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Palladium catalyzed intermolecular hydroamination of 1-substituted allenes: an atom-economical method for the synthesis of *N*-allylamines

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The palladium complex **[(3IP^{tBu})Pd(allyl)]OTf** previously displayed excellent catalytic activity for the hydroamination of 1,1-dimethylallene with anilines, selectively producing the branched substituted allylamine product (kinetic product) in high conversion. In the current report, the scope of this hydroamination reaction has been expanded to include both alkyl amines and anilines in combination with an array of seven alkyl and aryl allenes. For the majority of amines investigated, the hydroamination of 1,1-dimethylallene, cyclohexylallene, benzylallene, and select aryl allenes with alkyl amines gave the branched substituted allylamine product in nearly quantitative conversion at ambient temperature in less than 1 hour. In contrast, anilines displayed a more limited reaction scope and yielded the linear hydroamination product (thermodynamic product) with all allenes other than 1,1-dimethylallene. Both branched and linear products could be formed selectively in the hydroamination of *p*-fluorophenylallene with alkyl amines through careful control of **[(3IP^{tBu})Pd(allyl)]OTf** catalyst loading and reaction duration. Overall, the branched allylamines produced are useful synthetic intermediates due to their available unsaturated vinyl group, while the linear allylamine products are chemically similar to a class of known pharmaceuticals.

Introduction

Functionalized allylamines are a class of molecules that constitute a useful synthetic target due to their importance as intermediates in the synthesis of indoles[1–5] and heterocycles,[6–15] as well as their prevalence in pharmaceuticals, including drugs such as cinnarizine,[16] flunarizine,[17] naftifine,[18] terbinafine,[19,20] and zimelidine (Fig. 1).[21] These compounds play important and diverse biological roles. For example, cinnarizine acts as a calcium channel blocker in the treatment of vertigo[22] and nausea associated with motion sickness.[23] Likewise, flunarizine acts as a calcium channel blocker in the relief of chronic migraines.[24] Naftifine and terbinafine are antifungal drugs for the treatment of athlete's foot (tinea pedis), jock itch (tinea cruris), and ringworm (tinea corporis), whose modes of action involve inhibition of squalene epoxidase, an enzyme involved in the growth of fungal cell walls.[25] Zimelidine inhibits serotonin reuptake acting as an anti-depressant, although it is been subsequently replaced by more effective remedies.[26] The traditional stepwise synthesis of substituted allylamines is both time and material intensive, commonly requiring the use of both protecting groups and multiple purifications.[2,3,27] Recent advances in catalytic allylic amination have provided far greener methods for the synthesis of allylamines; however, even in the best cases, a coproduct such as water is formed.[28–30] For example, both flunarizine and naftifine were synthesized by Ohshima *et al. via* direct catalytic substitution of allylic alcohols, each forming water as the sole byproduct.[31] Although allylic amination presents a distinct improvement over the traditional methods for synthesis of these compounds,[17,32] production of allylamines *via* hydroamination offers an even greener synthetic alternative because all the atoms present in the starting materials are incorporated into a single product. Hydroamination is the direct addition of a nitrogen–hydrogen bond across a carbon–carbon unsaturated bond, allowing for the formation of complex molecular frameworks from inexpensive precursors.[33] Hydroamination is also the only 100% atom economical method available to prepare allylamines.[34]

Intermolecular hydroamination of allenes can produce several different regio- and stereoisomers depending primarily on the functionality present on the substrate allene and the catalyst employed to effect the addition reaction. In general, early transition metal catalysts yield hydroamination products where the amino group is added to the central carbon of the allene,[35,36] while late transition metal catalysts install the amine functionality at a terminal carbon atom.[37] For asymmetrically substituted allenes (such as monosubstituted allenes), the terminal carbons are inequivalent, allowing the possibility of regioselective hydroamination to give either branched or linear products. In fact,

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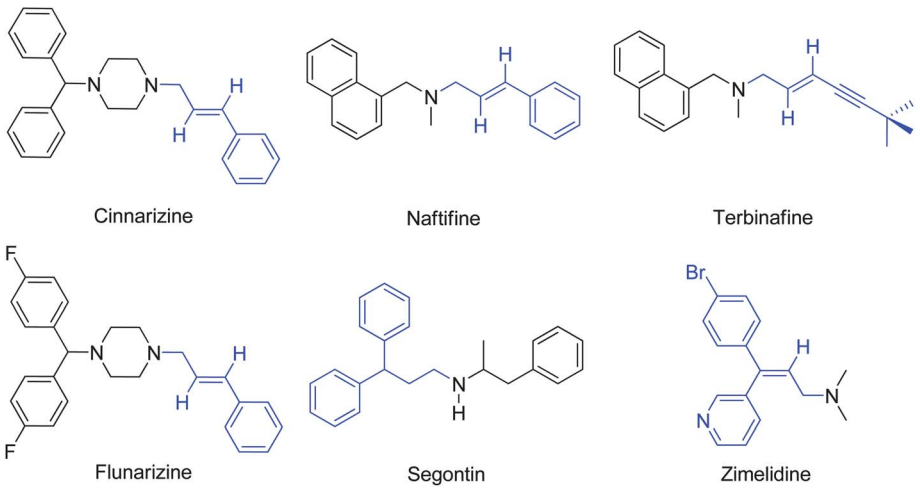


Fig. 1 Pharmacologically active allylamine or allylamine derived compounds.

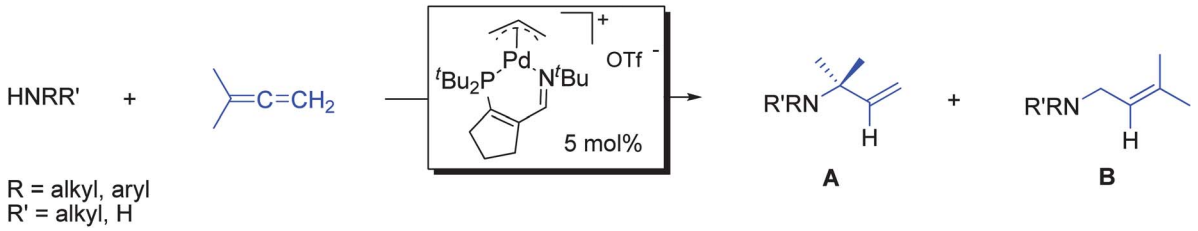
regioselective addition to the substituted carbon atom of a monosubstituted allene also creates a new stereocenter; chiral rhodium catalysts for asymmetric hydroamination of allenes have recently been disclosed in an elegant study by Breit and coworkers.[38] In the past several years, the intermolecular hydroamination of allenes has come under great scrutiny, and it has become clear that many late metal systems are capable of selectively producing the linear (thermodynamic) product,[39–42] while selectivity for the branched (kinetic) product remains difficult.[38] The relatively low cost of palladium compared to rhodium or gold makes the continued development of palladium based hydroamination catalysts an attractive pursuit. A new system capable of utilizing the less expensive palladium center while still allowing for the facile isolation of the kinetic product with broad substrate scope would represent a significant advancement in palladium catalyzed amination. Unfortunately, there are exceptionally few palladium complexes that will perform hydroamination[43,44] or allylic amination[45–48] in a manner that allows for the isolation of the branched product, mostly due to limitations in turnover frequency and necessary reaction temperatures.

We have previously established alicyclic 3-iminophosphines as effective supporting ligands for use in palladium-catalyzed hydroamination of allenes,[49–51] 1,3-dienes[50] and alkynes.[52] Our initial allene hydroamination study focused on **[3IP^{Ar}Pd(allyl)]OTf**, which performed well in the hydroamination of allenes with secondary amines.[50] Regrettably, in this initial study, the hydroamination of 1,1-dimethylallene with secondary alkyl amines yielded only the linear allylamines (thermodynamic products).[50] The ability to isolate the branched allylamines (kinetic products), where the double bond is terminal (vinylic), is highly desirable due to the ease in which these compounds can be further derivatized *via* reactions such as hydroformylation[53] and alkene metathesis.[54] In order to obtain these more valuable and thermodynamically less favorable products, modifications to the substituents on the ligand were investigated, ultimately resulting in the development of **[3IP^{tBu}Pd(allyl)]OTf**.[49] This complex was found to effectively produce the branched isomer in good to excellent yield when used for the hydroamination of allenes with anilines.[49] Isomerization to the linear product was minimal and in most cases the reaction operated well at room temperature. It was further shown that the branched isomer could be used in an aryl amino Claisen rearrangement, producing 2-allyl anilines in good yield *via* a one-pot two-step synthesis.[49] Herein, we report a broadly expanded catalytic scope for the 3-iminophosphine precatalyst **[3IP^{tBu}Pd(allyl)]OTf**, which has been utilized in the hydroamination of a diverse series of mono- and 1,1-disubstituted allenes with both alkyl amines and anilines. These reactions have resulted in the successful synthesis and isolation of a wide range of new allylamines, demonstrating the broad utility of this new catalytic system.

