***NOTE:***

# Sonochemical and Mechanochemical Synthesis of Alcohols from Aldehydes and Ketones

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***Abstract:*** *A green, convenient, and scalable synthesis of alcohols through the reduction of aldehydes and ketones has been developed. The green reduction was conducted using two different methods, namely sonochemistry and mechanochemistry. In the former method, the solution of aldehydes or ketones and sodium borohydride was irradiated under ultrasound irradiation. In the latter technique, the reaction mixture was ground under solvent-free conditions. The reduction reaction was performed at room temperature and completed in only 10 min using both protocols. The results showed that aldehydes and ketones with aromatic, heteroaromatic, and aliphatic motifs were tolerated under the reaction conditions, allowing the formation of the corresponding alcohols with the synthetic yields of 75–98% and 77–95% for grinding and sonication methods, respectively. In addition, the reaction can be carried out on a multigram scale.*

***Keywords:*** *alcohols; aldehydes; ketones; mechanochemistry; sonochemistry*

## ■ INTRODUCTION

Alcohols are versatile chemicals that play significant roles in our daily lives. These compounds have been widely applied in various industries such as pharmaceutical, cosmetic, energy, textile, food as well as fine chemical industries. Owing to their properties and reactivities, alcohols are important chemical intermediates in the synthesis of natural products, agrochemical products, drugs, and other functional materials [1].

The extensive applications of alcohols lead synthetic chemists to develop convenient and sustainable synthetic strategies to access diversely functionalized alcohols. To illustrate, benzyl halides were converted into benzyl alcohols under visible light in the presence of photocatalysts [2-3]. Visible light-induced-oxidative hydroxylation of boronic acids has also been employed for the synthesis of alcohols [4-5]. A previous study reported the application of iron(IV)oxo complex in the oxidation of toluene derivatives into their corresponding benzyl alcohols [6]. Vinyl ethers have been transformed into alcohols in acidic conditions [7]. Alcohols have been prepared through typical transition metal-catalyzed-hydrogenation of reducible functional groups such as esters [8-10], amides [11-12], and nitriles [13].

The previously mentioned protocols, unfortunately, suffered from limitations. For instance, the hydrogenation reaction required specific equipment, harsh conditions (high temperature and pressure), as well as expensive and fancy catalysts. Other methods were carried out using toxic solvents, long reaction times, and small scales. Therefore, developing synthetic methods of alcohols that can be efficiently carried out under milder conditions and are more sustainable is still highly desirable.

Reduction of aldehydes or ketones is considered a simple and straightforward method to synthesize

alcohols. Various reductants have been utilized in this reaction, for example, $ZrOCl_2$ [14], $Na_2S_2O_4$ [15], $Zn/NH_4Cl$ [16], ammonia borane [17], $LiAlH_4$ [18], $Zn(BH_4)_2$ [19], and $NaBH_4$ [20-21]. The reduction using $NaBH_4$ is considered convenient and simple since it can be carried out under milder conditions and does not require specific equipment. In addition, $NaBH_4$ is cheap and readily available [22].

Organic synthesis has been directed to sustainable synthesis, which involves clean, efficient, and environmentally friendly processes. The elimination of toxic chemicals and the application of sustainable methods are significant for academic and industrial applications. In this context, considerable attention has been dedicated to sonochemistry and mechanochemistry as green and powerful techniques for the synthesis of organic building blocks [23-25]. Both sonochemical and mechanochemical activations may improve reaction rates and yields which are relevant to green chemistry principles [26-28].

In this study, we report the application of sonochemistry and mechanochemistry in the synthesis of various alcohols from their corresponding aldehydes and ketones via reduction reaction.

## ■ EXPERIMENTAL SECTION

### Materials

Materials utilized in this study were purchased from Merck, including benzaldehyde, *p*-tolualdehyde, *m*-tolualdehyde, *o*-tolualdehyde, 4-methoxybenzaldehyde, 4-chlorobenzaldehyde, 4-bromobenzadehyde, 3-nitrobenzaldehyde, furfural, thiophene-2-carboxaldehyde, indole-3-carboxaldehyde, pyridine-2-carboxaldehyde, isovaleraldehyde, acetophenone, cyclohexanone, sodium borohydride, sodium hydrogen carbonate, sodium sulfate, ethanol, and dichloromethane. 2-Methoxybenzaldehyde was prepared from 2-hydroxybenzaldehyde, while 3,4-dimethoxybenzaldehyde and 4-ethyl-3-methylbenzaldehyde were synthesized from vanillin using our previously reported method [29]. The chemicals were P.A. grade and directly used without any further purification.

### Instrumentation

Instrumentations employed in this research were laboratory glassware, mortar, pestle, ultrasonic bath (Powersonic 505, 40 KHz, 300 W), melting point analyzer (Electrothermal 9100), Fourier transform infra-red spectrophotometer (FTIR, Shimadzu Prestige-21), gas chromatography-mass spectrometer (GC-MS, Shimadzu QP-2010S), $^1$H-nuclear magnetic resonance spectrometer ($^1$H-NMR, JEOL 500 MHz) and $^{13}$C-nuclear magnetic resonance spectrometer ($^{13}$C-NMR, JEOL 125 MHz).

