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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b00161 • Publication Date (Web): 12 Mar 2019

Iodine(III)-Mediated, Controlled Di- or Monoiodination of Phenols

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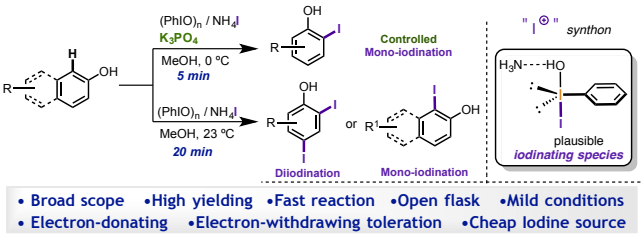


ABSTRACT: An oxidative procedure for the electrophilic iodination of phenols was developed by using iodosylbenzene as a non-toxic iodine(III)-based oxidant and ammonium iodide as a cheap iodine atom source. A totally controlled mono-iodination was achieved by buffering the reaction medium with K_3PO_4. This protocol proceeds with short reaction times, at mild temperatures, in an open flask and generally with high yields. Gram scale reactions, as well as the scope of this protocol, were explored with electron-rich and electron-poor phenols as well as heterocycles. Quantum chemistry calculations revealed PhI(OH)·NH_3 to be the most plausible iodinating active species as a reactive " I^+ " synthon. In light of the relevance of the iodoarene moiety, we present herein a practical, efficient and simple procedure with a broad functional group scope that allows access to the iodoarene core unit.

INTRODUCTION

Iodinated arenes and heteroarenes including indophenols are an important class of organic structures.[1] They are ubiquitous in marine natural products such as the terpenes or prostanoids isolated from sponges *Topsentia sp.*[2] or from corals of genus *Clavularia viridis*.[3] In the field of medical research, iodoarenes are found in pharmacologically active drugs,[4] in non-steroidal hormones L-thyroxine (T_4) and Liothyronine (T_3)[5] or in antifungal[6] or bactericidal compounds.[7] In chemistry, iodoarenes are found as starting materials in the synthesis of hypervalent I(V)[8] or iodine(III)[9] derivatives. They have also been found to be the best electrophiles in the Suzuki and Stille cross-coupling reactions, as well as the Sonogashira alkynylation and the Mizoroki-Heck olefination (Figure 1).[10]

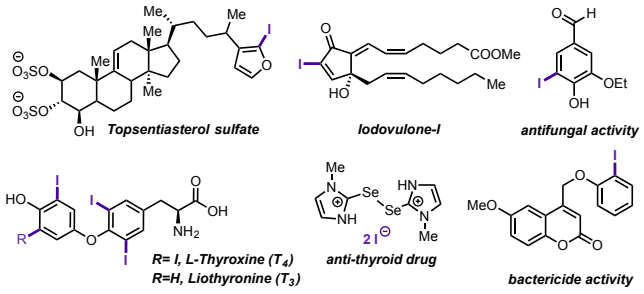
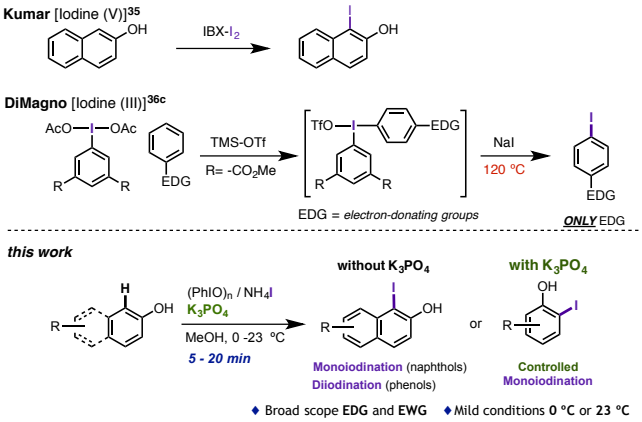


Figure 1. Relevance of the iodoarene moiety.

Due to the high relevance of the iodophenol moiety, several procedures have been developed to date for its synthesis. Among the most significant iodination strategies are those involving transition metals such as Ru,[11] In,[12] Pd,[13] Mo,[14] Hg,[15] Fe,[16] Ce,[17] Yb[18] or Ag.[19] A number of transition-metal-free iodination procedures have also been described using I_2 in combination with 1,4-bis(triphenylphosphonium)-2-butene peroxodisulfate,[20] DMSO,[21] HIO_3,[22] urea-H_2O_2,[23] or NO_2.[24] An additional strategy consists of the oxidation of iodide salts using the systems NH_4I/H_2O_2,[25] $NaI/NaClO_2$[26] or $NaClO_2$/NaI/HCl.[27] On the other hand, iodination reactions based on the use of (I^+) synthons are frequently carried out with ICl,[28] *N*-iodosaccharin,[29] IPy_2BF_4[30] and NIS in harsh acidic media such as TFA,[31] TfOH,[32] and HFIP.[33] Additionally, radical iodination using I_2/TBHP[34] has recently been developed. Finally, a much less well exploited strategy for the oxidative iodination of arenes and phenols involves the use of hypervalent iodine(V)[35] or iodine(III) reagents. The few procedures using iodine(III)[36] have a common strategy involving the synthesis of a diaryliodonium salt as an intermediate, which then reacts with a metallic iodide, typically NaI. This intermediate undergoes a thermally-promoted reductive elimination, allowing the formation of two different aryl iodides[37] from the iodonium salt at high temperatures (Scheme 1).

Scheme 1. Hypervalent iodine strategies for the iodination of arenes and phenols.

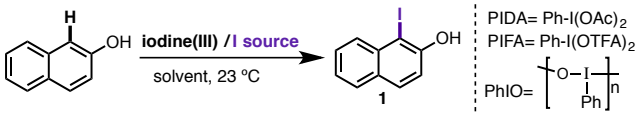


In general, iodination methods of phenols require expensive transition metals or are based on oxidative procedures using strong oxidants, leading to poor functional group compatibility. To overcome this problem, hypervalent reagents appear to be an excellent alternative. With respect to the known hypervalent-based iodination procedures of phenols, the very few of them that available are synthetically restricted in several ways, the most significant being low selectivity,[35] polyhalogenation, expensive starting materials,[36] more than one preparation step, limitation to electron-rich arenes, very narrow scope, and the requirement for high temperatures, strong Lewis acids and/or long reaction times. All of the aforementioned aspects make an efficient iodine(III)-based iodination procedure elusive. Therefore, we were interested in developing a new and systematic alternative iodination of phenols by using the hypervalent iodine(III) reagent iodosylbenzene (PhIO) in combination with NH_4I, an inexpensive source of iodine atoms. The scope and advantages of our new method are detailed herein, and theoretical calculations supporting the plausible operation of $PhI(OH)\cdot NH_3$ as the iodinating species are provided.

RESULTS

Our initial optimization of the iodination reaction used 2-naphthol as a model system, the results of which are tabulated in Table 1.

Table 1. Optimization of the iodine(III)-mediated electrophilic iodination of 2-naphthol.[a]



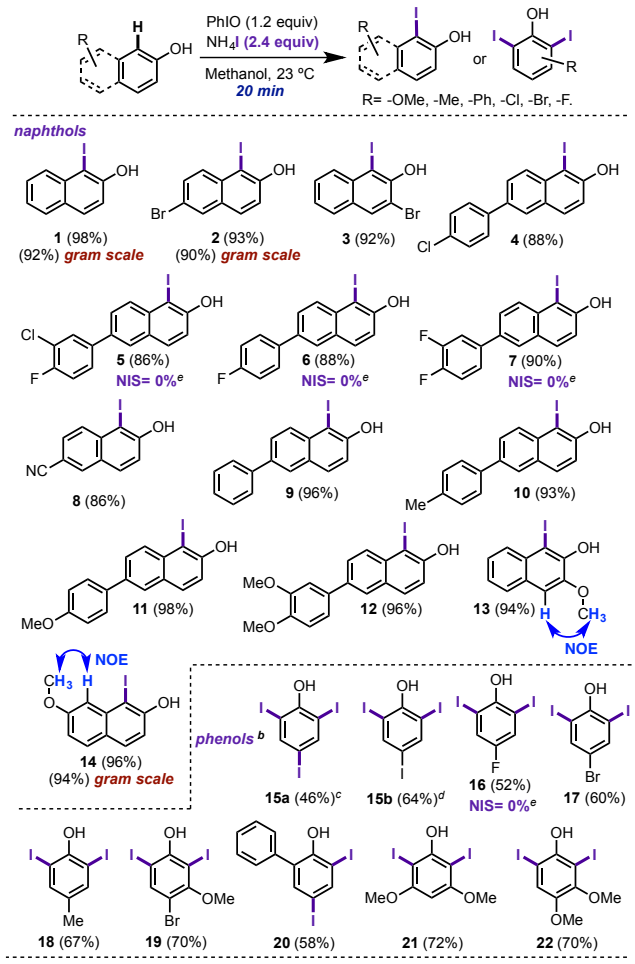
Entry	iodine(III) (equiv)	I Source (equiv)	Solvent	Yield (%)[b]
1	PIDA (1.2)	AlI_3 (2.4)	MeCN	-- [c]
2	PIFA (1.2)	AlI_3 (2.4)	MeCN	-- [c]
3	PhIO (1.2)	KI (2.4)	MeOH	17
4	PhIO (1.2)	KI (2.4)	H_2O	< 5
5	PhIO (1.2)	KI (2.4)	MeOH	86[d]
6	PhIO (1.2)	KI (2.4)	H_2O	25 [d]
7	PhIO (1.2)	KI (2.4)	MeOH / H_2O	38
8	***PhIO (1.2)***	***NH_4I (2.4)***	***MeOH***	***98***[e]
9	PhIO (1.2)	NH_4I (2.4)	MeCN	70
10	PhIO (1.0)	NH_4I (2.4)	MeOH	80
11	PhIO (0.5)	NH_4I (2.4)	MeOH	40
12	PhIO (1.2)	NH_4I (1.5)	MeOH	68
13	-	I_2 (1.0)	MeOH	58
14	-	I_2 (1.5)	MeOH	52
15	-	I_2 (2.0)	MeOH	46
16	-	I_2 (1.0)	TFE	57
17	PhIO (1.2)	-	MeOH	n.r.
18	--	NH_4I (2.4)	MeOH	n.r.

[a] Reaction conditions: 2-naphthol (0.5 mmol), solvent (0.15 *M*), open flask. [b] Yields as average of two runs. [c] I_2 was obtained. [d] 5 mol% of H_2SO_4 used as additive. [e] Yields as average of three runs. n.r. = no reaction observed.

The starting conditions were based on our previous chlorination[38] and bromination[39] procedures. Thus, 1.2 equivalents of PIDA or PIFA were used, along with 2.4 equivalents of AlI_3 in acetonitrile at room temperature (entries 1 and 2). Unfortunately, only molecular iodine was obtained as product in this trial. Different conditions were explored by changing the iodine(III) reagent from PIDA / PIFA to iodosylbenzene (PhIO). Iodide salts were also considered as the iodine atom source. In line with the results of Kita and coworkers, both PIFA and PIDA are prone to generate radicals when mixed with halogen salts having cations different to ammonium.[40] The topic about radical generation is outside of this work scope, hence PhIO was chosen as the iodine(III) reagent. Initial trials used potassium iodide in methanol to solubilize both PhIO and KI. In this way, **1** was isolated in a 17% yield (entry 3). The reaction in water as solvent showed poor conversion (<5%) and large quantities of unreacted starting material (entry 4). The use of 5 mol% of sulfuric acid as additive significantly increased the yield to 86% in methanol (entry 5) and 25% in water (entry 6). The (1:1) solvent combination of methanol and water did not improve the yield (entry 7), however it demonstrated that the reaction is water tolerant. As acidic media gave considerably better yields, another protic iodide salt was explored. Surprisingly, use of 1.2 equivalents of PhIO and 2.4 equivalents of ammonium iodide in methanol at 23 ºC provided 1-iodo-2-naphthol in nearly quantitative yield (98%) within 20 minutes (entry 8). This result highlighted several aspects of the process, such as the fast and high-yield reactions as well as its economical iodine atom source. Additionally, we avoid the possibility of the radical generation in the process since is used the ammonium cation. Changing the solvent to acetonitrile lowered the yield to 70% (entry 9). Decreasing the amount of PhIO (to 1.0 and 0.5 equivalents) provided yields of only 80% and 40%, respectively (entries 10 and 11). On the other hand, the yield was not improved by decreasing the ammonium iodide loading to 1.5 equivalents (entry 12). At this point the possibility of the iodide anion oxidation generating molecular iodine was considered, which could be the iodinating active species in the process. To test this mechanistic hypothesis, experiments using molecular iodine in absence of an iodine(III) reagent were carried out, using the conditions found to be best in the initial optimizations (entry 8). Thus, the reaction was tested with 1.0, 1.5 and 2.0 equivalents of molecular iodine at 23 ºC in methanol (entries 13-15) or trifluoroethanol (entry 16). Interestingly, the desired iodination was achieved with yields of 58%, 52%, 46% and 57% respectively. However, the yields remain far below that obtained in entry 8, thus molecular iodine was ruled out as the iodinating species. Control experiments were then carried out in order to complete the optimization. The use of PhIO in the absence of ammonium salt led to no reaction (entry 17). Similarly, the use of ammonium iodide without the iodine(III) reagent failed to produce **1**.

This set of experiments allowed reliable determination of the optimal iodination conditions, thus we proceeded to explore the scope of the new procedure with respect to changes in the aryl unit (Scheme 2).

