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PAPER

Solvent-free bromination reactions with sodium bromide and oxone promoted by mechanical milling

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New solvent-free brominations of 1,3-dicarbonyl compounds, phenols, various alkenes including chalcones, azachalcones, 4-phenylbut-3-en-2-one, methyl cinnamate, styrene and 1,3-cyclohexadiene were efficiently achieved by employing sodium bromide and oxone under mechanical milling conditions. The brominated products were obtained in good to excellent yields.

Introduction

Bromination reactions have been drawing extensive interest in the field of organic synthesis due to the commercial importance of bromoorganics in the synthesis of various natural products, as well as in the manufacture of pharmaceuticals, intermediates for agrochemicals, and other speciality chemicals. For example, a large number of industrially valuable products such as pesticides, herbicides, fire retardants, and other new materials, carry bromo functionality.[1] Traditional methods of bromination usually involve the use of elemental bromine under harsh reaction conditions,[2] and require careful control of the addition rate and temperature to avoid undesirable side reactions. Due to its toxic nature, the use of elemental bromine is troublesome and environmentally hazardous. Therefore, new bromination protocols have been developed.[3–9] As an alternative reagent to the highly toxic liquid bromine, solid organic ammonium tribromides such as Me_4NBr_3,[4a] 2,4-diamino-1,3-thiazole hydrotribromide,[4b] 1,8-diazabicyclo[5.4.0]undec-7-ene hydrobromide perbromide ($DBUHBr_3$),[4c] Bu_4NBr_3,[4d,e] phenyltrimethylammonium tribromide,[4e] $PyHBr_3$,[4e–g] and 1,2-dipyridiniumditribromide-ethane (DPTBE)[4h] have been utilized. However, these brominating agents need to be prepared in advance from elemental bromine and/or bromides. Another method involves using the bromide generated *in situ* from the oxidation of bromide ions.[3,5–9] The combinations of oxidants and bromides such as H_2O_2–HBr,[5a–c] H_2O_2–V_2O_5–Et_4NBr,[5d] *t*-BuOOH–HBr,[5b,c] oxone (potassium peroxymonosulfate, $2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$, the active component is potassium monopersulfate, $KHSO_5$)/NaBr,[6a] oxone/HBr,[6b] cerium(IV) ammonium nitrate (CAN)/KBr,[7a] CAN/LiBr,[7b] Selectfluor®/KBr[8] and $NaBrO_3$–NaBr[9] have been employed in these bromination reactions, but require a two-phase (water and an organic solvent) system.

On the other hand, solvent-free organic reactions have drawn increasing attention for many years for their environmentally friendly protocols and convenient means of product purification. The mechanical ball-milling technique is a powerful tool in promoting various solvent-free reactions.[10–13] As an effective oxidant, oxone is finding increasing applications in synthetic transformations due to its high stability, simple manipulation, non-toxic nature, versatility and cheapness.[12f,14,15] Although solvent-free allylic bromination in a ball mill with NBS has been reported,[16] to the best of our knowledge, the solvent-free bromination reaction using a combination of sodium bromide and oxone has not been disclosed. In the continuation of our interest in the utilization of oxone in mechanochemical reactions,[12f] we report a highly efficient method for the bromination of 1,3-dicarbonyl compounds, phenols, chalcones, azachalcones, 4-phenylbut-3-en-2-one, methyl cinnamate, styrene and 1,3-cyclohexadiene by employing a mixture of oxone and sodium bromide under ball milling and solvent-free conditions.

Results and discussion

Firstly, the bromination of representative 1,3-dicarbonyl compounds including 5,5-dimethylcyclohexane-1,3-dione (dimedone) (**1a**), 1,3-indandione (**1b**), barbituric acid (**1c**), 1,3-diphenylpropane-1,3-dione (**1d**), 1-(4-methoxyphenyl)-3-phenylpropane-1,3-dione (**1e**) and ethyl benzoylacetate (**1f**) was investigated. In a typical experiment, a mixture of dimedone (**1a**), oxone and NaBr in a molar ratio of 1 : 1 : 2.5 was introduced in a stainless steel jar (5 mL) together with a stainless steel ball of 7.0 mm diameter. The same mixture was also introduced into another parallel jar. Then the two reaction vessels were closed and fixed on the vibration arms of the ball-milling apparatus (Retsch MM200 mixer mill, Retsch GmbH, Haan, Germany) and were vibrated vigorously at a rate of 1800 rounds per minute (30 Hz) at room temperature for 20 min. The isolated product proved to be a dibromated compound **2a**. The same procedure was then applied to substrates **1b–f**.

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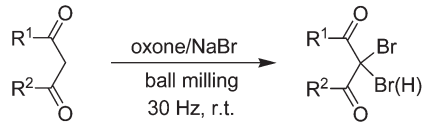
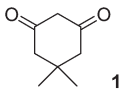
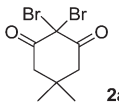
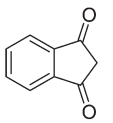
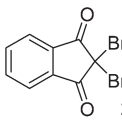
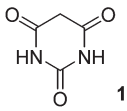
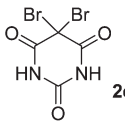
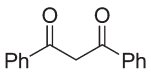
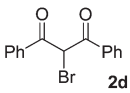
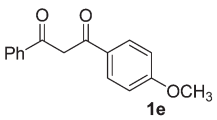
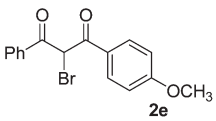
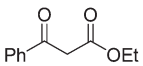
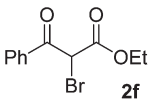
Table 1 Bromination of 1,3-dicarbonyl compounds **1a–f** using oxone with NaBr under mechanical milling conditions[a]

