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Nickel-catalyzed multi-component connection reaction of isoprene, aldimines (lactamines), and diphenylzinc

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This manuscript was dedicated to Professor Günther Wilke for his contribution to the field of organonickel chemistry

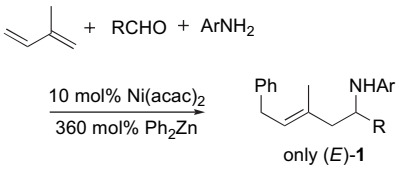
Abstract—$Ni(acac)_2$ catalyzes the four-component connection reaction of diphenylzinc, isoprene, aromatic aldehydes, and aromatic amines in this order and provides stereochemically homogeneous (*E*)-1-arylamino-1-aryl-3-methyl-5-phenyl-3-pentenes (**1**) in excellent yields. Aliphatic aldehydes react similarly and give (*E*)-1-arylamino-1-alkyl-3-methyl-5-phenyl-3-pentenes (**1**) in slightly reduced yields. When the alkyl groups are bulky, in addition to **1** are formed (*E*)-1-arylamino-1-alkyl-*4-methyl*-5-phenyl-3-pentenes (**1′**) as the minor products. Lactamines prepared in situ from five- and six-membered lactols and aromatic amines are more reactive than alkyl aldehyde aldimines and furnish (*E*)-4-arylamino-6-methyl-8-phenyl-6-octen-1-ols (**4**) and (*E*)-5-arylamino-7-methyl-9- phenyl-7-nonen-1-ols (**5**), respectively, in good yields with excellent *E*-stereoselectivity.

1. Introduction

Multi-component connection reactions of simple molecules are straightforward and efficient methods to construct desired molecules which have been realized mostly by making the best use of transition-metal catalysis.[1] Isoprene and aldimines are among the most important building blocks; isoprene is a ubiquitous constituent of the carbon frameworks of natural products and aldimines serve as a nitrogen source of many physiologically interesting compounds. Regio- (C1 vs C4) and stereoselective (*E* vs *Z*) incorporation of isoprene into molecules is a rather difficult task and it has been a challenge for synthetic organic chemists to establish methods to manipulate isoprene in desired ways.[2] Aldimines are among the least reactive carbonyl compounds and many studies, particularly in the past decade, have been devoted to their activation and utilization as electrophiles toward carbonucleophiles.

Recently, we demonstrated that a nickel(0) species nicely catalyzed the three-component connection reaction of organometals (M=Zn and B), isoprene, and aldehydes to afford homoallyl alcohols, where isoprene reacted regioselectively with aldehydes at the C1 position and with organometals at the C4 position.[3]

We also clarified that a similar methodology could be applied to the reactions with aldimines; phenylative multi-component connection reaction was best performed with diphenylzinc (Eq. 1), while methylative reaction was most successful with trimethylaluminum (Eq. 2).[4,5] Methylative reaction, however, is still not at a practically useful level; the reaction yields **2** with modest stereoselectivity (*E*:*Z*= 2:1–10:1) along with **3** as minor products, both being inseparable by conventional column chromatography. Further improvement of the reaction conditions, enabling the stereoselective formation of (*E*)-**2** minimizing the formation **3**, has been under our ongoing extensive study.



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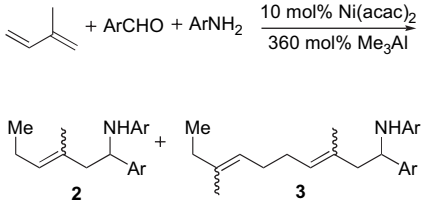

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Keywords: Aldimine; Diphenylzinc; Isoprene; Lactol; Multi-component connection; Nickel catalysis.
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In this article, we disclose a full account of phenylative multi-component connection reaction, which provides (*E*)-**1** in good yields and with excellent stereoselectivity for a variety of aldimines prepared in situ from aromatic aldehydes and aromatic amines (R=Ar, Eq. 1). The reaction can be successfully extended to aliphatic aldehyde-*p*-anisidine imines (R=alkyl, Ar=*p*-anisyl, Eq. 1), which is highlighted by the reaction with lactamines, generated in situ from lactols (cyclic hemiacetals) and aromatic amines (Eq. 3). This might be a great achievement, not only because two important building blocks, isoprene and aldimines, are incorporated in the products, but also because tri-substituted (*E*)-homoallylamines **1** and (*E*)-homoallylamino alcohols **4** and **5** are produced with a single operation in one flask in the yields of a synthetically useful level under nickel catalysis. These products may be of great concern for synthetic organic chemists and also for life science researchers.

2. Results and discussion

2.1. Ni-catalyzed four-component connection reaction of Ph_2Zn, isoprene, aldehydes, and aromatic amines

The reaction of benzaldehyde-*p*-anisidine imine under the identical conditions established for the multi-component connection reaction of aldehydes[3] was quite disappointing and provided the expected product **1a** (**1**, R=Ph, Ar=*p*-anisyl, Eq. 1) in as low as 14% yield among many other intractable products (*Experiment* 1). Use of 1 equiv *p*-anisidine as an additive turned out very effective to increase the yield of **1a** (63%, 30 °C for 2 h, *Experiment* 2). Remarkable improvement in the yield was brought about when the reaction was conducted using the aldimine formed in situ from benzaldehyde and *p*-anisidine (2 equiv), where **1a** was obtained in 80% yield (run 1, Table 1, *Experiment* 3). *Experiments* 2 and 3 only differ in the absence or presence of water (1 equiv), respectively. *Experiment* 4, which was undertaken under the identical conditions to those of *Experiment* 1 in the presence of 1 equiv of water, gave **1a** (24%) in a slightly better yield than *Experiment* 1. All these results combine to indicate that both water and *p*-anisidine, 1 equiv each, are essential to give rise to **1a** in satisfactory yield.

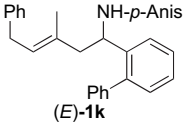
Many precedents point to the success of nucleophilic alkylation of aldimines[6] depending on the steric and electronic effects of both the aldehyde[7] and the nitrogen substituents,[8] and sometimes heteroatoms on these substituents exert tremendous effects on the reaction efficiency.[6,9]

In order to optimize the nitrogen substituents, we examined a wide range of aniline derivatives either bearing an electron-donating or an electron-withdrawing substituent under the conditions established above. The results are summarized in runs 2–9 (Table 1). Except for *o*-chloro- and *o*-bromoanilines (runs 6 and 8), no significant differences in reactivity and yields were observed over a wide range of pK_a of aniline derivatives[10] (e.g., pK_a(*o*-Br)=2.53, pK_a(*p*-OMe)=5.36). In most cases, the reactions were complete within 1–3 h and provided **1** in more than 90% yields. The reactions were monitored with TLC. The sluggishness and the low yields observed for *o*-chloro- and *o*-bromoanilines might be attributed to deactivation of a nickel catalyst rather than steric hindrance of the reaction (vide infra).

