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Palladium-Based Hydroamination Catalysts Employing Sterically Demanding 3-Iminophosphines: Branched Kinetic Products by Prevention of Allylamine Isomerization

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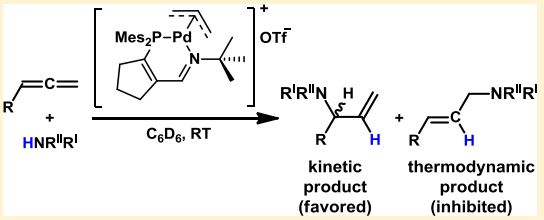
Supporting Information

ABSTRACT: A new allylpalladium triflate catalyst with a dimesitylphosphine moiety was synthesized, isolated, and characterized. The greatly increased steric bulk on the phosphine of this palladium catalyst inhibited product isomerization, which is often observed after hydroamination of terminal allenes with secondary amines. The considerably reduced rate of isomerization facilitated the isolation of many previously unknown branched allylamines, products that were inaccessible when using other, more active 3-iminophosphine palladium catalysts.



INTRODUCTION

Catalytic hydroamination is a green chemical method for the production of new C−N bonds through the 100% atom-economic addition of an amine to an alkene or alkyne. This approach to creating C−N bonds can be used in the formation of a variety of nitrogen-containing organic building blocks,[1] but a catalyst is necessary for hydroamination because of high activation barriers and an unfavorable entropy term. Additionally, [2 + 2] cycloaddition of an N−H bond and a C−C unsaturated system is orbitally forbidden.[2] So, a variety of metals supported by a wide range of ligands have been used for this reaction over the years.[3] Hydroamination has been successfully employed to regio- and enantioselectively yield N-containing products as an economic means to synthesize biologically active molecules or pharmaceuticals.[3,4] With many years of intense study, mechanistic analysis has enabled chemists to decipher the critical steps in the relevant catalytic cycles, leading to logical modulation of the ligands utilized in a quest for the best catalytic process.[5]

One significant method to synthesize allylamines is through the hydroamination of allenes with primary or secondary amines.[3,4c,6] Allylamines are useful building blocks in the synthesis of heterocycles and complex bioactive molecules.[7] Driven by this synthetic utility, there has been a substantial interest in the hydroamination of allenes with various transition-metal catalysts investigated to date.[4c,8] The presence of cumulated double bonds in an allene means that three possible hydroamination regioisomeric products could be produced, but only two regioisomers are expected to form when using a late metal catalyst because of the operable mechanisms. For a monosubstituted allene, a less stable kinetic product is formed by addition of N to the substituted terminal carbon of the 3-carbon cumulated system, whereas the thermodynamic product is formed by addition of N to the unsubstituted terminal carbon atom. Because of the mechanisms available for the late transition metal, addition of nitrogen to the central carbon atom is not observed. Unsurprisingly, the more stable thermodynamic product is usually produced, as seen with gold,[6b,9] platinum,[10] palladium,[11] copper,[8a] nickel,[12] and other transition-metal catalysts.[6b] Successful synthesis and isolation of the kinetic product has been limited to very few catalysts, such as only those using rhodium and palladium.[4c,13] These branched products, bearing a terminal vinyl group adjacent to a secondary or tertiary carbon atom, are synthetically quite useful, and thus catalysts capable of producing this isomer in isolable quantities remain attractive goals in this field.

Given the usefulness of allylamines, our group has been studying the hydroamination of allenes with primary and secondary amines using 3-iminophosphine palladium complexes over the past decade.[4c,5f,6a,12,14] With respect to catalytic hydroamination activity, we have studied the interrelationships of the imine substituents, the ring size of the backbone, and the phosphine substituents on these 3-iminophosphine ligands.[14b] We previously reported that more electron-donating phosphines enhance the catalytic activity of their palladium complexes.[14b] We also deduced that the electronics of the imine substituent must be carefully optimized to maximize catalytic activity.[5f] Furthermore, we showed that smaller backbone ring sizes with decreased bite angles favor higher catalytic activity by increasing the ring strain, an effect that seems to be related to detaching the imine substituent from palladium upon coordination of amines.[14b,15] Throughout all of our previous studies, relatively small phenyl and *tert*-butyl groups were studied on the phosphine unit; so the effect of sterically bulky phosphines has not been investigated. Herein, we present the synthesis of sterically encumbered 3-

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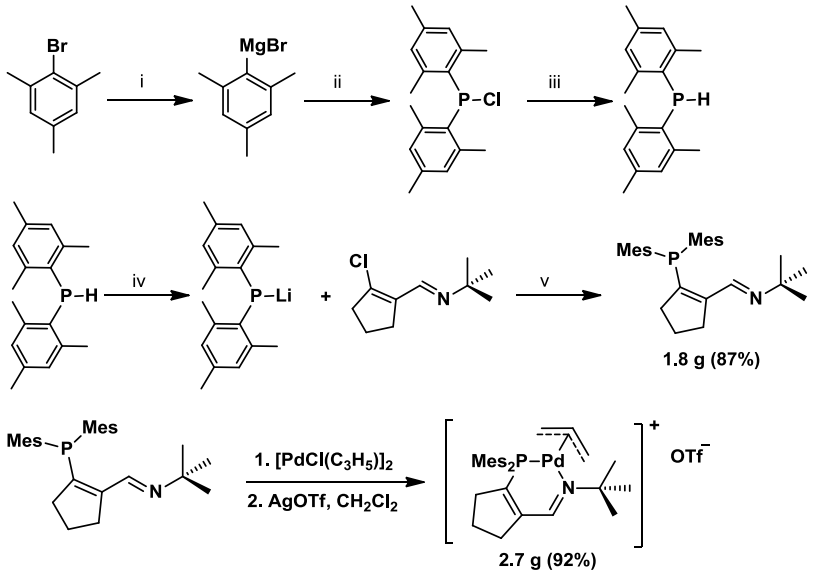
Organometallics XXXX, XXX, XXX−XXX

Scheme 1. Synthesis of (3-Iminophosphine)palladium Triflate Complex[a]



[a]Legend: (i) 1.2 equiv mg, THF, 0 °C, 1 h and then RT. (ii) 0.45 equiv PCl_3, THF, −78 °C and slow increase to RT. (iii) 1.5 equiv $LiAlH_4$, Et_2O, 0 °C and then RT. (iv) 1.1 equiv *n*-BuLi, Et_2O, 0 °C and then RT. (v) Et_2O, 0 °C for 1 h and then RT.

iminophosphine palladium complexes and the resulting impact on product selectivity in their catalytic hydroamination of allenes.

RESULTS AND DISCUSSION

3-Iminophosphine ligands have three permutable components: the alicyclic ring, the imine substituent, and the phosphine group. On the basis of our previous reports, we have observed that the ligand containing a cyclobutenyl backbone, a *tert*-butyl substituent on the imine, and di*tert*-butylphosphine provides the palladium complex that is most effective in catalytic hydroamination.[4c,14b] We also showed that the electron donation provided by the imine group was critically important for both the deprotonation of the amine substrate and the hemilabile displacement of the imine from the active palladium metal center.[5f] Hence, tuning of the electron donation of the imine substituent is crucial for effective catalytic hydroamination.[5f]

Additionally, we reported the successful synthesis of kinetic hydroamination products (addition of N- to the more substituted terminal carbon of the allene) using a di*tert*-butylphosphine-substituted catalyst for the hydroamination of monosubstituted allenes with various secondary amines.[4c] Unfortunately, a major drawback of this highly active system was that the kinetic products isomerized quickly to produce the thermodynamic products in the presence of the catalyst, especially after the substrates were completely consumed.[4c] In general, access to the branched kinetic hydroamination products in this chemistry proves to be a question of relative rates. The rate of hydroamination to yield the branched products must be substantially larger than the rate of the subsequent isomerization reaction converting these branched products to the linear isomers. This is especially relevant as the hydroamination reaction nears completion given the increasing concentration of the product branched allylamine and the decreasing concentrations of the initial substrates. In our previous work,[4c] there were several substrates where we could monitor and then quench the reaction before significant isomerization occurred, but unfortunately, many of the substrates proved to have rapid enough isomerization reactions that the amount of branched product never reached large enough levels to warrant quenching and attempted isolation, meaning that only the linear products were synthetically viable in those cases. So, in the present investigation, we hypothesized that by adding more steric bulk on the phosphine fragment, we could enhance selectivity for the kinetic products while simultaneously eliminating or reducing the relative rate of isomerization of the kinetic products in the hydroamination of monosubstituted allenes.

The desired sterically bulky ligand was synthesized similar to our previously reported 3-iminophosphines, and its palladium complex was produced in the usual fashion (Scheme 1).[14b] Specifically, the Grignard reagent of mesityl bromide was synthesized, and it was reacted with phosphorus trichloride to make dimesitylchlorophosphine.[16] After reduction with $LiAlH_4$,[17] deprotonation with *n*-butyl lithium yielded lithium dimesitylphosphide.[17] Next, the ligand was assembled by the reaction of dimesitylphosphide with the appropriate *β*-chloroimine. The palladium precatalyst was then formed by ligand coordination with allyl palladium chloride, followed by salt metathesis with silver triflate.

