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# C(sp$^3$)–F Bond Activation of $CF_3$-Substituted Anilines with Catalytically Generated Silicon Cations: Spectroscopic Evidence for a Hydride-Bridged Ru–S Dimer in the Catalytic Cycle

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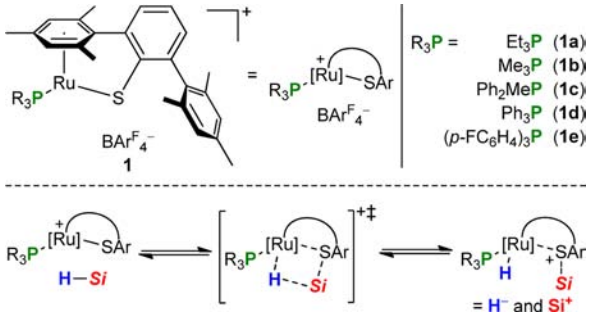
Supporting Information

**ABSTRACT:** Heterolytic splitting of the Si–H bond mediated by a Ru–S bond forms a sulfur-stabilized silicon cation that is sufficiently electrophilic to abstract fluoride from $CF_3$ groups attached to selected anilines. The ability of the Ru–H complex, generated in the cooperative activation step, to intramolecularly transfer its hydride to the intermediate carbenium ion (stabilized in the form of a cationic thioether complex) is markedly dependent on the electronic nature of its phosphine ligand. An electron-deficient phosphine thwarts the reduction step but, based on the Ru-S catalyst, half of an equivalent of an added alkoxide not only facilitates but also accelerates the catalysis. The intriguing effect is rationalized by the formation of a hydride-bridged Ru–S dimer that was detected by $^1$H NMR spectroscopy. A refined catalytic cycle is proposed.

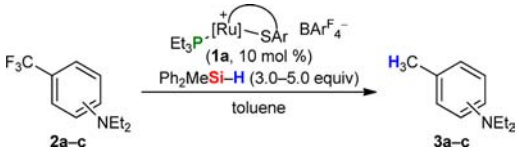
While the C–F bond is one of the thermodynamically strongest covalent single bonds, it is heterolytically activated by exceptionally potent, cationic[1,2] or neutral[3] main group element Lewis acids. Cationic silicon compounds in particular possess a high affinity to fluoride and are well-suited for fluoride abstraction[4−6] as independently shown by the laboratories of Ozerov[1a,c] and Müller.[1b] While these methods usually rely on the preformation of an inter-[1a,c] or intramolecularly[1b] stabilized cationic silicon catalyst, we recently disclosed a new way to catalytically generate a strong silicon electrophile.[7a] Inspired by the related H–H bond activation with late transition metal complexes containing a polar M–S bond,[8] we demonstrated that the tethered Ru–S complex **1a**[9] with an electron-rich phosphine ligand (Scheme 1, upper) is able to activate Si–H bonds to produce a transition metal hydride and a sulfur-stabilized silicon cation[10] (Scheme 1, lower).[7] Using that catalyst, this new methodology enables C-3-selective Friedel–Crafts-type silylation of indoles[7a] as well as direct dehydrogenative formation of silyl enol ethers from ketones.[7b] Both protocols do not require any added base, and dihydrogen is liberated as the sole byproduct. We now report on the hydrodefluorination of $CF_3$ groups catalyzed by a member of the family of those Ru–S complexes **1**. Unexpectedly, added alkoxide was found to accelerate the catalysis, and we provide a mechanistic rationale and propose a refined catalytic cycle based on the $^1$H NMR spectroscopic detection of intermediate mono- and dimeric Ru–H complexes.

**Scheme 1. Tethered Ruthenium Thiolate Complexes and Cooperative Si–H Bond Activation [Ar$^F$ = 3,5-Bis(trifluoromethyl)phenyl]**




Anilines emerged as suitable substrates from exploratory experiments. We were delighted to find that the *para*-$CF_3$-substituted aniline **2a** was hydrodefluorinated with full conversion in 48 h at ambient temperature (Table 1, entry 1). A catalyst loading of 10 mol % of **1a** appears reasonable, considering that the catalysis must pass through three cycles for complete transformation of a $CF_3$ into a $CH_3$ group. The use of regioisomeric anilines demonstrated a strong dependence on both the steric and electronic situation. The *meta*-$CF_3$-substituted aniline **2b** was not even transformed at high temperature and prolonged reaction time (entry 2), indicating

