Fast and Efficient Bromination of Aromatic Compounds with Ammonium Bromide and Oxone

Mameda Naresh,[a] Macharla Arun Kumar,[a] Marri Mahender Reddy,[a] Peraka Swamy,[a] Jagadeesh Babu Nanubolu,[b] Nama Narender*[a]

[a] I&PC Division, CSIR-Indian Institute of Chemical Technology, Hyderabad 500 007, India
Fax +91(40)27160387; E-mail: narendern33@yahoo.co.in

[b] X-ray Crystallography, CSIR-Indian Institute of Chemical Technology, Hyderabad 500 007, India

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Abstract: A highly efficient, rapid and regioselective protocol was developed for the ring bromination of aromatic compounds under mild conditions with ammonium bromide as a source of bromine source and Oxone® (potassium peroxysulfate) as an oxidant. No metal catalyst or acidic additive is required. A variety of aromatic compounds, including methoxy, hydroxy, amino, and alkyl arenes, reacted smoothly to give the corresponding monobrominated products in good to excellent yields in very short reaction times. Moreover, dibromination of deactivated anilines to give the corresponding dibromides proceeded in high yields. Interestingly, 1-(2-naphthyl)ethanone provided a ring-brominated product.

Key words: halogenation, bromination, arenes, regioselectivity, aryl halides

The bromination of aromatic compounds is an important electrophilic substitution reaction in organic chemistry[1] and the resultant bromoarenes are useful synthetic intermediates for the manufacture of pharmaceuticals, fine chemicals, agrochemicals, and other specialty chemicals, such as flame retardants, pesticides, and herbicides.[2] Bromoarenes are also useful and important intermediates for cross-coupling reactions[3] and as precursors to organometallic reagents.[4] In addition, several aryl bromides are biologically active and potentially useful as antitumor, antibacterial, antifungal, antineoplastic, or antiviral agents.[5]

Conventional nuclear bromination of aromatic substrates involves the use of molecular bromine, a hazardous, corrosive, and inconvenient reagent, and in some cases it requires expensive transition-metal-based catalysts.[6] Moreover, with bromine as the reagent, the atom efficiency is effectively reduced to 50%, as only half of the bromine atoms are used, the other half being converted into hydrobromic acid, which is corrosive, toxic, and a potential pollutant that must be neutralized before it can be discharged in effluent. Despite these problems, however, bromine is still being used in industry and in academia because of its ready availability and low cost, and because of the lack of a better alternative.

To overcome some of these problems, various alternative methods have recently been developed for the nuclear bromination of aromatic compounds. These employ a variety of brominating agents under a range of conditions. Among the brominating agents that have been used are calcium(II) bromide and bromine,[7] sodium bromide, sodium bromite, and sulfuric acid;[8] silica gel immobilized copper(II) perfluorophthalocyanine and potassium bromide;[9] *N*-bromosuccinimide (NBS) in the an ionic liquid;[10] ethylenebis(*N*-methylimadazolium ditribromide;[11] NBS and poly(ethylene glycol);[12] 1-butyl-3-methylpyridinium tribromide;[13] sodium bromide, hydrogen peroxide, and cerium(III) chloride;[14] isoamyl nitrite and hydrobromic acid;[15] photochemically activated NBS;[16] potassium bromide, hydrogen bromide, hydrogen peroxide, and ammonium metavanadate;[17] sodium bromide and hydrogen peroxide in a water/supercritical carbon dioxide biphasic medium;[18] bromine and β-cyclodextrin;[19] potassium bromide and benzyl(triphenyl)phosphonium peroxymonosulfate;[20] NBS and sulfonic acid functionalized silica;[21] sodium bromide and hydrobromic acid (electrochemical method);[22] hexamethylenetetramine and bromine;[23] ethylenebis(pyridinium ditribromide) (DPTBE);[24] 1-butyl-3-methylimidazolium tribromide;[25] bromine and a polymer-supported organotin reagent;[26] and pentylpyridinium tribromide.[27]

Although many methods are available for nuclear bromination of aromatic compounds, most suffer from one or more disadvantages. Some require prolonged reaction times, harsh reaction conditions, or complex experimental procedures; some give unsatisfactory product yields; and others involve the use of hazardous, toxic, expensive, or moisture-sensitive reagents, or reagents that are not readily available or need to be freshly prepared. These problems limit the use of many of these methods in situations where an environmentally benign process is required.

