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## Direct synthesis and applications of solid silylzinc reagents†

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The increased synthetic utility of organosilanes has motivated researchers to develop milder and more practical synthetic methods. Silylzinc reagents, which are typically the most functional group tolerant, are notoriously difficult to synthesize because they are obtained by a pyrophoric reaction of silyllithium, particularly  $\text{Me}_3\text{SiLi}$  which is itself prepared by the reaction of  $\text{MeLi}$  and disilane. Furthermore, the dissolved  $\text{LiCl}$  in silylzinc may have a detrimental effect. A synthetic method that can avoid silyllithium and involves a direct synthesis of silylzinc reagents from silyl halides is arguably the simplest and most economical strategy. We describe, for the first time, the direct synthesis of  $\text{PhMe}_2\text{SiZnI}$  and  $\text{Me}_3\text{SiZnI}$  reagents by employing a coordinating TMEDA ligand, as well as single crystal XRD structures. Importantly, they can be obtained as solids and stored for longer periods at  $4^\circ\text{C}$ . We also demonstrate their significance in cross-coupling of various free alkyl/aryl/alkenyl carboxylic acids with broader functional group tolerance and API derivatives. The general applicability and efficiency of solid  $\text{Me}_3\text{SiZnI}$  are shown in a wide variety of reactions including alkylation, arylation, allylation, 1,4-addition, acylation and more.

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## Introduction

Organosilicon compounds are widely utilized in various disciplines<sup>1</sup> and employed in a broad range of organic transformations.<sup>2</sup> Traditional silylating agents include silanes ( $\text{R}_3\text{SiH}$ ),<sup>2a,h</sup> disilanes,<sup>2f,i,3</sup> silylboranes,<sup>2c,4</sup> electrophilic silyl halides and nucleophilic silyl anions (Fig. 1a). While silanes are extensively utilized in hydrosilylations,<sup>2h,5</sup> silyl halides are usually combined with organometallic reagents to forge C–Si bonds. Noteworthy examples are the recently developed silyl–Negishi and cross-electrophile coupling reactions by Watson<sup>6</sup> and Shu<sup>7</sup> and co-workers. The complementary silyl anions are also well established, and silylzinc reagents in general are one of the most appealing<sup>8</sup> owing to their excellent functional group tolerance. Earlier in 1984, Oshima *et al.* described the synthesis of silylzinc reagents,<sup>9</sup> and Oestreich and co-workers followed up with elegant applications.<sup>10</sup>

However, it is notoriously difficult to synthesize silylzinc reagents because it requires the preparation of silyllithium reagents.<sup>11</sup> In particular, preparation of  $\text{Me}_3\text{SiLi}$  necessitates treating  $\text{MeLi}$  with hexamethyldisilane in HMPA, evincing the remarkably high activation barrier required for effecting Si–X

cleavage. Furthermore, the application of these reagents may be limited due to the dissolved lithium halides. The direct synthesis of silylzinc reagents is undoubtedly a desirable and economical route for the synthesis of silylzinc reagents, as it avoids the handling of pyrophoric silyllithium. Additional benefits may be obtained if the reagents are accessible as solids. Despite the fact that considerable advances have been made in the preparation of organozinc reagents, particularly by



Fig. 1 Synthesis of silylzinc reagents and acylsilanes.

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following Knochel's protocols,<sup>12</sup> the existing methods are not amenable to the synthesis of silylzinc reagents through reductive metalation of zinc to silyl halides.

Acylsilanes, on the other hand, are versatile and unique building blocks in organic synthesis.<sup>13</sup> They undergo a broad range of reactions including nucleophilic addition,<sup>14</sup> transition-metal mediated reactions<sup>15</sup> and intriguing transformations.<sup>16</sup> Importantly they have been utilized as acyl anion synthetic equivalents *via* the Brook rearrangement.<sup>13d,f,14d,15a,17</sup> It is ideal to employ carboxylic acid derivatives to synthesize acylsilanes; indeed, stoichiometric organosilicon reagents<sup>18</sup> or disilanes<sup>19</sup> or stannylsilanes<sup>20</sup> in the presence of catalytic palladium at 110 °C have been employed to synthesize acylsilanes. Despite the initial achievements, the synthesis of acylsilanes still involves a tedious protocol, as seen by the contemporary literature that uses the classical multistep 1,3-dithiane protocol,<sup>21</sup> or inconvenient protocols.<sup>16a</sup> Our attempts to couple silylzinc (prepared from silyllithium) and acid chlorides yielded poor results, perhaps owing to the dissolved LiCl, emphasizing the need for a new and facile synthetic strategy.

