Efficient Halogenation of Aromatic Systems Using *N*-Halosuccinimides in Ionic Liquids

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Abstract: A simple, rapid and highly regioselective green protocol has been developed for the halogenation of aromatic systems with *N*-halosuccinimides using room temperature ionic liquids (ILs) as novel and recyclable reaction media to produce the corresponding halogenated aromatic compounds in high to quantitative yields. *N*-Halosuccinimides show enhanced reactivity in ionic liquids thereby reducing the reaction times dramatically and improving the yields substantially.

Keywords: arenes; electrophilic halogenation; haloarenes; ionic liquids (ILs)

Introduction

Halogenation of aromatic systems is an important industrial process for the synthesis of drugs, pharmaceuticals, agrochemicals, pigments and photographic materials.[1] The direct method for the bromination of aromatic systems using Br_2 generates toxic and corrosive HBr, which causes serious environmental pollution.[2] Subsequently, several methods have been developed for the bromination of aromatic systems using a variety of brominating agents under various reaction conditions[3,4]. Among these reagents, NBS is one of the most popular and inexpensive brominating agents for allylic, benzylic and aromatic nuclear brominations under mild conditions.[5] The major advantage of the use of NBS as brominating agent is that the byproduct succinimide can be easily recovered and reconverted to NBS and can be reused in subsequent reactions. Allylic and benzylic bromination with NBS takes place in the presence of a radical initiator in CCl_4.[6] The bromination of unactivated aromatics with NBS proceeds only in the presence of stoichiometric amounts of strong Lewis acids or protic acids.[7] The nuclear bromination of activated aromatic systems with NBS is generally favored in polar solvents such as propylene carbonate, DMF and CH_3CN.[8] However, the use of solvents like water, supercritical fluids and ionic liquids has recently received a great deal of attention in different areas of organic chemistry.

Particularly, ionic liquids are being used as 'green solvents' with unique properties such as good solvating ability, wide liquid range, tunable polarity, high thermal stability, immiscibility with a number of organic solvents, negligible vapor pressure and ease of recyclability.[9]

[Bmim]PF_6 [Bmim]BF_4

Figure 1. Chemical structures of ionic liquids (ILs).

Due to the stabilization of charged intermediates by ionic liquids, the latter can promote unprecedented selectivities and reaction rates in comparison with conventional solvents. Because of their distinct advantages, ionic liquids can make a great contribution to green chemistry.[10] More recently, ionic liquids have also been used for the bromination of aromatic systems.[11]

Results and Discussion

We herein report the use of ionic liquids as novel and recyclable polar reaction media for the halogenation of aromatic systems using *N*-halosuccinimides (Scheme 1).

Accordingly, treatment of anisole with NBS and NIS in 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim]PF_6) ionic liquid afforded *p*-bromo- and *p*-iodoanisoles in 92% and 95% yields, respectively. In a similar manner, various substituted aromatic systems were converted to their corresponding bromo and iodo derivatives in high to quantitative yields by using this procedure. In all cases, the reactions proceeded rapidly at 27 °C with high regioselectivity. Interestingly, methyl-substituted aromatic compounds also reacted smoothly with *N*-halosuccinimides in ionic liquids to produce the corresponding halobenzenes without halogenation of the alkyl side-chain (entries **f**, **j** and **m**, Table 1). The substrates show significant enhancement in reaction

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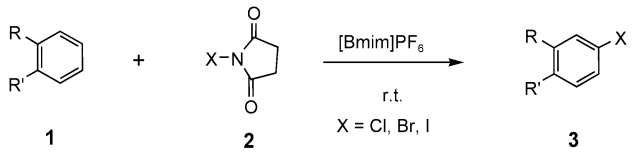

Scheme 1.

rates and yields in ionic liquids compared to molecular organic solvents. For example, treatment of *o*-methoxyphenol with NBS in [bmim]PF_6 ionic liquid for 15 min afforded the corresponding 4-bromo-2-methoxyphenol in 90% yield with *para*-selectivity whereas the same reaction in acetonitrile after 2.0 h gave the product in 79% yield as a mixture of *para*- (major) and *ortho*-isomers (minor). The rate enhancement in ionic liquids is probably due to the enhanced reactivity of *N*-halosuccinimides as result of increased polarization of the N–X bond in polar ionic media and also to the stabilization of the charged ionic intermediates by ionic liquids. This type of ionic environment might not be achieved in molecular organic solvents. It is also known that the polar solvents can enhance the polarization of NBS thereby making the ring bromination possible even in the case of polyalkylbenzenes.[12] Since the products were weakly soluble in the hydrophobic [bmim]PF_6 ionic liquid, they could be easily separated by simple extraction with toluene or ether. Then the rest of the ionic liquid was thoroughly washed with water to recover the water-soluble succinimide. The recovered succinimide was reconverted to the corresponding *N*-halosuccinimide and then reused in subsequent reactions. The rest of the ionic liquid was activated at 80 °C under reduced pressure and recycled in further runs without any loss of activity and, also, the products were obtained of the same purity as in the first run, in runs carried out using recycled activated ionic liquid. For instance, treatment of anisole with NIS in hydrophobic [bmim]PF_6 gave 95%, 93% and 94% yields over three cycles. Even though similar results were also obtained in hydrophilic [bmim]BF_4 ionic liquid, the recovery of succinimide is especially simple in [bmim]PF_6 ionic liquid due to its hydrophobic nature. To compare the efficiency of ionic liquids, the reactions were also carried out in various quaternary ammonium salts such as 1-butyl-3-methylimidazolium chloride [bmim]Cl and *n*-tetrabutylammonium chloride. High temperature reaction conditions (60 °C) and longer reaction times (5–8 h) are typical in these solvents to achieve comparable yields to those obtained at room temperature in ionic liquids. Lowering of the reaction temperature was detrimental to the efficiency of this procedure. The scope and generality of this process is illustrated with respect to various aromatic substrates and *N*-halosuccinimides and the results are presented in the Table 1.

