On the reactions of aryl and vinyl triflates with [Ni(COD)(dppf)]‡

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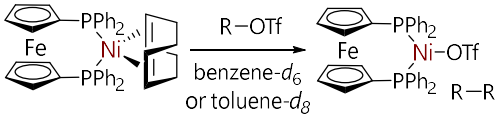
We report the experimental and computational investigations of the reactions of aryl and vinyl triflates with a model nickel(0) complex. Oxidative addition rates decrease in the order naphthyl > vinyl > phenyl, although 4-acetylphenyl triflate reacts most quickly due to favourable ketone coordination. Two possible reaction mechanisms are explored using DFT calculations.

Organotriflates are substrates for many nickel-catalysed reactions.[1-6] The reactions of a range of Ni^0 complexes with organohalides have been studied in some depth,[7] but less is known about the mechanisms of the reactions of aryl and vinyl triflates with Ni^0. We have previously studied the reactions of a range of aryl (pseudo)halides with [Ni(COD)(dppf)] (**1**),[8] which is a convenient, thermally-stable, catalytically-active model nickel(0) complex (COD = 1,5-cyclooctadiene; dppf = 1,1'bis(di-phenylphosphino)ferrocene).[9] We have studied the reactions of **1** with (hetero)aryl[8, 10-12] and alkyl[13, 14] halides, and ranked a series of aryl substrates of the form *p*-$F_3CC_6H_4X$ in order of their reactivity with **1**;[8] somewhat surprisingly, **1** undergoes reaction with *p*-$F_3CC_6H_4OTf$ more slowly than with *p*-$F_3CC_6H_4OTs$. Recently, we noted that the reaction of 2-pyridyl triflate (**2a**) with **1** forms [Ni(κ^2-*C*,*N*-2-pyridyl)(dppf)][OTf] in which the triflate moiety is present as an outer-sphere counterion to a pseudo-square planar cationic nickel(II) complex.[11] Neufeldt noted that selectivity for aryl sulfonate *versus* aryl chloride oxidative addition can be modulated *via* judicious ligand selection: Ni^0 complexes with most widely-used phosphine ligands preferentially activate aryl chlorides, while complexes of trimethylphosphine show the opposite selectivity by lowering the energy of the five-centre oxidative addition transition state for aryl triflate oxidative addition.[15] Here we examine the reactions of a series of aryl and vinyl triflates with **1**.

The reactions of **1** with phenyl (**2b**), 2-naphthyl (**2d**), or cycloalk-1-en-1-yl triflates (cyclopent-1-en-1-yl triflate (**3a**), cyclohex-1-en-1-yl triflate (**3b**), cyclohept-1-en-1yl triflate (**3c**), and cyclooct-1-en-1-yl triflate (**3d**)) ultimately form [Ni(OTf)(dppf)] (**4**) (Scheme 1), as confirmed by EPR analysis



Scheme 1. Product studies for the reaction of [Ni(COD)(dppf)] (**1**) with organotriflates.

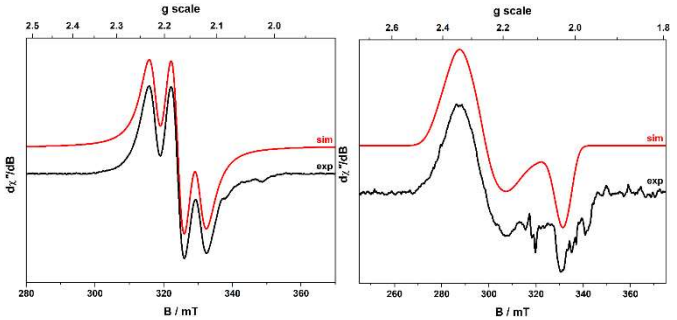


Figure 1. X-band EPR spectra of [Ni(OTf)(dppf)] (**4**) in THF solution (left) at 293 K (frequency, 9.8593 GHz; power, 6.3 mW; modulation, 0.6 mT) showing g_{iso} = 2.173 and A_{iso} = 65 × 10^{-4} cm^{-1} and (right) at 77K (frequency, 9.4215 GHz; power, 2.0 mW; modulation, 0.7 mT) showing *g* = (2.340, 2.265, 2.035) and *A* = (80, 80, 30) × 10^{-4} cm^{-1}. Experimental spectra are in black (bottom) and simulations are shown in red (at the top).

