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Mild and Efficient Nickel-Catalyzed Heck Reactions with Electron-Rich Olefins

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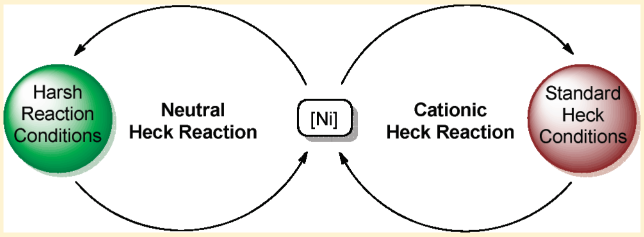
Supporting Information



ABSTRACT: A new efficient protocol for the nickel-catalyzed Heck reaction of aryl triflates with vinyl ethers is presented. Mild reaction conditions that equal those of the corresponding palladium-catalyzed Heck reaction are applied, representing a practical and more sustainable alternative to the conventional regioselective arylation of vinyl ethers. A catalytic system comprised of Ni(COD)$_2$ and 1,1′-bis(diphenylphosphino)ferrocene (DPPF) in combination with the tertiary amine Cy$_2$NMe proved effective in the olefination of a wide range of aryl triflates. Both electron-deficient and electron-rich arenes proved compatible, and the corresponding aryl methyl ketone could be secured after hydrolysis in yields approaching quantitative. Good functional group tolerance was observed matching the characteristics of the analogous Pd-catalyzed Heck reaction. The high levels of catalytic activity were explained by the intermediacy of a cationic nickel(II) complex potentially responsible for the successive β-hydride elimination and base promoted catalyst regeneration. Although these elementary reactions are normally considered challenging, DFT calculations suggested this pathway to be favorable under the applied reaction conditions.

INTRODUCTION

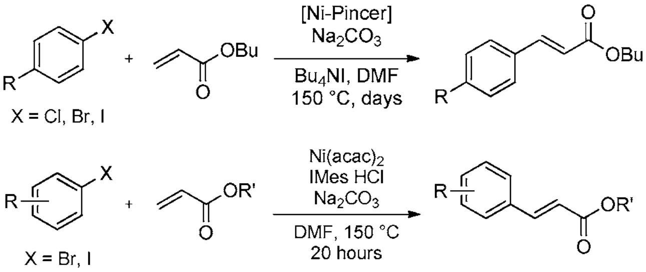
The Heck reaction represents one of the most important means for C−C bond formation in organic synthesis for the functionalization of olefins. Not only does this palladium-catalyzed reaction display an extraordinary functional group tolerance but due to the required *syn*-correlation during the β-hydride elimination, enantioselective variants of this reaction are also known.[1] Its immense applicability and many variations on both the laboratory and the industrial scale were recently recognized by the Nobel Prize Committee honoring Richard F. Heck for his discovery.[2] While palladium-based complexes are the most common catalysts for this reaction, efforts have been made to replace this metal with less expensive metals, such as nickel or cobalt.[3]

In the last 10 years, increasing attention has been directed toward nickel catalysis. The sustainability and relatively low prices of nickel precursors are important factors contributing to the attractiveness when considering transition-metal catalysis. Numerous reports have been disclosed on a wide variety of different nickel-catalyzed processes, including cross couplings,[4] cycloisomerization,[5] cycloadditions,[6] multicomponent couplings,[7] annulations,[8] reductive couplings,[9] and others.[10] Perhaps one of the most striking features of nickel catalysis compared to that of palladium is the broad range of adaptable electrophiles. In addition to aryl and vinyl halides and their corresponding sulfonates, functional groups traditionally inert toward oxidative addition, such as ethers,[11] metal alkoxides,[12] carboxylates,[13] carbamates[14] and so forth, have been accessed and utilized in a variety of cross coupling reactions.[15] Furthermore, alkyl halides have been employed with great success in various cross couplings creating both C(sp^3)−C(sp^3) and C(sp^3)−C(sp^2) σ-bonds under mild reaction conditions.[16,17] Alkyl halides possessing β-hydrogens proved perfectly suitable, and products arising from the undesired β-hydride elimination were not observed. This could be accounted for by an inherent reluctance of nickel to undergo β-hydride eliminations, although procedures relying on such transformations are well established, including the Shell higher olefin process.[18] Nevertheless, in contrast to other cross coupling reactions, nickel-catalyzed Heck couplings have only been scarcely described in the literature. This could indicate that the β-hydride elimination generating the nickel hydride intermediate, crucial to the Heck reaction, is in fact problematic.[19] Harsh reaction conditions, such as high temperatures, highly polar solvents, prolonged reaction times, or metal additives, are usually required for these reactions to proceed (Scheme 1).[20]

An alternative explanation for the observed difficulties in the Ni-catalyzed Heck reactions could also be the stronger bond energy of the Ni−H compared to the Pd−H, resulting in a more difficult reductive elimination step.[19] Hence, specific properties of both the base and the catalyst would be required

Received: September 7, 2011
Published: November 29, 2011

Scheme 1. Examples of Previously Reported Nickel-Catalyzed Heck Reactions



in order to regenerate the catalyst and complete the catalytic cycle.

