR spectra were recorded as solutions in $CDCl_3$ with complete proton decoupling. Chemical shifts are expressed in parts per million (ppm, δ) and are referenced to $CDCl_3$ (δ = 77.0 ppm) as an internal standard. High Resolution Mass Spectral analyses were performed using Q-TOF mass analyzer by ESI method. The molecular fragments in High Resolution Mass Spectra (HRMS) are quoted as the relation between mass and charge (*m*/*z*). The routine monitoring of reactions was performed with silica gel pre-coated Al plate, which was analyzed with iodine and/or uv light, ^{1}H NMR analysis, and GC / GCMS analysis of crude reaction mixture. All reactions were executed with oven-dried glassware under nitrogen atmosphere.

Representative experimental procedure for the synthesis of 2-(Heptan-2-yloxy)naphthalene (3a):

Catalyst *p*-TSA·H_2O (19 mg, 10 mol%), 2-Naphthol **1a** (144 mg, 1.0 mmol) and 2-heptanol **2a** (349 mg, 3.0 mmol) were taken in a 5 mL VWR reaction vial under nitrogen atmosphere. The cap of the vial was closed and the reaction mixture was stirred at 120 °C for 48 h. After completion of the reaction (by TLC, GC or NMR), the crude was directly purified by silica-gel (230–400 mess) column chromatography (flash) using 2% (*v*/*v*) ethyl acetate / hexane solution to afford the desired product **3a** as a colourless liquid (174 mg, 0.72 mmol, 72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93–0.97 (m, 3 H), 1.35–1.40 (m, 4 H), 1.41 (dd, *J*=6.04, 1.01 Hz, 3 H), 1.45–1.58 (m, 2 H), 1.63–1.73 (m, 1 H), 1.77–1.92 (m, 1 H), 4.56 (sxt, *J* = 5.99 Hz, 1 H), 7.10–7.22 (m, 2 H), 7.29–7.40 (m, 1 H), 7.41–7.51 (m, 1 H), 7.68–7.83 (m, 3 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.0, 19.6, 22.6, 25.2, 31.8, 36.4, 73.8, 108.3, 119.8, 123.4, 126.2, 126.6, 127.6, 128.8, 129.4, 134.6, 156.0 ppm; HRMS (ESI) calcd. for $C_{17}H_{23}O$ $[M+H]^+$ *m/z* 243.1743 found *m/z* 243.1730.

2-(Hexyloxy)naphthalene (3b):[19]

p-TSA·H_2O (10 mg, 5 mol%), 2-Naphthol **1a** (144 mg, 1.0 mmol) and 1-hexanol **2b** (306 mg, 3.0 mmol) were treated as described for the synthesis of **3a** for 24 h to obtain **3b** as a colorless liquid (223 mg, 0.98 mmol, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90–1.06 (m, 3 H), 1.44 (dq, *J* = 7.27, 3.62 Hz, 4 H),1.50–1.65 (m, 2 H), 1.83–1.98 (m, 2 H), 4.13 (t, *J* = 6.55 Hz, 2 H), 7.12–7.26 (m, 2 H), 7.39 (ddd, *J* = 8.06, 6.92, 1.13 Hz, 1 H), 7.50 (ddd, *J* = 8.18, 6.92, 1.26 Hz, 1 H), 7.71–7.87 (m, 3 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.0, 22.6, 25.8, 29.2, 31.6, 68.0, 106.5, 119.0, 123.4, 126.2, 126.7, 127.6, 128.9, 129.3, 134.6, 157.1 ppm.

2-(Heptyloxy)naphthalene (3c):

p-TSA·H_2O (10 mg, 5 mol%), 2-Naphthol **1a** (144 mg, 1.0 mmol) and 1-heptanol **2c** (348 mg, 3.0 mmol) were treated as described for the synthesis of 3b to obtain **3c** as a colourless liquid (237 mg, 0.98 mmol, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, J = 6.80 Hz, 3 H), 1.22–1.46 (m, 6 H), 1.46–1.62 (m, 2 H), 1.79–1.96 (m, 2 H), 4.10 (t, J = 6.55 Hz, 2 H), 7.10–7.22 (m, 2 H), 7.34 (ddd, J = 8.06, 6.92, 1.13 Hz, 1 H), 7.45 (td, J = 7.55, 1.26 Hz, 1 H), 7.69–7.83 (m, 3 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ = 14.1, 22.6, 26.1, 29.1, 29.2, 31.8, 68.0, 106.5, 119.0, 123.4, 126.3, 126.7, 127.6, 128.8, 129.3, 134.6, 157.1 ppm; HRMS (ESI) calcd. for $C_{17}H_{23}O$ $[M+H]^+$ *m/z* 243.1743 found *m/z* 243.1730.

2-(Naphthalen-6-yloxy)ethanol (3d):[20]

p-TSA·H_2O (10 mg, 5 mol%), 2-Naphthol **1a** (144 mg, 1.0 mmol) and ethane-1,2-diol **2d** (372 mg, 6.0 mmol) were treated as described for the synthesis of **3b** to obtain **3d** as a reddish oil (150 mg, 0.80 mmol, 80%). ^{1}H NMR (400 MHz, $CDCl_3$); δ = 2.20 (br. s., 1 H), 4.02 (br. s., 2 H), 4.14–4.25 (m, 2 H), 7.10–7.22 (m, 2 H), 7.34 (t, J = 7.55 Hz, 1 H), 7.44 (t, J = 7.55 Hz, 1 H), 7.74 (q, J = 8.73 Hz, 3 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ = 61.4, 69.1, 106.8, 118.7, 123.8, 126.4, 126.7, 127.6, 129.1, 129.5, 134.4, 156.5 ppm.