Scheme 2. Phenol ring scope in the PhIO/NH_4I-mediated iodination of phenols.[a]

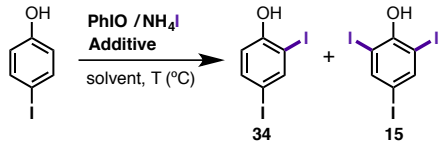


[a] Reaction conditions: 2-naphthol (0.5 mmol), methanol (0.15 *M*), open flask. [b] PhIO (2.4 equiv) / NH_4I (4.8 equiv) were used. [c] Synthesized from phenol. [d] Synthesized from 4-iodophenol. [e] Reaction conditions: phenol (0.5 mmol), NIS (1.2 equiv), TFA (10 mol%), MeCN (0.15 *M*) at 23 ºC by 12 h.

Several mono-annular phenols and naphthols were submitted to our optimized iodination conditions. We observed that the reaction shows great tolerance towards naphthols containing the electron-withdrawing groups bromine (**2** and **3**), chlorine (**4** and **5**), fluorine (**6** and **7**) or nitrile (**8**); as well as the electron-donating groups phenyl (**9**), tolyl (**10**), and methoxyl (**11** and **12**). The reaction took place regioselectively at the *ortho* position with respect to the hydroxyl group, in no more than 20 minutes and with good yields ranging from 86% to 98%. The NOESY correlation of methoxyl protons in **13** and **14** with the *ortho* protons at C4 and C8 demonstrated the observed regiochemistry (Scheme 2). Moreover, the scalability was illustrated by the gram-scale preparation of **1**, **2** and **14** in excellent yields (93-98%). On the other hand, when the procedure was applied to the iodination of mono-annular phenols, a mixture of unreacted starting material, mono- and diiodinated derivatives was obtained, in which case an additional amount of PhIO/NH_4I was necessary to complete the reaction. Under these conditions a range of phenols bearing electron-attracting fluorine, bromine or iodine groups (**15**-**17**), as well as electron-rich phenols bearing methyl, methoxyl and phenyl groups (**18**-**22**) were diiodinated in moderate to good yields (46-72%). Although it was expected to obtain the monoiodination products, the synthesized derivatives **15**-**22** are also important building blocks in synthetic chemistry.[8-10] On the other hand, the reactivity of our system was compared against the commonly used reagent NIS. Different phenols containing strong electron-withdrawing groups (**5**- **7** and **16**) which usually show great difficulties to react, undergo iodination reaction with moderate (52%) to excellent yields (86-90%) by using our system.

From this initial scope exploration, it is possible to conclude that the optimized conditions allow the controlled monoiodination of naphthols, while phenols are diiodinated. Inspired by these results, we were interested in developing controlled monoiodination reactions, thus a new optimization was initiated using 4-iodophenol as the model system (Table 2).

Table 2. Optimization of the PhIO/NH_4I-mediated, controlled monoiodination of phenols.[a]



Entry	PhIO (equiv)	NH_4I (equiv)	Additive (equiv)	Solvent	T (ºC)	Yield (%) 34 / 15
1	1.2	2.4	--	MeOH	23	-- / 64
2	1.2	2.0	--	MeOH	23	-- /56
3	1	1.5	--	MeOH	23	-- / 60
4	1.2	2.4	--	MeCN	23	n.r.
5	1.2	2.4	--	H_2O	23	n.r.
6	1.2	2.4	--	MeOH	0	25 / 36
7	1.2	2.4	K_3PO_4 (1.5)	MeOH	0	80 / 5
8	***1.2***	***2.4***	***K_3PO_4 (1.0)***	***MeOH***	***0***	***88 / --***
9[b]	1.2	2.4	H_2SO_4	MeOH	23	-- / 55
10[b]	1.2	2.4	H_2SO4	MeOH	0	10 / 28

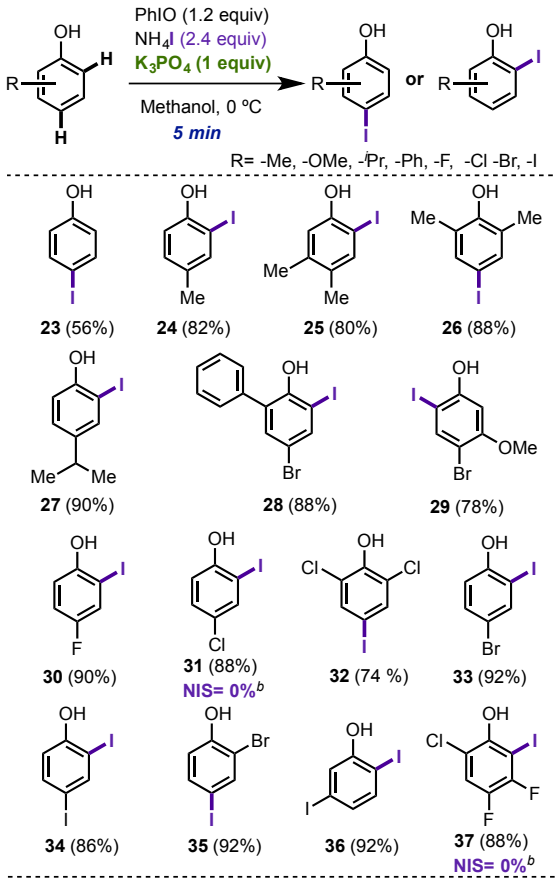
[a] Reaction conditions: 4-iodophenol (0.5 mmol), solvent (0.15 *M*), open flask. [b] 5 mol% of additive was used. n.r. = no reaction observed.

The optimal previous conditions afforded the diiodinated phenol **15** in 64% yield at 23 ºC (entry 1). By reducing the NH_4I loading to 2.0 or 1.5 equivalents, and the PhIO loading to 1.0 equivalent, **15** was systematically obtained in lower yields (entries 2 and 3). Changing the solvent to acetonitrile or water did not yield any product (entries 4 and 5). However, when the reaction was carried at 0 ºC in methanol, a mixture of mono- and diiodinated phenols was observed, but the starting material was not fully consumed (entry 6). This result highlights the important role of the temperature in controlling the reaction. At this point we hypothesized that a slightly acidic media could be influencing the outcome due to the inherently acidic nature of NH_4I, as well as the release of H^+ after the aromatization process. This could be eroding the control over the monoiodination process, since it is well known that acidic media accelerates the iodination process, leading to unwanted polyhalogenation.[22,27,31-33] In consequence, we decided to buffer the reaction pH by using tribasic potassium phosphate as an additive.[41] To

our delight, the use of 1.5 equivalents of K_3PO_4 at 0 ºC gave rise to the monoiodination product **34** in 80% yield in *only five minutes of reaction*, in addition to a small amount (5%) of the diiodination product **15** (entry 7). Upon decreasing the phosphate salt loading to 1.0 equivalents, the yield of **34** increased to 88% and the diiodination derivative **15** was not observed. These reaction conditions finally facilitated the totally ***controlled mono-iodination*** of the 4-iodophenol. To validate if the acidic medium is responsible for the observed diiodination in the reaction we performed the reaction with 5 mol% of sulfuric acid as additive. Under these conditions (at 23 ºC) the complete consumption of the starting material was observed, but with only a 55% yield to the diiodination product **15**, in a complex reaction mixture (entry 9). When the reaction was carried at 0 ºC, a mixture of **34** and **35** was obtained (entry 10). These results strongly point towards the diiodination being promoted by acidic medium.

After this analysis and determination of the optimal conditions, we explored the scope of the controlled monoiodination of phenols (Scheme 3).

Scheme 3. Scope of the PhIO/NH_4I-mediated, controlled monoiodination of phenols[a]



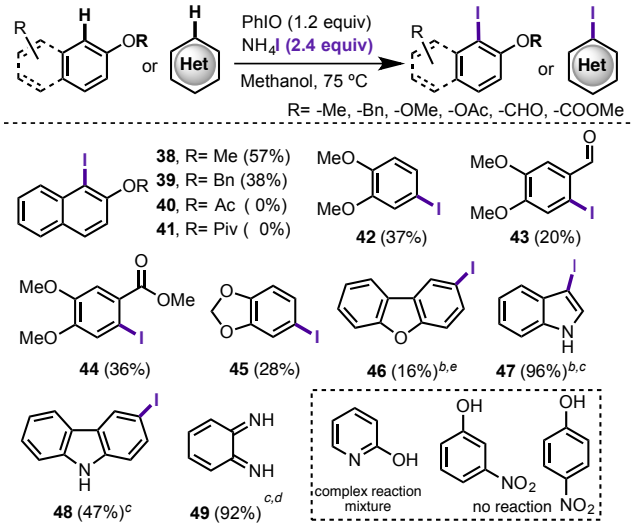
[a] Reaction conditions: phenol (0.5 mmol), methanol (0.15 *M*), open flask. [b] Reaction conditions: phenol (0.5 mmol), NIS (1.2 equiv), TFA (10 mol%), MeCN (0.15 *M*) at 23 ºC by 12 h.

A number of monoannular phenols bearing groups with different electronic nature were tested in the controlled monoiodination reaction. The exploration started with the simplest phenol (hydroxybenzene), leading to the monoiodinated product **23** in 56% yield in only five minutes. Neither the *ortho* regioisomer nor the diiodinated product were observed. Other monoiodinated phenols bearing alkyl groups, such as one (**24**) or two methyl groups (**25** and **26**) or an isopropyl (**27**) were successfully obtained in good yields ranging from 80 to 90%. Phenols containing electron-rich groups such as phenyl or methoxyl (**28** and **29**) afforded excellent monoiodination yields (88 and 78%). Additional examples involving phenols with the electron-attracting fluoride (**30**), chloride (**31** and **32**), bromide (**33** and **35**) or iodide (**34** and **36**) groups were tolerated very well, leading to the totally controlled introduction of a single iodine atom in high to excellent yields (86-92%). Even the strongly deactivated 2-chloro-4,5-difluorophenol led to the monoiodinated **37** in 88% yield. This starting phenol as well as the 4-chlorophenol did not react under the typically iodination conditions with NIS.

This set of monoiodinated phenols obtained demonstrated the scope and the excellent applicability of this methodology, allowing the use of both electron-rich and -poor monoannular phenols. The short reaction times (ca. 5 min.), good yields, and mild and open-flask reaction conditions are important aspects to be highlighted. To the best of our knowledge this is the first report describing a totally controlled monoiodination of phenols using a buffered system.

The following set of trials was devised to determine the tolerance of our procedure in the presence of: 1) different functional groups at the phenolic oxygen, 2) functionalized phenols with more than one functional group, 3) functionalities other than phenol present in the aryl moiety, and 4) heterocycles (Scheme 4).

Scheme 4. Functional group scope in the PhIO/NH_4I-mediated iodination of arenes and heteroarenes.[a]



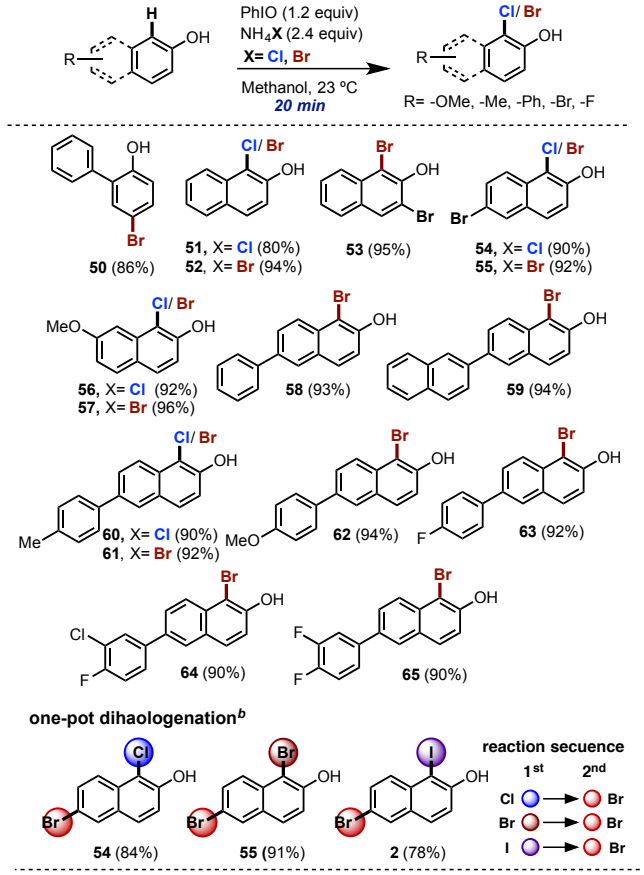
[a] Reaction conditions: arene (0.5 mmol), methanol (0.15 *M*), open flask. [b] One equivalent of NH_4I was used. [c] Reaction carried out at 23 ºC. [d] *o*-phenylenediamine was the starting material. [e] Combined yield of the mono- and diiodination at the 2,8 positions in a (1.5:1) ratio.

The first attempts to carry out the iodination reaction were evaluated using 2-methoxynaphthalene as the model system. However, no reaction was observed when the standard conditions (PhIO 1.2 equiv / NH_4I 2.4 equiv, 23 ºC) were applied, suggesting the importance of the hydroxyl group. By heating this reaction to 75 ºC, using the same stoichiometry, the iodination provided a 57% yield of **38**. By increasing the size of

the alkyl group through the use of a benzyl-substituted substrate, iodide **39** was obtained in only 38% yield. When the acetyl **40** and pivaloyl **41** derivatives were submitted to the same reaction conditions, no product was formed. Functionalities at the aryl moiety other than phenol, such as phenol-ether (**42**), aldehyde (**43**) or ester (**44**) could only be iodinated in moderate to low yields (20-37%). Moreover, oxy-heterocycles as well as nitrogenated heterocycles were tested. In these cases, the iodination of a 1,3-benzodioxole, dibenzofuran, as well as free N-H indoles and carbazoles (**45**-**48**) were achieved in low to excellent yields (16-96%) by using only one equivalent of NH_4I. Is important to mention that dibenzofuran gave rise to a (1.5:1) ratio of mono- and diiodinated products. Finally, *o*-phenylenediamine gave rise to the 1,2-diimine oxidation product **51** in 91% yield rather than the expected iodination product. Other substrates such as pyridine-2-ol, as well as 3-nitro- and 4-nitrophneol showed complex reaction mixtures or did not react even by heating at 75 ºC for a period of 24 h.