There is still need, therefore, to develop an efficient, rapid, ecofriendly, atom-economic (100% with respect to bromine), cheap, and selective procedure for nuclear bromination of aromatic compounds. In continuation of our research program on the development of environmentally benign halogenation processes,[28] we previously reported a bromination of aromatic rings by using ammonium bromide and Oxone® (potassium peroxysulfate) in acetonitrile, methanol or water as a solvent to give moderate to excellent yields of the bromo derivatives in moderately short times.[29] Here, we report, in detail, a very simple, rapid, mild, and efficient modified procedure for ring bromination of aromatic compounds by using ammonium

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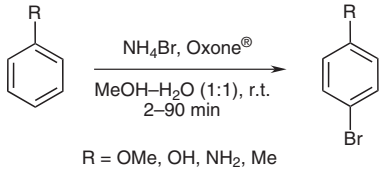
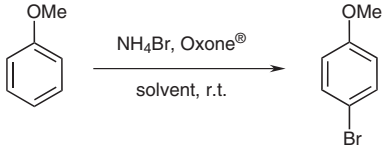
bromide and Oxone® in 1:1 methanol–water as the reaction medium (Scheme 1).



Scheme 1 Bromination of aromatic compounds

Initially, we attempted to brominate anisole with ammonium bromide and Oxone® in various solvents (methanol, acetonitrile, acetone, tetrahydrofuran, or ethanol) alone or in combination with water (Table 1). The best results, particularly in terms of the reaction yields and time, were obtained when we used a 1:1 mixture of methanol and water as the solvent system (Table 1, entry 7).

Table 1 Bromination of Anisole with Ammonium Bromide and Oxone®: Solvent Effects



Entry[a]	Solvent	Time	Yield[b] (%)
1	MeOH	1.3 h	90
2	MeCN	5 h	97[29a]
3	acetone	5 h	25
4	THF	5 h	15
5	EtOH	5 h	42
6	H_2O	5 h	39
7	MeOH–H_2O (1:1)	2 min	97
8	MeCN–H_2O (1:1)	2 min	89
9	acetone–H_2O (1:1)	2 min	89
10	THF–H_2O (1:1)	5 min	90
11	EtOH–H_2O (1:1)	3 min	90

[a] Reaction conditions: substrate (2 mmol), NH_4Br (2.2 mmol), Oxone® (2.2 mmol), solvent (10 mL), r.t.
[b] The product was characterized by ^1H NMR and MS, and quantified by GC.

Having optimized the reaction conditions, we subjected a variety of aromatic compounds, including anisoles, phenols, anilines, and alkylaromatic compounds to the bromination process to explore its scope and generality. The results are summarized in Table 2. Various functional groups played significant roles in governing the yield of the product.

Table 2 Monobromination of Aromatic Compounds with Ammonium Bromide and Oxone®

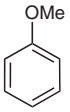
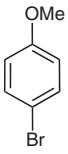
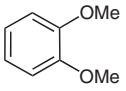
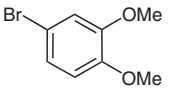
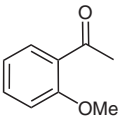
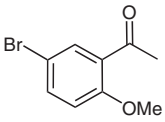
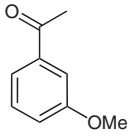
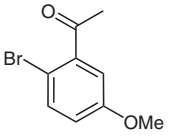
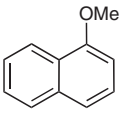
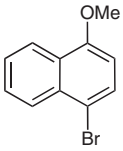
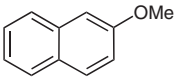
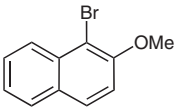
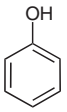
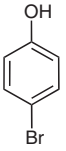
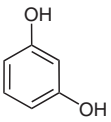
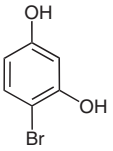
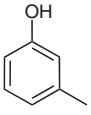
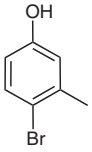
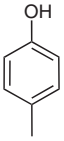
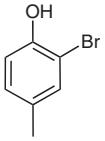
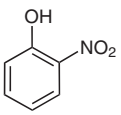
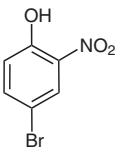
Entry[a]	Substrate	Time (min)	Product	Yield (%)[b]
1		2	**1a** 	97
2		4	**1b** 	96
3		4	**1c** 	98
4		4	**1d** 	98
5		3	**1e** 	77
6		2	**1f** 	89
7		2	**1g** 	79 (9)[c] (8)[d]
8		2	**1h** 	89 (9)[d]
9		2	**1i** 	79
10		2	**1j** 	95
11		6	**1k** 	16 (41)[d]

Table 2 Monobromination of Aromatic Compounds with Ammonium Bromide and Oxone® (continued)