2-(But-3-enyloxy)naphthalene (3e):[21]

p-TSA·H_2O (10 mg, 5 mol%), 2-Naphthol **1a** (144 mg, 1.0 mmol) and but-3-en-1-ol **2e** (216 mg, 3.0 mmol) were treated as described for the synthesis of **3b** to obtain **3e** as a colorless liquid (160 mg, 0.81 mmol, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.57–2.70 (m, 2 H), 4.17 (t, J = 6.80 Hz, 2 H), 5.09–5.30 (m, 2 H), 5.99 (ddt, J = 17.12, 10.32, 6.67, 6.67 Hz, 1 H), 7.10–7.22 (m, 2 H), 7.31–7.41 (m, 1 H), 7.41–7.50 (m, 1 H), 7.66–7.85 (m, 3 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 33.6, 67.1, 106.6, 117.2, 118.9, 123.5, 126.3, 126.7, 127.7, 128.9, 129.3, 134.4, 134.5, 156.8 ppm.

2-Phenoxynaphthalene (3f):[3e]

p-TSA·H_2O (10 mg, 5 mol%), 2-Naphthol **1a** (144 mg, 1.0 mmol) and phenol **2f** (282 mg, 3.0 mmol) were treated as described for the synthesis of **3b** to obtain **3f** as a colorless oil (136 mg, 0.62 mmol, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.14 (d, *J* = 7.81 Hz, 2 H), 7.20 (t, *J* = 7.43 Hz, 1 H), 7.29–7.55 (m, 6 H), 7.76 (d, *J* = 8.06 Hz, 1 H), 7.88 (dd, *J* = 8.31, 4.03 Hz, 2 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ = 114.1, 119.1, 120.0, 123.4, 124.7, 126.5, 127.1, 127.7, 129.8, 129.8, 130.1, 134.3, 155.1, 157.1 ppm.

(Naphthalen-6-yl)(phenyl)sulfone (3g):[22]

p-TSA·H_2O (10 mg, 5 mol%), 2-Naphthol **1a** (144 mg, 1.0 mmol) and benzenethiol **2g** (330 mg, 3.0 mmol) were treated as described for the synthesis of **3b** to obtain **3g** as a colorless oil (227 mg, 0.96 mmol, 96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.35 (m, 1 H), 7.35–7.42 (m, 2 H), 7.42–7.48 (m, 2 H), 7.49 (dd, *J* = 4.03, 1.76 Hz, 1 H), 7.51–7.59 (m, 2 H), 7.74–7.83 (m, 2 H), 7.83–7.89 (m, 1 H), 7.89–7.96 (m, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 126.2, 126.5, 127.0, 124.4, 127.7, 128.7, 128.8, 129.2, 129.8, 130.9, 132.2, 132.9, 133.7, 135.8 ppm.

N-Phenylnaphthalen-2-amine (3h):[23]

p-TSA·H_2O (19 mg, 10 mol%), 2-Naphthol **1a** (144 mg, 1.0 mmol) and aniline **2h** (279 mg, 3.0 mmol) were treated as described for the synthesis of **3a** to obtain **3h** as a pale yellow solid (160 mg, 0.73 mmol, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.89 (br. s., 1 H), 7.10 (t, *J* = 7.30 Hz, 1 H), 7.16–7.34 (m, 3 H), 7.42 (t, *J* = 7.81 Hz, 3 H), 7.46–7.57 (m, 2 H), 7.75 (d, *J* = 8.31 Hz, 1 H), 7.79–7.90 (m, 2 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 111.5, 118.2, 120.0, 121.3, 123.4, 126.4, 126.4, 127.6, 129.1, 129.4, 134.5, 140.7, 142.8 ppm.

N-(4-Fluorophenyl)naphthalen-2-amine (3i):[24]

p-TSA·H_2O (19 mg, 10 mol%), 2-Naphthol **1a** (144 mg, 1.0 mmol) and 4-fluoroaniline **2i** (333 mg, 3.0 mmol) were treated as described for the synthesis of **3a** to obtain **3i** as a grey

solid (180 mg, 0.76 mmol, 76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.75 (br. s., 1 H), 6.96–7.11 (m, 2 H), 7.11–7.23 (m, 3 H), 7.30–7.39 (m, 2 H), 7.45 (t, *J* = 7.15 Hz, 1 H), 7.67 (d, *J* = 8.17 Hz, 1 H), 7.71–7.83 (m, 2 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 110.3, 115.9, 116.1, 119.3, 121.0, 121.0, 123.3, 126.3, 126.5, 127.6, 128.9, 129.3, 134.6, 138.7, 141.6, 157.0, 159.4 ppm.

N-(4-Methoxyphenyl)naphthalen-2-amine (3j):[24]

p-TSA·H_2O (19 mg, 10 mol%), 2-Naphthol **1a** (144 mg, 1.0 mmol) and 4-methoxyaniline **2j** (369 mg, 3.0 mmol) were treated as described for the synthesis of **3a** to obtain **3j** as a brown solid (177 mg, 0.71 mmol, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.86 (s, 3 H), 5.69 (br. s., 1 H), 6.87–6.99 (m, 2 H), 7.14 (dd, *J* = 8.80, 2.35 Hz, 1 H), 7.17–7.23 (m, 2 H), 7.25 (d, *J* = 2.35 Hz, 1 H), 7.27–7.33 (m, 1 H), 7.36–7.46 (m, 1 H), 7.63 (d, *J*,=,7.63 Hz, 1 H) 7.75 (dd, *J* = 8.22, 4.11 Hz, 2 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 55.6, 108.7, 114.7, 118.8, 122.5, 122.8, 126.2, 126.4, 127.6, 128.5, 129.1, 134.8, 135.5, 142.9, 155.5 ppm.

N-(Naphthalen-6-yl)pyridin-2-amine (3k):[25]

p-TSA·H_2O (38 mg, 20 mol%), 2-Naphthol **1a** (144 mg, 1.0 mmol) and 2-aminopyridine **2k** (282 mg, 3.0 mmol) were treated as described for the synthesis of **3a** at 200°C to obtain **3k** as a yellowish solid (136 mg, 0.62 mmol, 62%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.81 (br. s., 1 H), 7.03 (d, *J* = 8.31 Hz, 1 H), 7.35–7.53 (m, 3 H), 7.56 (t, *J* = 7.68 Hz, 1 H), 7.76–7.91 (m, 4 H), 8.30 (s, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 108.5, 115.2, 115.4, 121.3, 124.2, 126.4, 127.0, 127.6, 129.0, 129.9, 134.3, 137.8, 138.1, 148.3, 156.0 ppm.

