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An Efficient and Convenient Palladium Catalyst System for the Synthesis of Amines from Allylic Alcohols

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A novel catalyst system for efficient amination of allylic alcohols with aryl and alkyl amines is presented. By applying a convenient combination consisting of $Pd(OAc)_2$/1,10-phenanthroline, a variety of allylic alcohols reacted smoothly to give the corresponding secondary and tertiary amines in good to excellent yields with high regioselectivity. The usefulness of our protocol is demonstrated in the one-step synthesis of the antifungal drug naftifine and the calcium channel blocker flunarizine.

Introduction

Amines and their derivatives are widely used for the synthesis of a variety of pharmaceuticals, dyes, agrochemicals, and polymers.[1] A variety of them have significant importance as fundamental building blocks for the bulk- and fine-chemical industries, as well as for the synthesis of numerous bioactive molecules such as alkaloids, amino acids, and nucleotides.[2] Among the different types of amines allylic amines also represent a common structural motif present in various biologically active compounds. Selected examples include the antifungal drug naftifine[3a,b] and the calcium channel blocker flunarizine.[3c] Furthermore, allylic amines are of interest as advanced intermediates for ring-closing metathesis,[4a] asymmetric isomerization,[4b] and the total synthesis of several natural products.[2] Therefore, the development of novel and improved catalysts for the synthesis of allyl amines is of continuing interest.

Transition-metal-catalyzed substitution reactions of activated allylic alcohol derivatives with nitrogen nucleophiles have become the most attractive synthetic tool for their synthesis.[5] These reactions are known to proceed through a π-allyl metal intermediate generated by the oxidative addition of the allylic substrate to a low-valence metal center, followed by addition of the nitrogen nucleophile to form the new C–N bond in a regio-, stereo-, and enantioselective manner. The pioneering work in this area was reported by Tsuji and Trost.[5a,b] Thereafter, palladium-catalyzed allylation reactions have become one of the most powerful methods for the construction of allylic C–C and carbon–heteroatom (N, O, S) bonds.

A considerable disadvantage of most reported metal-catalyzed allylic substitution reactions is the required preactivation of the hydroxyl group[6] because of its poor leaving ability. Hence, in general, these reactions are performed with allylic halides, acetates, carbonates, phosphonates, and related compounds with better leaving groups. In contrast, the direct use of readily available allylic alcohols would represent a cost-effective, salt-free, atom-economic, more benign C–N bond-forming process.[7] In such a transformation water is formed as the only byproduct, whereas conventional allylic esters and halides produce stoichiometric amounts of undesired salt waste. Advantageously, the use of allylic alcohols as substrates might also avoid additional activation and (de)protection steps.

In the last two decades, significant progress has been achieved in the direct amination of alcohols mainly by using ruthenium- and iridium-based catalysts. Applying these catalysts in so-called "borrowing hydrogen"[8] or "hydrogen autotransfer" reactions,[9] the alcohol is dehydrogenated in situ followed by subsequent formation of the respective imine. Final re-hydrogenation leads to the desired amine. Alternatively, allylic alcohols can be activated by palladium and related catalysts, which often requires the addition of catalytic or stoichiometric amounts of additives, such as As_2O_3,[10] B_2O_3,[11] BPh_3,[12] BEt_3,[13] $SnCl_2$,[14] CO_2,[15] $Ti(iOPr)_4$,[16] $Nb(OEt)_5$,[17] and carboxylic acids,[6] to activate the C–O bond and promote the leaving ability of the hydroxyl group.

Notably, in the last decade, several reports showed that palladium- and platinum-catalyzed reactions of allylic alcohols were possible without the use of activators. In this respect, the recent work of Ghosh and Sarkar[18a] as well as Mashima and co-workers[18b,c] is of special interest. Ozawa and co-workers reported an atom-economic synthesis of allyl amines using π-allylpalladium complexes with the diphosphinidenecyclobutene ligand (DPCB).[19] Particularly, le Floch and co-workers studied the reactivity of a range of cationic palladium complexes in combination with variety mono- or bidentate phosphine ligands for the amination of allyl alcohols.[20] Moreover, the research groups of Ikariya,[21] Shinokubo and Oshima,[22] and Berit[23] also considerably contributed to the development of this methodology. Nevertheless, limited substrate scope and

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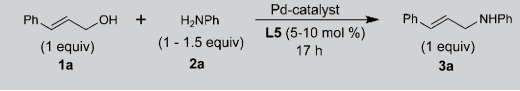
selectivity in terms of mono- and diallylations are limitations of most protocols. So far, no systematic studies have been performed for aminations of aliphatic allyl alcohols and primary aliphatic amines showed only poor reactivity. Importantly, in all reported reactions the use of fancy phosphorus ligands was necessary to achieve efficient allylic aminations.[24]

To the best of our knowledge, to date, there are no reports for catalytic aminations of readily available allylic alcohols in the presence of nitrogen donor ligands. Herein, we show that the combination of $Pd(OAc)_2$ with 1,10-phenanthroline (**L5**) allows for efficient conversion of a variety of aromatic and aliphatic allylic alcohols.