Herein we describe the first direct preparation of silylzinc reagents from silyl iodides and subsequent cross-coupling reactions with *in situ* prepared acid chlorides to generate a library of acylsilanes with broad functional group tolerance. In addition, the newly developed solid Me<sub>3</sub>SiZnI was successfully employed in a broad range of organic transformations including alkylation, arylation, allylation, 1,4-addition, acylation, cross-coupling *via* C–N bond cleavage, Brook rearrangement and decarboxylation.

## Results and discussion

We began our studies with silyl iodide **1a** which was prepared from the corresponding PhMe<sub>2</sub>SiH.<sup>6,22</sup> It has been reported in the literature that the activation of zinc is crucial and there are multiple methods known for the activation of zinc<sup>23</sup> including HCl wash,<sup>24</sup> Me<sub>3</sub>SiCl,<sup>25</sup> iodine,<sup>26</sup> ultrasound<sup>27</sup> and dibromoethane activation.<sup>28</sup> We have also followed these protocols for the activation of zinc and subjected them to reductive metalation to silyl iodide **1a**, and the results are summarized in Table 1. As expected, no silylation was observed in the absence of an activator or additive (entry 1). Initially, activation was carried out with Me<sub>3</sub>SiCl (entries 2 and 5); later iodine (entries 3 and 6–8) and DBE (entry 5) were employed to activate Zn. In general, THF was not suitable (entries 1, 2, and 5), and the C–O bond in THF was cleaved under reflux conditions (Fig. 1 and S5–S7 in the ESI†); a similar observation was reported during the synthesis of silylmagnesium reagents.<sup>29</sup> The group of Knochel extensively studied the role of LiCl in the preparation of organometallic reagents including organozinc reagents.<sup>12</sup> The same group reported the combination of LiCl, dibromoethane and Me<sub>3</sub>SiCl which is highly efficient for the preparation of alkyl zinc reagents.<sup>12e</sup> Unfortunately, the inclusion of LiCl as an additive or DBE as an activator was inconsequential (entries 4 and 5).

In the backdrop of our recent findings on the preparation of Me<sub>3</sub>SiMgI from Me<sub>3</sub>SiI<sup>30</sup> and the literature reports on polar solvents such as dimethylacetamide,<sup>26,31</sup>

Table 1 Synthesis of silylzinc reagents<sup>a</sup>

$\text{PhMe}_2\text{Si-I} \xrightarrow[\text{solvent (1.2 M)}]{\text{Zn (2 eq.) activator/additive}} \text{PhMe}_2\text{Si-ZnI} \quad \text{Me}_3\text{Si-ZnI}$ <p style="text-align: center;"><b>1a</b> <span style="margin-left: 150px;"><b>2a</b></span> <span style="margin-left: 50px;"><b>0.56 M 2b</b></span></p>			
Entry	Activator	Additive, solvent, temperature	<b>2a</b> (M)
1	—	THF, 60 °C	ND
2	TMSCl	THF, 60 °C/toluene, 70 °C	ND
3	Iodine	DMA, 80 °C/toluene, 70 °C	ND
4	—	LiCl, toluene, 70 °C	ND
5	DBE	LiCl, toluene, 70 °C/THF, 60 °C	ND <sup>b</sup>
6	Iodine	TMEDA, toluene, 66 °C, 63 h	0.21
7	Iodine	TMEDA, toluene, 70–90 °C, 63 h	0.68 <sup>c</sup>
8	Iodine	NMP/DMA, toluene, 85 °C	ND

<sup>a</sup> Reaction conditions: additive/activator: Me<sub>3</sub>SiCl (0.12 eq.), iodine (0.03/0.05 eq.), DBE (0.03 eq.), LiCl (1.0 eq.), TMEDA (1.1 eq.), NMP/DMA (1.5 eq.). <sup>b</sup> Me<sub>3</sub>SiCl (1.5 mol%) was used. <sup>c</sup> An average of 5 isolated runs. M: molarity, DBE: 1,2-dibromoethane, NMP: *N*-methyl-2-pyrrolidone, DMA: dimethylacetamide, ND: not detected.