(Figure 1). The corresponding reactions with 1-naphthyl triflate (**2c**) and 4-(trifluoromethyl)phenyl triflate (**2e**) are known to lead to [Ni(1-naphthyl)(OTf)(dppf)] (**4**) and **2**, respectively.[8] Homocoupling by-products were identified by GC-MS analysis; in the case of the reactions of **3a**, the identity of this by- product was confirmed by the analysis of an authentic sample. §

Kinetic studies of the oxidative addition step were performed by monitoring the decrease in the concentration of **1** over time by $^{31}P\{^1H\}$ NMR spectroscopy when it was exposed to **2a-d**, **2f**, and **3a-d** in benzene-d_6 solution under an argon atmosphere (Scheme 2).§ The rate of reaction decreases in the order 2-naphthyl > 4-acetylphenyl ≈ 1-naphthyl > 2-pyridyl > phenyl. The increased rate of reaction of heteroaryl halides compared to aryl halides has been noted previously in the oxidative addition reactions of nickel[11] and palladium.[16] The increased reactivity of **2f** with respect to **2b** is consistent with our previous studies, in which ketone coordination accelerates oxidative addition when 'ring-walking' across the π-system is possible;[10, 12] the present study establishes that this behaviour extends beyond aryl halides to other nickel catalysis substrates.

Intrigued by the possible role of alkene coordination in reaction rate and selectivity,[10, 12] four vinyl triflate substrates were prepared from the corresponding cycloalkanone.[5,§]

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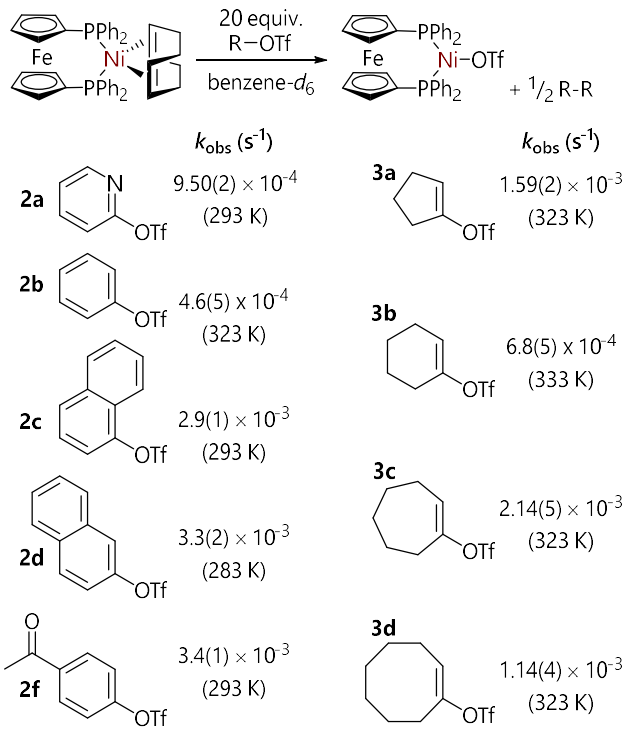
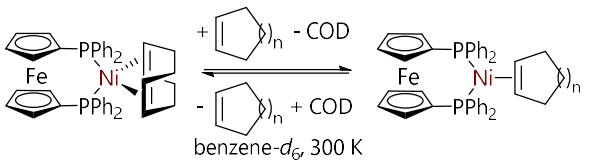
Electronic Supplementary Information (ESI) available: characterisation data for chemical compounds, kinetic data, and information about computational calculations.



Scheme 2. Kinetic studies of the oxidative addition of aryl and vinyl triflates to **1**.



n = 1 K_{eq} = 7.6 × 10^{-4} n = 3 K_{eq} = 1.6 × 10^{-4}
n = 2 K_{eq} < 4.4 × 10^{-10} n = 4 K_{eq} = 2.9 × 10^{-4}

Scheme 3. Measurement of K_{eq} for the displacement of COD from **1** by cycloalkenes.

Substrates **3a**, **3c**, and **3d** undergo reaction at *ca.* two to four times the rate of phenyl triflate. However, cyclohex-1-en-1-yl triflate (**3b**) undergoes reaction at *ca.* half the rate of phenyl triflate (**2b**), for which k_{obs} = 1.3(1) x 10^{-3} at 333 K. This anomalous result was explored further (*vide infra*).

