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Cu–Mn Spinel Oxide Catalyzed Regioselective Halogenation of Phenols and *N*-Heteroarenes

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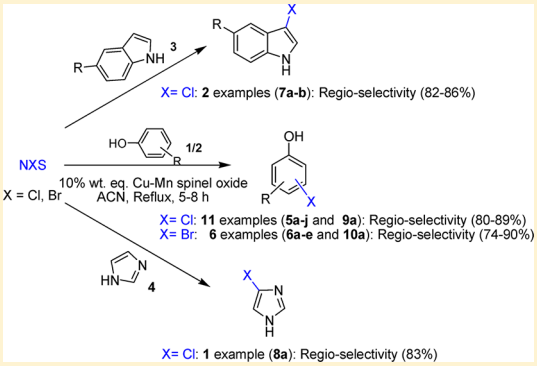
Supporting Information

ABSTRACT: A novel simple, mild chemo- and regioselective method has been developed for the halogenation of phenols using Cu–Mn spinel oxide as a catalyst and *N*-halosuccinimide as halogenating agent. In the presence of Cu–Mn spinel oxide B, both electron-withdrawing and electron-donating groups bearing phenols gave monohalogenated products in good to excellent yields with highest *para*-selectivity. The *para*-substituted phenol gave monohalogenated product with good yield and *ortho*-selectivity. *N*-Heteroarenes such as indoles and imidazoles also gave monohalogenated products with high selectivity. Unlike the copper-catalyzed halogenation, the present method works well with electron-withdrawing group bearing phenols and gives comparatively better yields and selectivity. The Cu–Mn spinel catalyst is robust and reused three times under optimized conditions without any loss in catalytic activity. Nonphenolics did not undergo this transformation.



Halogenated phenols and heteroarenes are widely used as synthons[1] for the synthesis of various drugs, insecticides, herbicides, dyestuffs, etc. Apart from their use as synthons, these are also present in large number of biologically active marine natural products.[2,3] The classical approach for their synthesis is the direct electrophilic halogenation using molecular chlorine/bromine.[4] Apart from this, numerous methods have been developed,[5] but most of the methods have several drawbacks such as toxic reagents, harsh conditions, low yields, and low chemo- and regioselectivity.[4,5] After the discovery of *N*-halosuccinimide as halogenating agents, numerous methods have been developed for the variety of substrates utilizing various catalysts such as SiO_2, HZSM-5, $HBF_4{\cdot}Et_2O$, TBAB, SO_3H-functionalized silica, ammonium acetate, and *p*-TSA.[5,6] In the past decade, several palladium-catalyzed regioselective halogenation methods have been developed,[7] but these methods are either limited to specific substrates (such as amides, pyridines, pyrimidine, carboxylic acids, and oxazolines)[7] or require expensive reagents. In recent years, copper salts have been also utilized as catalysts for the regioselective halogenation of several arenes and heteroarenes such as phenol, aniline, etc.[8] Literature survey on copper-catalyzed halogenation of phenol/aniline revealed that in spite of high yield and regioselectivity, this method is limited only to electron-rich arenes.[8] More recently, a study by Shen et al. on halogenations of 2-phenylpyridine reported that copper in the presence of MnO_2 favor the halogenation on *ortho*-position of phenyl ring.[9] We recently reported a Cu–Mn-based catalyst[10] for ligand-free Huisgen [3 + 2] cycloaddition reaction. Moreover, copper–manganese spinels have also attracted significant attention for their potential applications in catalysis[11] as well as in electrochemical systems.[12] Keeping in mind the recent finding regarding the catalytic properties of copper and magnesium-based catalysts,[10−12] we have explored Cu–Mn spinel oxide for halogenation reactions and successfully developed a mild and regioselective Cu–Mn spinel oxide catalyzed halogenation method for phenols and *N*-heteroarenes.

We began our studies by screening a series of Cu–Mn spinel oxide A–C (variation in their composition) for the halogenation of phenol using *N*-chlorosuccinimide (NCS) as halogenating agent and acetonitrile (ACN) as solvent (results summarized in Table 1). All the optimization reactions were performed in 1 mmol scale. Among the three Cu–Mn spinel oxides used, 10% weight equivalent of Cu–Mn spinel oxide (B)

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Table 1. Screening of Different Copper-Based Catalysts for Regioselective Halogenations[f]

					product composition[a](%)			
entry	catalyst	qty[b]	temp (°C)	time (h)	S	4-Cl	2-Cl	2,4-DiCl
a	Cu−Mn (A)	10[c]	80	10	26	60	10	3
b	**Cu−Mn (B)**	10[c]	**80**	**10**	**7**	**70**	**3**	**12**
c	Cu−Mn (C)	10[c]	80	10	25	61	8	3
d	Cu−Mn (B)	10[d]	80	10	3	70	2	21
e	**Cu−Mn (B)**	10[e]	**80**	**08**	**9**	**80**	**2**	**3**
f	Cu−Mn (B)	20[e]	80	10	24	54	9	9
g	Cu−Mn (B)	5[e]	80	10	13	68	6	8
h	Cu−Mn (B)	1[e]	80	10	28	53	5	10
i			80	10	20	45	33	
J	Cu−Mn (B)	10[e]	rt	36	33	40	27	
k			rt	36	35	42	23	
1	CuI	10[e]	80	10	17	43	32	
m	Cu_2O	10[e]	80	10	18	44	34	
n	$Cu(OAc)_2$	10[e]	80	10	50	25	20	
o	$CuCl_2$	10[e]	80	10	33	49	13	4