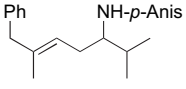
Table 1. Ni-catalyzed four-component connection reaction of Ph_2Zn, isoprene, aldehydes, and amines (Eq. 1)[a]

Run	Aldehyde	Amine	Time (h)	Yield[b]
	R			**3**
1	Ph	*p*-MeOPh	2	(*E*)-**1a**:80
2	Ph	*p*-MePh	1	(*E*)-**1b**:96
3	Ph	Ph	1	(*E*)-**1c**:90
4	Ph	*o*-(F)Ph	3	(*E*)-**1d**:**98**
5	Ph	*p*-(F)Ph	2	(*E*)-**1e**:94
6	Ph	*o*-(Cl)Ph	24	(*E*)-**1f**:30
7	Ph	*p*-(Cl)Ph	2	(*E*)-**1g**:78
8	Ph	*o*-(Br)Ph	24	—[c]
9	Ph	*p*-(Br)Ph	3	(*E*)-**1h**:94
10	Ph	*n*-Hexyl	6	—[c]
11	*p*-Tol	*p*-MeOPh	2	(*E*)-**1i**:83
12	*p*-Anis	*p*-MeOPh	6	(*E*)-**1j**:44
13	*o*-(Cl)Ph	*p*-MeOPh	6	(*E*)-**1k**:87[d]
14	*p*-(Cl)Ph	*p*-MeOPh	1	(*E*)-**1l**:61
15	*o*-(F)Ph	*p*-MeOPh	2	(*E*)-**1m**:94
16	*p*-(F)Ph	*p*-MeOPh	1	(*E*)-**1n**:96
17	2-Furyl	*p*-MeOPh	1	(*E*)-**1o**:98
18	2-Furyl	*p*-(Cl)Ph	1	(*E*)-**1p**:81
19	n-C_7H_{15}	*p*-MeOPh	6	(*E*)-**1q**:76
20	*i*-Pr	*p*-MeOPh	6	(*E*)-**1r**:57[e]

[a] Reaction conditions: an aldehyde (1 mmol) and an amine (2 mmol) in THF (2mL) at 30 °C overnight, and then $Ni(acac)_2$ (0.1 mmol in 3 mL of THF), isoprene (4 mmol), and Ph_2Zn (3.6 mmol) at 30 °C.
[b] Yields for the isolated spectroscopically homogeneous materials.
[c] Complex mixture of products.
[d] (*E*)-1-*p*-Anisylamino-3-methyl-5-phenyl-1-[(2-phenyl)phenyl]-3-pentene ((*E*)-**1k**, see below).
[e] A mixture of (*E*)-**1r** and its regioisomer (*E*)-**1r′** (see below) in a ratio of 2:1.



(*E*)-**1k**



(*E*)-**1r'**

Benzaldehyde imines of alkyl amines, e.g., *n*-hexylamine, on the other hand, showed completely different reactivity and gave intractable mixtures of products (run 10).

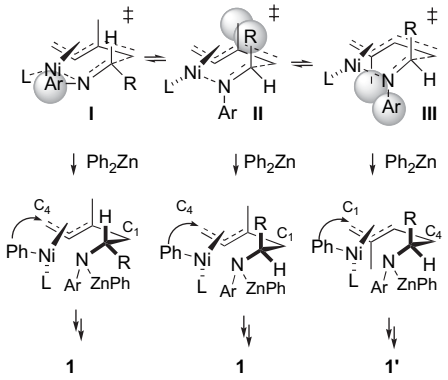
We next examined applicability of the present reaction to other aromatic aldehydes including 2-furaldehyde using *p*-anisidine as an aromatic amine (runs 11–18). Judging from the yields of **1a–h**, *p*-anisidine may not be the best choice of aromatic amines; however, we used it from a practical viewpoint. The *p*-methoxyphenyl group might be regarded as a protecting group of amines; it could be easily removed oxidatively, yielding free primary amines of the product **1** in good yields.[7c,9d,11]

All aromatic aldehydes, irrespective of the steric (*o*- and *p*-) and electronic (electron-donating and electron-withdrawing) nature of the substituents, reacted smoothly at 30 °C and provided the expected products **1** in modest to excellent yields. Interestingly, while the C–Cl bond of the *p*-chloro isomer **1l** remained intact, the C–Cl bond of the *o*-chloro isomer underwent cross-coupling reaction[12] with Ph_2Zn and provided **1k** exclusively in good yield (runs 13 and 14, footnote d, Table 1). The *o*-fluoro counterpart **1m** withstood the cross-coupling reaction (run 15).

The reaction could be extended to aliphatic aldehydes with limited success. Two typical examples, *n*-octanal (a primary

aldehyde) and 2-methylpropanal (a secondary aldehyde), were examined. The results are shown in runs 19 and 20. *n*-Octanal-*p*-anisidine imine provided the expected homoallylamine (*E*)-**1q** as a single isomer in good yield (run 19); however, sterically demanding 2-methylpropanal-*p*-anisidine imine provided an inseparable mixture of two isomers **1r** and **1r′**, the latter arising from incorporation of isoprene in an opposite direction (run 20, see footnote e).

This erosion of regioselectivity might be rationalized on the steric ground as discussed before (Scheme 1);[5c] the reaction would avoid a putative transition state **I** that places both the imine substituents at a di-equatorial position of a cyclic structure, since it suffers from severe gauche repulsion between the ligand on Ni and the aromatic ring on N. Instead, the reaction would proceed through a transition state **II**, where both the aldimine substituents locate in a diaxial position.[13] When R is of great steric bulk, 1,3-quasi-diaxial repulsion between R and the methyl group of isoprene becomes substantial in a transition state **II**, and another transition state **III**, placing isoprene in an opposite direction, would become to contribute to the reaction to a certain extent and would lead to **1′** as a side product.



Scheme 1. Transition states leading to regioisomers **1** and **1′**.

The stereochemical homogeneity of **1** was confirmed with ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectroscopies. The *E* structure of **1** was determined on the basis of NOE experiments. Some representative data are shown in Figure 1. The *E* structure of the regioisomer **1′** was also determined by NOE experiments.

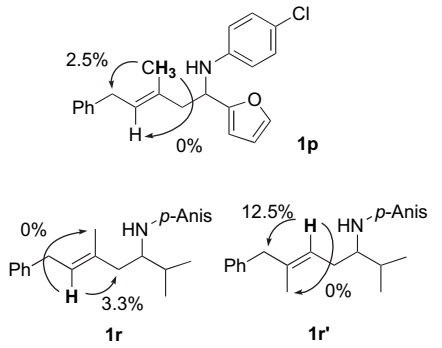
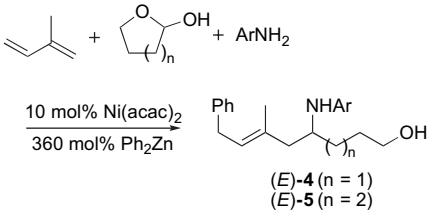


Figure 1. Percent increments of area intensities observed by irradiation at the boldface protons.