Results and Discussion

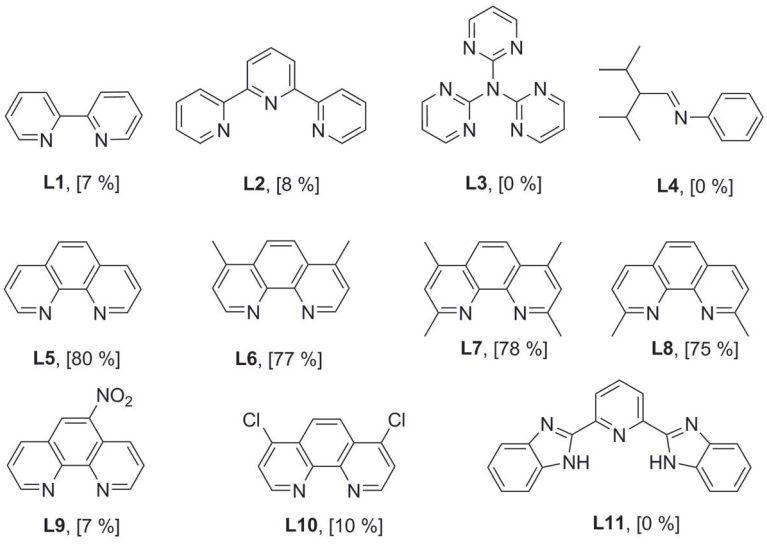
Based on our work on the borrowing-hydrogen methodology using alcohols and amines,[25] we became interested in the reaction of allylic alcohols with primary and secondary amines. In our initial investigations, we chose cinnamyl alcohol (**1a**) and aniline (**2a**) as model substrates. Different active catalysts were generated in situ in the presence of 5 mol% $Pd(OAc)_2$ and 10 mol% of **L1**–**L11** in toluene at 100 °C (Scheme 1). Good isolated yields of the desired product **3a** (75–80%) were obtained by using **L5** and its derivatives (**L6**–**L8**). Other mono-, bi-, tri-, and multidentate nitrogen ligands were inefficient and showed poor or no reactivity towards the amination reaction.

Table 1. Palladium-catalyzed amination of cinnamyl alcohol (**1a**) with aniline (**2a**).[a]



Entry	Catalyst	Amount [mol%]	Solvent	T [°C]	Ratio 1a/2a	Yield[b] [%]
1	$Pd(OAc)_2$	5	toluene	100	1:1.5	80
2	$[Pd(acac)_2]$	5	toluene	100	1:1.5	21
3	$[Pd(dba)_2]$	5	toluene	100	1:1.5	20
4	$Pd(OCOCF_3)_2$	5	toluene	100	1:1.5	0
5	$PdCl_2$	5	toluene	100	1:1.5	0
6	$Pd(OAc)_2$	5	dioxane	100	1:1.5	60
7	$Pd(OAc)_2$	5	*n*-octane	100	1:1.5	65
8	$Pd(OAc)_2$	5	*n*-heptane	100	1:1.5	55
9	$Pd(OAc)_2$	5	*t*-amyl alcohol	100	1:1.5	25
10	$Pd(OAc)_2$	1	toluene	100	1:1.5	62
11	$Pd(OAc)_2$	2.5	toluene	100	1:1.5	85
12	$Pd(OAc)_2$	2.5	toluene	100	1:1.5	69[c]
13	$Pd(OAc)_2$	2.5	toluene	100	1:1.2	87
14	$Pd(OAc)_2$	2.5	toluene	100	1:1.1	89
15	$Pd(OAc)_2$	2.5	toluene	80	1:1.1	50
16	$Pd(OAc)_2$	2.5	toluene	60	1:1.1	35
17	$Pd(OAc)_2$	2.5	toluene	25	1:1.1	15
18	no catalyst	–	toluene	100	1:1.1	0
19	$Pd(OAc)_2$	2.5	toluene	100	1:1.1	10[d]

[a] Reaction conditions: **1a** (1 mmol), **2a** (1–1.5 mmol), catalyst (1–5 mol%), **L5** (5–10 mol%), solvent (3 mL), 17 h. acac = acetylacetonate, dba = dibenzylideneacetone. [b] Isolated yields. [c] 20 mol% of **L5** used. [d] No ligand used.



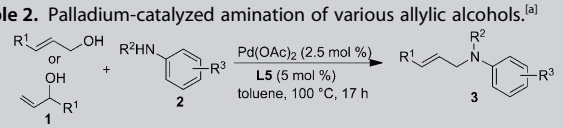
Scheme 1. Ligand screening for the palladium-catalyzed amination of cinnamyl alcohol (**1a**) and aniline (**2a**) (isolated yields are presented in parentheses).