Furthermore, NCS also reacted similar to NBS and NIS, with aromatic systems to give the corresponding chloroaromatics in 79–92% yields within 0.5–1.5 h in [bmim]PF_6 ionic liquid and the results are presented in Table 2. [Bmim]BF_4 and [bmim]PF_6 ionic liquids were obtained from Fluka and used without any further purification. The purity of [bmim]PF_6 is $\geq$ 97.0% (NMR).

Table 1. Halogenation of arenes using *N*-halosuccinimides in [bmim]PF_6 ionic liquid.

Entry	Arene 1	Product[a] X = 3 Br, 3' = I	NBS Time (min)	NBS Yield (%)[b]	NIS Time (min)	NIS Yield (%)[b]
a			25	92	20	95
b			20	90	25	92
c			25	93	25	94
d			55	84	45	87
e			45	86	40	89
f			30	89	35	92
g			35	90	25	91
h			20	92	15	95
i			15	90	10	93
j			35	85	40	89
k			25	92	20	92
l			35	87	40	90
m			50	82	45	85
n			40	90	35	92
o			35	89	30	90
p			20	92	25	94

[a] All products were characterized by ^{1}H NMR, IR and mass spectroscopy.
[b] Yield refers to pure products after column chromatography.

Conclusion

In summary, [bmim]PF_6 ionic liquid has proved to be a useful and polar alternative reaction media for the regioselective halogenation of aromatic compounds using *N*-halosuccinimides, avoiding the use of environ-

Table 2. Chlorination of arenes using NCS in [bmim]PF_6 ionic liquid.

Entry	Arene 1	Product[a] 4	NCS Time (min)	NCS Yield (%)[b]
a			65	87
b			55	90
c			60	92
d			70	89
e			30	90
f			45	87
g			40	90
h			55	85
i			75	78
j			45	87
k			55	85
l			60	90

[a] All products were characterized by ^{1}H NMR, IR and mass spectroscopy.
[b] Yield refers to pure products after column chromatography.

mentally unfavorable organic solvents by playing a dual role of solvent as well as promoter. The substrates show significant increases in reactivity thereby reducing the reaction times and improving the yields substantially. The simple experimental and product isolation procedures combined with ease of recovery and reuse of this novel reaction media are expected to contribute to the development of a green strategy for the halogenation of aromatic systems. The recoverability of succinimide and recyclability of [bmim]PF_6 is facilitated by its hydrophobic nature.

Experimental Section

A mixture of aromatic substrate (1 mmol) and *N*-halosuccinimide (1.2 mmol) in [bmim]PF_6 or [bmim]BF_4 (2 mL) was stirred at 27 °C for the appropriate time (Tables 1 and 2). After completion of the reaction, as indicated by TLC, the reaction mixture was washed with toluene or diethyl ether (3 × 10 mL). The combined organic extracts were concentrated under vacuum and the resulting product was directly charged onto a small silica gel column and eluted with a mixture of ethyl acetate:*n*-hexane (1:9) to afford the pure halogenated arene. The rest of the [bmim]PF_6 ionic liquid was washed with water to remove the succinimide; the ionic liquid was reactivated at 80 °C under reduced pressure and recycled in subsequent runs without any loss of activity. In the case of liquids, the products were easily be separated by distillation. All the products are known compounds. Their identities were confirmed by comparison of their IR, NMR and mass spectroscopic as well as their physical data with those of authentic samples. The spectral data of all the products were identical with those of authentic samples.[13]

1-Bromo-4-methoxybenzene (3a, Table 1): Liquid; IR (neat): ν = 2936, 2838, 1605, 1597, 1518, 1472, 1426, 1293, 1226, 1171, 1097, 1028, 926, 869, 792, 697 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.75 (s, 3H), 6.76 (d, 2H, *J* = 8.0 Hz), 7.36 (d, 2H, *J* = 8.0 Hz); EIMS: *m/z* (%): = 187 (M^+, 17), 172 (10), 156 (13), 107 (100), 92 (42), 76 (63), 51 (37).

