

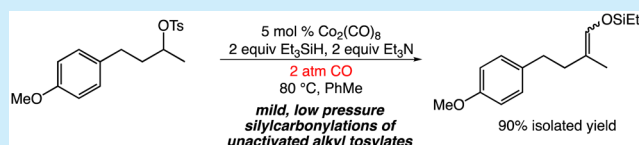
# Cobalt-Catalyzed Silylcarbonylation of Unactivated Secondary Alkyl Tosylates at Low Pressure

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**S** Supporting Information

**ABSTRACT:** A catalytic preparation of silyl enol ethers from unactivated secondary alkyl tosylates is reported. An inexpensive cobalt catalyst is used under mild conditions with low pressures of carbon monoxide. Nucleophilic, anionic cobalt carbonyls facilitate the catalytic activation of a range of alkyl tosylates. The silylcarbonylation offers a practical approach to synthetically valuable silyl enol ethers from simple starting materials.



Catalytic carbonylations of organohalides and sulfonates are important processes for the preparation of a range of valuable chemotypes.<sup>1</sup> Recent studies have developed carbonylations<sup>2</sup> and carboxylations<sup>3</sup> of alkyl electrophiles, which have been much less studied than aryl or vinyl substrates. These catalytic transformations are proposed to involve radical intermediates produced from the activation of alkyl halide substrates. There are few reports involving carbonylations of aliphatic alcohol derivatives (e.g., sulfonates), which are unlikely to participate in single electron processes and require a different approach.<sup>4,5</sup>

A previous report demonstrated the utility of cobalt catalysts in the carbonylation of alkyl sulfonates, but the use of iodide salts suggests the reaction proceeds via alkyl iodides formed in situ (Figure 1).<sup>4</sup> A general approach to the carbonylation of substrates containing C–O bonds was developed by Murai using a catalytic system involving  $\text{Co}_2(\text{CO})_8$  and silanes under a CO atmosphere.<sup>5</sup> The impressive scope of this catalytic system extended to the reactions of esters and lactones to afford silyl

enol ether products. These transformations required elevated CO pressures (50 atm CO) and high temperatures, however.

In previous studies, we developed low-pressure alkoxy carbonylations of secondary alkyl bromides using palladium catalysis.<sup>6</sup> As this system involved carbon-centered radical intermediates formed from single-electron processes, it was ineffective with alkyl sulfonates. We therefore became interested in developing an alternative system for low pressure, carbonylative transformations of alkyl sulfonates. Herein, we report our initial studies in this area which involve a cobalt-catalyzed silylcarbonylation of alkyl sulfonates providing valuable silyl enol ethers under mild conditions.

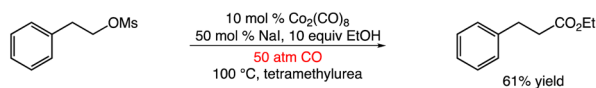
Our studies began by investigating the cobalt-catalyzed silylcarbonylation of secondary alkyl tosylate **1** (Table 1).

**Table 1. Cobalt-Catalyzed Silylcarbonylation of an Unactivated Secondary Alkyl Tosylate<sup>a</sup>**

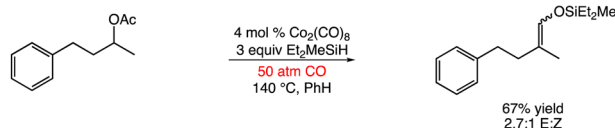
entry	variation from standard conditions above	yield (%) <sup>b</sup>
1	none	77
2	10 mol % $\text{K}[\text{Co}(\text{CO})_4]$ instead of 5 mol % $\text{Co}_2(\text{CO})_8$	78
3	40 °C instead of 80 °C	15
4	8 atm of CO instead of 2 atm of CO	70
5	2 equiv of $\text{K}_3\text{PO}_4$ instead of 2 equiv of $\text{Et}_3\text{N}$	52
6	1 atm of Ar instead of 2 atm of CO	16
7	no $\text{Et}_3\text{SiH}$	0
8	no $\text{Co}_2(\text{CO})_8$	0
9	no $\text{Et}_3\text{N}$	28(13) <sup>c</sup>

<sup>a</sup>Reactions were performed with  $[\text{substrate}]_0 = 0.5 \text{ M}$ . <sup>b</sup>Yields determined by <sup>1</sup>H NMR spectroscopy of crude reaction mixture using HMDS as the internal standard. <sup>c</sup>Yield of aldehyde derivative.