Recrystallization of the final palladium complex from a solution of tetrahydrofuran (THF) layered with pentane resulted in X-ray quality crystals of the mesityl-substituted catalyst, and its crystal structure was solved (Figure 1). As has been the case with many of the related catalysts synthesized in our group, the allyl group was disordered over two positions, which we have previously termed the cis and trans isomers of these complexes.[15] In this case, refinement of the occupancy of these allyl groups yielded a 56:44 ratio of the two isomers. Despite the presence of the sterically bulky mesityl groups bound to the phosphorus atom and flanking the metal center, the ligand−metal bond lengths and the relevant bond angles about the pseudo-square planar palladium center were near the middle of the ranges found in related complexes and proved unremarkable.[6a,13a,14,15] As such, the unique reactivity

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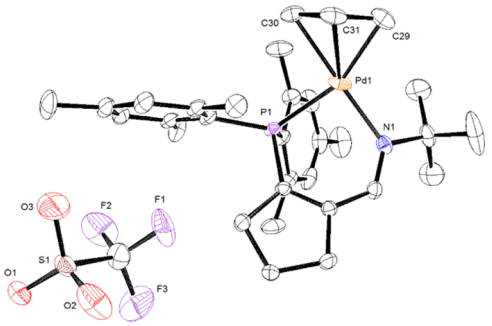


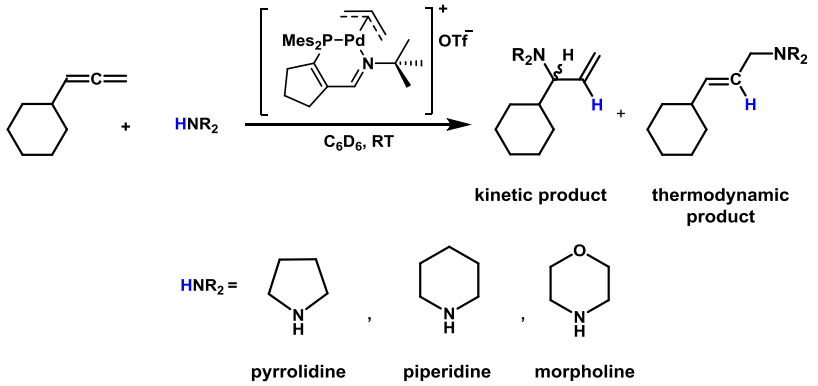
Figure 1. Oak Ridge thermal ellipsoid plot diagram (50% thermal ellipsoids) of the mesityl-substituted palladium complex. Hydrogen atoms and disordered allyl carbon atoms have been omitted for clarity. Selected bond lengths (in Å): Pd1−P1 = 2.3153(5), Pd1−N1 = 2.157(2), Pd1−C29 = 2.164(6), Pd1−C30 = 2.254(6). Bond angles (in deg): P1−Pd1−N1 = 87.03(4), C29−Pd1−C30 = 65.7(3), N1−Pd1−C29 = 114.5(2), N1−Pd1−C30 = 175.5(2), P1−Pd1−C29 = 158.3(2), P1−Pd1−C30 = 93.1(2).

displayed by this catalyst (as described below) must result from the large area occupied by the mesityl groups near the metal center rather than any significant changes in the ligand−metal bond strengths. Thus, the main role of these mesityl groups is likely in restricting access to palladium by substrates within these catalytic reactions.

A few years ago, we showed that catalysts using *tert*-butylphosphine substituents provided for the successful synthesis and isolation of the kinetic (branched) products in the hydroamination of cyclohexylallene with various secondary amines, but we also observed that these kinetic products quickly isomerized to their thermodynamically more stable isomers when the reaction mixture was left unquenched after reaction completion.[4c] As an initial screening of our new mesityl-substituted catalyst, we tested the hydroamination of cyclohexylallene with morpholine, pyrrolidine, and piperidine (Table 1). Overall, the catalytic results using cyclohexylallene were disappointing as catalysis was very slow (requiring 14−48 h to reach completion), taking substantially longer than our previous report (reaching completion in 30−60 min for the same substrates). Because of this long reaction time, we observed formation of the thermodynamic product exclusively with pyrrolidine and piperidine, as has been the case with other similarly slow catalysts we have investigated previously.[5f,6a,12] Surprisingly, the reaction between cyclohexylallene and morpholine using the mesitylphosphine catalyst, though much slower than the *tert*-butylphosphine substituted analogue, yielded a 47:53 ratio of the kinetic and thermodynamic isomers after reaction completion at 14 h. This was the first time we had observed a very slow catalysis (requiring many hours to reach completion) that yielded anything other than exclusively the linear (thermodynamic) isomers. Continued observation of this reaction mixture revealed very slow isomerization of the kinetic product into the thermodynamic product in this sterically bulky system, taking nearly 3 days to fully isomerize (Table 2). In our previous work,[4c] the kinetic hydroamination products isomerized to the thermodynamic products quite rapidly after reaction completion, yielding only the linear products if the reaction was left unquenched for 1−2 h after hydroamination was complete. The slow isomerization observed after nearly complete hydroamination with the mesityl-substituted catalyst proved to be the case with many substrate combinations, especially those with moderate hydroamination reactivity (see the Supporting Information file for detailed data). Because of the very slow isomerization rates relative to the hydroamination rate, we set out to utilize this catalyst system to isolate various branched products that had proven untenable with our previously published highly active catalysts.[4c]

Another substrate that we tested thoroughly in the past is phenylallene, whose hydroamination with various secondary amines and anilines met with only limited success using one of our most active catalysts.[4c] For example, the reaction of phenylallene with morpholine was so fast that both hydroamination and complete isomerization occurred within 10 min, making it very challenging for us to isolate the kinetic product in this reaction.[4c] The hydroamination of phenylallene with 1-methylpiperazine, 1-(diphenylmethyl)piperazine, and various substituted anilines also failed to yield the kinetic products.[4c] In each of these cases, the isomerization rate was observed to be very competitive with the hydroamination rate, and we were unable to find a combination of catalyst loading and time point

Table 1. Hydroamination of Cyclohexylallene with Secondary Amines[a]



entry	amine	time (h)	conversion (br:l)
1.1	morpholine	14	95 (47:53)
1.2	pyrrolidine	48	95 (0:100)
1.3	piperidine	46	95 (0:100)

[a]br is branched allylamine (kinetic product) and l is linear allylamine (thermodynamic product).

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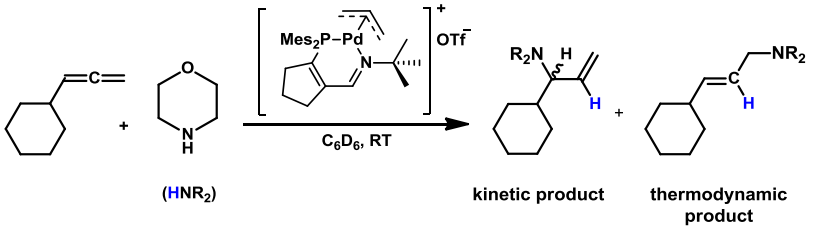
Organometallics XXXX, XXX, XXX−XXX

Table 2. Hydroamination Followed by Slow Isomerization of the Kinetic Product to the Thermodynamic Product[a]



time (h)	conversion (%)	conversion (branched/linear)
1	18	50/50
2	26	50/50
4	42	48/52
6	59	47/53
8	72	47/53
11	88	47/53
14	95	47/53
20	95	43/57
24	95	40/60
30	95	34/66
36	95	27/73
48	95	15/85
60	95	8/92
72	95	0/100

[a]Catalytic procedure: Reactions were carried out at 25 °C in NMR tubes prepared in a glovebox using benzene-d_6 as the solvent (800 μL), catalyst (0.025 mmol), secondary amine (0.50 mmol), and allene (0.50 mmol). Conversion was monitored by ^{1}H NMR spectroscopy.

where quenching would allow a synthetically useful amount of branched product to be isolated.[4c] Given the very slow isomerization of the kinetic product to the thermodynamic product observed using the mesityl catalyst above, we set out to study the hydroamination of phenylallene with various secondary amines and anilines in the hope that our new sterically bulky catalyst would allow access to the elusive kinetic products. Hydroamination of phenylallene with aniline was very slow, taking several days and forming the thermodynamic product only; however, we were pleased to find that hydroamination of phenylallene with morpholine produced almost entirely the kinetic product (the ratio of kinetic to thermodynamic product was 92:8) and required only 30 min to reach completion (Table 3, entry 3.1). Moreover, since the amount of isomerization product was minimal, the kinetic product was readily isolated via column chromatography. Similarly, we successfully isolated the kinetic products from hydroamination of phenylallene with 2,6-dimethylmorpholine, 1-methylpiperazine, 1-(diphenylmethyl)piperazine, indoline, and thiomorpholine (Table 3, entries 3.2−3.6). Note that for each entry in Table 3, reactions were monitored by nuclear magnetic resonance (NMR) spectroscopy, and the data is reported at the time point at which 95% conversion of the starting material was observed (with the corresponding branched to linear ratios). In general, all of the reactions with phenylallene proceeded at a moderate rate, reaching completion within a few hours and producing primarily the branched kinetic products. Similarly, kinetic products were strongly favored in a series of three representative reactions to test the hydroamination of *p*-fluorophenylallene (Table 3, entries 4.1−4.3).

To expand the scope of this reaction, two aliphatic allenes were also tested using the representative set of secondary amines (Table 3, entries 5.1−5.3 and 6.1−6.2). Both *n*-hexylallene and *n*-butylallene showed good selectivity for kinetic products in each of these reactions. Overall, hydroamination of *n*-hexylallene and *n*-butylallene was generally complete within 2 to 3 h and usually gave >80% selectivity for branched products. Furthermore, we also successfully carried out hydroamination of 5-phenyl-1,2-pentadiene with morpholine, 2,6-dimethylmorpholine, and thiomorpholine to predominantly yield their corresponding branched products (Table 3, entries 7.1−7.3). Again, the reactions were complete within 1 to 3 h. All of these branched products were successfully isolated by column chromatography.