Due to its availability and best reactivity, we chose **L5** as the ligand for further optimization studies (Table 1). A survey of different Pd precursors under similar reaction conditions showed that $Pd(OAc)_2$ was optimal, whereas $PdCl_2$ and $Pd(OCOCF_3)_2$ gave no product **3a** at all (Table 1, entries 1, 4, and 5). Reactions in the presence of $[Pd(acac)_2]$ and $[Pd(dba)_2]$ proceeded with low product yield (Table 1, entries 2 and 3). Changing the solvent from toluene to 1,4-dioxane, linear alkanes, or *t*-amyl alcohol, the product yield decreased to 25–65% (Table 1, entries 6–9). Testing different Pd concentrations revealed that a catalyst concentration of 2.5 mol% of $Pd(OAc)_2$ was optimal and afforded 85% isolated yield of **3a** (Table 1, entries 10 and 11). Interestingly, a large excess of ligand is not necessary for successful conversion and a Pd/**L5** ratio of 1:2 was optimal to achieve an excellent yield of *N*-cinnamylaniline (**3a**; Table 1, entries 11 and 12).

With respect to atom economy, it is interesting to note that 1 equivalent of **1a** reacted well with 1.1 equivalents of **2a** to afford **3a** in 89% yield (Table 1, entries 13 and 14). It is possible to run the amination process even at room temperature, albeit with lower yield of product (Table 1, entry 17). As expected, we did not observe any product in the absence of palladium (Table 1, entry 18). In all reactions in which we observed lower yields of **3a**, unreacted **1a** and **2a** could be recovered from the reaction mixture. In all these cases we also recovered some amount of the corresponding imine.

Encouraged by the results obtained in the model reaction, we were interested to check the compatibility of our protocol with a range of aromatic and aliphatic allylic alcohols. The results are summarized in Table 2. We also studied the regioselectivity of a variety of allylic alcohols with phenyl or methyl substituents at the α-, β-, or γ-positions. In all cases, only the linear substituted amines were obtained and we did not ob-

Table 2. Palladium-catalyzed amination of various allylic alcohols.[a]



Entry	Allylic alcohol	Amine	Product	Yield[b] [%]
1	**1a**	**2a**	**3a**	89
2	**1a**	**2b**	**3b**	80
3	**1a**	**2c**	**3c**	76
4	**1a**	**2d**	**3d**	79
5	**1a**	**2e**	**3e**	73
6	**1b**	**2b**	**3b**	77
7[c]	**1c**	**2e**	**3f**	50
8[c]	**1d**	**2e**	**3g**	60
9[c]	**1e**	**2e**[d]	**3h**	59[e]

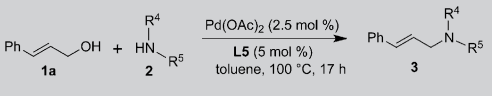
[a] Reaction conditions: allylic alcohol (1 mmol), amine (1.1 mmol), catalyst (2.5 mol%), **L5** (5 mol%), solvent (3 mL), 17 h. [b] Isolated yields. [c] Alcohols (2 mmol), 40 h. [d] *E*/*Z* mixture of **1e** (*E*/*Z* = 96:4) was used. [e] **3h** was obtained as an *E*/*Z* mixture (97:3).

serve either branched isomers or bis-allylation products of the corresponding amines.

The reaction of **1a** and α-phenyl-substituted allylic alcohol (**1b**) with electron-donating *p*-anisidine (**2b**) gave *N*-(4-methoxy)cinnamylaniline (**3b**) as the linear product and no branched isomer or diallylation product was detected by GC–MS analysis (Table 2, entries 2 and 6). Apparently, both reactions proceed via a common π-allylpalladium intermediate. Furthermore, reaction of **1a** with the electron-withdrawing aniline **2c** gave the monoallylation product in 76% isolated yield (Table 2, entry 3). Reactions of **1a** with *o*-toluidene (**2d**) or the secondary amine **2e** run with comparable efficiency, producing only linear *trans*-cinnamyl derivatives (Table 2, entries 4 and 5). Further reaction of the allylic alcohol **1c** with the secondary amine **2e** afforded the tertiary amine **3f** in 50% isolated yield (Table 2, entry 7). The β- or γ-methyl-substituted allylic alcohols also regioselectively produced the corresponding allylic amines in moderate to good yields (Table 2, entries 8 and 9).