1-Bromo-3,4-dimethoxybenzene (3b, Table 1): Liquid, IR (neat): ν = 2941, 2839, 1698, 1603, 1528, 1486, 1440, 1297, 1231, 1212, 1184, 1139, 1019, 932, 841, 798, 781, 695 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.83 (s, 3H), 3.84 (s, 3H), 6.75 (d, 1H, *J* = 8.1 Hz), 6.99 (d, 1H, *J* = 2.1 Hz), 7.13 (m, 1H); EIMS: *m/z* (%) = 217 (M^+, 29), 202 (12), 186 (38), 171 (63), 91(100), 75 (27), 50 (43).

3,4-Methylenedioxybromobenzene (3c, Table 1): Liquid, IR (neat): ν = 2941, 2849, 1674, 1505, 1479, 1435, 1376, 1297, 1123, 1045, 943, 848, 773, 650 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.91 (s, 2H), 6.59 (d, 1H, *J* = 8.3 Hz), 7.11 (d, 1H, *J* = 8.3 Hz), 7.20 (dd, 1H, *J* = 8.3, 2.0 Hz); EIMS: *m/z* (%) = 201 (M^+, 34), 171 (100), 91 (60), 75 (41), 51 (28).

2-Bromo-4,5-dimethoxy-acetophenone (3d, Table 1): Liquid, IR (neat): ν = 2921, 2851, 1683, 1591, 1502, 1371, 1258, 1218, 1171, 1011, 773, 649 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.50 (s, 3H), 3.89 (s, 3H), 3.90 (s, 3H), 6.80 (d, 1H, *J* = 8.1 Hz), 7.50 (m, 1H). EIMS: *m/z* (%) = 259 (M^+, 23), 228 (12), 213 (18), 133 (100), 90 (60), 74 (57), 50 (30).

5-Bromovaniline (3e, Table 1): Solid, mp 163 – 165 °C, IR (KBr): ν = 3497, 2963, 2847, 1706, 1634, 1596, 1523, 1469, 1398, 1276, 1218, 1183, 1096, 1018, 953, 869, 760, 659 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.98 (s, 3H), 6.63 (br s, 1H, OH), 7.34 (d, 1H, *J* = 2.0 Hz), 7.80 (d, 1H, *J* = 1.9 Hz), 9.85 (s, 1H, CHO); EIMS: *m/z* (%) = 231 (M^+, 29), 199 (100), 119 (73), 90 (34), 74 (53), 50 (20).

1-Bromo-2,4-dimethoxy-3-methylbenzene (3f, Table 1): Liquid, IR (neat): ν = 2947, 2851, 1635, 1603, 1571, 1479, 1423, 1306, 1278, 1215, 1180, 1097, 1022, 930, 865, 790, 669 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.18 (s, 3H), 3.78 (s, 3H), 3.80 (s, 3H), 6.48 (d, 1H, *J* = 8.2 Hz), 7.22 (d, 1H, *J* = 8.2 Hz); EIMS: *m/z* (%) = 231 (M^+, 40), 200 (18), 185 (67), 105 (100), 89 (53), 51 (20).

1,2-Dibromo-4,5-dimethoxybenzene (3g, Table 1): Solid, mp 88 – 89 °C, IR (KBr): ν = 2949, 2841, 1608, 1576, 1472, 1419, 1297, 1225, 1181, 1093, 1026, 929, 864, 789, 692 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.86 (s, 3H), 3.88 (s, 3H), 7.05 (s, 2H); EIMS: *m/z* (%) = 297 (M^+, 25), 252 (91), 206 (28), 191 (18), 172 (10), 133 (81), 128 (78), 113 (43), 99 (37), 70 (41), 56 (81), 42 (100).

1-Bromo-2,3,4-trimethoxybenzene (3h, Table 1): Liquid, IR (neat): ν = 2939, 2839, 1605, 1578, 1473, 1422, 1295, 1220, 1175, 1093, 1021, 928, 865, 789, 694 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.82 (s, 3H), 3.84 (s, 3H), 3.90 (s, 3H), 6.58 (d, 1H, *J* = 8.1 Hz), 7.15 (d, 1H, *J* = 8.1 Hz). EIMS: *m/z* (%) = 247 (M^+ 21), 232 (10), 217 (16), 201 (37), 186 (21), 170 (40), 167 (20), 90 (67), 74 (100), 50 (31).

4-Bromo-2-methoxyphenol (3i, Table 1): Liquid, IR (neat): ν = 3506, 2947, 2839, 1608, 1580, 1479, 1420, 1295, 1220, 1185, 1096, 1037, 930, 869, 785, 658 cm^{-1}; ^{1}H NMR (200 MHz,

$CDCl_3$): δ = 3.89 (s, 3H), 5.55 (s, 1H), 6.79 (d, 1H, *J* = 8.0 Hz), 6.95 (d, 1H, *J* = 2.1 Hz), 6.98 (dd, 2H, *J* = 8.0, 2.1 Hz). EIMS: *m/z* (%) = 204 (M^+, 100), 202 (98), 189 (74), 187 (72), 171 (34), 161 (38), 159 (41), 91 (34), 75 (53), 51 (35).

