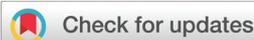


## RESEARCH ARTICLE

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Alkali/alkaline earth metal-mediated  
mechanochemical Wurtz reactions

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The Wurtz reaction is a classical C(sp<sup>3</sup>)–C(sp<sup>3</sup>) bond-forming reaction involving alkyl halides and alkali metals. However, this reaction generally requires molten or dispersed metals in large amounts of solvent, and has poor functional-group tolerance. Herein, we report a mechanochemical Wurtz reaction by the direct ball-milling of bulk Li, Na, and Ca with haloalkanes. The mechanochemical grinding of these bulk metals with a small amount of a liquid additive (THF) generates highly dispersed reactive metal species, enabling efficient C–C bond formation at room temperature even under air. Under optimized reaction conditions with Li and Na, various primary and secondary haloalkanes are converted into higher-order alkanes. Furthermore, the mechanochemical grinding of Ca is particularly effective for the Wurtz reaction of bromoalkanes bearing various functional groups such as fluoro, chloro, keto, and ester groups, achieving unprecedented C–C coupling and one-step furan synthesis. The developed reaction also allows gram-scale synthesis with a minimal amount of solvent, offering a practical and complementary method to the classical in-solution Wurtz reaction.

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## Introduction

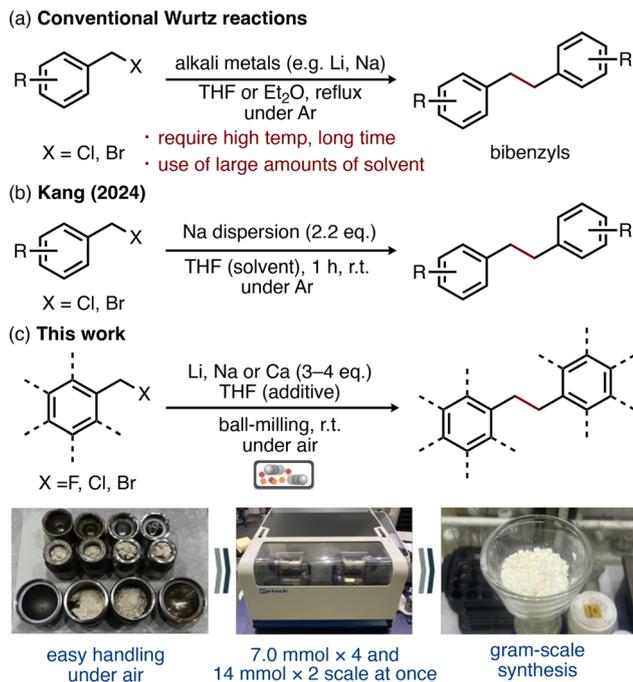
The Wurtz reaction is a classical method for forming C(sp<sup>3</sup>)–C(sp<sup>3</sup>) bonds using alkali metals and alkyl halides, and has been widely used to synthesize higher-order hydrocarbons (Fig. 1a).<sup>1</sup> Since the first report on sodium-mediated reactions in 1855,<sup>2</sup> related protocols employing other alkali metals such as Li<sup>3</sup> and K,<sup>4</sup> as well as transition metal-mediated variants (In, Co, Mn, Cu, Ni), have also been reported.<sup>5–9</sup> Particularly, alkali metals have been widely used as standard reductants owing to their high reduction potentials<sup>10</sup> and relatively low melting points.<sup>11</sup> However, for the reaction to proceed efficiently, the alkali metals should be dispersed in solution to increase the active reaction surface area. This typically entails heating (to melt the metals) and prolonged reaction times. Li is potentially more reactive owing to its highest reduction potential among metals (–3.04 V), but is less reactive as a bulk metal owing to its higher atomization enthalpy and melting point than Na and K.<sup>12</sup> Although it is more hazardous and pyrophoric to treat bulk Na and K than Li, these metals have been employed in the Wurtz reaction owing to their ease of dispersion and melting in solution, and consequently, their high practical reactivities.<sup>13</sup> As a further practical demonstration, Kang recently reported a safer and rapid alternative Wurtz

reaction<sup>14</sup> of benzyl halides using a Na dispersion,<sup>15</sup> where the safer, free-flowing metallic Na dispersion offered a high reaction surface area (Fig. 1b). Nevertheless, under the strongly reducing conditions using alkali metals, the functional-group tolerance inevitably remains poor, and large-scale reactions require the use of large amounts of solvent with hazardous alkali metals.<sup>1,2,13</sup> Therefore, the development of complementary Wurtz reactions is imperative and of significant importance in organic synthesis.