[a]The products were characterized by GC−MS. [b]Catalyst wt % equiv w.r.t. phenol. [c]Reaction condition: Phenol (1 mmol) and NCS (1 mmol) in ACN. [d]Reaction condition: Phenol (1 mmol) and NCS (1.2 mmol) in ACN. [e]Reaction condition: Phenol (1 mmol) and NCS (0.9 mmol) in ACN. [f]The number in the product composition denotes the position of chlorination w.r.t. −OH group. S refers to the substrate and Cu−Mn (A) = (Cu/Mn 2:0.25), Cu−Mn (B) = (Cu/Mn 1:0.25), Cu−Mn (C) = (Cu/Mn 3:0.25).

at 80 °C gave *p*-chlorophenol **5a** with 70% selectivity along with 3% of *o*-chlorophenol and 12% of dichlorophenol (Table 1, entry b). The composition of products was determined by GC−MS. Variation in the amount of NCS greatly affected the yields and selectivity (Table 1, entries d and e). Increase in the amount of NCS led to greater byproduct formation (Table 1, entry d), but 0.9 mmol of NCS per 1 mmol of phenol in the presence of 10 wt % equiv of Cu−Mn spinel oxide B at 80 °C increased the yield of **5a** from 70 to 80% and suppressed the formation of dichlorophenol from 12 to 3% (Table 1, entry e). Further, considering this best condition, the effect of amount of catalyst and temperature on this transformation was also evaluated (Table 1, entries f−k). An increase or decrease in the amount of Cu−Mn spinel oxide B did not provide a significant effect toward yield and selectivity (Table 1, entries f−h), but there was substantial loss in the yield and selectivity when reaction was performed at room temperature (Table 1, entry j). Further, no selectivity was observed even when the reactions were performed without Cu−Mn spinel oxide (B) at 80 °C and at room temperature, respectively (Table 1, entries i and k), suggesting that Cu−Mn spinel oxide might interact and activate the substrate at higher temperature, and therefore enhanced yield and *para*-selectivity was observed. We further screened other copper salts, viz., CuI, Cu_2O, $Cu(OAc)_2$, $CuCl_2$, in order to find whether these Cu salts catalyze this reaction, but none of these gave selectivity (Table 1, entries l−o). These findings suggested that it was not the copper but Cu−Mn spinel oxide that mediated the reaction and provided regioselectivity. In order to understand the efficiency and catalytic activity as a function of overall composition, powder X-ray diffraction (Figure S1, Supporting Information (SI)) and specific surface area (Table S1, SI) of the catalysts were studied. Among the three Cu−Mn spinel oxide (A−C) with varying amount of copper (Table S1, SI), the best conversion was observed in Cu−Mn spinel oxide (B). XRD of Cu−Mn spinel oxide (B) shows the presence of distinct Mn−Cu phases with comparatively less intensity of tenorite. On the other hand, Cu−Mn spinel oxide (C) having more intensity of tenorite and very small amount of Mn−Cu phases showed no activity (Figure S1, SI). Further, Cu−Mn spinel oxide (A) and (B) contain the same type of phases (Table S1, SI), but spinel oxide (B) possesses comparatively less intensity of tenorite. These results suggested that presence of tenorite (CuO) greatly affects the yield and selectivity. The presence of distinct Mn−Cu phases in the form of near spherical nanoparticles (Figure S3, SI) and comparatively larger surface area (Table S2, SI) of Cu−Mn spinel oxide (B) might be responsible for enhanced yield and selectivity. The optimization results suggested that 10% weight equivalent of Cu−Mn spinel oxide (B) and 0.9 mmol of NCS per 1 mmol of phenol is the best condition.

In order to see the diversity, tolerability, and feasibility of different functionalities, various substituted phenols were studied under optimized conditions (Table 2). All the experiments were performed without catalyst for comparative study, and results are summarized in Table 2. Both electron-donating group (EDG) and electron-withdrawing group (EWG) bearing phenol gave good to excellent yield as monochlorinated product (Table 2, entries b−j). Among EDG-bearing phenols, 2-methylphenol under optimized conditions provided the 4-chloro-2-methylphenol **5b** in high yields with 85% selectivity as compared to reaction performed without catalyst, which gave a mixture of 46% 4-chloro-2-methylphenol **5b** and 38% 6-chloro-2-methylphenol (Table 2, entry b). The phenol possessing group at *para*-position also underwent chlorination smoothly and gave *ortho*-chlorinated product with good yield and selectivity (Table 2, entries c, h−j). 4-Methylphenol gave 80% 2-chloro-4-methylphenol **5c** (Table 2, entry c).