1-Methyl-3-(naphthalen-6-yl)-1H-indole (3l):[26]

p-TSA·H_2O (19 mg, 10 mol%), 2-Naphthol **1a** (144 mg, 1.0 mmol) and 1-methyl-1H-indole **2l** (393 mg, 3.0 mmol) were treated as described for the synthesis of **3a** to obtain **3l** as brown liquid (128 mg, 0.50 mmol, 50%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.90 (s, 3 H), 7.23–7.33 (m, 1 H), 7.33–7.41 (m, 2 H), 7.42–7.58 (m, 3 H), 7.81–7.99 (m, 4 H), 8.11 (d, *J* = 7.81 Hz, 1

H), 8.15 (s, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 109.6, 116.6, 120.0, 120.0, 122.1, 124.9, 125.1, 126.1, 126.2, 126.4, 127.0, 127.7, 127.7, 128.2, 131.9, 133.1, 134.0, 137.6 ppm.

2-Bromo-3-(hexyloxy)naphthalene (3m):

p-TSA·H_2O (19 mg, 10 mol%), 3-bromonaphthalen-2-ol **1b** (223 mg, 1.0 mmol) and 1-hexanol **2b** (306 mg, 3.0 mmol) were treated as described for the synthesis of **3a** to obtain **3m** as a colorless oil (248 mg, 0.81 mmol, 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80–1.01 (m, 3 H), 1.30–1.47 (m, 4 H), 1.57 (q, *J* = 7.05 Hz, 2 H), 1.79–2.00 (m, 2 H), 4.14 (t, *J* = 6.55 Hz, 2 H), 7.15 (s, 1 H), 7.29–7.40 (m, 1 H), 7.40–7.51 (m, 1 H), 7.58–7.76 (m, 2 H), 8.08 (s, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.0, 22.6, 25.7, 29.0, 31.5, 69.1, 107.4, 113.9, 124.3, 126.5, 126.5, 126.7, 129.3, 132.1, 133.5, 153.1 ppm; HRMS (ESI) calcd. for $C_{16}H_{20}BrO$ $[M+H]^+$ *m/z* 307.0692 found *m/z* 307.0696.

2-Bromo-6-(hexyloxy)naphthalene (3n):[6]

p-TSA·H_2O (10 mg, 5 mol%), 6-bromonaphthalen-2-ol **1c** (223 mg, 1.0 mmol) and 1-hexanol **2b** (306 mg, 3.0 mmol) were treated as described for the synthesis of **3b** to obtain **3n** as a colorless oil (276 mg, 0.90 mmol, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, *J* = 6.55 Hz, 3 H), 1.40 (m, 4 H), 1.47–1.60 (m, 2 H), 1.81–1.93 (m, 2 H), 4.07 (t, *J* = 6.55 Hz, 2 H), 7.10 (s, 1 H), 7.15–7.22 (m, 1 H), 7.51 (d, *J* = 8.56 Hz, 1 H), 7.60 (d, *J* = 8.56 Hz, 1 H), 7.66 (d, *J* = 9.06 Hz, 1 H), 7.93 (s, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.0, 22.6, 25.8, 29.1, 31.6, 68.0, 106.4, 116.8, 120.1, 128.3, 128.4, 129.5, 129.6, 129.9, 133.1, 157.4 ppm.

2-(Hexyloxy)-6-methoxynaphthalene (3o):

p-TSA·H_2O (10 mg, 5 mol%), 6-methoxynaphthalen-2-ol **1d** (174 mg, 1.0 mmol) and 1-hexanol **2b** (306 mg, 3.0 mmol) were treated as described for the synthesis of **3b** at 80°C to obtain **3o** as a colorless oil (188 mg, 0.73 mmol, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 6.55 Hz, 3 H), 1.30–1.45 (m, 4 H), 1.46–1.57 (m, 2 H), 1.79–1.93 (m, 2 H), 3.92 (s, 3 H), 4.07 (t, *J* = 6.55 Hz, 2 H), 7.05–7.20 (m, 4 H), 7.65 (dd, *J* = 8.56, 5.29 Hz, 2 H) ppm; ^{13}C

NMR (101 MHz, $CDCl_3$): δ = 14.0, 22.6, 25.8, 29.3, 31.6, 55.3, 68.0, 106.0, 106.9, 118.8, 119.2, 128.0, 128.1, 129.6, 129.8, 155.6, 156.0 ppm; HRMS (ESI) calcd. for $C_{17}H_{23}O_2$ $[M+H]^+$ *m/z* 259.1693 found *m/z* 259.1684.

2-(Heptan-2-yloxy)-6-methoxynaphthalene (3p):

p-TSA·H_2O (19 mg, 10 mol%), 6-methoxynaphthalen-2-ol **1d** (174 mg, 1.0 mmol) and 2-heptanol **2a** (349 mg, 3.0 mmol) were treated as described for the synthesis of **3a** to obtain **3p** as a colorless oil (207 mg, 0.76 mmol, 76%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 6.67 Hz, 3 H), 1.31–1.40 (m, 7 H), 1.41–1.69 (m, 3 H), 1.72–1.89 (m, 1 H), 3.92 (s, 3 H), 4.48 (sxt, *J* = 6.04 Hz, 1 H), 7.07–7.18 (m, 4 H), 7.59–7.70 (m, 2 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.0, 19.7, 22.6, 25.3, 31.8, 36.5, 55.3, 74.0, 105.9, 109.0, 118.8, 120.1, 128.1, 129.6, 129.8, 154.5, 156.1 ppm; HRMS (ESI) calcd. for $C_{18}H_{25}O_2$ $[M+H]^+$ *m/z* 273.1849 found *m/z* 273.1849.