Jamison and co-workers recently reported a protocol describing the nickel-catalyzed vinylation of allylic ethers and carbonates producing 1,4-dienes at ambient temperature (Scheme 2).[21] The underlying mechanism was proposed to proceed through an operational β-hydride elimination reaction from a cationic nickel(II) complex forming a cationic hydrido-nickel(II) intermediate. Subsequent base induced reductive elimination then regenerated the catalyst. Trimethylsilyl trifluoromethanesulfonate (TESOTf) was added to the reaction mixture in order to secure the formation of the cationic nickel-(II) intermediate, abstracting the alkoxylate from the nickel nucleus and leaving the poorly coordinating triflate counterion behind. Noteworthy, the reaction proceeded smoothly without the need of ionic liquids, high temperatures, or strong base, which could imply that the cationic nickel(II) intermediate is of utmost importance.

Traditionally, aryl and vinyl triflates have been used in the regioselective palladium-catalyzed Heck reaction of electron-rich olefins, facilitated by a cationic pathway, forming the α-substituted alkenes.[22] In this regard, bidentate ligands, such as bisphosphines, are typically employed in order to secure an effective generation of the cationic palladium(II) center responsible for the formation of the branched α-substituted olefins. On the other hand, monodentate phosphines tend to produce mixtures of both isomers as the competing neutral pathway then will operate.[23] The generation of the central cationic palladium(II) intermediate is, on the other hand, considerably hampered when introducing the halide equivalents. Consequently, mixtures of both regioisomers are often encountered, and certain requirements to the catalytic system are therefore needed.[24] Besides employing bidentate phosphine ligands, the choice of solvent may induce a dramatic impact on the regioselective outcome of the reaction. Hence, highly polar solvents or ionic liquids favoring the cationic pathway have efficiently been applied in the α-arylation of electron-rich olefins using aryl halides, as reported by the groups of Xiao, Larhed, and Hallberg.[25] Alternatively, silver- or thallium-based halide scavengers can be used.[26]

In light of the results presented by the group of Jamison and our own experiences with the regioselective palladium-catalyzed reaction between aryl and vinyl tosylates and electron-rich olefins, we set forth to investigate the nickel-catalyzed arylation of electron-rich olefins in more detail.[27,28] In this paper, we wish to report our discoveries regarding the implementation of nickel as an efficient catalyst for the regioselective coupling of aryl triflates and alkyl vinyl ethers. To the best of our knowledge this constitutes the first Ni-catalyzed Heck reaction of aryl substrates proceeding under mild reaction conditions competitive to those of the corresponding Pd-catalyzed Heck reaction. Furthermore, mechanistic insight is provided based on DFT calculations supporting the cationic nickel(II) complex as the key intermediate.

■ RESULTS AND DISCUSSION

A catalytic system derived from Ni(COD)$_2$ and a bidentate phosphine ligand in combination with a tertiary amine base (Cy$_2$NMe) was envisioned to be a suitable starting point in the coupling of 4-biphenyl triflate **1** and butyl vinyl ether.[29] Preliminry screenings revealed that this was indeed possible (Table 1). Conducting the reaction in dioxane at 100 °C for approximately 20 h resulted in a 21% conversion using 1,2-bis(diphenylphosphino)ethane (DPPE) as the ligand (entry 1). Increasing the bite angle of the bisphosphine facilitated the desired reaction to a greater extent (entries 2 and 3).[30] Gratifyingly, full conversion was obtained when 1,1′-bis(diphenylphosphino)ferrocene (DPPF) was employed, and a 90% isolated yield of 4-phenylacetophenone **2** could be secured after hydrolysis of the initially formed α-arylated butyl vinyl ether (entry 4). Changing to solvents such as toluene or THF proved less effective compared to dioxane (entries 5 and 6). However, applying diglyme as the solvent restored the high catalytic outcome forming the α-substituted vinyl ether selectively in a 90% isolated yield (entry 7). Catalytic systems carrying more bulky and electron-donating ligands did not provide any detectable amounts of the desired product (entries 8——11). Applying monodentate phosphine ligands, which have demonstrated to be of high value in other coupling reactions, turned out to be nonproductive (entries 12 and 13).[31] Different amine bases were then evaluated. Diisopropylethylamine (DIPEA) and triethylamine, often used in palladium-catalyzed Heck reaction, were inferior compared to Cy$_2$NMe (entries 14 and 15). On the other hand, no reaction was observed when changing the base to pyridine or increasing the basicity, as in the case of DBU (entries 16 and 17). A significant drop in the reaction turnover was observed when lowering the reaction temperature to 80 °C. Moreover, changing the catalyst precursor to Ni-(acac)$_2$ resulted in no reaction (results not shown).

