Nickel-Catalyzed Trifluoromethylselenolation of Aryl and Alkenyl-Triflates: Scope and Mechanism

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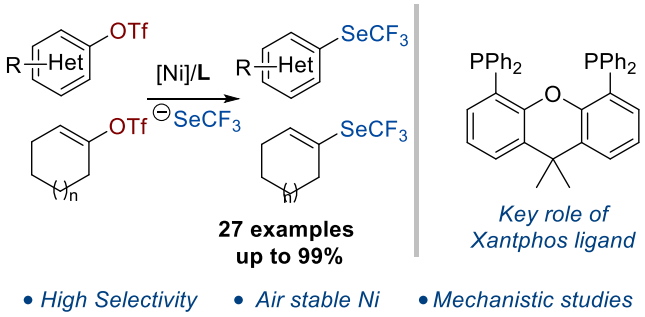
ABSTRACT:

The nickel-catalyzed trifluoromethylselenolation of aryl and vinyl triflates is described herein, encompassing synthesis method development and reaction understanding. The challenge lies in the propensity of the Csp^2-$SeCF_3$ product to undergo reversible oxidative addition to nickel(0) intermediates, potentially initiating catalyst deactivation pathways. In this study, we disclose that Xantphos/$Ni(COD)_2$ catalytic system is efficient for the synthesis of aryl and vinyl trifluoromethylselenides. The key elementary steps that delineate the catalytic cycles have been investigated by a joint experimental and computational mechanistic investigation and support a Ni^0/Ni^{II} process. The Xantphos/Ni^0 system was found to react with both ArOTf and $ArSeCF_3$ to

give the corresponding (Xantphos)Ni^{II}Ar(X) intermediates (X = OTf or $SeCF_3$), with the complex (Xantphos)Ni^{II}Ar(OTf) emerging as the most stable. In line with experimental observations, computational studies indicate that oxidative addition of $ArSeCF_3$ to Xantphos/Ni^0 is fastest than the oxidative addition of ArOTf but is thermodynamically much less favorable. Thereof, the oxidative addition of $ArSeCF_3$ is reversible and the product of the ArOTf oxidative addition is yielded as the most stable product. The relative stability of oxidative addition products is attributed to the coordination mode of the Xantphos ligand (κ2 *vs.* κ3) at nickel (II) intermediates. Finally, we demonstrate that $ArSeCF_3$ compounds can be prepared using an air-stable (Xantphos)Ni(II) pre-catalyst.

TOC graphic:



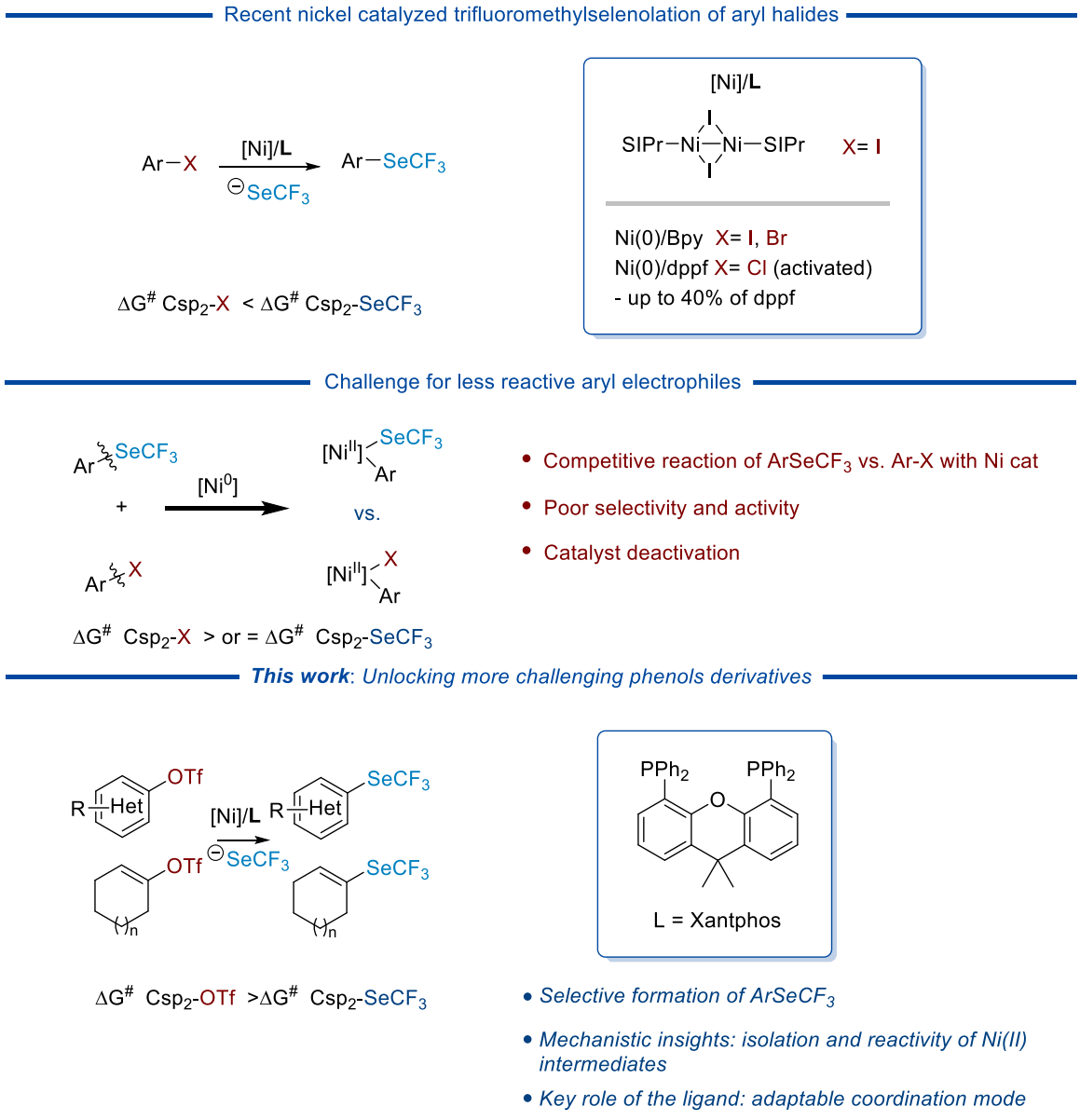
INTRODUCTION

Fluorinated motifs have gained widespread interest and several fluorinated compounds are currently finding applications in life science technology.[1] In this context, the association of chalcogens (O, S and Se) with trifluoromethyl group is covetable due to their interesting physicochemical properties and high lipophilicity.[2] Though several pharmaceuticals and agrochemicals compounds supporting the OCF_3 motif are commercialized,[3] their analogues displaying SCF_3 or $SeCF_3$ are more scarcely applied.[1,4] Regarding $SeCF_3$, attempts to develop