N-Phenylquinolin-6-amine (3q):[27]

p-TSA·H_2O (19 mg, 10 mol%), quinolin-6-ol **1e** (145 mg, 1.0 mmol) and aniline **2h** (279 mg, 3.0 mmol) were treated as described for the synthesis of **3a** at 160°C to obtain **3q** as a reddish solid (134 mg, 0.61 mmol, 61%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.19 (br. s., 1 H), 7.02–7.09 (m, 1 H), 7.19–7.26 (m, 2 H), 7.29–7.40 (m, 4 H), 7.44 (dd, *J* = 9.06, 2.52 Hz, 1 H), 7.95 (d, *J* = 8.31 Hz, 1 H), 8.01 (d, *J* = 9.06 Hz, 1 H), 8.73 (d, *J* = 2.77 Hz, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 109.3, 119.0, 121.5, 122.1, 123.0, 129.5, 129.6, 130.5, 134.4, 141.7, 142.1, 144.3, 147.5 ppm.

N-(4-Fluorophenyl)quinolin-6-amine (3r):

p-TSA·H_2O (19 mg, 10 mol%), quinolin-6-ol **1e** (145 mg, 1.0 mmol) and 4-fluoroaniline **2i** (333 mg, 3.0 mmol) were treated as described for the synthesis of **3q** to obtain **3r** as a brown solid (167 mg, 0.70 mmol, 70%). Melting point range: 70–72 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.18 (br. s., 1 H), 7.00–7.11 (m, 2 H), 7.11–7.23 (m, 3 H), 7.29–7.40 (m, 2 H),

7.84–8.07 (m, 2 H), 8.61–8.79 (m, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 107.8, 116.0, 116.3, 121.5, 122.0, 122.1, 122.7, 129.7, 129.9, 134.8, 137.8, 137.8, 142.7, 143.4, 146.9, 157.5, 159.9 ppm; HRMS (ESI) calcd. for $C_{15}H_{12}FN_2$ $[M+H]^+$ *m/z* 239.0979 found *m/z* 239.0976.

N-(4-Methoxyphenyl)quinolin-6-amine (3s):[27]

p-TSA·H_2O (19 mg, 10 mol%), quinolin-6-ol **1e** (145 mg, 1.0 mmol) and 4-methoxyaniline **2j** (369 mg, 3.0 mmol) were treated as described for the synthesis of **3q** to obtain **3s** as a brown solid (158 mg, 0.63 mmol, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.85 (s, 3 H), 5.89 (br. s., 1 H), 6.82–7.02 (m, 2 H), 7.11 (d, *J*=2.52 Hz, 1 H), 7.15–7.25 (m, 2 H), 7.25–7.37 (m, 2 H), 7.91 (d, *J*=8.56 Hz, 1 H), 7.98 (d, *J*=9.06 Hz, 1 H), 8.68 (s, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ = 55.5, 106.7, 114.8, 121.4, 122.1, 123.4, 129.8, 130.2, 134.3, 134.6, 143.5, 143.7, 146.7, 156.0 ppm.

1-(Hexyloxy)naphthalene (3t):[6]

p-TSA·H_2O (10 mg, 5 mol%), 1-naphthol **1f** (144 mg, 1.0 mmol) and 1-hexanol **2b** (306 mg, 3.0 mmol) were treated as described for the synthesis of **3b** to obtain **3t** as a colorless liquid (214 mg, 0.94 mmol, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.95–1.08 (m, 3 H), 1.40–1.48 (m, 4 H), 1.56–1.69 (m, 2 H), 1.92–2.02 (m, 2 H), 4.18 (t, *J* = 6.42 Hz, 2 H), 6.85 (dd, *J* = 7.55, 1.01 Hz, 1 H), 7.35–7.50 (m, 2 H), 7.50–7.63 (m, 2 H), 7.79–7.95 (m, 1 H), 8.32–8.47 (m, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ = 14.0, 22.6, 25.9, 29.3, 31.6, 68.1, 104.5, 119.9, 122.1, 125.0, 125.8, 125.9, 126.3, 127.4, 134.5, 154.9 ppm.

5-(Heptyloxy)naphthalen-1-ol (3u1):

p-TSA·H_2O (10 mg, 5 mol%), naphthalene-1,5-diol **1g** (160 mg, 1.0 mmol) and 1-heptanol **2c** (696 mg, 6.0 mmol) were treated as described for the synthesis of **3b** to obtain **3u1** as a colorless oil (49 mg, 0.20 mmol, 20%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 6.67 Hz, 3 H), 1.29–1.49 (m, 6 H), 1.54–1.68 (m, 2 H), 1.86–2.01 (m, 2 H), 4.14 (t, *J* = 6.42 Hz, 2 H),

5.23 (s, 1 H), 6.86 (t, *J* = 7.18 Hz, 2 H), 7.31 (t, *J* = 8.06 Hz, 1 H), 7.40 (t, *J* = 8.06 Hz, 1 H), 7.73 (d, *J* = 8.31 Hz, 1 H), 7.90 (d, *J* = 8.56 Hz, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ = 14.1, 22.6, 26.2, 29.1, 29.3, 31.8, 68.2, 105.2, 109.3, 113.4, 114.7, 125.0, 125.3, 127.1, 151.2, 154.8 ppm; HRMS (ESI) calcd. for $C_{17}H_{23}O_2$ $[M+H]^+$ *m/z* 259.1693 found *m/z* 259.1691.