Next, we studied the reaction of allylic alcohols with more challenging alkyl amines. Especially for primary amines, the resulting secondary products are more prone to undergo further allylation; hence, it is more difficult to achieve regio- and stereoselective monoallylation. To our delight, when applying the combination of $Pd(OAc)_2$ with **L5** under the previously optimized conditions, various primary aliphatic amines reacted well with **1a**. As shown in Table 3, we did not observe either any undesired higher alkylated products or any branched isomers of the corresponding aliphatic amines in any of these reactions. For example, the reaction of **1a** with diphenylmethanamine (**2f**), 1-naphthylmethylamine (**2g**), and 1-phenylethylamine (**2h**) proceeded in 64–70% yield of the monoallylation products (Table 3, entries 1–3). Monoallylation of cyclohexylamine (**2i**) and cyclooctylamine (**2j**) gave 79% and 82% isolated yields of **3l** and **3m**, respectively (Table 3, entries 4 and 5). Further reactions of **1a** with 1-octylamine (**2k**) and 2-octylamine (**2l**) delivered the corresponding monoallylated products with similar efficiency (Table 3, entries 6 and 7). As expect-

Table 3. Palladium-catalyzed amination of **1a** with various aliphatic amines.[a]

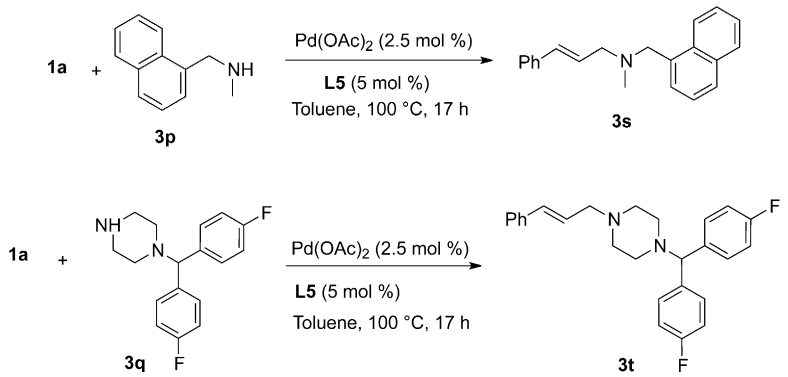


Entry	Aliphatic amine	Product	Yield[b] [%]
1	**2f**	**3i**	70
2	**2g**	**3j**	64
3	**2h**	**3k**	65
4	**2i**	**3l**	79
5	**2j**	**3m**	82
6	**2k**	**3n**	65
7	**2l**	**3o**	70
8	**2m**	**3p**	84
9[c]	**2n**	**3q**	87
10[c]	**2o**	**3r**	81

[a] Reaction conditions: **1a** (1 mmol), amine (1.1 mmol), catalyst (2.5 mol%), **L5** (5 mol%), solvent (3 mL), 17 h. [b] Isolated yields. [c] 1.5 equiv amine used.

ed, the reactions of **1a** with secondary amines gave excellent yields of the corresponding tertiary amine derivatives (Table 3, entries 8–10). Again, in some of the reactions with lower product yields, we recovered allylic alcohols as well as amine substrates.

Finally, we demonstrated the practical utility of our catalytic amination protocol in the one-step synthesis of the antifungal drug naftifine (**3s**) and the calcium channel blocker flunarizine (**3t**; Scheme 2). So far, these bioactive products have been synthesized by multiple synthetic steps[3b] or using harsh reaction conditions. In the presence of $Pd(OAc)_2$ (2.5 mol%) and **L5** (5 mol%), the desired products were obtained in 83% and 70% isolated yield, respectively.



Scheme 2. Synthesis of the antifungal drug naftifine (**3s**) and calcium channel blocker flunarizine (**3t**).

Conclusions

We have shown that the combination of $Pd(OAc)_2$ and **L5** efficiently catalyzes the direct amination of allylic alcohols. This catalytic protocol proceeds straightforward with high atom economy and does not need any additive for the activation of the alcohol. A variety of aryl and alkyl amines reacted highly selectively with allylic alcohols with phenyl or alkyl substituents at the α-, β-, or γ-positions. No branched isomers or bis-allylation products of the corresponding amines were obtained. The synthetic utility of our catalytic method was successfully applied in the one-step synthesis of the biologically active molecules naftifine and flunarizine.

Experimental Section

General: Unless otherwise stated, commercial reagents were used without further purification. Organic solvents were distilled and dried over molecular sieves. All reactions were performed under an argon atmosphere by using an oven-dried Schlenk tube. All products were purified by silica-gel column chromatography and characterized by using ^1H and ^{13}C NMR spectroscopy, HRMS, and FTIR spectroscopy. NMR spectra were recorded by using a Bruker AV 300 spectrometer. All chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz. All chemical shifts are related to solvent peaks (chloroform: $\delta = 7.26$ (^1H) and 77.00 ppm (^{13}C)). All measurements were performed at room temperature unless otherwise stated. MS were recorded by using a Finnigan MAT 95-XP (Thermo Electron, Agilent) instrument. IR spectra were recorded by using an FTIR Nicolet 6700 (Thermo Electron) instrument.

