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Visible-Light-Driven Oxidative Mono- and Dibromination of Benzylic sp³ C–H Bonds with Potassium Bromide/Oxone at Room Temperature

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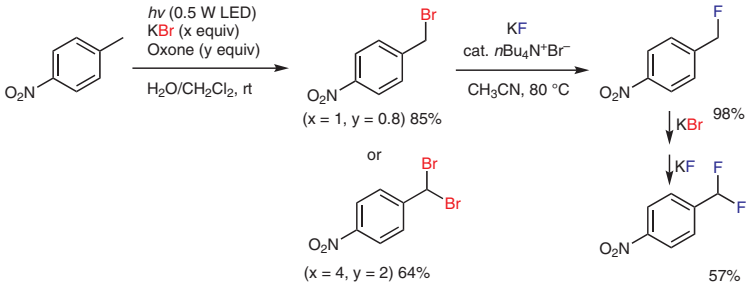

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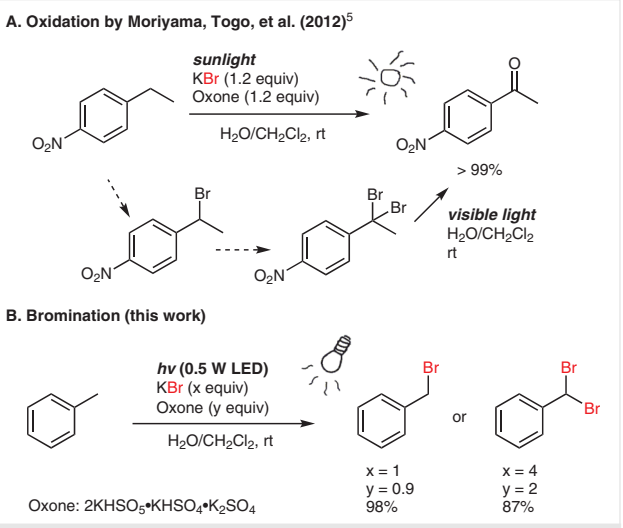
Abstract Benzylic sp³ C–H bonds have been successfully brominated with potassium bromide by using Oxone as an oxidant in water/dichloromethane under visible light at room temperature. Toluene, ethylbenzene and other alkylbenzenes bearing an electron-withdrawing group, such as Br, Cl, COMe, CO_2Et, CO_2H, CN or NO_2, provide the corresponding benzylic monobromides in good to excellent yields in this reaction. Dibromides can also be produced in the presence of excess potassium bromide in a prolonged reaction time. Control of the illuminance of visible light (~500 lux) is crucial to achieving both high yield and high selectivity in these brominations. Mono- and difluorides can be conveniently prepared through nucleophilic substitutions of the benzylic bromides with potassium fluoride.

Key words benzylic C–H bond, bromination, oxidation, photochemistry, room temperature

In comparison with benzylic sp³ C–H bonds, benzylic sp³ C–Br bonds as active bonds are converted very easily into the corresponding C–C, C–O and C–N bonds in current chemical synthesis.[1] Therefore, exploration of an efficient and convenient bromination of benzylic sp³ C–H bonds is an interesting subject to many researchers.[2] Multiple monobromination methods are known, including the use of bromine,[2d,h] *N*-bromosuccinimide,[2a,i] bromotrichloromethane,[2b] tetramethylammonium tribromide,[2c] $NaBrO_3$,[2e] tetrabromomethane[2f] and bromide salts[3] as a bromine source under mild conditions. Among them, transition-metal-free oxidative bromination is a promising approach when it proceeds by using NaBr or KBr as the brominating reagent with an inexpensive and nontoxic oxidant such as H_2O_2[3b,c] or Oxone ($2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$).[3d] However, these monobromination methods are usually not effective for benzylic dibromination.[4] One reason is that the benzylic bromides, especially dibromides, are readily transformed to aryl ketones or aryl carbolic acids under visible light in aqueous solution at room temperature, as suggested by Minisci,[3b] and Moriyama and Togo,[5] in their benzylic oxidation of alkylarenes with KBr/Oxone under mild conditions (Scheme 1, A).

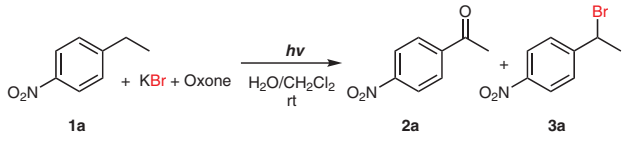
Most recently, we established the visible-light-driven monochlorination and monobromination of simple alkanes with NaCl/Oxone[6a] and KBr/air (O_2),[6b] respectively, combining the oxidation of halogen anion to halogen and the radical halogenation of C–H bonds under irradiation by visible light at room temperature. Herein, we report an effective mono- or dibromination of benzylic sp³ C–H bonds with KBr/Oxone under weak visible light at room temperature (Scheme 1, B).