2-Bromo-4-isopropylphenol (3j, Table 1): Liquid, IR (neat): ν = 3507, 2962, 2872, 2361, 1711, 1606, 1559, 1496, 1476, 1414, 1364, 1324, 1276, 1184, 1039, 873, 848, 823, 735, 670 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 1.22 (s, 3H), 1.28 (s, 3H), 2.75 – 2.90 (m, 1H), 6.93 (d, 1H, *J* = 8.1 Hz), 7.05 – 7.12 (dd, 1H, *J* = 8.1, 2.0 Hz), 7.28 (s, 1H); EIMS: *m/z* (%) = 215 (M^+, 11), 172 (19), 91(56), 74 (41), 43 (100).

2-Bromo-4,5-methylenedioxyphenol (3k, Table 1): Solid, mp 150 – 152 °C, IR (KBr): ν = 3489, 2924, 2854, 1619, 1469, 1379, 1164, 1014, 963, 827, 650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 5.30 (br s, 1H, OH), 5.92 (s, 2H), 6.58 (s, 1H), 6.88 (s, 1H); EIMS: *m/z* (%) = 217 (M^+, 28), 187 (11), 106 (100), 90 (48), 74 (69), 50 (31).

5-Bromo-2-hydroxybenzaldehyde (3l, Table 1): Solid, mp 104 – 105 °C, IR (KBr): ν = 3226, 2876, 2364, 1673, 1610, 1563, 1467, 1373, 1305, 1276, 1207, 1155, 1114, 890, 828, 766, 697, 624 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 6.90 (d, 1H, *J* = 8.0 Hz), 7.60 (dd, 1H, *J* = 8.0, 2.0 Hz), 7.70 (s, 1H), 9.95 (s, 1H, -CHO), 10.9 (br s, 1H, OH); EIMS: *m/z* (%) = 201 (M^+, 95), 200 (100), 157 (12), 144 (16), 65 (34), 63 (38), 43 (21).

1-Bromo-2-methylnaphthalene (3m, Table 1): Liquid, IR (neat): ν = 3052, 2979, 2867, 2361, 1714, 1595, 1556, 1501, 1440, 1326, 1259, 1221, 1138, 1034, 964, 898, 862, 808, 763, 642 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 2.65 (s, 3H), 7.30 (d, 1H, *J* = 8.1 Hz), 7.55 (d, 1H, *J* = 8.0 Hz), 7.60 (dd, 1H, *J* = 8.1, 2.0 Hz), 7.70 (m, 1H), 7.80 (d, 1H, *J* = 8.1 Hz), 8.30 (d, 1H, *J* = 8.0 Hz); EIMS: *m/z* (%) = 221 (M^+ 19), 142 (100), 126 (14), 116 (20), 91 (31), 43 (20).

1-Bromo-2-methoxynaphthalene (3n, Table 1): Liquid, IR (neat): ν = 2978, 2843, 1604, 1574, 1469, 1423, 1294, 1225, 1180, 1093, 1022, 920, 893, 859, 809, 766, 652 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 3.98 (s, 3H), 7.26 (d, 1H, *J* = 8.0 Hz), 7.39 – 7.41 (m, 1H), 7.54 – 7.56 (m, 1H), 7.72 (d, 1H, *J* = 7.9 Hz), 7.80 (d, 1H, *J* = 8.0 Hz), 8.22 (d, 1H, *J* = 7.9 Hz); EIMS: *m/z* (%) = 237 (M^+, 19), 206 (41), 194 (11), 181 (28), 157 (12), 130 (15), 126 (100), 114 (23), 104 (58), 102 (32), 76 (69), 51 (20).

1-Bromo-4-methoxynaphthalene (3o, Table 1): Liquid, IR (neat): ν = 2959, 2847, 1608, 1571, 1465, 1427, 1291, 1223, 1182, 1091, 1026, 923, 891, 861, 812, 765, 650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 3.92 (s, 3H), 6.61 (d, 1H, *J* = 7.9 Hz), 7.53 (m, 1H), 7.59 (m, 1H), 7.62 (d, 1H, *J* = 8.0 Hz), 8.14 (d, 1H, *J* = 7.9 Hz), 8.25 (d, 1H, *J* = 8.0 Hz); EIMS: *m/z* (%) = 237 (M^+, 28), 222 (16), 206 (38), 194 (19), 181 (25), 157 (13), 126 (100), 114 (20), 104 (39), 76 (48), 51 (30).