trifluoromethylselenolation reactions through electrophilic, nucleophilic or radical reactions design have been implemented, particularly for the forging of Csp^2-$SeCF_3$ bonds.[5] From a retrosynthetic perspective, the trifluoromethylselenolation of aryl halides constitutes an attractive route due to the availability of starting material as well as the potential use of the technology in late-stage functionalization. However, the few methodologies reported mostly involve aryl iodide as starting electrophiles. Additionally, these methodologies rely on the arylation of Me_4NSeCF_3 reagent using either stoichiometric amount of copper under harsh reaction conditions,[6] or palladium-based catalysis.[7] More recently, interesting nickel catalyzed trifluoromethylselenolation processes have been reported (Scheme 1). On the one hand, the employment of NHC-Ni(I) dimer proved to be an efficient catalyst for the trifluoromethylselenolation of aryl iodides.[8] On the other hand, the use of the Ni(0)/Bpy catalytic system revealed its efficiency toward the synthesis of Ar-$SeCF_3$ starting from aryl-iodides or -bromides.[9,10] Aryl chlorides can also be used as starting electrophiles, but their require the use of Ni(0)/Dppf catalytic loadings up to 40 mol%.[9] To date, the trifluoromethylselenolation of activated phenol derivatives has not been reported. The main challenge for the development of the trifluoromethylselenolation of Csp^2-O bonds stands in the inherent reactivity aryl(Csp^2)-$SeCF_3$ towards oxidative addition to nickel(0) species.[8] Thereof, the trifluoromethylselenolation of aryl electrophiles that are as or less reactive towards Ni(0) than the selenolated awaited product is expected to be intractable.

In this study we report the Ni-catalyzed trifluoromethylselenolation of aryl and vinyl triflates derivatives, under mild conditions. While most of the ancillary ligands provided discouraging results, the use of Xantphos ligand enabled the efficient formation of the desired $ArSeCF_3$ compounds. Mechanistic investigations combining stoichiometric experiments and computational

studies shed light on the key parameters governing the reactivity of XantphosNi(0) species towards the formation of trifluoromethylselenated compounds.



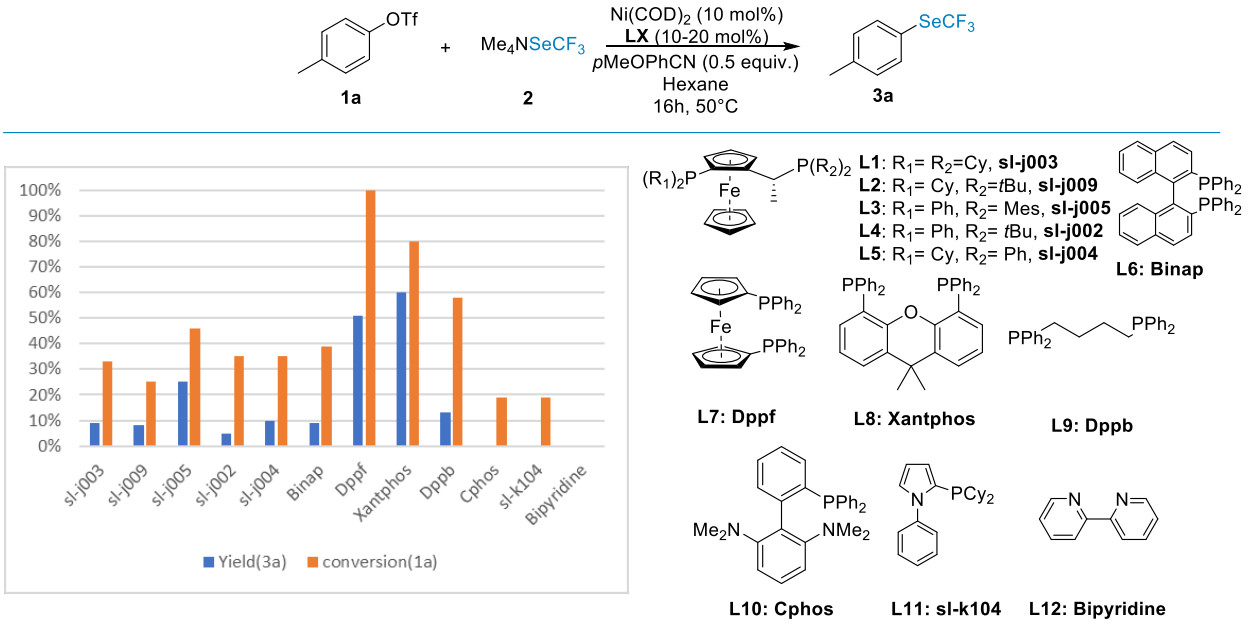
Scheme 1. Current development and challenges for nickel catalyzed trifluoromethylselenolation.

Results and Discussion

Catalyst optimization. The first stage of the investigation began with the identification a ligated Ni complexes that enable the activation of aryl triflates and deliver the desired $ArSeCF_3$ compounds (Scheme 2). Initial tests were devoted to investigating several Josiphos ligands with different electronic properties in conjunction with $Ni(COD)_2$. We have previously observed that this ligand platform efficiently sustains Ni(0)/Ni(II) redox pathways, allowing for the nickel-catalyzed selective monoarylation of acetone.[11] For preliminary assays, we selected 4-methyl-phenyltriflate (**1a**) as a model substrate, along with Me_4NSeCF_3 (**2**) as a nucleophile for reactions performed in hexane at 50 °C for 6 h. Importantly, we have used *p*$MeOC_6H_4CN$ as an additive in the aim of generating a more robust and reactive Ni(0) (pre)catalyst.[12]

Under these conditions, Josiphos-type ligands (**L1**-**L5**) exhibited poor reactivity towards the desired product (Scheme 1). Other diphosphine-ligands such as Binap, Dppf, and Xantphos-type ligands and which have proven efficient in nickel catalyzed cross-coupling reactions of aryl electrophiles including aryl triflates were then screened.[13] The use of Binap (**L6**) afforded very low amounts of the desired product. Dppf ligand (**L7**) showed 90% conversion of **3a** but with a maximum yield of 50% for the desired product **3a**. This observation contrasts with the reported efficiency of the Dppf/$Ni(COD)_2$ catalyst for the trifluoromethylthiolation of ArOTf,[14] which points out the enhanced reactivity of $ArSeCF_3$ *vs.* $ArSCF_3$.