With these optimized conditions in hand, we set forth to investigate the generality of this reaction. A variety of aryl triflates were synthesized using standard procedures and evaluated

Scheme 2. Nickel Catalyzed Allylic Substitutions of Simple Alkenes

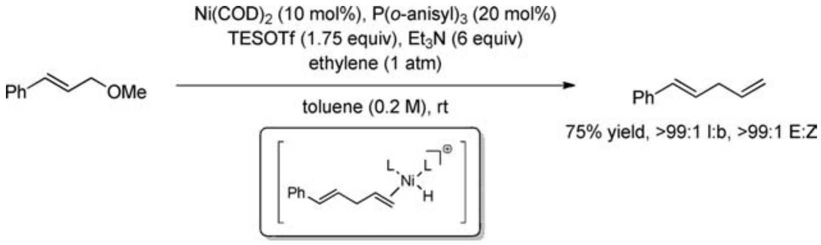
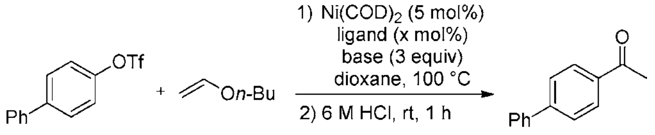


Table 1. Screening the Nickel-Catalyzed Heck Reaction of 4-Biphenyl Triflate and Butyl Vinyl Ether[a]



1 2

entry	ligand (mol %)	base	conversion (%)[b]
1	DPPE (5)	Cy_2NMe	21
2	DPPP (5)	Cy_2NMe	46
3	BINAP (5)	Cy_2NMe	42
4	DPPF (5)	Cy_2NMe	100 (90)
5	DPPF (5)	Cy_2NMe	66[c]
6	DPPF (5)	Cy_2NMe	80[d]
7	DPPF (5)	Cy_2NMe	100 (90)[e]
8	PPF-*t*Bu (5)	Cy_2NMe	<5
9	D*i*PrPF (5)	Cy_2NMe	<5
10	D*t*BuPF (5)	Cy_2NMe	<5
11	Xantphos (5)	Cy_2NMe	<5
12	PCy_3HBF_4 (10)	Cy_2NMe	<5
13	PPh_3 (10)	Cy_2NMe	<5
14	DPPF (5)	DIPEA	76
15	DPPF (5)	Et_3N	69
16	DPPF (5)	pyridine	<5
17	DPPF (5)	DBU	<5

[a] Aryl triflate (0.15 mmol), butyl vinyl ether (0.6 mmol), base (0.45 mmol), and dioxane 1 mL at 100 °C for 20 h. [b] Isolated yields. [c] Toluene as solvent. [d] THF as solvent. [e] Diglyme as solvent. [f] (2R)-1-[(1R)-1-[Bis(1,1-dimethylethyl)phosphino]ethyl]-2-(diphenylphosphino)ferrocene. [g] 1,1′-bis(diisopropylphosphino)ferrocene. [h] 1,1′-Bis(di-tert-butylphosphino)ferrocene.

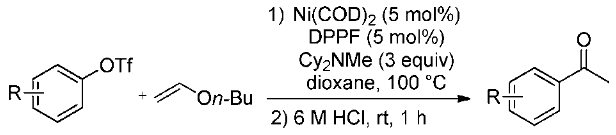
with butyl vinyl ether (Table 2).[32] In general, good to excellent yields of the desired aryl methyl ketones were obtained after treating the resulting aryl vinyl ether with 6 M HCl at room temperature for approximately 1 h. Aryl triflates containing both electron-withdrawing and -donating groups performed well under the applied reaction conditions. Functionalities, such as esters, amides, cyano, diazo, and acetals, and trifluoromethyl groups were allowed, paralleling the functional group tolerance observed in the analogous palladium-catalyzed Heck reaction (entries 4–13). Furthermore, acetylation of biological relevant structures represented by carbazole,[33] eugenol,[34] isoeugenol,[34] and coumarin[35] were successfully achieved attaining near quantitative yields (entries 14–17). Interestingly, isomerization of the allyl double bond in the coupling of eugenol triflate was identified generating mixtures of the conjugated cis- and trans-adducts along with the nonisomerized ketone product (entry 16). Potentially, this could be explained by a long-lived nickel hydride complex responsible for a consecutive hydronickelation and β-hydride elimination forming the thermodynamically more stable styrene derivative.[36] Somewhat lower yields were obtained in some cases, when electron-donating groups were positioned para to the triflate or ortho-substituents were introduced on the aromatic ring (entries 3 and 7–9). However, a slight increase in the catalytic loading restored the high levels of the synthetically useful outcome. Even heteroaromatic systems, such as quinolines, turned out to be adaptable to the optimized reaction conditions resulting in a 56% isolated yield of the heteroaryl ketone after hydrolysis (entry 18). Finally, an example with a vinyl triflate (entry 19) proved also effective for these Ni-catalyzed transformations. The coupling yield for this substrate was nevertheless lower than that obtained for the corresponding aromatic counterpart (entry 2).