Results and discussion

In our previous communication,[49] we used **[3IP^{tBu}Pd(allyl)]OTf** in the hydroamination of 1,1-dimethylallene with various anilines; some of these results are reproduced herein (Table 1; entries 1.6–1.9). In order to expand the scope of 1,1-dimethylallene reactivity, primary and secondary alkyl amines were subsequently investigated with this catalyst. Primary amines, cyclohexylamine and 2-octylamine, proceeded slowly (Table 1; entries 1.10 and 1.11), although they did react faster than even the most competent anilines.[49] The hydroamination of 1,1-dimethylallene with secondary alkyl amines proceeded much more rapidly, yielding exclusively the branched isomer in as little as 30 minutes (Table 1; entries 1.1–1.5). There seems to be a relationship between the pK_a of the amine's conjugate acid and the rate of hydroamination. For example, the pK_a of the conjugate acid of morpholine is 8.50 while that for *para*-toluidene is 5.08.[55] Given the increased rate of hydroamination of morpholine compared to *para*-toluidene, it is clear that basic, electron-rich amines make better substrates for allene hydroamination (Table 1). Generally, anilines are much less basic than alkyl amines due to delocalization of the nitrogen lone pair into the π system of the aromatic ring. Amine basicity is not the only factor affecting the rate of the reaction; steric factors also play a role. We have previous noted that 2-substituted anilines are ineffective substrates for the

Table 1 The hydroamination of 1,1-dimethylallene with primary and secondary amines



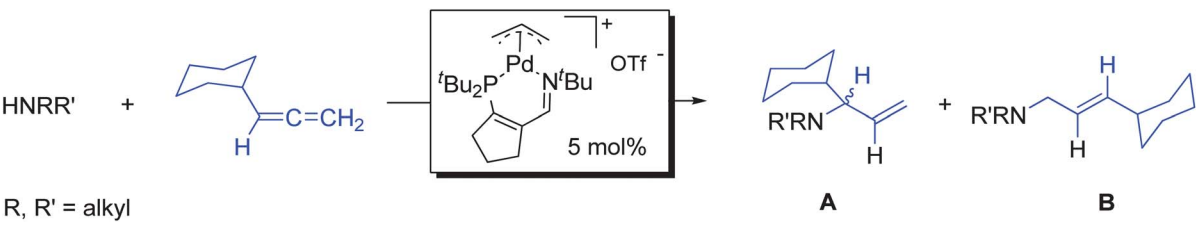
Entry	Amine	Time (h)	Conversion (A : B)
1.1	Morpholine	0.5	95 (100 : 0)
1.2	Piperidine	0.5	95 (100 : 0)
1.3	1-Methylpiperazine	0.5	95 (100 : 0)
1.4	Pyrrolidine	0.5	95 (100 : 0)
1.5	1,2,3,4-Tetrahydroisoquinoline	0.5	95 (100 : 0)
1.6	3-Methylaniline	20	62 (100 : 0)[a]
1.7	4-Methylaniline	20	95 (100 : 0)[a]
1.8	3-Methoxyaniline	20	73 (100 : 0)[a]
1.9	4-Methoxyaniline	20	95 (100 : 0)[a]
1.10	Cyclohexylamine	3	95 (100 : 0)
1.11	2-Octylamine	3	95 (100 : 0)

[a] Ref. 49.

hydroamination of 1,1-dimethylallene.[49] With a conjugate acid pK_a of 4.45,[55] *ortho*-toluidene is more basic than many of the halogenated anilines that act as competent coupling partners with 1,1-dimethylallene, but *ortho*-toluidene was found to be unreactive even at elevated temperature.[49] This is likely due to steric congestion around the palladium center caused by the *ortho* substituent during catalysis. Neither steric nor electronic arguments alone can adequately explain why primary alkyl amines react slowly. For example, cyclohexylamine is reasonably basic (conjugate acid pK_a of 10.64),[55] but reacts slowly compared to secondary alkyl amines. It may be that different steps in the catalytic mechanism are rate-limiting depending on the type of amine used. A full kinetic and mechanistic evaluation of this system remains a subject of future work in our group.

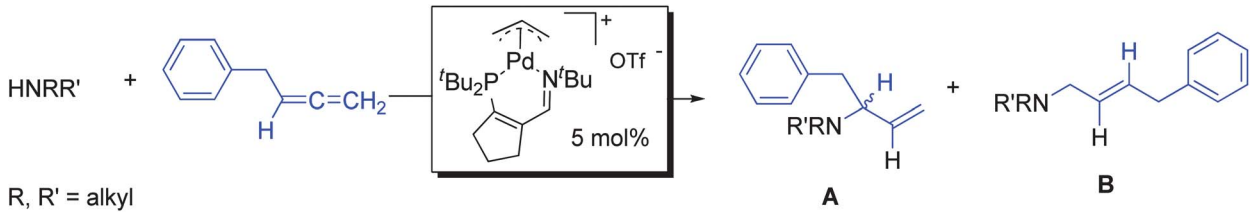
The main focus of the study reported herein was to investigate the hydroamination of other allenes. We were especially interested in mono-substituted allenes since formation of the branched isomer in these cases would create a new chiral center. Though a racemic mixture would result with the current catalyst, the successful creation of new chiral centers would inspire development of chiral versions of this catalyst system. The hydroamination of cyclohexylallene with secondary alkyl amines proceeded readily at room temperature to yield the branched products as racemic mixtures in 30 to 60 minutes (Table 2). Unfortunately, anilines were unreactive with cyclohexylallene in the presence of **[3IP$^{t\mathrm{Bu}}$Pd(allyl)]OTf**. 1,2,3,4-Tetrahydroquinoline was also found to be completely unreactive, similar to the *ortho*-substituted anilines tested with this catalyst

Table 2 The hydroamination of cyclohexylallene with secondary amines



Entry	Amine	Time (h)	Conversion (A : B)
2.1	Morpholine	0.5	95 (100 : 0)
2.2	Piperidine	0.5	91 (100 : 0)
2.3	1-Methylpiperazine	0.5	85 (100 : 0)
2.4	Pyrrolidine	0.5	56 (100 : 0)
2.5	1,2,3,4-Tetrahydroisoquinoline	1	95 (100 : 0)

Table 3 The hydroamination of benzylallene with secondary amines



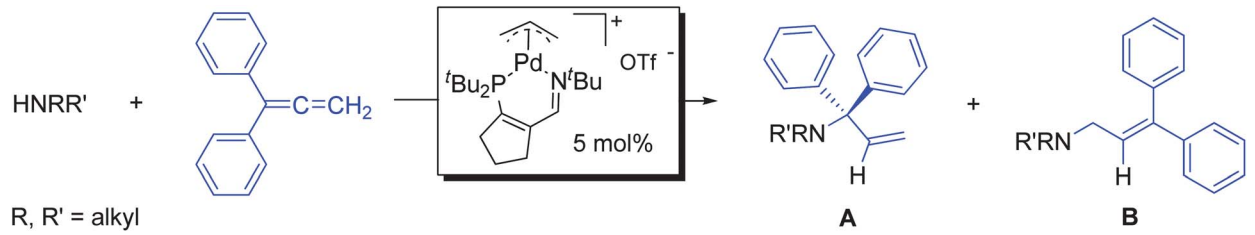
Entry	Amine	Time (h)	Conversion (A : B)
3.1	Morpholine	1.0	95 (100 : 0)
3.2	Piperidine	1.0	95 (100 : 0)
3.3.1	1-Methylpiperazine	0.75	95 (100 : 0)
3.3.2	1-Methylpiperazine	1.0	95 (87 : 13)
3.3.3	1-Methylpiperazine	2.0	95 (100 : 0)[a]
3.4	Pyrrolidine	1.0	95 (100 : 0)
3.5	1,2,3,4-Tetrahydroisoquinoline	1.0	95 (100 : 0)[a]

[a] Conversion reported at a catalyst loading of 1 mol%.

system. Its isomer, 1,2,3,4-tetrahydroisoquinoline, although slower than the other secondary alkyl amines, readily hydroaminated cyclohexylallene. The inclusion of a methylene group between the aromatic ring and the amine was enough to allow hydroamination to proceed. The reactivity difference between these two isomers fits well within both the electronic and steric considerations discussed above, allowing 1,2,3,4-tetrahydroisoquinoline to react, while 1,2,3,4-tetrahydroquinoline does not. Overall, cyclohexylallene underwent hydroamination effectively in the presence of **[3IP$^{t\mathrm{Bu}}$Pd(allyl)]OTf** and secondary amines.