### Procedure

#### *General procedure for the synthesis of alcohols using grinding technique*

Aldehydes or ketones (5 mmol, 1 equiv.) and sodium borohydride (189 mg, 5 mmol, 1 equiv.) were placed in a mortar. After 10 min of grinding (based on TLC), the saturated aqueous solution of sodium hydrogen carbonate was added to quench the reaction. Extraction of the reaction mixture was carried out using dichloromethane (3 × 10 mL). Sodium sulfate was then added to the combined organic layer. The solvent was removed under reduced pressure. The products were characterized using $^1$H-NMR, $^{13}$C-NMR, FTIR, and GCMS spectrometers.

#### *General procedure for synthesis of alcohols under ultrasound irradiation*

Into solution of aldehydes or ketones (5 mmol, 1 equiv.) in ethanol (2.5 mL) was slowly added sodium borohydride (189 mg, 5 mmol, 1 equiv.). The mixture was sonicated in an ultrasonic bath for 10 min (based on TLC). The reaction was terminated using a saturated aqueous solution of sodium hydrogen carbonate. The mixture was extracted using dichloromethane (3 × 10 mL). The combined organic phase was dried using sodium sulfate and evaporated. The structure elucidation of the products was carried out by means of $^1$H-NMR, $^{13}$C-NMR, FTIR, and GCMS spectrometers.

*Phenylmethanol* (**2a**) was prepared from benzaldehyde **1a** (5 mmol, 530 mg, 0.53 mL, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.),

colorless liquid; yield: 90% (mechanochemistry) and 92% (sonochemistry); $^1$H-NMR (500 MHz, $CDCl_3$, ppm) δ: 7.40–7.34 ($H_{Ar}$, m, 5H), 4.58 ($CH_2$, s, 2H), 3.73 (OH, br s, 1H); $^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ: 140.9 ($C_{Ar}$), 128.5 ($2CH_{Ar}$), 127.5 ($CH_{Ar}$), 127.0 ($2CH_{Ar}$), 64.9 ($CH_2$); FTIR (neat, $cm^{-1}$): 3350, 3016, 2978, 1512; GC-MS (EI): *m/z* (%): 108 [$M^+$], 107, 91, 79 [base peak], 77, 51.

p-*Tolylmethanol* (**2b**) was prepared from *p*-tolualdehyde **1b** (5 mmol, 600 mg, 0.59 mL, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.), white solid, yield: 95% (mechanochemistry) and 93% (sonochemistry); m.p.: 57–62 °C; $^1$H-NMR (500 MHz, $CDCl_3$, ppm) δ: 7.25 ($H_{Ar}$, d, *J* = 10.0 Hz, 2H), 7.17 ($H_{Ar}$, d, *J* = 10.0 Hz, 2H), 4.65 ($CH_2$, d, *J* = 5.0 Hz, 2H), 2.36 ($CH_3$, s, 3H); $^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ: 138.0 ($C_{Ar}$), 137.5 ($C_{Ar}$), 129.4 ($2CH_{Ar}$), 127.2 ($2CH_{Ar}$), 65.4 ($CH_2$), 21.3 ($CH_3$); FTIR (KBr, $cm^{-1}$): 3364, 2916, 1512, 1443, 1019; GC-MS (EI): *m/z* (%): 122 [$M^+$], 107, 91, 79 [base peak], 39.

*(4-Methoxyphenyl)methanol* (**2c**) was prepared from 4-methoxybenzaldehyde **1c** (5 mmol, 680 mg, 0.61 mL, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.), yellowish liquid; yield: 91% (mechanochemistry) and 93% (sonochemistry); $^1$H-NMR (500 MHz, $CDCl_3$, ppm) δ: 7.23 ($H_{Ar}$, d, *J* = 9.0 Hz, 2H), 6.85 ($H_{Ar}$, d, *J* = 9.0 Hz, 2H), 4.53 ($CH_2$, s, 2H), 3.77 ($CH_3$, s, 3H); $^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ: 159.1 ($C_{Ar}$), 133.2 ($C_{Ar}$), 128.7 ($2CH_{Ar}$), 113.9 ($2CH_{Ar}$), 64.7 ($CH_2$), 55.2 ($CH_3$); FTIR (neat, $cm^{-1}$): 3356, 2939, 1589, 1512, 1249; GC-MS (EI): *m/z* (%): 138 [$M^+$], 121, 109, 77 [base peak], 39.

*(4-Bromophenyl)methanol* (**2d**) was prepared from 4-bromobenzaldehyde **1d** (5 mmol, 925 mg, 0.50 mL, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.), white solid; yield: 82% (mechanochemistry) and 85% (sonochemistry); m.p: 75–77 °C $^1$H-NMR (500 MHz, $CDCl_3$, ppm) δ: 7.47 ($H_{Ar}$, d, *J* = 9.0 Hz, 2H), 7.22 ($H_{Ar}$, d, *J* = 9.0 Hz, 2H), 4.63 ($CH_2$, d, *J* = 4.0 Hz, 2H); $^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ: 139.9 ($C_{Ar}$), 131.7 ($2CH_{Ar}$), 128.7 ($2CH_{Ar}$), 121.5 ($C_{Ar}$), 64.6 ($CH_2$); FTIR (KBr, $cm^{-1}$): 3363, 2916, 1597, 1512, 1450, 833; GC-MS (EI): *m/z* (%): 188 [$M^+$], 186, 107 [base peak], 79, 77.