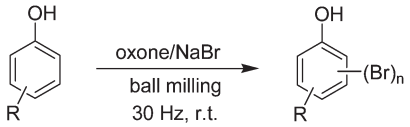


1 **2**

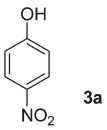
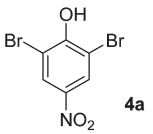
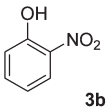
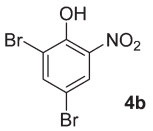
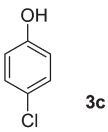
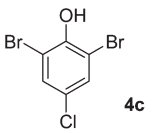
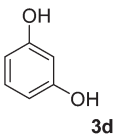
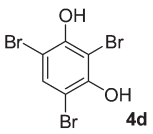
Entry	Substrate	Product	Yield (%)[b]
1	 **1a**	 **2a**	94
2	 **1b**	 **2b**	96
3	 **1c**	 **2c**	96
4[c]	 **1d**	 **2d**	97
5[c]	 **1e**	 **2e**	96
6[c,d]	 **1f**	 **2f**	98

[a] Unless otherwise specified, the reaction mixture of substrate **1** (1.0 equiv), oxone (1.0 equiv) and NaBr (2.5 equiv) was milled at 30 Hz for 20 min. [b] Isolated yields obtained by chromatography on silica gel. [c] 2.0 equiv of NaBr were used. [d] Reaction time was 90 min.

Table 2 Bromination of phenols **3a–d** using oxone with NaBr under mechanical milling conditions[a]



3 **4**

Entry	Substrate	Product	Yield (%)[b]
1	 **3a**	 **4a**	97
2	 **3b**	 **4b**	95
3	 **3c**	 **4c**	99
4[c]	 **3d**	 **4d**	99

[a] Unless otherwise specified, the reaction mixture of substrate **3** (1.0 equiv), oxone (2.0 equiv) and NaBr (2.5 equiv) was milled at 30 Hz for 40 min. [b] Isolated yields obtained by chromatography on silica gel. [c] 4.0 equiv of NaBr were used.

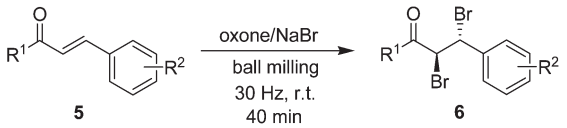
The reaction conditions and results for the solvent-free reaction of 1,3-dicarbonyl compounds **1a–f** with oxone and NaBr under ball milling conditions are listed in Table 1. As can be seen from Table 1, cyclic 1,3-dicarbonyl compounds **1a–c** afforded α,α-dibromo derivatives **2a–c** in 94–96% yields (Table 1, entries 1–3). In contrast, acyclic 1,3-dicarbonyl compounds **1d–f** selectively gave α-monobromo derivatives **2d–f** in nearly quantitative yields (96–98%), although an excess amount (2 equiv) of NaBr was employed (Table 1, entries 4–6). Notably, cyclic and acyclic 1,3-dicarbonyl compounds generated dibrominated and monobrominated products respectively. This difference may be due to the higher activity of cyclic 1,3-dicarbonyl compounds. Although, the same α,α-dibromo derivatives from **1a–c** were obtained when the amount of NaBr was 2 equiv or less, we employed 2.5 equiv of NaBr to guarantee the complete conversion of **1a–c** and excellent yields for **2a–c**.

We next explored the bromination of substituted phenols. When *p*-nitrophenol (**3a**), *o*-nitrophenol (**3b**), *p*-chlorophenol (**3c**) and resorcinol (**3d**) were employed, the corresponding poly-brominated products were selectively obtained in nearly quantitative yields (95–99%).

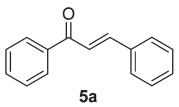
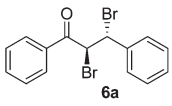
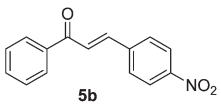
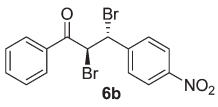
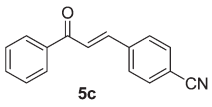
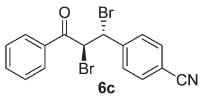
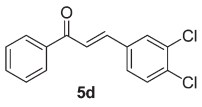
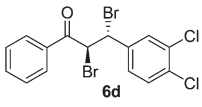
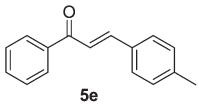
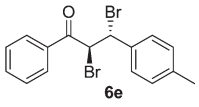
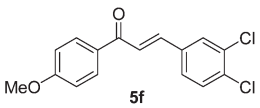
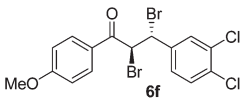
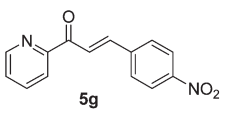
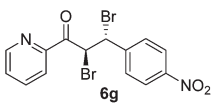
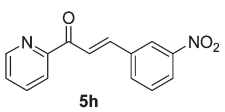
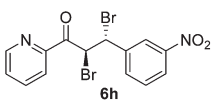
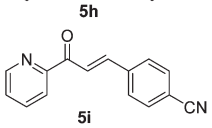
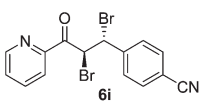
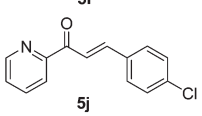
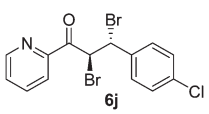
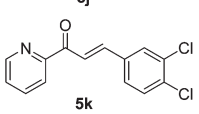
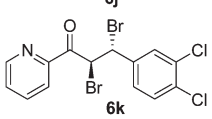
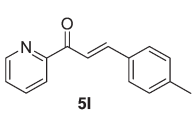
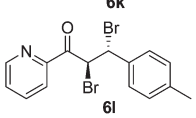
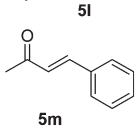
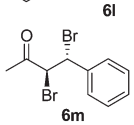
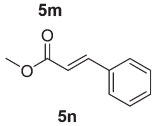
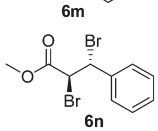
The reaction conditions and results for the solvent-free reaction of phenols **3a–d** with oxone and NaBr under ball milling conditions are shown in Table 2. It can be found from Table 2 that pure multibrominated phenols could be obtained exclusively from substituted phenols with extremely high efficiency. The substituent on the phenols had a vital and cooperative effect on the regioselectivity of the bromination reactions. The bromination took place in the *ortho*- and *para*-positions of the hydroxyl group on the phenyl ring (Table 2, entries 1–4). Our current procedure provided a mild and effective alternative to the synthesis of multisubstituted bromophenols. A larger amount (2 equiv) of oxone was required to achieve high yields of **4a–d**, although the exact reason is currently unknown. The attempted monobromination of **3a–d** using 1 equiv of NaBr failed because the reaction tended to give a mixture of products.