To put the results displayed in Table 3 into proper context, a comparison with our fastest and most effective hydroamination catalyst to date is warranted. Table 4 shows the allene/amine combinations that are present in both Table 3 and our previous report.[4c] Because all entries with the mesityl catalyst are reported at the time point in which 95% conversion was achieved, it is clear that the rate of hydroamination with the sterically hindered catalyst is generally slower than that observed using the more active *tert*-butyl substituted ligand. For example, in the hydroamination of phenylallene with morpholine, it requires 30 min for the mesityl catalyst to reach 95% conversion (with a 92:8 branched to linear ratio), whereas the same catalyst loading with the *tert*-butyl catalyst completes not only the hydroamination step but also the isomerization in just 10 min. For additional comparison data, see the Supporting Information file. It also seems that the rate of isomerization is much slower when employing the mesityl-substituted species. If the mesityl catalyst effected isomerization at the same rates as the *tert*-butyl catalyst, the branched products would not be observed at all because they would be isomerized almost as soon as they were produced, given that hydroamination is so much slower with the mesityl catalyst. Thus, the presence of the mesityl group in these catalysts causes both the hydroamination and the subsequent isomerization reactions to take place slower than in our previously

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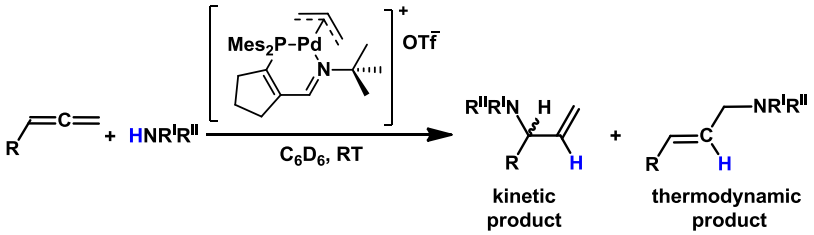
Organometallics XXXX, XXX, XXX−XXX

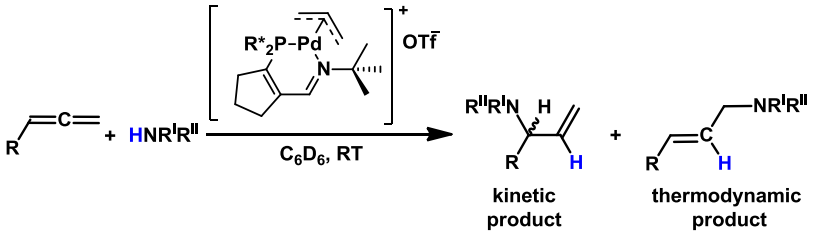
Table 3. Hydroamination of Allenes with Secondary Amines[a]



Entry	Allene	Amine	Time	Conversion (br : l)
3.1		Morpholine	30 min	95 (92 : 8)
3.2		2,6-Dimethylmorpholine	1 h	95 (83 : 17)
3.3		N-Methylpiperazine	6.5 h	95 (74 : 26)
3.4		N-(Diphenylmethyl)piperazine	2.5 h	95 (80 : 20)
3.5		Indoline	30 min	95 (68 : 32)
3.6		Thiomorpholine	2 h	95 (88 : 12)
4.1		1-Methylpiperazine	1 h	95 (91 : 9)
4.2		2,6-Dimethylmorpholine	1 h	95 (89 : 11)
4.3		Thiomorpholine	3 h	95 (87 : 13)
5.1		Morpholine	30 min	95 (92 : 8)
5.2		2,6-Dimethylmorpholine	1 h	95 (85 : 15)
5.3		Thiomorpholine	2 h	95 (83 : 17)
6.1		2,6-Dimethylmorpholine	1 h	95 (81 : 19)
6.2		Thiomorpholine	3 h	95 (78 : 22)
7.1		Morpholine	1 h	95 (89 : 11)
7.2		2,6-Dimethylmorpholine	1 h	95 (81 : 19)
7.3		Thiomorpholine	3 h	95 (78 : 22)

[a]Catalytic procedure: Reactions were carried out at 25 °C in NMR tubes prepared in a glovebox using benzene-d_6 as the solvent (800 μL), catalyst (0.025 mmol), secondary amine (0.50 mmol), and allene (0.50 mmol). Conversion was monitored by ^{1}H NMR spectroscopy. Products were subsequently isolated by column chromatography (see the Experimental Section for isolated yields).

Table 4. Comparison of Hydroamination Results Using Mesityl- and *tert*-Butyl-[4c] Substituted Ligands[a]



allene	amine	conversion (br:l) (R* = Mes)	conversion (br:l) (R* = ^{t}Bu)
phenylallene	morpholine	95 (92:8) (30 min)	95 (72:28) (1 min) 95 (5:95) (4 min) 95 (0:100) (10 min)
phenylallene	*N*-methylpiperazine	95 (74:26) (6.5 h)	95 (0:100) (30 min)
phenylallene	*N*-(diphenylmethyl)piperazine	95 (80:20) (2.5 h)	95 (0:100) (3 h)
p-fluorophenylallene	*N*-methylpiperazine	95 (91:9) (1 h)	95 (40:60) (1.5 h) 95 (0:100) (2 h)

[a]Catalytic procedure: Reactions were carried out at 25 °C in NMR tubes prepared in a glovebox using benzene-d_6 as the solvent (800 μL), catalyst (0.025 mmol), secondary amine (0.50 mmol), and allene (0.50 mmol). Conversion was monitored by ^{1}H NMR spectroscopy.

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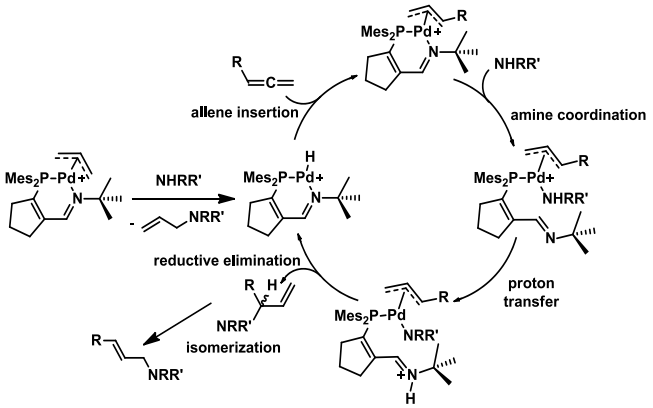
Organometallics XXXX, XXX, XXX−XXX

reported *tert*-butyl analogues. Although this means that the reactions are longer overall, these slower rates allow for much more facile synthesis and isolation of the kinetic (branched) products. This is evident in the straightforward isolation of the branched product resulting from phenylallene and morpholine, a reaction that almost fully isomerizes from branched to linear products in the period between 1 and 4 min of reaction time with the previously reported catalyst.[4c] The other three comparative reactions show that the mesityl-substituted catalyst allows access to other branched allylamines that were difficult or impossible to isolate in our previous report.[4c]

On the basis of the kinetics experiments and a Hammett plot analysis, we recently proposed a catalytic cycle explaining the reactivity of (3-iminophosphine)palladium catalysts in the hydroamination of monosubstituted allenes with secondary amines (Scheme 2).[5f] In the first step, an amine substrate

Scheme 2. Catalytic Cycle[5f] Adapted to the Present Sterically Bulky System



reacts with the 3-iminophosphine palladium precatalyst to generate the active Pd(II) hydride complex, which enters the catalytic cycle. After allene insertion, a substrate amine coordinates with palladium by displacing the imine unit of the ligand. Then, there is a proton transfer from the substrate amine to the imine, followed by reductive elimination of the kinetic product, regenerating the Pd(II) hydride catalyst.

Invoking this catalytic cycle, regiocontrol during hydroamination depends entirely on the orientation of the allene during the insertion step. Of the two regioisomers, **a** forms the kinetic product, whereas **b** gives the thermodynamic product after reductive elimination (Figure 2). Thus, we believe that the added sterics provided by the dimesitylphosphine group restrict the orientation, which in turn inhibits the formation of the thermodynamic product. Furthermore, in the cases where isomerization occurs after reaction completion, we believe that this is due to oxidative addition of the product allylamine to

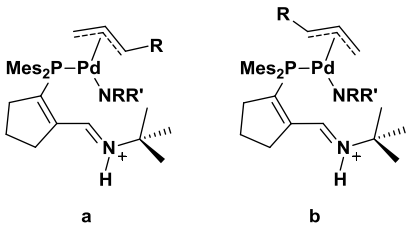


Figure 2. Possible orientations of the allyl group after insertion.

the palladium center (via the principle of microscopic reversibility), rotation of the allyl group to the opposite orientation, and then reductive elimination to give the final thermodynamic product. Thus, by using our bulky dimesitylphosphine substituent, it seems that this isomerization pathway is almost completely inhibited.

CONCLUSIONS

A new 3-iminophosphine ligand with a sterically bulky dimesitylphosphine group and its corresponding precatalyst [3IP^{Mes}Pd(allyl)]OTf were synthesized. The additional steric bulk on the phosphine moiety of the ligand led to a considerable decrease in the rate of isomerization of the kinetic product to the thermodynamic product following hydroamination of monosubstituted allenes with various secondary amines. Although the overall catalysis was slower than some of our previously published catalysts, the very slow isomerization rates displayed by this new catalyst enabled the successful isolation of branched, kinetic products in significant amounts. Thus, despite its overall slower hydroamination reaction rates, the new sterically bulky catalyst reported herein provides a synthetically viable route for the production of significant quantities of many branched allylamine hydroamination products. Additionally, several previously unattainable kinetic products were produced through the hydroamination of phenylallene and *p*-fluorophenylallene with various secondary amines. Overall, this new mesityl catalyst has allowed for the isolation of 13 new branched allylamine products, several of which had previously proven impossible to isolate using our related catalysts. Our laboratory continues to pursue new catalysts with sufficient steric bulk to completely shut down isomerization of the kinetic product to the thermodynamic product while in turn still maintaining overall acceptable hydroamination reaction rates.