hexamethylphosphoramide,<sup>32</sup> *N,N*-dimethylformamide,<sup>26,27,31</sup> dimethylsulfoxide,<sup>32</sup> acetonitrile,<sup>33</sup> tetramethylurea,<sup>27a</sup> CH<sub>3</sub>CN-pyridine<sup>33</sup> and *N*-methyl-2-pyrrolidone (NMP<sup>27a</sup>) favoring the generation of organozinc reagents, we envisioned that amine additives may assist the formation of silylzinc reagents. Pleasingly, we observed a successful reductive metalation of zinc when an industrially friendly solvent,<sup>34</sup> toluene, along with 1.1 eq. of TMEDA was employed as an additive (entry 6). An increase in the reaction temperature also increased the concentration of PhMe<sub>2</sub>SiZnI (entry 6 vs. 7). As shown in entry 8, no reactivity was observed with either NMP or DMA as additives. The methodology is not limited to the synthesis of PhMe<sub>2</sub>SiZnI **2a**; even the relatively less reactive Me<sub>3</sub>SiI was successfully employed to generate more productive Me<sub>3</sub>SiZnI **2b** with 0.56 M (average of 4 runs) concentration. Attempts to synthesize Et<sub>3</sub>SiZnI from Et<sub>3</sub>SiI were made, and although a concentration of 0.16 M was obtained for Et<sub>3</sub>SiZnI, subsequent application utilizing Et<sub>3</sub>SiZnI was unsuccessful. Using Me<sub>3</sub>SiBr instead of Me<sub>3</sub>SiI was likewise unsuccessful, and a poor concentration of 0.04 M was observed. Moreover, these silylzinc reagents (in toluene) stored at 4 °C did not decompose even after six months. Importantly, we obtained the structures of PhMe<sub>2</sub>SiZnI·TMEDA and Me<sub>3</sub>SiZnI·TMEDA from single crystal XRD for the first time (Fig. 2). It is apparent from these structures that TMEDA stabilizes **2a** and **2b**, the driving force for the reductive metalation.

At the outset of our studies, we screened a range of nickel catalysts to obtain the acylsilane **5a** (see ESI S11 and S12† for complete tables). The initial experiments were carried out with the isolated acid chloride **4a** derived from 3-(4-methoxyphenyl) propanoic acid **3a**; however, the later experiments (entries 8–16 and 20) were carried out with free carboxylic acid **3a** *via in situ* generation of acid chloride **4a**. When 10 mol% of NiBr<sub>2</sub>·diglyme was employed, we observed 60% of the cross-coupling product **5a** (entry 1, Table 2). The yield of **5a** was greatly improved by increasing the reaction temperature from 45 °C to 60 °C (entry 1





Fig. 2 X-ray crystal structures of (a)  $\text{PhMe}_2\text{SiZnI} \cdot \text{TMEDA}$  and (b)  $\text{Me}_3\text{SiZnI} \cdot \text{TMEDA}$  complexes; the hydrogen atoms have been omitted for clarity.

vs. 2). It is important to note that the activation of  $\text{NiBr}_2 \cdot \text{diglyme}$  (10 mol%) requires 20 mol% of  $\text{PhMe}_2\text{SiZnI}$ . The other nickel catalysts including  $\text{NiCl}_2$ ,  $\text{Ni}(\text{acac})_2$  and  $\text{NiBr}_2\text{bpy}$  afforded **5a** in only 29%, 66% and 21% yields, with the hydrolyzed acid **3a** being formed as the major byproduct (entries 3–5). To our surprise, the hydrated and air-stable  $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$  afforded the cross-coupled product **5a** in 86% yield (entry 6). A library of ligands was also screened: a simple bipyridine caused a significant reduction in the yield (entry 8), and TMEDA and dppe gave poor yields (entries 9 and 10). The non-polar toluene was not compatible (entry 11). A remarkable improvement in yield to 95% was obtained in DME (entry 12), although the dielectric constant (polarity) and coordinating ability of DME do not significantly vary from those of THF.

Pleasingly, the reaction can be performed at room temperature without a compromise in the yield (entry 13). Interestingly, 5 mol% of  $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$  afforded the cross-coupled **5a** in 86% isolated yield (entry 14). A further decrease in the loading of catalyst (2 mol%) decreased the yield of **5a** (entry 15). When  $\text{Ni}(\text{COD})_2$  was employed as a catalyst, 1.5 eq. of carboxylic acid **3a** was sufficient to obtain excellent yield (entry 16). Virtually no cross-coupled product **5a** was observed in the absence of  $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$  (entry 17). Notably,  $(\text{PhMe}_2\text{Si})_2\text{Zn}^{\text{sa,h}}$  and  $\text{PhMe}_2\text{SiZnCl}^{\text{g}}$  reagents prepared from silyllithium were found to be incompatible and product **5a** was observed in only 23% yield (entry 18); the dissolved LiCl may be at play. The detrimental effect of LiCl was confirmed by the addition of 1 eq. of LiCl to the standard reaction that significantly reduced the yield (entry 19). To expand the synthetic utility, we also conducted the reaction on a 4.2 mmol scale using 5 mol% of  $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$  and obtained **5a** in 80% isolated yield (entry 20). We also found that the mode of addition is critical to obtain a consistent result;  $\text{PhMe}_2\text{SiZnI}$  must be added dropwise at the end of sequential addition, and a change in the sequence resulted in a significant loss of yield.