Recently, mechanochemical reactions using a ball-milling apparatus have pioneered a new trend in organic synthesis in terms of not only improving the reaction efficiency and reducing solvent usage to an additive level, but also enabling difficult-to-achieve reactions that do not occur in solution.<sup>16,17</sup> Mechanochemical grinding without a solvent or with the minimum required amount of solvent additives efficiently generates highly reactive species/intermediates that are difficult to produce in solution.<sup>18–20</sup> For example, the direct grinding of aromatic substrates with pieces of Li wire, which is less reactive as a bulk metal, enables unprecedented cyclodehydrogenation,<sup>18</sup> Birch reduction<sup>19</sup> and Birch reductive arylation,<sup>20</sup> as recently demonstrated by us as well as the Ito/Kubota group. Ito/Kubota,<sup>21–23</sup> Aav/Kananovich,<sup>24</sup> and Lu<sup>25</sup> also demonstrated the usefulness of Na(0),<sup>21</sup> K(0),<sup>25</sup> Mg(0),<sup>22,24</sup> and Ca(0)<sup>23,24</sup> as reducing agents in Birch reduction and metal-halogen-exchanging reactions. The main advantages of these reactions are the ability to generate highly dispersed reactive metal-reactant mixtures from sluggish but intrinsically active

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**Fig. 1** (a) Conventional Wurtz reaction. (b) Recent report of a Wurtz reaction using a Na dispersion. (c) This work.

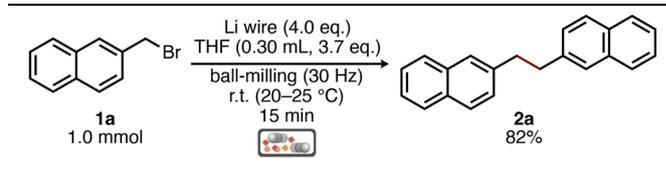
bulk metals while minimizing solvent usage, along with air tolerance and the capability for reactions at lower temperatures.

Although the advantages of mechanochemical reactions are remarkable, mechanochemical organometallic transformations<sup>26</sup> are still under development, and mechanochemical Wurtz reactions are yet to be realized. As explained above, the development of the mechanochemical Wurtz reaction using bulk metals is expected to offer a higher efficiency and better synthetic benefits than the reaction in solution. Herein, we report the mechanochemical Wurtz reaction using alkali/alkaline earth metals.<sup>27</sup> As shown in Fig. 1c, the direct mixing of Li(0), Na(0), and Ca(0) with various alkyl halides and an additive amount of THF using a ball-milling machine enables dimerization very quickly at room temperature (r.t.) even under air. One of the advantages of ball-milling is the flexibility it offers in the selection of the optimal metal reducing agents (Li, Na, or Ca) based on the substrates and reaction scale. The use of Ca(0) also promotes the Wurtz reaction; although the reaction is slower, it is far superior to reactions involving Li or Na in terms of the functional-group tolerability. The use of Ca(0) in this reaction also enables the one-step synthesis of functionalized 1,2-diarylethanes and substituted furans from various alkyl halides and  $\alpha$ -bromoketones. In addition, the mechanochemical method presented in this study enables the column chromatography-free, gram-scale synthesis of 1,2-di(naphthalen-2-yl)ethane, which can be easily converted into benzo[ghi]perylene<sup>28</sup> by stepwise oxidation. With the optimized reaction conditions using various haloalkanes, diverse kinds of diarylethanes, cycloalkanes, and diarylfuranes are successfully synthesized.

## Results and discussion

We first optimized the mechanochemical Wurtz reaction of 2-(bromomethyl)naphthalene (**1a**, 1.0 mmol, 1.0 eq.) as a model substrate (Table 1). Guided by our previous studies on Li(0)-mediated mechanochemical reactions with minor modifications,<sup>18–20</sup> Li(0) pieces cut from Li wire (4.0 eq.) and dry THF (0.30 mL, 3.7 eq.) were employed as a reductant and liquid-assisted grinding (LAG) additive,<sup>29</sup> respectively. In the optimal protocol, **1a**, Li(0), THF, and a 10 mm stainless-steel ball were charged in a 5.0 mL stainless-steel jar under air, which was sealed with a cap and polyethylene O-shape packing, and subjected to ball-milling at 30 Hz for 15 min at room temperature (r.t.: 20–25 °C). After quenching with sat.  $\text{NH}_4\text{Cl}$  aq., 1,2-di(naphthalen-2-yl)ethane (**2a**) was isolated in 82% yield (Table 1, entry 1). Control experiments showed that extending the reaction time from 15 to 60 min did not improve the yield, whereas shortening it to 5 min led to a significant decrease in the yield (entries 2 and 3). These results implied that although the present mechanochemical Wurtz reaction requires an induction period for efficient mixing over 5 min, the reaction exponentially proceeds and completes within 15 min. Other LAG additives such as ethylenediamine, *N,N,N',N'*-tetramethylethylenediamine (TMEDA), 1,4-dioxane, and 2-methyltetrahydrofuran (2-MeTHF) significantly decreased the yield (entries 4–7). A reduction in the amount of lithium(0) to 2.1 eq. reduced the yields of **2a** to 16% (entry 8). Notably, we often found that a slightly larger amount of lithium(0) than is theoretically required is needed for small-scale mechanochemical reactions due to lithium entering the gaps in the container or