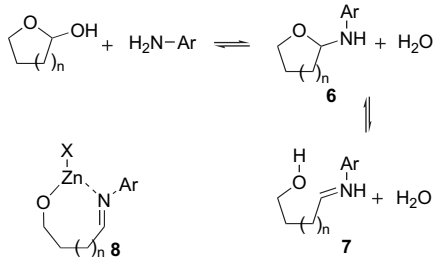
2.2. Ni-catalyzed four-component connection reaction of Ph_2Zn, isoprene, lactols, and aromatic amines

Lactols (2-hydroxy-oxacycloalkanes) share the fundamental skeleton with many carbohydrates, and establishment of methodology for their derivatization, enabling of elongation of carbon chains and especially enabling of introduction of an amino group, is of significant importance in organic synthesis and life science research.[14] The outstanding characteristics of the present methodology, compatibility with water and acceleration of the reaction in the presence of a limited amount of water, encouraged us to examine the multi-component connection reaction with lactols (Eq. 3).



(3)

^{1}H NMR studies revealed that a mixture of 2-hydroxytetrahydrofuran and *p*-anisidine cleanly formed 2-(*p*-anisidyl)-tetrahydrofuran (**6**, *n*=1) (Scheme 2). The mixture did not contain 4-hydroxybutanal-*p*-anisidine imine (**7**, *n*=1) in any detectable amounts. The extremely low concentration of **7** in the equilibrium with **6** suggested us that phenylative multi-component connection reaction using lactols and *p*-anisidine might proceed with difficulty or, if any, very slowly as compared with the reactions of alkyl aldehyde-*p*-anisidine imines.



Scheme 2.

To our pleasant surprise, however, the reaction of 2-hydroxytetrahydrofuran and *p*-anisidine under usual conditions proceeded smoothly, completing within 2 h even at ambient temperature (cf., run 1, Table 2 and runs 19–20, Table 1). The expected product (*E*)-**4a** (Ar=*p*-anisyl) was obtained as a single isomer in remarkably good yield. The parent aniline and *p*-chloroaniline showed almost the same results regarding the reactivity and the product yields (runs 2 and 3, Table 2).

2-Hydroxytetrahydropyran reacted similarly well for variety combinations with aniline derivatives and provided the expected products **5** in modest to good yields (runs 4–13, Table 2). *o*-Chloro- and *o*-bromoaniline gave rise to the expected products **5g** and **5i** about half the yields of the corresponding *p*-isomers, **5h** and **5j** (runs 10–13), respectively. On the other hand, *o*-methoxyaniline gave rise to the expected products

Table 2. Ni-catalyzed four-component connection of Ph_2Zn, isoprene, lactols (n=1 and 2), and anilines (Eq. 3)[a]

Run	n	Anilines	Time (h)	Yield[b] (%)
1	1	*p*-MeO	2	(*E*)-**4a**:83
2	1	H	2	(*E*)-**4b**:84
3	1	*p*-Cl	2	(*E*)-**4c**:88
4	2	*o*-MeO	4	(*E*)-**5a**:68
5	2	*p*-MeO	2	(*E*)-**5b**:76
6	2	H	1	(*E*)-**5c**:81
7	2	*p*-Me	2	(*E*)-**5d**:86
8	2	*o*-F	2	(*E*)-**5e**:45
9	2	*p*-F	3	(*E*)-**5f**:56
10	2	*o*-Cl	2	(*E*)-**5g**:44
11	2	*p*-Cl	2	(*E*)-**5h**:89
12	2	*o*-Br	4	(*E*)-**5i**:34
13	2	*p*-Br	6	(*E*)-**5j**:64

[a] Reaction conditions: a lactol (1 mmol) and an aniline derivative (2 mmol) in THF (2 mL) at room temperature overnight, and then $Ni(acac)_2$ (0.1 mmol in 3 mL of THF), isoprene (4 mmol), and Ph_2Zn (3.6 mmol) at room temperature.

[b] Yields for the isolated and spectroscopically homogeneous materials.

5a in almost the same yield as *p*-methoxyaniline (runs 4 and 5). These results suggest that the decrease in the yields that *o*-bromo- and *o*-chloro-isomers display is not due to steric hindrance but probably due to decomposition of products that might be triggered by oxidative addition of a Ni(0) species upon the *ortho* C-halogen bond followed by elimination of a Ni-amide species. Although the reason is not clear at the moment, the decomposition of **5g** and **5i** is not so serious as that encountered in runs 6 and 8 in Table 1.

The unexpectedly smooth reaction of lactamines might be attributed to an intermediacy of **8**, which is formed by chelation of **7** to zinc(II) through its hydroxy and imine nitrogen (Scheme 2); the C=N→Zn(II) bond would increase the electrophilic reactivity of the imine moiety, hence facilitate the reaction.[6a,15]

3. Conclusion

This paper demonstrates that $Ni(acac)_2$ serves as an efficient catalyst for the four-component connection reaction of diphenylzinc, isoprene, aromatic aldehydes, and aromatic amines and provides (*E*)-1-arylamino-1-aryl-3-methyl-5-phenyl-3-pentenes (**1**) in excellent yields. Aliphatic aldehydes show limited success; primary aldehydes provide (*E*)-1-arylamino-1-alkyl-3-methyl-5-phenyl-3-pentenes (**1**) selectively, while secondary aldehydes provide mixtures of **1** and (*E*)-1-arylamino-1-alkyl-*4-methyl*-5-phenyl-3-pentenes (**1′**), the positional isomers of the isoprene methyl group, as the minor products. Lactamines prepared in situ from five- and six-membered lactols and aromatic amines undergo the multi-component connection reaction smoothly and furnish (*E*)-4-arylamino-6-methyl-8-phenyl-6-octen-1-ols (**4**) and (*E*)-5-arylamino-7-methyl-9-phenyl-7-nonen-1-ols (**5**), respectively, in good yields with excellent *E*-selectivity. The reaction presented here is operationally simple and can be performed with a single flask procedure. The products, tri-substituted (*E*)-homoallylamines **1** and (*E*)-homoallylamino alcohols **4** and **5**, may be of great interest for synthetic organic chemists as synthetic intermediates and for life science researchers as probes in their studies.

4. Experimental

4.1. General

Reactions employed oven-dried glassware unless otherwise noted. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates with UV indicator (Merck, Silica gel 60F254). Flash chromatography columns were packed with 230–400 mesh silica gel as a slurry in *n*-hexane. Gradient flash chromatography was conducted eluting with a continuous gradient from *n*-hexane to the indicated solvent. Proton and carbon NMR data were obtained with a JEOL-GX400 with tetramethylsilane as an internal standard. Chemical shift values were given in parts per million downfield from the internal standard. Infrared spectra were recorded with a JASCO A-100 FTIR spectrophotometer. High-resolution mass spectra (HRMS) were measured with a JEOL JMS-DX303. Combustion analyses were performed by the Instrumental Analysis Center of Nagasaki University. Analysis agreed with the calculated values within ±0.4%.