The reactions of **2b** and **3a** were repeated with the addition of 1, 2, or 3 equivalents of COD; in both cases the rate of reaction decreased with increasing $[COD]_{t=0}$ consistent with the need to generate a vacant site for oxidative addition.§

The surprisingly low rate of oxidative addition for **3b** prompted further investigation. Equilibrium constants were measured by $^{31}P\{^1H\}$ NMR spectroscopy for the displacement of COD from **1** by cyclopentene, cyclohexene, cycloheptene, and *cis*-cyclooctene (Scheme 3); we have previously shown that ketones and aldehydes can coordinate to dppf-nickel(0),[10] even displacing good ligands such as COD, and we have noted that a whole range of coordinating functional groups affect the outcomes of nickel-catalysed Suzuki-Miyaura cross-coupling reactions.[12] The data in Scheme 3 show that K_{eq} decreases in the order cyclopentene > *cis*-cyclooctene > cycloheptene >> cyclohexene. The reticence of **3b** to engage in oxidative addition with **1** may be due to less favourable substrate coordination to the dppf-Ni^0 complex.

Computational studies, for which full details can be found in the supporting information,§ were used to further explore these reactions. Calculations were carried out at the MN15/6-311+G(d,p)/SMD(benzene)//B3LYP-D3/6-31G(d)+LANL2TZ(f) level of theory. This level of theory was benchmarked against DLPNO-CCSD(T)/cc-pVTZ/SMD(benzene) calculations.§

The exchange of COD for a cycloalkene at [Ni(dppf)] was explored first. The value of ΔG° increased in the order cyclopentene (3.4 kcal/mol; K_{eq} = 3 × 10^{-3}) < *cis*-cyclooctene (3.8 kcal/mol; K_{eq} = 2 × 10^{-3}) < cycloheptene (5.4 kcal/mol; K_{eq} = 1 × 10^{-4}) << cyclohexene (7.4 kcal/mol; K_{eq} = 4 × 10^{-6}), entirely consistent with the order of K_{eq} obtained experimentally.

The oxidative addition reactions proceed *via* displacement of COD from **1** by the substrate to form an intermediate η^2-complex, followed by oxidative addition *via* an S_N-type or five-centre transition state. The S_N-type transition states exhibit Ni···C interactions but no Ni···O interactions, while the latter show Ni···C and Ni···O interactions, as judged by QTAIM. § The profiles for the oxidative addition of phenyl, 1-naphthyl, and 2-naphthyl triflate (**2b-d**) are shown in Figure 2(a)-(c), as well as structures of the S_N-type and five-centre transition states. The two possible oxidative addition transition states for **2b** are within 1 kcal/mol, but naphthyl systems show a small preference for a five-centre transition state. These calculations correctly rank the aryl triflate substrates in order of reactivity, but somewhat overestimate the differences in reaction rate (k_{rel} = 5 × 10^4 : 6 × 10^2 : 1 for **2d** : **2c** : **2b**), assuming that the reaction rates approximately double for every 10 K increase in temperature.

The computational modelling of the reactions of *cis*-cycloalk-1-en-1-yl triflates are complicated by the various conformations that cycloalkenes can adopt.[17, 18] Data reported here are for the lowest energy pathway for each substrate (Figure 2).§§ The formation of an η^2-substrate complex ranges from slightly endergonic to slightly exergonic (G_{rel} = 0.7 to -2.8 kcal/mol). In most cases, the most favourable pathway for oxidative addition is *via* **TS^5**, with the exception of cyclohex-1-en-1-yl triflate (**3b**). DFT calculations suggest that the barrier to oxidative addition decreases in the order **3a** (12.6 kcal/mol) >**3b** (9.5 kcal/mol) > **3c** (7.1 kcal/mol) > **3d** (6.2 kcal/mol). §§§ The calculations therefore correctly rank three of the four substrates in the order of their reactivity.