Further, phenol bearing EWGs such as chloro, nitro, formyl, and acetyl groups (Table 2, entries d−i) gave better yields and *para*-selectivities (if *para*-position is free) as compared to EDG bearing phenols. The present method is also suitable for double bond bearing substrates. Eugenol possessing *para*-allyl group also underwent chlorination reaction and gave *o*-chlorinated product **5j** with 86% selectivity (Table 2, entry j). The effectiveness of the present method is further revealed in the reaction of several *N*-heteroarenes and 2-naphthol (result summarized in Table 3). Indole **3a** and 5-nitroindole **3b** under optimized condition gave 3-chlorosubstituted product **7a** and **7b** with 82 and 86% selectivity, respectively. But in the absence of catalyst, a substantial quantity of dichlorinated product along with unreacted starting material were observed (Table 3, entries a and b). Similarly, imidazole **4a** gave monochloro product **8a** with 83% selectivity as compared to uncatalyzed reaction (Table 3, entry c). The sterically hindered 2-naphthol **2a** also gave monochlorinated product **9a** with 89% selectivity as compared to uncatalyzed reaction (Table 3, entry d).

In order to further know the diversity of present method, the bromination with *N*-bromosuccinimide (NBS) was also explored with various unsubstituted and substituted phenols.

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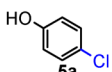
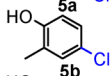
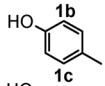
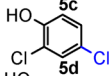
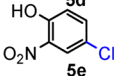
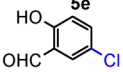
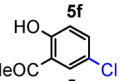
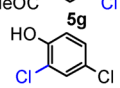
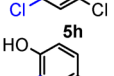
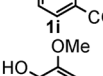
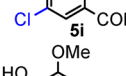
Table 2. Cu–Mn Spinel Oxide (B) Catalyzed Regioselective Chlorination of Phenols[c]

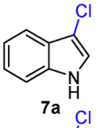
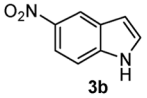
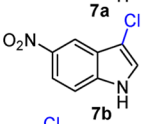
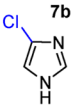
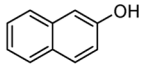
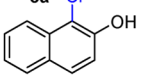
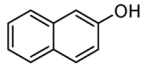
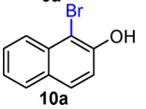
Entry	Substrate	Condition	Time (h)	Product composition (%)[a] S	4-Cl	2-Cl	6-Cl	Di-Cl	Product[b]
a	 1a	A	8	9	**80**	2	-	3	 5a
		B	10	20	45	33	-	-	
		C	36	33	40	27	-	-	
b	 1b	A	8	8	**85**	-	4	-	 5b
		B	10	16	46	-	38	-	
c	 1c	A	8	8	-	**80**	-	3	 5c
		B	10	23	-	42	-	33	
d	 1d	A	8	5	**82**	-	2	3	 5d
		B	10	19	55	-	8	18	
e	 1e	A	8	7	**85**	-	-	2	 5e
		B	10	40	41	-	3	9	
f	 1f	A	8	6	**86**	-	-	1	 5f
		B	10	20	45	-	20	15	
g	 1g	A	8	3	**85**	-	1	2	 5g
		B	10	22	55	-	3	30	
h	 1h	A	8	5	-	**82**	-	4	 5h
		B	10	15	-	55	-	18	
i	 1i	A	8	3	-	**84**	-	3	 5i
		B	10	22	-	52	-	15	
j	 1j	A	8	9	-	**86**	-	-	 5j
		B	10	85	-	7	-	-	

[a]The products were characterized by GC–MS. [b]Isolated yields of major products are provided in the Experimental Section. [c]Reaction condition (A): Phenol (1 mmol), NCS (0.9 mmol), 10 wt % equiv of Cu–Mn spinel oxide (B) w.r.t. phenol at 80 °C. Reaction condition (B): Phenol (1 mmol), NCS (0.9 mmol) at 80 °C. Reaction condition (C): Phenol (1 mmol), NCS (0.9 mmol), 10 wt % equiv of Cu–Mn spinel oxide (B) w.r.t. phenol at rt. The number in the product composition denotes the position of chlorination w.r.t. –OH group. S refers to the substrate.