1-Bromo-2-naphthol (3p, Table 1): Solid, mp 79 – 80 °C, IR (KBr): ν = 3498, 2983, 2848, 1615, 1583, 1511, 1476, 1410, 1286, 1217, 1181, 1083, 1026, 931, 893, 866, 817, 768, 665 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 7.91 (d, 1H, *J* = 8.1 Hz), 7.72 – 7.74 (m, 2H), 7.56 (t, 1H, *J* = 8.2 Hz), 7.41 (t, 1H, *J* = 8.2 Hz), 7.28 (d, 1H, *J* =8.1 Hz); EIMS: *m/z* (%) = 223 (M^+, 63), 194 (36), 168 (21), 148 (18), 114 (100), 88 (19), 76 (59), 64 (27), 51 (30).

1-Iodo-4-methoxybenzene (3a′, Table 1): Colorless solid, mp 51 – 52 °C, IR (KBr): ν = 2939, 2837, 1659, 1606, 1518, 1473, 1429, 1297, 1221, 1176, 1094, 1027, 929, 749, 692, 671 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 3.80 (s, 3H, OCH_3), 6.58 (d, 2H, *J* = 8.1 Hz), 7.48 (d, 2H *J* = 8.1 Hz); ^{13}C NMR (200 MHz, $CDCl_3$): δ = 142.7, 136.3, 129.2, 126.7, 112.8, 68.6; EIMS: *m/z* (%) = 234 (M^+, 19), 108 (100), 77 (21), 65 (59).

1-Iodo-3,4-dimethoxybenzene (3b′, Table 1): Solid, mp 76 – 78 °C, IR (KBr): ν = 2938, 2836, 1573, 1478, 1432, 1409, 1293, 1227, 1220, 1179, 1134, 1010, 920, 837, 796, 774, 693 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 3.83 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3) 6.60 (d, 1H *J* = 8.0 Hz), 7.21 (d, 1H, *J* = 2.1 Hz) 7.23 (dd, 1H, *J* = 8.0, 2.1 Hz); ^{13}C NMR ($CDCl_3$): δ = 146.4, 126.8, 121.2, 118.7, 116.57.6. 56.8; EIMS: *m/z* (%) = 264 (M^+ 21), 137 (68), 122 (13), 106 (100), 75 (42), 50 (29).

1-Iodo-3,4-methylenedioxybenzene (3c′, Table 1): Liquid, IR (neat): ν = 2938, 2843, 1676, 1506, 1480, 1437, 1374, 1295, 1229, 1126, 1046, 1010, 949, 848, 774, 650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 5.93 (s, 2H), 6.58 (d, 1H, *J* = 8.1 Hz), 7.12 (d, 1H, *J* = 2.0, Hz). 7.18 (dd, 1H, *J* = 8.1, 2.0 Hz); EIMS: *m/z* (%) = 248 (M^+, 34), 218 (12), 91 (67), 75 (100), 51 (42).

2-Iodo-4,5-dimethoxyacetophenone (3d′, Table 1): Liquid, IR (neat): ν = 2926, 2849, 1690, 1593, 1506, 1426, 1374, 1259, 1220, 1173, 1013, 775, 650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 2.48 (s, 3H), 3.88 (s, 3H), 3.89 (s, 3H), 6.79 (d, 1H, *J* = 8.0 Hz), 7.48 (m, 1H); EIMS: *m/z* (%) = 306 (M^+, 36), 275 (21), 260 (12), 133 (74), 90 (57), 74 (100), 50 (41).

5-Iodovaniline (3e′, Table 1): Solid, mp 180 – 182 °C, IR (KBr): ν = 3504, 2961, 2843, 1706, 1630, 1592, 1520, 1467, 1396, 1273, 1215, 1185, 1094, 1016, 950, 865, 758, 650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 3.96 (s, 3H), 6.65 (br s, 1H, OH), 7.36 (d, 1H, *J* = 2.0 Hz). 7.84 (d, 1H, *J* = 2.0 Hz), 9.80 (s, 1H, CHO); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 188.2, 150.6, 145.8, 132.5, 128.3, 108.2, 82.6, 54.3; EIMS: *m/z* (%) = 278 (M^+, 20), 246 (57), 119 (70), 90 (100), 74 (36), 50 (31).

1,3-Dimethoxy-2-methyl-4-iodobenzene (3f′, Table 1): Liquid, IR (neat): ν = 2943, 2857, 1685, 1597, 1523, 1478, 1421, 1349, 1284, 1213, 1179, 1084, 1018, 935, 867, 794, 658 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 2.20 (s, 3H), 3.79 (s, 3H), 3.80 (s, 3H), 6.40 (d 1H, *J* = 8.0 Hz). 7.50 (d, 1H, *J* = 8.0 Hz); EIMS: *m/z* (%) = 278 (M^+, 72), 247 (27), 232 (10), 105 (100), 90 (60), 66 (11), 50 (30).

1-Bromo-2-iodo-4,5-dimethoxybenzene (3g′, Table 1): Solid, mp 89 – 91 °C, IR (KBr): ν = 2957, 2836, 1605, 1572, 1468, 1416, 1297, 1223, 1179, 1091, 1023, 927, 861, 784, 690 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 3.85 (s, 3H), 3.86 (s, 3H), 7.12 (s, 1H), 7.23 (s, 1H); EIMS: *m/z* (%) = 344 (M^+, 92), 342 (100), 329 (31), 327 (57), 311 (12), 296 (23), 169 (53), 89 (31), 74 (32), 50 (29).