**Table 1** Effect of parameters in the mechanochemical Wurtz reaction. The reactions were conducted in a 5.0 mL stainless-steel jar using a 10 mm-diameter stainless-steel ball



Entry	Deviation from standard conditions	Yield of <b>2a</b> <sup>a</sup>
1	None	82%
2	Ball-milling for 60 min	79%
3	Ball-milling for 5 min	trace
4	Ethylenediamine (0.30 mL, 4.5 eq.) used instead of THF	31%
5	TMEDA (0.30 mL, 2.0 eq.) used instead of THF	0%
6	1,4-Dioxane (0.30 mL, 3.5 eq.) used instead of THF	18%
7	2-MeTHF (0.37 mL, 3.7 eq.) used instead of THF	34%
8	Li wire (2.1 eq.) used	16%
9	Na lump (4.0 eq.) used instead of Li	71%
10	Ca shot (4.0 eq.) used instead of Li, and ball-milling for 120 min	51%
11	Ba shot (4.0 eq.) used instead of Li, and ball-milling for 120 min	0%

<sup>a</sup> Isolated yield. 2-MeTHF: 2-methyltetrahydrofuran.



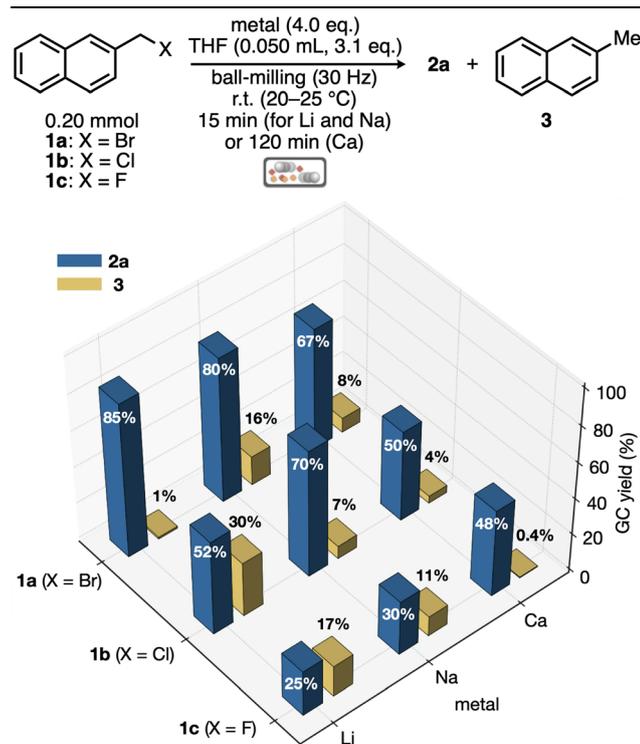
the surface oxide film on the lithium wire.<sup>18,20</sup> The use of a Na lump instead of Li wire in the Wurtz reaction at r.t. also resulted in high efficiency, affording **2a** in 71% yield (entry 9). The reaction with a Ca shot was very slow at r.t., and the product was obtained in 51% <sup>1</sup>H NMR yield after 120 min of reaction (entry 10). The bulk Ba shot was almost inert, likely due to the difficulty with finely crushing it during ball-milling, and most of the starting material **1a** remained unreacted after 120 min of reaction at r.t (entry 11). Consequently, the mechanochemical ball-milling process developed in this study using bulk Li, Na, and Ca was found to be effective for the *in situ* formation of highly dispersed organometallic species from bromoalkane without heating and prolonged reaction times, enabling rapid and efficient coupling at r.t. even under air. Notably, the Ca(0)-mediated Wurtz reaction was unprecedented but offered a lower reactivity, and would still be of interest in terms of functional-group tolerability (see following sections).

We next assessed the correlations between the yield and (i) the metal employed (Li(0), Na(0), and Ca(0)) and (ii) the halogen substituents (Br, Cl, and F) on 2-(halomethyl)naphthalene **1a–1c**, to clarify the reaction profile (Table 2). With all metals, the yields of **2a** increased in the order of ease of elimination for typical leaving groups: Br, Cl, and F. The use of **1a** (X = Br) and Li afforded the highest GC yield of **2a** (85%) with