To further demonstrate the versatility of our present methodology, the bromination of various α,β-unsaturated carbonyl compounds including chalcones (**5a–f**), azachalcones (**5g–l**), 4-phenylbut-3-en-2-one (**5m**), methyl cinnamate (**5n**) was scrutinized under the present conditions. The reaction conditions and results for the solvent-free reaction of α,β-unsaturated carbonyl compounds **5a–n** with oxone and NaBr under ball milling conditions are collected in Table 3.

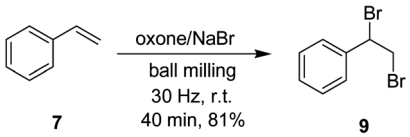
Table 3 Bromination of α,β-unsaturated carbonyl compounds **5a–n** using oxone with NaBr under mechanical milling conditions[a]



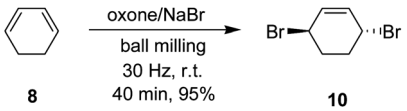
5 **6**

Entry	Substrate	Product	Yield (%)[b]
1	 **5a**	 **6a**	95
2	 **5b**	 **6b**	88
3	 **5c**	 **6c**	78
4	 **5d**	 **6d**	90
5	 **5e**	 **6e**	89
6	 **5f**	 **6f**	86
7	 **5g**	 **6g**	85
8	 **5h**	 **6h**	87
9	 **5i**	 **6i**	84
10	 **5j**	 **6j**	78
11	 **5k**	 **6k**	81
12	 **5l**	 **6l**	91
13	 **5m**	 **6m**	81
14	 **5n**	 **6n**	95

[a] The reaction mixture of substrate **5** (1.0 equiv), oxone (1.0 equiv) and NaBr (2.5 equiv) was milled at 30 Hz for 40 min. [b] Isolated yields obtained by chromatography on silica gel.



Scheme 1 Bromination of styrene using oxone/NaBr under mechanical milling conditions.



Scheme 2 Bromination of 1,3-cyclohexadiene using oxone/NaBr under mechanical milling conditions.

As shown in Table 3, a wide range of chalcones with either electron-withdrawing groups or electron-donating groups were successfully transformed into the corresponding *anti* α,β-dibromo derivatives **6a–f** in 78–95% yields (Table 3, entries 1–6). To our great delight, various aza-chalcones with substituents of different electronic properties also reacted efficiently under the same conditions, affording the corresponding brominated products **6g–l** in 78–91% yields (Table 3, entries 7–12). In addition, enone **5m** and cinnamate **5n** could also be converted nicely to *anti* α,β-dibromo derivatives **6m** and **6n** in yields of 81% and 95%, respectively. Nitro, cyano, chloro, keto and ester groups were unaffected, thus our protocol had excellent functional group compatibility for the bromination reaction. It should be noted that the bromination reaction of α,β-unsaturated carbonyl compounds was sensitive to ambient temperature, which should be about 25 °C.

Simple alkenes were also examined with styrene (**7**) and 1,3-cyclohexadiene (**8**) as representative examples. Both of them could be dibrominated efficiently with 1.0 equiv of oxone and 2.5 equiv of NaBr to give products **9** and **10** in 81% and 95% yields, respectively (Schemes 1 and 2).

It was reported that the reaction mixture of 1,3-cyclohexadiene with Br_2 in organic solvents at low temperature equilibrated at 25 °C to a mixture of three dibromocyclohexenes containing *trans*-3,6-dibromocyclohexene (**10**), its isomeric *cis*-3,6-dibromocyclohexene and *trans*-3,4-dibromocyclohexene in a ratio of ~3 : 1 : 1, which remained almost the same at 78 °C.[17] Intriguingly, the bromination of 1,3-cyclohexadiene under our conditions selectively gave only **10** rather than its *cis* isomer or *trans*-3,4-dibromocyclohexene, thus demonstrating the advantage of our protocol.

Conclusions

In summary, we have demonstrated a novel, efficient and environmentally friendly methodology for the bromination of various 1,3-dicarbonyl compounds, phenols, chalcones, aza-chalcones and simple alkenes. By simply mixing with the oxone/NaBr system in a ball mill, the brominated products were obtained in good to excellent yields. Compared with traditional bromination methodologies, milder reaction conditions, wider generality, higher yields, better selectivity and shorter reaction time are the main advantages of the present protocol. Furthermore, no use of any organic solvent makes the current method appealing.