Scheme 1 Oxidation and bromination of benzylic sp³ C–H bonds with KBr/Oxone under visible light at room temperature

In our study of the oxidative benzylic bromination of alkylarenes under mild conditions, we still employed the KBr/Oxone/H_2O/CH_2Cl_2 system which was very effective in the oxidation of alkylarenes to afford carbonyl compounds.[5] Initially, under indoor light on a clear day, an oxidation of *p*-ethylnitrobenzene (**1a**) with KBr/Oxone (1:1.2:1.2) occurred to give 1-(4-nitrophenyl)ethanone (**2a**) in 91% yield, as determined by ^{1}H NMR analysis, and no 1-(1-bromoethyl)-4-nitrobenzene (**3a**) was found at room temperature (Table 1, entry 1), like in the previous report. Interestingly, under similar conditions on a cloudy day, the yield of monobromide **3a** was up to 89% through a benzylic bromination (entry 2). Then, the following reactions were run under controlled light conditions. Under an 8 W light-emitting diode (LED) at a distance of 5 cm and 30 cm, benzylic oxidation and bromination, respectively, proceeded very well (entries 3 and 4). These results implied that the alkylarene undergoes benzylic bromination, rather than oxidation, under weak visible light. Moreover, **3a** was generated as the major product (59%) when 0.6 equivalents of KBr were added under an 8 W LED at 5 cm (entry 5), supporting the view that carbonyl products might arise from monobromides in further reactions with KBr/Oxone under strong light. Thus, when **1a**/KBr (1.1:1) was employed under a 0.5 W LED at 5 cm, only monobromide **3a** was obtained in excellent yield based on KBr (entry 7). In this case, the illuminance of visible light was ~500 lux.

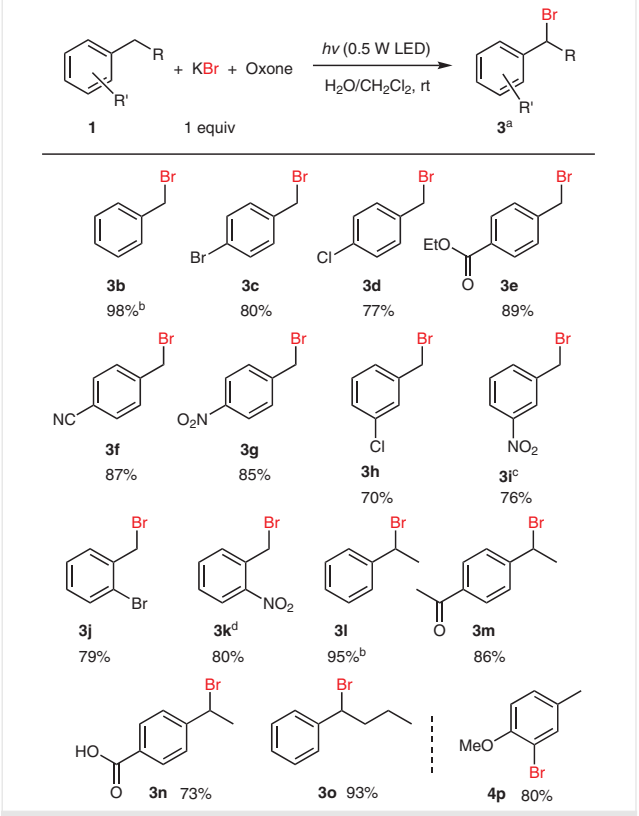
Table 1 Oxidation and Bromination of *p*-Ethylnitrobenzene (**1a**) with KBr/Oxone under Visible Light at Room Temperature[a]



Entry	*hv*	KBr (equiv)	Time (h)	**2a** Yield (%)[b]	**3a** Yield (%)[b]
1	indoor light (clear day)	1.2	3	91	0
2	indoor light (cloudy day)	1.2	4	10	89
3	8 W LED at 5 cm	1	16	96[c]	0
4	8 W LED at 30 cm	1	16	3	94
5	8 W LED at 5 cm	0.6	16	4	59
6[d]	3 W LED at 20 cm	1	4	0	85[c]
7[e]	0.5 W LED at 5 cm	1	20	0	93[c]

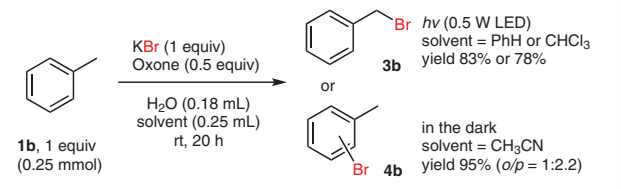
[a] Reaction conditions: **1a** (0.25 mmol, 1 equiv), KBr (0.6–1.2 equiv), Oxone (1.2 equiv), H_2O (0.18 mL), CH_2Cl_2 (0.25 mL), air, rt, 3–20 h.
[b] Yields are based on 1 equivalent of **1a** or KBr, and were determined by ^{1}H NMR analysis using CH_2Br_2 as an internal standard.
[c] Isolated yield.
[d] **1a** (1.1 mmol, 1.1 equiv), KBr (1 equiv), Oxone (1.2 equiv), H_2O (0.72 mL), CH_2Cl_2 (1 mL).
[e] **1a** (0.275 mmol, 1.1 equiv), Oxone (1 equiv).