Benzylallene was found to have a very similar reactivity profile to that of cyclohexylallene, although slightly longer reaction times were necessary, occasionally leading to small amounts of product isomerization (Table 3). Previous reports have shown that branched allylamines can be readily isomerized to linear allylamines using Lewis acid catalysts in the presence of a Brønsted acid.[47,48,56] The palladium complexes utilized in this study are no exception and generally, all of the branched allylamine products slowly convert to the linear isomer in a matter of hours in the presence of the catalyst; however, the branched benzylallene hydroamination products undergo this isomerization somewhat faster than many of the other products reported herein. Thus, the longer reaction times necessary for hydroamination of benzylallene led to some cases where the branched product had partially isomerized. For example, hydroamination of benzylallene with 1-methylpiperazine in the presence of **[3IP$^{t\mathrm{Bu}}$Pd(allyl)]OTf** (5 mol%) resulted in partial isomerization after one hour. This isomerization was avoided by limiting the reaction time to 45 minutes or reducing the catalyst loading to 1 mol% with a reaction time of 2 hours. Either approach gave complete product formation with no

Table 4 The hydroamination of 1,1-diphenylallene with secondary amines



Entry	Amine	Time (h)	Conversion (A : B)
4.1	Morpholine	20	95 (0 : 100)
4.2	Piperidine	20	95 (0 : 100)
4.3	1-Methylpiperazine	20	95 (0 : 100)
4.4	Pyrrolidine	20	95 (0 : 100)
4.5	1,2,3,4-Tetrahydroisoquinoline	20	95 (0 : 100)

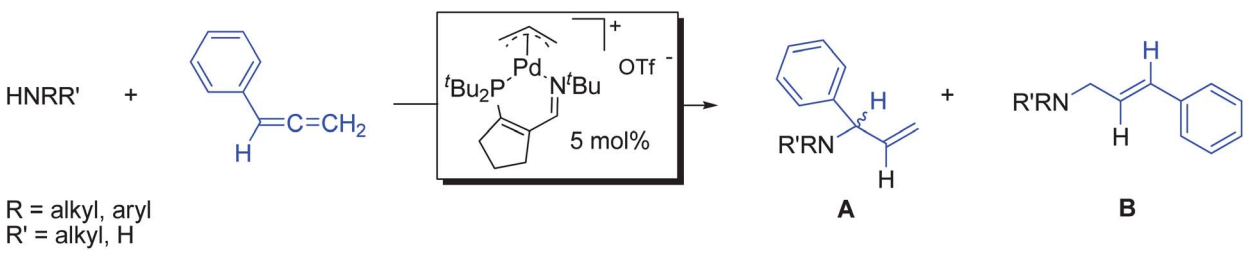
isomerization (Table 3; entries 3.3.1 to 3.3.3). Similarly, lower catalyst loading was necessary in the hydroamination using 1,2,3,4-tetrahydroisoquinoline (Table 3; entry 3.5). *para*-Toluidene was also found to hydroaminate benzylallene (with heating to 70 °C), but multiple inseparable isomers were observed. Overall, benzylallene proved to be a good substrate for hydroamination, with only minor procedural modifications necessary to achieve high yields of branched allylamine products.

1,1-Diphenylallene proved to be the least reactive of the allenes studied. It was completely inert towards anilines and hydroaminated slowly with all secondary alkyl amines studied, leading to isolation of linear isomers exclusively (Table 4). NMR spectroscopy was used to follow the progress of these reactions and small amounts of the branched isomers were observed in each reaction mixture throughout the course of the experiments; however, the rates of conversion from the branched to linear isomers appeared to be similar in magnitude to the rates of the hydroamination reactions, such that the branched isomers could not be isolated. The reactions were found to be complete at 20 hours for all secondary amines studied, leading to high yields of the linear hydroamination products for each secondary alkyl amine.

The hydroamination of phenylallene was incredibly facile for all alkyl amines studied. Unfortunately, the isomerization from branched to linear allylamine products was also very rapid with this system. Hydroamination using morpholine was complete in less than one minute with 28% of the material already isomerized to the linear product (Table 5; entry 5.1.1). This isomerization was nearly complete only 3 minutes later (Table 5; entry 5.1.2). In an effort to isolate the branched product, catalyst loading was reduced to 1 mol%, slowing both hydroamination and product isomerization. After 10 minutes, the reaction was complete with only 22% of the product isomerized to the linear isomer (Table 5; entry 5.1.4). Hydroamination of phenylallene with 1,2,3,4-tetrahydroisoquinoline reached completion in 90 minutes, while the other secondary alkyl amines were done in 30 minutes or less (Table 5; entries 5.2 to 5.5). Anilines required longer reaction times with conversions recorded at 20 hours and isomerization to the linear product complete by this time (Table 5; entries 5.6 to 5.9). Cinnamyl amines (*trans*-3-phenylallylamines) are found in *N*-cinnamyl-piperazines such as cinnarizine and flunarizine, both of which are medicinally active compounds, as discussed in the Introduction. Hydroamination of phenylallene with commercially available 1-(diphenylmethyl) piperazine yielded quantitative conversion to cinnarizine (Scheme 1) with 100% atom efficiency in only three hours (Table 5; entry 5.12), showing the utility of these catalysts in real world applications. Although it was difficult to isolate branched allylamine products, the hydroamination of phenylallene proved to be an exceptionally efficient method for installation of new nitrogen–carbon bonds, producing the particularly interesting cinnamyl moiety with 100% atom economy at room temperature.

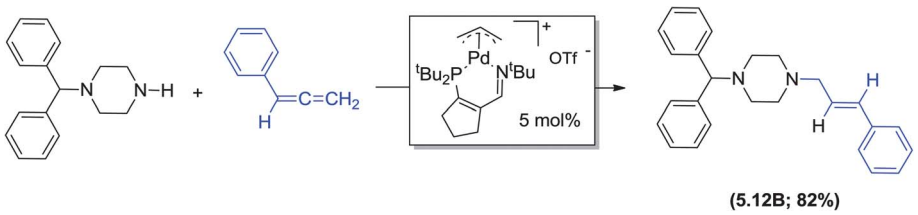
In order to investigate the role of electronics within the allene without varying the steric component, *para*-substituted phenylallene derivatives *p*-methoxyphenylallene and *p*-fluorophenylallene were tested in hydroamination. The reactions of *p*-methoxyphenylallene with morpholine and 4-methylaniline

Table 5 The hydroamination of phenylallene with anilines and secondary amines



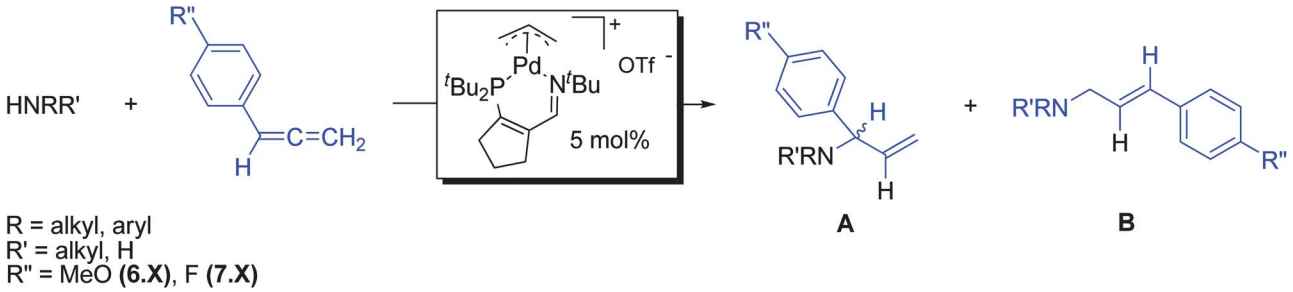
Entry	Amine	Time	Conversion (A : B)
5.1.1	Morpholine	1 min	95 (72 : 28)
5.1.2	Morpholine	4 min	95 (5 : 95)
5.1.3	Morpholine	10 min	95 (0 : 100)
5.1.4	Morpholine	10 min	99 (78 : 22)[a]
5.2	Piperidine	30 min	95 (0 : 100)
5.3	1-Methylpiperazine	30 min	95 (0 : 100)
5.4	Pyrrolidine	30 min	95 (0 : 100)
5.5	1,2,3,4-Tetrahydroisoquinoline	1.5 h	95 (0 : 100)
5.6	3-Methylaniline	20 h	95 (0 : 100)
5.7	4-Methylaniline	20 h	95 (0 : 100)
5.8	3-Methoxyaniline	20 h	95 (0 : 100)
5.9	4-Methoxyaniline	20 h	95 (0 : 100)
5.12	1-(Diphenylmethyl)piperazine	3 h	95 (0 : 100)

[a] Conversion reported at a catalyst loading of 1 mol%.



Scheme 1 Hydroamination of phenylallene with 1-(diphenylmethyl)piperazine yields the pharmaceutical cinnarizine (**5.12B**).