**Table 1. Regioisomeric Anilines in the Ru–S-Catalyzed Hydrodefluorination with Silanes[a]**




| entry | aniline w/ $CF_3$ group | aniline w/ $CH_3$ group | $T$ [°C] | $t$ [h] | conv. [%][b] |
|---|---|---|---|---|---|
| 1 | *para* (**2a**) | *para* (**3a**) | 20 | 48 | >99 |
| 2 | *meta* (**2b**) | *meta* (**3b**) | 100 | 72 | 0 |
| 3 | *ortho* (**2c**) | *ortho* (**3c**) | 100 | 72 | 77 |

[a]All reactions were performed according to the General Procedure 4. [b]Determined by GLC analysis using tetracosane as internal standard.

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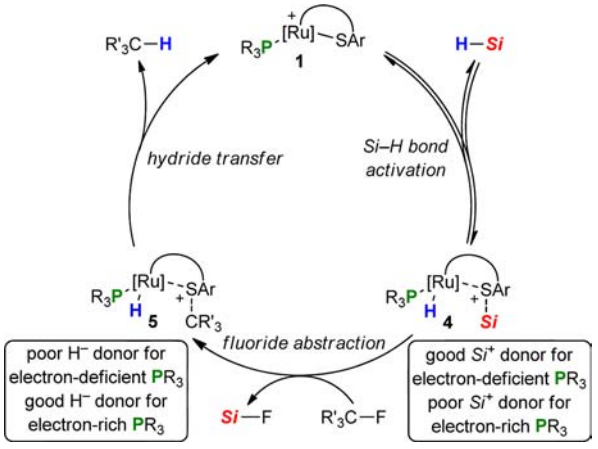
the importance of the electron-donating effect of the $Et_2N$ group. The *ortho*-$CF_3$-substituted aniline **2c**, an example of a good electronic but a poor steric situation, also afforded incomplete conversion after 72 h at 100 °C (entry 3). Partially fluorinated intermediates (with $CHF_2$ or $CH_2F$ groups) were not observed, even in reactions with incomplete conversion. This observation supports a mechanism involving carbenium ions as a result of the fluoride abstraction since its activation barrier is supposed to decrease in the order $CF_3$ > $CHF_2$ > $CH_2F$.

Referring to previous mechanistic insight[7a,9] and supported by experimental observations (see the Supporting Information (SI) for details), we conceived a basic catalytic cycle for the Ru–S-catalyzed hydrodefluorination with its elementary steps (Scheme 2). Si–H bond activation (**1** → **4**) is followed by

**Scheme 2. Elementary Steps of the Ru–S-Catalyzed Hydrodefluorination with Silanes ($BAr^F_4^-$ as Counteranion Omitted for Clarity)**

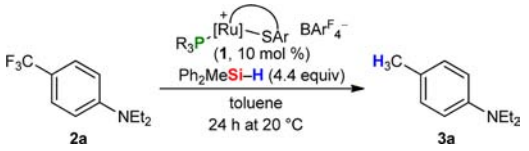



fluoride abstraction (**4** → **5**), forming a fluorosilane and a cationic thioether complex. Complexes similar to **5** arising from C($sp^3$)–X bond activation (X = Br and I) by the Ru–S bond had already been crystallographically characterized by Ohki, Tatsumi, and co-workers.[9] The 18e Ru–H complex **5** then transfers its hydride intramolecularly to afford the hydrocarbon, thereby regenerating the 16e Ru–S complex **1** (**5** → **1**). We assume fluoride abstraction to be rate-determining in the initial $CF_3$ → $CHF_2$ hydrodefluorination, and this is in accordance with the fact that partially fluorinated intermediates with $CHF_2$ and $CH_2F$ groups were not detected.

An obvious starting point for improving the catalyst performance is the variation of the phosphine ligand. We anticipated though that the effect would be antagonistic in the essential steps of the cycle, fluoride abstraction (**4** → **5**) and hydride transfer (**5** → **1**). The above results were obtained with $Et_3P$ as ligand where the latter step is likely to be favored. Changing the phosphine ligand from electron-rich to -poor, this step ought to be disfavored because it destabilizes the cationic 16e Ru–S complex **1**. Conversely, the same effect might be beneficial to the Lewis acidity of the silicon electrophile in **4**.