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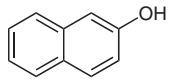
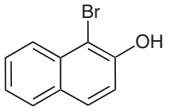
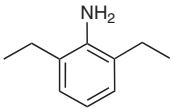
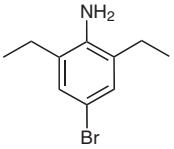
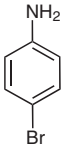
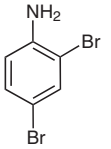
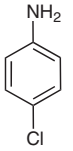
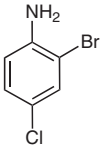
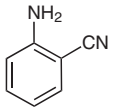
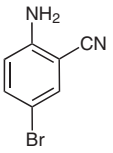
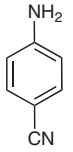
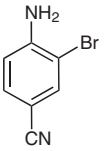
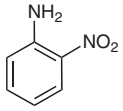
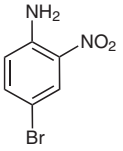
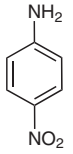
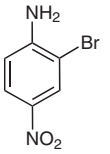
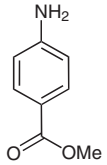
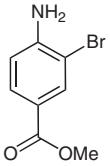
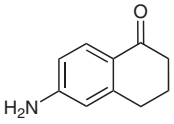
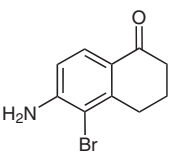
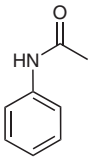
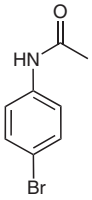
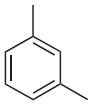
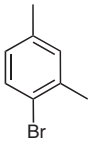
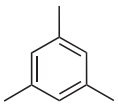
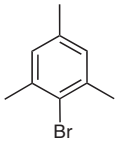
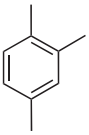
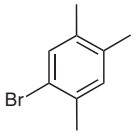
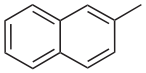
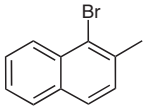
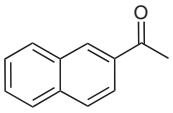
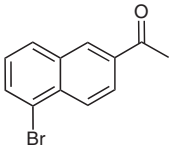
12		2	**1l** 	94
13		3	**1m** 	70
14		3	**1n** 	60 (25)[d]
15		5	**1o** 	20 (40)[d]
16		5	**1p** 	72
17		5	**1q** 	70 (15)[d]
18		4	**1r** 	70 (15)[d]
19		5	**1s** 	20 (45)[d]
20		5	**1t** 	50 (25)[d]
21		5	**1u** 	62 (31)[d]

Table 2 Monobromination of Aromatic Compounds with Ammonium Bromide and Oxone® (continued)

Entry[a]	Substrate	Time (min)	Product	Yield (%)[b]
22		4	**1v** 	85
23		30	**1w** 	97
24		10	**1x** 	79
25		30	**1y** 	96
26		30	**1z** 	82
27		90	**6** 	58

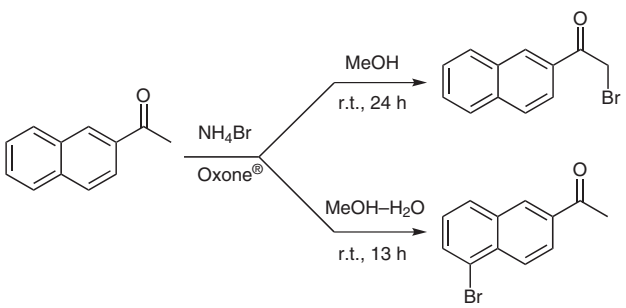
[a] Reaction conditions: substrate (2 mmol), NH_4Br (2.2 mmol), Oxone® (2.2 mmol), MeOH–H_2O (1:1; 10 mL), r.t.
[b] The products were characterized by ^1H NMR and MS, and quantified by GC.
[c] Yield of *o*-bromo product.
[d] Yield of dibromo product.

All the substrates were treated with 1.1 equivalents of ammonium bromide and 1.1 equivalents of Oxone® in a 1:1 mixture of methanol and water at room temperature. Within few minutes (2–90 min), each of the substrates gave the corresponding ring-brominated product in good to excellent yield and high regioselectivity. As can be seen from Table 2, bromination of methoxy and hydroxy derivatives by using this reagent system gave the corresponding ring-brominated products in high yields within very short reaction times (2–4 min), whereas much longer reaction times (5–8 h) were required when acetonitrile was used as the solvent.[29a] Anisoles containing electron-donating or electron-withdrawing functional groups in various positions on the aromatic ring worked well and did not show any marked difference in their yields of products or reaction times (entries 2–4). 2-Methoxynaphthalene and

2-naphthol were also rapidly (2 min) brominated under similar reaction conditions and afforded the corresponding 1-bromo derivatives exclusively in yields of 89% and 94%, respectively (entries 6 and 12). Phenol gave the *para*-brominated derivative as the major product (79%), along with smaller amounts of the corresponding *ortho*-brominated product (9%) and dibrominated product (8%) (entry 7). Resorcinol was also smoothly brominated to give the *para*-brominated and dibrominated products in yields of 89% and 9%, respectively (entry 8). However, in the case of strongly deactivated 2-nitrophenol, the dibrominated product (2,6-dibromo-4-nitrophenol) predominated; the dibrominated and monobrominated products were obtained in yields of 41% and 16%, respectively (entry 11).