A representative set of aryl and vinyl triflates was deployed in Kumada-Tamao-Corriu cross-coupling reactions to confirm that **1** is a competent catalyst for the cross-coupling reactions of these substrates (Scheme 4(a); Table 1). These conditions are unoptimised, but were previously deployed for the cross-coupling of alkyl halides with aryl Grignard reagents, and use only 1.1 equivalents of the latter.[13, 14] Reaction yields were quantified by GC-FID analysis using an internal standard, which was calibrated using authentic samples of each product; a substituted aryl triflate (**2g**) was used rather than **2a** in order to distinguish between cross- and homo-coupling processes. The reactions proceeded in moderate to excellent yields, confirming the competence of this catalyst system. There is not a correlation between oxidative addition rate and reaction yield, but these are single point yield measurements from catalytic reactions carried out at a higher temperature and for a longer

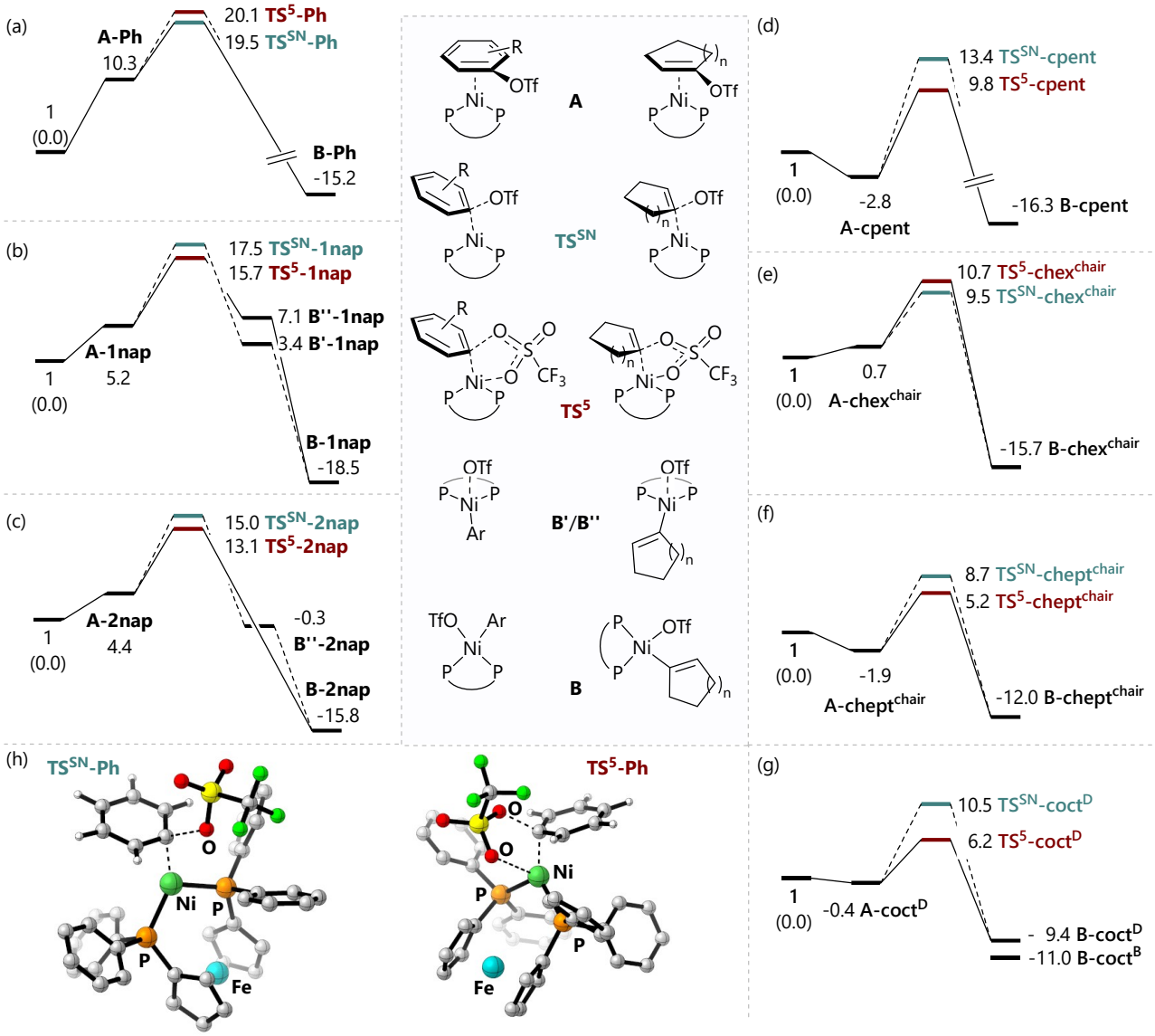
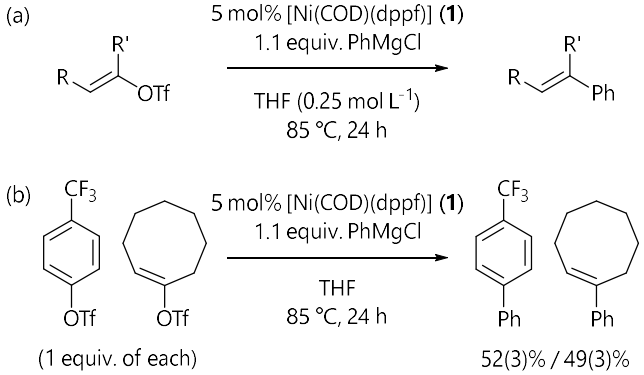