*(4-Chlorophenyl)methanol* (**2e**) was prepared from 4-chlorobenzaldehyde **1e** (5 mmol, 700 mg, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.), white solid; yield: 90% (mechanochemistry) and 94% (sonochemistry); m.p: 69–73 °C; $^1$H-NMR (500 MHz, $CDCl_3$, ppm) δ: 7.32 ($H_{Ar}$, d, *J* = 9.0 Hz, 2H), 7.29 ($H_{Ar}$, d, *J* = 9.0 Hz, 2H), 4.65 ($CH_2$, d, *J* = 5.0 Hz, 2H); $^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ: 139.4 ($C_{Ar}$), 133.5 ($C_{Ar}$), 128.8 ($2CH_{Ar}$), 128.4 ($2CH_{Ar}$), 64.6 ($CH_2$); FTIR (KBr, $cm^{-1}$): 3348, 2916, 1597, 1512, 1489, 802; GC-MS (EI): *m/z* (%): 142 [$M^+$], 107, 77 [base peak], 51.

*(3-Nitrophenyl)methanol* (**2f**) was prepared from 3-nitrobenzaldehyde **1f** (5 mmol, 755 mg, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.), brown liquid; yield: 97% (mechanochemistry) and 95% (sonochemistry); $^1$H-NMR (500 MHz, $CDCl_3$, ppm) δ: 8.14 ($H_{Ar}$, d, *J* = 10.0 Hz, 1H), 7.70 ($H_{Ar}$, d, *J* = 10.0 Hz, 1H), 7.53 ($H_{Ar}$, t, *J* = 10.0 Hz, 1H), 7.26 ($H_{Ar}$, s, 1H), 4.82 ($CH_2$, d, *J* = 5.0 Hz, 2H); $^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ: 148.5 ($C_{Ar}$), 143.0 ($C_{Ar}$), 132.8 ($CH_{Ar}$), 129.6 ($CH_{Ar}$), 122.7 ($CH_{Ar}$), 121.7 ($CH_{Ar}$), 64.1 ($CH_2$); FTIR (neat, $cm^{-1}$): 3356, 2870, 1528, 1350, 1042, 733; GC-MS (EI): *m/z* (%): 153 [$M^+$], 107, 89, 77 [base peak], 51.

m-*Tolylmethanol* (**2g**) was prepared from *m*-tolualdehyde **1g** (5 mmol, 600 mg, 0.55 mL, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.), colorless liquid, yield: 92% (mechanochemistry) and 92% (sonochemistry); $^1$H-NMR (500 MHz, $CDCl_3$, ppm) δ: 7.25 ($H_{Ar}$, t, *J* = 10.0 Hz, 1H), 7.17 ($H_{Ar}$, s, 1H), 7.14 ($H_{Ar}$, d, *J* = 10.0 Hz, 1H), 7.10 ($H_{Ar}$, d, *J* = 10.0 Hz, 1H), 4.61 ($CH_2$, d, *J* = 5.0 Hz, 2H), 2.36 ($CH_3$, s, 3H); $^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ: 140.9 ($C_{Ar}$), 139.3 ($C_{Ar}$), 128.6 ($CH_{Ar}$), 128.4 ($CH_{Ar}$), 127.9 ($CH_{Ar}$), 124.1 ($CH_{Ar}$), 65.3 ($CH_2$), 21.5 ($CH_3$); FTIR (neat, $cm^{-1}$): 3348, 3024, 2924, 1613, 1458, 1003; GC-MS (EI): *m/z* (%): 122 [$M^+$], 107, 91, 79 [base peak], 39.

o-*Tolylmethanol* (**2h**) was prepared from *o*-tolualdehyde **1h** (5 mmol, 600 mg, 0.58 mL, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.), yellow liquid, yield: 90% (mechanochemistry) and 88% (sonochemistry); $^1$H-NMR (500 MHz, $CDCl_3$, ppm) δ: 7.34–7.36 ($H_{Ar}$, m, 1H), 7.21–7.23 ($H_{Ar}$, m, 2H), 7.17–7.19 ($H_{Ar}$,m, 1H), 4.67 ($CH_2$, s, 2H), 2.36 ($CH_3$, s, 3H); $^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ: 138.8 ($C_{Ar}$), 136.2 ($C_{Ar}$), 130.4 ($CH_{Ar}$), 127.9 ($CH_{Ar}$), 127.6 ($CH_{Ar}$), 126.1

($CH_{Ar}$), 63.5 ($CH_2$), 18.7 ($CH_3$); FTIR (neat, $cm^{-1}$): 3333, 3024, 2924, 1604, 1458, 1003, 741; GC-MS (EI): *m/z* (%): 122 [$M^+$], 104 [base peak], 91, 79, 39.