the minimal generation of the dehalogenated side product **3** (1%). The reaction of **1a** with Na afforded **2a** in a comparable yield (80%) along with the increased formation of **3** (16%), whereas the yield of **2a** was slightly decreased using Ca (**2a**: 67%, **3**: 8%). Interestingly, Na provided the best result in terms of the yield of **2a** (70%) in all metals when **1b** (X = Cl) was used as the substrate. In the reactions of 2-(fluoromethyl)naphthalene (**1c**), all metals caused reduced GC yields of **2a** within 15 min (for Li and Na) and 120 min (for Ca); nevertheless, the use of Ca most effectively suppressed the formation of **3** (0.4%). To summarize these results: (i) the use of Li(0) is effective in the reaction of bromoalkene **1a** while minimizing the formation of the side product **3**, (ii) Na(0) exhibits similar reactivity to Li(0) in the reaction of bromoalkane **1a**, but affords superior results in the reaction of chloroalkane **1b**, and (iii) Ca(0) is less reactive than other metals and requires an extended reaction time at r.t., but is particularly effective in the reaction of fluoroalkane **1c**, minimizing the formation of the side product **3**. The reason for this metal-reactant compatibility is unclear at this time. Nevertheless, factors such as the crushability of bulk metals, atomization enthalpy (Li: 159 kJ mol<sup>-1</sup>; Na: 107 kJ mol<sup>-1</sup>, Ca: 177 kJ mol<sup>-1</sup>),<sup>30</sup> reduction electrode potential (Li: -3.04 V; Na: -2.71 V; Ca: -2.76 V vs. standard hydrogen electrode (SHE)),<sup>31</sup> and/or lattice enthalpies of the resulting salts (MX<sub>n</sub>) can influence the reaction progress.

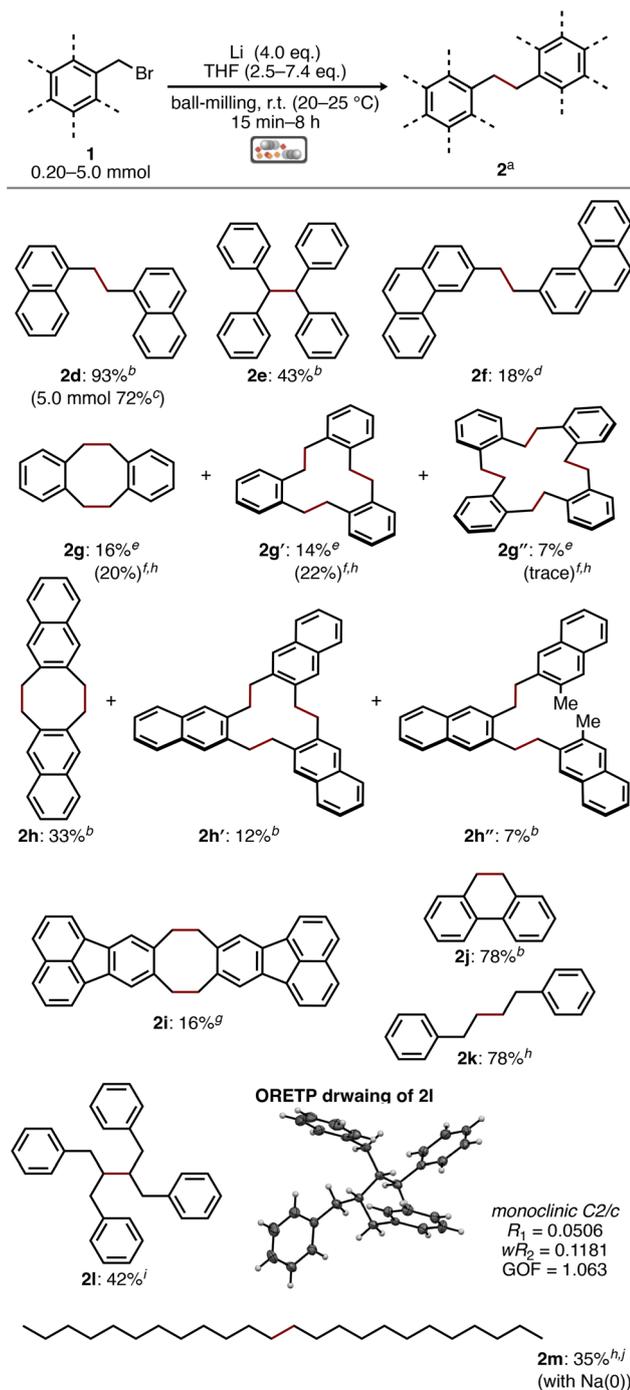
After establishing the optimal conditions for the Li(0)-mediated mechanochemical Wurtz reaction, the scope of alkyl bromides was investigated (Fig. 2). All experiments were performed under air at r.t. The use of 1-(bromomethyl)naphthalene (**1d**) afforded 1,2-di(naphthalen-1-yl)ethane (**2d**) in 58% yield. Gram-scale synthesis was also possible using a large-volume stainless-steel jar (10 mL volume) and two 10 mm-diameter stainless-steel balls with 1.11 g (5 mmol) of **1d**, affording **2d** in a satisfactory yield of 72% (510.9 mg). The reactions with  $\alpha$ -bromodiphenylmethane and 3-(bromomethyl)phenanthrene afforded the corresponding dimers **2e** and **2f** in 43 and 18% yields, respectively. The use of  $\alpha,\alpha'$ -dibromo-*o*-xylene (**1g**), which contains two benzylic bromides, afforded the corresponding octagonal cyclic dimer **2g** in 16% yield, together with the cyclic trimer **2g'** in 14% yield and cyclic tetramer **2g''** in 7% yield. When the amount of lithium(0) was reduced to 2.1 eq., **1g** remained unreacted and was recovered. On the other hand, the use of 6.0 eq. of lithium(0) afforded **2g** and **2g'** in 20% and 22% yields, respectively, along with a trace amount of **2g''**. The Wurtz coupling of **1g** has previously been achieved under solution conditions that required heating to disperse granular Li.<sup>32</sup> In comparison, the ball-milling protocol enables the reaction to proceed under simple, ambient conditions, thus providing a practical alternative to the solution-state method. Similarly, cyclization using 2,3-bis(bromomethyl)naphthalene (**1h**) afforded the cyclic dimer **2h**, cyclic trimer **2h'**, and linear trimer **2h''** in 33%, 12%, and 7% yields, respectively. When 8,9-bis(bromomethyl)fluoranthene (**1i**) was employed, an eight-membered ring compound **2i** was obtained in 16% yield. The mechanochemical Wurtz reaction can also be applied to intramolecular cyclization using 2,2'-bis(bromo-