Table 6 The hydroamination of *para*-substituted phenylallenes with anilines and secondary amines



Entry	Amine	Time (h)	Conversion (A : B)
6.1	Morpholine	1	95 (0 : 100)
6.7	4-Methylaniline	20	95 (0 : 100)
7.1.1	Morpholine	0.5	95 (100 : 0)[a]
7.1.2	Morpholine	1.5	95 (0 : 100)
7.2.1	Piperidine	10	84 (70 : 30)[b]
7.2.2	Piperidine	1.5	95 (0 : 100)
7.3.1	1-Methylpiperazine	1.5	95 (40 : 60)
7.3.2	1-Methylpiperazine	2	95 (0 : 100)
7.4.1	Pyrrolidine	10	80 (80 : 20)[b]
7.4.2	Pyrrolidine	1.5	95 (0 : 100)
7.5.1	1,2,3,4-Tetrahydroisoquinoline	0.6	70 (100 : 0)[a]
7.5.2	1,2,3,4-Tetrahydroisoquinoline	1.5	95 (0 : 100)
7.7	4-Methylaniline	20	95 (0 : 100)
7.12	1-(Diphenylmethyl)piperazine	3	95 (0 : 100)

[a] Conversion reported at a catalyst loading of 1 mol%. [b] Conversion reported at a catalyst loading of 2 mol%.

proceeded similarly to those of the unsubstituted phenylallene (Table 6; entries 6.1 and 6.7), and so this allene was not further tested. *p*-Fluorophenylallene underwent hydroamination at a slower rate than phenylallene for all amines investigated, yielding the linear allylamine as the only isolable product at 5 mol% catalyst loading (Table 6). Initial formation of the branched allylamine in the hydroamination of *p*-fluorophenylallene with morpholine followed by its subsequent conversion to the linear product was readily observed *via* NMR spectroscopy (Fig. 2). Isolation of significant yields of the branched isomer was achieved for morpholine, piperidine, pyrrolidine, and 1,2,3,4-tetrahydroisoquinoline (Table 6; entries 7.1.1–7.5.1) through careful control of catalyst loading and reaction time. Despite many attempts, isolation of the branched isomer in the hydroamination of *p*-fluorophenylallene with 1-methylpiperazine proved to be ineffective. The main problem was that virtually no hydroamination activity was observed at 1 mol% and 2 mol% catalyst loading. This may be caused by the presence of the extra lone pair on 1-methylpiperazine, which could bind to the palladium center, thus inhibiting catalysis. As with all other substrates, 4-methylaniline again reacted slowly compared to the secondary amines. Thus, because of the extremely slow rate of hydroamination when anilines are used, only the linear isomer was isolated from the hydroamination of *p*-fluorophenylallene with 4-methylaniline (Table 6; entry 7.7). Finally, we also used 1-(diphenylmethyl)piperazine in the hydroamination of *p*-fluorophenylallene, which produced the monofluorinated derivative of cinnarizine in nearly quantitative conversion (Table 6; entry 7.12). Given the simplicity of the synthesis of this pharmaceutical derivative, it is easy to envision the utility of allene hydroamination in the synthesis of compounds for structure–activity relationship studies.

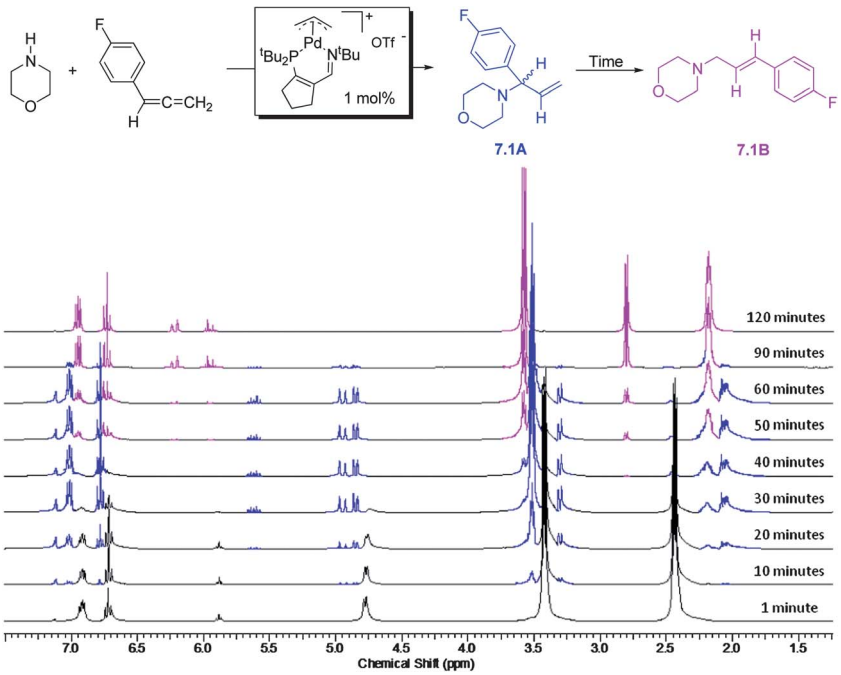


Fig. 2 Hydroamination yields *N*-(1-(4-fluorophenyl)-2-propenyl)-morpholine (**7.1A**), which subsequently isomerizes to *N*-(3-(4-fluorophenyl)-2-propenyl)-morpholine (**7.1B**) at low catalyst loading.

Ultimately, hydroamination of *p*-fluorophenylallene was very successful with selective isolation of either branched or linear allylamine products controlled merely by catalyst loading and reaction time.

Conclusion

The palladium complex **[3IP$^{t\mathrm{Bu}}$Pd(allyl)]OTf** efficiently catalyzed the room-temperature hydroamination of a diverse range of allenes with alkyl amines. This catalytic process is an effective means for the synthesis of branched allylamines in near quantitative conversion for many of the allenes investigated. The branched *N*-allylamines are the kinetic products of these hydroamination reactions and possess terminal vinylic moieties, making them especially useful species for further derivatization. Mono- and 1,1-diphenylallene gave the linear (thermodynamic) products in most cases. Utilizing this selectivity for the linear product, we successfully synthesized the medicinally active compound cinnarizine (Scheme 1), as well as its monofluorinated derivative *N*-(diphenylmethyl)-*N*′-(3-(4-fluorophenyl)-2-propenyl)-piperazine (Table 6; entry 7.12). A number of other piperazine based allylamines were also isolated. Hydroamination alone or coupled with hydrogenation could prove to be atom economical ways of building complex piperazine based therapeutics. The use of *p*-fluorophenylallene was especially interesting since catalyst loading and reaction time could be adjusted to allow for the selective isolation of either the branched or linear hydroamination product in high yield. Both branched and linear allylamines are desirable compounds due to their applicability as building blocks in the synthesis of heterocycles, natural products, and pharmaceuticals. In conclusion, we have shown that **[3IP$^{t\mathrm{Bu}}$Pd(allyl)]OTf** is a remarkably effective catalyst for the selective hydroamination of allenes, providing a high yielding route to many new allylamine products.

General methods and instrumentation

All manipulations involving **[(3IP$^{t\mathrm{Bu}}$)Pd(allyl)]OTf** were performed under an inert N_2 atmosphere using standard glove box and Schlenk techniques. Benzene-d_6 was dried over sodium metal, freeze–pump–thawed three times, and stored over 4 Å molecular sieves. Chloroform-*d* was dried and stored over 4 Å molecular sieves. Styrene, allylbenzene, 1,1-diphenylethylene, 4-methoxystyrene, bromoform, cyclohexylallene and 1,1-dimethylallene were purchased from Sigma-Aldrich and each was used as received. 4-Fluorostyrene was purchased from P212121, LLC and used as received. Amines were purchased from commercial sources and dried over calcium hydride, either neat (liquids) or as solutions in methylene chloride (solid amines). Liquid amines were freeze–pump–thawed three times, and vacuum distilled. Solutions of solid amines in methylene chloride were freeze–pump–thawed three times, filtered and the methylene chloride removed *via* reduced pressure. Non-commercially available allenes were dried as a solution in pentane using CaH_2, filtered and the pentane removed *via* reduced pressure. 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 Inova NMR or a 400 MHz VXRS NMR spectrometer at ambient temperature at 599.9 MHz for ^{1}H NMR and 150.8 MHz for ^{13}C NMR and 399.95 MHz for ^{1}H NMR and 100.56 MHz for ^{13}C NMR, respectively. All spectra were taken using C_6D_6 or $CDCl_3$

as the NMR solvent. ^{1}H NMR shifts are given relative to the residual solvent resonances at 7.16 ppm and 7.26 ppm, respectively, and ^{13}C NMR shifts are given relative to C_6D_6 (128.1 ppm) and $CDCl_3$ (77.16 ppm). Unless otherwise noted, all coupling constants are $^3J_{HH}$. High resolution mass spectrometry, using electrospray ionization, was performed at the University of Illinois Mass Spectrometry Laboratory, Urbana, IL.