Phenol on reaction with NBS at 80 °C gave mixture of mono- and dibrominated product along with 33% unreacted phenol, while in the presence of Cu–Mn spinel oxide (B), the selectivity toward the formation the *para*-bromophenol **6a** increased from 29 to 74% (Table 4, entry a). Similarly, in the presence of Cu–Mn spinel oxide (B)/NBS, EDG (such as *o*-methyl), and EWG (*o*-formyl, *o*-acetyl) bearing phenol also underwent bromination with excellent selectivity as compared to experiment performed without catalyst (Table 4, entries b–d). The sterically hindered phenol **1e** did not give brominating product in the absence of Cu–Mn spinel oxide (B), but in the presence of catalyst, it underwent bromination and gave *o*-brominated product **6e** with 90% selectivity (Table 4, entry e). The bromination of naphthol also underwent smoothly and gave monobromo-product **10a** with 84% selectivity (Table 3, entry e).

The present halogenation method was also tried for iodination with *N*-iodosuccinimide (NIS), but it did not give good selectivity; however, the mixture of mono, di, and other products were obtained. Further, regioselective halogenation was not achieved in nonphenolic compounds such as anisole and nitrobenzene, which suggested that the present method is specific to phenols and *N*-heterocycles.

Table 3. Cu–Mn Spinel Oxide (B) Catalyzed Regioselective Chlorination/Bromination of Naphthol and *N*-Heteroarenes[c]

Entry	Substrate	Condition	Time (h)	Product composition (%)[a] S	P	Other	Product[b]
a	 3a	A	8	9	**82**	-	 7a
		B	10	42	38	16	
b	 3b	A	8	3	**86**	4	 7b
		B	10	5	49	43	
c	 4a	A	8	5	**83**	-	 8a
		B	10	40	57	-	
d	 2a	A	8	3	**89**	-	 9a
		B	10	45	53	-	
e	 2a	D	8	3	**84**	-	 10a
		E	10	45	53	-	

[a]The products were characterized by GC–MS. [b]Isolated yields of major products are provided in the Experimental Section. [c]Reaction condition (A): Phenol (1 mmol), NCS (0.9 mmol), 10 wt % equiv of Cu–Mn spinel oxide (B) w.r.t. phenols/*N*-heteroarenes at 80 °C. Reaction condition (B): Phenol (1 mmol), NCS (0.9 mmol) at 80 °C. Reaction condition (D): Phenol (1 mmol), NBS (1 mmol), 10 wt % equiv of Cu–Mn spinel oxide (B) w.r.t. phenols/*N*-heteroarenes at 80 °C. Reaction condition (E): Phenol (1 mmol), NBS (1 mmol) at 80 °C. P refers to major product. S refers to the substrate.

In order to see the robustness of this Cu–Mn spinel oxide (B) catalyst, we carried out the reusability study with 2-formylphenol (Table 5). The Cu–Mn spinel oxide (B) was recovered by filtration after each experiment and could be reused for chlorination of phenol in three successive reactions without significant loss of the catalytic activity. A SEM image of used bimetallic catalyst shows that the morphology and the structural integrity of the Cu–Mn spinel oxide (B) remain same at the end of third run. This finding suggested that Cu–Mn spinel (B) is robust and was not affected under the reaction conditions.

Although the mechanism of present method cannot be clearly explained, some assumptions could be made on the basis of the available information. The applicability of present method toward EWG-bearing phenols suggests that it might not operate through free-radical mechanism, which is normally proposed for copper-catalyzed regioselective oxyhalogenation of phenols/anilines.[8] The above finding was confirmed when present halogenation method underwent smoothly in the presence of free-radical scavenger such as (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) and ruled out the possibility of involvement of free radical mechanism. Our careful examination of literature regarding catalysis of Cu–Mn spinel[11c] and other related bimetallic spinel[13] revealed that their catalytic activity and selectivity largely depends on acid–base properties as well as both structure of catalyst and orientation of substrate. On the basis of literature reports, we speculate that phenolate and aromatic interact with Cu–Mn spinel having an orientation that favors the *para*-selectivity. It is further assumed that Cu–

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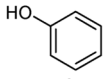
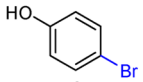
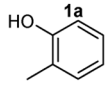
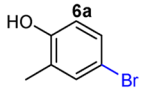
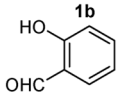
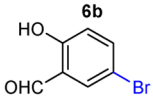
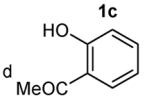
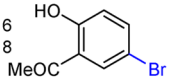
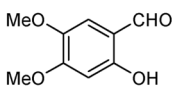
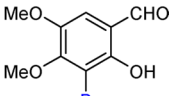
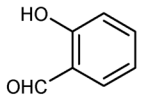
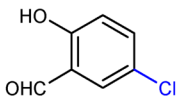
Table 4. Cu−Mn Spinel Oxide (B) Catalyzed Regioselective Bromination of Phenols[c]