**Table 2** Reactions were conducted in a 1.5 mL stainless-steel jar using a 7 mm-stainless-steel ball. The reactions were quenched with sat. NH<sub>4</sub>Cl aq. after the indicated reaction times. GC yields using dodecane as an internal standard are shown



Reaction times: 15 min for Li and Na, and 120 min for Ca. A Li wire, Na lump, and Ca shot were used for the reactions.





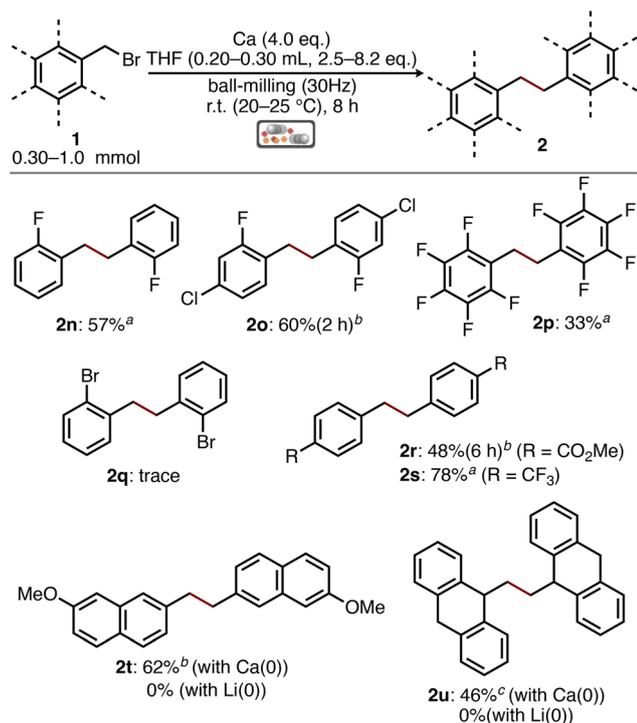
**Fig. 2** Substrate scope in the Li(0)-mediated mechanochemical Wurtz reaction and the ORTEP drawing of **2l**. Unless otherwise noted, the reactions were conducted in a 5.0 mL stainless-steel jar using a 10 mm stainless-steel ball under ball-milling at 30 Hz. <sup>a</sup>Isolated yields. <sup>b</sup>A 1.0 mmol-scale reaction for 15 min. <sup>c</sup>A 5.0 mmol-scale reaction in a 10 mL stainless-steel jar using two 10 mm-diameter stainless-steel balls for 60 min. <sup>d</sup>Combined yield in two runs of a 0.2 mmol-scale reaction using 4.0 eq. of a Na(0) lump in a 1.5 mL stainless-steel jar with two 7 mm-diameter stainless-steel balls for 3 h. <sup>e</sup>Combined yield in two runs of a 3.0 mmol-scale reaction in a 10 mL stainless-steel jar using four 10 mm-diameter stainless-steel balls for 120 min. <sup>f</sup>6.0 eq. of Li(0) was used. <sup>g</sup>A 1.0 mmol scale reaction for 8 h. <sup>h</sup>A 1.0 mmol scale for 60 min. <sup>i</sup>A 0.50 mmol scale for 8 h. <sup>j</sup>4.0 eq. of Na(0) lump was used.