A complementary scope exploration was considered in order to determine if different halogens can be introduced by changing the anion in the ammonium salt, thereby a range of phenols were examined (Scheme 5).

Scheme 5. Scope of the NH_4X salt in the PhIO/NH_4X-mediated chlorination and bromination of phenols.[a]



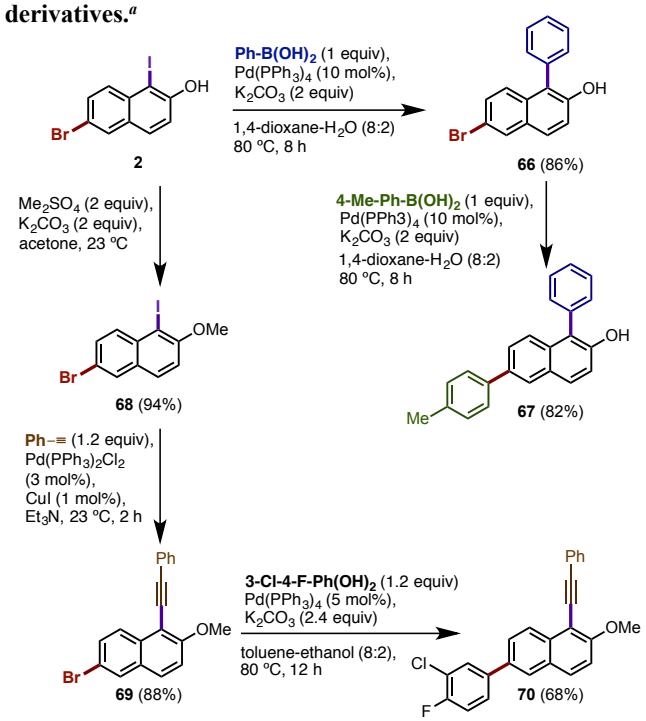
[a] Reaction conditions: phenol (0.5 mmol), methanol (0.15 *M*), open flask. [b] overall yield for the one-pot dihalogenation reaction using 2-naphthol as starting material.

The ammonium chloride and bromide were mainly employed under the optimized standard conditions (scheme 5) in order to introduce these halides into a range of phenols. In this way, 2-phenylphenol was brominated in 86% yield, giving rise to **50**. The chlorination and bromination of 2-naphthol, 6-bromo-2-naphthol, 7-methoxy-2-naphthol and 6-(*p*-tolyl)-2-naphthol also produced their corresponding chlorinated and brominated derivatives **51** and **52**, **54**-**57**, **60** and **61**, respectively, in 80-96% yields. A number of additional brominated phenols containing electron-withdrawing (**53**, **62**-**65**) and electron-donating groups (**58** and **59**) were isolated in high yields (90-95%), which demonstrated the excellent efficiency of our protocol. In fact, these described conditions resulted in a general improvement of our previous iodine(III)-mediated chlorination[38] and bromination[39] procedures. It is also important to mention that a very complex reaction mixture was observed when NH_4F was used, presumably due to formation of a strongly oxidizing reagent that degraded the starting material. To conclude the exploration of the scope of the halide salt, a one-pot two-halogenation-reaction sequence was attempted. Thus, starting from 2-naphthol, the one-pot chlorination-bromination sequence afforded **54** in an 84% overall yield. Similarly, tandem bromination-bromination and iodination-bromination sequences gave rise to **55** and **2** in 91% and 78% yields, respectively.

In addition to its broad scope, these tests demonstrated the exciting and varied possibilities of this reaction method, including high-yielding bis-iodination, fully controlled monoiodination, and chlorination or bromination of phenols possessing a free hydroxyl group.

To conclude the experimental part of this study, a series of reactions were devised to showcase the synthetic utility of the reaction (Scheme 6).

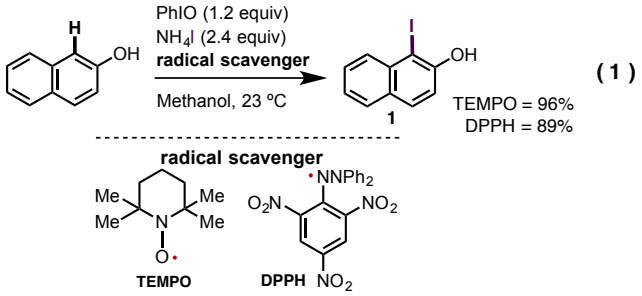
Scheme 6. Synthetic utility of the synthesized halogenated derivatives.[a]



The synthetic applicability of the derivatives obtained through our procedure was illustrated with the compound 6-bromo-1-iodo-2-naphthol (**2**) which possesses two halide groups with different reactivities. We considered the synthesis of **2** as an excellent opportunity to carry out two distinct orthogonal reaction sequences: sequential double Suzuki cross-coupling, and Sonogashira alkynylation / Suzuki cross-coupling. In

the first sequence, regioselective Suzuki cross-coupling at the C1 atom of **2** with phenyl boronic acid led to the formation of the 6-bromo-1-phenyl-2-naphthol **66** in 86% yield. The second Suzuki cross-coupling with 4-methylboronic acid introduced the *p*-tolyl fragment exclusively at the C6 position, affording the diarylated naphthol **67** in 82% yield. The second sequence started with the *O*-methylation of **2**, producing **68** in 94% yield. This compound was submitted to Sonogashira alkynylation conditions, giving rise to **69** in 88% yield with regioselective functionalization at the C1 position. The methylated alkynyl naphthol underwent subsequent Suzuki cross-coupling with (3-chloro-4-fluorophenyl)boronic acid leading to the formation of **70** in 68% yield with the regioselective functionalization at C6 of the naphthol.

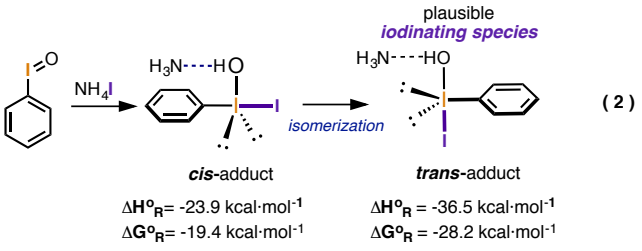
Finally, in order to gain more insight into the reaction mechanism, we decided to carry out the iodination of 2-naphthol in the presence of the radical scavengers TEMPO[42] (tetramethylpiperidine *N*-oxide) and DPPH (2,2-diphenyl-1-picrylhydrazyl) in order to determine if a radical or cationic pathway was operating (Eq. 1).



(1)

The presence of 1 equivalent of TEMPO or DPPH did not affect the reaction, and **1** was isolated in 96% and 89% yield respectively. This experiment ruled out a radical mechanism in the process, suggesting a cationic iodination as the more feasible pathway.

To provide a preliminary determination of the iodinating active species involved in this process, a DFT computational study was performed at the B3LYP/DGDZVP level[43] (Ec. 2).



(2)

The enthalpy and Gibbs free energy of the reaction between PhIO and NH_4I were calculated to evaluate the energetic stability of the obtained product. The resulting values strongly suggested the formation of the *trans*-adduct PhI(OH)·NH_3 as the most plausible active iodinating species. This hypervalent iodine(III) derivative is obtained after the isomerization of its corresponding *cis*-adduct which is formed initially as the kinetic product; while the aforementioned *trans*-PhI(OH)·NH_3 is the thermodynamic compound (see SI for full details).[44] We verified that the optimized geometry of the iodinating active species corresponds to a minimum on the potential energy surface by performing harmonic frequency calculations at 298 K and 1 atm (selected bond lengths and angles are included, see SI).

On the other hand, the electrophilic nature of the plausible iodinating species was analyzed by using the Fukui functions as the covalent descriptor[45-46] (Figure 2).

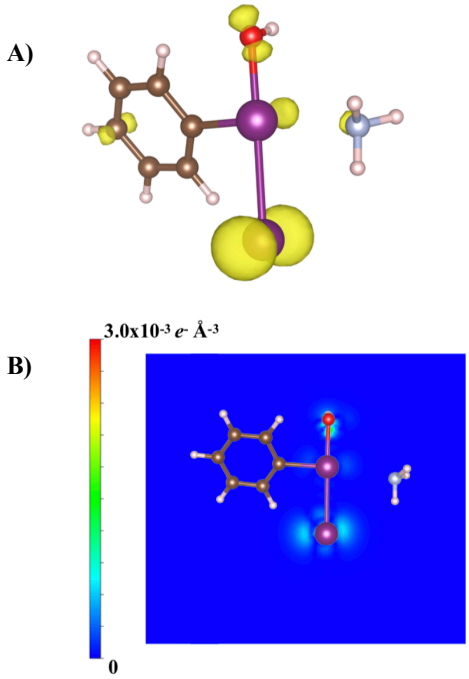


Figure 2. (a) The Fukui function for electrophilic attack of the plausible iodinating active species and (b) its 2D projection. Color code for atoms in brackets: C (Brown), O (red), I (purple), (N) light blue and H (pink).

The highest values of the calculated Fukui function (Figure 2a) showed the most electrophilic site[47] at the terminal iodine atom as an electrophilic center[48] which is identified with the isosurface in yellow color. It is clearly observed that the terminal iodine is the most electrophilic atom of the adduct PhI(OH)·NH_3, which is in agreement with our proposed cationic iodination mechanism. A 2D projection of the electrophilic form of the Fukui function (Figure 2b) is illustrated to evaluate the reactivity and susceptibility of the iodinating adduct towards electrophilic attacks. The full results of this mechanic study will be published separately.

CONCLUSIONS

In summary, we have developed a new hypervalent iodine(III)-based iodination procedure of phenols by using iodosylbenzene (PhIO) and ammonium iodide (NH_4I) as an inexpensive source of iodine atoms. This protocol was applied to a wide range of different arenes including aromatic and heteroaromatic derivatives. The best yields were obtained with phenols having at least one free hydroxyl group, and total control over the di- or monoiodination was achieved by buffering the reaction with tribasic potassium phosphate (K_3PO_4). This novel procedure takes place under mild, open-flask, one-step and operationally simple reaction conditions with short reaction times (5 to 20 min) and high yields. Initial mechanistic investigations showed PhI(OH)·NH_3 to be the most plausible iodinating species in the process.

EXPERIMENTAL SECTION

Organic synthesis.

General Information. All moisture- and oxygen-sensitive reactions were carried out in flame-dried round-bottom flasks under an inert atmosphere of nitrogen. Unless otherwise specified, all commercial materials were used as received without further purification. Anhydrous solvents were purchased from Sigma-Aldrich in SureSeal bottles. Column chromatography was performed using silica gel of sizes 100−200 and 230−400 mesh (Sigma-Aldrich). Thinlayer chromatography was performed with TLC silica gel 60 F256 plates, and visualization was effected with short wavelength UV light (254 nm). Compounds were characterized using ^{1}H NMR and ^{13}C NMR. (Copies of ^{1}H NMR and ^{13}C NMR spectra are provided for all the compounds in the SI.) Data of known compounds were compared with existing literature characterization data, and the references are given. ^{1}H and ^{13}C NMR spectra were recorded with 500 MHz and Bruker advance 400 MHz instruments using deuterated solvents purchased from Sigma-Aldrich like $CDCl_3$. ^{1}H spectra were referenced with tetramethyl silane (TMS, 0.0 ppm) or chloroform ($CDCl_3$, 7.26 ppm) and are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz), and integration. Chemical shifts of the ^{13}C NMR spectra were measured relative to CDCl3 (δ = 77.16 ppm). All the starting materials were synthesized according to reported procedures in the literature. High-resolution masses (HRMS) analyses were obtained under the following procedure: Samples were introduced by direct infusion at 3 μL min^{-1} to the electrospray ionization (ESI) source of a quadrupole time-of-flight mass spectrometer (Bruker Daltonics ESI-QTOF-MS maXis impact), equipped with Data Analysis 4.1. ESI was operated in positive mode with ion spray voltage 4 500 V, nitrogen dry gas 4 L min^{-1}, drying temperature 180 °C, and gas pressure 0.4 bar. Mass calibration was accomplished based on sodium formate clusters. Chemical nomenclature was generated using Chemdraw. Infrared (IR) spectra were recorded using PerkinElmer system 2000 FT-IR spectrometer. Melting points of solids were measured using a Fisher-Johns melting point apparatus.

Synthesis of iodosylbenzene $(PhIO)_n$. In a 250 mL round-bottom flask was suspended bis(acetoxy)iodobenzene (PIDA) (10 g, 31.04 mmol, 1 equiv) in 150 mL of a 3 *M* NaOH solution. The reaction was strongly stirred to room temperature during 12 h. Then, a precipitate was formed which was filtered-off and washed with cold water until pH of water was neutral. Then the solid was washed (3x10 mL) with $CHCl_3$ to remove impurities of PIDA. The obtained solid was dried at high vacuum without heating to yield $(PhIO)_n$ (6.2 g, 91%) as yellowish solid. *Caution: $(PhIO)_n$ is explosive upon drying at 110 ºC in vacuum conditions.*

General Procedure A. A 25 mL oven-dried round-bottom flask equipped with a magnetic stirrer bar was charged with the corresponding phenol (0.5 mmol, 1 equiv) and methanol (0.15 *M*) at 25 °C. After dissolving and obtaining homogeneous mixture, NH_4X (1.2 mmol, 2.4 equiv) (X= Cl, Br or I) was added and stirred for 2 min. Then iodosylbenzene (0.6 mmol, 1.2 equiv) was added and stirred at 25 °C until fully consumption of the starting material (usually 5 to 20 min). To quench the reaction, AcOEt (5 mL) was added and concentrated to vacuo. Purification was carried out by column chromatography with EtOAc-Hexanes system to give the desired product.