Catalyst and allene synthesis

The ligand **3IP^{tBu}** and catalyst **[(3IP^{tBu})Pd(allyl)]OTf** were prepared according to previously published procedures.[49] 2-Chlorocyclopent-1-enecarbaldehyde, the key precursor to **3IP^{tBu}**, was prepared *via* a recently published improved procedure.[51] All non-commercially available allenes were synthesized *via* the ring opening of the corresponding dibromocyclopropane.[57] Formation of the desired products was established *via* NMR spectroscopy for phenylallene,[58] diphenylallene,[58] benzylallene,[58] *p*-methoxyphenylallene[58] and *p*-fluorophenylallene.[59]

General catalytic procedure

All manipulations were performed in a nitrogen filled glove box. To a solution of **[(3IP^{tBu})Pd(allyl)]OTf** (14.8 mg, 0.025 mol, 5 mol %) in benzene-d_6 (0.8 ml), amine (0.5 mmol) was added. Subsequently, the allene (0.5 mmol) was added and the reaction was sealed and allowed to react at 25 °C. Conversion and product ratios were determined *via* ^{1}H NMR spectroscopy after the time noted. Conversion percentage reflects comparison of peak integrations for unreacted allene and the two product regioisomers. Ratios given for the two regioisomeric product allylamines are reported as whole numbers summing to 100%. Both values are subject to the usual experimental error associated with ^{1}H NMR experiments, perhaps as high as ±5%. The products were subsequently purified *via* column chromatography (silica gel; 5 : 1 pentane–ethyl acetate) to remove the catalyst and any unreacted starting materials prior to final ^{1}H and ^{13}C{^{1}H} NMR spectroscopic analysis of the products.

Characterization of hydroamination products

N-(1,1-Dimethyl-2-propenyl)-piperidine (**1.2A**),[47] *N*-(1,1-dimethyl-2-propenyl)-pyrrolidine (**1.4A**),[60] *N*-(1,1-dimethyl-2-propenyl)-1,2,3,4-tetrahydroisoquinoline (**1.5A**),[47] *N*-(1-phenyl-3-buten-2-yl)-morpholine (**3.1A**),[61] *N*-(3,3-diphenylallyl)-piperidine (**4.2B**),[62] *N*-(1-phenyl-2-propenyl)-morpholine (**5.1A**),[63] *N*-(3-phenyl-2-propenyl)-morpholine (**5.1B**),[64] *N*-(3-phenyl-2-propenyl)-piperidine (**5.2B**),[65] *N*-(3-phenyl-2-propenyl)-*N*′-methylpiperazine (**5.3B**),[31] *N*-(3-phenyl-2-propenyl)-pyrrolidine (**5.4B**),[60] *N*-(3-phenyl-2-propenyl)-1,2,3,4-tetrahydroisoquinoline (**5.5B**),[66] *N*-(3-phenyl-2-propenyl)-4-methylaniline (**5.7B**),[67] *N*-(3-phenyl-2-propenyl)-4-methoxyaniline (**5.9B**),[31] *N*-(diphenylmethyl)-*N*′-(3-phenyl-2-propenyl)-piperazine (**5.12B**),[68] and *N*-(1-(4-fluorophenyl)-2-propenyl)-piperidine (**7.2A**)[69] were identified by comparison to published NMR data.

***N*-(1,1-Dimethyl-2-propenyl)-morpholine (1.1A).** ^{1}H NMR (C_6D_6): δ 5.71 (dd, 17.2 Hz, 10.7 Hz, 1H), 4.90 (dd, 10.7 Hz, $^2J_{HH}$ = 2.0 Hz, 1H), 4.85 (dd, 17.2 Hz, $^2J_{HH}$ = 2.0 Hz, 1H), 3.56 (t, 4.7 Hz, 4H), 2.27 (t, 4.7 Hz, 4H), 0.90 (s, 6H); ^{13}C{^{1}H} NMR (C_6D_6): δ 146.2, 112.2, 67.8, 57.8, 46.8, 22.2; $HRMS_{calc}$: 156.1388 for $C_9H_{18}NO$ $[M + H]^+$; $HRMS_{meas}$: 156.1391.

***N*-(1,1-Dimethyl-2-propenyl)-*N*′-methylpiperazine (1.3A).** ^{1}H NMR ($CDCl_3$): δ 5.83 (dd, 16.7 Hz, 9.9 Hz, 1H), 5.02 (d, 9.9 Hz, 1H), 5.01 (d, 16.7 Hz, 1H), 2.57 (br. s, 4H), 2.41 (br. s, 4H), 2.25 (s, 3H), 1.11 (s, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$): δ 146.2, 117.7, 58.2, 56.1, 46.2, 46.1, 22.6; $HRMS_{calc}$: 169.1705 for $C_{10}H_{21}N_2$ $[M + H]^+$; $HRMS_{meas}$: 169.1705.

***N*-(1,1-Dimethyl-2-propenyl)-cyclohexylamine (1.10A).**[70] ^{1}H NMR ($CDCl_3$): δ 5.76 (dd, 17.3 Hz, 10.8 Hz, 1H), 4.97 (d, 17.3 Hz, 1H), 4.94 (d, 10.8 Hz, 1H), 2.33–2.29 (m, 1H), 1.73–1.71 (m, 2H), 1.66–1.63 (m, 2H), 1.54–1.52 (m, 1H), 1.26–1.16 (m, 3H), 1.13 (s, 6H), 1.08–1.02 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$): δ 147.4, 111.4, 54.9, 51.7, 36.9, 28.0, 25.9, 25.0; $HRMS_{calc}$: 168.1752 for $C_{11}H_{22}N$ $[M + H]^+$; $HRMS_{meas}$: 168.1753.

***N*-(1,1-Dimethyl-2-propenyl)-2-octylamine (1.11A).**[70] ^{1}H NMR (C_6D_6): δ 5.79 (dd, 17.6 Hz, 10.8 Hz, 1H), 4.97 (d, 17.6 Hz, 1H), 4.93 (d, 10.8 Hz, 1H), 2.61–2.56 (m, 1H), 1.40–1.21 (m, 10H), 1.11 (s, 3H), 1.10 (s, 3H), 1.01 (d, 6.4 Hz, 3H), 0.91 (t, 6.4 Hz, 3H); ^{13}C{^{1}H} NMR (C_6D_6): δ 148.3, 110.8, 54.6, 47.8, 40.5, 32.4, 30.0, 28.2, 27.9, 26.7, 24.4, 23.1, 14.4; $HRMS_{calc}$: 198.2222 for $C_{13}H_{28}N$ $[M + H]^+$; $HRMS_{meas}$: 198.2220.

***N*-(1-Cyclohexyl-2-propenyl)-morpholine (2.1A).** ^{1}H NMR ($CDCl_3$): δ 5.59 (dt, $^3J_{trans}$ = 17.2 Hz, $^3J_{cis}$ = $^3J_{C–H}$ = 10.0 Hz, 1H), 5.20 (dd, $^3J_{cis}$ = 10.0 Hz, $^2J_{HH}$ = 2.0 Hz, 1H), 4.98 (dd, $^3J_{trans}$ = 17.2 Hz, $^2J_{HH}$ = 2.0 Hz, 1H), 3.71–3.62 (m, 4H), 2.54–2.42 (m, 2H), 2.39–2.30 (m, 3H), 1.84–1.74 (m, 1H), 1.73–1.62 (m, 4H), 1.54–1.45 (m, 1H), 1.25–0.77 (m, 5H); ^{13}C{^{1}H} NMR ($CDCl_3$): δ 136.0, 118.6, 74.5, 67.6, 50.4, 37.6, 30.8, 29.5, 27.0, 26.6, 26.5; $HRMS_{calc}$: 210.1858 for $C_{13}H_{24}NO$ $[M + H]^+$; $HRMS_{meas}$: 210.1853.

***N*-(1-Cyclohexyl-2-propenyl)-piperidine (2.2A).** ^{1}H NMR ($CDCl_3$): δ 5.60 (dt, $^3J_{trans}$ = 17.2 Hz, $^3J_{cis}$ = $^3J_{C–H}$ = 10.0 Hz, 1H), 5.15 (dd, $^3J_{cis}$ = 10.0 Hz, $^2J_{HH}$ = 2.0 Hz, 1H), 4.93 (dd, $^3J_{trans}$ = 17.2 Hz, $^2J_{HH}$ = 2.0 Hz, 1H), 2.50–2.46 (m, 2H), 2.36 (t, 9.2 Hz, 1H), 2.25–2.22 (m, 2H), 1.90 (d, $^3J_{C–H}$ = 10.0 Hz, 1H), 1.77–1.38 (m, 11H), 1.27–1.06 (m, 3H), 0.95–0.74 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$): δ 136.8, 117.6, 74.8, 50.8, 38.2, 30.9, 30.4, 27.1, 26.70, 26.69, 26.65, 25.2; $HRMS_{calc}$: 208.2065 for $C_{14}H_{26}N$ $[M + H]^+$; $HRMS_{meas}$: 208.2060.