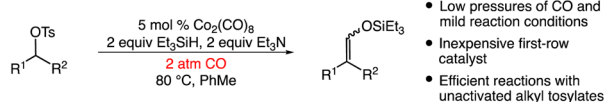
■ Cobalt-catalyzed alkoxy carbonylation of alkyl sulfonates: Fuchikami (1991)



■ Cobalt-catalyzed silylcarbonylation of alkyl acetates: Murai (1986)



■ This work: Cobalt-catalyzed silylcarbonylation of alkyl tosylates



**Figure 1.** Cobalt-catalyzed carbonylations of alkyl acetates and sulfonates.

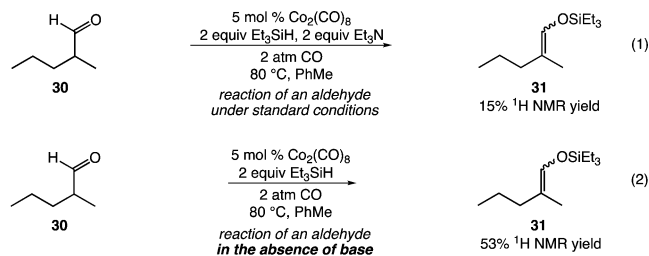
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Commercially available  $\text{Co}_2(\text{CO})_8$  (5 mol %) successfully catalyzed the silylcarbonylation using 2 equiv of  $\text{Et}_3\text{SiH}$  in toluene to afford silyl enol ether **2** in 77% yield (entry 1). Potassium tetracarbonylcobaltate catalyzed the reaction with comparable efficiency to the carbonyl dimer (78% yield, entry 2). Lowering the reaction temperature to 40 °C resulted in a significant decrease in product yield (15% yield, entry 3). Increasing the CO pressure from 2 to 8 atm slightly lowered the reaction yield (70%, entry 4), demonstrating that lower CO pressures are preferred for this transformation. The inorganic base  $\text{K}_3\text{PO}_4$  could also be used, albeit in lower yield (52%, entry 5). In the absence of CO, the reaction provides product **2** in low yield (16%, entry 6). Both  $\text{Et}_3\text{SiH}$  (entry 7) and  $\text{Co}_2(\text{CO})_8$  (entry 8) are required for the reaction to proceed. Finally, in the absence of base a mixture of silyl enol ether **2** (28% yield) and aldehyde (**13**% yield) forms, suggesting that base plays an important role in the silyl enol ether formation (entry 9).

With our optimized conditions in hand, we applied the silylcarbonylation to a range of secondary alkyl tosylates (Table 2). Importantly, the reaction tolerates ether and ester functionality, which underwent cleavage in previous catalytic silylcarbonylations (entries 3–5).<sup>5</sup> The silylcarbonylation of  $\beta$ -alkoxy substrate **13** delivered silyl enol ether **14** in 56% yield, although an increase in the amount of  $\text{Et}_3\text{SiH}$  to 5 equiv was required (entry 7). Silylcarbonylation of the primary chloride **15** proceeded chemoselectively to afford product **16** in 48% yield. Reactions involving more sterically hindered linear tosylates also delivered product, albeit in somewhat decreased yields (entries 9–10). Cyclic substrates were also well tolerated, as cyclopentyl and cycloheptyl tosylates (entries 11–12) as well as 2-norbornyl tosylate (entry 13) were successfully converted to silyl enol ether products.

The silylcarbonylation facilitates the efficient synthesis of a variety of products through elaboration of the versatile silyl enol ether functionality. Representative examples are shown in Scheme 1. In these transformations, the crude product from the silylcarbonylation is directly used in the second step. Desilylation with KF provides aldehyde **27** in 56% yield over two steps. Reduction produces branched alcohol **28** in 71% yield. Bromination of the silyl enol ether provides direct access to  $\alpha$ -bromo aldehyde **29**. Other manipulations of the silyl enol ether are easily envisioned.<sup>7</sup>

We next performed experiments aimed at probing the reaction mechanism of the silylcarbonylation. A major question was the potential intermediacy of an aldehyde prior to silyl enol ether formation. In order to test this possibility, we submitted 2-methylpentanal to the optimized reaction conditions (eq 1).