Having identified the optimal reaction conditions (Table 2, entry 14), we proceeded to examine the scope of carboxylic acids. The primary alkyl carboxylic acids **3a–3g** including the long-chain alkyl carboxylic acid afforded the cross-coupled products **5a–5g** in good to excellent yields. The  $\alpha$ -branched

secondary alkyl carboxylic acids **3h–3i** had no impact on the efficiencies and afforded the corresponding acylsilanes **5h–5i** in very good yields. Aryl carboxylic acids **3j–3no** including  $\pi$ -extended naphthalene-2-carboxylic acid **3k** and alkenyl carboxylic acids **3o–3q** were also compatible, affording the corresponding acylsilanes in good yields. The moderate yield concerning **5bc**, **5m**, **5mn** and **5r–5u** can be attributed to the incomplete reaction, as we observed a significant amount of  $\text{PhMe}_2\text{SiH}$  at the end of the reaction. We have also observed traces of the decarbonylated byproduct during the synthesis of acylsilanes **5mn**, **5no**, **5p**, **5r** and **5t–5u**. Various functional groups such as ethers (**3a**, **3n**, **3no**, and **3s**), alkyl/aryl bromides (**3e** and **3mn**), chloride **3s** and medicinally relevant fluoride **3m** were tolerated, affording the corresponding cross-coupled products in good to high yields. Carbonyls did not impede the reactivity of silylzinc reagents; ester **3f**, ketone **3u** and amide **3s** were compatible, despite their moderate yields. The *O*-tosyl protecting group **3g** was also compatible. The structurally complex API substances did not impede the reaction; indomethacin **3s**, probenecid **3t**, anti-inflammatory drug ibuprofen **3r**, and ketoprofen **3u** afforded the corresponding silylated products **5r–5u**. As we observed lower yields on a few substrates,

Table 2 Optimization<sup>a</sup>

Entry	Deviation from the above	Temp., time	<b>5a</b> <sup>a</sup> (%)
1	$\text{NiBr}_2 \cdot \text{diglyme}$ , THF	45 °C, 4 h	60 <sup>c</sup>
2	$\text{NiBr}_2 \cdot \text{diglyme}$ , THF	60 °C, 4 h	92
3	$\text{NiCl}_2$ , THF	60 °C, 4 h	29 <sup>d</sup>
4	$\text{Ni}(\text{acac})_2$ , THF	60 °C, 4 h	66
5	$\text{NiBr}_2\text{bpy}$ , THF	60 °C, 4 h	21
6	THF	60 °C, 4 h	86
7	20 mol% of CuI or CuCN	60 °C, 4 h	2
8	bpy instead of dtbpy, THF	60 °C, 4 h	70 <sup>d</sup>
9	TMEDA instead of dtbpy, THF	60 °C, 4 h	28 <sup>d</sup>
10	dppe instead of dtbpy, THF	60 °C, 4 h	10
11	Toluene	60 °C, 4 h	38
12	None	60 °C, 4 h	95
13	None	rt, 12 h	90
14	5 mol% $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$	rt, 12 h	94 (86) <sup>f</sup>
15	2 mol% $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$	rt, 12 h	52
16	$\text{Ni}(\text{COD})_2$ (1.5 eq. <b>3a</b> ), THF	rt, 12 h	95
17	Without $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$	rt, 12 h	2
18	Silylzinc from $\text{PhMe}_2\text{SiLi}$	rt, 12 h	23
19	1 eq. LiCl additive	rt, 12 h	42
20	4.2 mmol of <b>2a</b>	rt, 12 h	(80)

<sup>a</sup> Reaction conditions: 0.39 mmol of **3a**, 0.234 mmol of  $\text{PhMe}_2\text{SiZnI} \cdot \text{TMEDA}$  **2a** (0.66 M in toluene), 0.0195 mmol of  $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$  and dtbpy, 0.17 M (overall concentration). Isolated acid-chloride **4a** was used in entries 1–7 and 17–19; *in situ* acid-chloride **4a** was used in entries 8–16 and 20. <sup>b</sup> Yield determined by <sup>1</sup>H NMR using 1,3,5-trimethoxy benzene as an internal standard. <sup>c</sup> 1.3 eq. of  $\text{PhMe}_2\text{SiZnI}$ . <sup>d</sup> Incomplete reaction; unreacted starting material was observed in the crude NMR. <sup>e</sup> 1.0 eq. of  $\text{PhMe}_2\text{SiZnI}$  was used. <sup>f</sup> Reactions were repeated at least 10 times throughout the project. DME: 1,2-dimethoxy ethane, yield in parentheses is isolated yield.