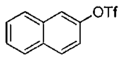
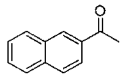
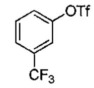
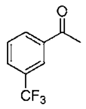
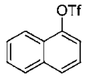
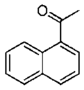
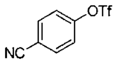
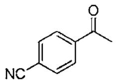
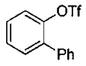
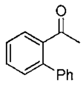
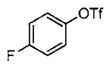
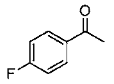
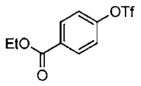
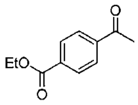
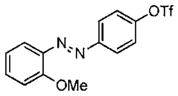
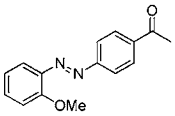
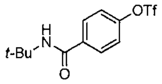
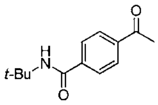
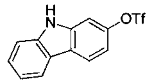
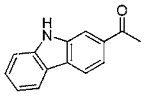
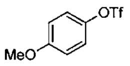
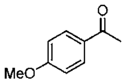
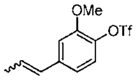
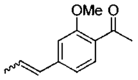
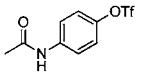
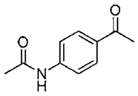
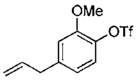
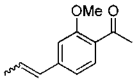
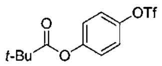
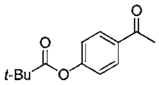
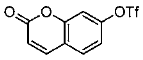
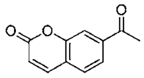
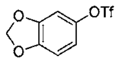
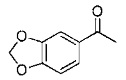
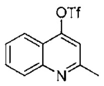
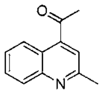
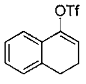
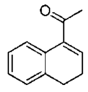
Having established an efficient catalytic system for the nickel-catalyzed Heck reaction with an electron-rich olefin, a more in-depth study of the mechanistic details was desired. In order to investigate the role of the leaving group, aryl sulfonates with different electronic properties were prepared from 2-naphthol and various arylsulfonyl chloride derivatives using known procedures (Table 3).[28] Relying on the optimized reaction conditions, the coupling between 2-naphthyl benzenesulfonate and butyl vinyl ether resulted in a 68% conversion (entry 1). Mixtures of regioisomers were obtained, suggesting that both the neutral and the cationic pathway are operating (entry 1). A slight increase in the electron density impeded the reaction, as illustrated by the reaction of 2-naphthyl tosylate (entry 2). In contrast, electron-withdrawing substituents, such as the trifluoromethyl group, favored the nickel-catalyzed Heck coupling although mixtures of regioisomers were again observed (entries 3 and 4). On the other hand, employing pentafluorophenyl sulfonate as the leaving group provided a clean reaction, generating the α-substituted butyl vinyl ether selectively, and a 91% yield of the corresponding 2-acetonaphthone **3** could be secured (entry 5). Reduced catalytic activity was observed, when a nitro group was introduced on the arylsulfonate (entries 6 and 7).

Furthermore, halide additives, such as LiCl and TBAB, completely inhibited the reaction presumably due to the trapping of the cationic nickel(II) complex, hence occupying the vacant site on the nickel nucleus and thereby preventing the β-hydride elimination step (results not shown).[25a,37,38]

Next, different olefins were tested in the coupling of 4-biphenyl triflate (Table 4). Introducing an isobutyl side chain on the vinyl ether did not affect the catalytic efficiency forming the 4-phenyl acetophenone in excellent yields after hydrolysis (entry 1). Employing a sterically encumbered vinyl ether or the cyclic olefin 2,3-dihydrofuran, traditionally used in the enantioselective Heck reaction, lowered the yield dramatically (entries 2 and 3). Moreover, essentially no reaction was obtained in the coupling of *N*-vinyl acetamide, *N*-vinyl 2-pyrrolidone, and vinyl

Table 2. Nickel-Catalyzed Heck Reaction of Aryl Triflates and Butyl Vinyl Ether[a]



entry	aryl triflate	product	compound	yield (%)[b]	entry	aryl triflate	product	compound	yield (%)[b]
1			**3**	91	10			**12**	81
2			**4**	97	11			**13**	78
3			**5**	88[c]	12			**14**	78[c]
4			**6**	79	13			**15**	75
5			**7**	90	14			**16**	76
6			**8**	93	15			**17**	97
7			**9**	56	16			**18**	92[d]
8			**10**	83[c]	17			**19**	78
9			**11**	77[c]	18			**20**	56
					19			**21**	67

[a] Aryl triflate (0.5 mmol), butyl vinyl ether (2.0 mmol), Cy_2NMe (1.5 mmol), DPPF (5 mol %), and $Ni(COD)_2$ (5 mol %) in dioxane 3 mL at 100 °C for 20 h. [b] Isolated yields. [c] DPPF (7 mol %) and $Ni(COD)_2$ (7 mol %). [d] A 7:10:2 mixture (*E*:*Z*:allyl) was obtained.

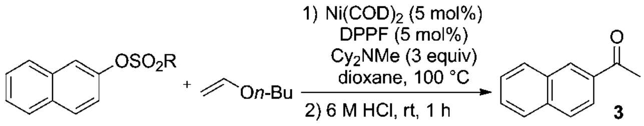
acetate (entries 4–6). Possibly, coordination of the amide/ester carbonyl group to the empty site on the metal center could potentially account for the lack of reactivity.[39] The cationic alkylnickel(II) complex formed after the olefin insertion, which is electron deficient and unsaturated, could therefore be stabilized and thus become reluctant to undergo *β*-hydride elimination (Scheme 3).