Entry	Substrate	Condition	Time (h)	Product composition (%)[a] S	4-Br	2-Br	6-Br Di-Br	Product[b]
a	 1a	D	5	9	**74**	4	- 4	 6a
		E	10	33	29	16	- 15	
b	 1b	D	8	5	**76**	-	2 4	 6b
		E	10	23	35	-	5 35	
c	 1c	D	8	6	**82**	-	3 5	 6c
		E	10	26	23	-	11 36	
d	 1d	D	8	5	**80**	-	4 6	 6d
		E	10	40	45	-	6 8	
e	 1e	D	8	9	-	**90**	- 0	 6e
		E	10	100	-	-	- -	

[a]The products were characterized by GC−MS. [b]Isolated yields of major products are provided in the Experimental Section. [c]Reaction condition (D): Phenol (1 mmol), NBS (1 mmol), 10 wt % equiv of Cu−Mn spinel oxide (B) w.r.t. phenol at 80 °C. Reaction condition (E): Phenol (1 mmol), NBS (1 mmol) at 80 °C. The number in the product composition denotes the position of bromination w.r.t. −OH group. S refers to the substrate.

Table 5. Reusability of Cu−Mn Spinel Oxide (B)[b]

Substrate	Run No.	Time (h)	S	Yield (%)[a]	Product
	1	8	6	86	
	2	8	7	84	
	3	8	7	84	

[a]The products were characterized by GC−MS. [b]Reaction condition (A): Phenol (1 mmol), NCS (0.9 mmol), 10 wt % equiv of Cu−Mn spinel oxide (B) w.r.t. phenols/*N*-heteroarenes at 80 °C. S refers to the substrate.

Mn spinel might also activate NCS/NBS to release chlorinium/brominium ion, which ultimately undergoes halogenation.

In summary, we have presented a new method for regioselective mono chlorination/bromination of phenols and *N*-heteroarenes in the presence of robust and reusable bimetallic Cu−Mn spinel oxide catalyst using simple and inexpensive *N*-halosuccinimides as halogenating agent. The present method is very general and is applicable to both EDG- and EWG-bearing phenols. Moreover, in the present method EWG-bearing phenols gave comparatively better results in terms of yield and selectivity. The present method is also suitable for various *N*-heteroarenes such as indole and imidazole. These transformations provide regioselectively for chlorination and bromination to a wide array of phenols and *N*-heteroarenes. Further exploration for full scope of these reactions and its extension to other arenes and heteroarenes as well as mechanistic study is underway and will be reported in due course.

EXPERIMENTAL SECTION

Preparation of Cu−Mn Spinel Oxide (A−C). A series of copper−manganese mixed oxides (A−C) were prepared by the coaddition of the aqueous solutions of $CuCl_2·2H_2O$ and $MnCl_2·4H_2O$ in a molecular weight ratio (2:0.25; 1:0.25; 3:0.25, respectively) at a rate of 1 mL min^{-1} under vigorous mechanical stirring at room temperature to form a uniform solution. Then ammonia solution was added drop by drop until it reached pH 8.5−8.7 and was allowed to stand overnight to form a gel, filtered, and washed with double distilled water until free from chloride ions. After being kept overnight at room temperature, the cake was allowed to dry in an air oven at 110 °C for 24 h and finally calcined (10 °C min^{-1}) in a muffle furnace at 425 °C for 3 h.

Catalysts were adequately characterized as reported previously[9] to understand the efficiency of catalytic activity. X-ray diffraction (XRD), specific surface area, and scanning electron micrograph (SEM) were studied and are provided in the Supporting Information.

General Procedure for Cu−Mn Spinel Oxide (B) Catalyzed Chlorination of Phenols/*N*-Heteroarenes. Substrate (1 mmol) was dissolved in acetonitrile (5 mL), and then bimetallic catalyst (Cu−Mn spinel oxide B, 10 wt % equiv) was added. The reaction mixture was heated and stirred at 80 °C for 10 min followed by slow addition of NCS (0.9 mmol). Heating was continued at 80 °C for the required time (Tables 2 and 3). After completion of reaction as indicated by TLC, the reaction mixture was filtered, and the filtrate was washed with ethyl acetate (5 mL × 3). The bimetallic catalyst was washed twice with ethyl acetate (5 mL × 2). The combined organic portion was dried over anhydrous Na_2SO_4. The solvent was removed by evaporation under reduced pressure to afford the crude product, which was analyzed by GC−MS to determine the product composition (given in Table 2 and 4). The crude product was then subjected to column chromatography (hexane/ethyl acetate as eluent) for final purification to isolate the respective major product. The products reported herein are characterized by NMR and GC−MS, and their values are in agreement with those reported in the literature.[5,7,14]

4-Chlorophenol ***5a****[5,14a] (Table 2, entry a).* Data: TLC (EtOAc/hexane 2:8) R_f = 0.45; Isolated yield 98.56 mg (77%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.06 (s, 1H), 6.75−6.78 (d, J = 9.03 Hz, 2H), 7.18−7.20 (d, J = 9.03 Hz, 2H); GC−MS (EI) m/z (relative intensity) 130.1 (M^++2, 29.8), 128.2 (M^+, 99.8), 92.0 (1.88), 63.1 (10.06).