we needed to design a complementary copper catalysis to obtain an increased yield. In place of  $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ , we employed catalytic  $\text{CuI}$  along with  $\text{LiCl}$  additive, which resulted in higher yields for substrates **5m** and **5u**. For substrate **5r**, a dual system incorporating both  $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$  and  $\text{CuI}$  resulted in a significant increase in yield (40% vs. 89%).

Importantly, the reaction is also compatible with  $\text{Me}_3\text{SiZnI}$  **2b**, affording the widely used TMS derived acylsilanes **7** in good to excellent yields. It was necessary to increase the loading of the catalyst to 10 mol% to improve the yield. Similar to  $\text{PhMe}_2\text{SiZnI}$  **2a**,  $\text{Me}_3\text{SiZnI}$  **2b** was also an efficient reagent (Table 4): primary and secondary alkyl carboxylic acids **3a–3i** with various functional groups afforded the cross-coupled products **7a–7i** in good to excellent yields. Aryl and vinyl carboxylic acids **3j–3q** were also compatible to yield the corresponding acylsilanes **7j–7q** in good yields. The API derivatives **7r–7u** were also silylated albeit in lower to moderate yields. In addition, the sterically hindered tertiary alkyl carboxylic acid **3ij** afforded acylsilane **7ij** in lower yield; an incomplete reaction and decarbonylative protonation may account for the lower yield. Both  $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$  and  $\text{Ni}(\text{COD})_2$  afforded the acylsilane **7ij** in similar yields. *N*-Tosyl protected isonipecotic acid **3hi** was compatible affording the acylsilane **7hi** in 58% isolated yield. In general, aryl carboxylic acids gave traces of decarbonylated products and increasing the reaction temperature further increased the undesired decarbonylative silylation. It is worth noting that the decarbonylation can generate catalytically inactive  $\text{L}_n\text{Ni}(\text{CO})_x$  species.<sup>35</sup> Additionally, copper catalysis was employed to improve the yield of product **7m**. Importantly, the dual  $\text{Ni}(\text{OAc})_2/\text{CuI}$  catalytic system significantly improved the yields for substrates **7r** and **7u**. Gram-scale synthesis of acylsilanes **5e** (3.5 mmol), **7a** (5 mmol), and **7e** (4 mmol) was promising with 82%, 70% and 76% isolated yields. Additional screening using  $\text{Ni}(\text{COD})_2$  and anhydrous  $\text{Ni}(\text{OAc})_2$  was done for the low yielding substrates, but no further improvement was observed.

A hypothetical mechanism is shown in Fig. 3. When  $\text{Ni}(\text{OAc})_2$  was exposed to  $\text{Me}_3\text{SiZnI}$  or  $\text{PhMe}_2\text{SiZnI}$ , we observed the formation of disilane with the concomitant formation of a low valent nickel complex, **I**. It has been reported in the literature that the use of organozinc reagents in cross-coupling reactions can lead to either  $\text{Ni}(0)^{12b,36}$  or  $\text{Ni}(I)^{37}$  intermediate complexes.

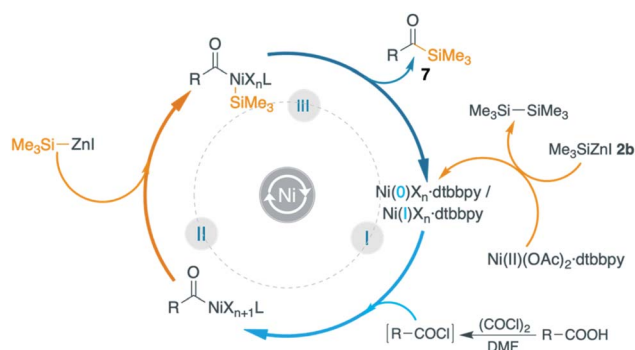


Fig. 3 Mechanistic hypothesis.

The low valent nickel complex **I** undergoes oxidative addition with the *in situ* generated acid chloride to generate the intermediate complex **II**. Subsequent transmetalation to intermediate **III** and reductive elimination affords the acylated product **5** or **7** while regenerating the active catalyst **I**.