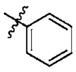
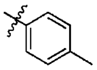
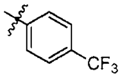
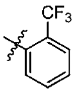
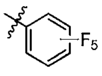
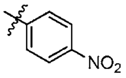
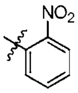
Finally, the couplings of ethyl vinyl sulfide and allyltrimethylsilane failed most likely due to catalyst poisoning by the sulfide and lack of nucleophilicity displayed by the less electron-rich allyltrimethylsilane (entries 7 and 8).[25a,40]

These results clearly demonstrate vinyl ethers to be the most suitable olefins in the nickel-catalyzed Heck reaction, contrasting the results obtained in the palladium-catalyzed Heck reactions of 2-pyridyl tosylates, in which *N*-vinyl acetamides were found to be considerably more reactive.[28] Hence, a competition experiment was set up adding a 1:1 mixture of butyl vinyl ether and *N*-vinyl acetamide to a mixture of 4-biphenyl triflate and the DPPF ligated nickel catalyst in combination with Cy_2NMe (Scheme 4). Only traces of the two possible 1,1-disubstituted alkenes were detected, implying that the nickel catalyst is truly obstructed by *N*-vinyl acetamide.

The results presented in Tables 2–4 suggest an unsaturated cationic nickel(II) intermediate to be essential in order to achieve successful coupling. In particular, the reductive elimination in transition metal catalysis has been shown to be influenced by a number of factors, including the electronic properties of the metal center and the steric effects of the chelating ligands.[1a] For instance, electron poor transition-metal complexes tend to be more prone to facilitate the reductive elimination in contrast to metal complexes with high electron densities.[41] Furthermore, Brown and co-workers have demonstrated that the bite angle of bidentate ligands has a great impact on this catalyst recovering step, whereby an increase in the rate of reductive elimination is observed with increasing bite angles of the ligand.[42] Thus, the electron deficient nature of the cationic hydridonickel intermediate and the bite angle of the bidentate ligand could possibly account for a more favorable *β*-hydride elimination and reductive elimination observed in this work, thereby representing a new strategy in the nickel-catalyzed Heck reaction.

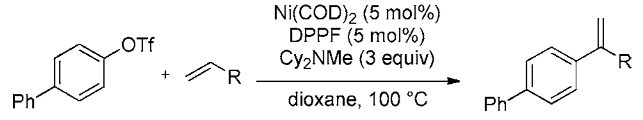
Table 3. Nickel-Catalyzed Heck Reaction of 2-Naphthyl Sulfonates and Butyl Vinyl Ether[a]

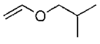
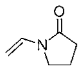
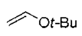
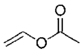
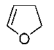
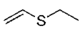
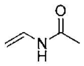
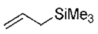


Entry	R	conversion (%)[b]
1		68[c]
2		40[c]
3		56[c]
4		85[c]
5		100 (91)
6		17
7		6

[a]Aryl sulfonate (0.15 mmol), butyl vinyl ether (0.60 mmol), Cy$_2$NMe (0.45 mmol), DPPF (5 mol %), and Ni(COD)$_2$ (5 mol %) dioxane 1 mL at 100 °C for 20 h. [b]Isolated yields. [c]Mixtures of regioisomers were observed.

Table 4. Nickel Catalyzed Heck Reaction of 4-Biphenyl Triflate and Various Olefins[a]



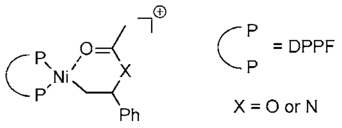
entry	olefin	conversion (%)[b]	entry	olefin	conversion (%)[b]
1		100 (91%)	5		10
2		37	6		< 5
3		35	7		< 5
4		11	8		< 5

[a]Aryl triflate (0.5 mmol), olefin (2.0 mmol), Cy$_2$NMe (1.5 mmol), DPPF (5 mol %), and Ni(COD)$_2$ (5 mol %) dioxane 3 mL at 100 °C for 20 h. [b]Isolated yields.

■ DFT STUDIES

In order to examine the influence of the intermediary cationic nickel(II) complexes on the elementary reactions constituting the catalytic cycle, a DFT study was performed. For computational efficiency, the catalytically competent ligand 1,3-bis(diphenylphosphino)propane (DPPP) was used in the calculations. Experimentally, DPPF is better, but the difference is not large enough to motivate the substantial computational resources needed to add a ferrocene moiety to the already large computational model. Phenyl triflate and ethyl vinyl ether were used as model substrates (Figure 1). The bisphosphine nickel(0) complex coordinating to the phenyl triflate prior to the oxidative addition (complex **I**) was selected as the starting point of the computational cycle. Reaction profiles are calculated from free energies, with dotted lines representing alternative paths that are excluded because of high barriers and dotted curves represent ligand exchange that could be either dissociative or associative, where the former can be monotonous processes on the potential energy surface (see Computational Details for further information).

