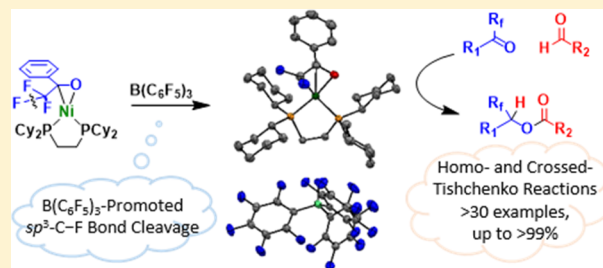


Synthesis, Characterization, and Unique Catalytic Activities of a Fluorinated Nickel Enolate

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S Supporting Information

ABSTRACT: We have synthesized a new nickel enolate $[(\text{PhCOCF}_2)\text{Ni}(\text{dcpe})][\text{FB}(\text{C}_6\text{F}_5)_3]$ featuring fluorine atoms on the enolate moiety via $\text{B}(\text{C}_6\text{F}_5)_3$ -promoted C–F bond activation of α,α,α -trifluoroacetophenone. X-ray diffraction study of $[(\text{PhCOCF}_2)\text{Ni}(\text{dcpe})][\text{FB}(\text{C}_6\text{F}_5)_3]$ revealed that the complex had adopted an η^3 -oxallyl coordination mode in the crystal lattice. The reaction of $^t\text{BuNC}$ with $[(\text{PhCOCF}_2)\text{Ni}(\text{dcpe})][\text{FB}(\text{C}_6\text{F}_5)_3]$ resulted in the coordination of isocyanide to the nickel center to form a C-bound enolate complex. The reactions of $[(\text{PhCOCF}_2)\text{Ni}(\text{dcpe})][\text{FB}(\text{C}_6\text{F}_5)_3]$ with aldehydes gave insertion products quantitatively which were fully characterized by NMR spectroscopy. Furthermore, we established unique catalytic applications for $[(\text{PhCOCF}_2)\text{Ni}(\text{dcpe})][\text{FB}(\text{C}_6\text{F}_5)_3]$ toward a Tishchenko reaction, along with a highly selective crossed-esterification of α,α,α -trifluoroacetophenones with aldehydes.



INTRODUCTION

The synthesis, structure, and reactivity of transition-metal enolates continues to garner interest because of their important roles in various organic transformations.¹ Many transition-metal enolates have been prepared via the nucleophilic displacement of carbonyl compounds bearing a leaving group at the α -position, via the transmetalation of a transition-metal salt with the enolate of a main group element and the oxidative cyclization of α,β -unsaturated carbonyl compounds on $\text{Ni}(0)$.^{2–4} These reactions result in the formation of transition-metal enolates with coordination modes that are classified as either O-bound, C-bound, or η^3 -oxallyl, although most main group elements preferentially bind to the oxygen atom of an enolate (Figure 1a). Despite numerous studies on

their chemistry, only a few examples of fluorinated transition-metal enolates have been established due to a lack of readily accessible synthetic routes. To date, oxidative addition of a C–Cl bond to $\text{Pt}(0)$ is the only method that has been used to successfully obtain the fluorinated analogues of transition-metal enolates (Figure 1b).⁵ Moreover, α -halogenated fluoroketones (such as A and B) are neither easy to prepare nor commercially available. Therefore, trifluoromethylketones could be ideal candidates for the precursors of fluorinated transition-metal enolates when using the well-established preparative procedure making use of inexpensive trifluoroacetic acid derivatives as starting materials.⁶ Amii and Uneyama have reported pioneering work that demonstrates an efficient synthetic method to gain fluorinated-silyl enolates via the treatment of α,α,α -trifluoroacetophenone with magnesium metal and chlorotrimethylsilane via C–F bond activation (Figure 1c).⁷ As far as we could ascertain, there is no precedence for the synthesis of fluorinated transition-metal enolates from trifluoromethylketones. Recently, we developed a Lewis acid-promoted C–F bond activation of perfluoroalkenes⁸ and perfluoroarenes⁹ on $\text{Pd}(0)$ or $\text{Ni}(0)$ to afford a series of fluorinated organometallic complexes. In those reactions, the Lewis acids that were effective were those bearing a strong affinity with fluoride anions such as lithium, magnesium, aluminum, and boron compounds.¹⁰ Herein, we report a C–F bond activation of α,α,α -trifluoroacetophenone coordinated to $\text{Ni}(0)$ promoted by the addition of $\text{B}(\text{C}_6\text{F}_5)_3$, which gives the first example of fluorinated $\text{Ni}(\text{II})$ enolate. Furthermore, a unique catalytic