Figure 2. Free energy profiles at MN15/6-311+G(d,p)/SMD(benzene)//B3LYP-D3/6-31G(d)+LANL2TZ(f) for the oxidative addition reactions of complex **1** with (a) phenyl triflate (**2b**), (b) 1-naphthyl triflate (**2c**), (c) 2-naphthyl triflate (**2d**),. (d) cyclopent-1-en-1-yl triflate (**3a**), (e) cyclohex-1-en-1-yl triflate (**3b**), (f) cyclohept-1-en-1-yl triflate (**3c**) and (g) cyclooct-1-en-1-yl triflate (**3d**). (h) S_N-type (left) and five-centre (right) transition states for the oxidative addition of phenyl triflate (**2b**) to [Ni(COD)(dppf)] (**1**).

time period than the oxidative addition studies. The rather low yield of 1-phenyl-cyclopentene is an outlier, and the fate of the missing 45% of the substrate is unclear at this stage; this may be due to formation of cyclopentene, which is sufficiently volatile to be lost in the solvent front during GC-FID analysis.

Finally, we wished to identify whether the more favourable coordination of vinyl triflates to Ni^0 (compared to aryl triflates) might allow a selective cross-coupling reaction to be achieved. Reactions were carried out in which one equivalent of each of 4-(trifluromethyl)phenyl triflate and cyclooct-1-en-1-yl triflate were exposed to 1.1 equivalents of phenylmagnesium chloride and 5 mol% of [Ni(COD)(dppf)]; these reactions were unselective, and produced the corresponding products in approximately equal yield (Scheme 4(b)).



Scheme 4. Prototypical Kumada-Tamao-Corriu cross-coupling reactions.

Table 1. Outcomes of Kumada-Tamao-Corriu Cross-Coupling Reactions[a]

Substrate	Conversion	Yield
Cyclopent-1-en-1-yl Triflate (**3a**)	95%	50(2)%
Cyclohex-1-en-1-yl Triflate (**3b**)	100%	85(1)%
Cyclohept-1-en-1-yl Triflate (**3c**)	100%	87(5)%
Cyclooct-1-en-1-yl Triflate (**3d**)	100%	96%
para-(Trifluoromethyl)phenyl triflate (**2g**)	90(3)%	79(1)%

a) All reactions were conducted in duplicate under the conditions noted in Scheme 4, and results are reported as the average of two replicates. Yields determined by calibrated GC-FID analysis using an internal standard.§

In conclusion, we have systematically studied the reactions of a model Ni^0 complex with aryl and vinyl triflates. The preference for S_N-type *versus* five-centre oxidative addition transition states is a function of the substrate. The order of reactivity is approximately naphthyl > 2-pyridyl > vinyl > phenyl. The coordination of vinyl substrates to Ni^0 is likely to play a key role in determining the rate of oxidative addition but does not appear to enable vinyl-over-aryl selectivity.

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Author Contributions

M.E.G.: data curation; formal analysis; investigation; methodology; writing – original draft. S.S.: data curation; formal analysis; investigation; methodology; resources. T.O.R.: funding acquisition; project administration; supervision. D.J.N.: conceptualisation; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; supervision; visualisation; writing – original draft; writing – review & editing.

Notes and references

‡ Dedicated to Patricia Keating on her retirement after 40 years working within the Department of Pure & Applied Chemistry.
§ See the Supporting Information for full details.
§§ Conformations were generated based on the literature and/or using CREST/xTB. Pathways for each conformation are reported in the supporting information,§ and were explored in case the lowest energy pathway involved a conformational change.
§§§ It is unclear why the results for **3a** are not consistent with experimental observations. Repeated attempts to find alternative, lower-energy transition states were unsuccessful.

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