Interestingly, the use of Xantphos (**L8**) offered an optimal balance with 80% conversion and 60% yield of the desired product. A low yield of 12% was obtained with Dppb (**L9**), and monophosphines (**L10** & **L11**) revealed inefficient as only low conversions were observed without a trace of the desired product. Finally, the use of bipyridine ligand (**L12**), which was recently reported to be an effective ligand for the activation of aryl halides,[9] was also ineffective for the trifluoromethylselenolation of aryl triflate **1a**.

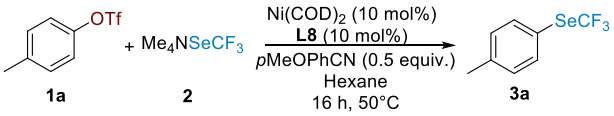


Scheme 2. Ligand screening for the trifluoromethylselenolation of **1a**. [a] Reactions were performed with **1a** (0.1 mmol, 1 equiv.), $Ni(COD)_2$ (0.01 mmol, 0.1 equiv.), **LX** (0.01 mmol, 0.1 equiv.), 2 (0.15 mmol, 1.5 equiv.), *p*$MeOC_6H_4CN$ (0.05 mmol, 0.5 equiv.) and solvent (1 mL) for 16 hours. Yields determined by ^{19}F NMR spectroscopy with $PhCF_3$ as an internal standard. [b] **LX** (0.02 mmol, 0.2 equiv.).

In the second stage, we have investigated other reaction parameters using Xantphos (**L8**) as an optimal ligand. Increasing the reaction temperature to 60 °C raised the yield of the desired product **3a** to 78% (Table 1, entry 2). Further increase in the reaction temperature to 70 °C proved to be detrimental as **3a** were obtained in 68% yield. Performing the reaction without the nitrile additive (*4*- *p*$MeOC_6H_4CN$) was also detrimental to the reaction outcome, in this case only traces of the desired product were observed (Table 1, entry 4). It is noteworthy that using MeCN as an additive (0.5 equiv.) was not as efficient as *p*$MeOC_6H_4CN$ for this transformation, as **3a** was obtained only in 6% yield. This suggests that the formation of the reactive [Ni(0)-nitrile] adduct is not favorable with acetonitrile (vide infra).[12] In contrast, aromatic nitriles such as PhCN and NaphCN proved to be beneficial for the catalytic activity, although slightly lower yields were obtained than with

*p*MeOC$_6$H$_4$CN (Table 1, entries 6 and 7). Performing the reaction in toluene provided the same results as in hexane (Table 1, entry 8), but the combination of hexane and toluene in a 1:1 ratio resulted in the formation of the desired product in 83% yield (entry 9).

Table 1. Optimization of the reaction.[a]

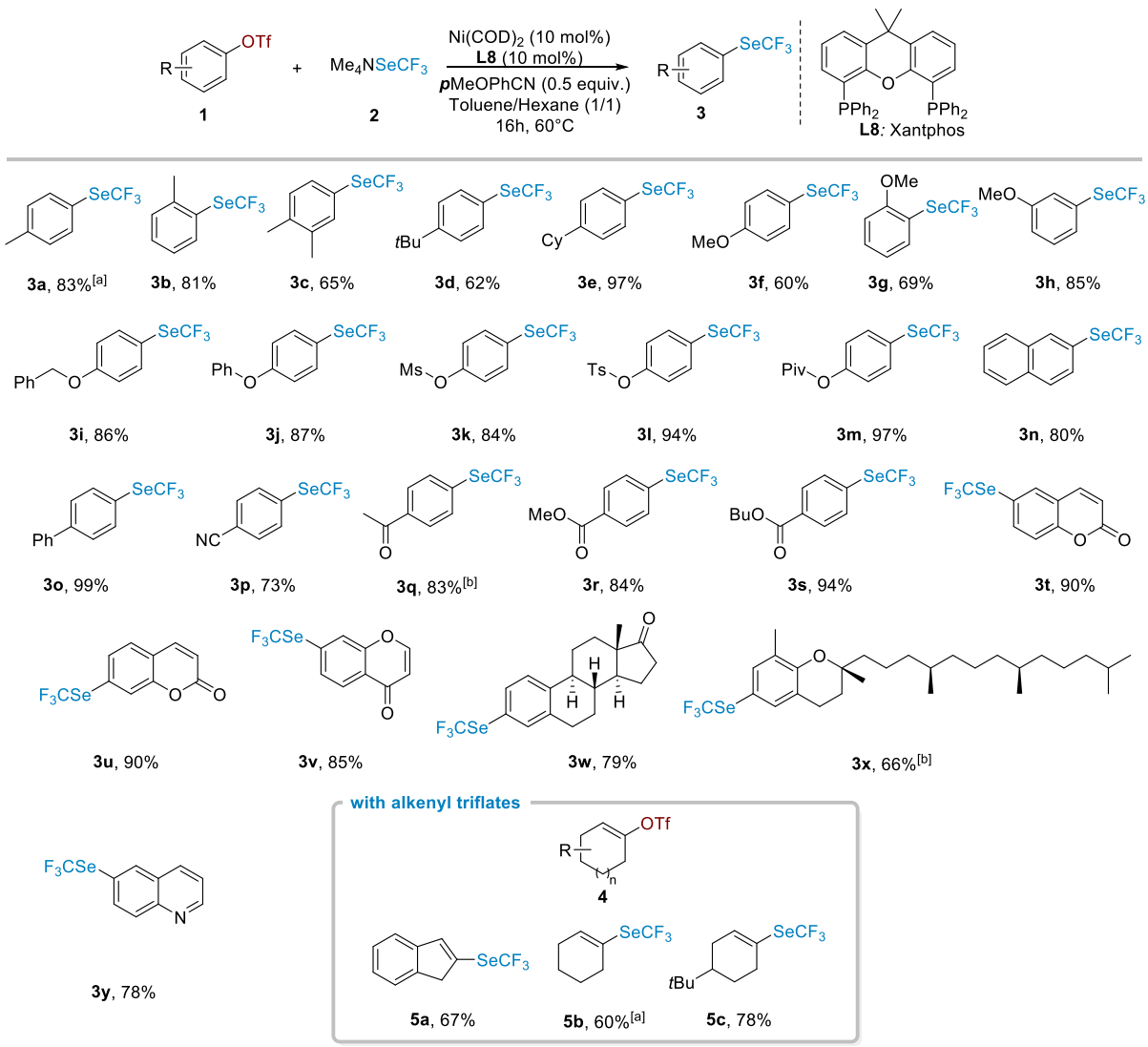


Entry[a]	Deviation from standard conditions	Yield[b]
1	None	60%
2	60°C instead of 50°C	78%
3	70°C instead of 50°C	68%
4	No *p*MeOC$_6$H$_4$CN	traces
5	MeCN instead of *p*MeOC$_6$H$_4$CN	7%
6	PhCN instead of *p*MeOC$_6$H$_4$CN	68%
7	NaphCN instead of *p*MeOC$_6$H$_4$CN	66%
8	Toluene	60%
9	**Toluene/Hexane (1/1)**	**83%**

[a] Reactions were performed with **1a** (0.1 mmol, 1 equiv.), Ni(COD)$_2$ (0.01 mmol, 0.1 equiv.), **L8** (0.01 mmol, 0.1 equiv.), **2** (0.15 mmol, 1.5 equiv.), *p*MeOC$_6$H$_4$CN (0.05 mmol, 0.5 equiv.) and solvent (1 mL) for 16 hours. [b] Determined by ^{19}F NMR spectroscopy with PhCF$_3$ as an internal standard.