4.2. Solvents and reagents

Tetrahydrofuran was dried and distilled from benzophenone and sodium immediately prior to use under nitrogen atmosphere. $Ni(acac)_2$ (purity 95%, Aldrich), PhMgBr (1.0 M THF solution, KANTO), $ZnCl_2$ (1.0 M ether solution, Aldrich), isoprene (Tokyo Kasei Kogyo Co., Ltd), aniline, *o*-anisidine, *p*-anisidine, *o*-fluoroaniline, *p*-fluoroaniline, *o*-chloroaniline, *p*-chloroaniline, *o*-bromoaniline, and *p*-bromoaniline were purchased and used as received. The following aldehydes were purchased and distilled prior to use by Kugelrohr apparatus: benzaldehyde, *o*-tolualdehyde, *p*-tolualdehyde, *o*-anisaldehyde, *p*-anisaldehyde, *o*-fluorobenzaldehyde, *p*-fluorobenzaldehyde, *o*-chlorobenzaldehyde, *p*-chlorobenzaldehyde, 2-furaldehyde, 1-octanal, and 2-methylpropanal.

4.2.1. Preparation of Ph_2Zn. Into a N_2 purged Schlenk flask, were introduced dry THF (10 mL) and $ZnCl_2$ (10 mL, 1 M ether solution; 10 mmol) via syringe. PhMgBr (20 mL, 1 M THF solution; 20 mmol) was successively added to the solution, and then the mixture was stirred at ambient temperature for 3 h. This stock solution was used as 0.25 M Ph_2Zn.

4.2.2. Preparation of hemiacetals. 3,4-Dihydro-2*H*-pyran (8.3 g, 100 mmol) was added into 2 M HCl (20 mL) at 0 °C over 30 min. The mixture was allowed to warm to room temperature, stirred for an additional 1 h, neutralized with satd $NaHCO_3$, and then extracted with dichloromethane (2×20 mL). The combined extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by means of Kugelrohr distillation (85 °C/2 mmHg) to give 2-hydroxytetrahydropyran in 93% yield. 2-Hydroxytetrahydrofuran was prepared from 2,3-dihydrofuran as described above (67%, 75 °C/2 mmHg).

4.3. New compounds listed in Table 1

4.3.1. A typical procedure for the Ni-catalyzed four-component connection reaction of Ph_2Zn, isoprene, an aldehyde and an aromatic amine (run 17, Table 1). Into

a N_2 purged two-necked round-bottomed flask containing *p*-anisidine (246 mg, 2.0 mmol), were added dry THF (2.0 mL) and 2-furaldehyde (96 mg, 1.0 mmol) via syringe. The mixture was stirred at 30 °C overnight to form aldimine, which was detected by TLC (R_f=0.59, *n*-hexane/ethyl acetate = 2:1, v/v). A solution of $Ni(acac)_2$ (25.7 mg, 0.1 mmol) in THF (3.0 mL) was introduced into the aldimine solution via a cannula. Isoprene (400 μl, 4.0 mmol) and a Ph_2Zn solution (14.4 mL, 0.25 M, 3.6 mmol) were successively introduced via syringe and the homogeneous mixture was stirred for 1 h. After completion of reaction (TLC), the mixture was poured into ice-water (20 mL) and extracted with ethyl acetate (30 mL). The water phase was extracted with ethyl acetate (2×20 mL). Combined organic extracts were washed with 2 M HCl (20 mL) and satd $NaHCO_3$ (25 mL), and then dried ($MgSO_4$) and concentrated in vacuo. The residue was subjected to column chromatography over silica gel (eluent: *n*-hexane/ethyl acetate = 100:1, v/v) to provide **1o** (R_f=0.74, *n*-hexane/ethyl acetate = 2:1, v/v) in 98% as a single isomer.

4.3.1.1. (*E*)-*N*-(1-(Furan-2-yl)-3-methyl-5-phenylpent-3-enyl)-4-methoxybenzenamine (1o). IR (neat) 3396 (w), 2831 (w), 1603 (w), 1514 (s), 1238 (m), 1037 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.68 (s, 3H), 2.52 (dd, *J*=13.4, 8.5 Hz, 1H), 2.65 (dd, *J*=13.4, 5.9 Hz, 1H), 3.33 (dd, *J*=15.1, 7.3 Hz, 1H), 3.39 (dd, *J*=15.1, 7.3 Hz, 1H), 3.71 (s, 3H), 4.47 (dd, *J*=8.5, 5.9 Hz, 1H), 5.47 (t, *J*=7.2 Hz, 1H), 6.13 (d, *J*=3.2 Hz, 1H), 6.26 (dd, *J*=3.2, 1.7 Hz, 1H), 6.48 (d, *J*=8.9 Hz, 2H), 6.71 (d, *J*=8.9 Hz, 2H), 7.12 (d, *J*=7.3 Hz, 2H), 7.18 (t, *J*=7.3 Hz, 1H), 7.26 (t, *J*=3.3 Hz, 2H), 7.32 (d, *J*=1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.8, 34.3, 45.7, 51.3, 55.7, 105.7, 110.0, 114.6, 114.8, 125.7, 127.4, 128.1, 128.3, 132.3, 141.0, 141.1, 141.4, 152.2, 156.5; HRMS calcd for $C_{23}H_{25}NO_2$: 347.4501; Found *m*/*z* (relative intensity): 347.1869 (M^+, 100).

4.3.1.2. (*E*)-4-Methoxy-*N*-(3-methyl-1,5-diphenylpent-3-enyl)benzenamine (1a). IR (neat) 3387 (w), 2831 (w), 1605 (w), 1512 (s), 1242 (s), 1034 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.76 (s, 3H), 2.34 (dd, *J*=13.7, 10.1 Hz, 1H), 2.52 (dd, *J*=13.7, 4.5 Hz, 1H), 3.34 (dd, *J*=15.4, 7.4 Hz, 1H), 3.44 (dd, *J*=15.4, 7.4 Hz, 1H), 3.67 (s, 3H), 3.87 (br s, 1H), 4.30 (dd, *J*=10.1, 4.5 Hz, 2H), 5.53 (t, *J*=7.4 Hz, 1H), 6.34 (d, *J*=8.9 Hz, 2H), 6.64 (d, *J*=8.9 Hz, 2H), 7.12–7.38 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.7, 34.3, 50.0, 55.7, 56.5, 114.4, 114.6, 125.8, 126.0, 126.7, 127.6, 128.2, 128.4, 132.9, 141.0, 141.9, 144.6, 151.8; HRMS calcd for $C_{25}H_{27}NO$: 357.2093; Found *m*/*z* (relative intensity): 357.2100 (M^+, 100).

4.3.1.3. (*E*)-4-Methyl-*N*-(3-methyl-1,5-diphenylpent-3-enyl)benzenamine (1b). IR (neat) 3395 (w), 3024 (m), 2916 (m), 1620 (m), 1520 (s), 1450 (m), 1304 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.76 (s, 3H), 2.17 (s, 3H), 2.42 (dd, *J*=13.7, 10.2 Hz, 1H), 2.54 (dd, *J*=13.7, 4.6 Hz, 1H), 3.33 (dd, *J*=15.4, 7.3 Hz, 1H), 3.44 (dd, *J*=15.4, 7.3 Hz, 1H), 3.99 (br s, 1H), 4.34 (dd, *J*=10.2, 4.6 Hz, 1H), 5.51 (t, *J*=7.3 Hz, 1H), 6.32 (d, *J*=8.5 Hz, 1H), 6.86 (d, *J*=8.5 Hz, 1H), 7.13–7.37 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.7, 20.4, 34.4, 50.1, 56.0, 113.5, 125.9, 126.1, 126.4, 126.7, 127.6, 128.2, 128.47, 128.51, 129.4, 133.0, 141.1, 144.6, 145.4; HRMS calcd for $C_{25}H_{27}N$: 341.2143; Found *m*/*z* (relative intensity): 341.2131 (M^+, 100).