4-Chloro-2-methylphenol ***5b****[14b] (Table 2, entry b).* Data: TLC (EtOAc/hexane 2:8) R_f = 0.25; Isolated yield 115.02 mg (81%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.21 (s, 3H), 4.95 (s, 1H), 6.68−6.70 (d, J = 8.49 Hz, 1H), 7.01−7.03 (dd, J = 2.15, 8.46 Hz, 1H), 7.09 (d, J = 1.88 Hz, 1H); GC−MS (EI) m/z (relative intensity) 144.0 (M^++2, 17.13), 142.1 (M^+, 54.92), 107.1 (99.98), 89.0 (13.79), 77.0 (44.77), 63.0 (7.04), 51.0 (9.92).

2-Chloro-4-methylphenol ***5c****[5,14c] (Table 2, entry c).* Data: TLC (EtOAc/hexane 2:8) R_f = 0.38; Isolated yield 68.16 mg (48%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (s, 3H), 5.80 (s, 1H), 6.98 (m, 2H), 7.21 (m, 1H); GC−MS (EI) m/z (relative intensity) 144.1 (M^++2, 13.37), 142.1 (M^+, 47.43), 107.1 (99.99), 79.1 (12.29).

2,4-Dichlorophenol ***5d*** *and* ***5h****[14a] (Table 2, entries d and h).* Data: TLC (EtOAc/hexane 2:8) R_f = 0.31; Isolated yield 126.36 mg (78% for **5d**) and 123.50 (76% for **5h**); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93−6.95 (d, J = 8.79, 1H), 7.13−7.15 (dd, J = 2.51, 8.54 Hz, 1H), 7.31−7.32 (d, J = 2.63, 1H); GC−MS (EI) m/z (relative intensity) 164.0 (M^++2, 10.53), 162.2 (M^+, 99.95), 126.2 (20.08), 99.0 (13.73), 73.1 (5.71), 63.1 (60.27), 53.1 (6.58).

4-Chloro-2-nitrophenol ***5e****[14d] (Table 2, entry e).* Data: TLC (EtOAc/hexane 2:8) R_f = 0.39; Isolated yield 138.40 mg (80%); ^{1}H NMR (400 MHz $CDCl_3$) δ 7.13−7.15 (d, J = 8.62 Hz, 1H), 7.53−7.56 (d, J = 9.54 Hz, 1H), 8.11 (s, 1H), 10.48 (s, 1H); GC−MS (EI) m/z (relative intensity)174.9 (M^++2, 33.9), 173.0 (M^+, 99.93), 157.0 (10.4), 143.1 (44.04), 128.1 (10.10), 115.1 (66.14), 99.0 (45.67), 73.0 (16.17), 63.0 (69.49), 52.9 (10.56).

4-Chloro-2-formylphenol ***5f****[14e] (Table 2, entry f).* Data: TLC (EtOAc/hexane 2:8) R_f = 0.41; Isolated yield 124.80 mg (80%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96−6.98 (d, J = 8.53 Hz, 1H), 7.46−

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7.49 (dd, J = 2.38, 9.67 Hz, 1H), 7.53−7.57 (d, J = 3.01 Hz, 1H), 9.85 (s, 1H), 10.92 (s, 1H); GC−MS (EI) m/z (relative intensity) 158.2 (M^++2, 31.71), 156.2 (M^+, 99.98), 127.5 (12.81), 99.1 (25.49), 74.2 (6.24), 63.2 (30.28).

2-Acetyl-4-chlorophenol ***5g***[14f,g] *(Table 2, entry g).* Data: TLC (EtOAc/hexane 2:8) R_f = 0.32; Isolated yield 120.70 mg (71%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.61 (s, 3H), 6.93−6.95 (d, J = 8.8 Hz, 1H), 7.40−7.43 (dd, J = 2.56, 8.62 Hz, 1H), 7.69−7.70 (d, J = 2.56 Hz, 1H), 12.14 (s, 1H); GC−MS (EI) m/z (relative intensity) 172 (M^++2, 17.5), 170 (M^+, 96.36), 155.4 (100), 99.0 (4.72), 63.1 (9.62).

4-Acetyl-2-chlorophenol ***5i***[14g] *(Table 2, entry i).* Data: TLC (EtOAc/hexane 2:8) R_f = 0.38; Isolated yield 134.30 mg (79%); ^{1}H NMR (500 MHz $CDCl_3$) δ 2.56 (s, 3H), 6.05 (s, 1H), 7.07−7.09 (d, J = 8.51 Hz, 1H), 7.81−7.84 (dd, J = 1.78, 8.76 Hz, 1H), 7.99 (d, J = 1.96 Hz, 1H); GC−MS (EI) m/z (relative intensity) 172.0 (M^++2, 6.05), 170.0 (M^+, 17.25), 155.1 (99.94), 127.2 (19.00), 99.0 (24.56), 63.0 (17.58), 51.0 (3.11).