1,2,3-Trimethoxy-4-iodobenzene (3h′, Table 1): Liquid, IR (neat): ν =2937, 2838, 1572, 1476, 1430, 1405, 1292, 1221, 1176, 1132, 1091, 1009, 918, 834, 794, 772, 690 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 3.79 (s, 3H), 3.80 (s, 3H), 3.85 (s, 3H), 6.51 (d, 1H, *J* = 8.0 Hz). 7.42 (d, 1H, *J* = 8.0 Hz); EIMS: *m/z* (%) = 294 (M^+, 100), 179 (10), 109 (12), 77 (10).

2-Methoxy-4-iodophenol (3i′, Table 1): Liquid, IR (neat): ν = 3497, 2963, 2847, 1604, 1582, 1478, 1423, 1296, 1221, 1187, 1095, 1038, 927, 867, 793, 685 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 3.90 (s, 3H), 5.42 (s, 1H, OH), 6.78 (d, 1H, *J* = 8.2 Hz), 6.90 – 7.00 (m, 2H); EIMS: *m/z* (%) = 250 (M^+, 42), 218 (100), 91 (67), 75 (30), 51 (18).

4-Isopropyl-6-iodophenol (3j′, Table 1): Liquid, IR (neat): ν = 3506, 2961, 2874, 2363, 1709, 1607, 1558, 1493, 1473, 1416, 1361, 1322, 1278, 1183, 1037, 871, 846, 823, 736, 675 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 1.20 (s, 3H,), 1.22 (s, 3H), 2.80 (q, 1H *J* = 7.0 Hz), 6.90 (d, 1H, *J* = 8.0 Hz), 7.08 (dd, 1H, *J* =

8.0, 2.0 Hz), 7.48 (m, 1H); EIMS: *m/z* (%) = 262 (M^+, 18), 219 (26), 92 (67), 74 (36), 43 (100).

3,4-Methylenedioxy-6-iodophenol (3k', Table 1): Solid, mp 191 – 193 °C, IR (KBr): ν = 3465, 2937, 2859, 1619, 1468, 1378, 1163, 1017, 963, 829, 654 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 5.91 (s, 2H), 6.52 (s, 1H), 6.65 (s, 1H), 8.75 (br s, 1H, OH). EIMS: *m/z* (%) = 264 (M^+, 30), 250 (12), 234 (19), 107 (100), 91 (67), 75 (41), 51 (37).

2-Hydroxy-5-iodobenzaldehyde (3l', Table 1): Solid, mp 63 – 65 °C, IR (KBr): ν = 3479, 2968, 28874, 1698, 1607, 1561, 1469, 1371, 1302, 1273, 1205, 1152, 1110, 897, 826, 763, 695, 635 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 6.88 (d, 1H, *J* = 8.1 Hz), 7.62 (dd, 1H, *J* = 8.1, 2.0 Hz), 7.72 (s, 1H), 9.94 (s, 1H, CHO), 10.9 (br s, 1H, OH); EIMS: *m/z* (%) = 248 (M^+, 100), 230 (37), 202 (18), 121 (10), 103 (41), 75 (59), 50 (63).

1-Iodo-2-methylnaphthalene (3m', Table 1): Liquid, IR (neat): ν = 3049, 2967, 2851, 1605, 1579, 1508, 1443, 1328, 1257, 1219, 1137, 1032, 965, 896, 861, 763, 652 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 2.63 (s, 3H), 7.29 (d, 1H, *J* = 8.1 Hz), 7.52 (t, 1H, *J* = 8.0 Hz), 7.62 (dd, 1H, *J* = 8.0, 2.0 Hz), 7.73 (m, 1H), 7.84 (d, 1H, *J* = 8.1 Hz), 8.32 (d, 1H, *J* = 8.0 Hz); EIMS: *m/z* (%) = 268 (M^+, 87), 241 (19), 215 (36), 177 (69), 141 (100), 102 (16), 76 (25), 51 (18).

1-Iodo-2-methoxynaphthalene (3n', Table 1): Solid, mp 86 – 87 °C, IR (KBr): ν = 2973, 2843, 1676, 1506, 1483, 1437, 1374, 1296, 1229, 1126, 1046, 1010, 949, 848, 774, 650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 3.99 (s, 3H), 7.24 (d, 1H *J* = 8.3 Hz), 7.36 (dd, 1H, J = 8.3, 2.0 Hz), 7.52 (dd, 1H, *J* = 8.3, 2.1 Hz), 7.76 (d, 1H, *J* = 8.3 Hz), 7.85 (d, 1H, *J* = 8.2 Hz), 8.23 (d, 1H, *J* = 8.3 Hz); EIMS: *m/z* (%) = 284 (M^+, 11), 169 (19), 168 (100), 128 (10), 127 (12), 115 (89), 63 (9), 51 (20).