4.3.1.4. (*E*)-*N*-(3-Methyl-1,5-diphenylpent-3-enyl)-benzenamine (1c). IR (neat) 3402 (w), 3024 (w), 1605 (s), 1504 (s), 748 (s) 694 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.76 (s, 3H), 2.34 (dd, *J*=13.7, 10.2 Hz, 1H), 2.55 (dd, *J*=13.7, 4.3 Hz, 1H), 3.33 (dd, *J*=15.2, 7.5 Hz, 1H), 3.39 (dd, *J*=15.2, 7.5 Hz, 1H), 4.37 (dd, *J*=10.2, 4.3 Hz, 1H), 5.51 (t, *J*=7.5 Hz, 1H), 6.39 (d, *J*=7.4 Hz, 2H), 6.62 (t, *J*=7.4 Hz, 1H), 7.02–7.37 (m, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.7, 34.3, 50.0, 55.7, 113.3, 117.2, 125.8, 125.9, 126.7, 128.1, 128.4, 128.5, 128.8, 132.8, 141.0, 144.3, 147.5; HRMS calcd for $C_{24}H_{25}N$: 327.1987; Found *m*/*z* (relative intensity): 327.1967 (M^+, 100).

4.3.1.5. (*E*)-2-Fluoro-*N*-(3-methyl-1,5-diphenylpent-3-enyl)benzenamine (1d). Mp 71.1–71.6 °C (*n*-hexane); IR (KBr disk) 3425 (m), 3024 (w), 2909 (w), 1620 (m), 1520 (s), 1450 (m), 1335 (m), 1188 (m), 741(s), 702 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.75 (s, 3H), 2.44 (dd, *J*=13.8, 9.3 Hz, 1H), 2.58 (dd, *J*=13.8, 4.6 Hz, 1H), 3.36 (dd, *J*=15.9, 7.3 Hz, 1H), 3.43 (dd, *J*=15.9, 7.3 Hz, 1H), 4.42 (dd, *J*=9.3, 4.6 Hz, 1H), 4.44 (br s, 1H), 5.51 (t, *J*=7.3 Hz, 1H), 6.35 (t, *J*=7.8 Hz, 1H), 6.51–6.57 (m, 1H), 6.77 (t, *J*=7.8 Hz, 1H), 6.94 (dd, *J*=12.0, 7.8 Hz, 1H), 7.12–7.37 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.7, 34.2, 49.8, 55.6, 113.1, 113.2, 113.9, 114.1, 116.37, 116.44, 124.2, 124.2, 125.7, 125.9, 126.9, 127.6, 128.1, 128.3, 128.5, 132.5, 135.9, 136.0, 140.8, 143.8; HRMS calcd for $C_{24}H_{24}FN$: 345.1893; Found *m*/*z* (relative intensity): 345.1895 (M^+, 22), 278 (21), 277 (100). Anal. Calcd for $C_{24}H_{24}FN$: C, 83.44; H, 7.00; F, 5.55; N, 4.05. Found: C, 83.20; H, 7.20; N, 4.08.

4.3.1.6. (*E*)-4-Fluoro-*N*-(3-methyl-1,5-diphenylpent-3-enyl)benzenamine (1e). IR (neat) 3402 (w), 3024 (w), 2916 (w), 1605 (w), 1512 (s), 1219 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.76 (s, 3H), 2.34 (dd, *J*=13.8, 10.1 Hz, 1H), 2.54 (dd, *J*=13.8, 4.6 Hz, 1H), 3.34 (dd, *J*=15.4, 7.4 Hz, 1H), 3.44 (dd, *J*=15.4, 7.4 Hz, 1H), 3.99 (br s, 1H), 4.30 (dd, *J*=10.1, 4.6 Hz, 1H), 5.51 (br t, *J*=7.4 Hz, 1H), 6.29 (d, *J*=8.9 Hz, 1H), 6.30 (d, *J*=8.9 Hz, 1H), 6.74 (t, *J*=8.9 Hz, 2H), 7.13–7.36 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.7, 34.3, 50.0, 56.3, 114.0, 114.1, 115.1, 115.3, 125.8, 126.0, 127.7, 128.1, 128.4, 128.5, 132.7, 141.0, 143.9, 154.4, 156.7; HRMS calcd for $C_{24}H_{24}FN$: 345.1893; Found *m*/*z* (relative intensity): 345.1894 (M^+, 100).

4.3.1.7. (*E*)-2-Chloro-*N*-(3-methyl-1,5-diphenylpent-3-enyl)benzenamine (1f). IR (neat) 3395 (w), 3024 (w), 2924 (w), 1597 (s), 1504 (s), 1450 (m), 1319 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.74 (s, 3H), 2.46 (dd, *J*=13.7, 9.8 Hz, 1H), 2.60 (dd, *J*=13.7, 4.6 Hz, 1H), 3.40 (d, *J*=6.9 Hz, 2H), 4.44 (dt, *J*=9.8, 4.6 Hz, 1H), 4.88 (d, *J*=2.9 Hz, 1H), 5.55 (br t, *J*=6.9 Hz, 1H), 6.32 (d, *J*=7.8 Hz, 1H), 6.54 (t, *J*=7.8 Hz, 1H), 6.90 (t, *J*=7.8 Hz, 1H), 7.14–7.36 (m, 11H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.8, 34.4, 50.0, 55.8, 112.6, 117.1, 119.4, 125.8, 126.0,

127.0, 127.4, 127.9, 128.3, 128.4, 128.7, 128.8, 132.5, 140.8, 143.3, 143.7; HRMS calcd for $C_{24}H_{24}ClN$: 361.1597; Found *m*/*z* (relative intensity): 361.1581 (M^+, 100).

4.3.1.8. (*E*)-4-Chloro-*N*-(3-methyl-1,5-diphenylpent-3-enyl)benzenamine (1g). IR (neat) 3402 (w), 3024 (w), 2916 (w), 1597 (s), 1497 (s), 1312 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.76 (s, 3H), 2.33 (dd, *J*=13.7, 10.1 Hz, 1H), 2.55 (dd, *J*=13.7, 4.3 Hz, 1H), 3.35 (dd, *J*=15.4, 7.4 Hz, 1H), 3.44 (dd, *J*=15.4, 7.4 Hz, 1H), 4.10 (br s, 1H), 4.33 (m, 1H), 5.51 (br t, *J*=7.4 Hz, 1H), 6.29 (d, *J*=8.9 Hz, 1H), 6.97 (d, *J*=8.9 Hz, 1H), 7.12–7.34 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.7, 34.4, 49.9, 55.9, 114.5, 118.1, 118.8, 121.5, 121.9, 126.0, 127.0, 127.98, 128.2, 128.5, 128.6, 128.7, 129.2, 129.4, 132.7, 141.0, 143.8, 146.1; HRMS calcd for $C_{24}H_{24}ClN$: 361.1597; Found *m*/*z* (relative intensity): 361.1590 (M^+, 100).