EXPERIMENTAL SECTION

General Methods, Instrumentation, and Synthesis. All reactions and manipulations were performed under an inert atmosphere of nitrogen using a standard glovebox or Schlenk techniques. Benzene, C_6D_6, was purchased from Cambridge Isotope Laboratories, dried over sodium metal, freeze–pump–thawed three times, vacuum transferred, stored over 4 Å molecular sieves in the glovebox, and used for hydroamination reactions. Chloroform, $CDCl_3$, was purchased from Cambridge Isotope Laboratories and was directly used for product characterization. Solvents were dried and degassed before use. Pentane, diethyl ether, and THF were passed through columns of activated alumina and 4 Å molecular sieves and degassed with nitrogen. Methylene chloride was passed through two columns of 4 Å molecular sieves and degassed with nitrogen. Styrene was purchased from Acros Organics, and 1-hexene, 1-octene, and bromoform were purchased from Sigma-Aldrich and used as received. 4-Fluorostyrene was purchased from Matrix Scientific and used as received. (Allyl)-palladium(II) chloride dimer and silver triflate were purchased from Strem and used without further purification. Cyclohexylallene was purchased from Alfa Aesar and was used without further purification. Amines were purchased from commercial sources and dried over calcium hydride, freeze–pump–thawed three times, vacuum-transferred, and stored over 4 Å molecular sieves in the glovebox. Silica gel (porosity: 60 Å, particle size: 40–63 μm) was purchased from Sorbent Technologies and used as received. ^{1}H and ^{13}C NMR data were obtained on a 600 MHz Bruker AVANCE III spectrometer at 599.9 MHz for ^{1}H NMR and 150.8 MHz for ^{13}C NMR. ^{31}P NMR and ^{19}F NMR data were obtained on a 400 MHz Varian NMR spectrometer at 161.90 and 376.29 MHz, respectively. ^{1}H NMR shifts are given relative to residual solvent resonances at 7.26

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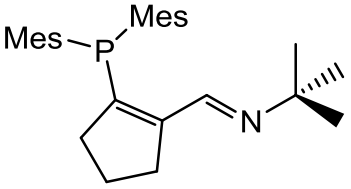
Organometallics XXXX, XXX, XXX–XXX

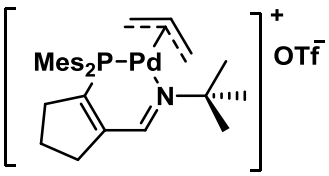
ppm, and ^{13}C NMR shifts are given relative to $CDCl_3$ (77.36 ppm). ^{19}F and ^{31}P NMR data were externally referenced to 0.00 ppm with $CFCl_3$ and 5% solution of H_3PO_4 in D_2O, respectively. High-resolution mass spectrometry data were determined by either The University of Illinois Mass Spectrometry Laboratory, Urbana, IL, USA or The University of Toledo Mass Spectrometry Laboratory, Toledo, OH, USA. All product spectra were taken using $CDCl_3$ as the NMR solvent. Elemental analyses were determined by Atlantic Microlab, Inc., Norcross, GA, USA. Infrared samples were prepared on NaCl plates as Nujol mulls and were obtained from a PerkinElmer Spectrum 2 Fourier transform infrared spectrometer. Melting points were determined in sealed capillary tubes under nitrogen using a capillary melting point apparatus.

Ligand and Catalyst Synthesis.



2-Dimesitylphosphinocyclopentene-1-(t-butyl)imine. 2-Chlorocyclopent-1-enecarbaldehyde and its corresponding *β*-chloroimine were prepared at an ambient temperature, and the reactions were performed under an inert atmosphere of nitrogen using standard Schlenk techniques via previously published procedures.[14a] A solution of freshly prepared chloroimine in dry ether was degassed and cooled to 0 °C. Lithium dimesitylphosphide was prepared by adapting the previously published procedure.[16,17] Lithium dimesitylphosphide (1.50 g; 1.1 equiv) was dissolved in diethyl ether and added to *β*-chloroimine (0.92 g) through a cannula. The mixture was allowed to warm to room temperature (RT) overnight. Then, the reaction mixture was passed through a pad of celite to remove the LiCl byproduct. The resulting solution was concentrated under reduced pressure and was kept under nitrogen at −20 °C overnight to give the 3-IP ligand as yellow crystals. Subsequently, the supernatant liquid was filtered, and the solid residue was placed under reduced pressure to remove volatiles.

Pale yellow solid, 1.81 g (87%). mp 105−106 °C. ^1H NMR ($CDCl_3$): δ 8.51 (d, $^4J_{P-H}$ = 4.0 Hz, 1H), 6.79 (d, $^4J_{P-H}$ = 2.8 Hz, 4H), 2.79−2.71 (m, 2H), 2.59−2.48 (m, 2H), 2.24 (s, 6H), 2.20 (s, 12H), 1.89−1.77 (m, 2H), 1.07 (s, 9H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 153.4 (d, $^3J_{P-C}$ = 19.6 Hz), 150.5 (d, $^1J_{P-C}$ = 21.1 Hz), 147.3 (d, $^1J_{P-C}$ = 22.7 Hz), 142.6 (d, $^2J_{P-C}$ = 15.1 Hz), 138.0, 131.3 (d, $^2J_{P-C}$ = 16.6 Hz), 130.0 (d, $^3J_{P-C}$ = 3.0 Hz), 57.6, 40.2, 34.3 (d, $^2J_{P-C}$ = 6.0 Hz), 30.1, 23.1 (d, $^3J_{P-C}$ = 16.6 Hz), 22.9 (d, $^3J_{P-C}$ = 3.0 Hz), 21.2. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −42.65. IR (cm^{-1}): 3018 (m), 2963 (m), 1912 (m), 1614 (s), 1598 (m), 1572 (m), 1495 (s), 1363 (m), 1183 (m), 806 (s), 512 (s). HRMS *m/z*: $[M + H]^+$ calcd for $C_{28}H_{39}NP$, 420.2820; found, 420.2816.



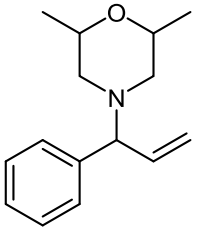
[(2-Dimesitylphosphinocyclopentene-1-(t-butyl)imine)Pd(allyl)]-OTf. The 3-iminophosphine ligand (1.05 equiv, 1.82 g) was dissolved in dichloromethane and added to allylpalladium chloride dimer (0.5 equiv, 0.76 g) in dichloromethane at an ambient temperature and stirred overnight. The resulting solution was placed under vacuum to remove the volatiles, and the residue was washed with pentane. The solid residue was then dissolved in dichloromethane and added to a slurry of silver triflate (0.65 equiv, 0.68 g) in dichloromethane and then stirred overnight in the dark. The reaction mixture was allowed to pass through a thick pad of celite, and the solvent was reduced under vacuum. The dark yellow solid was washed with pentane and dried under vacuum before transferring into the glovebox.

Pale yellow solid, 2.73 g (91.7%). mp 197 °C (dec). ^1H NMR ($CDCl_3$): δ 7.88 (d, $^4J_{P-H}$ = 4.0 Hz, 1H), 6.94 (d, $^4J_{P-H}$ = 3.1 Hz, 2H), 6.90 (d, $^4J_{P-H}$ = 3.3 Hz, 2H), 5.68−5.57 (m, 1H), 4.74−4.70 (m, 1H), 3.48 (dd, ^3J = 13.2 Hz, 11.2 Hz, 1H), 3.37 (d, ^3J = 7.9 Hz, 1H), 2.94 (m, 2H), 2.62 (d, ^3J = 13.2 Hz, 1H), 2.54 (d, ^3J = 7.9 Hz, 2H), 2.34 (s, 6H), 2.32 (s, 3H), 2.27 (s, 3H), 2.24 (s, 6H), 2.24−2.16 (m, 2H), 1.11 (s, 9H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 161.6 (d, $^3J_{P-C}$ = 6.0 Hz), 153.8 (d, $^1J_{P-C}$ = 16.6 Hz), 142.2 (d, $^2J_{P-C}$ = 10.6 Hz), 141.9 (d, $^2J_{P-C}$ = 10.6 Hz), 141.7 (d, $^2J_{P-C}$ = 7.5 Hz), 139.2 (d, $^1J_{P-C}$ = 31.6 Hz), 132.0 (d, $^3J_{P-C}$ = 9.0 Hz), 131.6 (d, $^3J_{P-C}$ = 7.5 Hz), 125.9, 125.6, 122.9 (d, $^1J_{P-C}$ = 42.2 Hz), 122.4 (q, $^1J_{F-C}$ = 316.7 Hz), 119.8 (d, $^2J_{P-C}$ = 7.5 Hz), 76.2 (d, $^2J_{P-C}$ = 33.2 Hz), 64.1, 62.1 (d, $^3J_{P-C}$ = 6.0 Hz), 38.5, 37.8 (d, $^2J_{P-C}$ = 10.6 Hz), 30.0, 25.0 (d, $^3J_{P-C}$ = 10.6 Hz), 24.1 (d, $^3J_{P-C}$ = 9.0 Hz), 23.1 (d, $^2J_{P-C}$ = 6.0 Hz), 21.2, 21.1. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ −7.20. $^{19}F\{^1H\}$ NMR ($CDCl_3$): δ −78.3. IR (cm^{-1}) 3027 (m), 2993 (m), 2834 (m), 1621 (s), 1585 (m), 1477 (s), 1360 (s), 1218 (s), 1022 (s), 680 (s). Anal. Calcd for $C_{32}H_{43}F_3NO_3PPdS{\cdot}0.4\ CH_2Cl_2$: C, 51.88; H, 5.89; N, 1.87. Found: C, 51.92; H, 6.16; N, 1.87.