1-Iodo-4-methoxynaphthalene (3o', Table 1): Colorless solid, mp 51 – 53 °C, IR (KBr): ν = 2967, 2834, 1604, 1579, 1468, 1439, 1298, 1227, 1186, 1089, 1034, 926, 893, 816, 743, 653 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 3.95 (s, 3H, OCH_3), 6.56 (d, 1H *J* = 8.0 Hz), 7.47 (m, 2H), 7.88 (d, 1H, *J* = 8.0, Hz), 8.0 (dd, 1H, *J* = 8.0 & 1.9 Hz), 8.32 (dd, 1H *J* = 8.0, 1.5 Hz); EIMS: *m/z* (%) = 284 (M^+, 45), 169 (24), 241 (26), 157 (10), 142 (20), 128 (12), 127 (19), 126 (22), 114 (100), 76 (33), 62 (18), 51 (20).

1-Iodo-2-hydroxynaphthalene (3p', Table 1): Solid, mp 90 – 92 °C, IR (KBr): ν = 3502, 2979, 2843, 1618, 1589, 1519, 1478, 1412, 1289, 1210, 1183, 1085, 1029, 932, 896, 863, 815, 769, 660 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 7.28 (d, 1H, *J* = 8.0 Hz), 7.36 (t, 1H, *J* = 8.0 Hz), 7.52 (t, 1H, *J* = 8.0, Hz), 7.78 (dd, 2H, *J* = 8.0, 2.0 Hz), 8.0 (d, 1H, *J* = 8.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 154.3, 135.7, 131.6, 130.9, 130.2, 126.9, 126.5, 124.7, 117.2, 86.4; EIMS: *m/z* (%) = 270 (M^+, 100), 252 (10), 241 (16), 228 (12), 215 (37), 177 (18), 143 (28), 88 (49), 63 (10), 51 (22).

4-Chloroanisole (4a, Table 2): Liquid, IR (neat): ν =2941, 2847, 1698, 1599, 1510, 1482, 1432, 1297, 1229, 1175, 1099, 1032, 936, 872, 794, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 3.82 (s, 3H), 6.78 (d, 2H, *J* = 8.1 Hz), 7.40 (d, 2H *J* = 8.1 Hz); EIMS: *m/z* (%) = 144 (M^+, 33), 142 (100), 127 (58), 112 (10), 99 (53), 77 (12), 63 (14), 58 (12).

3,4-Dimethoxychlorobenzene (4b, Table 2): Liquid, IR (neat): ν = 2947, 2839, 1702, 1691, 1605, 1582, 1491, 1446, 1399, 1238, 1218, 1189, 1146, 1023, 936, 847, 799, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 3.86 (s, 3H), 3.88 (s, 3H), 6.75 – 6.91 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 56.2, 56.6, 112.3, 112.7, 120.2, 120.6, 125.5, 149.8; EIMS: *m/z* (%) = 174 (M^{+2}, 32), 172 (100), 157 (11), 142 (17), 137 (20), 126 (31), 91 (61), 75 (42), 50 (16).

3,4-Methylenedioxychlorobenzene (4c, Table 2): Liquid, IR (neat): ν = 2943, 2852, 1678, 1506, 1481, 1379, 1299, 1126, 1047, 946, 851, 776, 651 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 5.90 (s, 2H), 6. 60 (d, 1H, *J* = 8.1 Hz), 7.15 – 7.25 (m, 2H); EIMS: *m/z* (%) = 158 (M^{+2}, 40), 156 (100), 126 (29), 91 (57), 75 (39), 51 (20).

2,4-Dimethoxy-3-methyl-1-chlorobenzene (4d, Table 2): Liquid, IR (neat): ν = 2948, 2853, 1698, 1605, 1573, 1481, 1426, 1298, 1210, 1179, 1096, 1020, 931, 867, 793, 696 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 2.18 (s, 3H), 3.78 (s, 3H), 3.80 (s, 3H), 6.55 (d, 1H, *J* = 8.0 Hz), 7.10 (d, 1H, *J* = 8.0 Hz); EIMS: *m/z* (%) = 188 (M^{+2}, 19), 186 (100), 171 (9), 156 (10), 140 (16), 105 (58), 89 (67), 51 (30).

1,2,3-Trimethoxy-4-chlorobenzene (4e, Table 2): Liquid, IR (neat): ν = 2941, 2840, 1722, 1581, 1466, 1414, 1297, 1221, 1177, 1094, 1070, 1017, 936, 896, 865, 774, 696 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 3.80 (s, 3H), 3.85 (s, 3H), 3.90 (s, 3H), 6.58 (d, 1H, *J* = 8.0 Hz), 7.00 (d, 1H, *J* = 8.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 56.4, 61.6, 107.5, 107.9, 123.6, 143.5, 150.2, 152.6; EIMS: *m/z* (%) = 204 (M^{+2}, 31), 202 (100), 187 (11), 172 (12), 156 (31), 141 (47), 125 (10), 121 (18), 90 (29), 74 (38), 50 (32).