4.3.1.9. (*E*)-4-Bromo-*N*-(3-methyl-1,5-diphenylpent-3-enyl)benzenamine (1h). IR (neat) 3402 (w), 3024 (w), 2916 (w), 1597 (m), 1497 (s), 1312 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.75 (s, 3H), 2.33 (dd, *J*=13.7, 10.2 Hz, 1H), 2.55 (dd, *J*=13.7, 4.1 Hz, 1H), 3.33 (dd, *J*=15.2, 7.4 Hz, 1H), 3.44 (dd, *J*=15.4, 7.4 Hz, 1H), 4.11 (br s, 1H), 4.32 (m, 1H), 5.51 (br t, *J*=7.4 Hz, 1H), 6.24 (d, *J*=8.8 Hz, 1H), 7.10 (d, *J*=8.8 Hz, 1H), 7.13 (d, *J*=7.6 Hz, 2H) 7.18–7.33 (m, 8H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.6, 34.3, 49.8, 55.7, 114.9, 125.9, 126.9, 127.9, 128.1, 128.4, 128.6, 131.5, 132.6, 140.9, 143.6, 146.4; HRMS calcd for $C_{24}H_{24}BrN$: 405.1092; Found *m*/*z* (relative intensity): 405.1094 (M^+, 100).

4.3.1.10. (*E*)-4-Methoxy-*N*-(3-methyl-5-phenyl-1-*p*-tolylpent-3-enyl)benzenamine (1i). IR (neat) 3386 (w), 2831 (m), 1605 (w), 1512 (s), 1242 (s), 1034 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.75 (s, 3H), 2.32 (s, 3H), 2.33 (dd, *J*=13.5, 10.1 Hz, 1H), 2.50 (dd, *J*=13.5, 4.7 Hz, 1H), 3.34 (dd, *J*=15.4, 7.5 Hz, 1H), 3.43 (dd, *J*=15.4, 7.5 Hz, 1H), 3.68 (s, 3H), 4.27 (dd, *J*=10.1, 4.7 Hz, 1H), 5.50 (br t, *J*=7.5 Hz, 1H), 6.35 (d, *J*=8.8 Hz, 2H), 6.64 (d, *J*=8.8 Hz, 2H), 7.09–7.30 (m, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.7, 34.3, 50.1, 55.7, 56.2, 114.4, 114.6, 125.8, 125.9, 127.4, 128.2, 128.4, 129.1, 133.0, 136.1, 141.0, 141.6, 142.0, 151.8; HRMS calcd for $C_{26}H_{30}NO$: 371.2249; Found *m*/*z* (relative intensity): 371.2259 (M^+, 100).

4.3.1.11. (*E*)-4-Methoxy-*N*-(1-(4-methoxyphenyl)-3-methyl-5-phenylpent-3-enyl)benzenamine (1j). IR (neat) 3384 (w), 2833–3026 (m), 1610 (w), 1512 (s), 1240 (s), 1035 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.75 (s, 3H), 2.33 (dd, *J*=13.5, 9.9 Hz, 1H), 2.49 (dd, *J*=13.5, 4.7 Hz, 1H), 3.34 (dd, *J*=15.4, 7.4 Hz, 1H), 3.43 (dd, *J*=15.4, 7.4 Hz, 1H), 3.68 (s, 3H), 3.78 (s, 3H), 3.85 (br s, 1H), 4.26 (dd, *J*=9.9, 4.7 Hz, 1H), 5.49 (br t, *J*=7.4 Hz, 1H), 6.35 (d, *J*=9.0 Hz, 2H), 6.50 (d, *J*=9.0 Hz, 2H), 6.50 (d, *J*=9.0 Hz, 2H), 6.83 (d, *J*=8.8 Hz, 1H), 7.14 (d, *J*=7.2 Hz, 2H), 7.20 (t, *J*=7.2 Hz, 1H), 7.27 (d, *J*=8.8 Hz, 2H), 7.28 (t, *J*=7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.7, 34.3, 50.1, 55.2, 55.7, 56.0, 113.9, 114.5, 114.6, 125.8, 127.1, 127.4, 128.2, 128.4, 133.0, 136.6, 141.0, 142.0, 151.8, 158.3; HRMS calcd for $C_{26}H_{29}NO_2$: 387.2198; Found *m*/*z* (relative intensity): 387.2195 (M^+, 100).

4.3.1.12. (*E*)-1-*p*-Anisylamino-3-methyl-5-phenyl-1-[(2-phenyl)phenyl]-3-pentene (1k). IR (neat) 3387 (w), 3024 (m), 2909 (m), 1597 (w), 1512 (s), 1242 (s), 1042 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.30 (s, 3H), 2.12 (dd, *J*=13.7, 10.6 Hz, 1H), 2.41 (br d, 1H), 3.24 (dd, *J*=15.3, 7.3 Hz, 1H), 3.36 (dd, *J*=15.3, 7.3 Hz, 1H), 3.69 (s, 3H), 3.74 (br s, 1H), 4.47 (dd, *J*=10.6, 3.4 Hz, 1H), 5.43 (br t, *J*=7.3 Hz, 1H), 6.31 (d, *J*=8.8 Hz, 2H), 6.65 (d, *J*=8.8 Hz, 2H), 7.09 (d, *J*=7.1 Hz, 2H), 7.16–7.44 (m, 11H), 7.58 (d, *J*=7.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.7, 34.3, 50.1, 55.2, 55.7, 56.0, 113.9, 114.5, 114.6, 125.8, 127.1, 127.4, 128.2, 128.4, 133.0, 136.6, 141.0, 142.0, 151.8, 158.3; HRMS calcd for $C_{31}H_{31}NO$: 433.2406; Found *m*/*z* (relative intensity): 433.2413 (M^+, 100), 432 (6).

4.3.1.13. (*E*)-*N*-(1-(4-Chlorophenyl)-3-methyl-5-phenylpent-3-enyl)-4-methoxybenzenamine (1l). IR (neat) 3384 (w), 2831–3026 (w), 1601 (w), 1512 (s), 1238 (m), 1038 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.74 (s, 3H), 2.32 (dd, *J*=13.5, 9.8 Hz, 1H), 2.48 (dd, *J*=13.5, 4.7 Hz, 1H), 3.33 (dd, *J*=15.3, 7.4 Hz, 1H), 3.42 (dd, *J*=15.3, 7.4 Hz, 1H), 3.67 (s, 3H), 4.27 (dd, *J*=9.8, 4.7 Hz, 1H), 5.48 (t, *J*=7.4 Hz, 1H), 6.33 (d, *J*=8.8 Hz, 2H), 6.65 (d, *J*=8.8 Hz, 2H), 7.12 (d, *J*=7.5 Hz, 2H), 7.20 (t, *J*=7.5 Hz, 1H), 7.27 (d, *J*=8.0 Hz, 4H), 7.28 (t, *J*=7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.7, 34.3, 49.8, 55.6, 55.7, 56.1, 56.2, 114.6, 125.8, 127.5, 127.9, 128.0, 128.4, 128.6, 132.3, 132.4, 140.9, 141.3, 143.0, 152.1; HRMS calcd for $C_{25}H_{26}ClNO$: 391.1703; Found *m*/*z* (relative intensity): 391.1738 (M^+, 10), 282 (3), 249 (10), 248 (66), 247 (32), 246 (100).