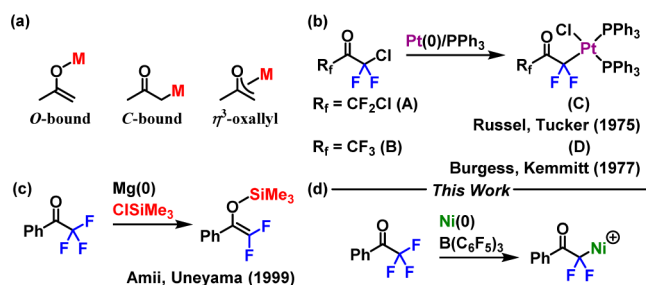


Figure 1. (a) Coordination modes of transition-metal enolates. (b) Fluorinated platinum enolates obtained via C–Cl bond cleavage. (c) Synthesis of fluorinated silyl enolate from readily available trifluoromethylketones. (d) This work: Synthesis of fluorinated $\text{Ni}(\text{II})$ enolate starting from α,α,α -trifluoroacetophenone.

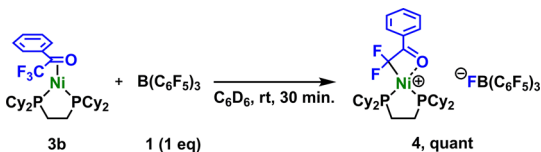
Received: November 14, 2014

activity of the nickel enolate has been demonstrated for the crossed-esterification of aldehydes with α -fluorinated ketones.

RESULTS AND DISCUSSION

We recently reported the selective C–F bond activation of a CF_3 group of hexafluoropropylene on $\text{Pd}(0)$ via the addition of $\text{B}(\text{C}_6\text{F}_5)_3$ (**1**).^{8d} Thus, the C–F bond cleavage of α,α,α -trifluoroacetophenone (**2a**) was also expected by the combination of **1** and low valent transition metals. There are some reports dealing with η^2 -ketone complexes of $\text{Ni}(0)$, including the ones bearing trifluoromethylketones.^{11,12} For instance, Yamamoto et al. have described the synthesis of $(\eta^2\text{-PhCOCF}_3)\text{Ni}(\text{dppe})$ ^{12g} (**3a**, $\text{dppe} = 1,2$ -bis-(diphenylphosphino)ethane). However, complex **3a** led to decomposition following treatment with **1**. Therefore, we decided to use a more electron-rich bidentate phosphine ligand, 1,2-bis(dicyclohexylphosphino)ethane (DCPE) that would result in a nickel center that was more suitable for C–F bond activation by increasing the electron density,¹³ with a resultant $\text{Ni}(\text{II})$ complex that was more stable. The reaction of $\text{Ni}(\text{cod})_2$ and DCPE with **2a** resulted in the formation of $(\eta^2\text{-PhCOCF}_3)\text{Ni}(\text{dcpe})$ (**3b**) in an 85% isolated yield. The signal attributable to the carbonyl carbon in **3b** (73.8 ppm) was observed in the upfield region relative to that of **3a** (79.4 ppm).^{12g} This upfield-shift would be invoked by the stronger electron-donating ability of the DCPE ligand that would enhance $\text{d} \rightarrow \pi^*$ back-donation. Treatment of **3b** with **1** in C_6D_6 afforded $[(\text{PhCOCF}_2)\text{Ni}(\text{dcpe})][\text{FB}(\text{C}_6\text{F}_5)_3]$ (**4**) in a quantitative yield (Scheme 1). It is noteworthy that in the

Scheme 1. Treatment of 3b with 1 To Yield the Fluorinated Nickel Enolate 4



absence of **1**, complex **3b** was thermally stable. In fact, no decomposition was observed after heating the C_6D_6 solution of **3b** at 100°C in a sealed NMR tube for a period of several days.

Nickel complex **4** was fully characterized by NMR, elemental analysis and X-ray crystallography. The ^{19}F NMR spectrum of **4** exhibited a signal that was attributable to CF_2 at $\delta = -100$ ppm (2F, dd, $J_{\text{PF}} = 7, 18$ Hz) and resembled that of previously reported analogous platinum complex **D** (Figure 1b)^{5b} as well as a set of resonances for the $[\text{FB}(\text{C}_6\text{F}_5)_3]$ counteranion.¹⁴ In the ^{31}P NMR spectrum, two sets of doublet of triplets with the same intensity were observed at $\delta = 80$ ($J_{\text{PF}} = 7$ Hz, $J_{\text{PP}} = 11$ Hz) and 82 ppm ($J_{\text{PF}} = 18$ Hz, $J_{\text{PP}} = 11$ Hz). The presence of two ^{31}P resonances was probably due to a weak interaction between the carbonyl oxygen atom and the nickel center preventing a fluxional rotation around the Ni–C bond.¹⁵

Fine crystals of **4** were obtained from the toluene/pentane layer at -35°C . The ORTEP diagram of the cationic portion of **4** depicts a fluorinated enolate complex of $\text{Ni}(\text{II})$ coordinated in an η^3 -oxallyl fashion (Figure 2). The C1–O1 bond length of 1.313(3) Å was an intermediate between a typical C–O double bond (ca. 1.22 Å) and a single bond (ca. 1.44 Å). The bond length of the C1–C2 bond of 1.426(5) Å was also within the range of standard C–C (ca. 1.54 Å) and $\text{C}=\text{C}$ (ca. 1.34 Å) bond lengths.