*(2-Methoxyphenyl)methanol* (**2i**) was prepared from 2-methoxybenzaldehyde **1i** (5 mmol, 680 mg, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.), brownish liquid; yield: 87% (mechanochemistry) and 89% (sonochemistry); $^1$H-NMR (500 MHz, $CDCl_3$, ppm) δ: 7.27–7.30 ($H_{Ar}$, m, 2H), 6.90–7.03 ($H_{Ar}$, m, 2H), 4.70 ($CH_2$, d, $J$ = 6.0 Hz, 2H), 3.88 ($CH_3$, s, 3H); $^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ: 159.5 ($C_{Ar}$), 132.9 ($C_{Ar}$), 129.7 ($CH_{Ar}$), 129.1 ($CH_{Ar}$), 128.6 ($CH_{Ar}$), 124.0 ($CH_{Ar}$), 64.8 ($CH_2$), 55.3 ($CH_3$); FTIR (neat, $cm^{-1}$): 3332, 2978, 1597, 1519, 1234; GC-MS (EI): m/z (%): 138 [$M^+$, base peak], 121, 105, 91, 77, 65.

*(3,4-Dimethoxyphenyl)methanol* (**2j**) was prepared from 3,4-dimethoxybenzaldehyde **1j** (5 mmol, 830 mg, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.), yellow liquid; yield: 98% (mechanochemistry) and 95% (sonochemistry); $^1$H-NMR (500 MHz, $CDCl_3$, ppm) δ: 6.51–6.83 ($H_{Ar}$, m, 3H), 4.51 ($CH_2$, s, 2H), 3.91 ($CH_3$, s, 6H), 3.22 (OH, br s, 1H); $^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ: 149.3 ($C_{Ar}$), 148.5 ($C_{Ar}$), 134.3 ($C_{Ar}$), 119.1 ($CH_{Ar}$), 111.6 ($CH_{Ar}$), 111.1 ($CH_{Ar}$), 64.9 ($CH_2$), 56.1 ($CH_3$), 56.0 ($CH_3$); FTIR (neat, $cm^{-1}$): 3402, 2931, 1597, 1512, 1234; GC-MS (EI): *m/z* (%): 168 [$M^+$, base peak], 151, 137, 121.

*(4-Ethoxy-3-methoxyphenyl)methanol* (**2k**) was prepared from 4-ethoxy-3-methoxybenzaldehyde **1k** (5 mmol, 900 mg, 0.53 mL, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.), yellowish solid; yield: 94% (mechanochemistry) and 94% (sonochemistry); m.p.: 54–56 °C; $^1$H-NMR (500 MHz, $CDCl_3$, ppm): δ 6.86–6.99 ($H_{Ar}$, m, 3H), 4.58 ($CH_2$, d, 2H, $J$ = 5.9 Hz), 4.10 ($CH_2$, q, $J$ = 7.3 Hz, 2H), 3.85 ($CH_3$, s, 3H), 1.46 ($CH_3$, t, $J$ = 7.3 Hz 3H); $^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ:149.5 ($C_{Ar}$), 147.8 ($C_{Ar}$), 133.9 ($C_{Ar}$), 119.4 ($CH_{Ar}$), 112.7 ($CH_{Ar}$), 110.9 ($CH_{Ar}$), 65.2 ($CH_2$), 64.5 ($CH_2$), 55.8 ($CH_2$), 14.7 ($CH_3$); FTIR (KBr, $cm^{-1}$): 3403, 3078, 2978, 1597, 1519, 1465, 1234; GC-MS (EI): *m/z* (%): 182 [$M^+$, base peak], 153, 137, 121, 93.

*Furan-2-ylmethanol* (**2l**) was prepared from furfural **1l** (5 mmol, 480 mg, 0.42 mL, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.), yellowish liquid, yield: 90% (mechanochemistry) and 91% (sonochemistry); $^1$H-NMR (500 MHz, $CDCl_3$, ppm) δ: 7.37–7.40 ($H_{Ar}$, m, 1H), 6.25–6.33 ($H_{Ar}$, m, 2H), 4.54 ($CH_2$, s, 2H), 2.95 (OH, br s, 1H); $^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ: 154.1 ($C_{Ar}$), 142.6 ($CH_{Ar}$), 110.6 ($CH_{Ar}$), 107.9 ($CH_{Ar}$), 57.3 ($CH_2$); FTIR (neat, $cm^{-1}$): 3332, 2931, 1435, 1010, 702; GC-MS (EI): *m/z* (%): 98 [$M^+$], 81, 42, 39 [base peak].

*Thiophen-2-ylmethanol* (**2m**) was prepared from 2-thiophenecarboxaldehyde **1m** (5 mmol, 560 mg, 0.7 mL, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.), brownish liquid, yield: 91% (mechanochemistry) and 92% (sonochemistry); $^1$H-NMR (500 MHz, $CDCl_3$, ppm) δ: 7.24 ($H_{Ar}$, dd, $J$ = 5 and 1.5 Hz, 1H), 6.94-6.97 ($H_{Ar}$, m, 2H), 4.73 ($CH_2$, s, 2H), 2.89 (OH, br s, 1H); $^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ: 144.1 ($C_{Ar}$), 126.9 ($CH_{Ar}$), 125.6 ($CH_{Ar}$), 125.5 ($CH_{Ar}$), 59.8 ($CH_2$); FTIR (neat, $cm^{-1}$): 3332, 2931, 1435, 1010, 702; GC-MS (EI): *m/z* (%): 114 [$M^+$], 85 [base peak], 45, 39.