4-Allyl-2-chloro-6-methoxy phenol ***5j***[7b,c] *(Table 2, entry j).* Data: TLC (EtOAc/hexane 2:8) R_f = 0.41; Isolated yield 158.40 mg (80%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.24−3.29 (m, 2H), 3.88 (s, 3H), 5.06−5.10 (d, J = 15.01 Hz, 2H), 5.73−5.80 (m, 1H), 5.84−5.96 (m, 1H), 6.59 (s, 1H), 6.77 (s, 1H); GC−MS (EI) m/z (relative intensity) 200.0 (M^++2,32.29), 198.0 (99.99), 183.0 (17.20), 163.1 (21.36), 131.1 (54.50), 119.1 (51.78), 103.1 (67.46), 91.0 (51.78), 77.0 (7.52), 63 (10.17), 51.0 (4.76).

3-Chloro-1H-indole[14h] ***7a*** *(Table 3, entry a).* Data: TLC (EtOAc/hexane 2:8) R_f = 0.32; Isolated yield 117.78 mg (78%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09−7.12 (t, J = 7.73 Hz, 1H), 7.16−7.20 (t, J = 8.04 Hz, 1H), 7.41−7.43 (d, J = 8.13 Hz, 1H),7.47−7.53 (m, 2H), 11.34 (brs, 1H); GC−MS (EI) m/z (relative intensity) 153.0 (M^++2, 30.11), 151.2 (M^+, 99.98), 123.4 (6.69), 116.4 (18.40), 89.1 (49.96), 63.1 (8.39).

3-Chloro-5-nitro-1H-indole[14i] ***7b*** *(Table 3, entry b).* Data: TLC (EtOAc/hexane 3:7) R_f = 0.36; Isolated yield 158.76 (81%); ^{1}H NMR (400 MHz $CDCl_3$) δ 7.62 (d, J = 9.04 Hz, 1H), 7.85 (s, 1H), 8.06−8.09 (dd, J = 2.27, 9.03 Hz, 1H), 8.32−8.40 (d, J = 2.04 Hz, 1H), 12.12 (brs, 1H); GC−MS (EI) m/z (relative intensity) 198.0 (M^++2, 30.16), 196.1 (99.99), 180 (14.87), 166.1 (62.04), 150.1 (21.56), 138.1 (26.76), 123.1 (37.20), 115.2 (17.0), 87.1 (13.40).

4-Chloro-1H-imidazole[14j] ***8a*** *(Table 3, entry c).* Data: TLC (EtOAc/hexane 3:7) R_f = 0.39; Isolated yield 80.58 mg (79%); ^{1}H NMR (200 MHz $CDCl_3$) δ 6.99 (s, 1H), 7.57 (s, 1H); GC−MS (EI) m/z (relative intensity) 104.0 (M^++2, 31.08), 102.0 (M^+, 99.85), 75.0 (35.25), 48.0 (12.66), 40.0 (12.01).

1-Chloro-2-naphthol[14k,l] ***9a*** *(Table 3, entry d).* Data: TLC (EtOAc/hexane 2:8) R_f = 0.32; yield 151.30 mg (85%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89 (s, 1H), 7.25−7.27 (m, peak merged with $CDCl_3$, 1H), 7.38−7.42 (t, J = 7.28 Hz, 1H), 7.55−7.59 (t, J = 7.13 Hz, 1H), 7.70−7.72 (d, J = 8.89 Hz, 1H), 7.78−7.80 (d, J = 8.17 Hz,1H), 8.05−8.07 (d, J = 8.49 Hz, 1H); GC MS (EI) m/z (relative intensity) 180.1 (M^+ +2, 31.3), 178.3 (M^+, 99.9), 149.4 (9.08), 114.4 (35.59), 87.1 (7.30), 63.1 (5.20).

General Procedure for Cu−Mn Spinel Oxide (B) Catalyzed Bromination of Phenols/*N*-Heteroarenes. Substrate (1 mmol) was dissolved in acetonitrile (5 mL), and then bimetallic catalyst (Cu−Mn spinel oxide B, 10 wt % equiv) was added. The reaction mixture was heated and stirred at 80 °C for 10 min followed by slow addition of NBS (0.9 mmol). Heating was continued at 80 °C for the required time (Tables 3 and 4). After completion of reaction as indicated by TLC, the reaction mixture was filtered, and the filtrate was washed with ethyl acetate (5 mL × 3). The bimetallic catalyst was washed twice with ethyl acetate (5 mL × 2). The combined organic portion was dried over anhydrous Na_2SO_4. The solvent was removed by evaporation under reduced pressure to afford the crude product, which was analyzed by GC−MS and NMR spectroscopic methods to determine the product composition (given in Tables 3 and 4). The crude product was then subjected to column chromatography (hexane/ethyl acetate as eluent) for final purification to isolate the respective major product. The products reported herein are characterized by NMR and GC−MS and their values are in agreement with those reported in the literature.[15]

4-Bromophenol[15a] ***6a*** *(Table 4, entry a).* Data: TLC (EtOAc/hexane 3:7) R_f = 0.35; Isolated yield 122.12 mg (71%); ^{1}H NMR (400 MHz $CDCl_3$) δ 4.96 (s, 1H), 6.71−6.73 (dd, J = 2.17, 6.81 Hz, 2H), 7.32−7.34 (dd, J = 2.08, 6.72 Hz, 2H); GC−MS (EI) m/z (relative intensity) 174.1 (M^++2, 97.59), 172.0 (M^+, 99.99), 131.2 (5.54), 63.1 (21.15).