Scheme 3. Nickel-Catalyzed Allylic Substitutions of Simple Alkenes

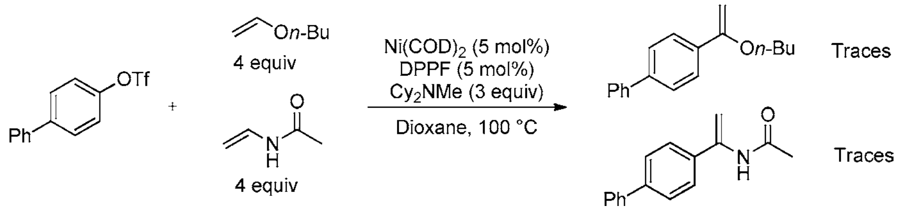


The oxidative addition of phenyl triflate to the nickel(0) complex resulting in the bisphosphine phenylnickel(II) triflate complex **II** was found to be highly exergonic (−131 kJ mol^{-1}) with an activation barrier of 15 kJ mol^{-1} (Figure 1). The exchange of the weakly coordinating triflate anion forming the cationic nickel(II) complex **III** coordinated by the ethyl vinyl ether revealed itself slightly more stable than the parent neutral nickel(II) complex **II**. The regioselective outcome of the reaction is determined in the subsequent carbonickelation of the olefin forming the α- or β-substituted alkene via **TS-b** and **TS-c**, respectively (Figure 2). However, under the applied reaction conditions the primary alkylnickel(II) complex **TS-b** leading to the branched α-arylated alkene was strongly favored over the secondary alkylnickel(II) species **TS-c** by 20 kJ mol^{-1}, resulting in less than 0.1% of the linear product, in good agreement with the results observed experimentally.

Displacement of the coordinated phenyl group in complex **IV** with the oxygen moiety via a rotation of the C−C bond was found to proceed with a barrier of 18 kJ mol^{-1} compared to 31 kJ mol^{-1}, leading to the agostic complex through **TS-e**. The generation of the kinetically favored oxygen coordinated cationic alkylnickel(II) complex **V** represents the most stable complex obtained after olefin insertion with a free energy 37 kJ mol^{-1} below that of complex **IV**. The formation of the agostic nickel(II) complex **VI** by a consecutive rotation of the C−C bond in **V** proved to be a demanding process, with a barrier of 68 kJ mol^{-1} (Figure 3). Interestingly, this C−C bond rotation **TS-f** demonstrated to be of higher energy than the following β-hydride elimination via **TS-g** in accordance to the observations reported by Norrby and co-workers in the palladium-catalyzed Heck reaction.[43]

The cationic nickel(II) hydride complex **VII** then undergoes a base induced reductive elimination **TS-h** regenerating the nickel(0) catalyst coordinated by the α-arylated vinyl ether product **VIII**. The barrier for this process was calculated to be 47 kJ mol^{-1} using the computationally more simplistic trimethyl amine as a model base compared to Cy$_2$NMe. Several different base promoted hydrogen abstractions were investigated, including the reductive elimination from an amine coordinated hydridonickel(II) complex.[29] However, none of these were found to be more efficient than the bimolecular process depicted as **TS-h** in Figure 3. Endergonic ligand exchange (30 kJ mol^{-1}) substituting the olefinic product with another phenyl triflate completes the catalytic cycle.

Scheme 4. Competition Experiment Between Butyl Vinyl Ether and *N*-Vinyl Acetamide



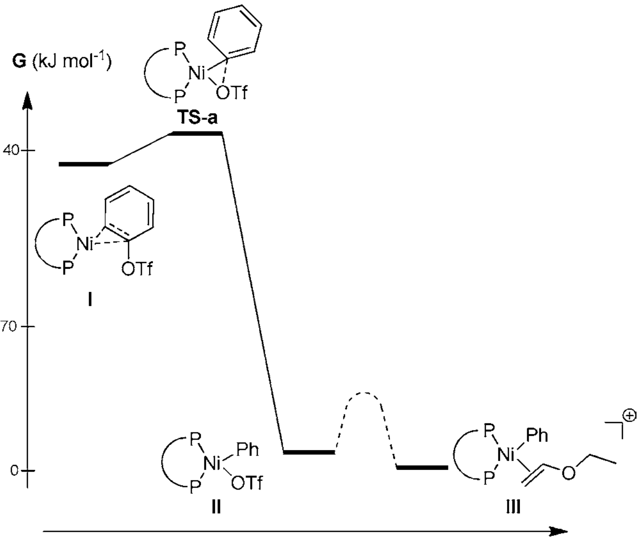


Figure 1. Oxidative addition and ligand exchange.

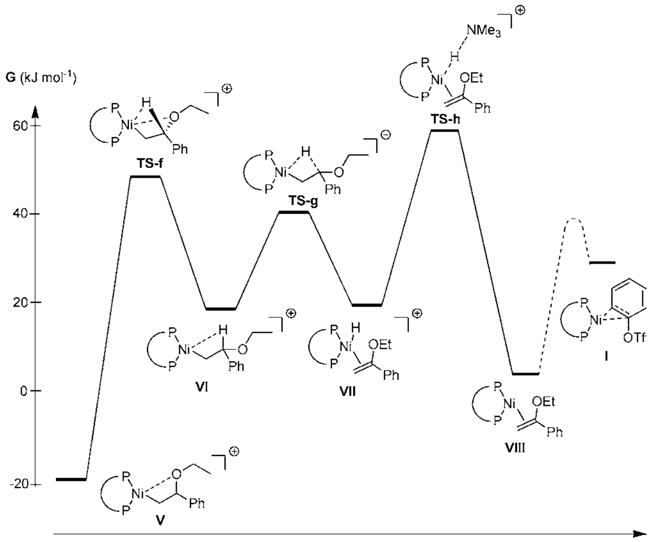


Figure 3. β-Hydride elimination and reductive elimination.