***N*-(1-Cyclohexyl-2-propenyl)-*N*′-methylpiperazine (2.3A).** ^{1}H NMR ($CDCl_3$): δ 5.58 (dt, $^3J_{trans}$ = 17.2 Hz, $^3J_{cis}$ = $^3J_{C–H}$ = 10.4 Hz, 1H), 5.15 (dd, $^3J_{cis}$ = 10.4 Hz, $^2J_{HH}$ = 1.6 Hz, 1H), 4.96 (dd, $^3J_{trans}$ = 17.2 Hz, $^2J_{HH}$ = 1.6 Hz, 1H), 2.56–2.27 (m, 9H), 2.24 (s, 3H), 1.79 (d, $^3J_{C–H}$ = 10.4 Hz, 1H), 1.72–0.87 (m, 10H); ^{13}C{^{1}H} NMR ($CDCl_3$): δ 136.4, 118.3, 74.1, 55.8, 46.3, 38.0, 30.9, 29.9, 29.7, 27.1, 26.7, 26.6; $HRMS_{calc}$: 223.2174 for $C_{14}H_{27}N_2$ $[M + H]^+$; $HRMS_{meas}$: 223.2175.

***N*-(1-Cyclohexyl-2-propenyl)-pyrrolidine (2.4A).** ^{1}H NMR ($CDCl_3$): δ 5.68 (dt, $^3J_{trans}$ = 16.8 Hz, $^3J_{cis}$ = $^3J_{C–H}$ = 10.2 Hz, 1H), 5.05 (dd, $^3J_{cis}$ = 10.2 Hz, $^2J_{HH}$ = 2.4 Hz, 1H), 4.99 (dd, $^3J_{trans}$ = 16.8 Hz, $^2J_{HH}$ = 2.4 Hz, 1H), 2.43–2.42 (br. s, 4H), 2.34 (dd, $^3J_{C–H}$ = 10.2 Hz, 5.7 Hz, 1H), 1.80–1.23 (m, 10H), 1.22–0.89 (m, 5H); ^{13}C{^{1}H} NMR ($CDCl_3$): δ 138.0, 117.0, 74.5, 51.8, 40.6, 31.2, 27.7, 27.0, 26.9, 26.8, 23.3; $HRMS_{calc}$: 194.1909 for $C_{13}H_{24}N$ $[M + H]^+$; $HRMS_{meas}$: 194.1910.

***N*-(1-Cyclohexyl-2-propenyl)-1,2,3,4-tetrahydroisoquinoline (2.5A).** ^{1}H NMR ($CDCl_3$): δ 7.12–7.02 (m, 4H), 5.70 (dt, $^3J_{trans} = 17.2$ Hz, $^3J_{cis} = {}^3J_{C-H} = 10.4$ Hz, 1H), 5.26 (dd, $^3J_{cis} = 10.4$ Hz, $^2J_{HH} = 2.4$ Hz, 1H), 5.10 (dd, $^3J_{trans} = 17.2$ Hz, $^2J_{HH} = 2.4$ Hz, 1H), 3.77 (d, 14.7 Hz, 1H), 3.58 (d, 14.7 Hz, 1H), 2.94–2.79 (m, 3H), 2.67–2.54 (m, 2H), 1.95 (d, $^3J_{C-H} = 10.4$ Hz, 1H), 1.78–1.60 (m, 5H), 1.32–0.87 (m, 5H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 136.2, 136.1, 135.2, 128.9, 126.9, 125.9, 125.6, 118.7, 73.7, 53.3, 46.3, 38.4, 30.9, 30.3, 27.1, 26.7; $HRMS_{calc}$: 256.2065 for $C_{18}H_{26}N$ $[M + H]^+$; $HRMS_{meas}$: 256.2058.

***N*-(1-Phenyl-3-buten-2-yl)-piperidine (3.2A).** ^{1}H NMR ($CDCl_3$): δ 7.27–7.23 (m, 2H), 7.18–7.15 (m, 3H), 5.77–5.68 (m, 1H), 5.04 (dd, 10.0 Hz, $^2J_{HH} = 1.6$ Hz, 1H), 4.80 (dd, 17.2 Hz, $^2J_{HH} = 1.6$ Hz, 1H), 3.09–3.02 (m, 2H), 2.71–2.59 (m, 3H), 2.55–2.49 (m, 2H), 1.64–1.56 (m, 4H), 1.48–1.43 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 140.2, 136.8, 129.7, 128.2, 126.0, 117.9, 70.9, 50.9, 38.6, 26.6, 25.0; $HRMS_{calc}$: 216.1752 for $C_{15}H_{22}N$ $[M + H]^+$; $HRMS_{meas}$: 216.1761.

***N*-(1-Phenyl-3-buten-2-yl)-*N*′-methylpiperazine (3.3A).** ^{1}H NMR ($CDCl_3$): δ 7.32–7.22 (m, 2H), 7.18–7.10 (m, 3H), 5.69 (dt, $^3J_{trans} = 16.8$ Hz, $^3J_{cis} = {}^3J_{C-H} = 9.9$ Hz, 1H), 5.04 (d, $^3J_{cis} = 9.9$ Hz, 1H), 4.83 (d, $^3J_{trans} = 16.8$ Hz, 1H), 3.08–3.02 (m, 2H), 2.68–2.45 (m, 9H), 2.29 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 139.6, 136.5, 129.6, 128.1, 125.9, 118.1, 70.1, 55.5, 49.6, 46.1, 38.3; $HRMS_{calc}$: 231.1861 for $C_{15}H_{23}N_2$ $[M + H]^+$; $HRMS_{meas}$: 231.1867.

***N*-(1-Phenyl-3-buten-2-yl)-pyrrolidine (3.4A).** ^{1}H NMR ($CDCl_3$): δ 7.27–7.23 (m, 2H), 7.18–7.12 (m, 3H), 5.73–5.64 (m, 1H), 4.94 (dd, 10.3 Hz, $^2J_{HH} = 1.9$ Hz, 1H), 4.77 (dd, 17.2 Hz, $^2J_{HH} = 1.9$ Hz, 1H), 3.14 (dd, $^2J_{HH} = 13.2$ Hz, 4.0 Hz, 1H), 2.88 (dt, 9.5 Hz, 4.0 Hz, 1H), 2.68–2.59 (m, 5H), 1.84–1.74 (m, 4H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 139.5, 138.9, 129.9, 128.2, 126.1, 117.2, 70.8, 52.1, 41.1, 23.5; $HRMS_{calc}$: 202.1596 for $C_{14}H_{20}N$ $[M + H]^+$; $HRMS_{meas}$: 202.1593.

***N*-(1-Phenyl-3-buten-2-yl)-1,2,3,4-tetrahydroisoquinoline (3.5A).** ^{1}H NMR ($CDCl_3$): δ 7.30–7.12 (m, 8H), 7.05 (d, 7.4 Hz, 1H), 5.81 (ddd, 17.4 Hz, 12.0 Hz, 10.2 Hz, 1H), 5.15 (dd, 10.2 Hz, $^2J_{HH} = 1.7$ Hz, 1H), 4.96 (dd, 17.4 Hz, $^2J_{HH} = 1.7$ Hz, 1H), 3.86 (d, $^2J_{HH} = 10.2$ Hz, 1H), 3.80 (d, $^2J_{HH} = 10.2$ Hz, 1H), 3.33–3.29 (m, 1H), 3.18 (dd, 12.0 Hz, 10.2 Hz, 1H), 3.04–3.00 (m, 1H), 2.94–2.93 (m, 2H), 2.84–2.79 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 139.8, 136.4, 135.5, 134.9, 129.8, 128.9, 128.4, 126.9, 126.24, 126.21, 125.8, 118.6, 69.8, 53.1, 46.9, 38.8, 29.9; $HRMS_{calc}$: 264.1752 for $C_{19}H_{22}N$ $[M + H]^+$; $HRMS_{meas}$: 264.1750.

***N*-(3,3-Diphenylallyl)-morpholine (4.1B).** ^{1}H NMR ($CDCl_3$): δ 7.41–7.33 (m, 4H), 7.31–7.25 (m, 4H), 7.17–7.15 (m, 2H), 6.21 (t, 6.0 Hz, 1H), 3.74–3.72 (m, 4H), 3.08 (d, 6.0 Hz, 2H), 2.45 (br. s, 4H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 130.0, 128.5, 128.4, 127.6, 127.5, 125.6, 67.2, 57.9, 53.9; $HRMS_{calc}$: 280.1701 for $C_{19}H_{22}NO$ $[M + H]^+$; $HRMS_{meas}$: 280.1705.