Allene Synthesis. All allenes were synthesized following the previously reported procedure via ring opening of the corresponding dibromocyclopropane.[18,19] The synthetic allenes were freeze−pump−thawed three times, vacuum-transferred, and stored over 4 Å molecular sieves in the glovebox freezer. The allenes were confirmed by ^1H and ^{13}C NMR spectroscopies.

Catalytic Reactions and Isolation of Allylamines. All hydroamination reactions were carried out inside a nitrogen-filled glovebox in NMR tubes. $[(3IP)Pd(allyl)]^+OTf$ (0.025 mmol, 17.9 mg) was dissolved in deuterated benzene (800 μL), and the secondary amine (0.50 mmol) was added. Finally, the allene (0.50 mmol) was added to the mixture. The ratio of each substrate to the hydroamination product was monitored by ^1H NMR spectroscopy. After reaction completion was observed, the reaction mixture was passed through a plug of silica. Solvents were removed under reduced pressure, and the colorless liquid was isolated by column chromatography using pentane/ethyl acetate (9/1 by volume) as an eluent. Linear hydroamination products: (3-cyclohexyl-2-propenyl)-morpholine (**1.1 l**),[12] (3-cyclohexyl-2-propenyl)-1-pyrrolidine (**1.2 l**),[12] (3-cyclohexyl-2-propenyl)-piperidine (**1.3 l**),[12] (3-phenyl-2-propenyl)-morpholine (**3.1 l**),[12] (3-phenyl-2-propenyl)-1-methylpiperazine (**3.3 l**),[12] (3-phenyl-2-propenyl)-*N*-diphenylmethylpiperazine (**3.4 l**),[12] [3-(4-fluorophenyl)-2-propenyl]-1-methylpiperazine (**4.1 l**),[12] 4-(non-2-en-1-yl)-morpholine (**5.1 l**),[12] 4-(non-2-en-1-yl)-2,6-dimethylmorpholine (**5.2 l**),[12] 4-(non-2-en-1-yl)-thiomorpholine (**5.3 l**),[12] 4-(hept-2-en-1-yl)-2,6-dimethylmorpholine (**6.1 l**),[12] 4-(hept-2-en-1-yl)-thiomorpholine (**6.2 l**)[12] and branched hydroamination products: (1-cyclohexyl-2-propenyl)-morpholine (**1.1 br**),[4c] (1-cyclohexyl-2-propenyl)-1-pyrrolidine (**1.2 br**),[4c] (1-cyclohexyl-2-propenyl)-piperidine (**1.3 br**),[4c] (1-phenyl-2-propen-1-yl)-morpholine (**3.1 br**),[20] (1-phenyl-2-propen-1-yl)-1-methyl-piperazine (**3.3 br**),[21] (1-phenyl-2-propen-1-yl)-2,3-dihydroindoline (**3.5 br**),[22] and (non-1-en-3-yl)morpholine (**5.1 br**),[20] were reported previously.

Characterization of New Hydroamination Products.



*(1-Phenyl-2-propenyl)-2,6-dimethylmorpholine (**3.2 br**).* Colorless liquid, 84.1 mg (72.7%). ^1H NMR ($CDCl_3$): δ 7.38−7.32 (m, 4H), 7.30−7.25 (m, 1H), 5.93 (ddd, ^3J = 17.1, 10.0, 8.8 Hz, 1H), 5.25 (dd, ^3J = 17.1 Hz, ^2J = 1.5 Hz, 1H), 5.13 (dd, ^3J = 10.0 Hz, ^2J = 1.5 Hz, 1H), 3.75 (dqd, ^3J = 10.3, 6.2, 1.9 Hz, 1H), 3.65 (dqd, ^3J = 10.3, 6.2, 1.9 Hz, 1H), 3.62 (d, ^3J = 8.8 Hz, 1H), 2.99 (dd, ^2J = 11.4 Hz, ^3J = 1.9 Hz, 1H), 2.53 (dd, ^2J = 11.4 Hz, ^3J = 1.9 Hz, 1H), 1.75 (dd, ^2J = 11.4

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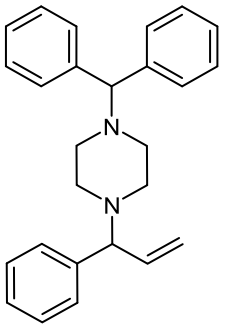
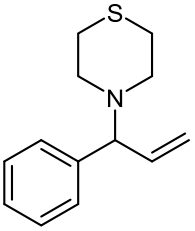
Organometallics XXXX, XXX, XXX−XXX

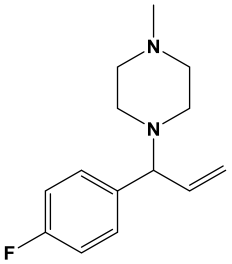
Hz, ^3J = 10.3 Hz, 1H), 1.60 (dd, ^2J = 11.4 Hz, ^3J = 10.3 Hz, 1H), 1.20 (d, ^3J = 6.2 Hz, 3H), 1.08 (d, ^3J = 6.2 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 142.0, 140.1, 128.9, 128.3, 127.6, 116.9, 75.5, 72.13, 72.09, 58.01, 57.98, 19.6, 19.5. IR (cm^{-1}): 3117 (m), 3083 (m), 2952 (m), 2804 (m), 1639 (br), 1415 (m), 1015 (s), 758 (s), 619 (s). HRMS *m/z*: calcd for $C_{15}H_{22}NO$, 232.1701 $[M + H]^+$; found, 232.1690.



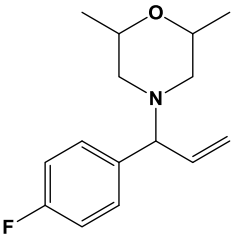
(1-Phenyl-2-propenyl)-N-diphenylmethylpiperazine (***3.4 br***). White solid, 124.2 mg (67.4%). ^1H NMR ($CDCl_3$): δ 7.51−7.39 (m, 5H), 7.39−7.23 (m, 8H), 7.23−7.14 (m, 2H), 5.91 (ddd, ^3J = 17.1, 10.1, 8.8 Hz, 1H), 5.25 (dd, ^3J = 17.1 Hz, ^2J = 1.6 Hz, 1H), 5.12 (dd, ^3J = 10.1 Hz, ^2J = 1.6 Hz, 1H), 4.27 (s, 1H), 3.71 (d, ^3J = 8.8 Hz, 1H), 2.54−2.36 (br, 8H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 143.12, 143.06, 142.1, 140.3, 128.78, 128.73, 128.69, 128.30, 128.27, 128.26, 127.4, 127.17, 127.15, 116.7, 76.5, 75.5, 52.3, 51.9. IR (cm^{-1}): 3063 (m), 3033 (m), 2956 (m), 2807 (m), 1662 (m), 1643 (m), 1603 (m), 1489 (m), 1451 (m), 1131 (s), 995 (s), 704 (s). HRMS *m/z*: $[M + H]^+$ calcd for $C_{26}H_{29}N_2$, 369.2331; found, 369.2331.



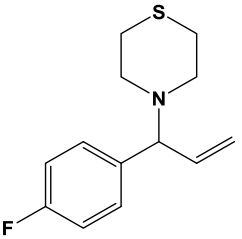
(1-Phenyl-2-propenyl)-thiomorpholine (***3.6 br***). Colorless liquid, 69.6 mg (63.6%). ^1H NMR ($CDCl_3$): δ 7.43−7.28 (m, 4H), 7.28−7.21 (m, 1H), 5.90 (ddd, ^3J = 17.1, 10.0, 8.6 Hz, 1H), 5.22 (dd, ^3J = 17.1 Hz, ^2J = 1.5 Hz, 1H), 5.15 (dd, ^3J = 10.0 Hz, ^2J = 1.5 Hz, 1H), 3.82 (d, ^3J = 8.6 Hz, 1H), 2.86−2.72 (m, 2H), 2.72−2.57 (m, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 141.9, 139.4, 128.8, 128.2, 127.5, 117.3, 74.8, 53.2, 28.5. IR (cm^{-1}): 3067 (m), 2991 (m), 2861 (m), 1641 (m), 1627 (m), 1450 (m), 1013 (s), 701 (s). HRMS *m/z*: $[M + H]^+$ calcd for $C_{13}H_{18}NS$, 220.1160; found, 220.1156.