For a systematic screening of phosphine ligands, in situ formation of the coordinatively unsaturated Ru–S catalysts **1** from the corresponding chloride complexes by treatment with $NaBAr^F_4$ would avoid the capricious small-scale preparation of these reactive 16e complexes. We quickly found out that results are similar with in situ-formed and preformed catalyst **1a** (with $Et_3P$, Table 2, entry 1). We, therefore, tested several phosphines in the in situ protocol. While the reactivity of

**Table 2. Variation of the Phosphine Ligand in In Situ-Formed or Preformed Ru–S Complexes (cf. Scheme 3 for Catalyst Formation)[a]**




| entry | phosphine (complex) | in situ-formed[c] conv. [%][b] | preformed conv. [%][b] |
|---|---|---|---|
| 1 | $Et_3P$ (**1a**) | 67 | 82 |
| 2 | $Me_3P$ (**1b**) | 26 | 17 |
| 3 | $Ph_2MeP$ (**1c**) | 20 | 0 |
| 4 | $Ph_3P$ (**1d**) | >99 | 0 |
| 5 | $(p\text{-}FC_6H_4)_3P$ (**1e**) | >99[d] | 0 |

[a,b]For footnotes *a* and *b*, see Table 1. [c]Complex **1** is formed in situ by using [$(R_3P)Ru(SDmp)Cl$] (**6**, 10 mol %) and $NaBAr^F_4$ (10 mol %). [d]Full conversion after 18 h.

complexes **1b** ($Me_3P$) and **1c** ($Ph_2MeP$) was poor (entries 2 and 3), we were delighted to see that **1d**[9] ($Ph_3P$) resulted in full conversion after 24 h (entry 4). An even more reactive complex formed with *para*-fluorinated aryl groups at the phosphorus atom; full conversion was obtained with **1e** at ambient temperature in 18 h (entry 5). Perfluorinated triarylphosphine $(C_6F_5)_3P$ was too electron-deficient to act as a ligand. To further verify these results, we prepared and characterized complex **1e** separately. Surprisingly, preformed **1e** was inactive (entry 5). The same was true for preformed complexes **1c** and **1d** (entries 3 and 4). Conversely, preformed **1b** behaves similarly to its in situ-formed counterpart (entry 2). These unexcepted findings indicated a subtle influence of the electronic nature of the phosphine on catalyst formation.

A closer look at the ruthenium complex synthesis provided an explanation for the striking reactivity difference of in situ-formed and preformed **1** with electron-deficient phosphines (Scheme 3). For electron-donating phosphine ligands, chloride abstraction from the corresponding Ru–Cl complex **6** with $NaBAr^F_4$ is quantitative at ambient temperature (**6** → **1**). The situation changes with electron-withdrawing phosphine ligands since these impede the formation of cationic complexes **1** with a vacant coordination site. When monitoring the chloride abstraction by $^{31}P$ NMR spectroscopy (in $CD_2Cl_2$ and/or $C_6D_6$ at 20 °C, selected data for the latter in Scheme 3), we observed an additional resonance signal that we assign to the phosphorus atoms of a chloride-bridged ruthenium dimer (**1** + **6** → **7**). This dimer formation appears plausible as it stabilizes these otherwise disfavored 16e complexes **1**. "Free" complexes **1** with electron-deficient phosphines are obtained at higher reaction temperatures with full conversion.

The insight that remaining **6** is critical in lending stabilization to **1** also serves to rationalize the activity of **7** (in situ formation) and inactivity of **1** (preformation) in the hydrodefluorination. The intramolecular hydride transfer that regenerates the coordinatively unsaturated Ru–S complex (cf. **5** → **1**, Scheme 2) becomes rate-determining with electron-withdrawing phosphine ligands. For the in situ protocol, **6** will assist the Ru-to-C hydride transfer through coordination to released **1** (**5** + **6** → **7**, Scheme 4, upper), thereby closing the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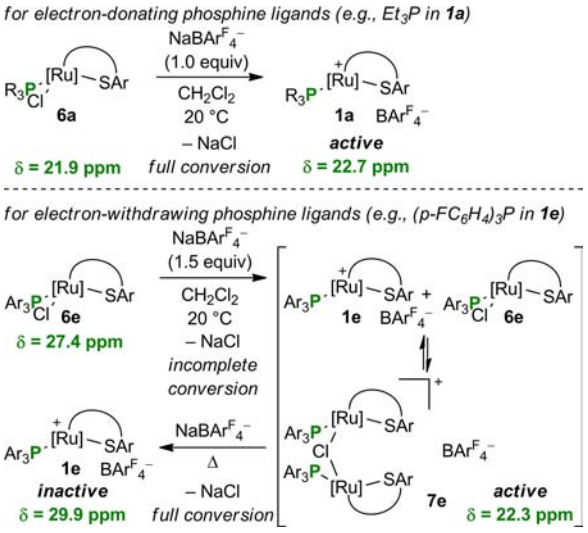
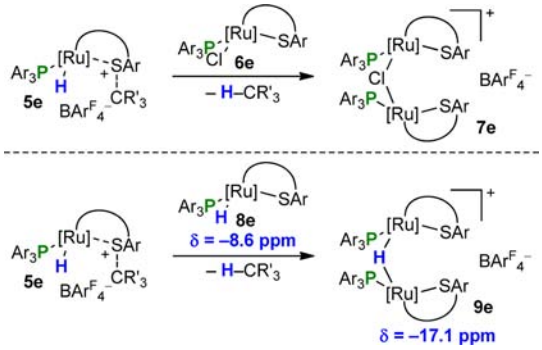
**Scheme 3. Dichotomy in the Catalyst Formation: Electron-Donating vs Electron-Withdrawing Phosphine Ligands (Ar = *p*-$FC_6H_4$)**[a]