***N*-(3,3-Diphenylallyl)-*N*′-methylpiperazine (4.3B).** ^{1}H NMR ($CDCl_3$): δ 7.41–7.16 (m, 10H), 6.28 (t, 6.8 Hz, 1H), 3.05 (d, 6.8 Hz, 2H), 2.38 (br. s, 4H), 1.63–1.57 (m, 4H), 1.42 (br. s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 129.9, 128.2, 127.3, 127.2, 127.1, 126.9, 58.3, 54.8, 26.1, 24.4.

***N*-(3,3-Diphenylallyl)-pyrrolidine (4.4B).** ^{1}H NMR ($CDCl_3$): δ 7.39–7.16 (m, 10H), 6.22 (t, 6.8 Hz, 1H), 3.74–3.72 (m, 4H), 3.08 (d, 6.8 Hz, 2H), 2.45 (br. s, 4H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 129.8, 128.3, 128.2, 127.4, 127.3, 125.7, 57.8, 57.1, 53.8; $HRMS_{calc}$: 264.1752 for $C_{19}H_{22}N$ $[M + H]^+$; $HRMS_{meas}$: 264.1761.

***N*-(3,3-Diphenylallyl)-1,2,3,4-tetrahydroisoquinoline (4.5B).** ^{1}H NMR ($CDCl_3$): δ 7.46–7.41 (m, 14H), 6.39 (t, 5.2 Hz, 1H), 3.67 (s, 2H), 3.30 (d, 5.2 Hz, 2H), 2.96 (t, 5.9 Hz, 2H), 2.77 (t, 5.9 Hz, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 130.0, 128.8, 128.7, 128.3, 128.2, 127.4, 127.39, 127.30, 126.7, 126.5, 126.2, 125.7, 65.3, 57.3, 50.9, 29.4; $HRMS_{calc}$: 326.1909 for $C_{24}H_{24}N$ $[M + H]^+$; $HRMS_{meas}$: 326.1906.

***N*-(3-Phenyl-2-propenyl)-3-methylaniline (5.6B).** ^{1}H NMR ($CDCl_3$): δ 7.40 (d, 8.8 Hz, 2H), 7.34 (t, 8.8 Hz, 2H), 7.25 (t, 6.8 Hz, 1H), 7.11 (t, 8.8 Hz, 1H), 6.64 (d, 16.0 Hz, 1H), 6.58 (d, 6.8 Hz, 1H), 6.52 (s, 1H), 6.49 (d, 6.8 Hz, 1H), 6.35 (dt, 16.0 Hz, 5.6 Hz, 1H), 3.94 (dd, 5.6 Hz, 1.7 Hz, 2H), 3.78 (br. s, 1H), 2.32 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 148.3, 139.3, 137.1, 131.7, 129.4, 128.8, 127.7, 127.4, 126.6, 118.8, 114.1, 110.4, 46.5, 21.9; $HRMS_{calc}$: 224.1439 for $C_{16}H_{18}N$ $[M + H]^+$; $HRMS_{meas}$: 224.1447.

***N*-(3-Phenyl-2-propenyl)-3-methoxyaniline (5.8B).** ^{1}H NMR ($CDCl_3$): δ 7.37 (d, 6.8 Hz, 2H), 7.35 (s, 1H), 7.31 (t, 7.9 Hz, 2H), 7.23 (t, 6.8 Hz, 1H), 7.10 (t, 7.9 Hz, 1H), 6.62 (d, 15.6 Hz, 1H), 6.37–6.28 (m, 4H), 3.93 (dd, 6.8 Hz, 1.2 Hz, 2H), 3.77 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 160.9, 136.9, 132.3, 130.3, 128.78, 128.77, 127.8, 126.5, 126.4, 106.4, 103.7, 99.8, 55.3, 46.9; $HRMS_{calc}$: 240.1388 for $C_{16}H_{18}NO$ $[M + H]^+$; $HRMS_{meas}$: 240.1397.

***N*-(3-(4-Methoxyphenyl)-2-propenyl)-morpholine (6.1B).** ^{1}H NMR ($CDCl_3$): δ 7.30 (d, 8.8 Hz, 2H), 6.84 (d, 8.8 Hz, 2H), 6.46 (d, 15.6 Hz, 1H), 6.10 (dt, 15.6 Hz, 7.2 Hz, 1H), 3.79 (s, 3H), 3.74–3.72 (m, 4H), 3.21 (d, 7.2 Hz, 2H), 2.48 (br. s, 4H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 128.2, 128.1, 115.8, 115.6, 93.1, 79.2, 68.1, 31.8, 22.8, 14.3; $HRMS_{calc}$: 234.1494 for $C_{14}H_{20}NO_2$ $[M + H]^+$; $HRMS_{meas}$: 234.1504.

***N*-(3-(4-Methoxyphenyl)-2-propenyl)-4-methylaniline (6.7B).**[70] ^{1}H NMR ($CDCl_3$): δ 7.28 (d, 6.0 Hz, 2H), 6.98 (d, 6.0 Hz, 2H), 6.82 (d, 6.0 Hz, 2H), 6.57 (d, 6.0 Hz, 2H), 6.53 (d, 12.0 Hz, 1H), 6.17 (dt, 12.0 Hz, 6.0 Hz, 1H), 3.85 (d, 6.0 Hz, 2H), 3.77 (s, 3H), 2.23 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 130.9, 129.8, 127.8, 127.5, 126.8, 125.0, 115.3, 114.2, 114.0, 113.3, 55.3, 46.7, 22.5; $HRMS_{calc}$: 254.1545 for $C_{17}H_{20}NO$ $[M + H]^+$; $HRMS_{meas}$: 254.1553.

***N*-(1-(4-Fluorophenyl)-2-propenyl)-morpholine (7.1A).** ^{1}H NMR ($CDCl_3$): δ 7.37–7.33 (m, 2H), 7.05 (t, $^3J_{HH} = {}^3J_{HF} = 8.7$ Hz, 2H), 5.95–5.86 (m, 1H), 5.26 (dd, 16.7 Hz, $^2J_{HH} = 1.7$ Hz, 1H), 5.15 (dd, 10.1 Hz, $^2J_{HH} = 1.7$ Hz, 1H), 3.74–3.72 (m, 4H), 3.65 (d, 9.9 Hz, 1H), 2.51 (br. s, 2H), 2.37–2.33 (m, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 162.1 (d, $^1J_{CF} = 243.8$ Hz), 139.6, 129.5 (d, $^3J_{CF} = 7.8$ Hz), 128.9 (d, $^4J_{CF} = 7.0$ Hz), 116.8, 115.6 (d, $^2J_{CF} = 20.0$ Hz), 74.7, 67.2, 51.9; $HRMS_{calc}$: 222.1294 for $C_{13}H_{17}FNO$ $[M + H]^+$; $HRMS_{meas}$: 222.1298.

***N*-(3-(4-Fluorophenyl)-2-propenyl)-morpholine (7.1B).** ^{1}H NMR ($CDCl_3$): δ 7.31 (dd, 8.8 Hz, $^4J_{HF} = 5.6$ Hz, 2H), 6.99 (t, $^3J_{HH} = {}^3J_{HF} = 8.8$ Hz, 2H), 6.48 (d, 15.9 Hz, 1H), 6.16 (dt, 15.9 Hz, 6.7 Hz, 1H), 3.74–3.72 (m, 4H), 3.13 (d, 6.7 Hz, 2H), 2.49 (br. s, 4H); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 162.5 (d, $^1J_{CF} = 245.5$ Hz), 133.4, 133.2, 128.0 (d, $^3J_{CF} = 7.9$ Hz), 125.9, 115.7 (d, $^2J_{CF} = 21.9$ Hz), 67.2, 61.6, 53.9; $HRMS_{calc}$: 222.1294 for $C_{13}H_{17}FNO$ $[M + H]^+$; $HRMS_{meas}$: 222.1298.

***N*-(3-(4-Fluorophenyl)-2-propenyl)-piperidine (7.2B).** ^{1}H NMR ($CDCl_3$): δ 7.31 (dd, 8.4 Hz, $^4J_{HF} = 6.6$ Hz, 2H), 6.97 (t, $^3J_{HH} = {}^3J_{HF} = 8.4$ Hz, 2H), 6.45 (d, 15.6 Hz, 1H), 6.21 (dt, 15.6 Hz, 6.4

Hz, 1H), 3.10 (d, 6.4 Hz, 2H), 2.40 (br. s, 4H), 1.63–1.57 (m, 4H), 1.43 (br. s, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 162.4 (d, $^{1}J_{CF} = 246.1$ Hz), 133.4 (d, $^{4}J_{CF} = 3.8$ Hz), 131.8, 128.0 (d, $^{3}J_{CF} = 7.9$ Hz), 126.9, 115.6 (d, $^{2}J_{CF} = 21.4$ Hz), 61.9, 54.8, 26.1, 24.5; $HRMS_{calc}$: 220.1502 for $C_{14}H_{19}FN$ $[M + H]^+$; $HRMS_{meas}$: 220.1500.

