Cobalt-catalyzed synthesis of silyl ethers via cross-dehydrogenative coupling between alcohols and hydrosilanes

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ABSTRACT

Various commercially available primary and secondary hydrosilanes were exploited for versatile direct dehydrocoupling with alcohols and phenols through cobalt catalysis. The protocol enables efficient Si–O bond formation with a host of O–nucleophiles and silanes (27 examples, 67–91% yield), with precatalyst loadings of 0.5–2 mol%. Beyond enabling a practical and greener approach to silyl ethers, this type of pincer-supported cobalt catalysis provides a blueprint for the development of a broad range of efficient reactions leading to synthetically relevant organometalloids. Moreover, the use of silanes as substrates and precatalyst activators permits the use of inexpensive and easily accessible Earth-abundant metal complexes and avoids the presence of additional activators.

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1. Introduction

Silyl ethers (alkoxysilanes) have found broad applications and thus the development of efficient and practical routes for their synthesis has been a long-standing goal of organic and organometalloidal synthesis (1). Moreover, typically, a direct silylation (mainly trimethylsilylation) arguably represents an important strategy for the protection of the reactive moieties (2–7), including O–H bonds (8–13). To bypass the limitations of stoichiometric approaches that employ sensitive reagents and require large amounts of Brønsted bases to neutralize corrosive by-products (8,14) dehydrogenative coupling methods have been introduced (1,9,10,15,16). From the viewpoint of atom economy, the dehydrocoupling between alcohols and hydrosilanes seems to be the most attractive route, due to the formation of dihydrogen as the sole by-product (17–31). While the use of earth-abundant metals as catalysts and primary/secondary hydrosilanes as substrates remains challenging, the most severe drawback of the vast majority of the current methods continues to be reliance upon strongly basic species (32–37) or expensive transition-metal species (30,38) as catalysts. Moreover, narrow scope of some protocols (39) significantly minimizes their practicability.

Sustainable synthetic methods that proceed in the presence of Earth-abundant catalysts have gained significant attention recently (40–45). In general, these approaches enable cheaper synthesis, which, coupled with lower toxicity and eco-friendly character of 3d-metals is a highly attractive alternative to traditional routes based on noble metal species. Among numerous types of complexes, those stabilized by pincer ligands are known as very robust, chemo-, and regioselective catalysts (46–55). Despite the indisputable progress, cobalt-catalyzed functionalization within the field of organosilicon chemistry is still largely limited to a few examples (56–61). Among these, Chang and Park developed a cobalt-catalyzed hydrosilylation of 3-alkynes with accompanying π-bond migration. The Pawluc group reported on regioselective hydrosilylation of terminal alkynes mediated by Schiff base cobalt(II) complexes (62,63). Then, Gunanathan and co-workers developed a Co-catalyzed synthesis of
symmetrical and unsymmetrical disiloxanes (64). Very recently, the Ye group and the Arzumanyan group reported on independent hydroxylations of hydrosilanes, featuring the utilization of the earth-abundant cobalt catalysts (65,66). Finally, two heterogeneous systems based on cobalt were developed for hydrolysis (67) and alcoholysis (39) of hydrosilanes.

Within our program on cobalt catalysis (68,69), we wondered whether Co-mediated Si–H alkoxylation would be viable. In this article, we report on the catalytic silylation of alcohols and phenols with hydrosilanes for the selective formation of several silyl ethers, by using cobalt complexes stabilized by PN5P ligands as the (pre)-catalysts (Scheme 1). In the context of green and sustainable chemistry, we set out to develop a method for the selective formation of silyl ethers from simple alcohols and phenols.

**Scheme 1. Context of the investigation.**

| Step | Reaction Scheme | Conditions | References |
|------|-----------------|------------|------------|
| **a** | \( RO - H + Cl - SiR_3^\text{Pr} \rightarrow RO - SiR_3^\text{Pr} \) | corrosive HCl, stoichiometric amounts of bases |  |
| **b** | \( PhO - H + H - SiR_3^\text{Pr} \rightarrow PhO - SiR_3^\text{Pr} \) | CoCl\(_2\), 162-245 °C | 1959, 8, 1195–1200, Chem. Commun. 2019, 55, 6563–6566 |
| **c** | \( Co(PN5P)Cl_2 \rightarrow R'_3Si + H - SiR_3^\text{Pr} \rightarrow R'_2B + SiR_3^\text{Pr} \) | our previous works on Co-catalysis | Chem. Eur. J. 2022, 28, e202103629, J. Catal. 2022, 413, 728–734 |
| **d** | \( RO - H + H - SiR_3^\text{Pr} \rightarrow RO - SiR_3^\text{Pr} \) | substantial scope including 1°, 2°, and 3° alcohols, operational simplicity (mild conditions, purification via distillation), commercially available substrates |  |