In Tables 2–4, the silylzinc reagents **2a** and **2b** were employed as 0.68 M and 0.56 M solutions, respectively. While studying the stability of these reagents, we discovered that they are quite stable in the form of a solid. To study the general applicability of this new solid  $\text{Me}_3\text{SiZnI}$  **2b**, we performed a wide range of organic transformations and the results are summarized in Fig. 4. Initially, both branched and linear allylsilanes **8b** and **9b** were synthesized through allylation. In the presence of catalytic  $\text{CuCN}$ , allyl chloride **8a** was treated with **2b** to generate the branched allylated product **8b** in 73% isolated yield.<sup>8g,38</sup> Using allylic alcohol **9a** in the presence of a nickel catalyst, the linear silane **9b** was likewise produced in 69% yield as a single isomer.<sup>8d,39</sup> Because aryl silanes are commonly used in synthetic applications,<sup>40</sup> we employed **2b** in a nickel-mediated cross-coupling process of aryl bromide **10a**, which resulted in the synthesis of aryl silane **10b** in 70% isolated yield.<sup>41</sup> Cross-coupling of a 2°-alkyl bromide and  $\text{PhMe}_2\text{SiZnCl}$  was recently

Table 3 Cross-coupling with  $\text{PhMe}_2\text{SiZnI}^a$

Reaction scheme	
$\text{R}-\text{COOH} \xrightarrow[\text{DME, rt, 12 h}]{\text{i. (COCl)}_2 (3.0 \text{ eq.}), \text{DMF (20 mol\%)}, \text{DCM}} \text{R}-\text{CO}-\text{SiMe}_2\text{Ph}$	$\text{R}-\text{COOH} \xrightarrow[\text{DME, rt, 12 h}]{\text{ii. Ni(OAc)}_2 \cdot 4\text{H}_2\text{O (5 mol\%)}, \text{dtbpy (5 mol\%)}, \text{PhMe}_2\text{SiZnI (1.1 eq.)}} \text{R}-\text{CO}-\text{SiMe}_2\text{Ph}$
R = alkyl/aryl/alkenyl	

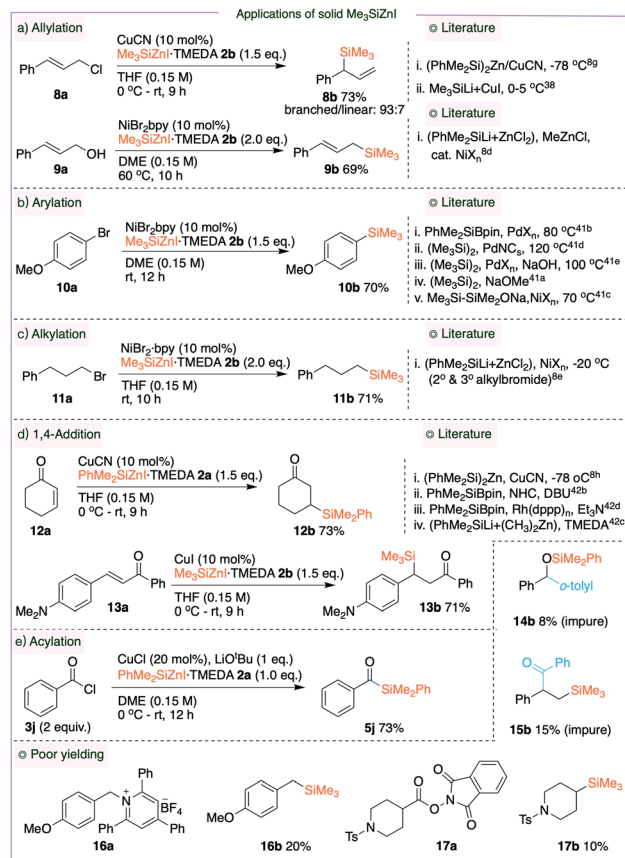
<sup>a</sup> Reaction conditions: 2 eq. of **3**, 1.1 eq. of  $\text{PhMe}_2\text{SiZnI} \cdot \text{TMEDA}$  **2a** (0.66 M in toluene), 5 mol% of  $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ , 5 mol% of dtbpy, 1,2-dimethoxy ethane (0.17 M). <sup>b</sup> Unreactive  $\text{PhMe}_2\text{SiZnI} \cdot \text{TMEDA}$  was observed as  $\text{PhMe}_2\text{SiH}$ . <sup>c</sup> NMR yield. <sup>d</sup> Conditions: 2 eq. of **3**, 1 eq. of  $\text{PhMe}_2\text{SiZnI} \cdot \text{TMEDA}$  (0.71 M in toluene), 20 mol% of  $\text{CuI}$ , 1 eq. of  $\text{LiCl}$ , 1,2-dimethoxy ethane (0.15 M overall concentration), 0 °C – rt. <sup>e</sup> A decarbonylative byproduct was observed. <sup>f</sup> 10 mol%  $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ , 10 mol% 1,10-phen, and 20 mol% of  $\text{CuI}$  were added. <sup>g</sup> The Brook rearrangement was observed.