General procedure for the amination of allylic alcohols: Under an argon atmosphere, an oven-dried Schlenk tube was charged with allylic alcohol (1 mmol) and amine (1.1 mmol) followed by $Pd(OAc)_2$ (2.5 mol%, 5.6 mg) and **L5** (5 mol%, 9.0 mg). Toluene (3 mL) and a magnetic stirrer bar were added and the reaction mixture was stirred at 100 °C for 17 h. The reaction mixture was then cooled to RT, diluted with ethyl acetate (10 mL), and dried over anhydrous Na_2SO_4. The filtrate was concentrated under reduced pressure and the residue was purified by silica-gel column chromatography using ethyl acetate/hexane as the eluent to afford the corresponding allyl amine.

N-Cinnamylaniline (**3a**):[18c] Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.05–7.29$ (m, 7H), 6.48–6.66 (m, 4H), 6.19–6.28 (m, 1H), 3.83 (dd, $J = 1.5$, 6.06 Hz, 2H), 3.48 ppm (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 148.0$, 136.9, 131.6, 129.3, 128.6, 127.6, 127.0, 126.4, 117.7, 113.1, 46.4 ppm; HRMS (ESI-TOF): m/z calcd for $C_{15}H_{15}N$: 210.1283 $[M+H]^+$; found: 210.1280; IR (ATR): $\tilde{\nu} = 3411$, 3085, 3055, 3020, 2910, 2827, 2735, 1602, 1505, 1413, 1298, 1217, 1170, 976 cm^{-1}.

N-Cinnamyl-4-methoxyaniline (**3b**):[18c] White solid; m.p. 66–68 °C; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.15–7.31$ (m, 6H), 6.72 (d, $J = 9.0$ Hz, 2H), 6.51–6.60 (m, 3H), 6.22–6.31 (m, 1H), 3.82 (dd, $J = 1.4$, 5.8 Hz, 2H), 3.67 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 152.4$, 142.1, 136.9, 131.5, 128.6, 127.5, 127.2, 126.3, 114.9, 114.6, 55.9, 47.4 ppm; HRMS (ESI-TOF): m/z calcd for $C_{16}H_{17}NO$: 240.1388 $[M+H]^+$; found: 240.1386; IR (ATR): $\tilde{\nu} = 3387$, 3026, 2831, 1625, 1511, 1463, 1296, 1235, 1179, 1118, 1036, 967 cm^{-1}.

N-Cinnamyl-4-trifluoromethylaniline (**3c**):[18c] White powder; m.p. 72–74 °C; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.16–7.35$ (m, 7H), 6.51–6.59 (m, 3H), 6.16–6.25 (m, 1H), 4.15 (br s, 1H), 4.03 ppm (d, $J = 6.0$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 150.4$, 136.5, 132.0, 128.6, 127.7, 126.6, 126.3, 125.9, 112.1, 45.6 ppm; HRMS (ESI-TOF): m/z calcd for $C_{16}H_{14}NF_3$: 278.1157 $[M+H]^+$; found: 278.1151; IR (ATR): $\tilde{\nu} = 3421$, 3029, 2845, 1889, 1615, 1528, 1479, 1449, 1413, 1319, 1187, 1099, 1059, 965, 825 cm^{-1}.

N-Cinnamyl-2-methylaniline (**3d**):[18a] Light-yellow oil; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 6.99–7.30$ (m, 8H), 6.54–6.66 (m, 3H), 6.25–6.35 (m, 1H), 3.90 (dd, $J = 1.5$, 5.9 Hz, 2H), 2.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 145.9$, 136.8, 131.6, 130.1, 128.6, 127.6, 127.2, 127.1, 126.3, 122.1, 117.2, 110.1, 46.2, 17.6; HRMS (ESI-TOF): m/z calcd for $C_{15}H_{17}N$: 224.1439 $[M+H]^+$; found: 224.1433; IR (ATR): $\tilde{\nu} =$ 3408, 3058, 3025, 2891, 1677, 1598, 1505, 1447, 1354, 1209, 1118, 1037, 964, 748, 732, 691 cm^{-1}.

N-Cinnamyl-*N*-methylaniline (**3e**):[18c] Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.13–7.29$ (m, 7H), 6.62–6.67 (m, 3H), 6.43 (d, $J = 16.2$ Hz, 1H), 6.12–6.21 (m, 1H), 3.99 (d, $J = 6.3$ Hz, 2H), 2.89 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 149.5$, 136.9, 131.2, 129.2, 128.5, 127.4, 126.3, 125.7, 116.6, 112.6, 54.9, 38.0 ppm; HRMS (ESI-TOF): m/z calcd for $C_{15}H_{17}N$: 224.1439 $[M+H]^+$; found:

224.1436; IR (ATR): $\tilde{\nu}$ = 3024, 2923, 2851, 1676, 1626, 1605, 1586, 1512, 1448, 1316, 1255, 1127, 1051, 967, 746, 691 cm^{-1}.