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sustainable chemistry, several important challenges have been addressed. With the motivation to move away from precious metal complexes and strong bases as well as highly sensitive reagents, we developed an efficient silylation strategy making use of Earth-abundant 3d-metal catalysis (Co) and robust Si sources (hydrosilanes). Notably, considering the combination of desirable features, such as operational simplicity, high chemoselectivity, a wide scope of substrates including challenging tertiary alcohols, excellent atom economy, no need for an external activator, and benign reaction conditions, the presented reaction system provides a promising alternative to existing methodologies. Moreover, some of the reactions were performed under solvent-free conditions (16 examples).

2. Results and discussion

In optimization studies, summarized in Table 1, we investigated catalytic O–H silylation of 3-methyl-3-pentanol (1a). Initial success was achieved using phenylsilane (2a) as the silylating agent, and cobalt complex A as the precatalyst. Using THF as a solvent at 40 °C, this combination of reagents afforded the desired product 3aa in 83% yield (Table 1, entry 1). Control experiments showed that other cobalt precatalysts (B–D) were also active in this transformation (Table 1, entries 7–9), but gave inferior results (e.g., worse chemoselectivity and conversion). The catalyst-free attempt was also carried out and proved the essential role of the 3d metal catalysis (Table 1, entry 2). Here, the reaction was performed in a brand-new Schlenk tube and magnetic stirrer, which is highly important to exclude the influence of even traces of other transition metals (70). Subsequently, a simple cobalt chloride was also examined in this process (Table 1, entry 3), but gave no product as well. Then, we also tried CoCl2 with triphenylphosphine (Table 1, entry 4). It is worth noting that a similar combination with copper is known to be an efficient system for dehydrocoupling reactions (71–73). In this case, we observed only traces of the desired product (<5%). Moreover, it turned out that 0.25 mol% of A enables only slightly lower conversion (Table 1, entries 5), but the presence of monoalkoxylated product was higher as well. We also demonstrated that our process can be performed at room temperature, although the conversion rate was slightly lower (~94%; Table 1, entry 12). Screening of the solvents showed that THF and toluene gave the best conversions and isolated yields (Table 1, entries 1 and 10), with dioxane giving only 30% yield of 3aa. In

![Chemical Structures](image)

**Table 1. Optimization of cobalt-catalyzed O–H silylation.**

| Entry | Variation from standard condition | Conversion of 2a [%]b | Yield of 3aa [%]c | Selectivity [%]d [3aa]: [3aa'] |
|-------|----------------------------------|----------------------|------------------|-----------------------------|
| 1     | no change                        | 100                  | 83               | 100: 0                      |
| 2     | no catalyst                      | 0                    | –                | –                           |
| 3     | CoCl2 instead of A               | 0                    | –                | –                           |
| 4     | CoCl2/PPh3 instead of A          | <5                   | –                | 100: 0                      |
| 5     | 0.25% of A                       | 97                   | 78               | 92: 8                       |
| 6     | 2.5 eq of 1a                     | 98                   | 79               | 95: 5                       |
| 7     | B instead of A                   | 98                   | 74               | 94: 6                       |
| 8     | C instead of A                   | 96                   | 60               | 76: 24                      |
| 9     | D instead of A                   | 21                   | –                | 29: 71                      |
| 10    | in toluenee                      | 91                   | 74               | 96: 4                       |
| 11    | in dioxane                       | 88                   | 30               | 54: 46                      |
| 12    | at room temperature             | 94                   | 77               | 95: 5                       |

General reaction conditions: 1a (3 eq.), 2a (1 eq.), A (0.5 mol%), under argon atmosphere, 40°C, 22 h. bConversion of 2a determined by GC with n-hexane. cIsolated yield. dSelectivity of [double]:[mono] dehydrogenative coupling products determined by GC. eA (1 mol%).
this particular case (Table 1, entry 11), it is worth noting, that precatalyst was much less soluble. Finally, this led to lower conversion and chemoselectivity.