[a]All reactions were performed according to the General Procedure 2.

**Scheme 4. Catalyst Dimerization through Chloride and Hydride Bridging: Increasing the Hydride Donor Strength (Ar = *p*-$FC_6H_4$)**

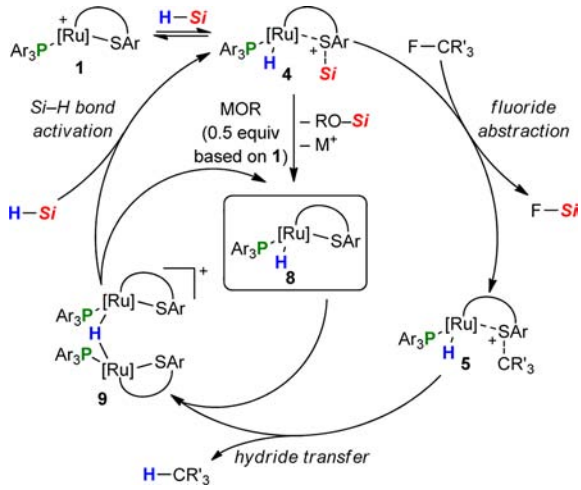



catalyic cycle. It is that step that cannot occur in the absence of any stabilizing donor, and Ru–H complexes **5** with electron-deficient phosphine ligands mark a dead end of the catalytic cycle.

The activating role of remaining Ru–Cl complex **6** through formation of chloride-bridged dimer **7** prompted us to consider hydride bridging to bring about the same net effect (**5** + **8** → **9**, Scheme 4, lower). We hypothesized that deliberate generation of monomeric Ru–H complex **8** would render the formation of hydride-bridged dimer **9** possible. We assumed that sub-stoichiometric amounts (based on catalyst) of alkoxide or hydroxide additives would sequester the silicon electrophile from intermediate **4** (cf. Scheme 2), partially yielding complex **8** required for subsequent stabilization of the vacant coordination site in **1** (**5** + **8** → **9**, Scheme 4, lower). A screening of various additives in the reactions with the inactive preformed complexes **1c**–**1e** (cf. Table 2, entries 3–5) revealed a dramatic effect on catalyst performance (see the SI for details). The catalyses proceeded smoothly at accelerated reaction rate. In turn, stoichiometric amounts of the additive thwarted the hydrodefluorination completely. We were then able to verify the formation of the proposed hydride-bridged dimer **9e** derived from complex **1e** by careful $^1$H NMR analysis (in $C_6D_6$ at 20 °C). A resonance signal at −17.1 ppm is a strong indication for the existence of **9e**; the nonbridged hydride complex **8e** was detected at −8.6 ppm. A similar hydride-bridged dimer with a chemical shift of −17.8 ppm was reported by Shvo et al.[11]

In view of these findings, the catalytic cycle must be extended for the case where electron-withdrawing phosphine ligands are used in combination with an alkoxide additive (Scheme 5).