Next, we explored the scope of the method by treating anilines under our optimized reaction conditions. 2,6-Diethylaniline exclusively gave the corresponding 4-brominated product in 70% yield in three minutes (entry 13). On the other hand, when acetonitrile, methanol, or water was used as the solvents, the yields were 48%, 45% and 28%, respectively, even after three hours. Deactivated anilines gave the corresponding monobrominated product, along with substantial amounts of the dibrominated product (entries 14–16 and 18–20), except for 2-aminobenzonitrile which gave the monobrominated product exclusively (entry 17). 1,2,3,4-Tetrahydronaphthalen-2-amine also reacted smoothly to give mono- and dibrominated products in 62% and 31% yield, respectively (entry 21).

Next, we investigated the efficiency of the method with alkylaromatic compounds, which are moderately activated, under similar reaction conditions. *m*-Xylene, mesitylene, and 1,2,4-trimethylbenzene reacted exclusively at the aromatic ring to give ring-brominated monobromo compounds in excellent yields, without forming any side-chain brominated products (Table 2, entries 23–25); however, the reaction took a little longer (10–30 min) than that of the highly activated aromatics. In methanol or water as the solvent, bromination of alkylaromatic compounds to give ring-brominated products required 40 minutes to 24 hours.[29b] Bromination of 2-methylnaphthalene gave the corresponding 1-bromo derivative in 82% yield in 30 minutes (entry 26), whereas the corresponding reaction in methanol or water gave 80% and 75% yields, respectively, in 24 hours.[29b]



Scheme 2 Bromination of 1-(2-naphthyl)ethanone

It is noteworthy that 1-(2-naphthyl)ethanone provided the ring-brominated product 1-(5-bromo-2-naphthyl)ethanone (**6**) in 58% yield by this method (Table 2, entry 27), whereas the α-brominated product was obtained in methanol (Scheme 2).[28b] Product **6** was unambiguously characterized by means of X-ray crystallography (Figure 1).[30]

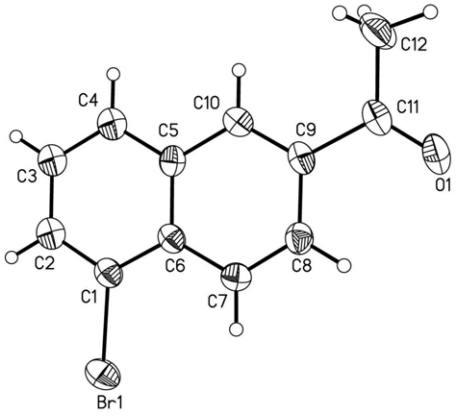


Figure 1 ORTEP diagram of compound **6** (30% probability)

The systems described above selectively gave the corresponding aromatic derivatives that were brominated in the *para*-position with respect to the activating substituent. However, when the *para*-position of the substrate was blocked by a substituent, the *ortho*-brominated product was obtained.

Encouraged by these results, we also successfully carried out dibrominations of several deactivated anilines by using 2.2 equivalents of each of the reagents (ammonium bromide and Oxone®), and we obtained excellent yields of the corresponding products, which are industrially important compounds or pharmaceutical intermediates, within a short reaction time (5 min) (Table 3).

Table 3 Dibromination of Substituted Anilines with Ammonium Bromide and Oxone®

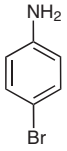
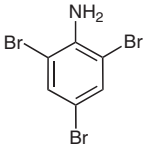
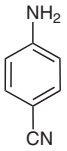
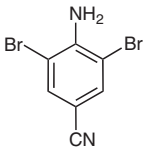
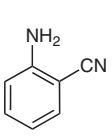
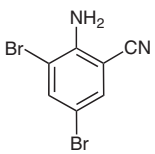
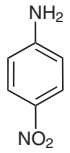
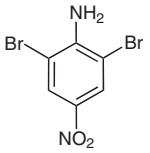
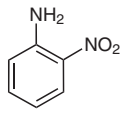
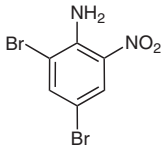
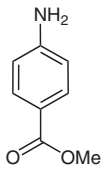
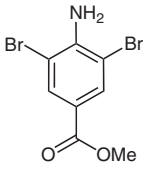
Entry[a]	Substrate	Product	Yield[b] (%)
1		**2a** 	95
2		**2b** 	95
3		**2c** 	95

Table 3 Dibromination of Substituted Anilines with Ammonium Bromide and Oxone® (continued)

Entry[a]	Substrate	Product	Yield[b] (%)
4		**2d** 	90
5		**2e** 	95
6		**2f** 	95

[a] Reaction conditions: substrate (2 mmol), NH_4Br (4.4 mmol), Oxone® (4.4 mmol), MeOH–H_2O (1:1; 10 mL), 5 min, r.t.
[b] The products were characterized by ^1H NMR and MS, and quantified by GC.