With optimized reaction conditions, we investigated a wide variety of alcohols in the dehydrogenative coupling process with hydrosilanes such as phenylsilane (2a), p-tolylsilane (2b), n-hexylsilane (2c), methylphenylsilane (2d) and diphenylsilane (2e). In this way, we obtained a wide variety of alkoxysilanes in very good yields with low catalyst concentrations and under mild reaction conditions (Scheme 2). Notably, for simple aliphatic alcohols such as methanol (1e) or ethanol (1f), we specifically obtained trisubstituted products (3ae and 3af). Gratifyingly, 2° and 3° alcohols were readily adopted in this protocol, which is quite challenging, especially for analogous base-catalyzed approaches. Unfortunately, selective obtainment of monoalkoxylated products was not possible, whereas a mixture of monosubstituted and disubstituted products was detected. Subsequently, we performed the reaction between 2a and 1,4-pentanediol. Under different conditions, it consistently led to an equimolar mixture of several products.

Moreover, we also tested thiophenol and aniline as the coupling partners. In the case of thiol, we observed no product, only traces of disulfide byproduct (∼2%). On the other hand, the desired silylamine was observed, but the conversion and isolated yield were low (<10%).

Encouraged by these results, we then investigated the use of secondary hydrosilanes (2d and 2e). All of them afforded the expected monoalkoxylated products (Scheme 3) in high yields (3da–3dl and 3ea–3el, 70–87%). These examples include ones bearing halogen (chloro and perfluorinated derivatives), and thioether functionalities. Here, a slightly higher concentration of precatalyst A was required (1 mol%). All these examples highlight both the electronic generality of this method and its tolerance for typically existing organic motifs, showcasing the unique robustness and versatility of our strategy.

Later, we also performed the hydroxylation of 2e. It resulted with 7% of disiloxane product and no traces observed for the corresponding silanol (standard conditions, 24 h). Subsequently, we also investigated the use of tertiary hydrosilanes such as triethylsilane and

Scheme 2. Scope of dehydrogenative coupling products from primary silanes.
dimethylphenylsilane. Unfortunately, they were not reactive under tested conditions. This outcome is in line with our previous studies, where we have shown that tertiary hydrosilanes cannot serve as precatalyst activators.

Finally, our protocol was scaled up to a 10 mmol scale yielding 82% (1.59 g) of the silylated product 3dc (Scheme 4). This once again makes it clear that the proposed methodology has significant application potential.

To gain some mechanistic insights into this 3d metal catalysis, we conducted preliminary experiments. Considering our previous investigations ([68]), again, we confirmed the formation of silyl Co–H species by using General conditions: 1a (2.5 eq.), 2d-e (1 eq.), B (1 mol%), under argon atmosphere, 40 °C, 22 h, [a] 3 eq. of alcohol, [b] A (1 mol%), [c] in THF, [d] B (2 mol%).

Scheme 3. Scope of dehydrogenative coupling products from secondary silanes.

Scheme 4. Scaled up synthesis of 3dc.
1H NMR analysis (please see SI). In this regard, 10 eq. of 2e were added to 1 eq. of precatalyst \( \text{A} \) in [D\(_8\)]THF and stirred at 40°C for 24 h. The result indicates the generation of (PN5P)Co IIIH\(_2\)(SiHPh\(_2\)) (Scheme 5). Moreover, the CoI/CoIII pathway is in line with previous investigations (74,75).

A plausible catalytic cycle based on previous literature and our experimental results is presented in Scheme 6. The silyl Co–H species underwent ligand replacement with alcohol, with simultaneous liberation of H\(_2\). Consequently, the alkoxy silyl cobalt complex is generated, but due to the large thermodynamic driving force, a reductive elimination immediately occurred to give the desired silyl ether. Finally, the active cobalt(I) catalyst is regenerated.

Scheme 5. Proposed activation of the precatalyst \( \text{A} \).

Scheme 6. The plausible mechanism.

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3. Conclusions

In conclusion, we have developed a very efficient protocol for catalytic O–H silylation of primary, secondary, and tertiary alcohols with primary or secondary hydrosilanes under 3d metal catalysis. This transformation does not require any additional activator or harsh conditions (40°C), making it a sustainable alternative to traditional stoichiometric and catalytic reactions. In a broader context, this new example of dehydrogenative coupling significantly expands the scope of this emerging class of reactions. We expect that this external activator-free strategy will streamline the development of several synthetic pathways involving hydrosilanes as the reagents. Thus, further investigations are ongoing in our laboratory.
Disclosure statement
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