The benzylic bromination of some alkylarenes with KBr/Oxone was screened, and the results are listed in Scheme 2. Both toluene (**1b**) and ethylbenzene (**1l**) gave their monobromides **3b** and **3l** in excellent yields based on KBr if 1.2 equivalents of the substrate were used under a 0.5 W LED at room temperature. When the aromatic ring was substituted with an electron-withdrawing group, including Br, Cl, COMe, CO_2H, CO_2Et, CN or NO_2, the corresponding monobromides were obtained in 70–89% isolated yield. In the case of *m*-methylnitrobenzene (**1i**) and *o*-methylnitrobenzene (**1k**) under a stronger light (3 W LED), the reaction rates were obviously accelerated and the brominations were complete in 3–4 hours. There is no very clear relationship between the electron-withdrawing groups or the substituted position (*o*, *m*, *p*) and the reaction performance. For *p*-methylanisole (**1p**) with a strong electron-donating group, however, instead of benzylic bromination, an electrophilic aromatic substitution occurred under the identical reaction conditions to afford the aryl bromide product **4p**. According to previous reports[2e,g,6] and this work, it is known that not only free-radical processes but also ionic



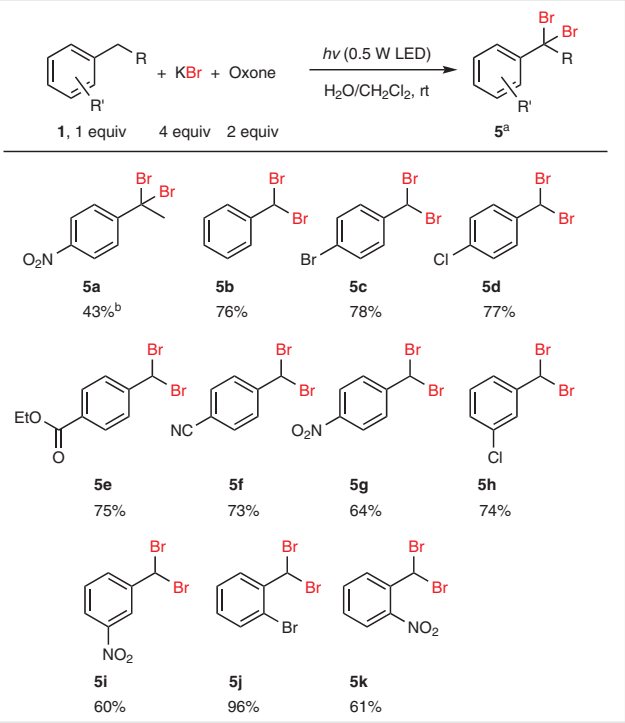
Scheme 2 Oxidative monobromination of benzylic sp^3 C–H bonds at room temperature. *Reagents and conditions*: **1** (1.1–1.2 equiv), KBr (0.25 mmol, 1 equiv), Oxone (0.8–1 equiv), H_2O (0.09–0.18 mL), CH_2Cl_2 (0.25 mL), 0.5 W LED at 5 cm, air, rt, 18–26 h. [a] Isolated yields based on KBr. [b] Yield determined by ^{1}H NMR analysis using CH_2Br_2 as an internal standard. [c] 3 W LED at 5 cm, 3 h. [d] 3 W LED at 5 cm, 4 h.

reactions can proceed very well in the halide salt/oxidant system, and the reaction selectivity depends on the substrates, solvents, light and other factors. For example, in the case of toluene (**1b**), as shown in Scheme 3 the occurrence of either aromatic or benzylic bromination can be controlled just by using different solvents with or without visible light (see the Supporting Information).



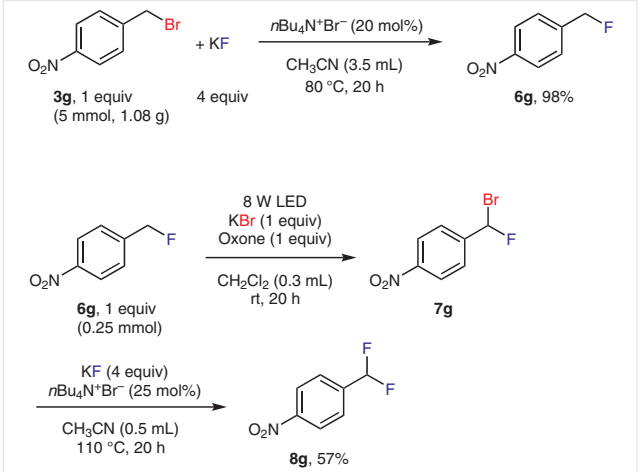
Scheme 3 Benzylic and aromatic bromination of toluene with KBr/Oxone at room temperature

Under weak visible light, no carbonyl products were found in the above benzylic monobrominations. Thus, dibrominations of benzylic sp^3 C–H bonds were investigated in the presence of excess KBr/Oxone under similar conditions, and the results are listed in Scheme 4. For toluene (**1b**) and its derivatives **1c–k** containing an electron-withdrawing group, such as Br, Cl, CO_2Et, CN or NO_2, dibromides **5b–k** were obtained in moderate to good yields at room temperature. However, for secondary benzylic sp^3 C–H bonds as in *p*-ethylnitrobenzene (**1a**), only a 43% yield of 1-(1,1-dibromoethyl)-4-nitrobenzene (**5a**) was obtained due to the steric hindrance of the large benzylic group. Although a prolonged reaction time was needed, this method of benzylic dibromination was successfully applied in the direct preparation of various benzylic dibromides from alkylarenes under very mild conditions.[4]