Experimental section

General procedure for the bromination of 1,3-dicarbonyl compounds

A mixture of **1** (0.1 mmol), oxone (61.4 mg, 0.1 mmol) and sodium bromide (25.8 mg, 0.25 mmol) (20.6 mg, 0.2 mmol for **1d–f**) was introduced, together with a stainless ball of 7.0 mm diameter, into a stainless jar (5 mL). The same mixture was also introduced into a second parallel jar. The two reaction vessels were closed and fixed on the vibration arms of a ball-milling apparatus (Retsch MM200 mixer mill, Retsch GmbH, Haan, Germany) and were vibrated vigorously at a rate of 1800 rounds per minute (30 Hz) at room temperature for 20 min (90 min for **1f**). After that, the reaction mixture was collected and dissolved in ethyl acetate. The solution was filtrated to remove the residue and then evaporated until dry under high vacuum. Finally, the resulting solid **2** was purified by column chromatography on silica gel using ethyl acetate–petroleum ether as the eluent.

2,2-Dibromo-5,5-dimethylcyclohexane-1,3-dione 2a.[6b] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.01 (s, 4H), 1.02 (s, 6H).

2,2-Dibromo-1,3-indandione 2b.[18] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.14–8.08 (m, 2H), 8.04–7.98 (m, 2H).

5,5-Dibromopyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione 2c.[19] ^{1}H NMR (DMSO-d_6, 300 MHz) δ 11.82 (s, 2H).

2-Bromo-1,3-diphenylpropane-1,3-dione 2d.[20] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.99 (d, J = 7.6 Hz, 4H), 7.60 (t, J = 7.3 Hz, 2H), 7.47 (t, J = 7.7 Hz, 4H), 6.55 (s, 1H).

2-Bromo-1-(4-methoxyphenyl)-3-phenylpropane-1,3-dione 2e. IR (KBr) cm^{-1} 2999, 1702, 1654, 1602, 1571, 1509, 1447, 1426, 1322, 1300, 1261, 1203, 1180, 1156, 1029, 1001, 983, 850, 808, 775, 755, 688, 643, 610, 566; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.99 (d, J = 8.7 Hz, 4H), 7.59 (t, J = 7.5 Hz, 1H), 7.46 (t, J = 7.5 Hz, 2H), 6.93 (d, J = 8.7 Hz, 2H), 6.49 (s, 1H), 3.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 189.2, 187.6, 164.5, 134.2, 134.0, 131.8, 129.3, 129.0, 126.7, 114.4, 55.7, 53.0; HRMS calcd for $C_{16}H_{13}O_3{}^{79}Br$: m/z 332.0048, found m/z 332.0045.

Ethyl 2-bromo-3-oxo-3-phenylpropanoate 2f.[20] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.00 (d, J = 8.3 Hz, 2H), 7.63 (t, J = 7.3 Hz, 1H), 7.50 (t, J = 7.4 Hz, 2H), 5.65 (s, 1H), 4.29 (q, J = 7.0 Hz, 2H), 1.25 (t, J = 7.0 Hz, 3H).

General procedure for the bromination of phenols

The same procedure was applied to a mixture of **3** (0.1 mmol), oxone (122.8 mg, 0.2 mmol) and sodium bromide (25.8 mg, 0.25 mmol) (41.2 mg, 0.4 mmol for **3d**) for 40 min to obtain **4a–d**.

2,6-Dibromo-4-nitrophenol 4a.[21] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.42 (s, 2H), 6.52 (s, 1H).

2,4-Dibromo-6-nitrophenol 4b.[22] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 11.05 (s, 1H), 8.25 (d, J = 2.3 Hz, 1H), 7.99 (d, J = 2.3 Hz, 1H).

2,6-Dibromo-4-chlorophenol 4c.[23] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.46 (s, 2H), 5.85 (s, 1H).

2,4,6-Tribromobenzene-1,3-diol 4d.[24] ^{1}H NMR (DMSO-d_6, 300 MHz) δ 9.97 (s, 2H), 7.69 (s, 1H).

General procedure for the bromination of α,β-unsaturated carbonyl compounds and simple alkenes

The same procedure was applied to a mixture of **5**, **7** or **8** (0.1 mmol), oxone (61.4 mg, 0.1 mmol) and sodium bromide (25.8 mg, 0.25 mmol) for 40 min to obtain **6a–n**, **9** and **10**.

***trans*-2,3-Dibromo-1,3-diphenylpropan-1-one 6a.**[4h] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.11 (d, J = 8.0 Hz, 2H), 7.69–7.64 (m, 1H), 7.58–7.52 (m, 4H), 7.49–7.36 (m, 3H), 5.83 (d, J = 11.3 Hz, 1H), 5.65 (d, J = 11.3 Hz, 1H).

***trans*-2,3-Dibromo-3-(4-nitrophenyl)-1-phenylpropan-1-one 6b.**[25] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.30 (d, J = 8.7 Hz, 2H), 8.05 (d, J = 7.8 Hz, 2H), 7.73–7.67 (m, 3H), 7.57 (t, J = 7.6 Hz, 2H), 5.78 (d, J = 11.2 Hz, 1H), 5.69 (d, J = 11.2 Hz, 1H).

***trans*-1,2-Dibromo-3-oxo-3-phenylpropyl)benzonitrile 6c.** IR (KBr) cm^{-1} 2926, 2224, 1680, 1594, 1447, 1370, 1323, 1265, 1225, 1180, 1146, 974, 840, 809, 737, 685, 645, 634, 574, 472; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.09 (d, J = 7.9 Hz, 2H), 7.75–7.63 (m, 5H), 7.56 (t, J = 7.6 Hz, 2H), 5.75 (d, J = 11.2 Hz, 1H), 5.64 (d, J = 11.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 190.6, 143.5, 134.5, 134.3, 132.8, 129.4, 129.2, 129.0, 118.2, 113.3, 47.9, 46.1; HRMS [M^+–Br] calcd for $C_{16}H_{11}NO^{79}Br$: m/z 312.0024, found m/z 312.0053.