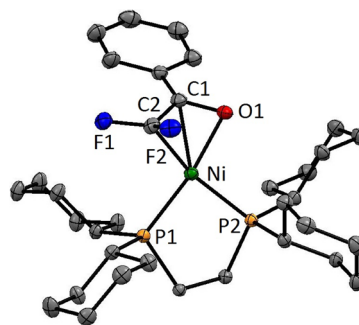
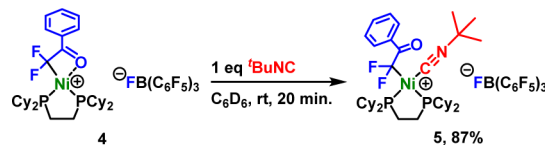


Figure 2. ORTEP representation of the cation of **4** with thermal ellipsoids at the 50% probability level. H atoms and the $[\text{FB}(\text{C}_6\text{F}_5)_3]$ counteranion were omitted for clarity. Selected bond lengths (Å): Ni–P1 2.1590(7), Ni–P2 2.1965(6), Ni–O1 1.922(2), Ni–C1 2.049(2), Ni–C2 1.989(3).

The reaction of **4** with $t\text{-BuNC}$ resulted in the coordination of isocyanide to the $\text{Ni}(\text{II})$ center to give η^1 -C-enolate **5** in an 87% yield (Scheme 2). ^{19}F NMR showed a signal derived from CF_2

Scheme 2. Treatment of 4 with t-BuNC



at $\delta = -79$ ppm (dd, $J_{\text{PF}} = 22, 30$ Hz). In the ^{31}P NMR spectrum, two signals were observed at $\delta = 79$ (dt, $J_{\text{PP}} = 29$ Hz, $J_{\text{PF}} = 22$ Hz) and 78 ppm (dt, $J_{\text{PP}} = 29$ Hz, $J_{\text{PF}} = 30$ Hz). The ^{13}C NMR spectrum exhibited a resonance of carbonyl carbon at $\delta = 194.1$ ppm as a triplet ($^2J_{\text{CF}} = 22.3$ Hz). This was unambiguously supported by X-ray analysis (Figure 3).

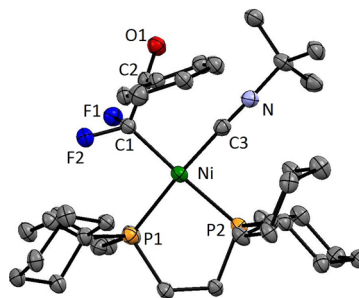


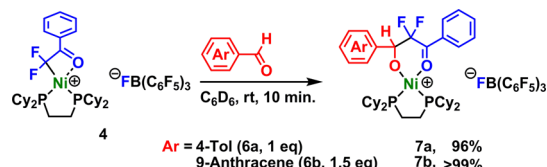
Figure 3. ORTEP representation of the cation of **5** with thermal ellipsoids at the 50% probability level. H atoms and the $[\text{FB}(\text{C}_6\text{F}_5)_3]$ counteranion were omitted for clarity. Selected bond lengths (Å): Ni–P1 2.215(2), Ni–P2 2.215(2), Ni–C1 1.966(7), Ni–C3 1.842(9).

The solid-state structure of **5** showed the square-planar geometry of the $\text{Ni}(\text{II})$ C-bound enolate. The observed C2–O1 bond lengths of 1.219(10) Å and C1–C2 of 1.495(9) Å were typical values of a C–O double bond and a C–C single bond, respectively.

Transition-metal enolates often act as nucleophiles toward aldehydes.¹⁶ For instance, a C-bound nickel enolate reacted with an aldehyde to give aldol products according to a report of Bergman and Heathcock.^{16a} The complex **4** containing electron-withdrawing fluorine atoms on an enolate moiety smoothly reacted with 1 equiv of *p*-tolualdehyde (**6a**) to allow

the migratory insertion of the carbonyl group into the Ni–C bond in a quantitative yield (Scheme 3). This was in sharp

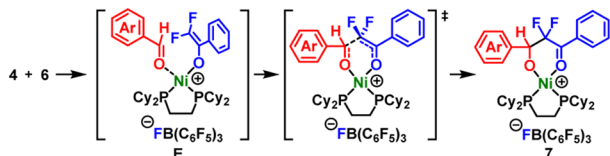
Scheme 3. Insertion of Aldehyde 6a and 6b into Ni–C Bond of 4



contrast to the reactions of corresponding silyl enolates with aldehydes that required the addition of Lewis acids and/or an excess amount of substrates and suffered from low yields.^{7,17}