methyl)-1,1'-biphenyl (**1j**) to afford 9,10-dihydrophenanthrene (**2j**) in 78% yield. We subsequently achieved the dimerization of alkyl bromides **1k** and **1l**, other than benzyl bromide derivatives. The use of phenethyl bromide (**1k**) afforded higher-order hydrocarbons **2k** in 78% yield. Notably, the reaction of a secondary alkyl bromide, (2-bromopropane-1,3-diyl)dibenzene (**1l**), also proceeded slowly, and the sterically congested branched alkane **2l** was obtained in 41% yield after reaction for 8 h. Single crystals of **2l** were successfully obtained by recrystallization from hexane, and their structure was elucidated by X-ray diffraction analysis. The use of 1-bromododecane (**1m**) was also applicable to this reaction and afforded *n*-tetraicosane (**2m**) in 35% isolated yield. Using a Na lump instead of Li(0) in this reaction resulted in a better yield. Note that several substrates bearing functional groups such as methoxy, trifluoromethyl, or ester groups were found to be incompatible under these conditions. Consequently, the developed Li(0)-mediated mechanochemical Wurtz reaction enables rapid, air-tolerant, and operationally simple C(sp<sup>3</sup>)-C(sp<sup>3</sup>) bond formation under ambient conditions, and is particularly adequate for the reaction of bromo alkanes including benzyl- and homobenzyl-type primary and secondary ones, as well as simple linear primary alkyl bromide.

Motivated by the fact that the reaction with Ca(0) also proceeded to some extent along with nearly no side reactions (Table 2) and considering the previous demonstrations by the Ito/Kubota group on the mechanochemical generation of Ca-based heavy Grignard reagents,<sup>23</sup> we carried out mechanochemical Wurtz reactions using a Ca shot to realize functional-group-tolerable Wurtz reactions (Fig. 3a). In the reactions of various benzyl bromides with *o*-fluoro (**1n**), *p*-chloro-*o*-fluoro (**1o**), perfluoro (**1p**), *p*-methoxycarbony (**1r**), and *p*-trifluoromethyl groups (**1s**) with Ca lumps (4.0 eq.) and THF (2.5–4.9 eq.), 1,2-diarylethanes (**2n–2p**, **2r**, and **2s**) were obtained in moderate yields (33–78%) without the marked loss of functional groups. In contrast, an *o*-bromo group on 1-bromo-2-(bromomethyl)benzene (**1q**) was incompatible with this reaction, likely due to the formation of aryl calcium species, resulting in an inseparable complex mixture.<sup>33</sup> We then achieved the coupling of 2-(bromomethyl)-7-methoxynaphthalene (**1t**) to afford the corresponding dimethoxynaphthalene dimer (**2t**) in 62% yield, while **2t** was not obtained in the reaction with Li(0) due to demethoxylation. Although the reaction of 9-bromomethylanthracene (**1u**) by the Li(0)-mediated mechanochemical Wurtz reaction exclusively afforded the dehydrobrominated product 9-methyl-9,10-dihydroanthracene, the Ca(0)-mediated reaction successfully provided the coupling product **2u** in 46% yield. Thus, the newly developed Ca(0)-mediated mechanochemical Wurtz reaction offers milder reactivity and a different reaction profile compared with conventional alkali metal-mediated reactions in the solution state, expanding the substrate scope.

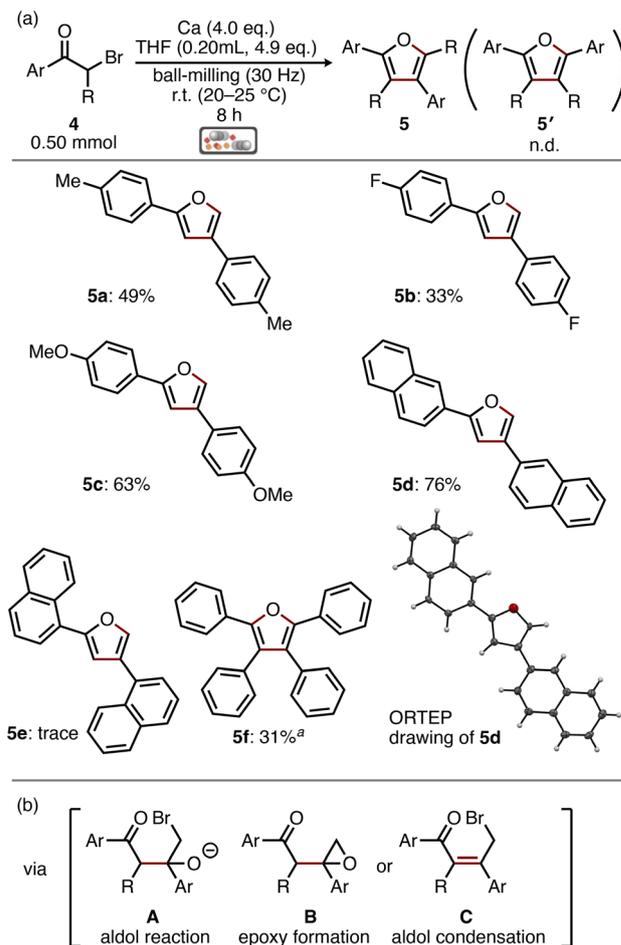
Encouraged by the broad functional-group compatibility, the Ca(0)-mediated mechanochemical Wurtz reaction was further applied to the reaction of phenacyl bromide derivatives **4** for the synthesis of 1,4-butanedione derivatives (Fig. 4a). Surprisingly, the mechanochemical grinding of *p*-(bromoace-