***trans*-2,3-Dibromo-3-(3,4-dichlorophenyl)-1-phenylpropan-1-one 6d.** IR (KBr) cm^{-1} 1686, 1594, 1475, 1448, 1409, 1364, 1292, 1263, 1221, 1136, 1031, 978, 723, 680, 635, 590; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.09 (d, J = 8.1 Hz, 2H), 7.68 (t, J = 7.4 Hz, 1H), 7.63 (d, J = 2.1 Hz, 1H), 7.56 (t, J = 7.6 Hz, 2H), 7.51 (d, J = 8.3 Hz, 1H), 7.36 (dd, J = 8.3, 2.1 Hz, 1H), 5.72 (d, J = 11.3 Hz, 1H), 5.57 (d, J = 11.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 190.7, 138.6, 134.5, 134.3, 133.5, 133.2, 130.9, 130.5, 129.2, 129.0, 127.8, 47.8, 46.5; HRMS [M^+–Br] calcd for $C_{15}H_{10}O^{35}Cl^{37}Cl^{79}Br$: m/z 356.9263, found m/z 356.9259.

***trans*-2,3-Dibromo-1-phenyl-3-p-tolylpropan-1-one 6e.** IR (KBr) cm^{-1} 2923, 1686, 1597, 1513, 1445, 1366, 1321, 1299, 1273, 1225, 1146, 980, 822, 744, 725, 687, 651, 580, 543, 511; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.12–8.09 (m, 2H), 7.66 (t, J = 7.3 Hz, 1 H), 7.58–7.53 (m, 2H), 7.42 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 5.83 (d, J = 11.3 Hz, 1H), 5.64 (d, J = 11.3 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 191.4, 139.5, 135.5, 134.8, 134.2, 129.7, 129.1, 129.0, 128.4, 50.2, 47.2, 21.4; HRMS calcd for $C_{16}H_{14}O^{79}Br_2$: m/z 379.9411, found m/z 379.9409.

***trans*-2,3-Dibromo-3-(3,4-dichlorophenyl)-1-(4-methoxyphenyl) propan-1-one 6f.** IR (KBr) cm^{-1} 3062, 2998, 1670, 1595, 1511, 1475, 1460, 1421, 1409, 1363, 1321, 1295, 1264, 1222, 1174, 1158, 1138, 1025, 983, 895, 841, 821, 783, 771, 694, 590, 467; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.07 (d, J = 8.9 Hz, 2H), 7.62 (d, J = 2.1 Hz, 1H), 7.50 (d, J = 8.3 Hz, 1H), 7.35 (dd, J = 8.3, 2.1 Hz, 1H), 7.02 (d, J = 8.9 Hz, 2H), 5.69 (d, J = 11.2 Hz, 1H), 5.56 (d, J = 11.2 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 189.2, 164.8, 138.9, 133.5, 133.2, 131.5, 130.9, 130.5, 127.9, 127.2, 114.5, 55.8, 48.1, 46.5; HRMS calcd for $C_{16}H_{12}O_2{}^{35}Cl_2{}^{79}Br_2$: m/z 463.8581, found m/z 463.8574.

***trans*-2,3-Dibromo-3-(4-nitrophenyl)-1-(pyridin-2-yl)propan-1-one 6g.** IR (KBr) cm^{-1} 2926, 1705, 1605, 1580, 1522, 1438, 1347, 1310, 1283, 1251, 1152, 1110, 994, 980, 858, 847, 821, 781, 747, 694, 616, 575; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.79 (d, J = 4.6 Hz, 1H), 8.30 (d, J = 8.7 Hz, 2H), 8.25 (d, J = 7.8 Hz, 1H), 7.95 (td, J = 7.8, 1.5 Hz, 1H), 7.75 (d, J = 8.7 Hz, 2H), 7.62–7.58 (m, 1H), 6.74 (d, J = 11.8 Hz, 1H), 5.70 (d, J = 11.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 191.3, 150.4, 149.3, 148.3, 145.5, 137.8, 129.6, 128.5, 124.2, 124.0, 47.1, 44.7; HRMS [M^+–HBr] calcd for $C_{14}H_9N_2O_3{}^{79}Br$: m/z 331.9797, found m/z 331.9802.

***trans*-2,3-Dibromo-3-(3-nitrophenyl)-1-(pyridin-2-yl)propan-1-one 6h.** IR (KBr) cm^{-1} 3012, 1702, 1580, 1528, 1436, 1350, 1309, 1278, 1250, 1220, 1156, 1090, 995, 980, 849, 820, 808, 743, 718, 690, 666, 617, 586; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.82 (d, J = 4.1 Hz, 1H), 8.46–8.45 (m, 1H), 8.28–8.24 (m, 2H), 7.98 (td, J = 7.7, 1.6 Hz, 1H), 7.92 (d, J = 7.7 Hz, 1H), 7.66–7.61 (m, 2H), 6.80 (d, J = 11.8 Hz, 1H), 5.72 (d, J = 11.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 191.4, 150.5, 149.4, 148.6, 140.9, 137.6, 134.6, 130.0, 128.4, 124.1, 123.9, 123.6, 47.4, 45.0; HRMS [M^+–Br] calcd for $C_{14}H_{10}N_2O_3{}^{79}Br$: m/z 332.9875, found m/z 332.9871.

***trans*-1,2-Dibromo-3-oxo-3-(pyridin-2-yl)propyl)benzonitrile 6i.** IR (KBr) cm^{-1} 3006, 2226, 1695, 1608, 1579, 1465, 1433, 1419, 1364, 1319, 1305, 1289, 1251, 1219, 1155, 1084, 994, 982, 841, 821, 748, 656, 616, 578; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.78 (d, J = 4.5 Hz, 1H), 8.24 (d, J = 7.8 Hz, 1H), 7.95 (td, J = 7.7, 1.6 Hz, 1H), 7.74 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 8.4 Hz, 2H), 7.62–7.58 (m, 1H), 6.71 (d, J = 11.8 Hz, 1H), 5.65 (d, J = 11.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 191.6, 150.6, 149.5, 143.7, 137.6, 132.8, 129.4, 128.4, 123.9, 118.3, 113.2, 47.7, 44.6; HRMS [M^+–Br] calcd for $C_{15}H_{10}N_2O^{79}Br$: m/z 312.9976, found m/z 312.9978.