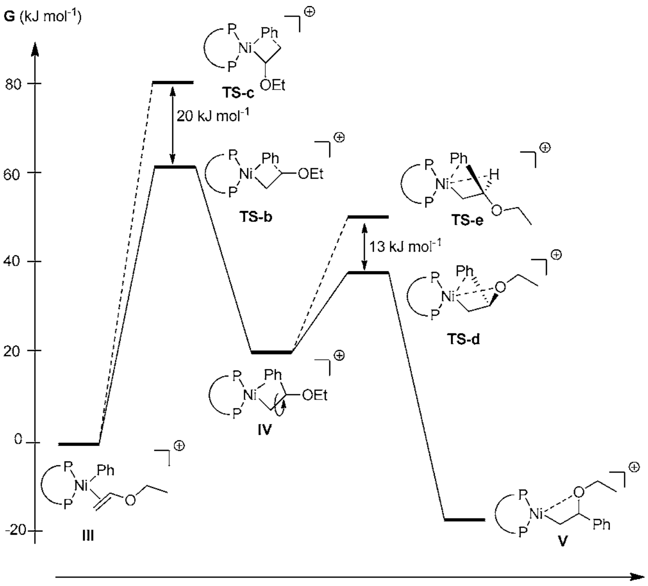


Figure 2. Carbonickelation and chelation.

From the simplified overall catalytic cycle depicted in Figure 4, two transition states can be identified as effectively irreversible (**TS-a** and **TS-h**), as they are higher than any subsequent point on the global free energy surface. The resting state of the nickel-catalyzed Heck reaction can be identified as the alkylnickel(II) complex **V** generated after the migratory insertion, which would imply that the migratory insertion can be reversible. However, the alternative reaction pathway forming a terminal alkylnickel(II) complex is still energetically inaccessible since **TS-c** is higher in energy than **TS-h**.[44] On the other hand, the β-hydride elimination and catalyst regeneration were both found to be endergonic and thus constitute the most demanding step with an overall barrier of 87 kJ mol^{-1} through **TS-h**. These findings parallel the calculations performed by Guo and co-workers suggesting the reductive elimination to be the rate-determining step in the nickel-catalyzed Heck reaction.[19] The highly exergonic oxidative addition ensures the total lowering in the energy facilitating the consecutive catalytic cycle.

On the other hand, impeded reaction rates could possibly be encountered if any of the other potential resting states including complex **II** obtained after the oxidative addition were significantly stabilized (Figure 1). During the investigations on the influence of the leaving group, a detrimental effect of added halides to the reaction mixture was observed. This effect was proposed to originate from the trapping of the crucial cationic nickel(II) intermediate blocking the vacant site mandatory in order to facilitate the olefin coordination.[38] Consequently, calculations regarding the dissociation of a bromide anion from the nickel(II) center were conducted (Scheme 5).

The presence of bromide anions proved to stabilize the neutral nickel(II) complex considerably by a free energy of 69 kJ mol^{-1} compared to complex **II** which would result in a carbonickelation barrier corresponding to 132 kJ mol^{-1}, essentially preventing further reaction.

Performing the nickel-catalyzed Heck reaction with olefins containing carbonyl groups, such as *N*-vinylacetamide, afforded the desired product only to a limited extent (Table 4). The potential coordination of the carbonyl oxygen to the electron deficient cationic nickel(II) intermediate was suggested to obstruct the β-hydride elimination. Hence, DFT calculations were

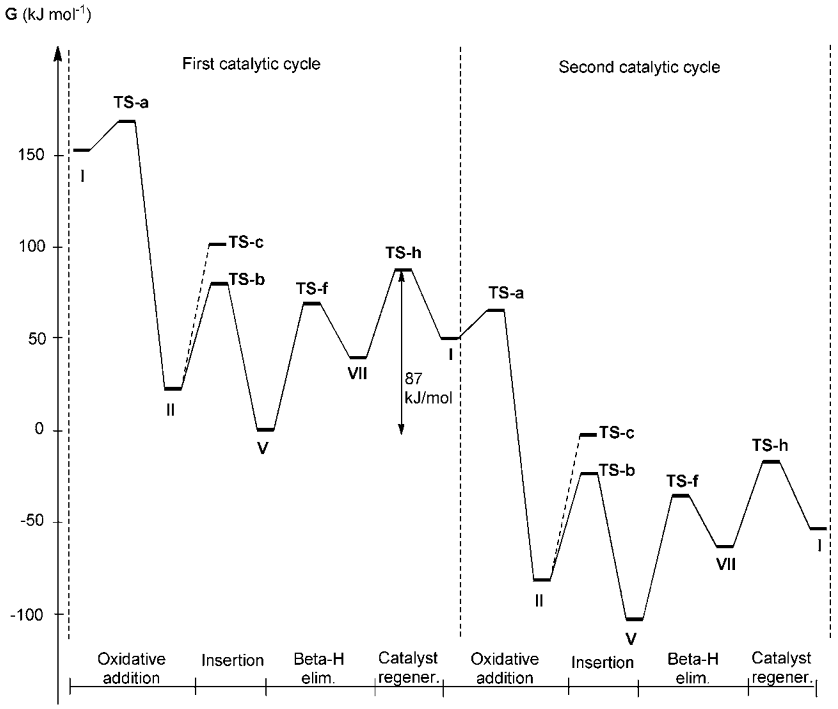
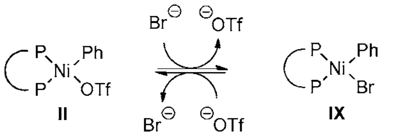
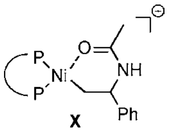


Figure 4. Simplified free energy surface of two sequential catalytic cycles.