1,5-Bis(heptyloxy)naphthalene (3u2):[28]

Obtained as colourless oil **3u2** (271 mg, 0.76 mmol, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.94 (t, *J* = 8.0 Hz, 6 H), 1.29–1.47 (m, 12 H), 1.55–1.62 (m, 4 H), 1.91–1.98 (m, 4 H), 4.14 (t, *J* = 8.0 Hz, 4 H), 6.85 (d, *J* = 7.81 Hz, 2 H), 7.38 (t, *J* = 8.06 Hz, 2 H), 7.88 (d, *J* = 8.56 Hz, 2 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ = 14.1, 22.6, 26.3, 29.1, 29.3, 31.8, 68.2, 105.2, 114.0, 125.0, 126.8, 154.7 ppm.

3-(hexyloxy)phenol (3v):[29]

p-TSA·H_2O (19 mg, 10 mol%), resorcinol **1h** (110 mg, 1.0 mmol) and 1-hexanol **2b** (612 mg, 6.0 mmol) were treated as described for the synthesis of **3a** to obtain **3v** as a colorless oil (140 mg, 0.72 mmol, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.95 (t, *J* = 6.29 Hz, 3 H), 1.34–1.42 (m, 3 H), 1.42–1.54 (m, 2 H), 1.71–1.86 (m, 2 H), 3.94 (t, *J* = 6.67 Hz, 2 H), 6.42–6.50 (m, 2 H), 6.53 (d, *J* = 8.31 Hz, 1 H), 7.14 (t, *J* = 8.44 Hz, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ = 14.0, 22.5, 25.6, 29.1, 31.5, 68.1, 102.2, 107.1, 107.8, 130.1, 156.6, 160.4 ppm.

3,5-Bis(hexyloxy)phenol (3w):

p-TSA·H_2O (19 mg, 10 mol%), benzene-1,3,5-triol **1i** (126 mg, 1.0 mmol) and 1-hexanol **2b** (612 mg, 6.0 mmol) were treated as described for the synthesis of **3v** to obtain **3w** as a white semi solid (235 mg, 0.80 mmol, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 6.55 Hz, 6 H), 1.30 (br. s., 1 H), 1.32–1.40 (m, 8 H), 1.40–1.54 (m, 4 H), 1.68–1.85 (m, 4 H), 3.90 (t, *J* = 6.55 Hz, 4 H), 6.05 (s, 2 H), 6.10 (s, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 13.9, 22.5, 25.6, 29.1, 31.5, 68.1, 94.3, 94.8, 157.3, 161.0 ppm. HRMS (ESI) calcd. for $C_{18}H_{31}O_3$ $[M+H]^+$ *m/z* 295.2268 found *m/z* 295.2260.

5-(Heptan-2-yloxy)benzene-1,3-diol (3x):[30]

p-TSA·H_2O (38 mg, 20 mol%), benzene-1,3,5-triol **1i** (126 mg, 1.0 mmol) and 2-heptanol **2a** (1.16 g, 10.0 mmol) in 1.5 mL dry toluene were treated as described for the synthesis of **3b** to obtain **3x** as a white solid (134 mg, 0.60 mmol, 60%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.55 Hz, 3 H), 1.24 (d, J = 6.04 Hz, 3 H), 1.26–1.34 (m, 5 H), 1.36–1.44 (m, 1 H), 1.45–1.58 (m, 1 H), 1.60–1.77 (m, 1 H), 4.24 (sxt, J = 5.94 Hz, 1 H), 5.95 (s, 1 H), 6.01 (s, 2 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.0, 19.6, 22.6, 25.1, 31.7, 36.3, 74.4, 95.7, 96.2, 157.4, 160.2 ppm.

N^1,N^3,N^5-Triphenylbenzene-1,3,5-triamine (3y):[31]

p-TSA·H_2O (38 mg, 20 mol%), benzene-1,3,5-triol **1i** (126 mg, 1.0 mmol) and aniline **2h** (558 mg, 6.0 mmol) were treated as described for the synthesis of **3a** to obtain **3y** as a brown solid (246 mg, 0.70 mmol, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.65 (br. s., 3 H), 6.36 (s, 3 H), 6.96 (t, J = 7.30 Hz, 3 H), 7.11 (d, J = 8.31 Hz, 6 H), 7.23–7.34 (m, 6 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 98.9, 118.7, 121.2, 129.3, 142.7, 145.3 ppm.

1-Fluoro-4-(hexyloxy)benzene (3z):[6]

p-TSA·H_2O (19 mg, 10 mol%), 4-fluorophenol **1j** (112 mg, 1.0 mmol) and 1-hexanol **2b** (306 mg, 3.0 mmol) were treated as described for the synthesis of **3a** to obtain **3z** as a reddish liquid (45 mg, 0.23 mmol, 23%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86–0.98 (t, J = 8.0 Hz, 3 H), 1.29–1.42 (m, 4 H), 1.42–1.54 (m, 2 H), 1.70–1.84 (m, 2 H), 3.93 (t, J = 6.55 Hz, 2 H), 6.79–6.88 (m, 2 H), 6.92–7.02 (m, 2 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.0, 22.6, 25.7, 29.2, 31.6, 68.6, 115.3, 115.4, 115.6, 115.8, 155.2, 155.2, 155.9, 158.3 ppm.

2-Methylnaphtho[2,1-b]furan (4a):[32]

p-TSA·H_2O (10 mg, 5 mol%), ß-Naphthol **1a** (144 mg, 1.0 mmol) and prop-2-yn-1-ol **2m** (168 mg, 3.0 mmol) were treated as described for the synthesis of **3b** for 12 h to obtain **4a** as a brown oil (109 mg, 0.60 mmol, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.59 (s, 3 H), 6.90

(d, *J* = 4.00 Hz, 1 H), 7.45–7.53 (m, 1 H), 7.54–7.73 (m, 3 H), 7.95 (d, *J* = 8.06 Hz, 1 H), 8.09 (d, *J* = 8.31 Hz, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ = 14.2, 101.7, 112.0, 123.4, 123.7, 124.1, 124.2, 125.9, 127.4, 128.6, 130.2, 151.9, 154.7 ppm.