We think that the C–C bond formation might occur via the Zimmerman–Traxler-type six-membered transition-state initiated by coordination of an aldehyde giving an O-bound enolate intermediate **E** (Scheme 4). This is partly supported by

Scheme 4. A Possible Reaction Pathway to Give Nickel Alkoxide Complex 7



the report of Cámpora et al. in which they concluded that only the O-bound enolate is sufficiently nucleophilic to afford the aldol product by a reaction with an aldehyde, based on unequivocal evidence for the difference of the reactivities between the O-bound Ni(II) enolate and its C-bound tautomer.^{16c} The reaction, however, was too fast to observe any intermediates when the reaction of **4** with **6a** was monitored by means of NMR at $-50\text{ }^{\circ}\text{C}$.

The ^{19}F NMR spectrum of the resultant complex **7a** showed two signals that could be attributable to a diastereotopic CF_2 group at $\delta = -103$ (dd, $J_{\text{HF}} = 9\text{ Hz}$, $J_{\text{FF}} = 270\text{ Hz}$) and -118 ppm (dd, $J_{\text{HF}} = 12\text{ Hz}$, $J_{\text{FF}} = 270\text{ Hz}$). Coupling constants of 9 and 12 Hz were attributable to the $^3J_{\text{HF}}$ coupling and suggested a C–C bond formation between an enolate and an aldehyde. This was consistent with the substantial upfield shift of a signal derived from a formyl group to 4.9 ppm in ^1H NMR that was observed as a broad triplet with a coupling constant of ca. 10 Hz that resulted from the coupling of two fluorine atoms at 9 and 12 Hz. A large coupling constant of 270 Hz for $^2J_{\text{FF}}$ in the ^{19}F NMR is characteristic of geminal coupling between fluorine atoms bound to $\text{sp}^3\text{ C}$. In the ^{31}P NMR spectrum, two signals with equivalent intensities were observed at 88 and 77 ppm and were coupled at 59 Hz. The two inequivalent phosphorus atoms indicated coordination of the carbonyl and newly formed carbinol oxygen atoms to the nickel center. The ^{13}C NMR spectrum of **7a** in CD_2Cl_2 gave signals attributable to CF_2 at 118.7 ppm as doublet of doublet bearing characteristic $^1J_{\text{CF}}$ coupling constants, 251 and 265 Hz, and α -carbons at 202.2 (t, $^2J_{\text{CF}} = 28.5\text{ Hz}$, carbonyl group) and 73.5 ppm (t, $^2J_{\text{CF}} = 23.0\text{ Hz}$, carbinol carbon). Although we could not obtain a single crystal of **7a**, an analogous complex **7b**, generated by the reaction of **4** with 9-anthracenecarboxaldehyde (**6b**), was isolated, and its single crystal was obtained. The molecular

structure of **7b** was determined by X-ray crystallography to be consistent with that deduced by NMR spectroscopy (Figure 4).

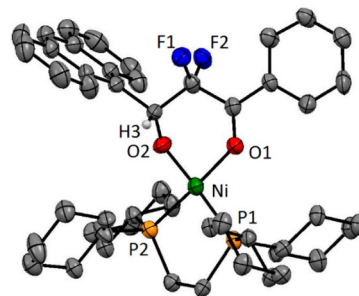
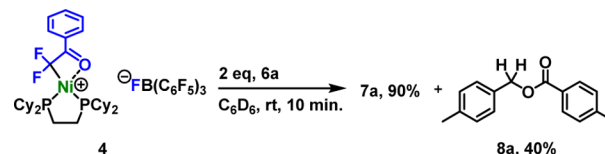


Figure 4. ORTEP representation of the cation of **7b** with thermal ellipsoids at the 30% probability level. H atoms except for H3 and the $[\text{FB}(\text{C}_6\text{F}_5)_3]$ counteranion were omitted for clarity. Selected bond lengths (Å): Ni–P1 2.180(2), Ni–P2 2.136(2), Ni–O1 1.932(5), Ni–O2 1.818(6).