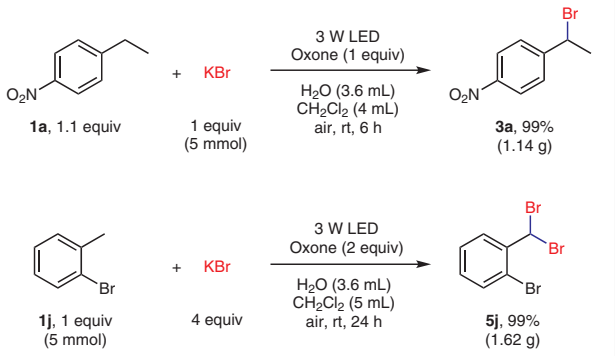
Scheme 4 Oxidative dibromination of benzylic sp^3 C–H bonds at room temperature. *Reagents and conditions*: **1** (0.25 mmol, 1 equiv), KBr (4 equiv), Oxone (2 equiv), H_2O (0.18 mL), CH_2Cl_2 (0.25 mL), 0.5 W LED at 5 cm, air, rt, 16–72 h. [a] Isolated yields based on **1**. [b] KBr (3 equiv), Oxone (1.5 equiv). Yield determined by ^1H NMR analysis using CH_2Br_2 as an internal standard.

Furthermore, we tried to prepare benzylic mono- and difluorides based on the oxidative bromination. After many tests, it was found that mono- and difluorides could be produced from benzylic monobromides and bromofluorides, respectively, in an effective nucleophilic substitution. The fluorinations of benzylic bromides with KF were carried out in the presence of catalytic $nBu_4N^+Br^-$ in CH_3CN at 80–110 °C. A benzylic monofluoride, 1-(fluoromethyl)-4-nitrobenzene (**6g**), was obtained from bromide **3g** in 98% yield in a gram-scale reaction. However, this substitution was not available for the direct formation of difluoride from the benzylic dibromide. The difluoride 1-(difluoromethyl)-4-nitrobenzene (**8g**) could be generated in 57% overall yield based on **6g** through a two-step process containing one monobromination and one fluorination, as shown in Scheme 5. This is a strategy for the preparation of benzylic fluorides, especially difluorides, without using HF or special fluorinating reagents.



Scheme 5 Preparation of benzylic mono- and difluorides from bromides

In addition, scale-up experiments for monobromination and dibromination were also conducted. Thus, 1-(1-bromoethyl)-4-nitrobenzene (**3a**) and 1-bromo-2-(dibromomethyl)benzene (**5j**) could be obtained in 99% isolated yield (Scheme 6).



Scheme 6 Gram-scale experiments for monobromination and dibromination

In summary, we have developed a very convenient method to prepare benzylic mono- and dibromides in moderate to excellent yields at room temperature. The method involves oxidative bromination of the benzylic sp^3 C–H bonds of toluene, ethylbenzene and their derivatives with KBr/Oxone in H_2O/CH_2Cl_2 under weak visible light. Alkylarenes bearing electron-donating groups are not suitable for this reaction, and their aromatic bromides may be produced under similar conditions in the dark. In addition, based on the monobromination, benzylic mono- and difluorides can also be produced successfully by catalytic nucleophilic substitution of the bromides with KF. Further studies on the reaction mechanism, scope and applications are underway.

All reagents were commercially available and weighed out under ambient conditions. All chemicals were used without further purification, except $CHCl_3$. Commercially purchased $CHCl_3$ was purified via washing with water and distillation to remove the stabilizer (CH_3CH_2OH). Analytical TLC was performed on precoated silica gel 60 F254 plates; visualization was achieved with UV light (254 nm). ^1H NMR spectra were recorded on Mercury Bruker AVANCE III HD 400 (400 MHz) or Bruker AVANCE III HD 500 (500 MHz) instruments. Chemical shifts are quoted in parts per million (ppm) referenced to the appropriate solvent peak or 0.0 ppm for TMS. Data for ^1H NMR spectra are reported as follows: chemical shift (δ), multiplicity (standard abbreviations), coupling constant(s) (Hz), integration. ^{13}C NMR spectra were recorded on Bruker AVANCE III HD 400 (101 MHz) or Bruker AVANCE III HD 500 (126 MHz) instruments. Chemical shifts are reported in ppm referenced to the center line of the triplet at 77.0 ppm of $CDCl_3$. ^{19}F NMR spectra were recorded on Bruker AVANCE III HD 400 (376 MHz) or Bruker AVANCE III HD 500 (471 MHz) instruments. Melting points were obtained on an INESA SGW X-4 melting point apparatus.