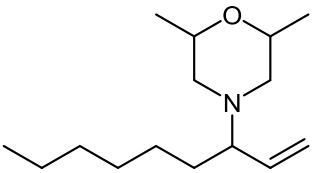
[1-(4-Fluorophenyl)-2-propenyl]-1-methylpiperazine (***4.1 br***). Colorless liquid, 77.9 mg (68.3%). ^1H NMR ($CDCl_3$): δ 7.36−7.27 (m, 2H), 7.04−6.93 (m, 2H), 5.87 (ddd, ^3J = 17.1, 10.0, 8.8 Hz, 1H), 5.21 (dd, ^3J = 10.0 Hz, ^2J = 1.1 Hz, 1H), 5.09 (dd, ^3J = 17.1 Hz, ^2J = 1.1 Hz, 1H), 3.63 (d, ^3J = 8.8 Hz, 1H), 2.72−2.14 (br, 8H), 2.27 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 162.6 (d, $^1J_{C-F}$ = 170.4 Hz), 140.2, 138.1 (d, $^4J_{C-F}$ = 3.0 Hz), 129.7 (d, $^3J_{C-F}$ = 7.5 Hz), 116.8, 115.7 (d, $^2J_{C-F}$ = 21.1 Hz), 74.5, 55.6, 51.5, 46.3. IR (cm^{-1}): 3103 (m), 3074 (m), 3016 (w), 2850 (m), 1665 (s), 1607 (s), 1448 (m), 1407 (m), 1087 (s), 999 (s), 659 (m), 537 (s). HRMS *m/z*: $[M + H]^+$ calcd for $C_{14}H_{20}FN_2$, 235.1611; found, 235.1597.



[1-(4-Fluorophenyl)-2-propenyl]-2,6-dimethylmorpholine (***4.2 br***). Colorless liquid, 88.1 mg (70.4%). ^1H NMR ($CDCl_3$): δ 7.34−7.32 (m, 2H), 7.03−6.99 (m, 2H), 5.86 (ddd, ^3J = 17.1, 10.1, 8.9 Hz, 1H), 5.21 (dd, ^3J = 17.1 Hz, ^2J = 1.5 Hz, 1H), 5.11 (dd, ^3J = 10.1 Hz, ^2J = 1.5 Hz, 1H), 3.70 (dqd, ^3J = 10.0, 6.3, 2.2 Hz, 1H), 3.61 (dqd, ^3J = 10.0, 6.3, 2.2 Hz, 1H), 3.58 (d, ^3J = 8.9 Hz, 1H), 2.93 (dd, ^2J = 11.3 Hz, ^3J = 2.2 Hz, 1H), 2.46 (dd, ^2J = 11.3 Hz, ^3J = 2.2 Hz, 1H), 1.71 (dd, ^2J = 11.3 Hz, ^3J = 10.0 Hz, 1H), 1.56 (dd, ^2J = 11.3 Hz, ^3J = 10.0 Hz, 1H), 1.16 (d, ^3J = 6.3 Hz, 3H), 1.06 (d, ^3J = 6.3 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 163.1 (d, $^1J_{C-F}$ = 245.8 Hz), 139.9, 137.8 (d, $^4J_{C-F}$ = 3.0 Hz), 129.7 (d, $^3J_{C-F}$ = 9.1 Hz), 117.0, 115.8 (d, $^2J_{C-F}$ = 21.1 Hz), 74.5, 72.14, 72.06, 57.9, 57.8, 19.6, 19.5. IR (cm^{-1}): 3052 (m), 3016 (m), 2988 (m), 2873 (w), 1654 (m), 1609 (m), 1449 (m), 1325 (s), 1287 (m), 738 (s), 640 (s), 593 (m). HRMS *m/z*: $[M + H]^+$ calcd for $C_{15}H_{21}FNO$, 250.1607; found, 250.1606.



[1-(4-Fluorophenyl)-2-propenyl]-thiomorpholine (***4.3 br***). Colorless liquid, 82.3 mg (69.1%). ^1H NMR ($CDCl_3$): δ 7.32−7.27 (m, 2H), 7.03−6.97 (m, 2H), 5.85 (ddd, ^3J = 17.1, 10.1, 8.6 Hz, 1H), 5.20 (dd, ^3J = 17.1 Hz, ^2J = 1.7 Hz, 1H), 5.16 (dd, ^3J = 10.1 Hz, ^2J = 1.7 Hz, 1H), 3.81 (d, ^3J = 8.6 Hz, 1H), 2.82−2.71 (m, 2H), 2.69−2.58 (m, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 163.1 (d, $^1J_{C-F}$ = 241.3 Hz), 139.0, 137.6 (d, $^4J_{C-F}$ = 3.0 Hz), 129.6 (d, $^3J_{C-F}$ = 7.5 Hz), 117.5, 115.4 (d, $^2J_{C-F}$ = 21.1 Hz), 74.0, 53.1, 28.5. IR (cm^{-1}): 3095 (m), 3058 (w), 3007 (m), 2973 (m), 2848 (w), 1642 (s), 1626 (m), 1322 (m), 1273 (s), 1131 (m), 873 (s), 751 (s), 649 (m). HRMS *m/z*: $[M + H]^+$ calcd for $C_{13}H_{17}FNS$, 238.1066; found, 238.1056.



3-(Non-1-enyl)-2,6-dimethylmorpholine (***5.2 br***). Colorless liquid, 81.7 mg (68.4%). ^1H NMR ($CDCl_3$): δ 5.65 (ddd, ^3J = 17.2, 10.3, 8.3 Hz, 1H), 5.16 (dd, ^3J = 10.3 Hz, ^2J = 1.8 Hz, 1H), 5.05 (dd, ^3J = 17.2 Hz, ^2J = 1.8 Hz, 1H), 3.66 (dqd, ^3J = 10.6, 6.3, 2.2 Hz, 1H), 3.61 (dqd, ^3J = 10.6, 6.3, 2.2 Hz, 1H), 2.79−2.72 (m, 1H), 2.69−2.59 (m, 2H), 1.89 (t, ^3J = 10.6 Hz, 1H), 1.77 (t, ^3J = 10.6 Hz, 1H), 1.67−1.55 (m, 1H), 1.43−1.33 (m, 1H), 1.33−1.17 (m, 8H), 1.13 (t, ^3J = 6.3 Hz, 6H), 0.92−0.81 (m, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 138.0, 117.9, 72.4, 72.2, 69.0, 57.6, 55.2, 32.1, 31.8, 29.7, 26.6, 23.0, 19.60, 19.59, 14.4. IR (cm^{-1}): 2854 (m), 2781 (m), 2719 (w), 1527 (s), 1448 (m), 1208 (m), 968 (s), 823 (m), 718 (s). HRMS *m/z*: $[M + H]^+$ calcd for $C_{15}H_{30}NO$, 240.2327; found, 240.2316.

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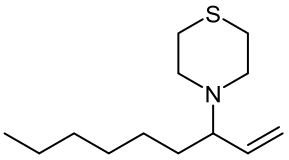
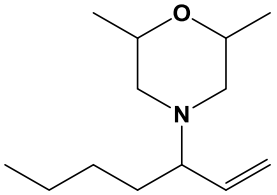
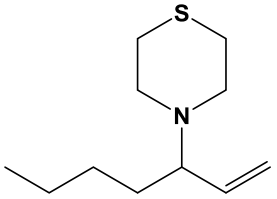
Organometallics XXXX, XXX, XXX−XXX



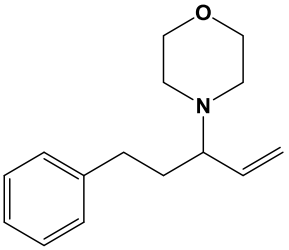
*3-(Non-1-enyl)-thiomorpholine (**5.3 br**).* Colorless liquid, 80.1 mg (71.2%). ^{1}H NMR ($CDCl_3$): δ 5.67 (ddd, ^3J = 17.1, 10.2, 8.6 Hz, 1H), 5.15 (dd, ^3J = 10.2 Hz, ^2J = 1.6 Hz, 1H), 5.04 (dd, ^3J = 17.1 Hz, ^2J = 1.6 Hz, 1H), 2.93−2.80 (m, 2H), 2.76 (dt, ^3J = 8.6 Hz, 5.2 Hz, 1H), 2.72−2.56 (m, 6H), 1.60−1.51 (m, 1H), 1.45−1.35 (m, 1H), 1.32−1.17 (m, 8H), 0.87 (t, ^3J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 137.4, 117.6, 69.6, 52.0, 32.1, 31.8, 29.6, 28.7, 26.8, 23.0, 14.4. IR (cm^{-1}): 2959 (m), 2924 (s), 2855 (m), 2806 (m), 1637 (s), 1450 (m), 1382 (m), 1107 (m), 920 (s), 699 (s). HRMS *m*/*z*: [M + H]$^+$ calcd for $C_{13}H_{26}NS$, 228.1786; found, 228.1780.



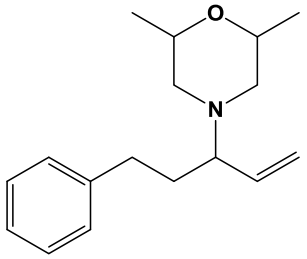
*3-(Hept-1-enyl)-2,6-dimethylmorpholine (**6.1 br**).* Colorless liquid, 77.9 mg (73.4%). ^{1}H NMR ($CDCl_3$): δ 5.63 (ddd, ^3J = 17.2, 10.1, 9.0 Hz, 1H), 5.15 (dd, ^3J = 10.1 Hz, ^2J = 1.8 Hz, 1H), 5.04 (dd, ^3J = 17.2 Hz, ^2J = 1.8 Hz, 1H), 3.73−3.63 (m, 1H), 3.63−3.54 (m, 1H), 2.74 (dd, ^2J = 11.3 Hz, ^3J = 1.7 Hz, 1H), 2.70−2.58 (m, 2H), 1.89 (t, ^3J = 10.6 Hz, 1H), 1.77 (t, ^3J = 10.6 Hz, 1H), 1.66−1.54 (m, 1H), 1.44−1.33 (m, 1H), 1.33−1.23 (m, 3H), 1.23−1.16 (m, 1H), 1.11 (dt, ^3J = 6.6 Hz, ^4J = 1.8 Hz, 6H), 0.87 (t, ^3J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 138.0, 117.9, 72.4, 72.1, 69.0, 57.6, 55.2, 31.5, 28.9, 23.1, 19.594, 19.585, 14.4. IR (cm^{-1}): 2976 (m), 2948 (w), 2879 (m), 2835 (m), 1637 (m), 1379 (m), 1257 (s), 1093 (m), 827 (m), 650 (m), 619 (s). HRMS *m*/*z*: [M + H]$^+$ calcd for $C_{13}H_{26}NO$, 212.2014; found, 212.2008.