4-Bromo-2-methylnaphtho[2,1-b]furan (4b):

p-TSA·H_2O (10 mg, 5 mol%), 3-bromonaphthalen-2-ol **1b** (223 mg, 1.0 mmol) and prop-2-yn-1-ol **2m** (168 mg, 3.0 mmol) were treated as described for the synthesis of **4a** for 12 h to obtain **4b** as a yellowish solid (149 mg, 0.57 mmol, 57%). Melting point range: 147–149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.62 (s, 3 H), 6.95 (s, 1 H), 7.44–7.52 (m, 1 H), 7.54–7.61 (m, 1 H), 7.73–7.90 (m, 2 H), 8.04 (d, *J*=8.06 Hz, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ = 14.3, 102.6, 104.6, 123.5, 125.0, 125.4, 125.7, 126.2, 126.4, 127.8, 131.2, 148.7, 155.7 ppm; HRMS (ESI) calcd. for $C_{15}H_{12}BrO_3$ $[M+OAc]^-$ *m/z* 318.9975 found *m/z* 318.9995.

7-Bromo-2-methylnaphtho[2,1-b]furan (4c):[33]

p-TSA·H_2O (10 mg, 5 mol%), 6-bromonaphthalen-2-ol **1c** (223 mg, 1.0 mmol) and prop-2-yn-1-ol **2m** (168 mg, 3.0 mmol) were treated as described for the synthesis of **4a** for 12 h to obtain **4c** as a yellowish solid (131 mg, 0.50 mmol, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.58 (s, 3 H), 6.85 (s, 1 H), 7.49–7.59 (m, 1 H), 7.59–7.66 (m, 2 H), 7.95 (d, *J*=8.22 Hz, 1 H), 8.09 (d, *J*=1.76 Hz, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ = 14.2, 101.6, 113.1, 117.8, 122.7, 125.2, 129.0, 130.6, 131.4, 152.0, 155.3 ppm.

2-Methyl-1-phenylnaphtho[2,1-b]furan (4d):[34]

p-TSA·H_2O (10 mg, 5 mol%), ß-Naphthol **1a** (144 mg, 1.0 mmol) and 1-phenylprop-2-yn-1-ol **2n** (396 mg, 3.0 mmol) were treated as described for the synthesis of **4a** to obtain **4d** as a brown oil (158 mg, 0.61 mmol, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.46 (s, 3 H), 7.29–7.35 (m, 1 H), 7.41 (td, *J* = 7.49, 1.13 Hz, 1 H), 7.44–7.59 (m, 5 H), 7.62–7.75 (m, 2 H), 7.79 (d, *J* = 8.31 Hz, 1 H), 7.94 (d, *J* = 8.06 Hz, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ = 12.3,

112.0, 118.9, 122.3, 123.2, 124.0, 124.5, 125.6, 127.5, 127.9, 128.6, 128.8, 130.5, 130.7, 134.2, 151.2, 151.2 ppm.

1,2-dimethylnaphtho[2,1-b]furan (4e):[35]

p-TSA·H_2O (10 mg, 5 mol%), ß-Naphthol **1a** (144 mg, 1.0 mmol) and but-3-yn-2-ol **2o** (210 mg, 3.0 mmol) were treated as described for the synthesis of **4a** to obtain **4e** as a reddish oil (102 mg, 0.52 mmol, 52%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.50 (s, 3 H), 2.59 (s, 3 H), 7.48 (t, *J*=7.05 Hz, 1 H), 7.52–7.63 (m, 2 H), 7.63–7.70 (m, 1 H), 7.96 (d, *J*=8.06 Hz, 1 H), 8.41 (d, *J*=8.06 Hz, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 11.4, 11.7, 111.7, 112.1, 123.0, 123.2, 123.7, 123.9, 125.7, 128.7, 128.9, 130.6, 149.9, 151.2 ppm.

7H-benzo[c]carbazole (4f):[36]

$Pd(OAc)_2$ (23 mg, 10 mol%), $Cu(OAc)_2$ (182 mg, 1.0 mmol) and *N*-phenylnaphthalen-2-amine **3h** (219 mg, 1.0 mmol) was refluxed in 3 mL dry acetonitrile for 24 h. $Pd(OAc)_2$ (23 mg, 10 mol%) and $Cu(OAc)_2$ (182 mg, 1.0 mmol) was added and the reaction was continued for another 24 h. After completion of the reaction, acetonitrile was evaporated and the residue was purified by flash column chromatography to obtain **4f** as a reddish brown oil (65 mg, 0.30 mmol, 30%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 (t, *J* = 7.43 Hz, 1 H), 7.45–7.54 (m, 2 H), 7.60 (d, *J* = 8.06 Hz, 1 H), 7.65 (d, *J* = 8.81 Hz, 1 H), 7.68–7.77 (m, 1 H), 7.89 (d, *J* = 8.56 Hz, 1 H), 8.03 (d, *J* = 8.31 Hz, 1 H), 8.47 (br. s., 1 H), 8.60 (d, *J* = 7.81 Hz, 1 H), 8.81 (d, *J* = 8.06 Hz, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 104.5, 111.1, 112.6, 120.2, 122.0, 123.0, 123.2, 124.0, 124.3, 126.9, 127.4, 129.2, 129.2, 129.9 ppm.

10-Fluoro-7H-benzo[c]carbazole (4g):[37]

$Pd(OAc)_2$ (46 mg, 20 mol%), $Cu(OAc)_2$ (364 mg, 2.0 mmol) and *N*-(4-fluorophenyl)naphthalen-2-amine **3i** (237 mg, 1.0 mmol) was refluxed as described for the synthesis of **4f** to obtain **4g** as a brown solid (73 mg, 0.31 mmol, 31%). ^{1}H NMR (400 MHz,

$CDCl_3$): δ = 7.22 (td, *J* = 8.88, 2.39 Hz, 1 H), 7.39–7.55 (m, 2 H), 7.62 (d, *J* = 8.81 Hz, 1 H), 7.74 (t, *J* = 7.68 Hz, 1 H), 7.89 (d, *J* = 8.81 Hz, 1 H), 8.02 (d, *J* = 8.06 Hz, 1 H), 8.22 (dd, *J* = 10.07, 2.27 Hz, 1 H), 8.42 (br. s., 1 H), 8.66 (d, *J* = 8.31 Hz, 1 H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 107.4, 107.6, 111.4, 111.5, 112.1, 112.4, 112.6, 122.8, 123.2, 127.1, 128.1, 129.1, 129.2, 129.7, 134.7, 138.3, 156.7, 159.1 ppm.