4.3.1.14. (*E*)-*N*-(1-(2-Fluorophenyl)-3-methyl-5-phenylpent-3-enyl)-4-methoxybenzenamine (1m). IR (neat) 3387 (w), 3024 (m), 2909 (m), 1589 (w), 1512 (s), 1242 (s), 1042 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.77 (s, 3H), 2.33 (dd, *J*=13.5, 9.7 Hz, 1H), 2.62 (dd, *J*=13.5, 4.8 Hz, 1H), 3.33 (dd, *J*=15.4, 7.5 Hz, 1H), 3.42 (dd, *J*=15.4, 7.5 Hz, 1H), 3.68 (s, 3H), 3.82 (br s, 1H), 4.70 (dd, *J*=9.7, 4.8 Hz, 1H), 5.47 (br t, *J*=7.5 Hz, 1H), 6.37 (d, *J*=9.0 Hz, 2H), 6.66 (d, *J*=9.0 Hz, 2H), 6.68–7.41 (m, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.6, 34.3, 47.7, 50.1, 55.2, 55.7, 56.0, 114.3, 114.6, 115.1, 115.3, 124.2, 124.3, 125.8, 127.5, 127.6, 127.7, 128.07, 128.13, 128.4, 130.9, 131.0, 132.8, 141.0, 141.4, 152.0, 159.0, 161.5; HRMS calcd for $C_{25}H_{26}FNO$: 375.1998; Found *m*/*z* (relative intensity): 375.1976 (M^+, 100).

4.3.1.15. (*E*)-*N*-(1-(4-Fluorophenyl)-3-methyl-5-phenylpent-3-enyl)-4-methoxybenzenamine (1n). IR (neat) 3387 (w), 2924 (m), 1605 (w), 1512 (s), 1234 (s), 1034 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.75 (s, 3H), 2.32 (dd, *J*=13.8, 9.9 Hz, 1H), 2.48 (dd, *J*=13.8, 4.9 Hz, 1H), 3.34 (dd, *J*=15.4, 7.4 Hz, 1H), 3.43 (dd, *J*=15.4, 7.4 Hz, 1H), 3.68 (s, 3H), 3.86 (br s, 1H), 4.28 (dd, *J*=9.9, 4.9 Hz, 1H), 5.49 (br t, *J*=7.4 Hz, 1H), 6.32 (d, *J*=9.0 Hz, 2H), 6.65 (d, *J*=9.0 Hz, 2H), 6.97 (t, *J*=8.6 Hz, 2H), 7.13 (d, *J*=8.6 Hz, 2H), 7.19–7.33 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.8, 34.4, 50.2, 55.8, 56.0, 114.6, 114.7,

115.2, 115.5, 125.9, 127.50, 127.53, 127.6, 127.8, 127.9, 128.2, 128.5, 132.7, 140.25, 140.27, 141.0, 141.8, 152.0, 160.5, 162.9; HRMS calcd for $C_{25}H_{26}FNO$: 375.1998; Found *m/z* (relative intensity): 375.1988 (M^+, 100).

4.3.1.16. (*E*)-4-Chloro-*N*-(1-(furan-2-yl)-3-methyl-5-phenylpent-3-enyl)benzenamine (1p). IR (neat) 3408 (w), 3026–2853 (w), 1601 (m), 1499 (s), 1313 (s), 1005 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.68 (s, 3H), 2.51 (dd, J=13.6, 8.7 Hz, 1H), 2.67 (dd, J=13.6, 5.7 Hz, 1H), 3.33 (dd, J=15.7, 7.7 Hz, 1H), 3.39 (dd, J=15.7, 7.7 Hz, 1H), 3.93 (br s, 1H), 4.50 (dd, J=8.7, 5.7 Hz, 1H), 5.48 (br t, J=7.7 Hz, 1H), 6.12 (d, J=3.3 Hz, 1H), 6.27 (dd, J=3.3, 1.8 Hz, 1H), 6.42 (d, J=8.8 Hz, 2H), 7.05 (d, J=8.8 Hz, 2H), 7.13 (d, J=7.5 Hz, 2H), 7.19 (t, J=7.5 Hz, 1H), 7.26 (d, J=7.5 Hz, 2H), 7.32 (d, J=7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.7, 34.3, 45.6, 50.4, 106.0, 110.2, 114.5, 122.4, 126.0, 127.9, 128.3, 128.6, 128.9, 132.1, 141.1, 141.5, 146.0, 155.9; HRMS calcd for $C_{22}H_{22}ClNO$: 351.139; Found *m/z* (relative intensity): 351.13850 (M^+, 100).

4.3.1.17. (*E*)-4-Methoxy-*N*-(3-methyl-1-phenyldodec-2-en-5-yl)benzenamine (1q). IR (neat) 3395 (w), 2924 (s), 1604 (w), 1512 (s), 1242 (m), 1041 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, a major isomer is assigned) δ 0.87 (t, J=6.9 Hz, 3H), 1.26–1.51 (m, 12H), 1.71 (s, 3H), 2.22 (d, J=5.9 Hz, 2H), 3.35 (d, J=7.3 Hz, 3H), 3.74 (br s, 1H), 5.40 (t, J=7.3 Hz, 1H), 6.51 (d, J=8.8 Hz, 2H), 6.75 (d, J=8.8 Hz, 2H), 7.13–7.28 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1, 16.3, 22.6, 25.8, 29.3, 29.8, 31.8, 34.3, 34.9, 45.3, 46.4, 52.3, 55.8, 114.5, 125.6, 126.1, 128.2, 128.3, 133.5, 141.3; HRMS calcd for $C_{26}H_{37}NO$: 379.2875; Found *m/z* (relative intensity): 379.2799 (M^+, 100).

4.3.1.18. (*E*)-*N*-(2,5-Dimethyl-7-phenylhept-5-en-3-yl)-4-methoxybenzenamine (1r). A mixture of **1r** and **1r′** in a ratio of 2:1; IR (neat) 3402 (w), 2955 (m), 1605 (w), 1512 (s), 1234 (m), 1041 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.90 (d, J=6.9 Hz, 3H), 0.95 (d, J=6.9 Hz, 3H), 1.67 (s, 3H), 1.96 (br hept, J=6.9 Hz, 1H), 2.05 (dd, J=13.7, 9.5 Hz, 1H), 2.27 (dd, J=13.7, 4.6 Hz, 1H), 3.29 (ddm, J=9.5, 4.6 Hz, 1H), 3.30 (m, 1H, coalescing to d, J=15.0 Hz by irradiation at 5.40), 3.35 (m, 1H, coalescing to d, J=15.0 Hz by irradiation at 5.40), 3.74 (s, 3H), 5.40 (t, J=7.6 Hz, 1H), 6.49 (d, J=8.8 Hz, 2H), 6.74 (d, J=8.8 Hz, 2H), 7.09–7.27 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.1, 18.07, 18.15, 30.7, 34.4, 41.5, 55.9, 56.9, 114.1, 114.9, 125.7, 126.0, 128.2, 128.3, 133.9, 136.3, 140.2, 141.3, 142.9, 151.4.