General Procedure B. A 25 mL oven-dried round-bottom flask equipped with a magnetic stirrer bar was charged with the corresponding phenol (0.5 mmol, 1 equiv) and methanol (0.15 *M*) at 0°C. After dissolving and obtaining homogeneous mixture, NH_4I (1.2 mmol, 2.4 equiv) was added and stirred for 2 min. Then K_3PO_4 (1 equiv) and iodosylbenzene (0.6 mmol, 1.2 equiv) was added and stirred at 25 °C until fully consumption of the starting material (usually 5 min). To quench the reaction, AcOEt (5 mL) was added and concentrated to vacuo. Purification was carried out by column chromatography with EtOAc-Hexanes system to give the desired product.

Suzuki-Miyaura Cross-Coupling procedure. The starting materials of the examples **4-12**[68, 69, 70] and **58-65**[68, 69, 70] were synthesized by Suzuki-Miyaura Cross-Coupling according to the following procedure. A 50 mL round bottom flask with a stir bar was fitted with a rubber septum and flame dried under high vacuum. The flask was purged with argon and charged with $Pd(PPh_3)_4$ (155.5 mg, 0.1 mmol), K_2CO_3 (580.5 mg, 4.2 mmol), 6-bromonaphthalen-2-ol (443.9 mg, 2.0 mmol), boronic acid (4.0 mmol), 10.0 mL 1,4-dioxane and 2 mL distilled water. The following boronic acids were purchased from Sigma Aldrich and used as such without additional purification: 4-chlorophenylbronic acid for compound **4**; 3-chloro-4-fluorophenylboronic acid for compounds **5** and **64**; 4-fluorophenylboronic acid for compounds **6** and **63**; 3,4-difluorofenilboronic acid for compounds **7** and **65**; 4-cyanophenylboronic acid for compound **8**; phenylboronic acid for compounds **9** and **58**; 4-methylboronic acid for compounds **10**, **60** and **61**; 4-methoxyphenyl boronic acid for compounds **11** and **62**; 3,4-dimethoxyphneylboronic acid for compound **12** and 2-naphthylboronic acid for compound **59**. The reaction mixture was then heated at 80 °C for 8 h. After the reaction was cooled down to room temperature, the organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 × 10 mL), and the combined organic layer was dried over Na_2SO_4 and concentrated. The crude products were purified by flash chromatography on silica gel.

Examples in Scheme 2. *1-iodonaphthalen-2-ol (**1**).*[21] The following compound was obtained according to the general procedure A, by using 2-naphthol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (3% EtOAc/Hexane) to afford the product **1** (92 mg, 98%); gram scale (1.72 g, 92%) as a white solid. m.p.= 89-91 °C. R_f= 0.5 (5% EtOAc/Hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.5 Hz, 1H), 7.76 (dd, *J* = 8.4, 3.3 Hz, 2H), 7.58 (t, 1H), 7.42 (t, 1H), 7.28 (d, *J* = 2.1 Hz, 1H), 5.79 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 153.9, 134.9, 130.7, 130.4, 129.8, 128.4, 128.4, 124.3, 116.9, 86.7. HRMS (ESI+): m/z calculated for $C_{10}H_8IO$ $[M+H]^+$=270.9620, found 270.9616.

*6-bromo-1-iodonaphthalen-2-ol (**2**).*[49] The following compound was obtained according to the general procedure A, by using 6-bromonaphthalen-2-ol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **2** (73 mg, 93%), gram scale (1.41 g, 90%). as a white solid. m.p.= 85-87 °C R_f = 0.2 (8% EtOAc/Hexane). IR (neat) ν/cm^{-1} = 3439, 3228, 2921, 1589. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 9.9 Hz, 1H), 7.82 (dd, *J* = 8.9, 5.2 Hz, 1H), 7.56 (dd, J = 8.7, 5.4 Hz, 2H), 7.27 (dd, *J* = 2.6 Hz, 1H), 5.81 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 154.1, 133.4, 132.1, 131.3, 130.4, 130.0, 129.6, 118.6, 117.5, 85.9. HRMS (ESI+): m/z calculated for $C_{10}H_7BrIO$ $[M+H]^+$= 348.8725, found 348.8705.

*3-bromo-1-iodonaphthalen-2-ol (**3**).* The following compound was obtained according to the general procedure A, by using 3-bromonaphthalen-2-ol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **3** (72 mg, 92%) as a white solid. m.p.= 67-69°C. R_f = 0.14 (10% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3390, 3023, 1560, 1429. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.97 (d, J = 8.4 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 1H), 6.22 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, CDCl3) δ 149.7, 134.7, 132.5, 130.8, 129.9, 128.6, 127.4, 125.1, 109.6, 84.7. HRMS (EI): m/z calculated for $C_{10}H_6BrIO$ [M]$^+$= 347.8647, found 347.8639.

*1-iodo-3-methoxynaphthalen-2-ol (**4**).* The following compound was obtained according to the general procedure A, by using 3-methoxynaphthalen-2-ol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **4** (81 mg, 94%), as a white solid. m.p.= 73-75 °C. R_f = 0.5 (10% EtOAc/Hexane). IR (neat) ν/cm^{-1} = 3328, 3012, 1620, 1478, 1439. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.7 Hz, 1H), 7.64 (d, *J* = 7.4 Hz, 1H), 7.43 (d, *J* = 7.5 Hz, 1H), 7.36 (d, *J* = 7.5 Hz, 1H), 7.12 (s, 1H), 6.58 (s, 1H), 4.04 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 146.6, 146.9, 130.8, 129.6, 127.7, 126.1, 126.3, 124.8, 106.6, 82.7, 56.9. HRMS (EI): m/z calculated for $C_{11}H_9IO2$ [M]$^+$= 299.9647, found 299.9641.

*1-iodo-7-methoxynaphthalen-2-ol (**5**).* The following compound was obtained according to the general procedure A, by using 7-methoxynaphthalen-2-ol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (6% EtOAc/Hexane) to afford the product **5** (83 mg, 96%), gram scale (1.62 g, 94%). as a white solid m.p.= 79-81°C. R_f = 0.15 (10% EtOAc/Hexane). IR (neat) ν/cm^{-1} = 3428, 3018, 1630, 1380, 1409. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 8.7, 5.7 Hz, 2H), 7.28 (s, 1H), 7.13 (d, *J* = 8.7 Hz, 1H), 7.05 (d, *J* = 8.8 Hz, 1H), 5.84 (s, 1H), 4.00 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 159.9, 154.4, 136.5, 130.6, 130.2, 124.9, 116.5, 114.3, 109.8, 85.6, 55.6. HRMS (ESI+): m/z calculated for $C_{11}H_{10}IO_2$ [M+H]$^+$= 300.9725, found 300.9715.

*1-iodo-6-phenylnaphthalen-2-ol (**6**).*[50] The following compound was obtained according to the general procedure A, by using 6-phenylnaphthalen-2-ol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (4% EtOAc/Hexane) to afford the product **6** (66 mg, 96%) as a white solid. m.p.= 138-140 °C. R_f = 0.42 (8% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3410, 3020, 1585, 1472, 1430. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.7 Hz, 1H), 7.92 (s, 1H), 7.77 (t, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 7.6 Hz, 2H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.23 (d, *J* = 3.3 Hz, 1H), 5.79 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 153.8, 140.4, 136.9, 134.5, 130.8, 130.8, 129.8, 128.9, 127.7, 127.4, 127.8, 126.1, 116.8, 85.9. HRMS (EI): m/z calculated for $C_{16}H_{11}IO$ [M]$^+$= 345.9855, found 345.9847.

*1-iodo-6-(p-tolyl)naphthalen-2-ol (**7**).*[50] The following compound was obtained according to the general procedure A, by using 6-(*p*-tolyl) naphthalen-2-ol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (6% EtOAc/Hexane) to afford the product **7** (62 mg, 93%) as a white solid. m.p.=132-134 °C. R_f = 0.55 (15% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3210, 3040, 1680, 1600, 1530, 1482, 1454. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.7 Hz, 1H), 7.88 (s, 1H), 7.77 (t, *J* = 8.2 Hz, 2H), 7.56 (d, *J* = 7.7 Hz, 2H), 7.24 (d, *J* = 4.1 Hz, 1H), 7.21 (s, 1H), 5.74 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 153.8, 137.6, 137.4, 137.2, 134.0, 130.9, 130.9, 129.8, 127.8, 127.3, 125.8, 116.9, 86.8, 21.9. HRMS (EI): m/z calculated for $C_{17}H_{13}IO$ [M]$^+$= 360.0011, found 360.0006.

*1-iodo-6-(4-methoxyphenyl)naphthalen-2-ol (**8**).* The following compound was obtained according to the general procedure A, by using 6-(4-methoxyphenyl) naphthalen-2-ol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (8% EtOAc/Hexane) to afford the product **8** (74 mg, 98%) as a white solid. m.p.= 140-142 °C. R_f = 0.12 (15% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3398, 3040, 1598, 1498, 1440. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.7 Hz, 1H), 7.88 (s, 1H), 7.75 (d, *J* = 8.9 Hz, 2H), 7.63 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 3.7 Hz, 1H), 7.01 (d, *J* = 8.3 Hz, 2H), 5.79 (s, 1H), 3.86 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.8, 153.7, 136.8, 133.8, 132.9, 130.8, 130.8, 130.4, 128.4, 127.8, 125.6, 116.9, 114.5, 86.8, 55.5. HRMS (EI): m/z calculated for $C_{17}H_{13}IO_2$ [M]$^+$= 375.9960, found 375.9955.

*6-(3,4-dimethoxyphenyl)-1-iodonaphthalen-2-ol (**9**).* The following compound was obtained according to the general procedure A, by using 6-(3,4-dimethoxyphenyl)naphthalen-2-ol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (10% EtOAc/Hexane) to afford the product **9** (70 mg, 96%) as a white solid. m.p.= 132-134 °C. R_f = 0.15 (15% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3330, 3020, 1610, 1491, 1425. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.8 Hz, 1H), 7.91 (d, *J* = 9.6 Hz, 1H), 7.80 – 7.75 (m, 2H), 7.27 (d, *J* = 9.2 Hz, 2H), 7.21 (d, J = 1.7 Hz, 1H), 6.99 (d, *J* = 8.1, 4.2 Hz, 1H), 5.79 (s, 1H), 3.99 (s, 3H), 3.95 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 153.7, 149.4, 148.8, 136.8, 133.9, 133.9, 130.8, 130.7, 129.8, 127.6, 125.5, 119.6, 116.8, 111.6, 110.5, 85.9, 56.0. HRMS (EI): m/z calculated for $C_{18}H_{15}IO_3$ [M]$^+$= 406.0066, found 406.0063.

*6-(4-chlorophenyl)-1-iodonaphthalen-2-ol (**10**).* The following compound was obtained according to the general procedure A, by using 6-(4-chlorophenyl) naphthalen-2-ol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (8% EtOAc/Hexane) to afford the product **10** (65 mg, 88%) as a white solid. m.p.= 160-162 °C. R_f= 0.20 (8% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3330, 3045, 1580, 1486, 1460. 1H NMR (500 MHz, CDCl3) δ 7.96 (d, *J* = 8.7 Hz, 1H), 7.88 (d, *J* = 1.5 Hz, 1H), 7.75 (d, *J* = 8.8 Hz, 1H), 7.72 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.44 – 7.40 (m, 2H), 7.24 (d, *J* = 6.7 Hz, 1H), 5.79 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 154.4, 138.8, 135.7, 134.9, 133.7, 131.2, 130.8, 129.8, 129.9, 128.8, 127.6, 126.2, 117.5, 85.8. HRMS (EI): m/z calculated for $C_{16}H_{10}ClIO$ [M]$^+$ = 379.9465, found 379.9460.

*6-(4-fluorophenyl)-1-iodonaphthalen-2-ol (**11**).* The following compound was obtained according to the general procedure A, by using 6-(4-fluorophenyl) naphthalen-2-ol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (12% EtOAc/Hexane) to afford the product **11** (67 mg, 88%) as a light yellowish solid. m.p.= 136-138 °C. R_f = 0.14 (20% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3400, 3035, 1580, 1485, 1454. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.7 Hz, 1H), 7.89 (d, *J* = 1.4 Hz, 1H), 7.78 (d, *J* = 8.8 Hz, 1H), 7.75 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.67 – 7.63 (m, 2H), 7.28 (d, *J* = 8.8 Hz, 1H), 7.17 (t, *J* = 8.7 Hz, 2H), 5.80 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ

162.74 (d, *J* = 247.0 Hz), 154.8, 136.7 (d, *J* = 3.3 Hz), 136.9, 134.8 (d, J = 3.1 Hz), 131.2 (d, J = 17.9 Hz), 130.1, 128.9 (d, *J* = 8.0 Hz), 127.7, 126.1, 117.1, 115.9 (d, *J* = 21.5 Hz), 86.4. HRMS (EI): m/z calculated for $C_{16}H_{10}FIO$ $[M]^+$= 363.9760, found 363.9753.

*6-(4-chloro-3-fluorophenyl)-1-iodonaphthalen-2-ol (**12**).* The following compound was obtained according to the general procedure A, by using 6-(4-chloro-3-fluorophenyl)-naphthalen-2-ol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (10% EtOAc/Hexane) to afford the product **12** (63 mg, 86%) as a light yellowish solid. m.p.= 142-144 °C. R_f= 0.55 (15% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3440, 3140, 1680, 1498, 1420. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.7 Hz, 1H), 7.84 (s, 1H), 7.74 (d, *J* = 8.7 Hz, 1H), 7.67 (t, *J* = 7.2 Hz, 2H), 7.53 – 7.47 (m, 1H), 7.22 (dd, *J* = 16.8, 9.0 Hz, 2H), 5.80 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 157.9 (d, *J* = 249.5 Hz), 154.3, 137.8 (d, *J* = 4.1 Hz), 134.8, 134.4, 131.8, 130.9, 129.8, 129.7, 127.4, 127.2 (d, *J* = 7.1 Hz), 126.7, 121.6 (d, *J* = 18.0 Hz), 117.7 (d, *J* = 13.7 Hz), 117.5, 86.1. HRMS (ESI-): m/z calculated for $C_{16}H_8ClFIO$ $[M-H]^-$ = 396.9298, found 396.9290.