***trans*-2,3-Dibromo-3-(4-chlorophenyl)-1-(pyridin-2-yl)propan-1-one 6j.** IR (KBr) cm^{-1} 3009, 1705, 1581, 1493, 1437, 1412, 1363, 1312, 1290, 1250, 1216, 1151, 1094, 1013, 994, 981, 821, 787, 749, 723, 701, 642, 617, 573; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.79 (dd, J = 4.7, 0.6 Hz, 1H), 8.24 (d, J = 7.7 Hz, 1H), 7.94 (td, J = 7.7 Hz, 1.6 Hz, 1H), 7.61–7.57 (m, 1H), 7.52 (d, J = 8.5 Hz, 2H), 7.40 (d, J = 8.5 Hz, 2H), 6.73 (d, J = 11.8 Hz, 1H), 5.63 (d, J = 11.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 191.9, 150.7, 149.4, 137.5, 137.2, 135.2, 129.9, 129.2, 128.3, 123.8, 48.6, 45.1; HRMS [M^+–HBr] calcd for $C_{14}H_9NO^{35}Cl^{79}Br$: m/z 320.9556, found m/z 320.9551.

***trans*-2,3-Dibromo-3-(3,4-dichlorophenyl)-1-(pyridin-2-yl) propan-1-one 6k.** IR (KBr) cm^{-1} 3014, 1704, 1581, 1474, 1437, 1409, 1356, 1308, 1288, 1247, 1218, 1152, 1133, 1033, 995, 984, 918, 819, 744, 681, 617, 593; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.78 (dd, J = 4.7, 0.6 Hz, 1H), 8.23 (d, J = 7.8 Hz, 1H), 7.94 (td, J = 7.7, 1.6 Hz, 1H), 7.67 (d, J = 2.1 Hz, 1H), 7.59 (ddd, J = 7.5, 4.7, 1.1 Hz, 1H), 7.51 (d, J = 8.3 Hz, 1H), 7.41 (dd, J = 8.3, 2.1 Hz, 1H), 6.67 (d, J = 11.8 Hz, 1H), 5.58 (d, J = 11.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 191.6, 150.6, 149.4, 138.9, 137.6, 133.5, 133.1, 131.0, 130.5, 128.3, 127.9, 123.8, 47.6, 45.0; HRMS [M^+–Br] calcd for $C_{14}H_9NO^{35}Cl_2{}^{79}Br$: m/z 355.9245, found m/z 355.9237.

***trans*-2,3-Dibromo-1-(pyridin-2-yl)-3-p-tolylpropan-1-one 6l.** IR (KBr) cm^{-1} 3017, 1706, 1612, 1581, 1513, 1435, 1362, 1319, 1301, 1250, 1219, 1146, 995, 981, 814, 753, 742, 722, 671, 617, 577; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.79 (dd, J = 4.7, 0.6 Hz, 1H), 8.24 (d, J = 7.8 Hz, 1H), 7.93 (td, J = 7.7, 1.7 Hz, 1H), 7.58 (ddd, J = 7.6, 4.7, 1.0 Hz, 1H), 7.47 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 6.79 (d, J = 11.9 Hz, 1H), 5.67 (d, J = 11.9 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 192.2, 150.9, 149.4, 139.4, 137.4, 135.6, 129.7, 128.4, 128.1, 123.7, 50.0, 45.5, 21.4; HRMS [M^+–Br] calcd for $C_{15}H_{13}NO^{79}Br$: m/z 302.0181, found m/z 302.0175.

***trans*-3,4-Dibromo-4-phenylbutan-2-one 6m.**[4h,6b,8] ^1H NMR ($CDCl_3$, 300 MHz) δ 7.43–7.36 (m, 5 H), 5.32 (d, J = 11.7 Hz, 1H), 4.93 (d, J = 11.7 Hz, 1H), 2.49 (s, 3H).

***trans*-Methyl 2,3-dibromo-3-phenylpropanoate 6n.**[5c,8] ^1H NMR ($CDCl_3$, 300 MHz) δ 7.41–7.37 (m, 5H), 5.34 (d, J = 11.7 Hz, 1H), 4.84 (d, J = 11.7 Hz, 1H), 3.90 (s, 3H).

1-(1,2-Dibromoethyl)benzene 9.[26] ^1H NMR ($CDCl_3$, 300 MHz) δ 7.41–7.32 (m, 5H), 5.15 (dd, J = 10.4, 5.7 Hz, 1H), 4.08 (dd, J = 10.4, 5.7 Hz, 1H), 4.02 (t, J = 10.4 Hz, 1H).

***trans*-3,6-Dibromocyclohexene 10.**[17b] ^1H NMR ($CDCl_3$, 300 MHz) δ 6.00 (bs, 2H), 4.90 (bs, 2H), 2.47 (d, J = 10.8 Hz, 2H), 2.17 (d, J = 10.8 Hz, 2H).