1-(1-Bromoethyl)-4-nitrobenzene (3a); Typical Bromination Procedure

KBr (29.8 mg, 0.25 mmol, 1.0 equiv), 1-ethyl-4-nitrobenzene (**1a**) (41.6 mg, 0.275 mmol, 1.1 equiv), Oxone (153.9 mg, 0.25 mmol, 1.0 equiv), CH_2Cl_2 (0.25 mL) and H_2O (180.0 mg, 0.18 mL, 40.0 equiv) were added, in accordance with the order, to a 15-mL oven-dried tube. The reaction tube was equipped with a magnetic stir bar and sealed with a Teflon-lined cap at once after the addition of the H_2O. Then, the tube was placed on a magnetic stirrer (speed 300 rpm) and irradiated with a 0.5 W LED at a distance of 5 cm for 20 h at rt. After the reaction was finished, the reaction mixture was quenched with Na_2SO_3. Water (15 mL) was added and the mixture extracted with CH_2Cl_2 (3 × 5 mL). The organic phase was combined and dried with anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to give the crude product that was purified by flash column chromatography (petroleum ether/EtOAc mixtures). Compound **3a** was obtained as a light yellow solid; yield: 53.6 mg (93%).

1-(4-Nitrophenyl)ethanone (2a)[5]

White solid; yield: 39.6 mg (96%).

Mp 76–78 °C (Lit.[7] 80–81 °C).

^1H NMR (400 MHz, $CDCl_3$): δ = 8.33 (d, *J* = 8.8 Hz, 2 H), 8.12 (d, *J* = 8.8 Hz, 2 H), 2.69 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 196.4, 150.4, 141.4, 129.4, 123.9, 27.1.

1-(1-Bromoethyl)-4-nitrobenzene (3a)[3b]

Light yellow solid; yield: 53.6 mg (93%).

Mp 29–31 °C (Lit.[8] 31–32.5 °C).

^1H NMR (400 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 8.8 Hz, 2 H), 7.61 (d, *J* = 8.8 Hz, 2 H), 5.21 (q, *J* = 6.8 Hz, 1 H), 2.06 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 150.2, 147.6, 128.0, 124.1, 46.6, 26.6.

(Bromomethyl)benzene (3b)[2i]

Light yellow liquid; yield: 98% (^1H NMR).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.30 (m, 5 H), 4.50 (s, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.9, 129.2, 128.9, 128.6, 33.7.

1-Bromo-4-(bromomethyl)benzene (3c)[2i]

White solid; yield: 50.0 mg (80%).

Mp 56–58 °C (Lit.[2b] 60.5–61 °C).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 8.4 Hz, 2 H), 7.28 (d, *J* = 8.4 Hz, 2 H), 4.44 (s, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 136.9, 132.1, 130.8, 128.6, 32.5.

1-(Bromomethyl)-4-chlorobenzene (3d)[2i]

White solid; yield: 39.6 mg (77%).

Mp 44–46 °C (Lit.[2b] 49.5–50.5 °C).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.32 (s, 4 H), 4.46 (s, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 136.4, 134.4, 130.5, 129.1, 32.5.

Ethyl 4-(Bromomethyl)benzoate (3e)[2i]

White solid; yield: 54.1 mg (89%).

Mp 34–35 °C (Lit.[9] 35 °C).

^1H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 8.4 Hz, 2 H), 7.45 (d, *J* = 8.4 Hz, 2 H), 4.51 (s, 2 H), 4.38 (q, *J* = 7.2 Hz, 2 H), 1.40 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.2, 142.6, 130.6, 130.2, 129.1, 61.3, 32.4, 14.5.

4-(Bromomethyl)benzonitrile (3f)[2i]

White solid; yield: 42.6 mg (87%).

Mp 111–112 °C (Lit.[2b] 112 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 8.0 Hz, 2 H), 7.50 (d, *J* = 8.0 Hz, 2 H), 4.48 (s, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 143.0, 132.7, 129.9, 118.5, 112.3, 31.6.

1-(Bromomethyl)-4-nitrobenzene (3g)[2i]

White solid; yield: 45.9 mg (85%).

Mp 98–99 °C (Lit.[3c] 98–99 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 8.8 Hz, 2 H), 7.57 (d, *J* = 8.8 Hz, 2 H), 4.52 (s, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 147.8, 144.9, 130.1, 124.2, 31.1.

1-(Bromomethyl)-3-chlorobenzene (3h)[10]

Colorless liquid; yield: 36.0 mg (70%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.89 (s, 1 H), 7.28 (m, 3 H), 4.44 (s, 2 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 139.7, 134.6, 130.2, 129.3, 128.7, 127.3, 32.3.

1-(Bromomethyl)-3-nitrobenzene (3i)[10]

White solid; yield: 41.0 mg (76%).

Mp 51–53 °C (Lit.[11] 55 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.27 (d, *J* = 6.8 Hz, 1 H), 8.17 (d, *J* = 6.8 Hz, 1 H), 7.74 (d, *J* = 6.8 Hz, 1 H), 7.55 (t, *J* = 6.8 Hz, 1 H), 4.55 (s, 2 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 148.5, 139.8, 135.1, 130.0, 124.0, 123.4, 31.2.