Table 4 Cross-coupling with  $\text{Me}_3\text{SiZnI}^a$ 

$\text{R}-\text{COOH} \xrightarrow[\text{DME, rt, 12 h}]{\text{i. (COCl)}_2 (3.0 \text{ eq.}), \text{DMF} (20 \text{ mol\%}), \text{DCM}} \text{R}-\text{CO}-\text{SiMe}_3$ $\text{R} = \text{alkyl/aryl/alkenyl}$	
<p><b>1° alkyl</b></p> <p>7a, 82%; 7b, 40% (57%)<sup>b</sup>; 7c, 91%; 7d, 86%; 7e, 77%<sup>c</sup></p> <p><b>2° alkyl</b></p> <p>7f, 35%<sup>c</sup>; 7g, 69%; 7h, 80%<sup>d</sup>; 7i, 58%; 7j, 62%<sup>d</sup></p> <p><b>3° alkyl</b></p> <p>7k, 43% (53%)<sup>b</sup>; 7l, 35% (54%)<sup>b</sup>; 7m, 35% (51%)<sup>b,g</sup></p> <p><b>Aryl carboxylic acids</b></p> <p>7n, 94%; 7o, 62%<sup>h</sup>; 7p, 42%<sup>c</sup>; 7q, 31%<sup>b</sup></p> <p><b>vinyl carboxylic acids</b></p> <p>7r, 46%, 71%<sup>i</sup>; 7s, 23%<sup>c</sup>; 7t, 19%<sup>c</sup>; 7u, 17%, 41%<sup>b,j</sup></p> <p><b>API derivatives</b></p>	<p><b>Applications of solid <math>\text{Me}_3\text{SiZnI}</math></b></p> <p><b>a) Allylation</b></p> <p>8a <math>\xrightarrow[\text{THF (0.15 M), 0 °C - rt, 9 h}]{\text{CuCN (10 mol\%), Me}_3\text{SiZnI-TMEDA 2b (1.5 eq.)}}</math> 8b 73% branched/linear: 93:7</p> <p>9a <math>\xrightarrow[\text{DME (0.15 M), 60 °C, 10 h}]{\text{NiBr}_2\text{bpy (10 mol\%), Me}_3\text{SiZnI-TMEDA 2b (2.0 eq.)}}</math> 9b 69%</p> <p><b>b) Arylation</b></p> <p>10a <math>\xrightarrow[\text{DME (0.15 M), rt, 12 h}]{\text{NiBr}_2\text{bpy (10 mol\%), Me}_3\text{SiZnI-TMEDA 2b (1.5 eq.)}}</math> 10b 70%</p> <p><b>c) Alkylation</b></p> <p>11a <math>\xrightarrow[\text{THF (0.15 M), rt, 10 h}]{\text{NiBr}_2\text{bpy (10 mol\%), Me}_3\text{SiZnI-TMEDA 2b (2.0 eq.)}}</math> 11b 71%</p> <p><b>d) 1,4-Addition</b></p> <p>12a <math>\xrightarrow[\text{THF (0.15 M), 0 °C - rt, 9 h}]{\text{CuCN (10 mol\%), PhMe}_3\text{SiZnI-TMEDA 2a (1.5 eq.)}}</math> 12b 73%</p> <p>13a <math>\xrightarrow[\text{THF (0.15 M), 0 °C - rt, 9 h}]{\text{CuI (10 mol\%), Me}_3\text{SiZnI-TMEDA 2b (1.5 eq.)}}</math> 13b 71%</p> <p><b>e) Acylation</b></p> <p>3j (2 equiv.) <math>\xrightarrow[\text{DME (0.15 M), 0 °C - rt, 12 h}]{\text{CuCl (20 mol\%), LiO}^t\text{Bu (1 eq.), PhMe}_3\text{SiZnI-TMEDA 2a (1.0 eq.)}}</math> 5j 73%</p> <p><b>Poor yielding</b></p> <p>16a <math>\xrightarrow[\text{DME (0.15 M), 0 °C - rt, 12 h}]{\text{CuI (10 mol\%), Me}_3\text{SiZnI-TMEDA 2b (1.5 eq.)}}</math> 16b 20%</p> <p>17a <math>\xrightarrow[\text{DME (0.15 M), 0 °C - rt, 12 h}]{\text{CuI (10 mol\%), Me}_3\text{SiZnI-TMEDA 2b (1.5 eq.)}}</math> 17b 10%</p>