In summary, we have developed an efficient, rapid, and versatile method for the regioselective nuclear bromination of aromatics by using ammonium bromide and Oxone® in aqueous methanol. A wide range of aromatic compounds were found to react under mild conditions (room temperature) to give good to excellent yields of the corresponding ring-brominated products. Salient features of this method are shorter reaction times (rapid conversion), simple reaction conditions, commercial availability of reagents, environmental compatibility, no evolution of hydrogen bromide, easy setup and workup, high yields, and low costs. An interesting feature of the method is that 1-(2-naphthyl)ethanone gave the corresponding ring-brominated product in good yield.

All chemicals used were of reagent grade and used as received without further purification. ^1H NMR spectra were recorded at 300 and 500 MHz and ^{13}C NMR spectra were recorded at 75 MHz in $CDCl_3$ or DMSO-d_6 with Bruker VX NMR FT-300 and Varian Unity 500 spectrometers. The chemical shifts (δ) are reported in ppm relative to TMS as internal standard for ^1H NMR and to $CDCl_3$ for ^{13}C NMR. Mass spectra were recorded with a Finnigan MAT 1020 mass spectrometer operating at 70 eV. Column chromatography was performed on 100–200 mesh silica gel.

Monobromination of Aromatic Compounds; General Procedure

NH_4Br (2.2 mmol) and Oxone® (2.2 mmol) were added to a stirred soln of substrate (2 mmol) in MeOH–H_2O (1:1; 10 mL), and the mixture was stirred at r.t. for the time shown in Table 2. When the reaction was complete (TLC), the mixture was filtered and the solvent was removed under reduced pressure. The residue was dissolved in EtOAc (25 mL) and the soln was filtered and washed successively with 0.2 M aq $Na_2S_2O_3$ (10 mL) and H_2O. The organic layer was dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, 5–50% EtOAc–hexane) to give pure products that were identified by means of ^1H NMR spectroscopy and mass spectrometry.

1-Bromo-4-methoxybenzene (1a)[31]
^1H NMR (500 MHz, $CDCl_3$): δ = 3.77 (s, 3 H), 6.76 (d, *J* = 8.61 Hz, 2 H), 7.36 (d, *J* = 8.61 Hz, 2 H).

MS (EI): *m/z* (%) = 188 (98) $[M + 2]^+$, 186 (100) $[M^+]$, 171 (50), 173 (50), 143 (45), 145 (45), 77 (20), 63 (35).

4-Bromo-1,2-dimethoxybenzene (1b)[32]
^1H NMR (300 MHz, $CDCl_3$): δ = 3.86 (s, 3 H), 3.87 (s, 3 H), 6.74 (d, *J* = 8.49 Hz, 1 H), 6.98 (d, *J* = 2.26 Hz, 1 H), 7.03 (dd, *J* = 8.68, 2.26 Hz, 1 H).

MS (EI): *m/z* (%) = 218 (58) $[M + 2]^+$, 216 (60) $[M^+]$, 201 (30), 203 (30), 173 (20), 138 (25), 94 (100), 79 (50), 51 (50).

1-(5-Bromo-2-methoxyphenyl)ethanone (1c)[33]
^1H NMR (300 MHz, $CDCl_3$): δ = 2.60 (s, 3 H), 3.90 (s, 3 H), 6.86 (d, *J* = 9.0 Hz, 1 H), 7.54 (dd, *J* = 9.0, 3.0 Hz, 1 H), 7.82 (d, *J* = 2.6 Hz, 1 H).

1-(2-Bromo-5-methoxyphenyl)ethanone (1d)[34]
^1H NMR (300 MHz, $CDCl_3$): δ = 2.63 (s, 3 H), 3.81 (s, 3 H), 6.85 (dd, *J* = 8.30, 3.02 Hz, 1 H), 6.98 (d, *J* = 3.02 Hz, 1 H), 7.49 (d, *J* = 9.06 Hz, 1 H).

1-Bromo-4-methoxynaphthalene (1e)[35]
^1H NMR (500 MHz, $CDCl_3$): δ = 3.99 (s, 3 H), 6.67 (d, *J* = 8.08 Hz, 1 H), 7.48–7.55 (m, 1 H), 7.58–7.68 (m, 2 H), 8.17 (d, *J* = 8.89 Hz, 1 H), 8.27 (d, *J* = 8.08 Hz, 1 H).

MS (EI): *m/z* (%) = 238 (98) $[M + 2]^+$, 236 (100) $[M^+]$, 221 (60), 223 (60), 193 (75), 195 (75), 158 (40), 114 (70), 88 (25), 63 (25).