Scope of the reaction. With the best reaction conditions in hand, we explored the scope of the reaction. A set of aryl triflates substituted with electron donating groups have been subjected for trifluoromethylselenolation. When the phenyl ring is substituted with a methyl group in *ortho*, *meta* or *para* position, good yields have been obtained ranging from 65% to 83% (Scheme 3, products **3a**-**3c**). Similarly, when the phenyl ring is substituted with a *t*-butyl or a cyclohexyl group in *para* position, the desired products have been obtained in 62% or 97% yield, respectively

(Scheme 3, products **3d** and **3e**). The reaction also proceeded well with ether substituents (Scheme 3, products **3f**-**3j**). The presence of other oxygenated leaving groups on the starting aryl triflates have been also investigated. Interestingly, the aryl triflate is selectively and smoothly converted in the presence of mesylate, tosylate as well as pivalate groups with reaction outcomes up to 97% yield (Scheme 3, products **3k**-**3m**). The naphthene starting material delivered the desired product with 80% yield (Scheme 3, product **3n**). Aryl triflates bearing electron withdrawing groups (Scheme 3, **3o-3s**) were also found to display good reactivity. However, the transformation was shown to be not compatible with carboxylic acids, amido, amino and hydroxyl functional groups, (unsuccessful substrates are provided in SI). The trifluoromethylselenolation of more complex substrates such as coumarin and chromone core structures (Scheme 3, **3t-3v**), an estrone derivative (Scheme 3, **3w**), and a derivative of vitamin E (Scheme 3, **3x**) proceeded with good to very good yields. The exploration of electrophiles was enlarged by considering alkenyl triflate derivatives **4**. Several alkenyl triflates were converted to their corresponding trifluoromethylselenolated analogues in good to very good yields (Scheme 3, products **5a**-**5c**).



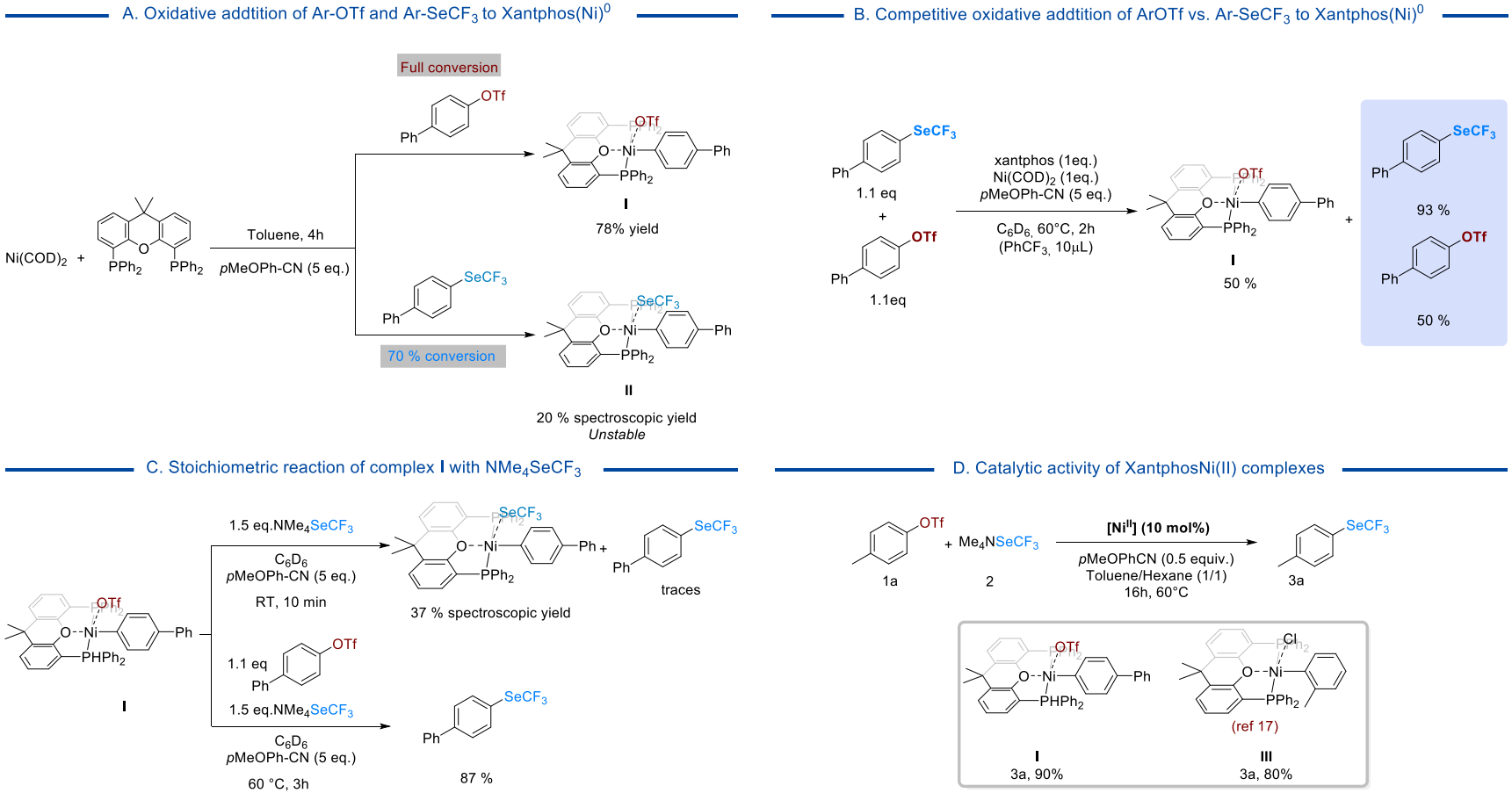
Scheme 3. Substrate scope. [a] Reactions were performed with **1** or **4** (0.2 mmol, 1 equiv.), $Ni(COD)_2$ (0.02 mmol, 0.1 equiv.), **L8** (0.02 mmol, 0.1 equiv.), **2** (0.3 mmol, 1.5 equiv.), *p*$MeOC_6H_4CN$ (0.1 mmol, 0.5 equiv.) and solvent (1 mL) for 16 hours. Yields of isolated products. [a] Determined by ^{19}F NMR spectroscopy with $PhCF_3$ as an internal standard. [b] $Ni(COD)_2$ (0.03 mmol, 0.15 equiv.), **L7** (0.03 mmol, 0.15 equiv.).

