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Iron-Catalyzed Silylation of Alcohols by Transfer Hydrosilylation with Silyl Formates

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Abstract An iron catalyst is shown for the first time to promote transfer hydrosilylation with silyl formates and utilized for the silylation of alcohols. Attractive features of this protocol include the use of an earth abundant transition metal catalyst, mild reaction conditions and the release of gases as the only by-products (H₂ and CO₂).

Key words silylation, iron catalysis, silanes, alcohols, silyl formates, hydrosilanes, CO₂

Transfer hydrosilylation consists in the formal transfer of a hydrosilane moiety (R₃SiH) from a silicon reagent (that bears no Si-H bond) to a substrate.¹ It is reminiscent of transfer hydrogenation where a hydrogen donor (e.g., isopropanol or formic acid) is used to deliver an equivalent of H₂ to reduce a C=C or C=O unsaturation.² Although the two methodologies are conceptually related, examples of transfer hydrosilylation reactions have only been disclosed recently with the use of silicon-substituted cyclohexa-1,4-dienes (1,4-CHDN) (1) able to deliver a hydrosilane equivalent with the concomitant release of a benzene derivative (Scheme 1). While Studer et al. explored the radical activation of these hydrosilane surrogates in the transfer hydrosilylation of alkenes,³-⁴ Oestreich et al. exploited their ionic activation for the transfer hydrosilylation of carbonyls, alcohols and alkenes.⁵-⁷ In 2016, Cantat et al. introduced a new type of hydrosilane surrogates with the use of silyl formates (2, R₃SiCHO).⁸ While silyl formates are usually observed as products or intermediates in the hydrosilylation of silyl formates with the use of silyl formates (2, R₃SiCHO).⁸ While silyl formates are usually observed as products or intermediates in the hydrosilylation of CO₂,⁹-¹² the reversible decarboxylation reaction was used to promote the transfer hydrosilylation of aldehydes (Scheme 1).⁶ An advantage of this methodology is the release of a gaseous by-product, CO₂. Earlier this year, the same methodology was employed to convert alcohols to silyl ethers by dehydrogenative and decarboxylative silylation of O-H bonds with silyl formates.¹³ Importantly, the use of silyl formates in transfer hydrosilylation reactions requires a catalyst able to promote the decarboxylation of a formate ligand and the silylation of alcohols and aldehydes could only be achieved using molecular ruthenium(II) complexes.¹⁰,¹³ Further utilization of silyl formates would strongly benefit from the use of noble metal free catalysts and, herein, we show for the first time that iron complexes, supported by a chelating tetraphosphine ligand, enable the silylation of alcohols by transfer hydrosilylation with silyl formates. An improved synthesis of silyl formates is also reported.

Scheme 1 Surrogates of hydrosilanes used in transfer hydrosilylation.

Although silyl formates can be obtained by catalytic hydrosilylation of CO₂,⁹-¹² a more convenient access to these reagents relies on the silylation of formic acid with chlorosilanes, in the presence of an organic base, such as pyridine or triethylamine.⁷ Nevertheless, using this synthesis, free formic acid can be found as an impurity in samples of silyl formates and the presence of such protic species influences the catalytic activity in transfer hydrosilylation. To circumvent this limitation, a new route was exploited where chlorosilanes are reacted with...
sodium formate in ethereal solutions (Scheme 2). Heating a Et₂O solution of Et₃SiCl at 90 °C in the presence of 1.4 equiv. NaOCHO after 12 h, results in the formation of Et₃SiOCHO (2a). After filtration aimed at removing the insoluble NaCl and NaOCHO precipitate and removal of the volatiles under reduced pressure, 2a was isolated in 94% yield. The procedure was successfully applied to the synthesis of a variety of silylformates, including trimethylsilyl (2b), tert-butylmethylsilyl (TBDMs, 2c), diphenyldimethylsilyl (DPMs, 2e), and phenyltrimethylsilyl (PDMS, 2f) substituents. The yield is somewhat lower for 2b (82%), compared to 2c-2g (92-99%), because of the high volatility of the product and TMSiCl, and the reaction was carried out at 60 °C. The bulky trisopropylsilyl (TIPS) formate (2d) could not be obtained in satisfactorily yields and its synthesis was performed with formic acid, in the presence of triethylamine.³ Diethylchlorosilane was efficiently converted to the bis-formate derivative 2g (94% yield) upon reaction with an excess sodium formate (Scheme 2). Silyl formates 2b and to a lesser extent 2a were found to be sensitive towards moisture as they are readily hydrolyzed to formic acid and silanols and siloxanes.