N-Allyl-*N*-methylaniline (**3f**): Light-yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.09–7.18 (m, 2H), 6.52–6.66 (m, 3H), 5.70–5.83 (m, 1H), 5.04–5.12 (m, 2H), 3.84 (d, J = 5.22 Hz, 2H), 2.86 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.6, 133.8, 129.2, 116.3, 116.1, 112.5, 55.4, 38.1 ppm; HRMS (ESI-TOF): *m/z* calcd for $C_{10}H_{13}N$: 148.1126 $[M+H]^+$; found: 148.1118; IR (ATR): $\tilde{\nu}$ = 3060, 2925, 2813, 1642, 1505, 1368, 1249, 1210, 1156, 1033, 992, 918, 747, 691 cm^{-1}.

N-(2-Methylallyl)-*N*-methylaniline (**3g**): Light-yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.10–7.19 (m, 2H), 6.58–6.62 (m, 3H), 4.71–4.78 (m, 2H), 3.72 (s, 2H), 2.53 (s, 3H), 1.65 ppm (d, J = 0.72 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.6, 141.4, 129.0, 116.0, 111.9, 110.6, 53.6, 38.3, 20.1 ppm; HRMS (ESI-TOF): *m/z* calcd for $C_{11}H_{15}N$: 162.1277 $[M+H]^+$; found: 162.1274; IR (ATR): $\tilde{\nu}$ = 3004, 2937, 2843, 1670, 1587, 1513, 1444, 1373, 1341, 1323, 1214, 1120, 985, 960, 742, 694 cm^{-1}.

N-(But-2-enyl)-*N*-methylaniline (**3h**): Light-yellow oil; ^1H NMR (300 MHz, $CDCl_3$) for (*E*)-**3h**: δ = 7.09–7.17 (m, 2H), 6.53–6.68 (m, 3H), 5.35–5.54 (m, 2H), 3.76 (d, J = 1.2, 5.28 Hz, 2H), 2.82 (s, 3H), 1.60 ppm (dd, J = 1.3, 5.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.7, 129.3, 127.5, 126.5, 116.3, 112.6, 54.5, 37.9, 17.8 ppm; HRMS (ESI-TOF): *m/z* calcd for $C_{11}H_{15}N$: 162.1277 $[M+H]^+$; found: 162.1274; IR (ATR): $\tilde{\nu}$ = 3024, 2917, 2813, 1677, 1597, 1503, 1449, 1371, 1349, 1320, 1204, 1117, 990, 966, 747, 691 cm^{-1}.

N-Cinnamyl-1,1-diphenylmethylamine (**3i**): Light-yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.10–7.35 (m, 15H), 6.41 (d, J = 15.99 Hz, 1H), 6.20–6.29 (m, 1H), 4.84 (s, 1H), 3.29 (d, J = 6.09 Hz, 2H), 1.68 ppm (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.9, 137.2, 131.3, 128.5, 128.4, 127.7, 127.4, 127.1, 126.3, 66.5, 49.9 ppm; HRMS (ESI-TOF): *m/z* calcd for $C_{22}H_{21}N$: 300.1746 $[M+H]^+$; found: 300.1746; IR (ATR): $\tilde{\nu}$ = 3421, 3058, 3023, 2822, 1948, 1597, 1491, 1448, 1301, 1277, 1115, 1072, 964, 741, 691 cm^{-1}.

N-Cinnamyl-naphthalen-1-ylmethanamine (**3j**): Light-yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.04 (d, J = 8.12 Hz, 1H), 7.67–7.79 (m, 2H), 7.14–7.45 (m, 9H), 6.49 (d, J = 15.12 Hz, 1H), 6.21–6.32 (m, 1H), 4.18 (s, 2H), 3.44 (d, J = 6.48 Hz, 2H), 1.53 ppm (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.1, 135.8, 133.9, 131.8, 131.6, 128.8, 128.6, 128.5, 127.8, 127.4, 126.3, 126.2, 125.7, 125.4, 123.7, 51.8, 50.9 ppm; HRMS (ESI-TOF): *m/z* calcd for $C_{20}H_{19}N$: 274.1596 $[M+H]^+$; found: 274.1594; IR (ATR): $\tilde{\nu}$ = 3411, 3024, 2813, 1648, 1596, 1493, 1446, 1355, 1261, 1211, 1114, 1070, 964, 790, 729, 690 cm^{-1}.

N-Cinnamyl-1-phenylethylamine (**3k**):[18c] Pale-yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.13–7.29 (m, 10H), 6.38 (d, J = 15.72 Hz, 1H), 6.15–6.24 (m, 1H), 3.79 (q, J = 5.97 Hz, 1H), 3.27 (d, J = 6.2 Hz, 2H), 1.71 (br s, 1H), 1.32 ppm (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.3, 137.1, 131.3, 128.5, 128.4, 127.3, 127.0, 126.6, 126.2, 57.6, 49.8, 24.3 ppm; HRMS (ESI-TOF): *m/z* calcd for $C_{17}H_{19}N$: 238.1596 $[M+H]^+$; found: 238.1592; IR (ATR): $\tilde{\nu}$ = 3415, 3059, 3025, 2964, 2924, 1681, 1599, 1493, 1449, 1368, 1305, 1205, 1118, 1071, 1027, 966, 761, 745, 699 cm^{-1}.