1-Bromo-2-(bromomethyl)benzene (3j)[12]

White solid; yield: 49.4 mg (79%).

Mp 21–22 °C (Lit.[12] 31 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.58 (dd, *J* = 7.5, 1.0 Hz, 1 H), 7.46 (dd, *J* = 7.5, 2.0 Hz, 1 H), 7.30 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1 H), 7.17 (ddd, *J* = 7.5, 7.5, 2.0 Hz, 1 H), 4.61 (s, 2 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 137.2, 133.5, 131.4, 130.3, 128.1, 124.6, 33.5.

1-(Bromomethyl)-2-nitrobenzene (3k)[10]

White solid; yield: 43.2 mg (80%).

Mp 42–43 °C (Lit.[13] 46–47.5 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 8.5 Hz, 1 H), 7.63–7.57 (m, 2 H), 7.51–7.48 (m, 1 H), 4.84 (s, 2 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 148.2, 133.8, 133.0, 132.7, 129.7, 125.6, 29.0.

(1-Bromoethyl)benzene (3l)[2i]

Colorless liquid; yield: 95% (^{1}H NMR).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53–7.45 (m, 2 H), 7.35 (dd, *J* = 8.0, 6.4 Hz, 2 H), 7.29 (d, *J* = 7.2 Hz, 1 H), 5.22 (q, *J* = 7.2 Hz, 1 H), 2.05 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 143.3, 128.8, 128.5, 126.9, 49.7, 27.0.

1-(4-(1-Bromoethyl)phenyl)ethanone (3m)[14]

Light yellow, oily liquid; yield: 48.8 mg (86%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 8.4 Hz, 2 H), 7.53 (d, *J* = 8.4 Hz, 2 H), 5.21 (q, *J* = 6.8 Hz, 1 H), 2.61 (s, 3 H), 2.06 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 197.6, 148.3, 137.0, 128.9, 127.2, 48.0, 26.8, 26.6.

4-(1-Bromoethyl)benzoic Acid (3n)[15]

White solid; yield: 41.8 mg (73%).

Mp 152–154 °C (Lit.[15] 225 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.49 (br, 1 H), 8.08 (d, *J* = 8.4 Hz, 2 H), 7.54 (d, *J* = 8.4 Hz, 2 H), 5.21 (q, *J* = 7.0 Hz, 1 H), 2.06 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.6, 149.1, 130.8, 129.2, 127.2, 47.9, 26.7.

(1-Bromobutyl)benzene (3o)[16]

Colorless liquid; yield: 49.5 mg (93%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40–7.27 (m, 5 H), 4.97 (t, *J* = 7.5 Hz, 1 H), 2.31–2.01 (m, 2 H), 1.54–1.29 (m, 2 H), 0.94 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 142.4, 128.8, 128.4, 127.4, 55.6, 42.2, 21.6, 13.5.

2-Bromo-1-methoxy-4-methylbenzene (4p)[17]

Colorless oily liquid; yield: 40.2 mg (80%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 1.6 Hz, 1 H), 7.05 (dd, *J* = 8.4, 1.6 Hz, 1 H), 6.79 (d, *J* = 8.4 Hz, 1 H), 3.86 (s, 3 H), 2.27 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 153.9, 133.9, 131.6, 129.0, 112.0, 111.4, 56.4, 20.3.

1-(1,1-Dibromoethyl)-4-nitrobenzene (5a)[18]

White solid; mp 44–46 °C (Lit.[8] 51–52 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.22 (d, *J* = 9.0 Hz, 2 H), 7.95 (d, *J* = 9.0 Hz, 2 H), 3.00 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 152.4, 147.8, 127.4, 123.6, 58.8, 41.0.

(Dibromomethyl)benzene (5b)

Colorless liquid; yield: 47.5 mg (76%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.57 (dd, *J* = 7.0, 1.6 Hz, 2 H), 7.39–7.31 (m, 3 H), 6.66 (s, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 142.1, 130.0, 128.8, 126.6, 41.2.

1-Bromo-4-(dibromomethyl)benzene (5c)[4c]

Colorless liquid; yield: 64.1 mg (78%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.50 (d, *J* = 8.5 Hz, 2 H), 7.44 (d, *J* = 8.5 Hz, 2 H), 6.59 (s, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 141.1, 132.0, 128.3, 124.0, 39.7.

1-Chloro-4-(dibromomethyl)benzene (5d)[19]

Colorless liquid; yield: 54.7 mg (77%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 9.0 Hz, 2 H), 7.35 (d, *J* = 9.0 Hz, 2 H), 6.61 (s, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 140.6, 135.8, 129.0, 128.0, 39.7.

Ethyl 4-(Dibromomethyl)benzoate (5e)[3c]

White solid; yield: 60.4 mg (75%).

Mp 96–98 °C (Lit.[3c] 98–99 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 8.0 Hz, 2 H), 7.63 (d, *J* = 8.0 Hz, 2 H), 6.66 (s, 1 H), 4.39 (q, *J* = 7.2 Hz, 2 H), 1.40 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 165.7, 146.1, 131.8, 130.1, 126.7, 61.4, 39.9, 14.5.