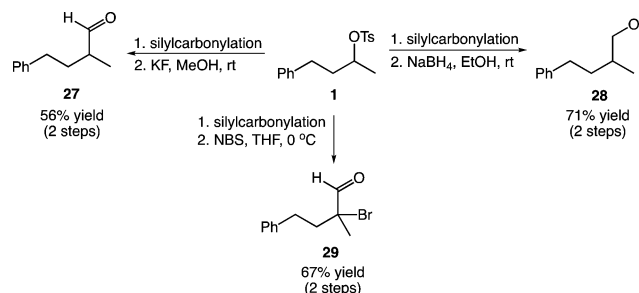
The  $^1\text{H}$  NMR analysis of the crude reaction mixture indicated a 15% yield of silyl enol ether (**31**), which is substantially lower than the silylcarbonylation of similar substrates in Table 2 (i.e., entry 6). However, when the aldehyde was submitted to the optimized reaction conditions *in the absence of base*, a 53% yield of silyl enol ether **31** was obtained (eq 2). These results suggest

Table 2. Low-Pressure Silylcarbonylations of Alkyl Tosylates<sup>a</sup>

entry	substrate	product	yield (%) <sup>b</sup>
1			70
2			82
3			90
4			78
5			74
6			68
7			56 <sup>c</sup>
8			48
9			57 <sup>c</sup>
10			47 <sup>d</sup>
11			57 <sup>d</sup>
12			60
13			61

<sup>a</sup>See Table 1 for conditions. For ratios of stereoisomers, see the Supporting Information. <sup>b</sup>Isolated yields. <sup>c</sup>5 equiv of  $\text{Et}_3\text{SiH}$ . <sup>d</sup>Determined by  $^1\text{H}$  NMR spectroscopy of the crude reaction mixture using HMDS as the internal standard.

Scheme 1. Functionalization of Silyl Enol Ether Products

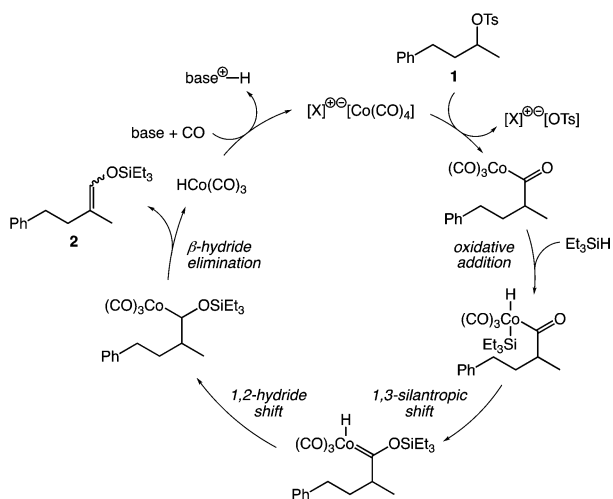


that under our standard conditions in the presence of base, free aldehyde is not a major reaction intermediate, as silyl enol ether formation from aldehydes is inefficient in these reactions.

Based upon our experiments and prior studies, a plausible catalytic cycle for the silylcarbonylation of alkyl tosylates is

depicted in Scheme 2. The reaction begins by substitution of the alkyl tosylate by a cobaltate nucleophile.<sup>8,9</sup> This is followed

**Scheme 2. Plausible Catalytic Cycle for the Silylcarbonylation**



by CO insertion to afford an acyl cobalt complex. Oxidative addition of  $\text{Et}_3\text{SiH}$  is then followed by a 1,3-silantropic shift to deliver a cobalt carbene intermediate.<sup>8,10</sup> A subsequent 1,2-hydride shift is then followed by  $\beta$ -hydride elimination to deliver the silyl enol ether product. Interestingly, the reaction performs poorly with primary alkyl tosylates,<sup>11</sup> which is potentially a result of the decreased rate of  $\beta$ -hydride elimination of alkyl cobalt species with less substitution.<sup>5</sup>

In conclusion, we have developed a cobalt-catalyzed, low pressure transformation of unactivated alkyl tosylates providing silyl enol ethers. This process is a rare example of the catalytic activation of secondary alkyl tosylates. The reaction proceeds under mild conditions and displays a broad substrate scope in the production of synthetically versatile silyl enol ethers. Mechanistic studies are consistent with the direct formation of product without the presence of aldehyde intermediates.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: [10.1021/acs.orglett.7b02117](https://doi.org/10.1021/acs.orglett.7b02117).

Experimental procedures and spectral data for all new compounds (PDF)

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### Notes

The authors declare no competing financial interest.

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