10-Methoxy-7H-benzo[c]carbazole (4h):[38]

$Pd(OAc)_2$ (46 mg, 20 mol%), $Cu(OAc)_2$ (364 mg, 2.0 mmol) and N-(4-methoxyphenyl)naphthalen-2-amine **3j** (249 mg, 1.0 mmol) was refluxed as described for the synthesis of **4f** to obtain **4h** as a deep green solid (94 mg, 0.38 mmol, 38%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.05 (s, 3 H), 7.15 (dd, *J*=8.81, 2.27 Hz, 1 H), 7.48–7.53 (m, 2 H), 7.64 (d, *J*=8.56 Hz, 1 H), 7.74 (ddd, *J*=8.31, 7.05, 1.26 Hz, 1 H), 7.87 (d, *J*=8.56 Hz, 1 H), 8.00–8.06 (m, 2 H), 8.36 (br. s., 1 H), 8.73 (d, *J*=8.56 Hz, 1 H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 56.2, 105.1, 111.6, 112.7, 113.5, 115.3, 122.8, 122.9, 124.4, 126.8, 127.4, 129.1, 129.2, 129.9, 133.4, 137.8, 154.4 ppm.

Gram Scale Experiment between 2-Naphthol (1a) and 1-Hexanol (2b): Catalyst *p*-TSA·H_2O (132 mg, 5 mol%), 2-Naphthol **1a** (2.00 g, 13.87 mmol) and 1-hexanol **2b** (4.25 g, 41.62 mmol) were taken in a 10 mL reaction vial under nitrogen atmosphere. The cap of the vial was closed and the reaction mixture was stirred at 120 °C for 12 h in an oil bath. After completion of the reaction (GCMS), the crude was directly purified by silica-gel (230–400 mess) column chromatography (flash) using 2% (*v*/*v*) ethyl acetate / hexane solution to afford the desired product 2-(hexyloxy)naphthalene **3b** as a colourless liquid (2.95 g, 12.90 mmol, 93%).

Acknowledgement

SB thanks DST-Inspire programme, Govt. of India for financial support and Faculty Award (DST/INSPIRE/04/2013/000017). AM thanks DST-Inspire for his project fellowship. We are thankful to Prof. Ganesh Pandey for his generous supports and Centre of Bio-Medical Research (CBMR) for infrastructural and financial assistances. We also thank Dr. Chattopadhaya for helpful discussions; Prof. Roy, Dr. Baishya and Mr. Ajay for their helps in NMR; Mr. Prashant and Mr. Durgaprasad for HRMS; and Ms. Ranjana for melting point determinations. We are extremely thankful to the corresponding reviewers for their valuable comments and suggestions.

Supporting Information Available

Optimization table, compound characterization checklist, and copies of ^{1}H and ^{13}C NMR Spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Footnotes

(1) For selected examples, see: Sach, N. W.; Richter, D. T.; Cripps, S.; Tran-Dubé, M.; Zhu, H.; Huang, B.; Cui, J.; Sutton, S. C. *Org. Lett.* **2012**, *14*, 3886.

(2) Mare, P. B. D. L. *Electrophilic halogenations*; Cambridge University Press: New York, **1976.**

(3) For selected examples, see: (a) Maiti, D.; Buchwald, S. L. *J. Org. Chem.* **2010**, *75*, 1791. (b) Larsson, P.-F.; Correa, A.; Carril, M.; Norrby P.–O.; Bolm, C. *Angew. Chem., Int. Ed.,* **2009**, *48*, 5691. (c) Buchwald S. L.; Bolm, C. *Angew. Chem., Int. Ed.*, **2009**, *48*, 5586. (d) Maiti, D.; Buchwald, S. L. *J. Am. Chem. Soc.,* **2009**, *131*, 17423. (e) Bistri, O.; Correa, A.; Bolm, C. *Angew. Chem., Int. Ed.,* **2008**, *47*, 586. (f) Shelby, Q.; Kataoka, N.; Mann, G.; Hartwig, J. F. *J. Am. Chem. Soc.,* **2000**, *122*, 10718.

(4) (a) Yu, D. –G.; Li, B. –J.; Zheng, S. –F.; Guan, B. –T.; Wang, B. –Q.; Shi, Z. –J. *Angew. Chem. Int. Ed.* **2010**, *49*, 4566. (b) Yu, D. –G. Shi, Z. –J. *Angew. Chem. Int. Ed.* **2011**, *50*, 7097. (c) Ackermann, L.; Pospech, J.; Potukuchi, H. K. *Org. Lett.* **2012**, *14*, 2146.

(5) (a) Furman, F. M.; Thelin, J. H.; Hein, D. W.; Hardy, W. B. *J. Am. Chem. Soc.* **1960**, *82*, 1450. (b) Charoonniyomporn, P.; Thongpanchang, T.; Witayakran, S.; Thebtaranonth, Y.; Phillips, K. E. S.; Katz, T. J.; *Tetrahedron Lett.* **2004**, *45*, 457. (c) Nakazawa, T.; Hirose, N.; Itabashi, K. *Synthesis* **1989**, 955.

(6) Murai, M.; Origuchi, K.; Takai, K. *Org. Lett.* **2014**, *16*, 3828.

(7) (a) A. Williamson, *Justus Liebigs Ann. Chem.* **1851**, *77*, 37. (b) J. March, March's Advanced Organic Chemistry, Reaction, Mechanisms and Structure, 5th ed., Wiley, New York, **2001**, p. 477.