Having in hand a collection of silyl formates bearing different allyl and aryl substituents on the silicon center, their reactivity was evaluated in the dehydrogenative and decarboxylative silylation of alcohols. Silyl ethers are useful chemicals, utilized for the temporary protection of alcohols but also for the synthesis of hybrid materials.¹⁴-¹⁸ Two main routes have been developed to access the O—Si linkage. They rely either on chlorosilanes or hydroxilanes. While the reaction between an alcohol and a chlorosilane, in the presence of a base, generates a stoichiometric amount of a salt,¹⁷-¹⁹ the catalytic dehydrogenative silylation with chlorosilanes has the advantage of releasing H₂ gas as the only by-product.²⁰-²⁶ This year, our group showed that replacing the hydroxilane reagent with a silyl formate enabled the silylation of a variety of alcohols when a catalytic amount of [triphos]Ru(OAc)₂ (triphos = 1,1,1-tris(diphenylphosphinomethyl)ethane) was added.¹³ The role of the Ru catalyst is to promote the decarboxylation of a formate ligand to yield a reactive hydride complex. Based on this assumption, we turned our attention to iron catalysts that are able to engage in similar reaction paths. In particular, Laurenz, Ludwig, Beller et al. demonstrated the potential of iron(II) salts supported by the tetraphosphine ligand P(C₅H₅PPh₂)₃ (4, also labelled PP₃) in the catalytic decomposition of formic acid to H₂ and CO₂.²⁷ Capitalizing on this work, the silylation of benzylalcohol (3) was attempted with Et₃SiOCHO (2a), in the presence of 2 mol% Fe(OAc)₃ and 2 mol% 4. After 5 h at 70 °C in CH₂Cl₂, the reagents were fully consumed and 5a was formed in quantitative yield (Scheme 3) [only 5% 5a were observed in the absence of catalyst].¹Ⅲ and ¹Ⅳ NMR spectra of the crude mixture also confirmed the production of H₂ and CO₂ as by-products of the reaction. The formation of silyl ether 5a from 2a represents the second example of a dehydorgenative silylation of alcohols using silyl formates as surrogates of hydroxilanes.¹³ Although the reaction proceeded well in THF, acetonitrile or benzene, the best conversions were noticed in CH₂Cl₂ (see SI). Decreasing the reaction temperature to 25 °C also enabled formation of 5a in 98% yield, after a prolonged reaction time of 21 h. In comparison, [triphos]Ru(OAc)₂ was found inactive at room temperature (RT).¹³

Scheme 2 Synthesis of silyl formates by salt metathesis from sodium formates and chlorosilanes. [a]The reaction was performed at 60 °C.

Scheme 3 Iron-catalyzed silylation of benzylalcohol (3) to 5a with triethylsilyl formate (2a).

The influence of the silyl group was then investigated on the influence of the transfer hydroxilation reaction. All the silyl formates 2a-2g successfully reacted with 3 to yield silyl ethers 5a-5g, respectively (Scheme 4). Full conversion of 3 was reached within 3 h at 70 °C for the trimethylsilyl derivative 2b while the production of the more congested congeners 5c and 5d, bearing TBDMs and TIPS groups, were limited to 56 and 34% yield, respectively, after 5 h. Interestingly, the aryl-substituted silyl formates 2e and 2f and the bis-formate 2g were fully converted to the corresponding silyl ethers 5e-5g within only 1.5 h, presumably because of the enhanced acidic character at the silicon center.