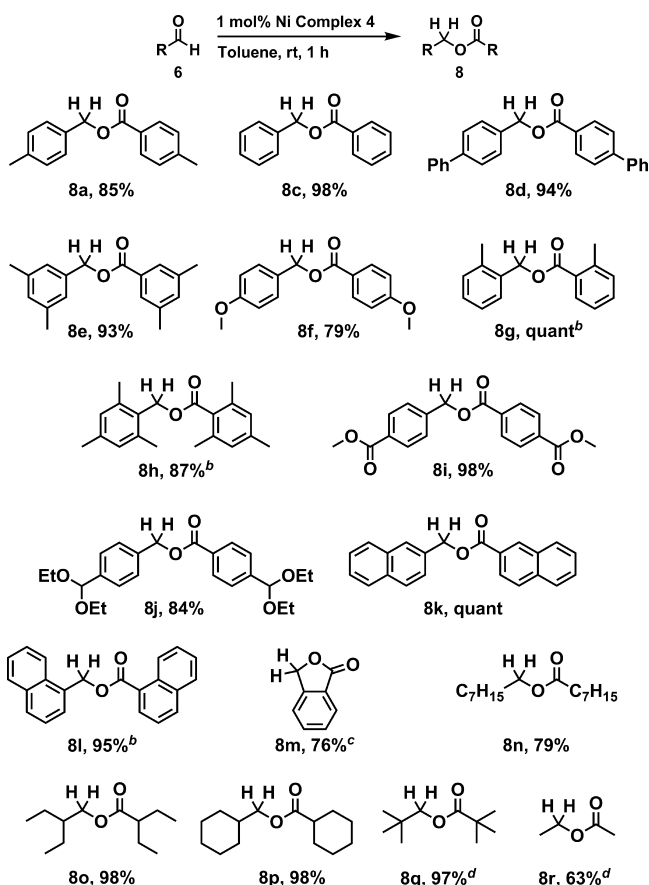
On the other hand, the reaction of **4** with 2 equiv of **6a** also resulted in the formation of **7a** and a homocoupled ester **8a**, which was unexpectedly formed from the residual aldehyde (Scheme 5). The dimerization of aldehydes to give an ester is

Scheme 5. Reaction of 4 with 2 equiv of 6a



known as the Tishchenko reaction, and it is one of the most famous methods of ester synthesis in an atom-economic and waste-free reaction manner.¹⁸ The classical Tishchenko reactions catalyzed by aluminum alkoxides, however, suffer from limited substrate scope. Thus, many catalyst systems have been developed for this promising reaction avoiding side reactions such as the aldol reaction, the Cannizzaro reaction, the Meerwein–Ponndorf–Verley reduction, and the Oppenauer oxidation. Encouraged by our results, we next investigated the catalytic activity of **4** in a Tishchenko reaction (Table 1).

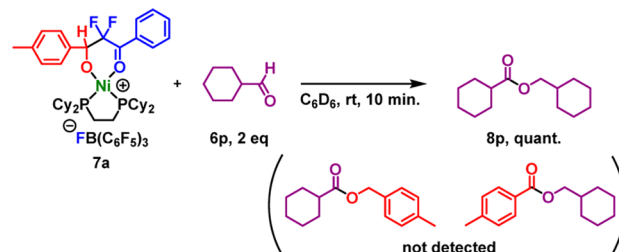
In the presence of 1 mol % of **4**, the reactions of **6a**, benzaldehyde (**6c**), 4-biphenylcarboxaldehyde (**6d**), 3,5-dimethylbenzaldehyde (**6e**), and 4-anisaldehyde (**6f**) afforded the corresponding esters **8a,c–f** in excellent isolated yields under ambient temperature for 1 h. Contrary to these results, 2-tolualdehyde (**6g**) did not react at ambient temperature. However, the reaction proceeded smoothly by heating at $60\text{ }^{\circ}\text{C}$ for 1 h to give the corresponding ester **8g** in a quantitative yield. Even very bulky mesitaldehyde (**6h**) reacted under these conditions to yield **8h** in an 87% yield. Aldehydes bearing either an ester **6i** or an acetal **6j** group were tolerated under these reaction conditions to give **8i** and **8j** in 98 and 84% yields, respectively. The reaction of 2-naphthaldehyde (**6k**) gave the corresponding ester **8k** in a quantitative yield; however, the reaction of 1-naphthaldehyde (**6l**) required an elevated temperature to obtain **8l**. The intramolecular Tishchenko reaction of *o*-phthalaldehyde (**6m**) occurred to give phthalide **8m** in the presence of 2 mol % of **4**, and no oligomer was observed in the crude reaction mixture. This result was in sharp contrast with that of our previous report employing a Ni(0)

Table 1. Substrate Scope of Homo-Esterification of Aldehydes^a

^aIsolated Yields. ^bReactions conducted at 60 °C. ^c2 mol % catalyst loading. ^dNMR yield.

catalyst wherein the reaction of **6m** yielded a complicated mixture as a result of oligomerization.^{19a} Not only aromatic aldehydes but also aliphatic aldehydes such as primary **6n**, secondary **6o** and **6p**, and tertiary alkylaldehyde **6q** were prone to esterification under the reaction conditions to afford the corresponding esters **8n–q** in good to high yields. Furthermore, the catalytic transformation of acetaldehyde (**6r**) into ethyl acetate (**8r**) was accomplished in moderate yield. Complex **4** proved to be an efficient catalyst for the Tishchenko reaction with utility toward both aromatic and aliphatic aldehydes and relatively low degree of catalyst loading.^{19,20}