(8) (a) Cazorla, C.; Pfordt, É.; Duclos, M. –C.; Métay, E.; Lemaire, M. *Green Chem.* **2011**, *13*, 2482 and references cited therein. (b) Bell, K. H.; Mccaffery, L. F. *Aust. J. Chem.* **1993**, *46*, 731.

(9) Veena, K.; Ramaiah, M.; Shashikaladevi, K.; Avinash, T. S.; Vaidya V. P. *J. Chem. Pharm. Res.* **2011**, *3*, 130.

(10) Schaefer, T.; Schildknecht, C.; Murer, P.; Lennartz, C.; Langer, N.; Wagenblast, G.; Metz, S. Phenanthro[9,10-*b*]furan derivatives and their preparation and use in electronic applications. PCT Int. Appl. 2012045710, April 12, 2012.

(11) (a) Mayr, H.; Kempf, B.; Ofial, A. R. *Acc. Chem. Res.* **2003**, *36*, 66; (b) Biswas, S.; Samec, J. S. M. *Chem. –Asian J.* **2013**, *8*, 974.

(12) Lee, D. –W.; Kwon, K. –H.; Yi, C. S. *J. Am. Chem. Soc.* **2012**, *134*, 7325.

(13) Schmidt, A. W.; Reddy, K. R.; Knölker, H. –J. *Chem. Rev.* **2012**, *112*, 3193.

(14) Bagdi, A. K.; Santra, S.; Monir, K.; Hajra, A. *Chem. Commun.* **2015**, *51*, 1555.

(15) Wang, H.; Wang, Y.; Peng, C.; Zhang, J.; Zhu, Q. *J. Am. Chem. Soc.* **2010**, *132*, 13217.

(16) No deuterium incorporation at any position of the aromatic ring was observed when **1a** or **1f** were treated with D_2O without using *p*-TSA even at 120 °C for 48 h.

(17) (a) For a mechanistic calculation, see, Jacobsson, M.; Oxgaard, J.; Abrahamsson, C. –O.; Norrby, P. –O.; Goddard III, W. A.; Ellervik, U. *Chem. –Eur. J.* **2008**, *14*, 3954; (b) Attempts to observe **B** by NMR spectroscopy have been unsuccessful, possibly because the equilibrium concentration is below the detectable range. Several ^{1}H, ^{13}C, No-D ^{1}H, ^{13}C NMR experiments were performed using different solvents and temperatures. Although small chemical shifting was observed in some cases, that did not provide sufficient characterizable data in support of intermediate **B**. Please refer to some copies of NMR spectra in the SI.

(18) Bunrit, A.; Dahlstrand, C.; Olsson, S. K.; Srifa, P.; Huang, G.; Orthaber, A.; Sjörberg, P.; Biswas, S.; Himo, F.; Samec, J. S. M. *J. Am. Chem. Soc.* **2015**, *137*, 4646.

(19) Sergeev, A. G.; Hartwig, J. F. *Science*, **2011**, *323*, 439.

(20) Liu, Y.; Park, S. K.; Xiao, Y. Chae, J. *Org. Biomol. Chem.* **2014**, *12*, 4747.

(21) Li, S.; Li, F.; Gong, J.; Yang, Z. *Org. Lett.* **2015**, *17*, 1240.

(22) Eichman, C. C.; Stambuli, J. P. *J. Org. Chem.* **2009**, *74*, 4005.

(23) Xie, Y.; Liu, S.; Liu, Y.; Wen, Y.; Deng, G. -J. *Org. Lett.* **2012**, *14*, 1692.

(24) Li, G.; Liu, Y.; Du, H. *Org. Biomol. Chem.* **2015**, *13*, 2875.

(25) Rao, D. N.; Rasheed, Sk.; Vishwakarma, R. A.; Das, P. *RSC Advances*, **2014**, *4*, 25600.

(26) Wang, Y. –F.; Zhang, F. –L.; Chiba, S. *Synthesis* **2012**, *44*, 1526.

(27) Xie, Y. –S.; Vijaykumar, B. V. D.; Jang, K.; Choi, K. –M.; Zuo, H.; Yoon, Y. –J.; Shin, D. –S. *Bull. Kor. Chem. Soc.* **2013**, *34*, 3881.

(28) Alvey, P. M.; Reczek, J. J.; Lynch, V.; Iverson, B. L. *J. Org. Chem.* **2010**, *75*, 7682.

(29) Tassoni, E.; Conti, R.; Gallo, G.; Vincenti, S.; Dell'Uomo, N.; Mastrofrancesco, L.; Ricciolini, R.; Cabri, W.; Carminati, P.; Giannessi, F. *ChemMedChem* **2010**, *5*, 666.

(30) Makriyannis, A.; Lu, D. *U.S. Pat. Appl. Publ.* **2007**, US 20070155701 A1.

(31) Pron, A.; Baumgarten, M.; Muellen, K. *Org. Lett.* **2010**, *12*, 4236.

(32) Youn, S. W.; Eom, J. I. *Org. Lett.* **2005**, *7*, 3355.

(33) Sharma, U.; Naveen, T.; Maji, A.; Manna, S.; Maiti, D. *Angew. Chem. Int. Ed.* **2013**, *52*, 12669.

(34) Kundu, D.; Samim, Md.; Majee, A.; Hajra, A. *Chem. –Asian J.* **2011**, *6*, 406.

(35) Kikas, I.; Skoric, I.; Marinic, Z.; Sindler-Kulyk, M. *Tetrahedron*, **2010**, *66*, 9405.

(36) Suzuki, C.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2015**, *17*, 1597.

(37) Jiang, Q.; Duan-Mu, D.; Zhong, W.; Chen, H.; Yan, H. *Chem. –Eur. J.* **2013**, *19*, 1903.

(38) Lim, Y. –K.; Jung, J. –W.; Lee, H.; Cho, C. –G. *J. Org. Chem.* **2004**, *69*, 5778.