Mechanistic investigations. Having identified optimal conditions for the trifluoromethylselenolation of aryl- and vinyl-triflates, we were eager to collect mechanistic rationale for the observed reactivity of the Xanthpos/Ni catalytic system, especially the role played by the nitrile additive and the relative reactivity of the catalysts between the triflate reagent and

the associated trifluoromethylselenolated product. Based on previous mechanistic observations, $ArSeCF_3$ was anticipated to be more reactive towards the oxidative addition to [Ni(0)] than ArOTf.[8] However, the trifluoromethylselenolated product can be isolated as the main product and in good yield using the Xantphos/Ni(0) catalytic system. This prompted us to investigate the mechanism of the reaction. More precisely, we were eager to examine the oxidative additions of both ArOTf **1o** and of $ArSeCF_3$ **3o** to Xantphos-ligated Ni(0) complexes.

As previously reported, attempts to prepare XantphosNi(COD) by reacting $Ni(COD)_2$ and 1 equivalent of the Xantphos ligand **L8** in toluene resulted in the precipitation of $(Xantphos)_2Ni$ as the major species.[15] This complex has poor solubility in most solvents, but its formation was confirmed by X-Ray diffraction analysis (See ESI for details).[16] This species is not reactive under our catalytic conditions (see Table 1, entry 4). Additionally, when $Ni(COD)_2$ and 1 equivalent of Xantphos were reacted in the presence of aryl triflate **1o**, only precipitation of $(Xantphos)_2Ni$ was observed, no oxidative addition product was detected. The beneficial effect of the nitrile additive, as observed during catalysis, was found to arise from the ability of the nitrile to displace one Xantphos ligand and form a catalytically active (Xantphos)Ni(nitrile) complex.[15] We have experimentally confirmed that the addition of 5 to 10 equivalents of *p*-methoxybenzonitrile to the reaction mixture led to an equilibrium between $(Xantphos)_2Ni$ and the nitrile adduct (Xantphos)Ni(pMeOC_6H_4CN) that is formed up to 34%. Notably, it was found that acetonitrile is not efficient in forming the (Xantphos)Ni(MeCN) complex, which explains the poor catalytic activity observed in the presence of acetonitrile (Table 1, entry 5).[17] Then, the oxidative addition of *p*-phenyl-phenyltriflate **1o** to Ni(0) complexes yielded from Xantphos and $Ni(COD)_2$ in the presence of 5 eq. of *p*-methoxybenzonitrile has been investigated. The reaction proceeded at room temperature and resulted in the rapid formation of the oxidative addition complex **I**, which was

isolated in 78% yield (Scheme 4A). The formation of complex **I** was confirmed in solution by NMR spectroscopy. The $^{31}P\{^{1}H\}$ NMR spectrum of complex **I** displayed a single resonance signal at $\delta = 11.4$ ppm indicating a *trans*-symmetric coordination of both phosphorus atoms.[18] In addition, the ^{19}F NMR resonance signal of the triflate moiety is shifted to $\delta = -78.8$ ppm, suggesting a weak coordination to the Ni center. ESI mass spectrometry analyses of **I** clearly indicated the formation of a cationic (Xantphos)nickel(II) aryl species (mass peak at 789.1981 m/z for $[C_{51}H_{41}OP_2Ni^+]$). Unfortunately, all attempts to characterize the corresponding complex by X-ray diffraction analysis were unsuccessful. The characterization data of complex **I** indicates the formation of a square planar nickel complex with a weakly coordinated OTf counter anion.[19]



Scheme 4. Mechanistic investigations: A, B. Comparative reactivity of Xantphos/Ni(COD)$_2$/*p*-methoxybenzonitrile with ArOTf **1o** and ArSeCF$_3$ **3o**. C. trifluoromethylselenolation of ArOTf using complex **I. D.** Catalytic reactivity of XantphosNi(II) complexes. Yields of complexes were determined by ^{31}P NMR and product yields by ^{19}F NMR spectroscopy with PhCF$_3$ as an internal standard.

Then, we investigated the reactivity of *p*-phenyl-phenylSeCF$_3$ **3o** towards oxidative addition to XantphosNi(0) in presence of nitrile was investigated. In this case, monitoring the reaction by ^{19}F NMR spectroscopy revealed significant consumption of **3o** (70 % conversion) after 4h at room temperature in C_6D_6, along with the formation of a single species appearing as a singlet at $\delta = -17$ ppm with an overall spectroscopic yield of 20%. The ^{19}F NMR chemical shift of the new species falls within the same region as trifluoromethylselenate metal complexes previously described.[20] Additionally, the new species displays a ^{31}P NMR resonance signal at $\delta = 7.5$ ppm, very close to that observed for complex **I**. These NMR data suggest that XantphosNi(0) also readily undergoes oxidative addition of ArSeCF$_3$ to give the corresponding (Xantphos)Ni(II)(Ar)(SeCF$_3$) species (Scheme 4B). The NiSeCF$_3$ intermediate was found to be unstable, as it gradually disappears over time or upon heating to 60°C, while ArSeCF$_3$ is further consumed. Unfortunately, all attempts to isolate and further characterize the NiSeCF$_3$ intermediate and its degradation product(s) were unsuccessful. After 20 hours of reaction the ^{19}F NMR spectrum of the reaction mixture showed only two minor resonance signals corresponding to residual ArSeCF$_3$ reactant **3o** (8%) and to PhSeCF$_3$ (30%).[21] The reaction of Xantphos/Ni(0) species with aryl halides has been previously shown to lead to the formation of Ni(I) intermediates concomitantly with high amount of bi-aryl compounds.[22] Such a pathway may also be operative for ArSeCF$_3$ to explain the decomposition process; however, no traces of bi-aryl compounds could be detected. These observations along with previous reports indicating that DppfNi(I) species are ineffective as catalyst for the formation of C-SCF$_3$ bonds[14,23] suggest that the formation of Ni(I) species in catalytic conditions is not predominant.