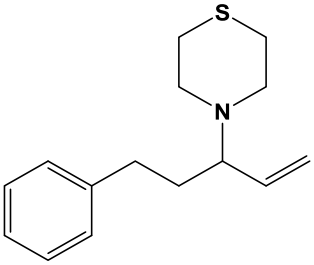
*3-(Hept-1-enyl)-thiomorpholine (**6.2 br**).* Colorless liquid, 69.3 mg (69.2%). ^{1}H NMR ($CDCl_3$): δ 5.66 (ddd, ^3J = 17.2, 10.2, 8.7 Hz, 1H), 5.14 (dd, ^3J = 10.2 Hz, ^2J = 1.8 Hz, 1H), 5.02 (dd, ^3J = 17.2 Hz, ^2J = 1.8 Hz, 1H), 2.91−2.82 (m, 2H), 2.74 (dt, ^3J = 8.7 Hz, 5.1 Hz, 1H), 2.72−2.55 (m, 6H), 1.63−1.53 (m, 1H), 1.48−1.35 (m, 1H), 1.35−1.17 (m, 4H), 0.86 (t, ^3J = 7.2 Hz, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 137.4, 117.6, 69.7, 52.0, 31.6, 29.1, 28.8, 23.1, 14.4. IR (cm^{-1}): 2983 (m), 2926 (w), 2884 (m), 2813 (m), 1603 (m), 1278 (m), 1192 (s), 947 (m), 797 (s), 704 (s), 583 (m). HRMS *m*/*z*: [M + H]$^+$ calcd for $C_{11}H_{22}NS$, 200.1473; found, 200.1467.



*3-(5-Phenyl-pent-1-enyl)-morpholine (**7.1 br**).* Colorless liquid, 83.1 mg (71.6%). ^{1}H NMR ($CDCl_3$): δ 7.33−7.28 (m, 2H), 7.23−7.19 (m, 3H), 5.77 (ddd, ^3J = 17.2, 10.3, 9.0 Hz, 1H), 5.28 (dd, ^3J = 10.3 Hz, ^2J = 1.7 Hz, 1H), 5.15 (dd, ^3J = 17.2 Hz, ^2J = 1.7 Hz, 1H), 3.78−3.69 (m, 4H), 2.81−2.77 (m, 1H), 2.74−2.69 (m, 1H), 2.64−2.57 (m, 3H), 2.51−2.45 (m, 2H), 2.09−1.97 (m, 1H), 1.78−1.72 (m, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 142.3, 137.1, 128.5, 128.4, 125.8, 118.3, 68.1, 67.3, 50.1, 33.3, 32.4. IR (cm^{-1}): 3041 (m), 3019 (w), 2965 (m), 2902 (m), 2853 (m), 1642 (m), 1615 (m), 1393 (m), 1315 (m), 1173 (m), 782 (m), 711 (s), 597 (s). HRMS *m*/*z*: [M + H]$^+$ calcd for $C_{15}H_{22}NO$, 232.1701; found, 232.1693.



*3-(5-Phenyl-pent-1-enyl)-2,6-dimethylmorpholine (**7.2 br**).* Colorless liquid, 96.7 mg (74.3%). ^{1}H NMR ($CDCl_3$): δ 7.36−7.23 (m, 2H), 7.23−7.08 (m, 3H), 5.71 (ddd, ^3J = 17.2, 10.3, 8.8 Hz, 1H), 5.25 (dd, ^3J = 10.3 Hz, ^2J = 1.7 Hz, 1H), 5.14 (dd, ^3J = 17.2 Hz, ^2J = 1.7 Hz, 1H), 3.72 (dqd, ^3J = 10.0, 6.3, 2.4 Hz, 1H), 3.65 (dqd, ^3J = 10.0, 6.3, 2.4 Hz, 1H), 2.83−2.71 (m, 2H), 2.71−2.64 (m, 1H), 2.62 (d, ^3J = 11.2 Hz, 1H), 2.60−2.52 (m, 1H), 2.01−1.94 (m, 1H), 1.99 (t, ^3J = 10.6 Hz, 1H), 1.83 (t, ^3J = 10.6 Hz, 1H), 1.77−1.74 (m, 1H), 1.18 (dd, ^3J = 6.3 Hz, ^4J = 2.4 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 142.7, 137.4, 128.7, 128.6, 126.0, 118.5, 72.4, 72.2, 68.3, 57.7, 54.6, 33.7, 32.8, 19.59, 19.56. IR (cm^{-1}): 3027 (m), 2997 (w), 2972 (m), 2856 (m), 1661 (m), 1603 (m), 1416 (m), 1371 (s), 1267 (m), 874 (m), 735 (s), 606 (m). HRMS *m*/*z*: [M + H]$^+$ calcd for $C_{17}H_{26}NO$, 260.2014; found, 260.2007.



*3-(5-Phenyl-pent-1-enyl)-thiomorpholine (**7.3 br**).* Colorless liquid, 81.8 mg (65.9%). ^{1}H NMR ($CDCl_3$): δ 7.34−7.23 (m, 2H), 7.22−7.12 (m, 3H), 5.75 (ddd, ^3J = 17.2, 10.3, 8.7 Hz, 1H), 5.22 (dd, ^3J = 17.2 Hz, ^2J = 1.8 Hz, 1H), 5.09 (dd, ^3J = 10.3 Hz, ^2J = 1.8 Hz, 1H), 2.93−2.86 (m, 2H), 2.83 (dd, ^3J = 14.5 Hz, 8.4 Hz, 1H), 2.73−2.56 (m, 8H), 1.97−1.92 (m, 1H), 1.81−1.62 (m, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 142.3, 136.5, 128.5, 128.3, 125.8, 117.8, 68.3, 51.6, 33.3, 32.6, 28.4. IR (cm^{-1}): 3075 (m), 3019 (m), 2956 (w), 2823 (m), 1638 (m), 1621 (m), 1395 (m), 1327 (m), 1193 (m), 790 (m), 673 (m), 629 (s). HRMS *m*/*z*: [M + H]$^+$ calcd for $C_{15}H_{22}NS$, 248.1473; found, 248.1467.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.9b00025.

NMR spectra for all newly reported compounds and conversion versus time data for four additional substrate combinations (PDF)

Crystal data including bond lengths and angles for the mesityl-substituted catalyst (TXT)

Accession Codes

CCDC 1891646 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing

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Organometallics XXXX, XXX, XXX−XXX

data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) Trost, B. M. Atom economy-A challenge for organic synthesis: Homogeneous catalysis leads the way. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259−281.

(2) Muller, T. E.; Hultzsch, K. C.; Yus, M.; Foubelo, F.; Tada, M. Hydroamination: Direct addition of amines to alkenes and alkynes. *Chem. Rev.* **2008**, *108*, 3795−3892.

(3) Huang, L.; Arndt, M.; Gooßen, K.; Heydt, H.; Gooßen, L. J. Late transition metal-catalyzed hydroamination and hydroamidation. *Chem. Rev.* **2015**, *115*, 2596−2697.

(4) (a) Beller, M.; Seayad, J.; Tillack, A.; Jiao, H. Catalytic Markovnikov and anti-Markovnikov functionalization of alkenes and alkynes: Recent developments and trends. *Angew. Chem., Int. Ed.* **2004**, *43*, 3368−3398. (b) Hultzsch, K. C. Catalytic asymmetric hydroamination of non-activated olefins. *Org. Biomol. Chem.* **2005**, *3*, 1819−1824. (c) Beck, J. F.; Samblanet, D. C.; Schmidt, J. A. R. Palladium catalyzed intermolecular hydroamination of 1-substituted allenes: An atom-economical method for the synthesis of *N*-allylamines. *RSC Adv.* **2013**, *3*, 20708−20718. (d) Hultzsch, K. C. Transition metal-catalyzed asymmetric hydroamination of alkenes (AHA). *Adv. Synth. Catal.* **2005**, *347*, 367−391. (e) Kinder, R. E.; Zhang, Z.; Widenhoefer, R. A. Intermolecular hydroamination of allenes with N-unsubstituted carbamates catalyzed by a gold(I) N-heterocyclic carbene complex. *Org. Lett.* **2008**, *10*, 3157−3159. (f) Goldfogel, M. J.; Roberts, C. C.; Meek, S. J. Intermolecular hydroamination of 1,3-dienes catalyzed by bis(phosphine)-carbodicarbene-rhodium complexes. *J. Am. Chem. Soc.* **2014**, *136*, 6227−6230. (g) Yang, X.-H.; Lu, A.; Dong, V. M. Intermolecular hydroamination of 1,3-dienes to generate homoallylic amines. *J. Am. Chem. Soc.* **2017**, *139*, 14049−14052. (h) Ickes, A. R.; Ensign, S. C.; Gupta, A. K.; Hull, K. L. Regio- and chemoselective intermolecular hydroamination of allyl imines for the synthesis of 1,2-diamines. *J. Am. Chem. Soc.* **2014**, *136*, 11256−11259. (i) Vanable, E. P.; Kennemur, J. L.; Joyce, L. A.; Ruck, R. T.; Schultz, D. M.; Hull, K. L. Rhodium-catalyzed asymmetric hydroamination of allyl amines. *J. Am. Chem. Soc.* **2019**, *141*, 739−742.