Scheme 4 Iron-catalyzed silylation of benzylalcohol (3) to 5 with silyl formates (2b-2g).
The potential of the Fe(0Ac)₂/4 catalytic system was further evaluated in the dehydrogenative and decarboxylative silylation of alcohols having various functional groups (Scheme 5). Aliphatic as well as aromatic alcohols were successfully silylated with Et₃SiOCHO (2a), as exemplified with the formation of 6a-15a (from primary and secondary alcohols) and 17a-18a (from phenols). Primary and secondary alcohols exhibit similar reactivities as attested with the formation of silyl ethers 8a and 13a in >96% yields from 2-phenyl-1-propanol and cyclohexanol, respectively. As such, the bis-silylation of the polyfunctional 1-phenyl-1,2-ethanediol to 20b is readily achieved with 2 equiv. 2b. Importantly, the method is also tolerant to oxidizing functional groups such as iodo, nitro, keto and vinyl groups (see 6a, 7a, 12a, and 16b). For example, despite the reductive conditions imposed by the combination of silyl formate 2b and the Fe(OAc)₂/4 catalyst, the silylation of testosterone to 16b is carried out in 92% yield within 2 h without reduction of the enone functionality. Overall, the Fe(OAc)₂/4 presents a catalytic activity and a reaction scope very similar to (triphos)Ru(OAc)₄, with the benefit of utilizing a first row transition metal complex. This is further confirmed with the isolation of silyl ester 21a that can be obtained from the silylation of benzoic acid with 2a and either the iron or ruthenium catalyst.¹³

Preliminary mechanistic investigations with (triphos)Ru(OAc)₂ have shown that the silylation of alcohols with silyl formates results from a two-step process where the metal complex first catalyzes a trans-silylation equilibrium between the reagents to yield the corresponding silyl ether and free formic acid.¹³ The ruthenium plays a second role by catalyzing the irreversible decomposition of formic acid to H₂ and CO₂, thereby driving the production of silyl ether to completion. The transient formation of free formic acid was observed by ‘H NMR spectroscopy upon silylation of 3 with silyl formate 2a and Fe(OAc)₂/4 (Scheme 3), suggesting that the iron catalyst follows a similar reaction path. The hypothesis was further confirmed as Fe(OAc)₂/4 readily dehydrogenates formic acid to H₂ and CO₂ at 90 °C under base-free conditions in CH₂Cl₂ (see SI). To gain deeper insights into the nature of the active iron(II) species, the stoichiometric reaction between Fe(OAc)₂/4 and 2 equiv. Et₃SiOCHO (2a) was carried out in CH₂Cl₂ at 70 °C. Rapid gas evolution indicated the transformation of the iron acetate complex. Isolation of the resulting iron complex by recrystallization from CH₂Cl₂/pentane enabled the structure determination of 22 by X-ray diffraction (Figure 1). 22 is an 18-electron iron(II) hydrido chloro complex supported by the tetraphosphine ligand 4, coordinated with a κ₄-mode.²⁰ The formation of 22 demonstrates the ability of Fe(OAc)₂/4 to yield iron-hydride species in the presence of silyl formates and this chemical behaviour is consistent with previous findings from Beller et al. on the reactivity of iron(II) complexes supported by 4 in the presence of formic acid.²¹