Overall, these observations indicate that both ArOTf and ArSeCF$_3$ can react readily with XantphosNi(0) species at room temperature. Remarkably, when the reaction is performed in the

presence of stochiometric amount of both substrates, only the triflate derivative is converted towards the formation of the corresponding nickel(II) aryl species **I** (50% ^{19}F NMR spectroscopic yield). Under the same conditions, the $ArSeCF_3$ substrate remained almost intact. To further confirm the formation of a $NiSeCF_3$ intermediate, a stoichiometric reaction between complex **I** and NMe_4SeCF_3 was carried out. Within 10 minutes at room temperature, ^{19}F and ^{31}P NMR spectroscopic analyses of the reaction mixture indicated the formation of complex **II** (37 % ^{31}P NMR spectroscopic yield) along with traces of the $ArSeCF_3$ coupling product. Upon further heating the reaction to 60°C for several hours, the signals associated with complexes **I** and **II** disappeared, with only a slight increase in the coupling product. However, when the reaction is carried out in the presence of one equivalent of ArOTf **1o,** the formation of the desired product **3o** is observed in high yield (87% yield, Scheme 4). These observations suggest that salt metathesis is operative to give a selenated nickel intermediate **II**. The C-$SeCF_3$ reductive elimination from complex **II** would proceed with an equilibrium constant favoring the reverse oxidative addition. Under stoichiometric conditions, the addition of ArOTf is necessary to shift the equilibrium toward the formation of thermodynamically stable complex **I** and the release of the desired product. The catalytic efficiency of complex **I** was further confirmed, providing the trifluoromethylselenated product in high yields. Notably, similar results were obtained using previously reported XantphosNi(II) aryl chloride analogue complex **III**.[24]

All together, these results support a Ni(0)/Ni(II) pathway, which is initiated by the oxidative addition of ArOTf to a mono-Xantphos-ligated Ni(0) complex, followed by salt metathesis and subsequent reductive elimination.

To complement the experimental mechanistic investigation, a computational study was conducted at the M06/CPCM(PhMe)/def2-TZVP:SDD-ECP//B3PW91/6-311G(2*d*,*p*):LANL2-

ECP DFT level (see ESI for computational details) to confirm the key intermediates and to assess the energetics of the most relevant reaction steps. Xantphos ligand was modeled without structural simplification, and PhOTf was used as a typical electrophile. Unless specified ionic species were considered separated from their counter ion. The (Xantphos)Ni(nitrile) adduct **A** was optimized as a minimum on the potential energy surface. Its formation is computed endergonic by only 7.8 kcal mol^{-1} relative to separated $(Xantphos)_2Ni$, $Ni(COD)_2$ and nitrile (Figure 1). This result is consistent with detailed experimental mechanistic observations and previous reports,[12,15] but also with the equilibrium in solution of $(Xantphos)_2Ni$, $Ni(COD)_2$ and complex **A** as previously discussed.

The oxidative addition of PhOTf to complex **A** requires overcoming a Gibbs energy barrier of 16.8 kcal.mol^{-1} to yield the nickel(II) aryl complex **B** whose formation is computed exergonic by 19.4 kcal.mol^{-1} relative to **A** and the associated reactants. In comparison, the oxidative addition of $PhSeCF_3$ to complex **A** is much faster, as indicated by a computed Gibbs energy barrier of 11.4 kcal.mol^{-1}. This is consistent with the observed experimental reactivity trend and in line with the computed (Ar)C-$SeCF_3$ bond dissociation energies that is weaker than the (Ar)C-OTf one by 21 kcal mol^{-1} (See ESI). Thermodynamically, formation of the resulting (Xantphos)Ni^{II}(Ph) ($SeCF_3$) complex in its singlet (**C**) or triplet state (**D**) is exergonic by ca. 4 kcal mol^{-1}, which is less stable by ca. 15 kcal.mol^{-1} than the PhOTf oxidative addition product. Therefore, it is likely that the (Xantphos)Ni^{II}(Ph)($SeCF_3$) (**C**) intermediate is formed but undergoes rapid reductive elimination ($\Delta G^{\#}$ = 15.4 kcal mol^{-1}) to regenerate the Ni(0) adduct **A**, which ultimately performs the oxidative addition of the triflate with an overall Gibbs energy barrier of 20.8 kcal.mol^{-1} and a global exergonicity of 15.4 kcal.mol^{-1}. This mechanistic picture is consistent with the experimental observation.