*6-(3,4-difluorophenyl)-1-iodonaphthalen-2-ol (**13**).* The following compound was obtained according to the general procedure A, by using 6-(3,4-difluorophenyl) naphthalen-2-ol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (15% EtOAc/Hexane) to afford the product **13** (67 mg, 90%) as a light yellowish solid. m.p.= 122-124 °C. R_f = 0.55 (20% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3400, 3040, 1600, 1498, 1445. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.7 Hz, 1H), 7.83 (s, 1H), 7.74 (dd, *J* = 8.8, 1.7 Hz, 1H), 7.69 – 7.65 (m, 1H), 7.49 – 7.42 (m, 1H), 7.39 – 7.33 (m, 1H), 7.26 – 7.19 (m, 2H), 5.80 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 154.9 , 151.9 – 150.9 (m), 150.6 – 148.8 (m), 137.7 (dd, *J* = 5.6, 3.9 Hz), 135.0, 134.4, 131.2, 130.9, 129.8, 127.2, 126.4, 123.7 (dd, *J* = 6.0, 3.3 Hz), 117.8 (d, *J* = 17.3 Hz), 117.3, 116.5 (d, *J* = 17.7 Hz), 86.0. HRMS (EI): m/z calculated for $C_{16}H_9F_2IO$ $[M]^+$= 381.9666, found 381.9662.

*6-hydroxy-5-iodo-2-naphthonitrile (**14**).*[50] The following compound was obtained according to the general procedure A, by using phenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (10% EtOAc/Hexane) to afford the product **14** (75 mg, 86%) as a yellow solid. From 6-hydroxy-2-naphthonitrile. R_f=0.55(15% EtOAc/Hexane). ^{1}H NMR (500 MHz, DMSO) δ 8.43 (d, *J* = 1.1 Hz, 1H), 8.04 (d, *J* = 8.8 Hz, 1H), 7.94 (d, *J* = 8.9 Hz, 1H), 7.78 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.35 (d, *J* = 8.8 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, DMSO) δ 158.9, 137.6, 135.6, 131.6, 131.8, 128.9, 127.9, 119.6, 119.6, 105.9, 84.7.

*2,4,6-triiodophenol (**15**).*[35] The following compound was obtained according to the general procedure A, by using phenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (2% EtOAc/Hexane) to afford the product **15a** (116 mg, 46%) as a white solid. From 4-iodophenol, **15b** (160 mg, 64%). m.p.= 137-139 °C. R_f= 0.46 (4% EtOAc/Hexane). ^{1}H NMR (500 MHz, CDCl3) δ 7.87 (s, 2H), 5.69 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 153.8, 146.4, 83.9, 83.5. HRMS (ESI+): m/z calculated for $C_6H_4I_3O$ $[M+H]^+$= 472.7396, found 472.7391.

*4-fluoro-2,6-diiodophenol (**16**).* The following compound was obtained according to the general procedure A, by using 4-fluorophenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (4% EtOAc/Hexane) to afford the product **16** (65 mg, 52%) as a white solid. m.p.= 64-66 °C. R_f= 0.15 (6% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3400, 290, 1580, 1498, 1465. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.3 Hz, 2H), 5.49 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 155.9 (d, *J* = 248.5 Hz), 150.8 (d, *J* = 3.0 Hz), 125.9 (d, *J* = 24.6 Hz), 80.6 (d, *J* = 8.5 Hz). HRMS (ESI-): m/z calculated for $C_6H_2FI_2O$ $[M-H]^-$ = 362.8179, found 362.8175.

*4-bromo-2,6-diiodophenol (**17**).*[51] The following compound was obtained according to the general procedure A, by using 4-bromophenol as starting material and NH_4I. The crude material was puri-fied by flash column chromatography over silica gel with the system (2% EtOAc/Hexane) to afford the product **17** (85 mg, 60%) as a white solid. m.p.= 115-117 °C. R_f= 0.4 (4% EtOAc/Hexane).^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (s, 2H), 5.65 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 153.7, 140.9, 113.6, 82.6.

*2,6-diiodo-4-methylphenol (**18**).*[51] The following compound was obtained according to the general procedure A, by using 4-methylphenol as starting material and NH_4I. The crude material was pu-rified by flash column chromatography over silica gel with the system (2% EtOAc/Hexane) to afford the product **18** (100 mg, 67%) as a white solid. m.p.= 49-51°C. R_f= 0.55 (6% EtOAc/Hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (s, 2H), 5.59 (s, 1H), 2.24 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 151.4, 139.6, 133.8, 82.5, 19.7. HRMS (ESI+): m/z calculated for $C_7H_7I_2O$ $[M+H]^+$= 360.8586, found 360.8577.

*4-bromo-2,6-diiodo-3-methoxyphenol (**19**).* The following compound was obtained according to the general procedure A, by using 4-bromo-3-methoxyphenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **19** (79 mg, 70%) as a white solid. m.p.= 64-68°C. IR (neat) ν/cm^{-1}= 3382, 3060, 1613, 1485, 1454. R_f= 0.2 (10% EtOAc/Hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (s, 1H), 5.84 (s, 1H), 3.86 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 157.8, 154.6, 141.5, 107.4, 82.3, 76.4, 60.8. HRMS (EI): m/z calculated for $C_7H_5BrI_2O_2$ $[M]^+$= 453.7562, found 453.7559.

*3,5-diiodo-[1,1'-biphenyl]-2-ol (**20**).* The following compound was obtained according to the general procedure A, by using [1,1'-biphenyl]-2-ol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (4% EtOAc/Hexane) to afford the product **20** (81 mg, 58%) as a colorless oil. R_f= 0.14 (10% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3480, 3010, 1485, 1470, 1430. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, *J* = 1.7 Hz, 1H), 7.53 (d, *J* = 1.7 Hz, 1H), 7.51 – 7.37 (m, 5H), 5.58 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 151.9, 145.2, 139.5, 135.9, 130.7, 129.2, 128.6, 87.1, 83.7. HRMS (ESI-): m/z calculated for $C_{12}H_7I_2O$ $[M-H]^-$ = 420.8292, found 420.8263.

*2,6-diiodo-3,5-dimethoxyphenol (**21**).*[52] The following compound was obtained according to the general procedure A, by using 3,5-dimethoxyphenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **21** (190 mg, 72%) as a white solid. m.p.= 149-141°C. R_f = 0.55 (15% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3430, 2920, 1810, 1488, 1428. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.01 (s, 1H), 5.92 (s, 1H), 3.83 (s, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 160.4, 154.9, 88.4, 64.5, 56.8. HRMS (ESI+):

m/z calculated for $C_8H_9I_2O_3$ $[M+H]^+$= 406.8641, found 406.8638.

*2,6-diiodo-3,4-dimethoxyphenol (**22**)*. The following compound was obtained according to the general procedure A, by using 3,4-dimethoxyphenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (6% EtOAc/Hexane) to afford the product **22** (186 mg, 70%) as a white solid. m.p.= 150-152 °C. R_f= 0.5 (10% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3400, 3030, 1595, 1492, 1430. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.01 (s, 1H), 5.92 (s, 1H), 3.83 (s, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 160.3, 154.9, 130.8, 128.8, 88.4, 68.7, 64.5, 56.8. HRMS (EI): m/z calculated for $C_8H_8I_2O_3$ $[M]^+$= 405.8563, found 405.8558.

Examples in Scheme 3. *4-iodophenol (**23**)*.[21] The following compound was obtained according to the general procedure B, by using phenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (2% EtOAc/Hexane) to afford the product **23** (133 mg, 56%) as a white solid. m.p.= 80-82 °C. R_f= 0.5 (6% EtOAc/Hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.7 Hz, 2H), 6.55 (d, *J* = 7.6 Hz, 2H), 4.91 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 155.8, 138.9, 117.9, 82.8.

*2-iodo-4-methylphenol (**24**)*.[21] The following compound was obtained according to the general procedure B, by using 4-methylphenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **24** (178 mg, 82%) as a white solid. m.p.= 96-98 °C. R*f* = 0.55 (10% EtOAc/Hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 1.4 Hz, 1H), 7.04 (dd, *J* = 8.2, 1.6 Hz, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 5.15 (s, 1H), 2.25 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 152.9, 138.4, 132.1, 130.9, 114.8, 85.5 20.8.

*2-iodo-4,5-dimethylphenol (**25**)*.[53] The following compound was obtained according to the general procedure B, by using 4,5-dimethylphenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (4% EtOAc/Hexane) to afford the product **25** (176 mg, 80%) as a white solid. m.p.= 50-52 °C. R_f= 0.12 (8% EtOAc/Hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (s, 1H), 6.79 (s, 1H), 5.04 (s, 1H), 2.18 (s, 3H), 2.15 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 152.80, 139.6, 138.6, 130.9, 116.4, 81.7, 19.9, 18.9.

*4-iodo-2,6-dimethylphenol (**26**)*.[51] The following compound was obtained according to the general procedure B, by using 2,6-dimethylphenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (6% EtOAc/Hexane) to afford the product **26** (178 mg, 88%) as a white solid. m.p.= 96-98°C. R_f= 0.2 (10% EtOAc/Hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (s, 2H), 4.62 (s, 1H), 2.19 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz, CDCl3) δ 152.8, 137.1, 125.7, 82.3, 15.5.

*2-iodo-4-isopropylphenol (**27**)*.[54] The following compound was obtained according to the general procedure B, by using 4-isopropylphenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (3% EtOAc/Hexane) to afford the product **27** (174 mg, 90%) as a colorless liquid. R_f = 0.55 (8% EtOAc/Hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 – 7.41 (m, 1H), 7.02 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.84 (d, *J* = 8.3 Hz, 1H), 5.05 (s, 1H), 2.72 (hept, *J* = 13.7, 6.9 Hz, 1H), 1.13 (d, *J* = 6.0 Hz, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 152.8, 143.3, 135.8, 128.3, 114.8, 85.6, 32.9, 24.6.

*5-bromo-3-iodo-[1,1'-biphenyl]-2-ol (**28**)*. The following compound was obtained according to the general procedure B, by using 5-bromo-[1,1'-biphenyl]-2-ol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **28** (66 mg, 88%) as a yellowish liquid. R_f= 0.55 (10% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3360, 3080, 1540, 1486, 1480. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.51 – 7.36 (m, 6H), 5.57 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 151.4, 139.5, 135.9, 133.5, 129.9, 128.9, 128.9, 128.5, 113.3, 86.6. HRMS (ESI-): m/z calculated for $C_{12}H_7BrIO$ $[M-H]^-$ = 372.8730, found 372.8727.

*4-bromo-2-iodo-5-methoxyphenol (**29**)*.[55] The following compound was obtained according to the general procedure B, by using 4-bromo-5-methoxyphenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **29** (66 mg, 78%) as a yellow liquid. R_f = 0.55 (10% EtOAc/Hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (s, 1H), 6.62 (s, 1H), 5.26 (s, 1H), 3.86 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 157.6, 155.4, 139.9, 103.9, 99.4, 73.8, 56.6. HRMS (ESI+): m/z calculated for $C_7H_7BrIO_2$ $[M+H]^+$= 328.8674, found 328.8661.

*4-fluoro-2-iodophenol (**30**)*.[56] The following compound was obtained according to the general procedure B, by using 4-fluorophenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **30** (96 mg, 90%) as a white solid. m.p.= 118-120 °C R_f = 0.55 (10% EtOAc/Hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 7.6, 2.9 Hz, 1H), 7.02 – 6.96 (m, 1H), 6.93 (dd, *J* = 9.0, 4.9 Hz, 1H), 5.11 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 156.6 (d, *J* = 243.4 Hz), 151.6 (d, *J* = 2.5 Hz), 124.5 (d, *J* = 25.4 Hz), 117.1 (d, *J* = 23.1 Hz), 115.5 (d, *J* = 7.8 Hz), 84.6.

*4-chloro-2-iodophenol (**31**)*.[17] The following compound was obtained according to the general procedure B, by using 4-chlorophenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **31** (87 mg, 88%) as a white solid. m.p.=76-78 °C. R_f = 0.4 (10% EtOAc/Hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 2.4 Hz, 1H), 7.24 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.94 (d, *J* = 8.7 Hz, 1H), 5.29 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 153.9, 137.3, 130.9, 126.5, 115.8, 85.6.

*2,6-dicholoro-4-iodophenol (**32**)*.[71] The following compound was obtained according to the general procedure B, by using 2,6-dichlorophenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (2% EtOAc/Hexane) to afford the product **32** (65 mg, 74%) as a white solid. R_f = 0.22 (5% EtOAc/Hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (s, 1H), 5.83 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 148.7, 136.6, 122.5, 80.5.

*4-bromo-2-iodophenol (**33**)*.[17] The following compound was obtained according to the general procedure B, by using 4-Bromophenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (4% EtOAc/Hexane) to afford the product **33** (79 mg, 92%) as a white solid. m.p.= 70-72 °C. R_f = 0.22 (8% EtOAc/Hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 2.3 Hz, 1H), 7.35 (dd, *J* = 8.7, 2.3 Hz, 1H), 6.87 (d, *J* = 8.7 Hz, 1H),

5.28 (s, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 154.3, 139.8, 133.7, 116.3, 113.6, 86.1.