(5) (a) Pawlas, J.; Nakao, Y.; Kawatsura, M.; Hartwig, J. F. A general nickel-catalyzed hydroamination of 1,3-dienes by alkylamines: catalyst selection, scope, and mechanism. *J. Am. Chem. Soc.* **2002**, *124*, 3669−3679. (b) Cochran, B. M.; Michael, F. E. Mechanistic studies of a palladium-catalyzed intramolecular hydroamination of unactivated alkenes: Protonolysis of a stable palladium alkyl complex is the turnover-limiting step. *J. Am. Chem. Soc.* **2008**, *130*, 2786−2792. (c) Takaya, J.; Hartwig, J. F. Mechanistic studies of ruthenium-catalyzed anti-Markovnikov hydroamination of vinylarenes: Intermediates and evidence for catalysis through π-arene complexes. *J. Am. Chem. Soc.* **2005**, *127*, 5756−5757. (d) Wang, Z. J.; Benitez, D.; Tkatchouk, E.; Goddard III, W. A., III; Toste, F. D. Mechanistic study of gold(I)-catalyzed intermolecular hydroamination of allenes. *J. Am. Chem. Soc.* **2010**, *132*, 13064−13071. (e) Nettekoven, U.; Hartwig, J. F. A new pathway for hydroamination. Mechanism of palladium-catalyzed addition of anilines to vinylarenes. *J. Am. Chem. Soc.* **2002**, *124*, 1166−1167. (f) Tafazolian, H.; Samblanet, D. C.; Schmidt, J. A. R. Electronic role of 3-iminophosphine ligands in palladium-catalyzed intermolecular hydroamination. *Organometallics* **2015**, *34*, 1809−1817. (g) Straub, B. F.; Bergman, R. G. The mechanism of hydroamination of allenes, alkynes, and alkenes catalyzed by cyclopentadienyltitanium-imido complexes: A density functional study. *Angew. Chem., Int. Ed.* **2001**, *40*, 4632−4635.

(6) (a) Kuchenbeiser, G.; Shaffer, A. R.; Zingales, N. C.; Beck, J. F.; Schmidt, J. A. R. Palladium(II) 3-iminophosphine (3IP) complexes: Active precatalysts for the intermolecular hydroamination of 1,2-dienes (allenes) and 1,3-dienes with aliphatic amines under mild conditions. *J. Organomet. Chem.* **2011**, *696*, 179−187. (b) Nishina, N.; Yamamoto, Y. Gold-catalyzed intermolecular hydroamination of allenes with arylamines and resulting high chirality transfer. *Angew. Chem., Int. Ed.* **2006**, *45*, 3314−3317. (c) Meguro, M.; Yamamoto, Y. A new method for the synthesis of nitrogen heterocycles via palladium catalyzed intramolecular hydroamination of allenes. *Tetrahedron Lett.* **1998**, *39*, 5421−5424. (d) Nobis, M.; Drießen-Hölscher, B. Recent developments in transition metal catalyzed intermolecular hydroamination reactions-A breakthrough? *Angew. Chem., Int. Ed.* **2001**, *40*, 3983−3985.

(7) (a) Schultz, D. M.; Wolfe, J. P. Synthesis of polycyclic nitrogen heterocycles via alkene aminopalladation/carbopalladation cascade reactions. *Org. Lett.* **2010**, *12*, 1028−1031. (b) Sharma, V.; Kumar, P.; Pathak, D. Biological importance of the indole nucleus in recent years: A comprehensive review. *J. Heterocycl. Chem.* **2010**, *47*, 491−502. (c) Caddick, S.; Kofie, W. Observations on the intramolecular Heck reactions of aromatic chlorides using palladium/imidazolium salts. *Tetrahedron Lett.* **2002**, *43*, 9347−9350.

(8) (a) Blieck, R.; Bahri, J.; Taillefer, M.; Monnier, F. Copper-catalyzed hydroamination of terminal allenes. *Org. Lett.* **2016**, *18*, 1482−1485. (b) Ackermann, L.; Bergman, R. G.; Loy, R. N. Use of group 4 bis(sulfonamido) complexes in the intramolecular hydroamination of alkynes and allenes. *J. Am. Chem. Soc.* **2003**, *125*, 11956−11963.

(9) (a) Zeng, X.; Soleilhavoup, M.; Bertrand, G. Gold-catalyzed intermolecular Markovnikov hydroamination of allenes with secondary amines. *Org. Lett.* **2009**, *11*, 3166−3169. (b) Khrakovsky, D. A.; Tao, C.; Johnson, M. W.; Thornbury, R. T.; Shevick, S. L.; Toste, F. D. Enantioselective, stereodivergent hydroazidation and hydroamination of allenes catalyzed by acyclic diaminocarbene (ADC) gold(I) complexes. *Angew. Chem., Int. Ed.* **2016**, *55*, 6079−6083.

(10) Toups, K. L.; Widenhoefer, R. A. Platinum(II)-catalyzed intermolecular hydroamination of monosubstituted allenes with secondary alkylamines. *Chem. Commun.* **2010**, *46*, 1712−1714.

(11) Besson, L.; Goré, J.; Cazes, B. Synthesis of allylic amines through the palladium-catalyzed hydroamination of allenes. *Tetrahedron Lett.* **1995**, *36*, 3857−3860.

(12) Tafazolian, H.; Schmidt, J. A. R. Cationic [(iminophosphine)-nickel(allyl)]$^+$ complexes as the first example of nickel catalysts for direct hydroamination of allenes. *Chem.—Eur. J.* **2017**, *23*, 1507−1511.

(13) (a) Beck, J. F.; Schmidt, J. A. R. Hydroamination of 1,1-dimethylallene with primary aryl amines under mild conditions: An atom-economical route to *N*-(1,1-dimethyl-2-propenyl)-anilines. *RSC Adv.* **2012**, *2*, 128−131. (b) Cooke, M. L.; Xu, K.; Breit, B. Enantioselective rhodium-catalyzed synthesis of branched allylic amines by intermolecular hydroamination of terminal allenes. *Angew. Chem., Int. Ed.* **2012**, *51*, 10876−10879. (c) Xu, K.; Wang, Y.-H.; Khakyzadeh, V.; Breit, B. Asymmetric synthesis of allylic amines via hydroamination of allenes with benzophenone imine. *Chem. Sci.* **2016**, *7*, 3313−3316. (d) Koschker, P.; Breit, B. Branching out: Rhodium-catalyzed allylation with alkynes and allenes. *Acc. Chem. Res.* **2016**, *49*, 1524−1536.

DOI: 10.1021/acs.organomet.9b00025
Organometallics XXXX, XXX, XXX−XXX

(14) (a) Shaffer, A. R.; Schmidt, J. A. R. Palladium(II) 3-iminophosphine complexes as intermolecular hydroamination catalysts for the formation of imines and enamines. *Organometallics* **2008**, *27*, 1259−1266. (b) Zingales, N. C.; Shaffer, A. R.; Schmidt, J. A. R. Investigation of steric and electronic features of 3-iminophosphine-based palladium catalysts for intermolecular hydroamination. *Organometallics* **2013**, *32*, 578−586.
(15) Shaffer, A. R.; Schmidt, J. A. R. Reactivity of (3-iminophosphine)palladium(II) complexes: Evidence of hemilability. *Organometallics* **2009**, *28*, 2494−2504.
(16) Campos, J.; Espada, M. F.; López-Serrano, J.; Carmona, E. Cyclometalated iridium complexes of bis(aryl) phosphine ligands: Catalytic C-H/C-D exchanges and C-C coupling reactions. *Inorg. Chem.* **2013**, *52*, 6694−6704.
(17) Bartlett, R. A.; Olmstead, M. M.; Power, P. P.; Sigel, G. A. Synthesis and spectroscopic and X-ray structural studies of the mesitylphosphines PH_2Mes and $PHMes_2$ (Mes = 2,4,6-$Me_3C_6H_2$) and their lithium salts $[Li(THF)_3PHMes]$ and $[\{Li(OEt_2)PMes_2\}_2]$. *Inorg. Chem.* **1987**, *26*, 1941−1946.
(18) Kidonakis, M.; Stratakis, M. Ligandless regioselective hydrosilylation of allenes catalyzed by gold nanoparticles. *Org. Lett.* **2015**, *17*, 4538−4541.
(19) Gao, S.; Liu, H.; Wu, Z.; Yao, H.; Lin, A. Palladium-catalyzed allylic alkylation with internal alkynes to construct C-C and C-N bonds in water. *Green Chem.* **2017**, *19*, 1861−1865.
(20) Takeuchi, R.; Ue, N.; Tanabe, K.; Yamashita, K.; Shiga, N. Iridium complex-catalyzed allylic amination of allylic esters. *J. Am. Chem. Soc.* **2001**, *123*, 9525−9534.
(21) Kawatsura, M.; Uchida, K.; Terasaki, S.; Tsuji, H.; Minakawa, M.; Itoh, T. Ruthenium-catalyzed regio- and enantioselective allylic amination of racemic 1-arylallyl esters. *Org. Lett.* **2014**, *16*, 1470−1473.
(22) Liu, W.-B.; Zhang, X.; Dai, L.-X.; You, S.-L. Asymmetric N-allylation of indoles through the iridium-catalyzed allylic alkylation/oxidation of indolines. *Angew. Chem., Int. Ed.* **2012**, *51*, 5183−5187.

DOI: 10.1021/acs.organomet.9b00025
Organometallics XXXX, XXX, XXX−XXX