4-Bromo-2-methylphenol[15b] ***6b*** *(Table 4, entry b).* Data: TLC (EtOAc/hexane 3:7) R_f = 0.35; Isolated yield 135.78 mg (73%); ^{1}H NMR (400 MHz $CDCl_3$) δ 2.22 (s, 3H), 5.05 (s, 1H), 6.64−6.66 (d, J = 8.47 Hz, 1H), 7.15−7.18 (dd, J = 2.27, 8.48 Hz, 1H), 7.23−7.24 (d, J = 2.01 Hz, 1H); GC−MS (EI) m/z (relative intensity) 190.0 (M^++2, 73.26), 188.0 (M^+, 74.66), 107.1 (99.99), 77.1 (74.49), 51.0 (15.6).

4-Bromo-2-formylphenol[15c] ***6c*** *(Table 4, entry c).* Data: TLC (EtOAc/hexane 3:7) R_f = 0.37; Isolated yield 156.00 mg (78%); ^{1}H NMR (400 MHz $CDCl_3$) δ 6.90−6.92 (d, J = 8.87 Hz, 1H), 7.59−7.62 (dd, J = 2.47, 8.87 Hz, 1H), 7.68 (d, J = 2.32 Hz, 1H), 9.84 (s, 1H), 10.93 (s, 1H); GC−MS (EI) m/z (relative intensity) 202.2 (M^++2, 95.65), 200.1 (M^+, 99.96), 182.1 (7.01), 156.1 (7.44), 143.1 (12.96), 92.1 (5.52), 75.1 (6.02), 63.1 (33.13).

2-Acetyl-4-bromo-phenol[15d] ***6d*** *(Table 4, entry d).* Data: TLC (EtOAc/hexane 3:7) R_f = 0.34; Isolated yield 164.78 mg (77%); ^{1}H NMR (400 MHz $CDCl_3$) δ 2.63 (s, 3H), 6.89−6.91 (d, J = 8.89 Hz, 1H), 7.54−7.56 (dd, J = 2.42, 8.89 Hz, 1H), 7.84 (d, J = 2.42 Hz, 1H), 12.16 (s, 1H); GC -MS (EI) m/z (relative intensity) 216.0 (M^++2, 44.30), 214.0 (M^+, 48.9), 199.1 (99.98), 143.1 (14.36), 89.1 (5.94), 63.1 (24.82), 43.0 (10.61).

3-Bromo-2-hydroxy-4,5-dimethoxybenzaldehyde[15e] ***6e*** *(Table 4, entry e).* Data: TLC (EtOAc/hexane 3:7) R_f = 0.36; Isolated yield 223.60 mg (86%); ^{1}H NMR (400 MHz $CDCl_3$) δ 3.89 (s, 3H), 4.00 (s, 3H), 7.02 (s, 1H), 9.75 (s, 1H), 11.57 (s, 1H); GC−MS (EI) m/z (relative intensity) 264.1 (M^++2, 26.11), 262.0 (M^++2, 30.11), 262.1(M^+, 97.46), 245.2 (13.68), 217.2 (5.86), 189.2 (6.47), 137.2 (17.11), 110.2 (49.11), 95.1 (6.40), 79.2 (6.52), 53.1 (10.95).

1-Bromo-2-napthol[15a] ***10a*** *(Table 3, entry e).* Data: TLC (EtOAc/hexane 3:7) R_f = 0.37; Isolated yield 175.38 mg (79%); ^{1}H NMR (400 MHz $CDCl_3$) δ 5.91 (s, 1H), 7.26−7.29 (m, 1H submerged with solvent peak), 7.38−7.42 (t, J = 7.14 Hz, 1H), 7.55−7.59 (t, J = 7.30 Hz, 1H), 7.74−7.76 (d, J = 8.83 Hz, 1H), 7.78−7.80 (d, J = 8.18 Hz, 1H), 8.02−8.04 (d, J = 8.48 Hz, 1H); GC−MS (EI) m/z (relative intensity) 224.2 (M^++2, 90.00), 222.1 (M^+, 99.93), 195.0 (6.05), 143.1 (5.84), 115 (89.85), 87.0 (15.76), 63 (13.49).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Characterization data of Cu−Mn spinel oxide along with ^{1}H NMRs and GC−MS of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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