*Pyridin-2-ylmethanol* (**2n**) was prepared from 2-pyridinecarboxaldehyde **1n** (5 mmol, 535 mg, 0.48 mL, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.), yellowish solid, yield: 85% (mechanochemistry) and 82% (sonochemistry); m.p.: 70–73 °C; $^1$H-NMR (500 MHz, $CDCl_3$, ppm) δ: 8.50–8.52 ($H_{Ar}$, m, 1H), 7.66–7.71 ($H_{Ar}$, m, 1H), 7.30–7.34 ($H_{Ar}$, m, 1H),7.19–7.21 ($H_{Ar}$, m, 1H), 4.77 ($CH_2$, s, 2H), 4.23 (OH, br s, 1H); $^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ: 159.7 ($C_{Ar}$), 148.5 ($CH_{Ar}$), 136.9 ($CH_{Ar}$), 122.4 ($CH_{Ar}$), 120.7 ($CH_{Ar}$), 64.4 ($CH_2$); FTIR (KBr, $cm^{-1}$): 3244, 2924, 1467, 1012, 821; GC-MS (EI): *m/z* (%): 109 [$M^+$], 80 [base peak], 53, 39.

*3-Methylbutan-1-ol (**2o**)* was prepared from isovaleraldehyde **1o** (5 mmol, 430 mg, 0.55 mL, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.), colorless liquid, yield: 75% (mechanochemistry) and 77% (sonochemistry); $^1$H-NMR (500 MHz, $CDCl_3$, ppm) δ: 3.55–3.59 ($CH_2$, m, 2H), 2.84 (OH, br s, 1H), 1.64 (CH, sept, $J$ = 7 Hz, 1H), 1.40 ($CH_2$, q, $J$ = 7 Hz, 2H), 0.85 ($CH_3$, d, $J$ = 7 Hz, 6H); $^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ: 61.0 ($CH_2$), 41.6 ($CH_2$), 24.7 (CH), 22.6 ($2CH_3$); FTIR

(KBr, $cm^{-1}$): 3370, 2960, 1467, 1366, 1058; GC-MS (EI): *m/z* (%): 70 [$M^+$-17], 55, 41 [base peak], 31.

*1-Phenylethanol* (**2p**) was prepared from acetophenone **1p** (5 mmol, 600 mg, 0.58 mL, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.), colorless liquid; yield: 91% (mechanochemistry) and 90% (sonochemistry); $^1$H-NMR (500 MHz, $CDCl_3$, ppm) δ: 7.31–7.35 ($H_{Ar}$, m, 4H), 7.24–7.28 ($H_{Ar}$, m, 1H), 4.82 (CH, q, *J* = 6.5 Hz, 1H), 2.67 (OH, br s, 1H) 1.46 ($CH_3$, d, *J* = 6.5 Hz, 3H); $^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ: 145.9 ($C_{Ar}$), 128.4 ($2CH_{Ar}$), 127.4 ($CH_{Ar}$), 125.5 ($2CH_{Ar}$), 70.2 ($CH_2$), 25.1 ($CH_3$); FTIR (neat, $cm^{-1}$): 3363, 3050, 2978, 1451, 1078, 700; GC-MS (EI): *m/z* (%): 122 [$M^+$], 107 [base peak], 77, 43.

*Cyclohexanol* (**2q**) was prepared from cyclohexanone **1q** (5 mmol, 490 mg, 0.52 mL, 1 equiv.) and sodium borohydride (5 mmol, 189 mg, 1 equiv.), colorless liquid, yield: 85% (mechanochemistry) and 89% (sonochemistry); $^1$H-NMR (500 MHz, $CDCl_3$, ppm) δ: 3.48–3.53 (CH, m, 1H), 2.83 (OH, br s, 1H), 1.79–1.83 ($CH_2$, m, 2H), 1.63–1.67 ($CH_2$, m, 2H), 1.06–1.48 ($CH_2$, m, 6H);$^{13}$C-NMR (125 MHz, $CDCl_3$, ppm) δ: 70.1 (CH), 35.4 ($2CH_2$), 25.5 ($CH_2$), 24.2 ($2CH_2$); FTIR (KBr, $cm^{-1}$): 3330, 2930, 1452, 1088; GC-MS (EI): *m/z* (%): 100 [$M^+$], 82, 67, 57 [base peak], 44.

## ■ RESULTS AND DISCUSSION

Our study was started by performing the reduction of benzaldehyde **1a** using equimolar of sodium borohydride under ultrasound irradiation at room temperature (Fig. 1, Method A). The reaction was carried out under mild conditions in a bio-based solvent of ethanol. To our delight, the reaction was complete in only 10 min, and the desired benzyl alcohol **2a** was obtained in very good yields. In previous reports [20-21], the reduction of benzaldehyde was carried out using conventional stirring using a higher molar equivalent of sodium borohydride in a more toxic solvent of methanol for 1 h, demonstrating that our methodology was more efficient and greener. As an environmentally benign method, the sonochemical process using ultrasound irradiation may lead to acoustic cavitation involving the formation, growth, and collapse of bubbles in a liquid medium. As a consequence, the cavity collapse may generate extremely high temperatures and pressure in the system, which may increase the reaction rate [30-31].