2-Methoxy-4-chlorophenol (4f, Table 2): Liquid, IR (neat): ν = 3478, 2949, 2863, 1606, 1581, 1473, 1422, 1293, 1229, 1185, 1091, 1026, 932, 865, 790, 694 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 3.88 (s, 3H), 5.65 (br s, 1H, OH), 6.81 (d, 1H, *J* = 8.0 Hz), 6.98 (d, 1H, *J* = 8.0 Hz), 6.95 – 7.05 (m, 1H); EIMS: *m/z* (%) = 160 (M^{+2}, 23), 158 (100), 143 (11), 126 (47), 91 (32), 76 (60), 51 (21).

4,5-Methylenedioxy-2-chlorophenol (4g, Table 2): Solid, mp 88 – 90 °C, IR (KBr): ν = 3463, 2902, 1631, 1480, 1376, 1305, 1188, 1110, 1036, 934, 841,767 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 5.95 (s, 2H), 6.59 (s, 1H), 6.79 (s, 1H), 9.40 (br s, 1H, OH); EIMS: *m/z* (%) = 174 (M^+, 44), 172 (100), 157 (91), 129 (36), 111 (17), 99 (13), 93 (43), 86 (16), 79 (28), 65 (34), 53 (26).

2-Bromo-4,5-dimethoxychlorobenzene (4h, Table 2): Solid, mp 110 – 112 °C, IR (KBr): ν = 2951, 2843, 1609, 1579, 1472, 1421, 1298, 1227, 1183, 1096, 1027, 931, 867, 791, 695 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 3.86 (s, 3H), 3.88 (s, 3H), 6.90 (d, 1H, *J* = 8.0 Hz), 7.05 (d, 1H, *J* = 8.0 Hz); EIMS: *m/z* (%) = 253 (M^{+2}, 11), 251 (100), 236 (15), 221 (28), 186 (42), 170 (17), 90 (59), 75 (71), 50 (30).

1-Chloro-2-methylnaphthalene (4i, Table 2): Liquid, IR (neat): ν = 3056, 2981, 2873, 2364, 1716, 1597, 1558, 1503, 1447, 1331, 1262, 1224, 1141, 1036, 967, 899, 867, 766, 643 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 2.60 (s, 3H), 7.20 – 7.30 (d, 1H, *J* = 8.0 Hz), 7.35 – 7.40 (m, 2H), 7.60 – 7.75 (m, 2H), 8.22 (d, 1H, *J* = 8.0 Hz); EIMS: *m/z* (%) = 178 (M^{+2}, 21), 176 (100), 141 (72), 126 (18), 116 (11), 91 (37), 66 (12), 43 (40).

1-Chloro-2-methoxynaphthalene (4j, Table 2): Solid, mp 68 – 69 °C, IR (KBr): ν = 2983, 2847, 1608, 1579, 1471, 1427, 1296, 1227, 1183, 1096, 1027, 924, 896, 862, 810, 764, 648 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ = 3.98 (s, 3H), 7.19 (d, 1H, *J* = 8.0 Hz), 7.32 (m, 1H), 7.48 (m, 1H), 7.75 (d, 1H, *J* = 7.9 Hz), 7.85 (d, 1H, *J* = 8.0 Hz), 8.20 (d, 1H, *J* = 7.9 Hz); EIMS: *m/z* (%) = 194 (M^{+2}, 31), 192 (100), 177 (12), 161 (37), 149 (11), 126 (18), 114 (62), 101 (42), 63 (20), 52 (13).

1-Chloro-4-methoxynaphthalene (4k, Table 2): Liquid, IR (neat): ν = 2976, 28859, 1605, 1584, 1509, 1483, 1420, 1283, 1223, 1187, 1089, 1023, 927, 893, 865, 809, 763, 650 cm^{-1};

^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.97 (s, 3H), 6.62 (d, 1H, *J* = 8.0 Hz), 7.40 – 7.45 (m, 1H), 7.90 (d, 1H, *J* = 8.0 Hz), 7.95 – 8.05 (m, 1H), 8.28 – 8.32 (m, 2H); EIMS: *m/z* (%) = 194 (M^{+2}, 23), 192 (100), 177 (18), 161 (57), 157 (20), 126 (11), 114 (72), 101 (8), 88 (16), 63 (10), 52 (32).

1-Chloro-2-naphthol (4l, Table 2): Solid, mp 69 – 70 °C, IR (KBr): ν = 3469, 2987, 2843, 1610, 1579, 1513, 1479, 1412, 1289, 1219, 1183, 1084, 1027, 932, 895, 867, 812, 765, 674 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.95 (d, 1H, *J* = 8.1 Hz), 7.76 (m, 2H), 7.50 (m, 1H), 7.41 (m, 1H), 7.30 (d, 1H, *J* = 8.0 Hz); EIMS: *m/z* (%) = 180 (M^+, 53), 178 (100), 149 (18), 114 (76), 89 (14), 63 (12).

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