Scheme 5. Nickel(II) Bromide and Triflate Complexes



Scheme 6. Coordination of Carbonyl Oxygen



commissioned in order to evaluate the coordinating abilities of the carbonyl moiety (Scheme 6).

The transition state for the *β*-hydride elimination from the cyclic cationic alkylnickel(II) complex **X** was located with a free energy barrier of 94 kJ mol^{-1} compared to 68 kJ mol^{-1} (from **V**–**VII**, Figure 4), accounting for the poor catalytic outcome observed using carbonyl containing olefins.

■ CONCLUSION

In summary, a new efficient strategy for the nickel-catalyzed Heck reaction of aryl triflates and vinyl ethers has been presented. The mild reaction conditions applied allow the presence of a wide range of functional groups complementing the palladium based analogous. This approach represents a more sustainable and less costly alternative for the vinylation of aromatic compounds. The high catalytic activity was attributed to the formation of a crucial cationic nickel complex formed during the catalytic cycle being responsible for a favorable *β*-hydride elimination step and subsequent reductive elimination. DFT calculations supported this assumption, revealing the cationic nickel intermediates to be of utmost importance.[45]

■ EXPERIMENTAL SECTION

General Methods. All reactions were carried out in 7.0 mL sample vials with a Teflon-sealed screwcap in a glovebox under an argon atmosphere. All purchased chemicals were used as received without further purification. Solvents were dried according to standard procedures, reactions were monitored by thin-layer chromatography analysis, and flash chromatography was carried out on silica gel 60 (230–400 mesh). The chemical shifts are reported in ppm relative to solvent residual peak.[46] The ^{1}H NMR spectra were recorded at 400 MHz, ^{13}C NMR spectra were recorded at 100 MHz, and ^{19}F NMR spectra were recorded at 376 MHz on a Varian Mercury 400 spectrometer (see Supporting Information). MS spectra were recorded on a LC TOF (ES) apparatus. The aryl triflates were synthesized according to known procedures.[47] The aryl sulfonates depicted in Table 3 were prepared using known procedures.[48]

7-Acetyl-2*H*-chromen-2-one (Table 2, entry 17). In dioxane (3 mL), 2-Oxo-2*H*-chromen-7-yl triflate (0.5 mmol), DPPF (5 mol %), Cy_2NMe (1.5 mmol), vinyl ether (2.0 mmol), and $Ni(COD)_2$ (5 mol %) were dissolved, and the sample vial was fitted with a Teflon-sealed screwcap and removed from the glovebox. The reaction mixture was stirred at 100 °C for 20 h. Hydrolysis was performed adding 6 M HCl (3 mL) to the reaction mixture and stirred at room temperature for 1 h. Diethyl ether was added, and the crude reaction mixture was washed twice with water and once with brine, dried over anhydrous $MgSO_4$, and filtrated. Flash chromatography using diethyl ether:-pentane:CH_2Cl_2 2:2:1 as eluent resulting in 73.0 mg (78% yield) of the title product obtained as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.82–7.79 (m, 2H), 7.73 (d, 1H, J = 9.5 Hz), 7.56 (d, 1H, J = 7.9 Hz), 6.48 (d, 1H, J = 9.5 Hz), 2.61 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 196.5, 160.1, 153.9, 142.5, 139.3, 128.3, 122.2, 118.9, 116.7, 26.9. HRMS $C_{11}H_{18}O_3$ [M + Na^{+}]: calculated 211.0371; found 211.0366.

■ COMPUTATIONAL DETAILS

The calculations were performed using Jaguar, version 7.6,[49] employing the B3LYP hybrid functional[50] with the LACVP* basis set, which uses an effective core potential[51] for Pd and 6-31G* for all other atoms. All geometries were optimized in the gas phase with a subsequent single-point energy calculation in the solution phase, utilizing the PBF solvation model[52] with parameters suitable for THF (ε = 7.6, probe radius =2.52 Å), which is a competent solvent for the title reaction and computationally more feasible than the experimentally preferred dioxane. Vibrational analysis was performed for the optimized geometries in the gas phase, and the free energies for the geometries were calculated by adding the thermodynamic contribution at 298.15 K to the solution phase energy. Dispersion corrections were calculated using the DFT-D3 program[53] and added to obtain the final energies. The transition states in the lowest free energy path on the potential energy surface were determined to be connected to their corresponding reactants and products via geometry optimization in the forward and backward direction from the transition state. All transition states presented have exactly one imaginary frequency, and the stationary minima have no imaginary frequencies.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details and copies of ^{1}H NMR and ^{13}C NMR spectra for all the coupling products. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENTS

We thank the Danish National Research Foundation, the Lundbeck Foundation, the Carlsberg Foundation, the iNANO and OChem Graduate Schools, and Aarhus University for generous financial support of this work

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