1-Bromo-2-methoxynaphthalene (1f)[36]
^1H NMR (500 MHz, $CDCl_3$): δ = 4.04 (s, 3 H), 7.23 (d, *J* = 9.35 Hz, 1 H), 7.35 (dd, *J* = 8.01, 1.2 Hz, 1 H), 7.53 (dt, *J* = 7.8, 1.2 Hz, 1 H), 7.71–7.79 (m, 2 H), 8.19 (d, *J* = 8.57 Hz, 1 H).

MS (EI): *m/z* (%) = 238 (98) $[M + 2]^+$, 236 (100) $[M^+]$, 221 (25), 223 (25), 193 (75), 195 (75), 114 (60), 88 (15), 63 (25).

4-Bromophenol (1g)[37]
^1H NMR (500 MHz, $CDCl_3$): δ = 5.20 (s, 1 H), 6.73 (d, *J* = 8.30 Hz, 2 H), 7.33 (d, *J* = 8.30 Hz, 2 H).

MS (EI): *m/z* (%) = 174 (8) $[M + 2]^+$, 172 (10) $[M^+]$, 143 (30), 93 (12), 62 (100), 39 (50).

4-Bromobenzene-1,3-diol (1h)[38]
^1H NMR (500 MHz, DMSO-d_6): δ = 6.18 (dd, *J* = 8.90, 1.98 Hz, 1 H), 6.45 (d, *J* = 1.98 Hz, 1 H), 7.12 (d, *J* = 7.91 Hz, 1 H), 8.99 (br s, 1 H), 9.33 (br s, 1 H).

4-Bromo-3-methylphenol (1i)[39]
^1H NMR (500 MHz, $CDCl_3$): δ = 2.33 (s, 3 H), 5.34 (br s, 1 H), 6.55 (dd, *J* = 9.06, 3.02 Hz, 1 H), 6.73 (d, *J* = 3.02 Hz, 1 H), 7.35 (d, *J* = 9.06 Hz, 1 H).

2-Bromo-4-methylphenol (1j)[40]
^1H NMR (500 MHz, $CDCl_3$): δ = 2.9 (s, 3 H), 5.32 (br s, 1 H), 6.81 (d, *J* = 8.0 Hz, 1 H), 7.0 (d, *J* = 8.0 Hz, 1 H), 7.26 (d, *J* = 2.02 Hz, 1 H).

MS (EI): *m/z* (%) = 186 (75) $[M + 2]^+$, 188 (73) $[M^+]$, 107 (100), 77 (40), 51 (25).

4-Bromo-2-nitrophenol (1k)[41]
^1H NMR (500 MHz, $CDCl_3$): δ = 7.08 (d, *J* = 8.8 Hz, 1 H), 7.66 (dd, *J* = 9.0, 2.4 Hz, 1 H), 8.24 (d, *J* = 2.4 Hz, 1 H), 10.49 (s, 1 H).

MS (EI): *m/z* (%) = 219 (73) $[M + 2]^+$, 217 (75) $[M^+]$, 202 (12), 200 (12), 143 (25), 63 (100).

2,4-Dibromo-6-nitrophenol (1k)[41]
^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 2.4 Hz, 1 H), 8.25 (d, *J* = 2.4 Hz, 1 H), 11.05 (s, 1 H).

MS (EI): *m/z* (%) = 299 (48) $[M + 4]^+$, 297 (100) $[M + 2]^+$, 295 (50) $[M^+]$, 250 (10), 143 (25), 141 (25), 62 (35).

1-Bromo-2-naphthol (1l)[42]
^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.92 (s, 1 H), 7.27 (d, *J* = 8.83 Hz, 1 H), 7.39 (t, *J* = 7.72 Hz, 1 H), 7.57 (t, *J* = 7.72 Hz, 1 H), 7.73–7.79 (m, 2 H), 8.03 (d, *J* = 7.72 Hz, 1 H).

MS (EI): *m/z* (%) = 222 (8) $[M + 2]^+$, 224 (10) $[M^+]$, 141 (10), 114 (15), 60 (20), 43 (100).

4-Bromo-2,6-diethylaniline (1m)[43]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.55 Hz, 6 H), 2.49 (q, *J* = 7.55 Hz, 4 H), 3.62 (br s, 2 H), 7.07 (s, 2 H).

MS (EI): *m/z* (%) = 229 (98) $[M + 2]^+$, 227 (100) $[M^+]$, 212 (95), 214 (93), 148 (20), 133 (40), 91 (35).

2,4-Dibromoaniline (1n)[26]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.09 (br s, 2 H), 6.64 (d, *J* = 8.49 Hz, 1 H), 7.20 (dd, *J* = 8.49, 2.07 Hz, 1 H), 7.52 (d, *J* = 2.07 Hz, 1 H).