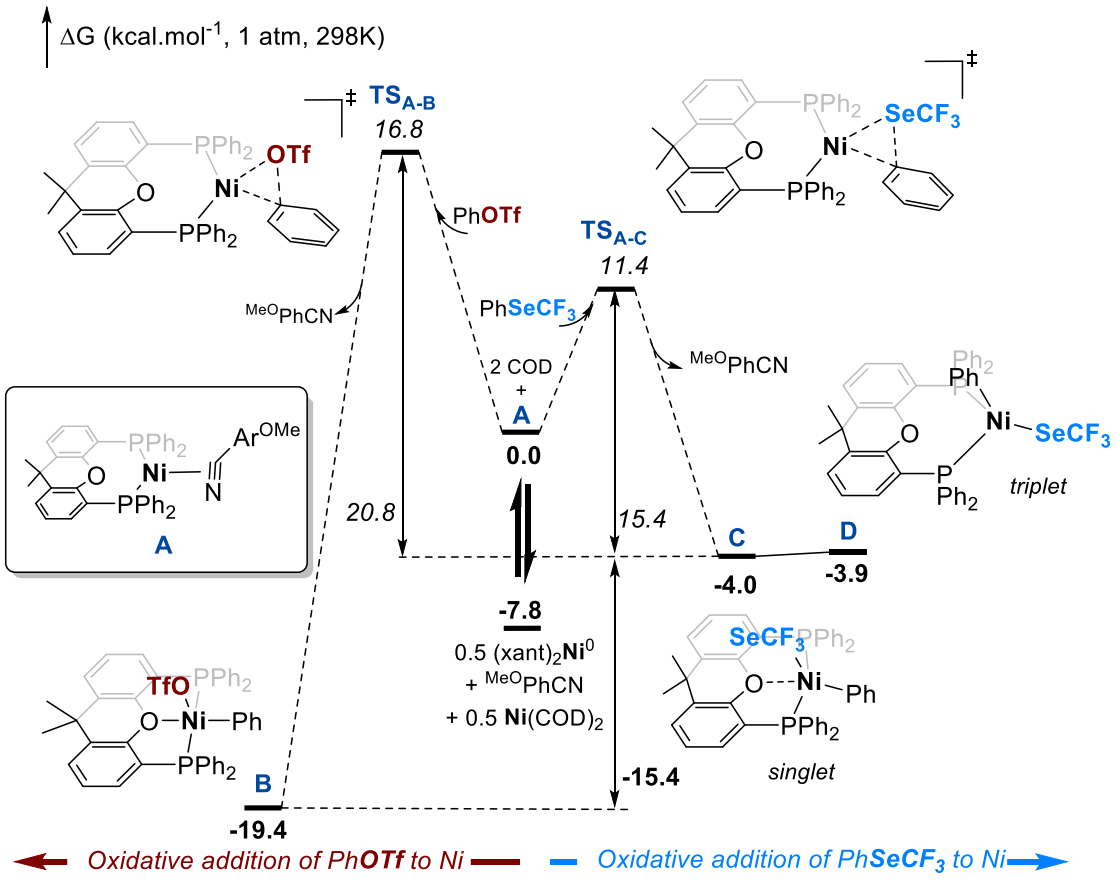


Figure 1. Simplified Gibbs energy profile for the oxidative addition of PhOTf *vs.* $PhSeCF_3$ (see level of theory in ESI).

For comparative analysis, we have conducted the same computational investigation using Dppf as a bidentate ligand (see ESI for details). Starting from the (Dppf)Ni(nitrile) adduct, the computed Gibbs energy barriers for the oxidative addition of PhOTf and $PhSeCF_3$ stand at 14.4 and 10.6 kcal.mol^{-1}, respectively. Both processes were also found to be thermodynamically favorable, by 13.8 kcal.mol^{-1} for (Dppf)Ni^{II}(Ph)($SeCF_3$) and by 21.2 kcal.mol^{-1} for (Dppf)Ni^{II}(Ph)(Otf).

Analogously to that observed with Xantphos ligand, these results indicate that both reactions are feasible and the kinetic preference for $PhSeCF_3$ oxidative addition. The resulting oxidative addition

intermediates are thermodynamically stable, with (Dppf)Ni^{II}(Ph)($SeCF_3$) being more stable than the corresponding (Xantphos)Ni^{II}(Ph)($SeCF_3$) intermediate.

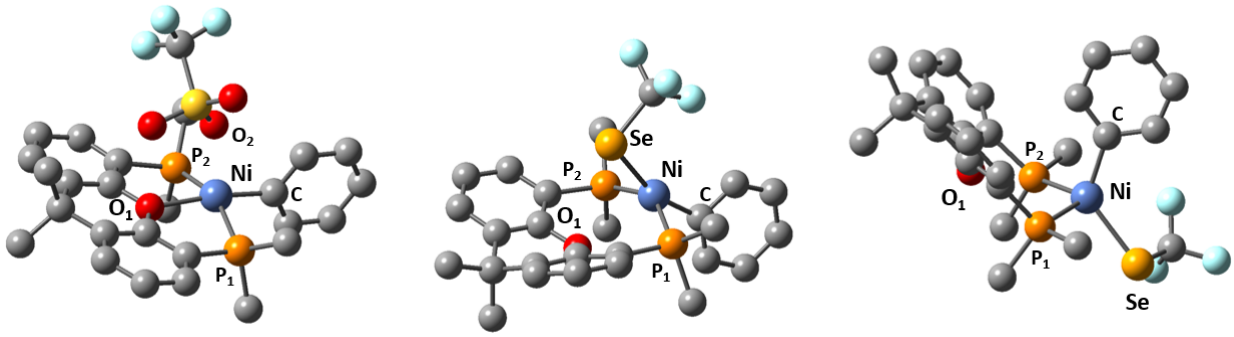
It is worth noting that the oxidative addition of $ArSCF_3$ to (Dppf)Ni(0) species was reported to lead to a catalytically inactive species.[14] This insight raises the possibility that the computed (Dppf)Ni(II)$SeCF_3$ intermediate may undergo decomposition rather than reversible reductive elimination. Additionally, the oxidative addition of ArOTf to (Dppf)Ni(0) species may lead to (DPPF)Ni(I) species, via a subsequent comproportionation pathway.[23] These species have been shown to lead to inactive species in the context of trifluoromethylthiolation of aryl halides. [23]

Thus, on one hand the thermodynamic stability of (Xantphos)Ni^{II}(Ph)(Otf) may prevent from the competitive formation of Ni(I) species. On the other hand, the comparatively diminished stability of (Xantphos)Ni^{II}(Ph)($SeCF_3$) enables facile reverse reductive elimination and thus do not eventually lead to catalytically inactive species.

To get more insights into the factors that account for the important difference of thermodynamic stability between (Xantphos)Ni^{II}(Ph)(OTf) and (Xantphos)Ni^{II}(Ph)($SeCF_3$) intermediates, optimized structures of XantphosNi(II) complexes **B** and **C** were analyzed. In complex **B**, the nickel center exhibits a square pyramidal geometry in which the tridentate κ^3-P,O,P Xantphos ligand and the phenyl ring form the base of the pyramid, while the OTf ligand occupies the apical position. The distance between the OTf anion and the metal center is relatively short (2.321 Å), much shorter than the sum of the van der Waals radii of Ni and O atoms (3.15 Å). The deviation of Ni from the base is only around 0.28 Å relative to an ideal square-based pyramid geometry, indicating a slightly distorted geometry. In contrast, complexes (Xantphos)Ni^{II}(Ph)($SeCF_3$) (**C** or **D**) display tetrahedral geometries in which the Xantphos ligand is no longer tridentate but κ^2-P,P

bidentate as illustrated in Table 2. The optimized Ni-Se distances of 2.44 Å in **C** and 2.40 Å in **D** are short relative to the sum of the Ni and Se van der Waals radii (3.53 Å), potentially indicating a strong interaction.

Table 2. Top: From left to right: computed structures of complexes **B**, **C** and **D**. Bottom: angles and distances of computed structures.



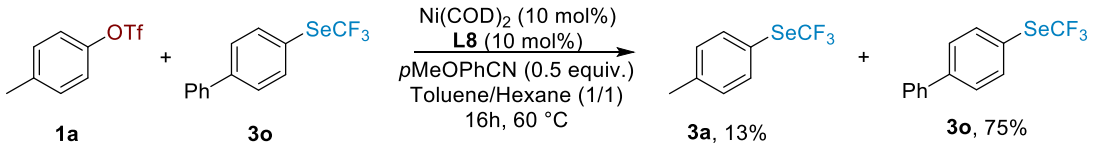
	Distance (Å)				Angles (°)			
	$Ni-O_1$	$Ni-O_2$	Ni-Se	Ni-C	P_1-Ni-P_2	O_1-Ni-C	C-Ni-Se	O_2-Ni-C
B	2.100	2.321	-	1.872	154.9	172.5	-	101.9
C	2.755	-	2.449	1.888	142.9	120.7	160.7	-
D	3.456	-	2.409	1.972	107.2	92.5	123.0	-

The weaker coordination of the OTf moiety to Ni compared to $SeCF_3$, induces a different coordination mode of the Xantphos ligand, which significantly impacts the coordination geometry around the nickel(II) center.