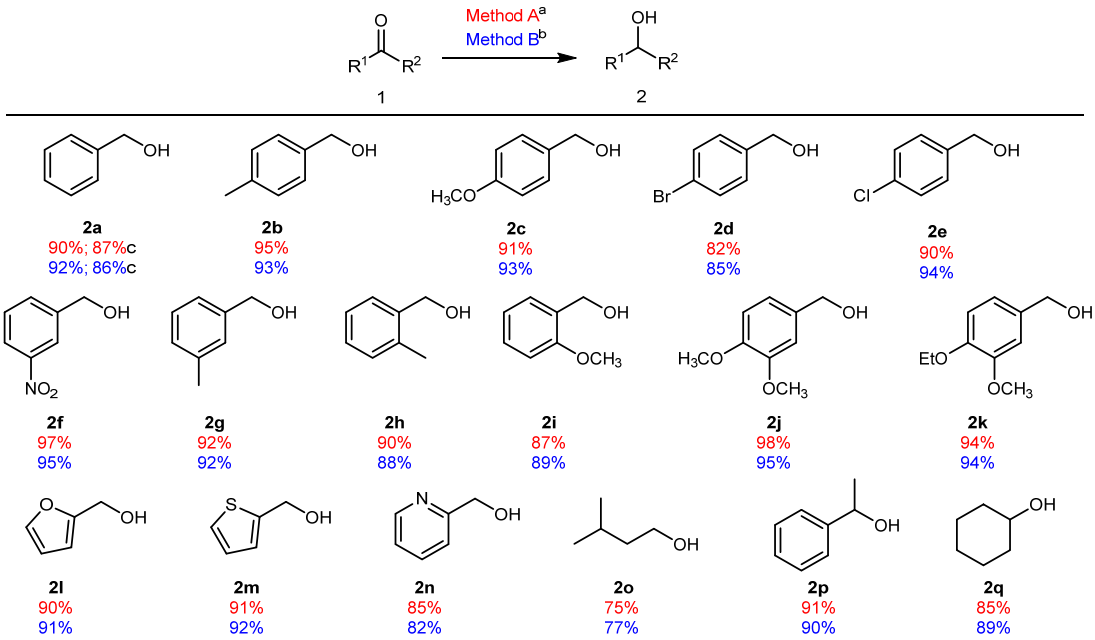


**Fig 1.** Scopes of reaction: a) reaction was carried out using grinding method at room temperature for 10 min; b) reaction was conducted under ultrasound irradiation at room temperature for 10 min, 40 kHz, 300 W; c) reaction was performed using 20 mmol of benzaldehyde

Mechanochemistry is a green method that provides alternative mechanical energy input to accelerate or catalyze chemical reactions. Moreover, it offers various advantages such as improving the reaction yields, avoiding the use of toxic solvents, and reducing energy consumption, which is in good agreement with green chemistry principles [28]. In this context, the grinding method was used in this study due to its simplicity. Benzaldehyde **1a** and sodium borohydride were then subjected to the mechanical-assisted-reduction reaction (Fig. 1, Method B). The completion of the reaction was achieved after 10 min of grinding. It should also be noted that the reaction was conducted without any solvent, and benzyl alcohol **2a** was furnished in 92% yield.

Encouraged by the promising preliminary results, we then decided to expand the scope of our methodology. Various benzaldehydes with different substitution types and positions were initially screened. We found that benzaldehyde bearing both electron donating- and withdrawing groups (**2b**-**e**) were suitable for sonochemical and mechanochemical reduction reaction. Interestingly, different position of substituents in aldehydes also produced the alcohols (**2f**-**k**) in very good yield. We also managed to reduce the heterocyclic aldehyde (**1l**-**n**) using our protocols. Performing the reaction using aliphatic aldehyde of isovaleraldehyde using both methods allowed us to obtain isoamyl alcohol (3-methylbutan-1-ol, **2o**) in lower yield. The loss of some product during the work up process might occur due to the slight solubility of isoamyl alcohol in water. It is interesting to note that secondary alcohols **2p** and **2q** were successfully synthesized from aromatic (acetophenone, **1p**) and aliphatic (cyclohexanone, **1q**) ketones, respectively. Recent report demonstrated that performing the reduction of acetophenone in ethanol solvent under stirring method for 2h generated the corresponding alcohol **1p** in 91% yield [32]. It should be noted that the alcohol **1p** can be obtained (with the same chemical yield) in only 10 min by using sonochemistry and mechanochemistry (Fig. 1). Evaluation of the reaction scopes demonstrated that our methodology was green, general, and efficient.

Structure elucidation of the products (**2a**-**q**) was carried out using $^{1}$H-NMR, $^{13}$C-NMR, FTIR, and GCMS spectrometers. The NMR spectra of the products showed no peak at the chemical shift around 9–10 ppm (for $^{1}$H-NMR) and 200–220 (for $^{13}$C-NMR) ppm, indicating that the aldehydes and ketones were reduced to alcohols. The formation of alcohols was strongly confirmed by the presence of a broad singlet peak from hydroxyl proton (–O**H**) at $^{1}$H-NMR spectra and a peak from the carbon adjacent to hydroxyl group (**C**-OH) in the region of 55–70 ppm at $^{13}$C-NMR spectra. According to FTIR spectra, the success of the reaction could be shown by the disappearance of the strong peak belong to carbonyl aldehydes and ketones at around 1700 $cm^{-1}$ and the appearance of a broad band from alcohols at the region of 3200–3500 $cm^{-1}$. Moreover, GCMS analysis showed that the generated $M^{+}$ ions corresponded to the molecular mass of the products.