**Fig. 3** Ca(0)-mediated mechanochemical Wurtz reaction. Unless otherwise noted, the reactions were conducted in a 5.0 mL stainless-steel jar using two 7 mm-diameter stainless-steel balls under ball-milling at 30 Hz. <sup>a</sup>0.50 mmol-scale reaction with 0.20 mL (4.9 eq.) of THF. <sup>b</sup>A 1.0 mmol-scale reaction with 0.20 mL (2.5 eq.) of THF. <sup>c</sup>A 0.30 mmol-scale reaction with 0.20 mL (8.2 eq.) of THF.

toluene (**4a**) with Ca(0) followed by an aqueous workup unexpectedly furnished 2,4-di(*p*-tolyl)furan (**5a**) in 49% yield. Based on related in-solution reactions reported in the literature,<sup>34–36</sup> this reaction is expected to proceed *via* (i) the generation of ketone enolate by the reaction of **4a** with Ca(0), (ii) an aldol reaction to form intermediate **A**, (iii) the formation of epoxide **B** or a  $\beta$ -(bromomethyl)chalcone derivative by aldol condensation, and (iv) oxy-cyclization and aromatization (Fig. 4b). This one-step furan synthesis typically occurs in the reaction of various phenacyl bromide derivatives including *p*-(bromoacetyl)fluorobenzene (**4b**), *p*-(bromoacetyl)anisole (**4c**), and 2-(bromoacetyl)naphthalene (**4d**), affording the corresponding 2,4-diarylfurans (**5b–5d**) in 33%, 63%, and 76% yields, respectively (Fig. 4a). The structure of **5d** was elucidated by X-ray crystallographic analysis. While this analysis unequivocally confirmed substitution by 2-naphthyl groups at the C2- and C4-positions, the absolute structure could not be reliably determined owing to weak anomalous scattering (see SI for details). Although a trace amount of 2,4-di(naphthalen-1-yl) furan (**5e**) was detected by GC-MS in a crude mixture of the reaction using 1-bromoacetylnaphthalene (**4e**), the product **5e** could not be isolated. A phenacyl bromide bearing a secondary  $\alpha$ -center, 2-bromo-1,2-diphenylethanone (**4f**), underwent annulation to afford 2,3,4,5-tetraphenylfuran (**5f**) in 31% yield. Similar reactions were previously demonstrated using CuCl<sub>2</sub>/

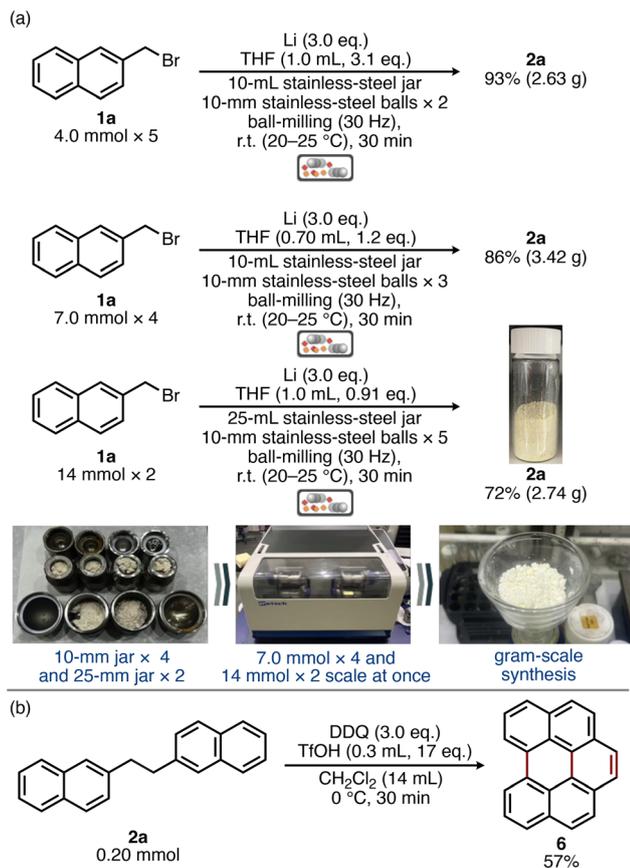


**Fig. 4** (a) Ca(0)-mediated mechanochemical reductive coupling of phenacyl bromide derivatives for the synthesis of 2,4-diarylfurans. Unless otherwise noted, the reactions were conducted in a 5.0 mL stainless-steel jar using two 7 mm-diameter stainless-steel balls under ball-milling at 30 Hz. <sup>a</sup>1.0 mmol-scale reaction with 0.30 mL (3.7 eq.) of THF. (b) Possible intermediates.