The catalytic implication of 22 was tested in the silylation of 3. As expected, 22 possesses a catalytic activity similar to Fe(OAc)₂/4 and the complex promotes the formation of 5a in the reaction described in Scheme 3. Based on these data, a mechanistic proposal is drawn in Scheme 6: an active iron(II) hydride species (likely 22) is formed from Fe(OAc)₂ in the presence of 4 and the silyl formate reductant. The complex is then able to decompose HCO₂H by successive dehydrogenation and decarboxylation steps, in order to displace the equilibrium involving the alcohol, the silyl ether, and free formic acid to the formation of the silyl ether product.
In conclusion, we have described an efficient synthetic route for the synthesis of silyl formates from chlorosilanes and sodium formates and the first iron catalysts able to utilize silyl formates as surrogates of hydrosilanes. Fe(OAc)$_2$, supported by P(C$_3$H$_5$P$_2$)$_2$Cl, is an efficient catalyst for the dehydrogenative and decarboxylative silylation of alcohols to silyl ethers. The iron catalyst exhibits a catalytic behaviour similar to [triphos]Ru(OAc)$_2$ in this reaction and was shown to produce iron-hydride species in dichloromethane, in the presence of silyl formates. Further efforts are underway in our laboratories to exploit the reducing ability of such intermediates in new transfer hydroxylation reactions.

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Click here to insert acknowledgment text. Funding sources and grant numbers should be given above in the Funding Information section.

**Supporting Information**

YES (this text will be updated with links prior to publication)

**Primary Data**

NO (this text will be deleted prior to publication)

**References and Notes**

31. General procedure for the synthesis of silylformates (2)

In a glovebox, a flame-dried round bottom flask equipped with a Solv-seal connection and a J-Young valve was charged with sodium formate (42 mmol, 1.4 equiv.) and suspended in diethyl ether (30 mL, C = 1 M). To the resulting suspension was added the silyl chloride (30 mmol, 1 equiv.). The flask was then sealed with a sintered glass funnel and the solvent removed by distillation under vacuum at 0 °C. No other purification was needed. The formation of silyl formate was confirmed by 1H, 13C NMR and elemental analysis.
**Analytical data for 2e** is provided below, as a representative example:

$^1$H NMR (200 MHz, d$_8$-THF) δ 8.18 (s, 1H), 7.71 – 7.56 (m, 4H), 7.38 (m, 6H), 0.85 (s, 3H). $^{13}$C NMR (50 MHz, d$_8$-THF) δ 160.88, 135.09, 134.47, 130.99, 128.53, -2.64. Elemental Analysis: calcd (%) for C$_{14}$H$_{14}$O$_2$Si (243.3 g mol$^{-1}$): C 69.39, H 5.82, found: C 69.03, H 5.67.

**General procedure for the transfer hydrosilylation of alcohols with silylformates (5-21)**

In a glovebox, a flame-dried flask equipped with a J-Young valve was charged with Fe(OAc)$_2$ (1.7 mg, 0.01 mmol, 2 mol%) and P(C$_2$H$_4$PPh$_2$)$_3$ (4) (6.7 mg, 0.01 mmol, 2 mol%) followed by CH$_2$Cl$_2$ (2 mL, C = 0.25 M). To the resulting white suspension were sequentially added the alcohol (0.5 mmol, 1 equiv) and the silyl formate (0.6 mmol, 1.2 equiv, per hydroxyl group) reagents. The flask was then sealed, brought out of the glovebox and immersed in a pre-heated oil bath at 90 °C (oil temperature). A purple coloration appeared when heated. At this temperature, all the reactions were generally complete within 1.5 h with silyl formates 2. The coloration observed turned from purple to bright orange. Yields of silyl ethers were determined after isolation and purification by column chromatography on silica gel.

**Analytical data for 16b** is provided below, as a representative example:

$^1$H NMR (200 MHz, d$_8$-THF) δ 5.59 (s, 1H), 3.58 (m, 2H), 1.89 (m, 14H), 1.20 (s, 3H), 1.12 – 0.78 (m, 4H), 0.75 (s, 3H), 0.06 (s, 9H). $^{13}$C NMR (50 MHz, d$_8$-THF) δ 195.30, 167.91, 122.75, 80.52, 49.26, 41.92, 37.52, 35.86, 35.00, 34.79, 32.75, 31.49, 30.85, 29.81, 22.38, 19.69, 15.74, 9.80, -1.61. HRMS (ESI) m/z [M + H]$^+$ calcd. for C$_{14}$H$_{25}$O$_2$Si$^+$: 361.2557; found: 361.2557.