4-(Dibromomethyl)benzonitrile (5f)[20]

White solid; yield: 50.2 mg (73%).

Mp 78–80 °C (Lit.[21] 81–82 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.69 (s, 4 H), 6.62 (s, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 146.3, 132.7, 127.5, 118.0, 113.7, 38.8.

1-(Dibromomethyl)-4-nitrobenzene (5g)[20]

White solid; yield: 47.2 mg (64%).

Mp 61–63 °C (Lit.[20] 73–75 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.25 (d, *J* = 7.2 Hz, 2 H), 7.76 (d, *J* = 7.2 Hz, 2 H), 6.67 (s, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 148.4, 148.0, 127.9, 124.2, 38.3.

1-Chloro-3-(dibromomethyl)benzene (5h)

Colorless liquid; yield: 52.6 mg (74%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.58 (s, 1 H), 7.45–7.43 (m, 1 H), 7.31–7.30 (m, 2 H), 6.68 (s, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 143.7, 134.6, 130.10, 130.06, 127.0, 124.8, 39.4.

1-(Dibromomethyl)-3-nitrobenzene (5i)[20]

White solid; yield: 44.2 mg (60%).

Mp 102–104 °C (Lit.[20] 99–101 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.44 (dd, *J* = 2.0, 2.0 Hz, 1 H), 8.21 (ddd, *J* = 8.0, 2.0, 0.9 Hz, 1 H), 7.93 (d, *J* = 8.0 Hz, 1 H), 7.60 (t, *J* = 8.0 Hz, 1 H), 6.69 (s, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 148.2, 143.8, 132.7, 130.1, 124.7, 121.8, 38.2.

1-Bromo-2-(dibromomethyl)benzene (5j)[20]

Colorless liquid; yield: 78.9 mg (96%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.02 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.49 (dd, *J* = 8.0, 1.0 Hz, 1 H), 7.41 (app ddd, *J* = 8.0, 8.0, 1.0 Hz, 1 H), 7.17 (app ddd, *J* = 8.0, 8.0, 1.5 Hz, 1 H), 7.09 (s, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 140.5, 132.7, 131.3, 131.2, 128.7, 119.8, 39.9.

1-(Dibromomethyl)-2-nitrobenzene (5k)[22]

Yellow solid; yield: 45.0 mg (61%).

Mp 44–46 °C (Lit.[22] 46 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.25 (dd, *J* = 8.0, 1.0 Hz, 1 H), 7.92 (dd, *J* = 8.0, 1.0 Hz, 1 H), 7.76–7.73 (m, 1 H), 7.53–7.49 (m, 1 H), 7.48 (s, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 144.3, 136.3, 134.3, 132.7, 130.6, 124.4, 34.3.

1-(Fluoromethyl)-4-nitrobenzene (6g)[23]

Pale yellow solid; yield: 0.76 g (98%).

Mp 37–38 °C (Lit.[24] 38.5 °C).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.27 (d, *J* = 8.0 Hz, 2 H), 7.54 (d, *J* = 8.0 Hz, 2 H), 5.52 (d, *J* = 46.5 Hz, 2 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 148.0, 143.5 (d, *J* = 18 Hz), 127.2 (d, *J* = 8 Hz), 124.0, 83.0 (d, *J* = 171 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = –215.7.

1-(Bromo(fluoro)methyl)-4-nitrobenzene (7g)

Yellow oily liquid; yield: 56.2 mg (96%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.30 (d, *J* = 9.0 Hz, 2 H), 7.69 (d, *J* = 9.0 Hz, 2 H), 7.49 (d, *J* = 45.5 Hz, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 148.7, 145.0 (d, *J* = 20 Hz), 126.2 (d, *J* = 6 Hz), 124.2, 89.6 (d, *J* = 257 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ = –136.4.

1-(Difluoromethyl)-4-nitrobenzene (8g)[25]

Yellow oily liquid; yield: 30.3 mg (70%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.34 (d, *J* = 8.4 Hz, 2 H), 7.72 (d, *J* = 8.4 Hz, 2 H), 6.75 (t, *J* = 55.6 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 149.5, 140.3 (t, *J* = 23 Hz), 127.0 (t, *J* = 6 Hz), 124.2, 113.3 (t, *J* = 242 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –113.0.

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Supporting Information

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References

(1) (a) Lin, R.; Amrute, A. P.; Pérez-Ramírez, J. *Chem. Rev.* **2017**, *117*, 4182. (b) Lu, W.; Zhou, L. *Oxidation of C–H Bonds*; John Wiley & Sons, Inc: Hoboken, **2017**. (c) Shimojo, H.; Moriyama, K.; Togo, H. *Synthesis* **2015**, *47*, 1280.

