

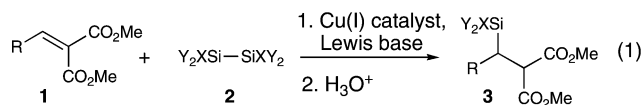
## Copper(I)-Catalyzed Disilylation of Alkylidene Malonates Employing a Lewis Base Activation Strategy

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The efficient incorporation of silicon into organic molecules provides important access to organosilicon compounds with significant utility in organic synthesis.<sup>1</sup> Of the many reactions that accomplish this goal, the conjugate addition of silyl nucleophiles to unsaturated systems is a particularly powerful method for the synthesis of functionalized  $\beta$ -silyl carbonyl compounds. Established approaches for this reaction manifold typically involve stoichiometric additions of anionic silyl nucleophiles.<sup>2</sup> However, an alternate strategy for the overall conjugate addition of silyl groups involves metal-catalyzed disilylations of  $\alpha,\beta$ -unsaturated ketones.<sup>3</sup> Although methods exist that employ this approach, the potentially more useful and general strategy for the disilylation of  $\alpha,\beta$ -unsaturated esters remains an unsolved challenge. In this communication, we report the copper(I)-catalyzed disilylation of alkylidene malonates (**1**) with disilanes (**2**) in the presence of Lewis bases to yield functionalized  $\beta$ -silyl diesters (**3**, eq 1).



The activation of disilanes to generate silyl anions is a well-known process.<sup>4</sup> Recently, it has been demonstrated that the addition of Lewis bases such as 1,3-dimethyl-2-imidazolidinone (DMI) and dimethylformamide (DMF) activate Si–Si bonds for disilylations of unsaturated organic molecules.<sup>5</sup> With this in mind, it was felt that coupling this activation strategy with the use of  $\alpha,\beta$ -unsaturated esters as substrates and readily available disilanes should afford a metal-catalyzed disilylation reaction that would generate highly useful  $\beta$ -silyl esters.

Our initial survey of potential activated unsaturated esters for the desired metal-catalyzed disilylation revealed that the combination of alkylidene malonates (**1**) with commercially available diphenyltetramethyldisilane (**2a**), copper(I) triflate (10 mol %) and tri-*n*-butylphosphine (20 mol %) in DMF gratifyingly afforded the desired  $\beta$ -silyl diester **3a** in moderate yield after in situ hydrolysis (Table 1, eq 2). An investigation of copper(I) sources indicated that, while multiple salts affected the desired reaction, copper(I) triflate was the optimal catalysts in terms of conversion and yield (entries 1–4).<sup>6</sup> Employing Lewis bases such as DMF, DMI, NMP, and HMPA (entries 4–7) were crucial for good levels of conversion, with DMF providing the greatest isolated yield (56%). While modulating the Lewis base component of the reaction has a relatively minimal impact on the process, the absence of such functionality affords no reaction (entry 8). In the cases where toluene is utilized as solvent and DMF is an additive (10 equiv), the reaction proceeds to complete conversion, even at catalyst loadings as low as 5 mol % (entry 9).<sup>7</sup>

With the optimal copper(I) catalyst and solvent mixture identified, the effects of ligand and disilane structure on the reaction were evaluated (Table 2). In the absence of *n*-Bu<sub>3</sub>P, the reaction still

**Table 1.** Effect of Solvent and Catalysts on the Catalytic Disilylation of Alkylidene Malonates **1a**<sup>a</sup>

entry	catalyst	mol%	solvent	conversion <sup>d</sup> (%)	yield (%) <sup>e</sup>
1	CuI	10	DMF <sup>f</sup>	16	4
2	CuCN	10	DMF	16	5
3	CuPF <sub>6</sub> <sup>g</sup>	10	DMF	65	54
4	[CuOTf] <sup>c</sup>	10	DMF	84	56
5	[CuOTf]	10	DMI <sup>h</sup>	75	42
6	[CuOTf]	10	NMP <sup>i</sup>	67	31
7	[CuOTf]	10	HMPA <sup>j</sup>	62	28
8	[CuOTf]	10	toluene	0	—
9	[CuOTf]	5	DMF/toluene <sup>k</sup>	>95	48
10	[CuOTf]	2.5	DMF/toluene	28	21

<sup>a</sup> All reactions are heated at 100 °C for 60 h then quenched with TsOH and H<sub>2</sub>O. <sup>b</sup> CuPF<sub>6</sub>(CH<sub>3</sub>CN)<sub>4</sub>. <sup>c</sup> [(CuOTf)<sub>2</sub>·benzene]. <sup>d</sup> Conversion based on <sup>1</sup>H NMR (500 MHz) spectroscopy. <sup>e</sup> Isolated yield after chromatography. <sup>f</sup> Dimethylformamide. <sup>g</sup> 1,3-Dimethyl-2-imidazolidinone. <sup>h</sup> *N*-Methyl-2-pyrrolidinone. <sup>i</sup> Hexamethylphosphoramide. <sup>j</sup> 10 equiv of DMF in toluene.