The scalability of this methodology was further evaluated by conducting the reaction in multigram scale. In this context, benzaldehyde **1a** (20 mmol, 2.05 g) was subjected to the sonochemical and mechanochemical reduction reaction. It is worth nothing that the synthetic yield of alcohol **2a** remained high. Based on our study, the diversely-substituted-alcohols could be accessed by simply grinding aldehydes or ketones and sodium borohydride using a mortar and pestle in a short reaction time. Additionally, the reaction could proceed using both liquid and solid reactants under solvent-free condition. However, the mechanical energy applied during the reaction could not be controlled [33].

The application of ultrasound irradiation to the synthesis of alcohols could reduce the reaction time compared to conventional stirring. Unlike the grinding method, a small amount of solvent should be employed to facilitate the reaction (particularly when solid aldehydes such as 4-chlorobenzaldehyde, 4-bromobenzaldehyde and 3-nitrobenzaldehyde were used). It should be noted that the ultrasound-assisted-reduction reaction could also be scaled up without losing its efficiency.

## ■ CONCLUSION

We have developed a green synthesis of alcohols via reduction reaction using either sonochemistry or mechanochemistry methods. The reactions were operated under mild conditions with short reaction times and could be carried out on a multigram scale. Various aldehydes and ketones could be used as synthetic precursors, showing the versatility of this methodology.

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## ■ AUTHOR CONTRIBUTIONS

All authors conducted the experiment, MIDM wrote and revised the manuscript. All authors agreed to the final version of this manuscript.

## ■ REFERENCES

[1] Scognamiglio, J., Jones, L., Vitale, D., Letizia, C.S., and Api, A.M., 2012, Fragrance material review on benzyl alcohol, *Food Chem. Toxicol.*, 50, S140–S160.

[2] Xu, J., Liu, N., Zou, L., Cheng, F., Shen, X., Liu, T., Lv, H., Khan, R., and Fan, B., 2019, Visible-light driven hydrolysis of benzyl halides with water for preparation of benzyl alcohols, *Asian J. Org. Chem.*, 8 (2), 261–264.

[3] Li, J., Wang, H., Liu, L., and Sun, J., 2014, Metal-free, visible-light photoredox catalysis: Transformation of arylmethyl bromides to alcohols and aldehydes, *RSC Adv.*, 4 (91), 49974–49978.

[4] Chen, Y., Hu, J., and Ding, A., 2020, Aerobic photooxidative hydroxylation of boronic acids catalyzed by anthraquinone-containing polymeric photosensitizer, *RSC Adv.*, 10 (13), 7927–7932.

[5] Ding, A., Zhang, Y., Chen, Y., Rios, R., Hu, J., and Guo, H., 2019, Visible light induced oxidative hydroxylation of boronic acids, *Tetrahedron Lett.*, 60 (9), 660–663.

[6] Park, J., Lee, Y.M., Nam, W., and Fukuzumi, S., 2013, Brønsted acid-promoted C–H bond cleavage via electron transfer from toluene derivatives to a protonated nonheme iron(IV)-oxo complex with no kinetic isotope effect, *J. Am. Chem. Soc.*, 135 (13), 5052–5061.

[7] Voronin, V.V., Ledovskaya, M.S., Rodygin, K.S., and Ananikov, V.P., 2020, Examining the vinyl moiety as a protecting group for hydroxyl (–OH) functionality under basic conditions, *Org. Chem. Front.*, 7 (11), 1334–1342.

[8] Li, X.G., Li, F., Xu, Y., Xiao, L.J., Xie, J.H., and Zhou, Q.L., 2022, Hydrogenation of esters by manganese catalysts, *Adv. Synth. Catal.*, 364 (4), 744–749.

[9] Wang, F., Tan, X., Lv, H., and Zhang, X, 2016, New ruthenium complexes based on tetradentate bipyridine ligands for catalytic hydrogenation of esters, *Chem. - Asian J.*, 11 (15), 2103–2106.

[10] Gonzalez-de-Castro, A., Cosimi, E., Aguila, M.J.B., Gajewski, P., Schmitkamp, M., de Vries, J.G., and Lefort, L., 2017, Long-chain α–ω diols from renewable fatty acids *via* tandem olefin metathesis–ester hydrogenation, *Green Chem.*, 19 (7), 1678–1684.

[11] Kawano, T., Watari, R., Kayaki, Y., and Ikariya, T., 2019, Catalytic hydrogenation of carboxamides with a bifunctional Cp*Ru catalyst bearing an imidazol-2-ylidene with a protic aminoethyl side chain, *Synthesis*, 51 (12), 2542–2547.

[12] Cabrero-Antonino, J.R., Alberico, E., Drexler, H.J., Baumann, W., Junge, K., Junge, H., and Beller, M., 2016, Efficient base-free hydrogenation of amides to alcohols and amines catalyzed by well-defined pincer imidazolyl–ruthenium complexes, *ACS Catal.*, 6 (1), 47–54.

[13] Tavakoli, G., and Prechtl, M.H.G., 2019, The reductive deaminative conversion of nitriles to alcohols using para-formaldehyde in aqueous solution, *Catal. Sci. Technol.*, 9 (21), 6092–6101.