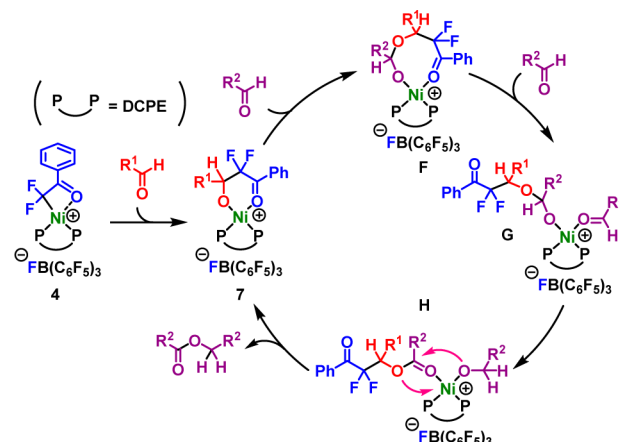
Although the complete reaction mechanism is unclear at this point, we propose that the nickel alkoxide complex **7** might be involved as an active catalyst. The reaction of **7a** with 2 equiv of aldehyde **6p** resulted in a quantitative formation of homoesterification product **8p** (Scheme 6). Note that ester products bearing a *p*-tolyl group derived from **7a** were not detected from the reaction mixture, and complex **7a** was recovered. We also tested the reaction of **7a** with **6k-d₂** with formyl proton deuterated to afford the **8k-d₂**, and no significant scrambling was observed. This result rules out the possibility of nickel-hydride species as an active catalyst, although other metal hydrides often catalyze the Tishchenko reaction. To gain deeper insight into the mechanism, we monitored the reaction of **4** with 2 equiv of **6a** in toluene-*d*₈ by use of a variable-temperature NMR from –50 to 25 °C. Formation of a nickel

Scheme 6. Treatment of **7a** with 2 equiv of **6p**

alkoxide complex **7a** was quite fast even at –50 °C, and complete conversion of the starting complex **4** was confirmed by ¹⁹F NMR. However, at this temperature, starting aldehyde **6a** was observed along with only trace amount of homo-Tishchenko product **8a**. Although the Tishchenko reaction mostly did not proceed below –10 °C, the broadening of the signal of the formyl proton of **6a** was observed by raising the temperature.

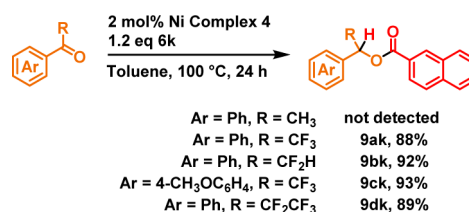
A possible reaction mechanism is described in Scheme 7. First, the reaction of **4** with an aldehyde generates the active

Scheme 7. A Possible Reaction Pathway of the Tishchenko Reaction



catalyst **7**. Insertion of aldehyde into the nickel alkoxide bond in **7** then gives intermediate **F**. The carbonyl group coordinated to the nickel center in an intermediate **F** is replaced by another aldehyde to generate an intermediate **G** that is transformed into **H** by β-hydrogen elimination–insertion sequence. Internal nucleophilic substitution of ester yields the homocoupling product with regeneration of the active catalyst **7**.

Next, we attempted the crossed-esterification of a ketone with an aldehyde (Scheme 8). In the presence of a catalytic amount of **4**, the reaction of acetophenone with **6k** gave no

Scheme 8. Crossed-Esterification of Ketones with Aldehyde **6k**

coupling product and both starting materials were recovered. However, reaction of **2a** with **6k** gave the desired product **9ak** in high yield. The crossed-esterification of **2a** with aldehydes was reported by Connon's group utilizing thiophenoxide or selenoxide catalysts.^{19b,21} The reaction also proceeded with difluoroacetophenone (**2b**) to give the corresponding ester compound **9bk** in a 92% yield. The reactions of 4'-methoxy-2,2,2-trifluoroacetophenone (**2c**) and 2,2,2,3,3-pentafluoropropiophenone (**2d**) were also successful. Note that no coupling product derived from nickel catalyst **4**, i.e., **9ak**, was observed from these reaction mixtures by GCMS. We also attempted the reaction with α -fluoroacetophenone, but the starting materials were recovered from the reaction mixture along with some unidentified products that were not isolable.