MS (EI): *m/z* (%) = 253 (58) $[M + 4]^+$, 251 (100) $[M + 2]^+$, 249 (60) $[M^+]$, 172 (18), 170 (20), 157 (20), 155 (20), 91 (20).

2-Bromo-4-chloroaniline (1o)[40]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.08 (br s, 2 H), 6.69 (d, *J* = 9.06 Hz, 1 H), 7.07 (dd, *J* = 8.30, 2.26 Hz, 1 H), 7.40 (d, *J* = 2.26 Hz, 1 H).

MS (EI): *m/z* (%) = 209 (30) $[M + 4]^+$, 207 (100) $[M + 2]^+$, 205 (75) $[M^+]$, 126 (25), 90 (18).

2-Amino-5-bromobenzonitrile (1p)[44]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.44 (br s, 2 H), 6.64 (d, *J* = 8.99 Hz, 1 H), 7.40 (dd, *J* = 8.99, 2.00 Hz, 1 H), 7.48 (d, *J* = 2.00 Hz, 1 H).

MS (EI): *m/z* (%) = 198 (98) $[M + 2]^+$, 196 (100) $[M^+]$, 117 (70), 90 (60), 63 (25).

4-Amino-3-bromobenzonitrile (1q)[45]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.63 (br s, 2 H), 6.77 (d, *J* = 8.30 Hz, 1 H), 7.38 (dd, *J* = 8.30, 2.26 Hz, 1 H), 7.70 (d, *J* = 2.26 Hz, 1 H).

MS (EI): *m/z* (%) = 198 (98) $[M + 2]^+$, 196 (100) $[M^+]$, 117 (30), 90 (30), 63 (20).

4-Bromo-2-nitroaniline (1r)[26]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.09 (br s, 2 H), 6.73 (d, *J* = 8.30 Hz, 1 H), 7.43 (dd, *J* = 9.06, 2.26 Hz, 1 H), 8.27 (d, *J* = 2.26 Hz, 1 H).

MS (EI): *m/z* (%) = 218 (98) $[M + 2]^+$, 216 (100) $[M^+]$, 186 (25), 188 (25), 170 (50), 172 (50), 143 (30), 145 (30), 90 (70), 63 (75).

2-Bromo-4-nitroaniline (1s)[46]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.83 (br s, 2 H), 6.75 (d, *J* = 9.06 Hz, 1 H), 8.04 (dd, *J* = 9.0, 2.26 Hz, 1 H), 8.38 (d, *J* = 2.26 Hz, 1 H).

MS (EI): *m/z* (%) = 218 (68) $[M + 2]^+$, 216 (70) $[M^+]$, 186 (75), 188 (75), 170 (25), 90 (100), 63 (60).

Methyl 4-Amino-3-bromobenzoate (1t)[47]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.86 (s, 3 H), 4.52 (br s, 2 H), 6.73 (d, *J* = 8.30 Hz, 1 H), 7.79 (dd, *J* = 8.30, 2.26 Hz, 1 H), 8.12 (d, *J* = 2.02 Hz, 1 H).

MS (EI): *m/z* (%) = 231 (68) $[M + 2]^+$, 229 (70) $[M^+]$, 200 (98), 198 (100), 150 (14), 90 (30).

6-Amino-5-bromo-3,4-dihydronaphthalen-1(2*H*)-one (1u)[48]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.07–2.15 (m, 2 H), 2.58 (t, *J* = 6.04 Hz, 2 H), 2.97 (t, *J* = 6.79 Hz, 2 H), 4.67 (br s, 2 H), 6.68 (d, *J* = 9.06 Hz, 1 H), 7.89 (d, *J* = 8.9 Hz, 1 H).

MS (EI): *m/z* (%) = 241 (86) $[M + 2]^+$, 239 (88) $[M^+]$, 211 (100), 250 (98), 185 (12), 183 (13), 143 (10), 104 (50).

***N*-(4-Bromophenyl)acetamide (1v)**[7]
^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.12 (s, 3 H), 7.36 (d, *J* = 8.8 Hz, 2 H), 7.54 (d, *J* = 8.87 Hz, 2 H), 9.73 (br s, 1 H).

MS (EI): *m/z* (%) = 214 (4) $[M + 2]^+$, 212 (5) $[M^+]$, 172 (30), 136 (25), 94 (100), 43 (50).

1-Bromo-2,4-dimethylbenzene (1w)[49]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.27 (s, 3 H), 2.36 (s, 3 H), 6.85 (d, *J* = 8.30 Hz, 1 H), 7.04 (s, 1 H), 7.39 (d, *J* = 8.30 Hz, 1 H).

MS (EI): *m/z* (%) = 186 (58) $[M + 2]^+$, 184 (60) $[M^+]$, 105 (100), 77 (50), 43 (60).