**Scheme 5. Refined Catalytic Cycle for Ru–S Complexes with Electron-Withdrawing Phosphine Ligands: Remarkable Effect of Alkoxides as Additive ($BAr^F_4^-$ as Counteranion Omitted for Clarity)**




Again, the catalysis commences with cooperative Si–H bond activation at the Ru–S bond (**1** → **4**). As long as the additive is present, the silicon cation will transfer to the alkoxide, yielding an unreactive silyl ether along with Ru–H complex **8** and a weakly Lewis acidic countercation $M^+$ (usually $Na^+$ or $K^+$). That controlled quench of the silicon electrophile secures a steady concentration of **8**. After full consumption of the alkoxide, complex **4** is finally available for fluoride abstraction (**4** → **5**). In the presence of **8**, Ru–H-assisted hydride transfer is now facile, accompanied by the formation of the hydride-bridged dimer **9**. Subsequent Si–H bond activation involving **9** regenerates **4** and releases the facilitator **8**.

With the understanding of the additive effect, we finally optimized the hydrodefluorination protocol by variation of the silane–additive–solvent combination (see the SI for details). Using $Ph_2MeSiH$ and NaOMe in *n*-hexane for the hydrodefluorination of *para*-$CF_3$-substituted aniline **2a** resulted in full conversion after just 6 h at ambient temperature (Table 3, entry 1). As expected, **2b** (*meta*) and **2c** (*ortho*) were far less reactive but **2b** now showed little conversion and **2c** was even fully hydrodefluorinated in 72 h at 60 °C (entries 2 and 3). Excellent conversion was obtained for $CF_3$-disubstituted **2d** at 100 °C (entry 4) but chemoselective hydrodefluorination of the *para*-$CF_3$ group was not possible. Aniline **2e** with a free $NH_2$ group also reacted, subsequent to dehydrogenative *N*-silylation[12] (entry 5). Current efforts are directed toward the expansion of the substrate scope.

To summarize, we disclosed a heterolytic C($sp^3$)–F bond cleavage of activated $CF_3$ groups using a catalytically generated silicon electrophile. The catalysis is likely to proceed through "sulfur-stabilized" silylium and carbenium ions, and the tethered


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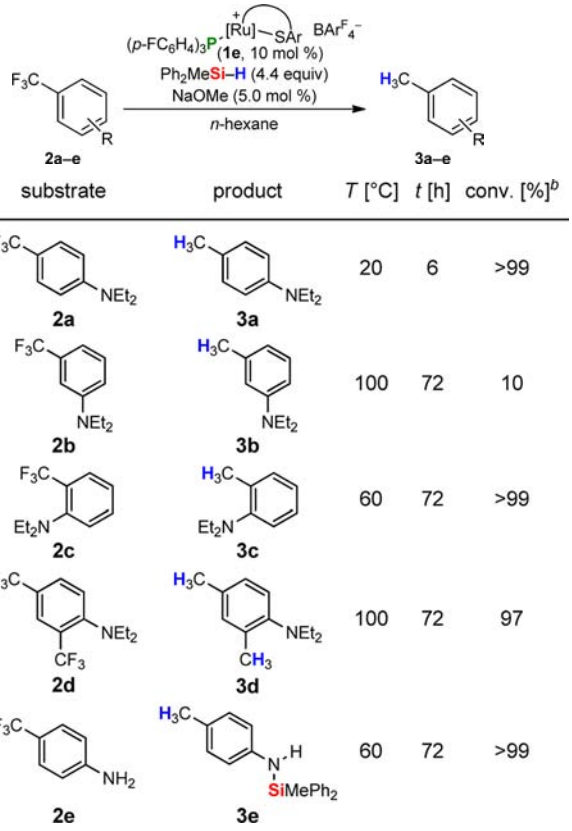
**Table 3. Ru−S-Catalyzed Hydrodefluorination in the Presence of Alkoxide Additive**[a]




[a]All reactions were performed according to the General Procedure 5. [b]Determined by GLC analysis using tetracosane as internal standard. [c]7.0 equiv of $Ph_2MeSiH$ were used. [d]5.0 equiv of $Ph_2MeSiH$ were used.

thiolate ligand in the Ru−S catalyst **1** is instrumental in that. Remarkably, regeneration of coordinatively unsaturated 16e complex **1** proved difficult when electron-withdrawing phosphine ligands were used. That was overcome by the deliberate addition of a silicon cation scavenger (alkoxides or hydroxide) to form a Ru−H (co)catalyst that facilitates the crucial intramolecular Ru-to-C hydride transfer by formation of a hydride-bridged dimeric complex.

## ■ ASSOCIATED CONTENT

### Supporting Information

Experimental details, characterization data, as well as $^{1}H$, $^{11}B$, $^{13}C$, $^{19}F$, $^{29}Si$, and $^{31}P$ NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

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