In this crossed-esterification reaction, a nickel alkoxide complex generated by insertion of a fluorinated ketone **2** to a fluorinated nickel enolate **4** would be involved as a resting state of the catalyst. The reaction of **2c** with **4** afforded a nickel alkoxide complex **10** that was characterized by NMR spectroscopy (Scheme 9). It is noteworthy that the complex

Scheme 9. Insertion of Ketone **2c** into Ni–C Bond of **4**



10 showed no catalytic activity for homoesterification of aldehyde **6a** at room temperature, probably because the insertion of aldehyde to complex **10**, a possible step involved in the homo-Tishchenko reaction, might not occur. The difference in catalytic activities between alkoxide complexes **10** and **7a** might be rationalized by lower nucleophilicity of **10** bearing a highly electron-withdrawing CF₃ group than that of complex **7a**. To gain further insight, we monitored the reaction of **2a** with **6k** in the presence of catalytic amount of **4** by use of variable-temperature NMR at 95 °C (Figure S1). As a result, interestingly, we observed an induction period that indicates formation of an active catalyst from nickel alkoxide species under the reaction condition. Mechanistic studies to elucidate this phenomenon are ongoing.

These results motivated us to develop a more practical catalyst system for the crossed-esterification of a trifluoromethylketone with an aldehyde in which an active nickel catalyst was generated *in situ* from the reaction of Ni(0), trifluoromethylketone **2**, and **1**. In the presence of 10 mol % of Ni(cod)₂, DCPE, and **1**, the reaction of **2a** with **6a** in toluene at 100 °C resulted in the formation of the corresponding cross-coupled ester **9aa** in an 88% yield (Table 2, run 1). The reaction did not work in the absence of Ni(cod)₂, DCPE, or **2** (runs 2–4). Reactions with other ligands (1,2-bis-(diphenylphosphino)ethane and 1,3-bis(2,6-diisopropylphenyl)imidazole-2-ylidene as well as 20 mol % of PCy₃) gave no coupling product. The use of THF as a solvent allowed the reaction to proceed at a temperature that was lower than that of the reaction conducted in toluene (runs 5, 6). The amount of catalyst loadings could be reduced to 2 mol %, and with this optimized condition, the desired product was successfully isolated in an 88% yield (run 7).

With the optimized reaction conditions in hand, substrate scope was studied (Table 3). The reactions of **2a** with 2,4-

Table 2. Optimization of the Reaction Condition of Crossed-Esterification of a Trifluoroacetophenone **2** with an Aldehyde

run	catalyst	conditions	yield ^{a,b}
1	10 mol %	toluene, 100 °C, 4 h	88%
2	10 mol % ^c	toluene, 100 °C, 4 h	ND
3	10 mol % ^d	toluene, 100 °C, 4 h	ND
4	10 mol % ^e	toluene, 100 °C, 4 h	ND
5	10 mol %	toluene, 60 °C, 5 h	64%
6	10 mol %	THF, 60 °C, 5 h	87%
7	2 mol %	THF, 60 °C, 24 h	88% ^f

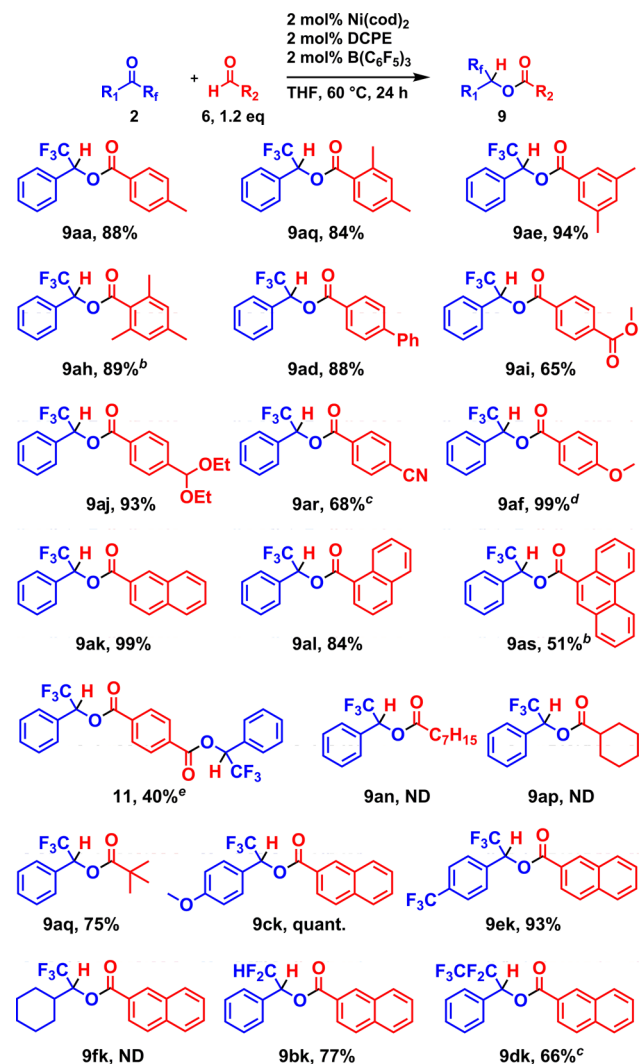
^aYields were determined by GC using tetradecane as an internal standard. ^bND = not detected. ^cWithout DCPE. ^dWithout **1**. ^eWithout Ni(cod)₂. ^fIsolated Yield.