*2,4-diiodophenol (**34**)*.[51] The following compound was obtained according to the general procedure B, by using 4-iodophenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (3% EtOAc/Hexane) to afford the product **34** (68 mg, 86%) as a colorless needle. m.p.= 72-74 °C. R_f = 0.5 (5% EtOAc/Hexane). ^1H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 2.3 Hz, 1H), 7.51 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.76 (d, *J* = 8.5 Hz, 1H), 5.32 (s, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 155.3, 145.7, 139.4, 117.9, 87.9, 82.9.

*2-bromo-4-iodophenol (**35**)*.[57] The following compound was obtained according to the general procedure B, by using 2-Bromophenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (4% EtOAc/Hexane) to afford the product **35** (79 mg, 92%) as a white solid. m.p.= 52-54 °C. R_f = 0.14 (8% EtOAc/Hexane). ^1H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* =1.5 Hz, 1H), 7.51 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.79 (d, *J* = 8.5 Hz, 1H), 5.52 (s, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 152.5, 139.7, 138.7, 118.3, 111.6, 82.6.

*2,5-diiodophenol (**36**).* The following compound was obtained according to the general procedure B, by using 3-iodophenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (2% EtOAc/Hexane) to afford the product **36** (73 mg, 92%) as a white solid. m.p.= 68-70 °C. R_f = 0.14 (5% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3390, 3023, 1580, 1450, 1429. ^1H NMR (500 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 4.8, 3.4 Hz, 2H), 7.00 (dd, *J* = 8.3, 1.3 Hz, 1H), 5.29 (s, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 155.0, 139.2, 131.0, 124.5, 94.4, 85.3. HRMS (ESI-): m/z calculated for $C_6H_4I_2O$ $[M-H]^-$ =345.8352, found 345.8350.

*6-chloro-3,4-difluoro-2-iodophenol (**37**).* The following compound was obtained according to the general procedure B, by using 6-chloro-3,4-difluorophenol as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (3% EtOAc/Hexane) to afford the product **37** (92 mg, 98%) as a white solid. m.p.= 80-82 °C. R_f = 0.5 (5% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3385, 3080, 1590, 1486, 1427. ^1H NMR (500 MHz, $CDCl_3$) δ 7.41 (t, *J* = 8.5 Hz, 1H), 5.86 (s, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 151.6 (d, *J* = 14.5 Hz), 149.8 – 149.1 (m), 144.1 (dd, *J* = 249.2, 15.8 Hz), 120.1 (d, *J* = 21.0 Hz), 101.8 (dd, *J* = 7.7, 4.2 Hz), 73.3 (d, *J* = 25.7 Hz). HRMS (EI): m/z calculated for $C_6H_2ClF_2IO$ $[M]^+$= 289.8807, found 289.8803.

Examples in Scheme 4. The starting materials for the examples **38**-**41**[39,67] were synthesized according to the previously described procedures.

2-methoxynaphthalene.[39,67] A 25 mL oven-dried round-bottom flask equipped with a magnetic stirrer bar was charged with 2-naphthol (2 mmol), dimethyl sulfate (2 mmol) and 3 mL of a solution (2 *M)* of Na_2CO_3. After dissolving in 8 mL of acetonitrile the mixture was stirred at 25 ºC overnight. After this period the starting material was fully consumed judging by TLC. To quench the reaction, AcOEt (5 mL) was added and concentrated to vacuo. Purification was carried out by column chromatography with EtOAc-Hexanes system to give the desired product.

2-benzyloxynaphthalene.[39,67] A 25 mL oven-dried round-bottom flask equipped with a magnetic stirrer bar was charged with 2-naphthol (2 mmol), benzyl bromide (2 mmol) and 3 mL of a solution (2 *M)* of Na_2CO_3. After dissolving in 8 mL of acetonitrile the mixture was stirred at 25 ºC overnight. After this period the starting material was fully consumed judging by TLC. To quench the reaction, AcOEt (5 mL) was added and concentrated to vacuo. Purification was carried out by column chromatography with EtOAc-Hexanes system to give the desired product.

2-acetylnaphthalene.[39,67] A 25 mL oven-dried round-bottom flask equipped with a magnetic stirrer bar was charged with 2-naphthol (2 mmol), acetyl chloride (2 mmol) and triethylamine (2mmol). After dissolving in 8 mL of dichloromethane the mixture was stirred at 25 ºC overnight. After this period the starting material was fully consumed judging by TLC. To quench the reaction, AcOEt (5 mL) was added and concentrated to vacuo. Purification was carried out by column chromatography with EtOAc-Hexanes system to give the desired product.

Naphthalene-2-yl pivalate.[39,67] A 25 mL oven-dried round-bottom flask equipped with a magnetic stirrer bar was charged with 2-naphthol (2 mmol), pivaloyl chloride (2 mmol) and triethylamine (2mmol). After dissolving in 8 mL of dichloromethane the mixture was stirred at 25 ºC overnight. After this period the starting material was fully consumed judging by TLC. To quench the reaction, AcOEt (5 mL) was added and concentrated to vacuo. Purification was carried out by column chromatography with EtOAc-Hexanes system to give the desired product.

*1-iodo-2-methoxynaphthalene (**38**)*.[21] The following compound was obtained according to a modified general procedure A, by using 2-methoxynaphthalene as starting material and NH_4I (reaction was in reflux overnight). The crude material was purified by flash column chromatography over silica gel with the system (3% EtOAc/Hexane) to afford the product **38** (52 mg, 57%) as a white solid. m.p.= 86-88 °C. R_f = 0.5 (5% EtOAc/Hexane). ^1H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.6 Hz, 1H), 7.83 (d, *J* = 8.9 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.54 (t, *J* = 7.7 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.22 (d, *J* = 8.9 Hz, 1H), 4.03 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 156.6, 135.6, 131.2, 130.7, 129.9, 128.9, 128.2, 124.6, 112.9, 87.7, 57.4.

*2-(benzyloxy)-1-iodonaphthalene (**39**)*.[58] The following compound was obtained according to a modified general procedure A, by using 2-(benzyloxy)naphthalene as starting material and NH_4I (reaction was in reflux overnight). The crude material was purified by flash column chromatography over silica gel with the system (3% EtOAc/Hexane) to afford the product **39** (30 mg, 38%) as a white solid. m.p.= 84-86 °C. R_f = 0.5 (5% EtOAc/Hexane). ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.6 Hz, 1H), 7.78 (d, *J* = 8.8 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.56 (t, *J* = 10.2 Hz, 3H), 7.40 (q, *J* = 7.5 Hz, 3H), 7.33 (t, *J* = 7.3 Hz, 1H), 7.22 (d, *J* = 8.9 Hz, 1H), 5.32 (s, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 155.8, 136.6, 135.7, 131.6, 130.3, 130.1, 128.6, 128.9, 128.9, 127.9, 127.4, 124.6, 114.7, 89.5, 71.9.

*4-iodo-1,2-dimethoxybenzene (**42**)*.[54] The following compound was obtained according to a modified general procedure A, by using 1,2-dimethoxybenzene as starting material and NH_4I (reaction was in reflux overnight). The crude material was purified by flash column chromatography over silica gel with the system (2% EtOAc/Hexane) to afford the product **42** (71mg, 37%) as a yellow liquid. Rf = 0.5 (5% EtOAc/Hexane). ^1H NMR (500 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 11.1, 4.6 Hz, 1H), 7.09 (s, 1H), 6.77 (d, *J* = 9.8, 4.9 Hz, 1H), 4.01 (s, 3H), 4.00 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 149.8, 149.2, 129.7, 120.8, 113.8, 111.3, 82.3, 55.9, 55.8.

*2-iodo-4,5-dimethoxybenzaldehyde (**43**)*.[33] The following compound was obtained according to a modified general procedure

A, by using 4,5-dimethoxybenzaldehyde as starting material and NH_4I (reaction was in reflux overnight). The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **43** (36 mg, 20%) as a white solid. R_f = 0.5 (10% EtOAc/Hexane). ^1H NMR (500 MHz, $CDCl_3$) δ 9.82 (s, 1H), 7.37 (s, 1H), 7.21 (s, 2H), 3.91 (s, 3H), 3.87 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 194.9, 154.5, 149.9, 128.4, 121.8, 111.2, 92.7, 56.9, 56.8.

*Methyl 2-iodo-4,5-dimethoxybenzoate (**44**)*.[59] The following compound was obtained according to a modified general procedure A, by using methyl 3,4-dimethoxybenzoate as starting material and NH_4I (reaction was in reflux overnight). The crude material was purified by flash column chromatography over silica gel with the system (3% EtOAc/Hexane) to afford the product **44** (59 mg, 36%) as a white solid. R_f = 0.5 (5% EtOAc/Hexane). ^1H NMR (500 MHz, $CDCl_3$) δ 7.44 (s, 1H), 7.39 (s, 1H), 3.91 (s, 6H), 3.90 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 166.5, 152.7, 148.8, 126.9, 123.8, 113.9, 84.8, 56.4, 56.8, 52.4.

*5-iodobenzo[d][1,3]dioxole (**45**)*.[54] The following compound was obtained according to a modified general procedure A, by using benzo[*d*][1,3]dioxole as starting material and NH_4I (reaction was in reflux overnight). The crude material was purified by flash column chromatography over silica gel with the system (3% EtOAc/Hexane) to afford the product **45** (58 mg, 28%) as a liquid. R_f = 0.5 (5% EtOAc/Hexane). ^1H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, J = 5.3 Hz, 2H), 6.71 (d, J = 8.0 Hz, 1H), 6.07 (s, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 148.8, 147.9, 130.7, 117.9, 110.6, 101.5, 82.5.

*2-iododibenzo[b,d]furan (**46**)*.[72] The following compound was obtained according to a modified general procedure A, by using dibenzo*[b,d]*furanas starting material and NH_4I (reaction was in reflux overnight). The crude material was purified by flash column chromatography over silica gel with the system (2% EtOAc/Hexane) to afford the product **46** (58 mg, 16%) as a white solid in a 1.5:1 mixture with its corresponding 2,8-diiododibenzo[*b,d*]furane. R_f = 0.15 (4% EtOAc/Hexane). Signals for monoiodinated derivative. ^1H NMR (500 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.74 (t, J = 12.0, 8.6, 1.8 Hz, 2H), 7.57 (d, J = 8.3 Hz, 1H), 7.51 – 7.46 (m, 1H), 7.36 (dt, J = 8.6, 3.0 Hz, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 156.3, 155.6, 136.4, 135.6, 129.8, 129.6, 127.9, 123.1, 120.8, 113.8, 113.7, 111.8, 85.7.

*3-iodo-1H-indole (**47**)*.[60] The following compound was obtained according to a modified general procedure A, by using 1*H*-indole as starting material and NH_4I (iodosylbenzene and ammonium iodide were used in 1 equiv each). The crude material was purified by flash column chromatography over silica gel with the system (2% EtOAc/Hexane) to afford the product **47** (99.5 mg, 96%) as a white solid. R_f = 0.54 (5% EtOAc/Hexane). ^1H NMR (500 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.39 (d, J = 7.5 Hz, 1H), 7.28 (d, J = 7.9 Hz, 1H), 7.22 – 7.10 (m, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 135.6, 129.8, 128.4, 123.2, 121.3, 120.8, 111.7, 57.6.

*3-iodo-9H-carbazole (**48**)*.[61] The following compound was obtained according to a modified general procedure A, by using 9*H*-carbazole as starting material and NH_4I (reaction was in reflux overnight). The crude material was purified by flash column chromatography over silica gel with the system (3% EtOAc/Hexane) to afford the product **48** (58 mg, 47%) as a liquid. R_f = 0.5 (5% EtOAc/Hexane). ^1H NMR (500 MHz, $CDCl_3$) δ 8.39 (d, J = 1.5 Hz, 1H), 8.08 (s, 1H), 8.02 (d, J = 7.8 Hz, 1H), 7.66 (dd, J = 8.5, 1.7 Hz, 1H), 7.47 – 7.41 (m, 2H), 7.26 – 7.24 (d, J = 8.2 Hz, 1H), 7.23 (d, J = 8.5 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 139.6, 138.9, 134.2, 129.9, 126.7, 126.7, 122.5, 120.6, 120.1, 112.7, 110.8, 82.3.

*cyclohexa-3,5-diene-1,2-diimine (**49**)*.[62] The following compound was obtained according to the general procedure A, by using *o*-phenylendiamine as starting material and NH_4I. The crude material was purified by flash column chromatography over silica gel with the system (4% EtOAc/Hexane) to afford the product **49** (56 mg, 38%) as a white solid. m.p.= 64-66°C. R_f = 0.4 (6% EtOAc/Hexane). IR (neat) ν/cm^{-1} = 3400, 3045, 1600, 1495, 1450, 1265. ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.29 (m, 1H), 5.74 – 5.70 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 142.6, 114.6, 106.2. HRMS (ESI+): m/z calculated for $C_6H_7N_2$ $[M+H]^+$= 107.0609, found 107.0602.

Examples in Scheme 5.

*5-bromo-[1,1'-biphenyl]-2-ol (**50**)*.[39] The following compound was obtained according to the general procedure A, by using [1,1'-biphenyl]-2-ol as starting material and NH_4Br. The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **50** (63 mg, 86%) as a yellow oil. R_f = 0.12 (8% EtOAc/Hexane). ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (t, J = 8.0 Hz, 2H), 7.43 (d, J = 8.1 Hz, 3H), 7.37-7.34 (m, 2H), 6.88 (d, J = 8.4 Hz, 1H), 5.22 (s, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 151.7, 135.8, 132.7, 131.9, 130.2, 129.6, 129.0, 128.5, 117.7, 112.9.