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Notes and references

1 (*a*) G. W. Gribble, *Chem. Soc. Rev.*, 1999, **28**, 335; (*b*) A. Butler and J. V. Walker, *Chem. Rev.*, 1993, **93**, 1937; (*c*) R. H. Seevers and R. E. Counsell, *Chem. Rev.*, 1982, **82**, 575.
2 (*a*) P. B. De la Mare, *Electrophilic Halogenation*, Cambridge University Press, Cambridge, UK, 1976, ch. 5; (*b*) R. Taylor, *Electrophilic Aromatic Substitution*, Wiley, Chichester, UK, 1990.
3 (*a*) M. Eissen and D. Lenoir, *Chem.–Eur. J.*, 2008, **14**, 9830; (*b*) M. Eissen, M. Strudthoff, S. Backhaus, C. Eismann, G. Oetken, S. Kaling and D. Lenoir, *J. Chem. Educ.*, 2011, **88**, 284; (*c*) V. V. K. M. Kandepi and N. Narender, *Synthesis*, 2012, 15.
4 (*a*) M. Avramoff, J. Weiss and O. Schächter, *J. Org. Chem.*, 1963, **28**, 3256; (*b*) L. Forlani, *Synthesis*, 1980, 487; (*c*) H. A. Muathen, *J. Org. Chem.*, 1992, **57**, 2740; (*d*) M. K. Chaudhuri, A. T. Khan, B. K. Patel, D. Dey, W. Kharmawophlang, T. R. Lakshmiprabha and G. C. Mandal, *Tetrahedron Lett.*, 1998, **39**, 8163; (*e*) K. Tanaka, R. Shiraishi and F. Toda, *J. Chem. Soc., Perkin Trans. 1*, 1999, 3069; (*f*) F. Toda and J. Schmeyers, *Green Chem.*, 2003, **5**, 701; (*g*) S. Nakamatsu, S. Toyota, W. Jones and F. Toda, *Chem. Commun.*, 2005, 3808; (*h*) V. Kavala, S. Naik and B. K. Patel, *J. Org. Chem.*, 2005, **70**, 4267.
5 (*a*) T. L. Ho, B. Gupta and G. A. Olah, *Synthesis*, 1977, 676; (*b*) N. B. Barhate, A. S. Gajare, R. D. Wakharkar and A. V. Bedekar, *Tetrahedron Lett.*, 1998, **39**, 6349; (*c*) N. B. Barhate, A. S. Gajare, R. D. Wakharkar and A. V. Bedekar, *Tetrahedron*, 1999, **55**, 11127; (*d*) U. Bora, G. Bose, M. K. Chaudhuri, S. S. Dhar, R. Gopinath, A. T. Khan and B. K. Patel, *Org. Lett.*, 2000, **2**, 247.
6 (*a*) R. K. Dieter, L. E. Nice and S. E. Velu, *Tetrahedron Lett.*, 1996, **37**, 2377; (*b*) K.-M. Kim and I.-H. Park, *Synthesis*, 2004, 2641.
7 (*a*) V. Nair, S. B. Panicker, A. Augustine, T. G. George, S. Thomas and M. Vairamani, *Tetrahedron*, 2001, **57**, 7417; (*b*) S. C. Roy, C. Guin, K. K. Rana and G. Maiti, *Tetrahedron Lett.*, 2001, **42**, 6941.
8 C. Ye and J. M. Shreeve, *J. Org. Chem.*, 2004, **69**, 8561.
9 A. Subbarayappa, S. Ghosh, P. U. Patoliya, G. Ramachandraiah, M. Agrawal, M. R. Gandhi, S. C. Upadhyay, P. K. Ghosh and B. C. Ranu, *Green Chem.*, 2008, **10**, 232.
10 For reviews, see: (*a*) G.-W. Wang, Fullerene mechanochemistry. in *Encyclopedia of Nanoscience and Nanotechnology*, ed. H. S. Nalwa, American Scientific Publishers, Stevenson Ranch, 2004, vol. 3, p. 557; (*b*) K. Komatsu, *Top. Curr. Chem.*, 2005, **254**, 185; (*c*) B. Rodríguez, A. Bruckmann, T. Rantanen and C. Bolm, *Adv. Synth. Catal.*, 2007, **349**, 2213; (*d*) A. L. Garay, A. Pichon and S. L. James, *Chem. Soc. Rev.*, 2007, **36**, 846; (*e*) A. Bruckmann, A. Krebs and C. Bolm, *Green Chem.*, 2008, **10**, 1131; (*f*) G. Kaupp, *CrystEngComm*, 2009, **11**, 388; (*g*) A. Stolle, T. Szuppa, S. E. S. Leonhardt and B. Ondruschka, *Chem. Soc. Rev.*, 2011, **40**, 2317.
11 For reactions of fullerenes under ball-milling conditions, see: (*a*) G.-W. Wang, Y. Murata, K. Komatsu and T. S. M. Wan, *Chem. Commun.*, 1996, 2059; (*b*) G.-W. Wang, K. Komatsu, Y. Murata and M. Shiro, *Nature*, 1997, **387**, 583; (*c*) K. Komatsu, G.-W. Wang, Y. Murata, T. Tanaka, K. Fujiwara, K. Yamamoto and M. Saunders, *J. Org. Chem.*, 1998, **63**, 9358; (*d*) G.-W. Wang, T.-H. Zhang, E.-H. Hao, L.-J. Jiao, Y. Murata and K. Komatsu, *Tetrahedron*, 2003, **59**, 55; (*e*) G.-W. Wang, T.-H. Zhang, Y.-J. Li, P. Lu, H. Zhan, Y.-C. Liu, Y. Murata and K. Komatsu, *Tetrahedron Lett.*, 2003, **44**, 4407; (*f*) G.-W. Wang, Y.-J. Li, R.-F. Peng, Z.-H. Liang and Y.-C. Liu, *Tetrahedron*, 2004, **60**, 3921; (*g*) R.-F. Peng, G.-W. Wang, Y.-B. Shen, Y.-J. Li, T.-H. Zhang, Y.-C. Liu, Y. Murata and K. Komatsu, *Synth. Commun.*, 2004, **34**, 2117; (*h*) T.-H. Zhang, G.-W. Wang, P. Lu, Y.-J. Li, R.-F. Peng, Y.-C. Liu, Y. Murata and K. Komatsu, *Org. Biomol. Chem.*, 2004, **2**, 1698; (*i*) Y.-J. Li, R.-F. Peng, Y.-C. Liu and G.-W. Wang, *Chin. Chem. Lett.*, 2004, **15**, 1265; (*j*) X. Cheng, G.-W. Wang, Y. Murata and K. Komatsu, *Chin. Chem. Lett.*, 2005, **16**, 1327; (*k*) G.-W. Wang, Z.-X. Chen, Y. Murata and K. Komatsu, *Tetrahedron*, 2005, **61**, 4851.
12 For reactions of non-fullerene molecules under ball-milling conditions, see: (*a*) Z. Zhang, Y.-W. Dong, G.-W. Wang and K. Komatsu, *Synlett*, 2004, 61; (*b*) Z. Zhang, G.-W. Wang, C.-B. Miao, Y.-W. Dong and Y.-B. Shen, *Chem. Commun.*, 2004, 1832; (*c*) Z. Zhang, J. Gao, J.-J. Xia and G.-W. Wang, *Org. Biomol. Chem.*, 2005, **3**, 1617; (*d*) G.-W. Wang and X.-L. Wu, *Adv. Synth. Catal.*, 2007, **349**, 1977; (*e*) X.-L. Wu, J.-J. Xia and G.-W. Wang, *Org. Biomol. Chem.*, 2008, **6**, 548; (*f*) J. Gao and G.-W. Wang, *J. Org. Chem.*, 2008, **73**, 2955; (*g*) G.-W. Wang, Y.-W. Dong, P. Wu, T.-T. Yuan and Y.-B. Shen, *J. Org. Chem.*, 2008, **73**, 7088; (*h*) G.-W. Wang and J. Gao, *Org. Lett.*, 2009, **11**, 2385.
13 For selected examples in other groups, see: (*a*) V. P. Balema, J. W. Wiench, M. Pruski and V. K. Pecharsky, *J. Am. Chem. Soc.*, 2002, **124**, 6244; (*b*) B. Rodríguez, T. Tantanen and C. Bolm, *Angew. Chem., Int. Ed.*, 2006, **45**, 6924; (*c*) F. Schneider and B. Ondruschka, *ChemSusChem*, 2008, **1**, 622; (*d*) R. Thorwirth, A. Stolle and B. Ondruschka, *Green Chem.*, 2010, **12**, 985; (*e*) W. C. Shearouse, C. M. Korte and J. Mack, *Green Chem.*, 2011, **13**, 598; (*f*) F. Ravalico, S. L. James and J. S. Vyle, *Green Chem.*, 2011, **13**, 1778.
14 (*a*) C. Bolm, A. S. Magnus and J. P. Hildebrand, *Org. Lett.*, 2000, **2**, 1173; (*b*) D. Yang and C. Zhang, *J. Org. Chem.*, 2001, **66**, 4814; (*c*) B. R. Travis, M. Sivakumar, G. O. Hollist and B. Borhan, *Org. Lett.*, 2003, **5**, 1031; (*d*) B. Plietker, *Org. Lett.*, 2004, **6**, 289; (*e*) R. Singh, R. M. Kissling, M.-A. Letellier and S. P. Nolan, *J. Org. Chem.*, 2004, **69**, 209.