N-Cinnamylcyclohexaneamine (**3l**):[18c] Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.13–7.30 (m, 5H), 6.43 (d, J = 16.05 Hz, 1H), 6.18–6.28 (m, 1H), 3.36 (d, J = 6.42 Hz, 2H), 2.39–2.46 (m, 1H), 1.82–1.86 (m, 2H), 1.53–1.69 (m, 3H), 0.95–1.25 ppm (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.2, 130.9, 129.0, 128.5, 127.3, 126.2, 56.2, 49.0, 33.6, 26.2, 25.1 ppm; HRMS (ESI-TOF): *m/z* calcd for $C_{15}H_{21}N$: 216.1746 $[M+H]^+$; found: 216.1745; IR (ATR): $\tilde{\nu}$ = 3411, 3025, 2923, 2851, 1677, 1598, 1494, 1447, 1374, 1259, 1124, 1070, 963, 908, 889, 729, 690 cm^{-1}.

N-Cinnamylcyclooctylamine (**3m**): Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.13–7.30 (m, 5H), 6.43 (d, J = 15.87 Hz, 1H), 6.17–6.27 (m, 1H), 3.32 (d, J = 6.78 Hz, 2H), 2.64–2.71 (m, 1H), 1.38–1.75 ppm (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.2, 131.2, 128.7, 128.5, 127.3, 126.3, 57.2, 49.5, 32.5, 27.3, 25.8, 24.1 ppm; HRMS (ESI-TOF): *m/z* calcd for $C_{17}H_{25}N$: 244.2065 $[M+H]^+$; found: 244.2064; IR (ATR): $\tilde{\nu}$ = 3410, 3025, 2916, 2849, 1674, 1598, 1494, 1446, 1360, 1101, 1028, 964, 805, 731, 690 cm^{-1}.

N-Cinnamyloctylamine (**3n**): Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.13–7.31 (m, 5H), 6.50 (d, J = 15.12 Hz, 1H), 6.18–6.28 (m, 1H), 3.33 (dd, J = 1.5, 6.6 Hz, 2H), 2.57 (t, J = 7.5 Hz, 2H), 1.39–1.46 (m, 3H), 1.18–1.23 (m, 10H), 0.80 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.2, 131.1, 128.7, 128.5, 127.3, 126.2, 52.1, 49.6, 32.0, 30.2, 29.6, 29.3, 27.4, 22.8, 14.2 ppm; HRMS (ESI-TOF): *m/z* calcd for $C_{17}H_{27}N$: 246.2216 $[M+H]^+$; found: 246.2219; IR (ATR): $\tilde{\nu}$ = 3411, 3026, 2954, 2923, 2853, 1681, 1599, 1494, 1449, 1377, 1121, 1070, 965, 743, 692 cm^{-1}.

N-Cinnamyl-2-octylamine (**3o**): Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.13–7.30 (m, 5H), 6.49 (d, J = 15.78 Hz, 1H), 6.18–6.28 (m, 1H), 3.26–3.57 (d, J = 6.02 Hz, 2H), 2.57–2.65 (m, 1H), 0.93–1.40 (m, 11H), 0.86–0.92 (m, 3H), 0.78–0.83 ppm (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.2, 131.0, 128.9, 128.5, 127.3, 126.2, 52.6, 49.4, 37.1, 32.0, 29.6, 26.0, 22.5, 20.3, 14.4 ppm; HRMS (ESI-TOF): *m/z* calcd for $C_{17}H_{27}N$: 246.2216 $[M+H]^+$; found: 246.2219; IR (ATR): $\tilde{\nu}$ = 3412, 3025, 2956, 2924, 2850, 1683, 1599, 1494, 1449, 1374, 1155, 1071, 964, 908, 730, 690 cm^{-1}.

N-Cinnamyl-*N*-methyloctylamine (**3p**): Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.13–7.31 (m, 5H), 6.42 (d, J = 15.23 Hz, 1H), 6.15–6.24 (m, 1H), 3.05 (dd, J = 1.5, 6.8 Hz, 2H), 2.17–2.31 (m, 2H), 1.52 (s, 3H), 1.39–1.44 (m, 2H), 1.00–1.19 (m, 10H), 0.77–0.98 ppm (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.1, 132.4, 128.5, 127.6, 127.3, 126.3, 60.4, 57.6, 42.3, 31.9, 29.7, 29.2, 27.5, 22.6, 14.2 ppm; HRMS (ESI-TOF): *m/z* calcd for $C_{18}H_{29}N$: 260.2372 $[M+H]^+$; found: 260.2374; IR (ATR): $\tilde{\nu}$ = 3026, 2924, 2853, 2785, 1682, 1599, 1495, 1450, 1359, 1132, 1027, 966, 810, 738, 690 cm^{-1}.

