Mechanochemical activation of metallic lithium enabling rapid generation of organolithium species and their applications to organic synthesis

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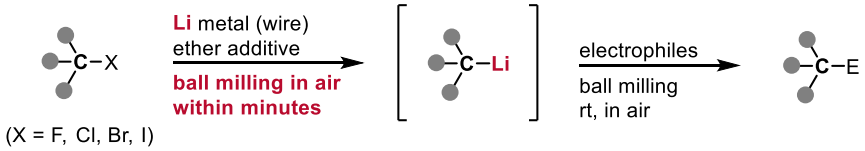
Mechanochemical synthesis, which uses ball-milling to induce chemical reactions, has garnered increased interest in various fields of organic chemistry in recent years.[1] In the area of organometallic synthesis, this method can eliminate the need for complicated operational setups involving inert gases and dry organic solvents and enhance reactivity by activating the surface of zero-valent metals.[2] However, the mechanochemical generation of organolithium compounds has not yet been explored systematically despite the widespread use of such compounds as arguably one of the most fundamental and valuable organometallic reagents in organic synthesis.

Here, we report the first mechanochemical protocol for the direct generation of organolithium reagents from readily available organic halides and unactivated lithium source (lithium wire) under bulk-solvent-free conditions.[3] These reactions rapidly (within minutes) generate a diverse array of organolithium compounds at room temperature without special precautions against moisture and temperature control, and the addition of these compounds to various electrophiles proceeds smoothly in a one-pot fashion. Moreover, the solid-state ball-milling conditions enable the generation of organolithium reagents from poorly soluble aryl halides, which are incompatible with conventional solution-based conditions. Furthermore, the present mechanochemical strategy allows the rapid and direct generation of organolithiums via C–F bond lithiation without using pre-activated lithium sources. Given these attractive features, the present study constitutes an important milestone in the field of organometallic mechanochemistry.



- Carried out under ambient conditions
- Bulk-solvent-free conditions
- Fast metalation (within minutes)
- Applicable to poorly soluble substrates
- No requirement for activated Li sources

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