15 For other application of oxone in ball-milled reactions, see: (*a*) R. Thorwirth, F. Bernhardt, A. Stolle, B. Ondruschka and J. Asghari, *Chem.–Eur. J.*, 2010, **16**, 13236; (*b*) T. Szuppa, A. Stolle, B. Ondruschka and W. Hopfe, *Green Chem.*, 2010, **12**, 1288; (*c*) T. Szuppa, A. Stolle, B. Ondruschka and W. Hopfe, *ChemSusChem*, 2010, **3**, 1181.
16 A. N. M. M. Rahman, R. Bishop, R. Tan and N. Shan, *Green Chem.*, 2005, **7**, 207.
17 (*a*) G. E. Heasley, V. L. Heasley, S. L. Manatt, H. A. Day, R. V. Hodges, P. A. Kroon, D. A. Redfield, T. L. Rold and D. E. Williamson, *J. Org. Chem.*, 1973, **38**, 4109; (*b*) X. Han, R. N. Khedekar, J. Masnovi and R. J. Baker, *J. Org. Chem.*, 1999, **64**, 5245.
18 R. Horcajada, B. Batanero, F. Barba and A. Martín, *Tetrahedron Lett.*, 2007, **48**, 6437.
19 V. N. Ingle, P. K. Gaidhane, S. S. Dutta, P. P. Naha and M. S. Sengupta, *J. Carbohydr. Chem.*, 2006, **25**, 661.
20 A. T. Khan, M. A. Ali, P. Goswami and L. H. Choudhury, *J. Org. Chem.*, 2006, **71**, 8961.
21 H. Zhang, M. K. Tse and K. S. Chan, *Synth. Commun.*, 2001, **31**, 1129.
22 W.-P. Yin and M. Shi, *Tetrahedron*, 2005, **61**, 10861.
23 P. Suresh, S. Annalakshmi and K. Pitchumani, *Tetrahedron*, 2007, **63**, 4959.
24 E. Kiehlmann and R. W. Lauener, *Can. J. Chem.*, 1989, **67**, 335.
25 N. O. Mahmoodi, M. R. Yazdanbakhsh, H. Kiyani and B. Sharifzadeh, *J. Chin. Chem. Soc. (Taipei)*, 2007, **54**, 635.
26 A. Podgoršek, M. Eissen, J. Fleckenstein, S. Stavber, M. Zupan and J. Iskra, *Green Chem.*, 2009, **11**, 120.