N,*N*-Dipropylcinnamylamine (**3q**): Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.13–7.31 (m, 5H), 6.42 (d, J = 15.72 Hz, 1H), 6.16–6.39 (m, 1H), 3.17 (d, J = 6.54 Hz, 2H), 2.35 (t, J = 7.5 Hz, 4H), 1.35–1.48 (m, 4H), 0.80 ppm (t, J = 7.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.3, 131.9, 128.5, 128.0, 127.2, 126.2, 56.8, 56.0, 20.2, 12.0 ppm; HRMS (ESI-TOF): *m/z* calcd for $C_{15}H_{23}N$: 218.1903 $[M+H]^+$; found: 218.1906; IR (ATR): $\tilde{\nu}$ = 3026, 2957, 2931, 2871, 2797, 1681, 1599, 1495, 1449, 1364, 1298, 1187, 1072, 966, 738, 691 cm^{-1}.

N-Cinnamylmorpholine (**3r**):[18c] Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.15–7.31 (m, 5H), 6.45 (d, J = 15.93 Hz, 1H), 6.13–6.48 (m, 1H), 3.66 (t, J = 4.6 Hz, 4H), 3.07 (d, J = 6.78 Hz, 2H), 2.42 ppm (t, J = 4.59 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.8, 133.4, 128.6, 127.6, 126.3, 126.0, 67.0, 61.5, 53.7 ppm; HRMS (ESI-TOF): *m/z* calcd for $C_{13}H_{17}NO$: 204.1382 $[M+H]^+$; found: 204.1384; IR (ATR): $\tilde{\nu}$ = 3025, 2956, 2853, 2804, 1679, 1598, 1494, 1451, 1350, 1291, 1276, 1114, 1069, 1005, 966, 867, 739 cm^{-1}.

N-Cinnamyl-*N*-methylnaphthalen-1-ylmethanamine (**3s**):[18c] Orange oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.22 (d, J = 8.67 Hz, 1H), 7.68–7.78 (m, 2H), 7.14–7.47 (m, 9H), 6.50 (d, J = 16.1 Hz, 1H), 6.25–6.34 (m, 1H), 3.88 (s, 2H), 3.21 (dd, J = 1.5, 5.9 Hz, 2H), 2.20 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.1, 134.9, 133.9, 132.7, 132.5, 128.6, 128.4, 127.9, 127.6, 127.5, 127.4, 126.3, 125.9, 125.6, 125.1, 124.6, 60.4, 60.1, 42.5 ppm; HRMS (ESI-TOF): *m/z* calcd for $C_{21}H_{21}N$:

288.1746 $[M+H]^+$; found: 288.1748; IR (ATR): $\tilde{\nu}$ = 3026, 2942, 2853, 2785, 1677, 1597, 1509, 1449, 1362, 1124, 1015, 967, 792 cm^{-1}.

1-[Bis(4-fluorophenyl)methyl]-4-cinnamylpiperazine (**3t**):[18c] Orange oil; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.14–7.29 (m, 9H), 6.85–6.92 (m, 4H), 6.43 (d, J = 15.8 Hz, 1H), 6.13–6.23 (m, 1H), 4.15 (s, 1H), 3.09 (d, J = 6.8 Hz, 2H), 2.18–3.11 ppm (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.8 (d, J(C,F) = 244.8 Hz), 138.2, 136.9, 133.3, 129.2 (d, J(C,F) = 8.27 Hz), 128.5, 127.6, 126.3, 115.4 (d, J(C,F) = 19.12 Hz), 74.4, 60.9, 53.3, 51.6 ppm; HRMS (ESI-TOF): m/z calcd for $C_{26}H_{26}F_2N_2$: 405.2136 $[M+H]^+$; found: 405.2141; IR (ATR): $\tilde{\nu}$ = 3027, 2961, 2809, 2766, 1602, 1504, 1455, 1351, 1260, 1221, 1151, 1097, 1005, 907, 823, 730, 692 cm^{-1}.

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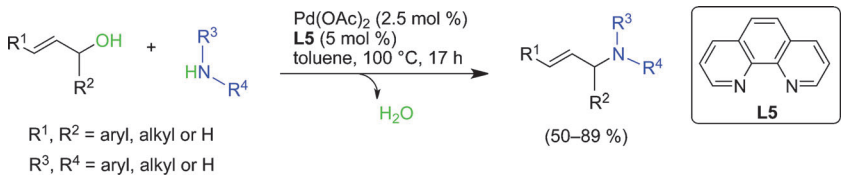

One pot is all it takes: By applying a convenient combination consisting of $Pd(OAc)_2$/1,10-phenanthroline, a variety of allylic alcohols reacts smoothly to give the corresponding secondary and tertiary amines in good to excellent yields with high regioselectivity (see picture).

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An Efficient and Convenient Palladium Catalyst System for the Synthesis of Amines from Allylic Alcohols