**Table 2.** Impact of Ligand on Efficiency of Catalytic Disilylation<sup>a</sup>

entry	ligand	R	DMF (equiv)	conversion <sup>c</sup> (%)	yield (%)
1	none	Ph ( <b>2a</b> )	10	60	32
2	<i>n</i> -Bu <sub>3</sub> P	Ph	1	0	0
3	<i>n</i> -Bu <sub>3</sub> P	Ph	10	>95	48
4	P(OPh) <sub>3</sub>	Ph	10	75	45
5	P(OEt) <sub>3</sub>	Ph	10	>95	52
6	pyridine	Ph	10	>95	67
7	pyridine	vinyl ( <b>2b</b> )	10	70	35

<sup>a</sup> All reactions were heated at 100 °C for 60 h (0.5 M in substrate). <sup>b</sup> [(CuOTf)<sub>2</sub>·benzene]. <sup>c</sup> Conversion based on <sup>1</sup>H NMR (500 MHz) spectroscopy.

proceeds, albeit in lower yield (32%, entry 1). Interestingly, increasing the concentration of *n*-Bu<sub>3</sub>P to 40 mol % (4 equiv relative to CuOTf) or utilizing other phosphines affords no product.<sup>8</sup> However, the use of phosphites (entries 4, 5), promotes the reaction up to 52% yield. In an effort to utilize more convenient ligands, pyridine was employed. Gratifyingly, the reaction proceeds to complete conversion in 67% yield (entry 6). The structure of the disilane also significantly impacts the outcome of the reaction. For example, although 1,2-disubstituted tetramethyldisilanes (diphenyl, divinyl) cleanly afford  $\beta$ -silyl diesters with 10 mol % [CuOTf], 20 mol % pyridine, and 10 equiv of DMF in toluene (entries 6, 7) after hydrolysis, the use of more hindered disilanes does not provide desired product.<sup>9</sup>

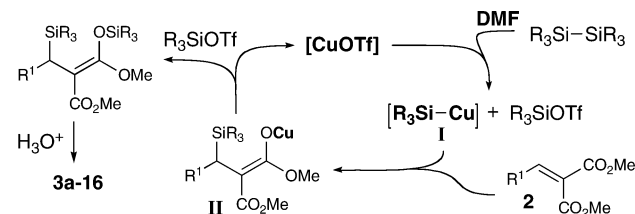
**Table 3.** Catalytic Disilylation of Various Alkylidene Malonates (**1**)<sup>a</sup>

1		2a		3a-16			
entry	R	yield (%)	product	entry	R	yield (%)	product
1	Ph	67	<b>3a</b>	8	1-naphthyl	84	<b>10</b>
2	Cl-Ph	87	<b>4</b>	9	2-naphthyl	84	<b>11</b>
3	4-F-Ph	53	<b>5</b>	10	<i>n</i> -pentyl	60 <sup>c</sup>	<b>12</b>
4	4-NO <sub>2</sub> Ph	0	<b>6</b>	11	(CH <sub>2</sub> ) <sub>2</sub> Ph	37 <sup>c</sup>	<b>13</b>
5	2-furyl	80	<b>7</b>	12	Me	40 <sup>c</sup>	<b>14</b>
6	4-MeOPh	67	<b>8</b>	13	NHCOCF <sub>3</sub>	57	<b>15</b>
7	2-MeOPh	64	<b>9</b>	14	CO <sub>2</sub> Et	— <sup>d</sup>	<b>16</b>

<sup>a</sup> All reactions were heated at 100 °C for 24–60 h. Reported yields are after chromatographic purification. <sup>b</sup> [(CuOTf)<sub>2</sub>·benzene]. <sup>c</sup> 15 mol % [CuOTf], 30 mol % pyridine. <sup>d</sup> Product de-silylates upon hydrolysis.

Once the best conditions had been identified, the scope of the reaction was explored (eq 3, Table 3). With aryl alkylidene malonates, our reaction generates  $\beta$ -silyl diesters in good yield. It is tolerant of both electron-rich and electron-poor aromatic rings. However, the incorporation of a nitro group (entry 4) surprisingly affords no desired product.<sup>10</sup> With slightly higher catalyst loadings, reactions employing alkyl alkylidene malonates generate  $\beta$ -silyl diesters in moderate yields (entries 10–12).<sup>11</sup> Notably, a  $\beta$ -silyl- $\beta$ -amino ester can be generated in moderate yield when  $\beta$ -trifluoroacetamido alkylidene malonate is utilized as a substrate (entry 13, 57% yield).<sup>12</sup>

A plausible catalytic cycle for this reaction is depicted in Scheme 1. Interaction between the Lewis base (DMF) and the disilane produces an activated electron-rich silicon species that undergoes transmetalation to copper(I) triflate. The nucleophilic activation of organosilanes has been observed by <sup>29</sup>Si NMR.<sup>13</sup> The copper intermediate **I** undergoes conjugate addition to alkylidene malonate (**2**), and the resulting copper enolate **II** is trapped by the silyl triflate/silyl Lewis base adduct, thus regenerating the copper(I) catalyst. Pyridine presumably acts as a ligand for copper throughout the catalytic cycle.

**Scheme 1.** Proposed Catalytic Cycle for Disilylation Reaction

The synthetic utility of our  $\beta$ -silyl diester products is highlighted in eq 5. The decarboxylation of **3a** followed by a highly diastereoselective alkylation (dr  $\geq$  20:1) affords  $\alpha$ -substituted- $\beta$ -silyl ester **17** in 62% for the two steps.<sup>14</sup> A straightforward oxidation produces  $\beta$ -hydroxy ester **18** in excellent yield (89%) without elimination.<sup>15</sup>

In conclusion, a copper(I)-catalyzed disilylation of alkylidene malonates has been described. The reaction is broad in scope, utilizes commercially available disilanes and ligands, and provides a new catalytic route to synthetically useful  $\beta$ -silyl diesters in good



yield. Further investigations into the mechanism of this reaction and the development of asymmetric variants of this process are currently under way and will be reported in due course.

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**Supporting Information Available:** Experimental procedures and spectral data for all new compounds (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (8) Phosphines such as (*t*-Bu)<sub>3</sub>P, Cy<sub>3</sub>P, Ph<sub>3</sub>P, and 2-di(*tert*-butylphosphino)-biphenyl give no conversion.
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