(2) (a) Djerassi, C. *Chem. Rev.* **1948**, *43*, 271. (b) Huyser, E. S. *J. Am. Chem. Soc.* **1960**, *82*, 391. (c) Avramoff, M.; Weiss, J.; Schächter, O. *J. Org. Chem.* **1963**, *28*, 3256. (d) Shaw, H.; Perlmutter, H. D.; Gu, C.; Arco, S. D.; Quibuyen, T. O. *J. Org. Chem.* **1997**, *62*, 236. (e) Kikuchi, D.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **1998**, *63*, 6023. (f) Smirnov, V. V.; Zelikman, V. M.; Beletskaya, I. P.; Levitskii, M. M.; Kazankova, M. A. *Mendeleev Commun.* **2000**, *10*, 175. (g) Shibatomi, K.; Zhang, Y.; Yamamoto, H. *Chem. Asian J.* **2008**, *3*, 1581. (h) Nishina, Y.; Hashimoto, H.; Kimura, N.; Miyata, N.; Fujii, T.; Ohtani, B.; Takada, J. *RSC Adv.* **2012**, *2*, 6420. (i) Cantillo, D.; de Frutos, O.; Rincon, J. A.; Mateos, C.; Kappe, C. O. *J. Org. Chem.* **2014**, *79*, 223.

(3) (a) Podgoršek, A.; Zupan, M.; Iskra, J. *Angew. Chem. Int. Ed.* **2009**, *48*, 8424. (b) Amati, A.; Dosualdo, G.; Zhao, L.; Bravo, A.; Fontana, F.; Minisci, F.; Bjørsvik, H. R. *Org. Process Res. Dev.* **1998**, *2*, 261. (c) Podgoršek, A.; Stavber, S.; Zupan, M.; Iskra, J. *Tetrahedron* **2009**, *65*, 4429. (d) Yin, L.; Wu, J.; Xiao, J.; Cao, S. *Tetrahedron Lett.* **2012**, *53*, 4418.

(4) (a) Mataka, S.; Kurisu, M.; Takahashi, K.; Tashiro, M. *Chem. Lett.* **1984**, 1969. (b) Kulangiappar, K.; Karthik, G.; Kulandainathan, M. A. *Synth. Commun.* **2009**, *39*, 2304. (c) Pingali, S. R. K.; Upadhyay, S. K.; Jursic, B. S. *Green Chem.* **2011**, *13*, 928.
(5) Moriyama, K.; Takemura, M.; Togo, H. *Org. Lett.* **2012**, *14*, 2414.
(6) (a) Zhao, M.; Lu, W. *Org. Lett.* **2017**, *19*, 4560. (b) Zhao, M.; Lu, W. unpublished results.
(7) Cui, L.; Liu, K.; Zhang, C. *Org. Biomol. Chem.* **2011**, *9*, 2258.
(8) Kochergin, P. M.; Bushueva, K. S. *Zh. Obshch. Khim.* **1962**, *32*, 3033.
(9) Snyder, H. R.; Merica, E. P.; Force, C. G.; White, E. G. *J. Am. Chem. Soc.* **1958**, *80*, 4622.
(10) Adimurthy, S.; Ghosh, S.; Patoliya, P. U.; Ramachandraiah, G.; Agrawal, M.; Gandhi, M. R.; Upadhyay, S. C.; Ghosh, P. K.; Ranu, B. C. *Green Chem.* **2008**, *10*, 232.
(11) Spickett, R. G. W.; Timmis, G. M. *J. Chem. Soc.* **1954**, 2887.
(12) Soran, L.; Coman, V.; Soran, A.; Silvestru, C. *Cent. Eur. J. Chem.* **2004**, *2*, 563.
(13) Daub, G. H.; Castle, R. N. *J. Org. Chem.* **1954**, *19*, 1571.
(14) Summers, J. B.; Gunn, B. P.; Martin, J. G.; Martin, M. B.; Mazdiyasni, H.; Stewart, A. O.; Young, P. R.; Bouska, J. B.; Goetze, A. M.; Dyer, R. D.; Brooks, D. W.; Carter, G. W. *J. Med. Chem.* **1988**, *31*, 1960.
(15) Thiessen, W.; Wolff, T. *Des. Monomers Polym.* **2011**, *14*, 287.
(16) Nagarapu, L.; Apuri, S.; Gaddam, C.; Bantu, R. *Org. Prep. Proced. Int.* **2009**, *41*, 243.
(17) Zysman-Colman, E.; Arias, K.; Siegel, J. S. *Can. J. Chem.* **2009**, *87*, 440.
(18) Lambooy, J. P. *J. Am. Chem. Soc.* **1950**, *72*, 2804.
(19) Rogers, R. B.; Herrero, M. P. EP 101288, **1983**.
(20) Xi, H.; Gibb, C. L. D.; Gibb, B. C. *J. Org. Chem.* **1999**, *64*, 9286.
(21) Di Mola, A.; Caruso, T.; De Caprariis, P.; Massa, A. *ARKIVOC* **2016**, *(iv)*, 10.
(22) Makosza, M.; Owczarczyk, Z. *J. Org. Chem.* **1989**, *54*, 5094.
(23) Blessley, G.; Holden, P.; Walker, M.; Brown, J. M.; Gouverneur, V. *Org. Lett.* **2012**, *14*, 2754.
(24) Beguin, C.; Meary-Tertian, A. *Bull. Soc. Chim. Fr.* **1967**, 795.
(25) Aikawa, K.; Serizawa, H.; Ishii, K.; Mikami, K. *Org. Lett.* **2016**, *18*, 3690.