*1-chloronaphthalen-2-ol (**51**)*.[38] The following compound was obtained according to the general procedure A, by using 2-napthol as starting material and NH_4Cl. The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **51** (49 mg, 80%) as a white solid. R_f = 0.2 (10% EtOAc/Hexane). ^1H NMR (500 MHz, $CDCl_3$): δ 8.07 (d, J = 8.6 Hz, 1H), 7.81 (d, J = 8.1 Hz, 1H), 7.73 (d, J = 8.9 Hz, 1H), 7.59 (t, J = 8.8 Hz ,1H), 7.42 (t, J = 7.9 Hz, 1H), 7.27 (s, 1H), 5.90 (s, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 149.3, 131.0, 129.4, 128.4, 128.1, 127.5, 124.1, 122.7, 117.2, 113.3.

*1-bromonaphthalen-2-ol (**52**)*.[39] The following compound was obtained according to the general procedure A, by using 2-naphthol as starting material and NH_4Br. The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **52** (69 g, 94%) as a white solid. R_f = 0.55 (10% EtOAc/Hexane). ^1H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, J = 8.5 Hz, 1H), 7.63 (d, J = 8.1 Hz, 1H), 7.59 (d, J = 8.8 Hz, 1H), 7.43 (t, J = 7.6 Hz, 1H), 7.26 (t, J = 7.4 Hz, 1H), 7.14 (s, 1H), 5.83 (s, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 150.6, 132.4, 129.8, 129.4, 128.3, 127.9, 125.4, 124.2, 117.2, 106.2.

*1,3-dibromonaphthalen-2-ol (**53**)*.[39] The following compound was obtained according to the general procedure A, by using 3-bromonaphthalen-2-ol as starting material and NH_4Br. The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **53** (65 mg, 95%) as a white solid. R_f = 0.10 (15% EtOAc/Hexane). ^1H NMR (500 MHz) δ 8.04 (d, J = 7.2 Hz, 2H), 7.70 (s, 1H), 7.58 (t, J = 7.8 Hz, 1H), 7.41 (t, J = 8.1 Hz, 1H), 6.21 (s, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 147.3, 131.9, 131.6, 129.9, 128.3, 127.4, 125.9, 125.2, 110.8. 106.5.

*6-bromo-1-chloronaphthalen-2-ol (**54**)*.[38] The following compound was obtained according to the general procedure A, by using 6-bromonaphthalen-2-ol as starting material and NH_4Cl. The crude material was purified by flash column chromatography over silica gel with the system (10% EtOAc/Hexane) to afford the product **54** (65 mg, 90%) as a white solid. R_f = 0.2

(15% EtOAc/Hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 9.9 Hz, 2H), 7.51 (d, *J* = 8.7 Hz, 2H), 7.17 (d, *J* = 7.4 Hz, 1H), 5.84 (s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 149.7, 130.9, 130.5, 130.2, 129.7, 127.6, 124.7, 118.5, 118.1, 113.6.

*1,6-dibromonaphthalen-2-ol (**55**)*.[39] The following compound was obtained according to the general procedure A, by using 6-bromonaphthalen-2-ol as starting material and NH_4Br. The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **55** (63 mg, 92%) as a white solid. R_f = 0.49 (10% EtOAc/Hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.81 (d, *J* = 9.0 Hz, 1H), 7.58-7.51 (m, 2H), 7.19 (d, *J* = 8.7 Hz, 1H), 5.85 (s, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 151.0, 131.8, 131.1, 130.7, 130.2, 128.5, 127.3, 118.4, 118.1, 106.2.

*1-chloro-7-methoxynaphthalen-2-ol (**56**)*.[38] The following compound was obtained according to the general procedure A, by using 1-chloro-7-methoxynaphthalen-2-ol as starting material. The crude material was purified by flash column chromatography over silica gel with the system (10% EtOAc/Hexane) to afford the product **56** (55 mg, 92%) as a white solid. R_f = 0.55 (15% EtOAc/Hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.8 Hz, 1H), 7.62 (d, *J* = 8.7 Hz, 1H), 7.33 (s, 1H), 7.11 (d, *J* = 8.7 Hz, 1H), 7.05 (d, *J* = 8.9 Hz, 1H), 5.90 (s, 1H), 3.97 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 159.4, 150.0, 132.6, 130.0, 128.2, 124.8, 116.7, 114.6, 112.6, 101.7, 55.5.

*1-Bromo-7-methoxynaphthalen-2-ol (**57**)*.[39] The following compound was obtained according to the general procedure A, by using 7-methoxynaphthalen-2-ol as starting material and NH_4Br. The crude material was purified by flash column chromatography over silica gel with the system (8% EtOAc/Hexane) to afford the product **57** (66 mg, 96%) as a white solid. R_f = 0.55 (15% EtOAc/Hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 9.2 Hz, 2H), 7.26 (d, *J* = 2.5 Hz, 1H), 7.06 (d, *J* = 8.7 Hz, 1H), 6.98 (dd, *J* = 8.9, 2.5 Hz, 1H), 5.89 (s, 1H), 3.91 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 159.6, 150.9, 133.8, 129.9, 129.1, 124.9, 116.4, 114.5, 105.3, 104.4, 55.4.

*1-bromo-6-phenylnaphthalen-2-ol (**58**)*.[63] The following compound was obtained according to the general procedure A, by using 2-naphthol as starting material and NH_4Br. The crude material was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product **58** (73 mg, 93%) as a white solid. m.p.=138-140 °C R_f = 0.12 (10% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3390, 3026, 1598, 1485, 1415. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.7 Hz, 1H), 7.99 (d, *J* = 1.6 Hz, 1H), 7.84 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.73 – 7.68 (m, 2H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.29 (d, *J* = 8.8 Hz, 1H), 5.93 (s, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 150.8, 140.9, 137.1, 131.5, 129.9, 129.9, 128.9, 127.5, 127.3, 127.7, 126.5, 125.9, 117.6, 106.3. HRMS (EI): m/z calculated for $C_{16}H_{11}BrO$ $[M]^+$ = 297.9993, found 297.9988.

*5-bromo-[2,2'-binaphthalen]-6-ol (**59**)*. The following compound was obtained according to the general procedure A, by using 5-bromo-[2,2'-binaphthalen]-6-ol as starting material and NH_4Br. The crude material was purified by flash column chromatography over silica gel with the system (10% EtOAc/Hexane) to afford the product **59** (69 mg, 94%) as a white solid. m.p.=144-146 °C R_f = 0.55 (15% EtOAc/Hexane) IR (neat) ν/cm^{-1}= 3386, 1717, 1600, 1450, 1258. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 8.12 (d, *J* = 5.7 Hz, 1H), 7.90 (ddd, *J* = 28.0, 19.6, 9.1 Hz, 5H), 7.57 – 7.48 (m, 2H), 7.31 (d, *J* = 8.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 150.7, 137.7, 136.8, 133.7, 132.8, 131.6, 130.2, 129.6, 128.6, 128.2, 127.7, 127.6, 126.4, 126.5, 126.9, 126.6, 125.9, 125.2, 117.7, 106.9. HRMS (EI): m/z calculated for $C_{20}H_{13}BrO$ $[M]^+$=348.0150, found 348.0145.

*1-chloro-6-(p-tolyl)naphthalen-2-ol (**60**)*. The following compound was obtained according to the general procedure A, by using 6-(*p*-tolyl)naphthalen-2-ol as starting material and NH_4Cl. The crude material was purified by flash column chromatography over silica gel with the system (10% EtOAc/Hexane) to afford the product **60** (52 mg, 90%) as a white solid. m.p.=146-148 °C R_f = 0.22 (15% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3398, 3032, 1600, 1498, 1429. 1H NMR (400 MHz, CDCl3) δ 8.04 (d, *J* = 8.7 Hz, 1H), 7.90 (s, 1H), 7.76 (d, *J* = 8.7 Hz, 1H), 7.68 (d, *J* = 8.9 Hz, 1H), 7.51 (t, *J* = 13.2 Hz, 2H), 7.21 (dd, *J* = 14.3, 5.6 Hz, 3H), 5.82 (s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 149.9, 137.6, 137.8, 136.9, 130.1, 129.9, 129.7, 128.6, 127.9, 127.1, 125.7, 123.6, 117.6, 113.3, 21.6. HRMS (EI): m/z calculated for $C_{17}H_{13}ClO$ $[M]^+$= 268.0655, found 268.0649.

*1-bromo-6-(p-tolyl) naphthalen-2-ol (**61**)*. The following compound was obtained according to the general procedure A, by using 6-(*p*-tolyl) naphthalen-2-ol as starting material and NH_4Br. The crude material was purified by flash column chromatography over silica gel with the system (8% EtOAc/Hexane) to afford the product **61** (62 mg, 92%) as a white solid. m.p.=150-152 °C R_f = 0.46 (15% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3400, 3043, 1603, 1490, 1450, 1260. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.8 Hz, 1H), 7.88 (s, 1H), 7.79 – 7.68 (m, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.20 (dd, *J* = 14.5, 5.9 Hz, 4H), 5.84 (s, 1H), 2.35 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 150.8, 137.7, 137.4, 137.7, 131.5, 130.5, 129.8, 129.8, 127.6, 127.4, 126.3, 125.8, 117.8, 106.8, 21.8. HRMS (EI): m/z calculated for $C_{17}H_{13}BrO$ $[M]^+$= 312.0150, found 312.0148.

*1-bromo-6-(4-methoxyphenyl) naphthalen-2-ol (**62**)*.[65] The following compound was obtained according to the general procedure A, by using 6-(4-methoxyphenyl) naphthalen-2-ol as starting material and NH_4Br. The crude material was purified by flash column chromatography over silica gel with the system (10 % EtOAc/Hexane) to afford the product **62** (62 mg, 94%) as a white solid. m.p.=156-158 °C R_f = 0.28 (15% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3400, 3033, 1590, 1495, 1429. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.8 Hz, 1H), 7.85 (d, *J* = 1.6 Hz, 1H), 7.75 – 7.68 (m, 2H), 7.59 – 7.53 (m, 2H), 7.19 (d, *J* = 3.6 Hz, 1H), 6.97 – 6.91 (m, 2H), 5.83 (s, 1H), 3.80 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 159.3, 150.5, 136.6, 132.9, 131.8, 130.5, 129.4, 128.8, 127.9, 125.8, 125.3, 117.5, 114.4, 106.4, 55.9. HRMS (EI): m/z calculated for $C_{17}H_{13}BrO_2$ $[M]^+$= 328.0099, found 328.0091.

*1-bromo-6-(4-fluorophenyl) naphthalen-2-ol (**63**)*. The following compound was obtained according to the general procedure A, by using 6-(4-fluorophenyl) naphthalen-2-ol and NH_4Br. The crude material was purified by flash column chromatography over silica gel with the system (10% EtOAc/Hexane) to afford the product **63** (61 mg, 92%) as a white solid. m.p.=124-126°C R_f = 0.45 (15% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3400, 3045, 2225, 1600, 1485, 1450. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.8 Hz, 1H), 7.93 (s, 1H), 7.85 – 7.70 (m, 2H), 7.68 – 7.62 (m, 2H), 7.29 (d, *J* = 8.8 Hz, 1H), 7.17 (t, *J* = 8.7 Hz, 2H), 5.95 (s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.6 (d, *J* = 246.7 Hz), 150.7, 136.8, 136.0, 131.4, 129.9, 129.54, 128.8 (d, *J* = 8.1 Hz), 127.7, 126.07, 125.9, 117.7, 115.8 (d, *J* = 21.5 Hz), 106.3. HRMS (EI): m/z calculated for $C_{16}H_{10}BrFO$ $[M]^+$= 315.9899, found 315.9895.

1-bromo-6-(3-chloro-4-fluorophenyl)naphthalen-2-ol ***(64)***. The following compound was obtained according to the general procedure A, by using 6-(3-chloro-4-fluorophenyl)naphthalen-2-ol as starting material and NH_4Br. The crude material was purified by flash column chromatography over silica gel with the system (10% EtOAc/Hexane) to afford the product **64** (61 mg, 90%) as a white solid. m.p.=136-138 °C R_f = 0.45 (15% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3395, 3060, 1660, 1540, 1427. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.87 (s, 1H), 7.80 – 7.63 (m, 3H), 7.49 (s, 1H), 7.22 (d, *J* = 13.2 Hz, 2H), 5.92 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 157.9 (d, *J* = 254 HZ), 151.1, 137.9, 134.8, 131.9, 130.0, 129.7, 129.5, 127.1, 127.0, 126.4, 126.2, 121.6 (d, *J* = 60 Hz), 118.1, 117.1 (d, *J* = 85 Hz), 106.2. HRMS (ESI+): m/z calculated for $C_{16}H_{10}BrClFO$ $[M+H]^+$= 350.9588, found 350.9580.

1-bromo-6-(3,4-difluorophenyl) naphthalen-2-ol ***(65)***. The following compound was obtained according to the general procedure A, by using 6-(3,4-difluorophenyl) naphthalen-2-ol and NH_4Br. The crude material was purified by flash column chromatography over silica gel with the system (10% EtOAc/Hexane) to afford the product **67** (88 mg, 90%) as a white solid. m.p.=124-126 °C. R_f = 0.14 (20% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3395, 3032, 1600, 1496, 1427. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.8 Hz, 1H), 7.84 (s, 1H), 7.72 (d, *J* = 8.9 Hz, 1H), 7.66 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.42 (ddd, *J* = 11.3, 7.6, 2.1 Hz, 1H), 7.35 – 7.30 (m, 1H), 7.25 – 7.17 (m, 2H), 5.91 (d, *J* = 4.6 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 151.5 (dd, J=256 Hz), 151.0, 149.1 (dd, *J* = 256 Hz), 137.6 (dd, *J* = 24 Hz), 134.9, 131.7, 129.8, 129.6, 126.9, 126.3, 126.1, 123.1 (dd, *J* = 24 Hz), 117.9, 117.7 (d, *J* = 68 Hz), 116.1 (d, *J* = 68 Hz), 106.0. HRMS (EI): m/z calculated for $C_{16}H_9BrF_2O$ $[M]^+$= 333.9805, found 333.9801.