<sup>a</sup> 2 eq. of 3; 1.2 eq. of  $\text{Me}_3\text{SiZnI-TMEDA 2b}$  (0.56 M in toluene, 1.19 mmol); 10 mol%  $\text{Ni(OAc)}_2 \cdot 4\text{H}_2\text{O}$ ; 10 mol% dtbpy; 1,2-dimethoxy ethane (0.17 M). <sup>b</sup> NMR yield. <sup>c</sup> A decarbonylative byproduct was observed. <sup>d</sup> Dimerization of 3 to a diketone was observed. <sup>e</sup>  $\text{Ni(COD)}_2$  (10 mol%) instead of  $\text{Ni(OAc)}_2 \cdot 4\text{H}_2\text{O}$ . <sup>f</sup> Decomposition on silica was observed. <sup>g</sup> Conditions: 2 eq. of 3, 1 eq. of  $\text{PhMe}_3\text{SiZnI-TMEDA}$  (0.71 M in toluene), 20 mol% of CuI, 1 eq. of LiCl, 1,2-dimethoxy ethane (0.15 M overall concentration), 0 °C - rt. <sup>h</sup> 6 mmol of 2b was employed. <sup>i</sup> 10 mol%  $\text{Ni(OAc)}_2 \cdot 4\text{H}_2\text{O}$ , 10 mol% 1,10-phen, 20 mol% of CuI was added.

realized,<sup>8e</sup> and we were ecstatic to see that the new reagent 2b was effective in undergoing the cross-coupling reaction with 1°-alkyl bromide 11a, yielding the alkyl silane 11b in a 71% isolated yield. Fortunately, the copper-mediated 1,4-addition of 2a and 2b with enones 12a and 13a yielded the β-silyl ketones 12b and 13b in 73% and 71% isolated yields, respectively.<sup>8h,42</sup> Acylsilane 5j was also synthesized by coupling of acid chloride 3j and 2a in the presence of CuCl. We also employed 2a in a novel Brook-rearrangement/cross-coupling of benzaldehyde and bromoarene;<sup>43</sup> however, 14b was observed in poor yield. A similar result was obtained in a multi-component reaction between styrene, acid chloride and 2b to yield product 15b.<sup>44</sup> Pyridinium salt 16a and redox ester 17a underwent cross-coupling reactions with 2b to afford alkyl silanes 16b and 17b in only 20% and 10% isolated yields respectively, indicating the need for dedicated studies. Samples of solid  $\text{Me}_3\text{SiZnI 2b}$  were stored at three different temperatures (rt, 4 °C and -23 °C) for a period of two months and subjected in the cross-coupling of 10a to afford the aryl silane 10b. The silylzinc 2b samples stored at 4 °C and -23 °C were equally effective as the freshly prepared reagent; however,  $\text{Me}_3\text{SiZnI}$  (two different batches) stored at room temperature gave poor yield (ESI S52†). It is worth noting that Apeloig and Zhivotovskii *et al.* described the synthesis of solid

Fig. 4 Synthetic applications of solid  $\text{Me}_3\text{SiZnI}$ .

$[(\text{Me}_3\text{Si})_3\text{Si}]_2\text{Zn}$  (stored in a glovebox),<sup>45</sup> which was later used in silylzincation of alkynes.<sup>46</sup>

## Conclusions

In summary, for the first time, we have developed a method for direct synthesis of silylzinc reagents from silyl iodides and their structures were confirmed by single-crystal XRD. Unlike the use of pyrophoric silyllithium in the synthesis of silylzinc reagents, the current method offers a simplified direct method to access them from silyl halides. The absence of dissolved lithium/magnesium salts in these reagents could be beneficial for various chemical processes. We have also demonstrated the practical synthesis of acylsilanes from unactivated alkyl acid chlorides by nickel, copper and dual catalysis. The methodology is compatible with various functional groups, and accommodates sterically hindered secondary and tertiary alkyl carboxylic acids. Structurally complex and API molecules are also silylated conveniently. The general synthetic utility of these reagents is shown in a broad range of reactions. Further study to expand the synthetic scope of these reagents is currently underway in our laboratory.

## Author contributions

The manuscript was written through the contributions of all authors. R. C., F. T. P. and K. S. performed the experiments. All authors have approved the final version of the manuscript.



## Conflicts of interest

The authors declare no competing financial interest.

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