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

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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.

Graphical Abstract

Catalytic carbonylations of organohalides and sulfonates are important processes for the preparation of a range of valuable chemotypes.¹ Recent studies have developed carbonylations² and carboxylations³ 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.^{4,5}

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).⁴ 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 CO atmosphere.⁵ 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.

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

In previous studies, we developed low-pressure alkoxycarbonylations of secondary alkyl bromides using palladium catalysis.⁶ 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). Commercially available $\text{Co}_2(\text{CO})_8$ (5 mol %) successfully catalyzed the silylcarbonylation using 2 equiv of Et_3SiH 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 atm to 8 atm slightly lowered the reaction yield (70%, entry 4), demonstrating that lower CO pressures are preferred for this transformation. The inorganic base K_3PO_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 Et_3SiH (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) form, 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).⁵ The silylcarbonylation of β -alkoxy substrate **13** delivered silyl enol ether **14** in 56% yield, although an increase in the amount of Et_3SiH to 5 equiv was required (entry 7). Silylcarbonylation of the primary chloride **15** proceeded chemoselectively to afford product **16** in 60% 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 α -bromo aldehyde **29**. Other manipulations of the silyl enol ether are easily envisioned.⁷

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 ^1H 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 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.

(1)

(2)

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 nucleophilic substitution of the alkyl tosylate by a cobaltate intermediate.^{8,9} This is followed by CO insertion to afford an acyl cobalt complex. Oxidative addition of Et_3SiH is then followed by a 1,3-silantropic shift to deliver a cobalt carbene intermediate.^{8,10} A subsequent 1,2-hydride shift is then followed by β -hydride elimination to deliver the silyl enol ether product. Interestingly, the reaction performs poorly with primary alkyl tosylates,¹¹ which is potentially a result of the decreased rate of β -hydride elimination of alkyl cobalt species with less substitution.⁵

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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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11. The silylcarbonylation of octyl tosylate under the standard conditions provided the silyl enol ether product in only 30% yield. See the Supporting Information for details.

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

■ *Cobalt-catalyzed silyl carbonylation of alkyl acetates: Murai (1986)*

■ **This work:** *Cobalt-catalyzed silyl carbonylation of alkyl tosylates*

- Low pressures of CO and mild reaction conditions
- Inexpensive first-row catalyst
- Efficient reactions with unactivated alkyl tosylates

Figure 1.

Cobalt-catalyzed carbonylations of alkyl acetates and sulfonates.

Scheme 1.
Functionalization of Silyl Enol Ether Products

Scheme 2.
Plausible Catalytic Cycle for the Silylcarbonylation

Table 1

Cobalt-Catalyzed Silylcarbonylation of an Unactivated Secondary Alkyl Tosylate

entry	variation from standard conditions above	yield (%) ^a
1	none	77
2	10 mol % K[Co(CO) ₄] instead of 5 mol % Co ₂ (CO) ₈	78
3	40 °C instead of 80 °C	15
4	8 atm CO instead of 2 atm of CO	70
5	2 equiv K ₃ PO ₄ instead of 2 equiv Et ₃ N	52
6	1 atm Ar instead of 2 atm CO	16
7	no Et ₃ SiH	0
8	no Co ₂ (CO) ₈	0
9	no Et ₃ N	28(13) ^b

Reactions were performed with [substrate]₀ = 0.5 M.^aYields determined by ¹H NMR spectroscopy of crude reaction mixture using HMDS as the internal standard.^bYield of aldehyde derivative.

Table 2

Low-Pressure Silylcarbonylations of Alkyl Tosylates

entry	substrate	product	yield (%) ^a
1	1: R = H	2: R = H	70
2	3: R = Cl	4: R = Cl	82
3	5: R = OMe	6: R = OMe	90
4	7: R = C(O)OMe	8: R = C(O)OMe	78
5			74
6			68
7			56 ^b
8			48
9			57 ^b

entry	substrate	product	yield (%) ^a
10	19	20	47 ^c
11	21	22	57 ^c
12	23	24	60
13	25	26	61

See Table 1 for conditions. For ratios of stereoisomers, see the Supporting Information.

^a Isolated yields.

^b 5 equiv Et₃SiH.

^c Determined by ¹H NMR spectroscopy of the crude reaction mixture using HMDS as the internal standard.