2-Bromo-1,3,5-trimethylbenzene (1x)[46]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.22 (s, 3 H), 2.36 (s, 6 H), 6.83 (s, 2 H).

MS (EI): *m/z* (%) = 200 (18) $[M + 2]^+$, 198 (20) $[M^+]$, 168 (100), 141 (80), 119 (75), 71 (70), 57 (100), 43 (90).

1-Bromo-2,4,5-trimethylbenzene (1y)[50]
^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.17 (s, 3 H), 2.20 (s, 3 H), 2.32 (s, 3 H), 6.98 (s, 1 H), 7.28 (s, 1 H).

MS (EI): *m/z* (%) = 200 (78) $[M + 2]^+$, 198 (80) $[M^+]$, 119 (100), 91 (25), 39 (12).

1-Bromo-2-methylnaphthalene (1z)[46]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.64 (s, 3 H), 7.32 (d, *J* = 8.30 Hz, 1 H), 7.41–7.60 (m, 2 H), 7.68 (d, *J* = 9.06 Hz, 1 H), 7.76 (d, *J* = 7.55 Hz, 1 H), 8.28 (d, *J* = 8.30 Hz, 1 H).

MS (EI): *m/z* (%) = 223 (48) $[M + 2]^+$, 221 (50) $[M^+]$, 142 (100), 116 (25), 92 (25), 43 (12).

1-(5-Bromo-2-naphthyl)ethanone (6)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.75 (s, 3 H), 7.41 (t, *J* = 7.55 Hz, 1 H), 7.88–7.97 (m, 2 H), 8.12 (dd, *J* = 8.30, 1.51 Hz, 1 H), 8.30 (d, *J* = 9.06 Hz, 1 H), 8.45 (d, *J* = 1.51 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.8, 122.7, 125.4, 127.2, 127.8, 129.5, 130.3, 132.4, 133.8, 134.0, 135.0, 197.6.

ESI-MS: *m/z* (%) = 249 (40) $[M + H]^+$.

Crystal data:[30] $C_{12}H_9BrO$; *M* = 249.10; monoclinic; *a* = 10.4152(7), *b* = 11.8496(8), *c* = 9.0740(6) Å; *V* = 1026.79(12) Å^3; *T* = 293(2) K; space group $P2_1/c$ (No. 14); 9463 reflections measured of which 1808 were unique reflections (R_{int} = 0.0359) used in all calculations. The final *wR2* was 0.1916.

Dibromination of Aromatic Compounds; General Procedure
This was performed by a similar procedure to monobromination, except that NH_4Br (4.4 mmol) and Oxone® (4.4 mmol) were used, and the reaction mixture was stirred at r.t. for the time shown in Table 3.

2,4,6-Tribromoaniline (2a)[26]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.55 (br s, 2 H), 7.51 (s, 2 H).

MS (EI): *m/z* (%) = 333 (48) $[M + 6]^+$, 331 (100) $[M + 4]^+$, 329 (100) $[M + 2]^+$, 327 (50) $[M^+]$, 252 (9), 250 (20), 248 (10), 170 (25), 168 (25).

4-Amino-3,5-dibromobenzonitrile (2b)[51]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.11 (br s, 2 H), 7.66 (s, 2 H).

MS (EI): *m/z* (%) = 278 (58) $[M + 4]^+$, 276 (100) $[M + 2]^+$, 274 (60) $[M^+]$, 195 (8), 197 (7), 116 (20), 88 (18).

2-Amino-3,5-dibromobenzonitrile (2c)[52]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.90 (br s, 2 H), 7.48 (d, *J* = 2.07 Hz, 1 H), 7.73 (d, *J* = 2.3 Hz, 1 H).

MS (EI): *m/z* (%) = 278 (35) $[M + 4]^+$, 276 (75) $[M + 2]^+$, 274 (35) $[M^+]$, 196 (100), 198 (98), 117 (40), 90 (30).

2,6-Dibromo-4-nitroaniline (2d)[46]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.30 (br s, 2 H), 8.34 (s, 2 H).

MS (EI): *m/z* (%) = 298 (50) $[M + 4]^+$, 296 (100) $[M + 2]^+$, 294 (50) $[M^+]$, 268 (35), 266 (75), 264 (36), 170 (45), 168 (45), 90 (40).

4,6-Dibromo-2-nitroaniline (2e)[53]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.60 (br s, 2 H), 7.82 (d, *J* = 2.26 Hz, 1 H), 8.28 (d, *J* = 2.26 Hz, 1 H).

MS (EI): *m/z* (%) = 298 (58) $[M + 4]^+$, 296 (100) $[M + 2]^+$, 294 (60) $[M^+]$, 252 (24), 250 (48), 264 (24), 90 (30).

1-(4-Amino-3,5-dibromophenyl)ethanone (2f)[47]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.87 (s, 3 H), 5.00 (br s, 2 H), 8.07 (s, 2 H).

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