dimethylbenzaldehyde **6q** and 3,5-dimethylbenzaldehyde **6e** gave corresponding cross-coupled esters **9aq** and **9ae** in 84 and 94% yields, respectively. A bulky aldehyde **6h** reacted to give ester **9ah** in a high yield using an elongated reaction time. The reaction of **6d** was also successful, and the structure of the product **9ad** was confirmed by X-ray crystallography (Figure S5). The ester and acetal groups on the aldehydes survived under these reaction conditions and gave the corresponding esters **9ai** and **9aj**. The reaction of *p*-formylbenzonitrile **6r** was unsuccessful under the optimized conditions listed above, and the starting materials were recovered. The reaction conducted in toluene at 100 °C, however, yielded the corresponding ester **9ar** in a moderate yield. In the same manner, the reaction of **2a** with **6f** afforded a quantitative product **9af** in toluene at 100 °C. Naphthaldehydes **6k** and **6l** reacted with **2a** to give the corresponding esters **9ak** and **9al** in THF at 60 °C for 24 h. Using an aldehyde bearing the phenanthrene structure **6s** required a much longer time to yield the ester product **9as**. The reaction of *p*-phthalaldehyde with 2 equiv of **2a** resulted in the conversion of both aldehyde moieties to afford diester **11** in a 40% yield. The reactions of **2a** with aliphatic aldehydes such as **6n** and **6m** were unsuccessful in delivering the required products **9an** and **9ap**. The reaction of **2a** with **6q**, however, gave the corresponding ester **9aq** in a 75% yield. Both trifluoroacetophenone bearing electron-donating methoxy group **9c** and -withdrawing CF₃ group **9e** reacted cleanly to give the desired product in high yields. The reaction of alkylketone **2f** with **6k** gave no coupling product. Difluorinated ketone **2b** reacted with **6k** to give the corresponding ester **9bk** in a good yield. This result implies formation of an active nickel catalyst from α,α -difluorinated ketone. The reaction of **9d** conducted in THF resulted in a low conversion of starting materials. Therefore, we attempted the reaction in toluene at an elevated temperature (100 °C), which afforded the desired ester **9dk** in a 66% yield.

CONCLUSION

In summary, we have demonstrated the first synthesis of a fluorinated analogue of nickel enolate **4**, via the C–F bond activation of trifluoroacetophenone, which was drastically accelerated by the addition of B(C₆F₅)₃. The combination of Ni(0) with an electron-rich DCPE ligand might be the key to

Table 3. Substrate Scope of Crossed-Esterification of Trifluoroacetophenone 2 with Aldehydes 6 by Using *in Situ*-Generated Catalyst^a



^aIsolated Yields. ND = not detected. ^b50 h. ^cReactions conducted at 100 °C in toluene. ^dReactions conducted at 100 °C in toluene for 48 h. ^e4 mol % catalyst loading.

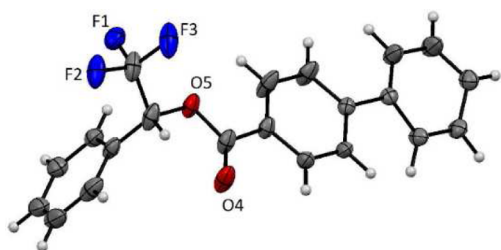


Figure 5. Molecular structure of 9ad.

observe successful activation of the C–F bond. The reaction of 3 with ^tBuNC resulted in coordination to the nickel center to give nickel C-bound enolate 5. The complex 4 was reactive to aldehyde, and the resultant complex 7 was fully characterized. Furthermore, complex 4 showed unique catalytic activities toward either the dimerization of aldehydes or the crossed-esterification of trifluoroacetophenone with aldehydes. The established method was further improved in a practical sense by

the *in situ* generation of a nickel-enolate catalyst. Thus, we have successfully developed an efficient Ni(cod)₂/DCPE/B(C₆F₅)₃ catalyst system for a highly selective crossed-esterification of trifluoroacetophenones with aldehydes. Detailed studies on the reaction mechanism of esterification are currently underway in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details of isolation and characterization of all the new compounds are described along with spectral data. 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.

■ ACKNOWLEDGMENTS

This work was partially supported by a Grant-in-Aid for Young Scientist (A) (25708018) and a Grant-in-Aid for Scientific Research on Innovative Areas “Molecular Activation Directed toward Straightforward Synthesis” (23105546) from MEXT and by the ACT-C and the A-STEP programs from JST. R.D. is grateful for support as a JSPS Research Fellow. M.O. also acknowledges The Noguchi Institute.

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