Na<sub>2</sub>Te (17% yield of 2,4-diphenylfuran<sup>34b</sup>) and [FeCp(cod)]<sup>−</sup> (Cp = cyclopentadienyl; cod = 1,5-cyclooctadiene, 13% yield of 2,4-diphenylfuran<sup>34b</sup>) in the solution state; however, notably, the present one-step mechanochemical synthesis of 2,4-di- and 2,3,4,5-tetra-substituted furans from  $\alpha$ -bromo ketones is easier to perform, practical, and more advantageous in terms of the yield and substrate scope compared to previous methods.

To further highlight the synthetic practicality of this protocol, a gram-scale mechanochemical Wurtz reaction was demonstrated at ambient temperature under air (Fig. 5a). The mechanochemical Wurtz reaction of **1a** was conducted in five parallel batches of 10 mL stainless-steel jars containing 4.0 mmol  $\times$  5 of **1a** using the mixer-mill Retsch MM-500 Vario. Upon ball-milling at r.t. after 30 min, the crude mixture presented as a white foam, with no macroscopic Li remaining. After extraction into organic solvents and concentration *in vacuo*, the solid residue was further washed with hexane to afford **2a** in 93% yield (2.63 g) with sufficient quality (Fig. 4a). Similarly, the parallel four-batch





**Fig. 5** (a) Large-scale synthesis of **2a** by the Li(0)-mediated mechanochemical Wurtz reaction. (b) Synthesis of benzo[ghi]perylene (**6**) from **2a**.

(7.0 mmol  $\times$  4) and two-batch (14 mmol  $\times$  2) reactions of **1a** in the appropriate jars with balls afforded **2a** in 86% yield (3.42 g) and 72% yield (2.74 g), respectively. Notably, the easily available Wurtz reaction product **2a** was useful in terms of its transformability to valuable benzo[ghi]perylene (**6**)<sup>37</sup> simply by reacting 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) and triflic acid (TfOH). Such a simple protocol including the cyclodehydrogenation and aromatization of **2a** is yet to be reported (Fig. 5b). Together with the observation that scaling up the reactions from the milligram to gram scale did not cause a loss of yield and significant extension of the reaction time, the use of the minimum amount of solvent (THF: 0.9–1.2 eq.) is also highly beneficial considering green chemistry and mass production in process chemistry. Accordingly, the developed mechanochemical Wurtz reaction provides a rapid and highly time-efficient route to preparative-scale synthesis, readily accommodating larger quantities of target materials.

## Conclusions

In summary, a complementary mechanochemical Wurtz reaction of haloalkanes was developed to access diarylethane and higher-

order hydrocarbons. The direct ball-milling of easy-to-handle Li wire, Na lump or Ca shot with bromomethyl arenes in the presence of a stoichiometric amount of THF under air at ambient temperature afforded the desired products rapidly. The developed protocol uses a minimal amount of solvent, features short reaction times with straightforward workups, and is readily scalable. Crucially, the ability to choose between Li, Na and Ca allows the reductant to be matched to the substrate class and reaction scale, providing a practical, safe, and robust alternative to conventional solution-state methods. Furthermore, the Ca(0)-mediated mechanochemical grinding of phenacyl bromide derivatives unexpectedly and effectively afforded 2,4-di- and 2,3,4,5-tetra-substituted furans by unsymmetric reductive coupling. We believe that the present work will contribute to advancements not only in mechanochemistry but also in organic synthesis and organometallic chemistry in solid/slurry states.

## Author contributions

Y. T. synthesized, analyzed, and characterized all compounds. H. I. designed the study and target compounds, supervised the experiments, and conducted data analyses. The draft manuscript was written by Y. T. and finalized by H. I. All authors approved the final version of the manuscript.

## Conflicts of interest

There are no conflicts to declare.

## Data availability

Supplementary information (SI): experimental and characterization data, including crystallographic data, and NMR spectra. See DOI: <https://doi.org/10.1039/d6qo00142d>.

CCDC 2519748 (**5d**) and 2513489 (**2l**) contain the supplementary crystallographic data for this paper.<sup>38a,b</sup>

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