[14] He, J., Xu, Y., Yu, Z., Li, H., Zhao, W., Wu, H., and Yang, S., 2020, $ZrOCl_2$ as a bifunctional and *in situ* precursor material for catalytic hydrogen transfer of bio-based carboxides, *Sustainable Energy Fuels*, 4 (6), 3102–3114.

[15] Neyt, N.C., and Riley, D.L., 2018, Mild and selective reduction of aldehydes utilising sodium dithionite under flow conditions, *Beilstein J. Org. Chem.*, 14, 1529–1536.

[16] Mandal, T., Jana, S., and Dash, J., 2017, Zinc-mediated efficient and selective reduction of carbonyl compounds, *Eur. J. Org. Chem*., 2017 (33), 4972–4983.

[17] Zhao, W., Meier, S., Yang, S., and Riisager, A., 2020, Ammonia borane enabled upgrading of biomass derivatives at room temperature, *Green Chem*., 22 (18), 5972–5977.

[18] Mohanty, A.D., and Bae, C., 2014, Mechanistic analysis of ammonium cation stability for alkaline exchange membrane fuel cells, *J. Mater. Chem. A*, 2 (41), 17314–17320.

[19] Shahinnoranikoliji, S., and Khezri, B., 2015, Reduction of carbonyl compounds with $Zn(BH_4)_2$ under microwave irradiation, *Orient. J. Chem*., 31 (4), 2449–2451.

[20] Cao, J., Ma, C., Zang, J., Gao, S., Gao, Q., Kong, X., Yan, Y., Liang, X., Ding, Q., Zhao, C., Wang, B., Xu, W., and Zhang, Y., 2018, Novel leucine ureido derivatives as aminopeptidase N inhibitors using click chemistry, *Bioorg. Med. Chem*., 26 (12), 3145–3157.

[21] Abdullaha, M., Ali, M., Kour, D., Mudududdla, R., Khajuria, P., Kumar, A., and Bharate, S.B., 2021, Tetramethoxystilbene inhibits NLRP3 inflammasome assembly via blocking the oligomerization of apoptosis-associated speck-like protein containing caspase recruitment domain: *In vitro* and *in vivo* evaluation, *ACS Pharmacol. Transl. Sci*., 4 (4), 1437–1448.

[22] Sri Ramya, P.V., Angapelly, S., Guntuku, L., Singh Digwal, C., Nagendra Babu, B., Naidu, V.G.M., and Kamal, A., 2017, Synthesis and biological evaluation of curcumin inspired indole analogues as tubulin polymerization inhibitors, *Eur. J. Med. Chem*., 127, 100–114.

[23] Chatel, G., and Varma, R.S., 2019, Ultrasound and microwave irradiation: Contributions of alternative physicochemical activation methods to green chemistry, *Green Chem*., 21 (22), 6043–6050.

[24] Mardjan, M.I.D., Hariadi, M.F., Putri, I.M., Musyarrofah, N.A., Salimah, M., Priatmoko, P., Purwono, B., and Commeiras, L., 2022, Ultrasonic-assisted-synthesis of isoindolin-1-one derivatives, *RSC Adv*., 12 (29), 19016–19021.

[25] Martínez, R.F., Cravotto, G., and Cintas, P., 2021, Organic sonochemistry: A chemist's timely perspective on mechanisms and reactivity, *J. Org. Chem*., 86 (20), 13833–13856.

[26] Varma, R.S., 2016, Greener and sustainable trends in synthesis of organics and nanomaterials, *ACS Sustainable Chem. Eng*., 4 (11), 5866–5878.

[27] da Silveira Pinto, L., and de Souza, M., 2017, Sonochemistry as a general procedure for the synthesis of coumarins, including multigram synthesis, *Synthesis*, 49 (12), 2677–2682.

[28] Liu, X., Li, Y., Zeng, L., Li, X., Chen, N., Bai, S., He, H., Wang, Q., and Zhang, C., 2022, A Review on mechanochemistry: Approaching advanced energy materials with greener force, *Adv. Mater*., 34 (46), 2108327.

[29] Fitriastuti, D., Mardjan, M.I.D., Jumina, J., and Mustofa, M., 2014, Synthesis and heme polymerization inhibitory activity (HPIA) assay of antiplasmodium of (1)-*N*-(3,4-dimethoxybenzyl)-1,10-phenanthrolinium bromide from vanillin, *Indones. J. Chem*., 14 (1), 1–6.

[30] Chavan, P.N., Pansare, D.N., and Shelke, R.N., 2019, Eco-friendly, ultrasound-assisted, and facile synthesis of one-pot multicomponent reaction of acridine-1,8(2*H*,5*H*)-diones in an aqueous solvent, *J. Chin. Chem. Soc*., 66 (8), 822–828.

[31] Dachi, F.D., 2022, Pengaruh sterik dan induksi benzaldehida terhadap sintesis turunan benzil alkohol melalui reaksi reduksi menggunakan metode sonokimia, *Undergraduate Thesis*, Universitas Gadjah Mada, Yogyakarta.

[32] Tanemura, K., 2022, Reduction of aldehydes and ketones by a stoichiometric amount of $NaBH_4$ using a small amount of MeOH or EtOH, *Results Chem*., 4, 100486.

[33] Pagola, S., 2023, Outstanding advantages, current drawbacks, and significant recent developments in mechanochemistry: A perspective view, *Crystals*, 13 (1), 124.