One-pot dihalogenations.

one-pot synthesis of ***54***. This compound was synthesized by two consecutive halogenations (chlorination-bromination) which were carried out in the same flask with only single purification after the second reaction. Starting from 2-naphthol and NH_4Cl the general procedure A was used to obtain 1-chloro-2-naphthol **51** (58 mg) as a dark solid. The ^{1}H and ^{13}C{^{1}H} of this derivative match perfectly with the previous obtained compound. Then, without purification this dark solid was submitted to the second halogenation reaction using the general procedure A and NH_4Br to yield the compound **56** (71 mg, 84%) after column chromatography as a withe solid. The ^{1}H and ^{13}C{^{1}H} of this compound match perfectly with the previously obtained.

one-pot synthesis of ***55***. This compound was synthesized by two consecutive halogenations (bromination-bromination) which were carried out in the same flask with only single purification after the second reaction. Starting from 2-naphthol and NH_4Br the general procedure A was used to obtain 1-bromo-2-naphthol **52** (72 mg) as a dark-yellow solid. The ^{1}H and ^{13}C{^{1}H} of this derivative match perfectly with the previous obtained compound. Then, without purification this dark-yellow solid was submitted to the second halogenation reaction using the general procedure A and NH_4Br to yield the compound **57** (89 mg, 91%) after column chromatography as a withe solid. The ^{1}H and ^{13}C of this compound match perfectly with the previously obtained.

one-pot synthesis of ***2***. This compound was synthesized by two consecutive halogenations (iodination-bromination) which were carried out in the same flask with only single purification in after the second reaction. Starting from 2-naphthol and NH_4I the general procedure A was used to obtain 1-iodo-2-naphthol **1** (88 mg) as a grey solid. The ^{1}H and^{13}C{^{1}H} of this derivative match perfectly with the previous obtained compound. Then, without purification this grey solid was submitted to the second halogenation reaction using the general procedure A and NH_4I to yield the compound **2** (89 mg, 78%) after column chromatography as a withe solid. The ^{1}H and ^{13}C of this compound match perfectly with the previously obtained.

Sequences followed in scheme 6.

6-bromo-1-phenylnaphthalen-2-ol ***(66)***.[66] The following substrate was prepared by Suzuki-Miyaura cross-coupling reactions between 6-bromo-1-iodonaphthalen-2-ol and phenylboronic acid. A 50 mL round bottom flask with a stir bar was fitted with a rubber septum and flame dried under high vacuum. The flask was purged with argon and charged with $Pd(PPh_3)_4$ (173.1 mg, 0.1 mmol), K_2CO_3 (445.2 mg, 4.2 mmol), 6-bromo-1-iodonaphthalen-2-ol (667.9 mg, 2.0 mmol), phenylboronic acid (4.0 mmol), 10.0 mL 1,4-dioxene, and 2 mL distiled water. The reaction mixture was then heated at 80 °C for 12 h. Afterwards the reaction was cooled down to room temperature, the organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 × 10 mL), and the combined organic layer was dried over Na_2SO_4 and concentrated. The crude products were purified by flash chromatography on silica gel (5% EtOAc/Hexane) to afford the product 6-Bromo-1-phenylnaphthalen-2-ol (420.1 mg, 86%) as a white solid. m.p.= 96-98°C. R_f = 0.2 (10% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3386, 3034, 1720, 1600, 1450, 1260. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.7 Hz, 1H), 7.94 (s, 1H), 7.83 – 7.75 (m, 2H), 7.62 (d, *J* = 7.9 Hz, 2H), 7.45 (d, *J* = 7.9 Hz, 2H), 7.30 (d, *J* = 8.8 Hz, 1H), 5.95 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 150.8, 138.9, 135.7, 133.8, 131.6, 129.8, 129.9, 129.8, 128.8, 127.8, 126.5, 125.9, 117.8, 106.4. HRMS (EI): m/z calculated for $C_{16}H_{11}BrO$ $[M]^+$= 297.9993, found 297.9985.

1-phenyl-6-(p-tolyl)naphthalen-2-ol ***(67)***. The following substrate were prepared by Suzuki-Miyaura cross-coupling reactions between 6-bromo-1-phenylnaphthalen-2-ol (**66**) obtained in the previous reaction and *p*-tolylboronic acid. A 50 mL round bottom flask with a stir bar was fitted with a rubber septum and flame dried under high vacuum. The flask was purged with argon and charged with $Pd(PPh_3)_4$ (106.24 mg, 0.1 mmol), K_2CO_3 (445.2 mg, 4.2 mmol), 6-bromo-1-phenylnaphthalen-2-ol (**66**) (410 mg, 2.0 mmol), *p*-tolylboronic acid (4.0 mmol), 10.0 mL 1,4-dioxene, and 2 mL distiled water. The reaction mixture was then heated at 80 °C for 12 h. After the reaction was cooled down to room temperature, the organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 × 10 mL), and the combined organic layer was dried over Na_2SO_4 and concentrated. The crude products were purified by flash chromatography on silica gel (10% EtOAc/Hexane) to afford the product 1-phenyl-6-(*p*-tolyl)naphthalen-2-ol (**67**) (349 mg, 82%) as a yellowish solid. m.p.=138-140°C. R_f = 0.2 (10% EtOAc/Hexane). m.p. = 92-94 °C. R_f = 0.2 (15% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3400, 3040, 2222, 1600, 1482, 1454. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.89 (d, *J* = 8.9 Hz, 1H), 7.63 (dd, *J* = 14.4, 6.8 Hz, 5H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.49 (d, *J* = 6.2 Hz, 3H), 7.31 (dd, *J* = 13.6, 7.0 Hz, 3H), 5.20 (s, 1H), 2.44 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 150.8, 138.4, 136.9, 136.5, 134.3, 132.2, 131.8, 129.7, 129.7, 129.7, 129.2, 128.6, 127.6, 126.1, 125.6, 125.4, 120.9, 117.8, 21.2. HRMS (EI): m/z calculated for $C_{23}H_{18}O$ $[M]^+$ = 310.1358, found 310.1355.

6-bromo-1-iodo-2-methoxynaphthalene ***(68)***.[50] To a solution of **2** (0.434 mg, 1.25 mmol) in acetone (5 mL) was added K_2CO_3 (0.345 mg, 10.0 mmol), dimethyl sulfate (0.2 mL, 10.0 mmol). The solution was heated to reflux for 4 h at which time TLC

indicated complete consumption of the naphthol. The reaction mixture was cooled to room temperature Et_3N (5.0 mL) was added and the reaction was stirred for 1 h. The layers were separated, and the aqueous layer was extracted with DCM (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure to give crude material, which was purified by flash column chromatography over silica gel with the system (5% EtOAc/Hexane) to afford the product 6-bromo-1-iodo-2-methoxynaphthalene **68** (0.413 mg, 94%) as a yellowish solid. R_f = 0.15 (8% EtOAc/Hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 9.1 Hz, 1H), 7.91 (s, 1H), 7.73 (d, *J* = 8.9 Hz, 1H), 7.58 (d, *J* = 9.0 Hz, 1H), 7.21 (d, *J* = 9.0 Hz, 1H), 4.02 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 156.9, 134.3, 133.2, 131.8, 130.6, 129.9, 129.4, 118.2, 113.7, 87.7, 57.2.

*6-bromo-2-methoxy-1-(phenylethynyl)naphthalene (**69**)*. A 50 mL round bottom flask with a stir bar was fitted with a rubber septum was flame dried under high vacuum. The flask was purged with nitrogen and sequentially charged with 6-bromo-1-iodo-2-methoxynaphthalene (**68**) (361.8 mg, 1.00 mmol) added Et_3N (2 mL), phenylacetylene (1.1 mmol), $PdCl_2(PPh_3)_2$ (0.1 mmol) and CuI (0.25 mmol). The mixture was stirred at 60 °C for 6 h until fully consumption of **68** by judging on TLC development. Then the mixture was filtered through a pad of Celite®. The solvent was removed under reduced pressure to afford the crude material which was purified by flash column chromatography over silica gel with the system (2% EtOAc/Hexane) giving rise to the product 6-bromo-2-methoxy-1-(phenylethynyl)-naphthalene (**69**) (0.296 mg, 88%) as a yellow liquid. R_f = 0.44 (5% EtOAc/Hexane). IR (neat) ν/cm^{-1}= 3400, 3360,3033, 1590, 1495, 1460. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.9 Hz, 1H), 7.93 (s, 1H), 7.71 (d, *J* = 9.1 Hz, 1H), 7.66 (d, *J* = 6.8 Hz, 2H), 7.60 (d, *J* = 8.9 Hz, 1H), 7.42 – 7.35 (m, 3H), 7.27 (d, *J* = 9.4 Hz, 1H), 4.04 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 159.1, 133.9, 131.9, 130.6, 130.0, 129.9, 129.1, 128.9, 128.7, 127.2, 123.7, 117.9, 113.7, 106.8, 99.4, 83.5, 56.7. HRMS (ESI+): m/z calculated for C19H13BrO $[M+H]^+$= 337.0228, found 337.0237.

*6-(3-chloro-4-fluorophenyl)-2-methoxy-1-(phenylethynyl)naphthalene (**70**)*. The following substrate was prepared by Suzuki-Miyaura cross-coupling reactions between 6-bromo-2-methoxy-1-(phenylethynyl)naphthalene (**69**) obtained in the previous reaction and (3-choloro-4-fluorophenyl)boronic acid. A 50 mL round bottom flask with a stir bar was fitted with a rubber septum and flame dried under high vacuum. The flask was purged with argon and charged with $Pd(PPh_3)_4$ (0.1 mmol), K_2CO_3 (4.2 mmol), 6-bromo-2-methoxy-1-(phenylethynyl)naphthalene (**69**) (56 mg, 2.0 mmol), (3-choloro-4-fluorophenyl)boronic acid (4 mmol), 1,4-dioxene(10.0 mL), and distilled water (2 mL). The reaction mixture was then heated at 80 °C for 12 h. Afterwards the reaction was cooled down to room temperature, the organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 × 10 mL), and the combined organic layer was dried over Na_2SO_4 and concentrated. The crude products were purified by flash chromatography on silica gel (5% EtOAc/Hexane) to afford the product 6-(3-chloro-4-fluorophenyl)-2-methoxy-1-(phenylethynyl)naphthalene (**70**) (45 mg, 68%) as a white solid. m.p.= 96-98 °C. R_f = 0.55 (8 % EtOAc/Hexane). IR (neat) ν/cm^{-1}=3460, 3320,2933, 1560, 1510, 1440. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.7 Hz, 1H), 7.93 (s, 1H), 7.89 (d, *J* = 9.1 Hz, 1H), 7.74 (s, 1H), 7.73 (t, *J* = 2.4 Hz, 1H), 7.69 (dt, *J* = 3.4, 1.9 Hz, 2H), 7.56 (t, *J* = 8.5, 4.5, 2.3 Hz, 1H), 7.43 – 7.35 (m, 3H), 7.33 (d, *J* = 9.1 Hz, 1H), 7.24 (d, *J* = 8.7 Hz, 1H), 4.09 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 159.4, 158.6, 156.6 (d, *J* = 1.1 Hz), 138.2 (d, *J* = 5.1 Hz), 134.9, 133.9, 131.9, 130.4, 129.3, 128.6, 128.3 (d, *J* = 11.6 Hz), 126.8 (d, *J* = 6.9 Hz), 126.5 – 125.9 (m), 123.6, 121.46, 121.3 (d, *J* = 1.3 Hz), 117.02, 116.85, 113.4, 106.3, 99.1, 83.6, 56.7. HRMS (EI): m/z calculated for $C_{25}H_{16}ClFO$ $[M]^+$= 386.0874, found 386.0866.

Computational Details.

The enthalpy and Gibbs free energy calculations for the adduct PhI(OH)·NH_3 were computed as the energy difference between the adduct and the sum of the energies of the optimized PhiIO and the NH_4I at the gas phase employing the Gaussian 16 software package.

Fukui function calculations for PhI(OH)·NH_3. The reactivity of the iodinating species was analyzed by exploring a very useful covalent reactivity descriptor: the Fukui or frontier function, which is usually a reliable predictor of the regioselectivity of soft molecules.[44-46] Fukui functions are defined as the response of the electron density when the number of electrons (*N*) suffers an infinitesimal change, providing us information about the reactive sites of a molecular system.[47] Particularly to indicate how the electron density is redistributed when molecules react, thus, molecular regions suffering more charge rearrangements are the most reactive sites. The Fukui functions are obtained calculating the electron density of the PhI(OH)·NH_3 with *N*, *N-1* and *N+1* electrons respectively at the ground state. The positive ($\boldsymbol{f}^+(\boldsymbol{r})$) and negative ($\boldsymbol{f}^-(\boldsymbol{r})$) forms of the Fukui functions are useful descriptors to evaluate nucleophilic or electrophilic attacks respectively.[48]

The transition state search for the PhI(OH)·NH_3 adduct was obtained by using the DL-FIND library[73] implemented in Terachem 1.9.3[74,75] employing the nudged elastic band method.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Copies of ^{1}H and ^{13}C NMR spectra of compounds **1-70** as well as computational details related to the energetic profile formation, MEP and general details regarding PhI(OH)·NH_3.

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

This work was supported by CONACyT (CB-2013/220836). We acknowledge the facilities of the DCNyE, the Chemistry Department, and the National Laboratory UG-CONACyT (LACAPFEM) at the University of Guanajuato, for full characterization. We thank CONACyT for PhD fellowships to Y.S., N.M. and D.B. We also thank M.C. Kevin Juárez for preliminary optimization assays.

Dedicated to Professor Keiji Maruoka in occasion of his 66th birthday.

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