Overall, this computational mechanistic study suggests that the formation of compound **C** is kinetically favored, yet reversible, while formation of compound **B** is thermodynamically favored. Consequently, the activation of $PhSeCF_3$ is unlikely to significantly disturb the catalytic trifluoromethylselenolation of PhOTf under the experimental conditions used. The important Gibbs free energy difference observed between compound **C** and compound **B** (ΔG = 15.4

kcal.mol^{-1}) may originate from the different coordination geometry around the nickel(II) center induced by the Xantphos ligand (κ^3-P,O,P *vs.* κ^2-P,P). This may explain the superior catalytic efficiency of Xantphos compared to other bidentate ligands.[25]

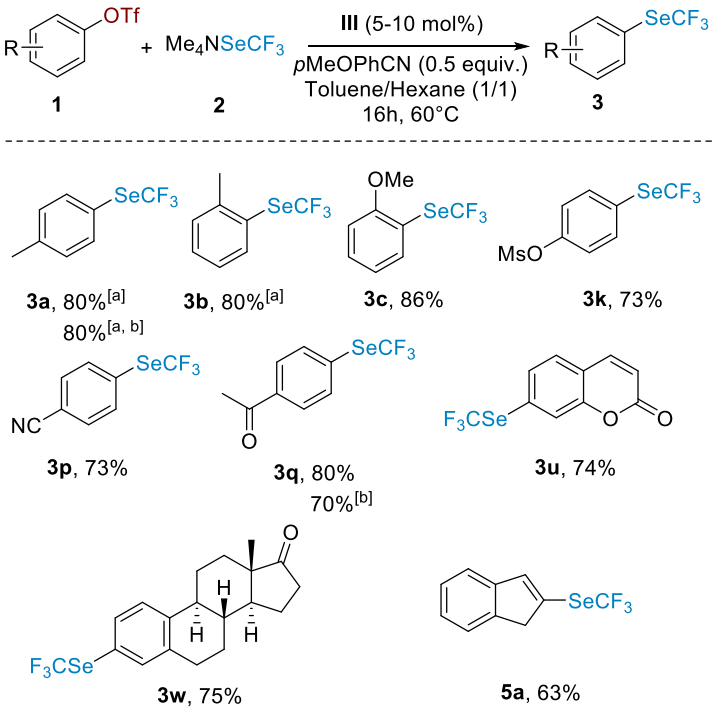
Finally, to further confirm that oxidative addition of $ArSeCF_3$ occurs during catalysis, we hypothesized that trifluoromethylselenolation of Ar^2OTf may be observed using one equivalent of Ar^1SeCF_3 as the -$SeCF_3$ precursor. This process would entail the concomitant oxidative addition of both Ar^1SeCF_3 and Ar^2OTf substrates, followed by ligand exchange and reductive elimination to give some Ar^2SeCF_3 product. To test this hypothesis, we conducted a catalytic reaction using a 1/1 ratio of 4-MePhOTf **1a** and 4-PhPhSeCF_3 **3o** under identical reaction conditions. We were delighted to observe the formation of the desired product **3a** 4-MePhSeCF_3 albeit in low yield of 13% and recovering of 75% of the starting **3o** (Scheme 5). This experiment evidences the occurrence of some $ArSeCF_3$ oxidative addition during catalysis.



Scheme 5. trifluoromethylselenolation of ArOTf **1a** using **3o** as $SeCF_3$ precursor.

Finally, we sought to evaluate the use of Ni(II) precatalysts instead of air sensitive Nickel(0) precursors. While the combination of Xantphos with nickel(II) salts in the presence of reductants (Zn, Mn or TDAE) is not operative for this transformation (see ESI for details), we found that the isolated (Xantphos)Ni(II)(OTf)PhPh complex **II** was very efficient for the trifluoromethylselenolation of **1a** affording the desired product in 90% yield. However, as complex

II was found to be air sensitive, our attention turned to complex **III** that is air stable. Using **III**, the trifluoromethylselenolation of aryl and vinyl triflates were explored. To our delight, complex **III** performs well the trifluoromethylselenolation independently of the stereo-electronic features of the electrophile substituents, encompassing more complex structures (Scheme 6). Interestingly, starting with **III** enabled us to decrease the catalyst loading down to 5 mol% with similar reaction outcome (compound **3a**, or **3q** Scheme 6). Notably, we also observed interesting reactivity with alkenyl triflates, and were able to obtain compound **5a** with a yield of 63% (Scheme 6).



Scheme 6. Substrate scope with complex **III** [a] Reactions were performed with **1** or **4** (0.2 mmol, 1 equiv.), **III** (0.02 mmol, 0.1 equiv.), **2** (0.3 mmol, 1.5 equiv.), *p*MeOC$_6$H$_4$CN (0.1 mmol, 0.5 equiv.) and solvent (1 mL) for 16 hours. Yields of isolated products. [a] Determined by ^{19}F NMR spectroscopy with PhCF$_3$ as an internal standard. [b] **III** (0.01, 0.05 equiv.)

Conclusion

In this study, we have presented the first example of a nickel-catalyzed trifluoromethylselenolation of C-O bonds, which is efficient for both electron donating and electron withdrawing substituted aryl triflates as well as more complex structures and alkenyl triflates. By conducting detailed mechanistic studies, combining experimental and computational investigations, we have been able to elucidate the feasibility and selectivity of each key elementary step involved in the catalytic cycle. Our investigations revealed that the XantphosNi(0) precursors are able to activate both Csp^2-OTf and Csp^2-$SeCF_3$ bonds, giving rise to the corresponding nickel(II) intermediates that have been spectroscopically assessed. However, only the (Xantphos)Ni(II)(Ar)(OTf) intermediate is thermodynamically stable, providing a driving force for the desired transformation. The ability of Xantphos ligand to accommodate different coordination modes was found to be at the origin of the different stability between Ni(II)-OTf and Ni(II)-$SeCF_3$ intermediates. Additionally, we have demonstrated that the reversibility of the Csp^2-$SeCF_3$ bond activation at XantphosNi(0) species open very promising opportunities to develop new synthetic pathways towards the formation of $SeCF_3$-product.

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ASSOCIATED CONTENT

Supporting Information.

Experimental procedures, spectral and analytical data including NMR spectra (PDF)

Crystallographic data for [(Xantphos)$_2$Ni] complex (CIF)

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