***N*-(3-(4-Fluorophenyl)-2-propenyl)-*N'*-methylpiperazine (7.3B).** ^{1}H NMR ($CDCl_3$): δ 7.32–7.25 (m, 2H), 7.02–6.70 (m, 2H), 6.46 (d, 15.9 Hz, 1H), 6.16 (dt, 15.9 Hz, 6.9 Hz, 1H), 3.12 (d, 6.9 Hz, 2H), 2.49 (br. s, 8H), 2.27 (s, 3H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 162.4 (d, $^{1}J_{CF} = 246.5$ Hz), 132.2, 129.5 (d, $^{4}J_{CF} = 7.8$ Hz), 128.0 (d, $^{3}J_{CF} = 8.3$ Hz), 126.4 (d, $^{5}J_{CF} = 2.5$ Hz), 115.6 (d, $^{2}J_{CF} = 21.5$ Hz), 61.2, 55.3, 53.3, 46.2; $HRMS_{calc}$: 235.1611 for $C_{14}H_{20}FN_2$ $[M + H]^+$; $HRMS_{meas}$: 235.1609.

***N*-(1-(4-Fluorophenyl)-2-propenyl)-pyrrolidine (7.4A).** ^{1}H NMR ($CDCl_3$): δ 7.30 (dd, 8.3 Hz, $^{4}J_{HF} = 5.9$ Hz, 2H), 6.98 (t, $^{3}J_{HF} = {}^{3}J_{HH} = 8.3$ Hz, 2H), 5.97 (ddd, 17.4 Hz, 10.2 Hz, 8.9 Hz, 1H), 5.17 (dd, 17.4 Hz, $^{2}J_{HH} = 2.0$ Hz, 1H), 4.99 (dd, 10.2 Hz, $^{2}J_{HH} = 2.0$ Hz, 1H), 3.56 (d, 8.9 Hz, 1H), 2.48–2.45 (m, 2H), 2.35–2.32 (m, 2H), 1.77–1.72 (m, 4H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 162.2 (d, $^{1}J_{CF} = 244.8$ Hz), 141.5, 129.2 (d, $^{3}J_{CF} = 7.5$ Hz), 128.3, 115.4 (d, $^{2}J_{CF} = 21.4$ Hz), 115.1, 74.5, 53.2, 23.5; $HRMS_{calc}$: 206.1345 for $C_{13}H_{17}FN$ $[M + H]^+$; $HRMS_{meas}$: 206.1343.

***N*-(3-(4-Fluorophenyl)-2-propenyl)-pyrrolidine (7.4B).** ^{1}H NMR ($CDCl_3$): δ 7.34–7.29 (m, 2H), 6.97–6.92 (m, 2H), 6.48 (d, 15.6 Hz, 1H), 6.24 (dt, 15.6 Hz, 6.4 Hz, 1H), 3.23 (d, 6.4 Hz, 2H), 2.57–2.51 (m, 4H), 1.84–1.78 (m, 4H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 162.4 (d, $^{1}J_{CF} = 246.2$ Hz), 133.5 (d, $^{4}J_{CF} = 3.7$ Hz), 130.8, 128.0 (d, $^{3}J_{CF} = 8.7$ Hz), 127.7, 115.6 (d, $^{2}J_{CF} = 21.4$ Hz), 58.6, 54.3, 23.6; $HRMS_{calc}$: 206.1345 for $C_{13}H_{17}FN$ $[M + H]^+$; $HRMS_{meas}$: 206.1353.

***N*-(1-(4-Fluorophenyl)-2-propenyl)-1,2,3,4-tetrahydroisoquinoline (7.5A).** ^{1}H NMR ($CDCl_3$): δ 7.33 (dd, $^{3}J_{HF} = 11.9$ Hz, 7.9 Hz, 2H), 7.13–7.03 (m, 3H), 6.98 (t, $^{3}J_{HH} = {}^{4}J_{HF} = 7.9$ Hz, 2H), 6.92 (d, 7.9 Hz, 1H), 6.10–5.98 (m, 1H), 5.23 (d, 15.9 Hz, 1H), 5.10 (d, 11.9 Hz, 1H), 3.81 (d, 7.9 Hz, 1H), 3.69 (d, $^{2}J_{HH} = 14.7$ Hz, 1H), 3.49 (d, $^{2}J_{HH} = 14.7$ Hz, 1H), 2.84–2.78 (m, 2H), 2.71–2.61 (m, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 162.1 (d, $^{1}J_{CF} = 241.2$ Hz), 139.9, 138.0 (d, $^{4}J_{CF} = 3.3$ Hz), 135.1, 134.7, 129.4 (d, $^{3}J_{CF} = 7.8$ Hz), 128.8, 126.6 (d, $^{2}J_{CF} = 65.5$ Hz), 125.8, 116.6, 115.6, 115.4, 73.7, 54.5, 48.3, 29.3; $HRMS_{calc}$: 268.1502 for $C_{18}H_{19}FN$ $[M + H]^+$; $HRMS_{meas}$: 268.1500.

***N*-(3-(4-Fluorophenyl)-2-propenyl)-1,2,3,4-tetrahydroisoquinoline (7.5B).** ^{1}H NMR ($CDCl_3$): δ 7.40–7.31 (m, 2H), 7.29–7.03 (m, 6H), 6.58 (d, 15.6 Hz, 1H), 6.31 (dt, 15.6 Hz, 6.4 Hz, 1H), 3.71 (s, 2H), 3.35 (d, 6.4 Hz, 2H), 2.95 (t, 5.6 Hz, 2H), 2.83 (t, 5.6 Hz, 2H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 162.5 (d, $^{1}J_{CF} = 245.5$ Hz), 134.7, 134.4, 133.3 (d, $^{4}J_{CF} = 3.7$ Hz), 132.1, 128.9, 128.1 (d, $^{3}J_{CF} = 8.2$ Hz), 126.9, 126.7 (d, $^{5}J_{CF} = 2.5$ Hz), 126.5, 125.9, 115.7 (d, $^{2}J_{CF} = 21.4$ Hz), 60.9, 56.3, 50.9, 29.3; $HRMS_{calc}$: 268.1502 for $C_{18}H_{19}FN$ $[M + H]^+$; $HRMS_{meas}$: 268.1499.

***N*-(3-(4-Fluorophenyl)-2-propenyl)-4-methylaniline (7.7B).**[70] ^{1}H NMR ($CDCl_3$): δ 7.38–7.34 (m, 2H), 7.10–7.01 (m, 4H), 6.64 (d, 8.4 Hz, 2H), 6.60 (d, 15.6 Hz, 1H), 6.27 (dt, 15.6 Hz, 6.0 Hz, 1H), 3.93 (d, 6.0 Hz, 2H), 2.90 (s, 3H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 161.3 (d, $^{1}J_{CF} = 255.2$ Hz), 145.9, 130.2, 129.9 (d, $^{3}J_{CF} = 9.1$ Hz), 129.8, 127.8, 127.0 (d, $^{4}J_{CF} = 1.5$ Hz), 126.9, 115.4 (d, $^{2}J_{CF} = 24.0$ Hz), 113.3, 46.5, 20.5; $HRMS_{calc}$: 242.1345 for $C_{16}H_{17}FN$ $[M + H]^+$; $HRMS_{meas}$: 242.1356.

***N*-(Diphenylmethyl)-*N'*-(3-(4-fluorophenyl)-2-propenyl)-piperazine (7.12B).** ^{1}H NMR ($CDCl_3$): δ 7.40 (d, 7.9 Hz, 4H), 7.32–7.28 (m, 2H), 7.26 (t, 7.9 Hz, 4H), 7.16 (t, 7.9 Hz, 2H), 6.99–6.96 (m, 2H), 6.45 (d, 15.6 Hz, 1H), 6.17 (dt, 15.6 Hz, 6.6 Hz, 1H), 4.24 (s, 1H), 3.14 (d, 6.6 Hz, 2H), 2.52 (br. s, 8H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 162.4 (d, $^{1}J_{CF} = 246.6$ Hz), 142.9, 133.3 (d, $^{4}J_{CF} = 3.8$ Hz), 132.0, 128.6, 128.2, 128.0 (d, $^{3}J_{CF} = 8.1$ Hz), 127.1, 126.5, 115.6 (d, $^{2}J_{CF} = 21.6$ Hz), 76.4, 61.2, 53.7, 52.2; $HRMS_{calc}$: 387.2237 for $C_{26}H_{28}FN_2$ $[M + H]^+$; $HRMS_{meas}$: 387.2232.

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