4.3.1.19. (*E*)-*N*-(2,6-Dimethyl-7-phenylhept-5-en-3-yl)-4-methoxybenzenamine (1r′). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.94 (d, J=6.8 Hz, 3H), 0.97 (d, J=6.8 Hz, 3H), 1.51 (s, 3H), 1.89 (dhept, J=4.9, 6.8 Hz, 1H), 2.15 (dt, J=14.5, 7.3 Hz, 1H), 2.27 (dm, J=14.5 Hz, 1H), 3.15 (dt, J=7.3, 4.9 Hz, 1H), 3.26 (s, 2H), 3.74 (s, 3H), 5.30 (t, J=7.3 Hz, 1H), 6.52 (d, J=8.9 Hz, 2H), 6.75 (d, J=8.9 Hz, 2H), 7.09–7.27 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.1, 18.5, 18.9, 30.1, 31.1, 46.5, 59.8, 114.3, 114.9, 123.3, 125.9, 128.1, 128.7, 133.9, 140.2, 141.3, 142.9, 151.4; HRMS calcd for $C_{22}H_{29}NO$: 323.2249; Found *m/z* (relative intensity): 323.2233 (M^+, 100).

4.4. New compounds listed in Table 2

4.4.1. A typical procedure for the four-component connection reaction of Ph_2Zn, isoprene, tetrahydro-*2H*-pyran-2-ol, and *p*-anisidine (run 5, Table 2). Into a N_2 purged two-necked round-bottomed flask containing *p*-anisidine (246 mg, 2.0 mmol), were added dry THF (2.0 mL) and 2-hydroxytetrahydropyran (102 mg, 1.0 mmol) via syringe. The mixture was stirred at room temperature. 2-*p*-Anisidyltetrahydropyran was detected by TLC (R_f=0.56, *n*-hexane/ethyl acetate = 2:1, v/v). A solution of $Ni(acac)_2$ (25.7 mg, 0.1 mmol) in THF (3.0 mL) was introduced into the lactamine solution via a cannula. Isoprene (400 μl, 4.0 mmol) and a Ph_2Zn solution (14.4 mL, 0.25 M, 3.6 mmol) were successively introduced via syringe and the homogeneous mixture was stirred for 2 h at room temperature. The reaction mixture was poured into ice-water (20 mL) and extracted with 30 mL of ethyl acetate. The water phase was extracted with ethyl acetate (2×20 mL). The combined organic extracts were washed with 2 M HCl (20 mL) and with satd $NaHCO_3$ (25 mL), and then dried ($MgSO_4$) and concentrated in vacuo. The residue was subjected to column chromatography over silica gel (eluent: *n*-hexane/ethyl acetate = 8:1, v/v) to give **5b** (R_f=0.66, *n*-hexane/ethyl acetate = 2:1, v/v) in 76% yield as a single isomer.

4.4.1.1. (*E*)-5-(4-Methoxyphenylamino)-7-methyl-9-phenylnon-7-en-1-ol (5b). IR (neat) 3387 (m), 2932 (s), 1736 (m), 1512 (s), 1450 (m), 1242 (s), 1042 (m), 818 (m), 741 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.24–1.59 (m, 7H), 1.71 (s, 3H), 2.23 (d, J=6.2 Hz, 2H), 3.35 (d, J=7.4 Hz, 2H), 3.39 (t, J=6.2 Hz, 1H), 3.60 (t, J=6.3 Hz, 2H), 3.74 (s, 3H), 5.40 (t, J=7.4 Hz, 1H), 6.50 (d, J=8.9 Hz, 2H), 6.75 (d, J=8.9 Hz, 2H), 7.14 (d, J=7.5 Hz, 2H), 7.17 (t, J=7.5 Hz, 1H), 7.26 (t, J=7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.4, 22.0, 32.9, 34.4, 34.7, 45.4, 52.1, 55.9, 62.8, 114.4, 115.0, 125.7, 126.3, 128.2, 128.4, 133.5, 141.3, 142.2, 151.7; HRMS calcd for $C_{23}H_{31}NO_2$: 353.2355; Found *m/z* (relative intensity): 353.2350 (M^+, 100).

4.4.1.2. (*E*)-4-(4-Methoxyphenylamino)-6-methyl-8-phenyloct-6-en-1-ol (4a). IR (neat) 3379 (m), 2931 (s), 1604 (m), 1512 (s), 1450 (m), 1234 (w), 740 (s), 702 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.44–1.66 (m, 4H), 1.69 (s, 3H), 2.16 (dd, J=6.9, 13.8 Hz, 1H), 2.25 (dd, J=6.9, 13.8 Hz, 1H), 2.79 (s, 1H), 3.34 (d, J=7.1 Hz, 2H), 3.39 (dd, J=4.4, 6.9 Hz, 1H), 3.56 (t, J=6.2 Hz, 2H), 3.71 (s, 3H), 5.39 (t, J=7.1 Hz, 1H), 6.51–7.25 (m, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.3, 29.2, 31.6, 34.3, 45.3, 51.5, 55.7, 62.8, 114.8, 115.0, 125.7, 126.4, 128.1, 128.3, 133.2, 141.2, 141.7, 152.0; HRMS calcd for $C_{22}H_{29}NO_2$: 339.2198; Found *m/z* (relative intensity): 339.2178 (M^+, 100).

4.4.1.3. (*E*)-6-Methyl-8-phenyl-4-(phenylamino)oct-6-en-1-ol (4b). IR (neat) 3394 (m), 2931 (s), 1604 (m), 1504 (s), 1434 (m), 1319 (w), 748 (s), 694 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.50–1.70 (m, 4H), 1.72 (s, 3H), 2.22 (dd, J=6.9, 13.5 Hz, 1H), 2.27 (dd, J=6.9, 13.5 Hz, 1H), 3.35 (dd, J=2.4, 7.4 Hz, 2H), 3.53 (dd, J=4.6, 6.9 Hz, 1H), 3.62 (t, J=6.0 Hz, 2H), 5.41 (t, J=7.4 Hz, 1H), 6.54–7.25 (m, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.4, 29.2,

31.4, 34.4, 45.5, 51.2, 63.0, 113.2, 117.1, 125.7, 126.5, 128.2, 128.4, 129.2, 133.2, 141.2, 147.7; HRMS calcd for $C_{21}H_{27}NO$: 309.2093; Found *m/z* (relative intensity): 309.2074 (M^+, 100).

4.4.1.4. (*E*)-4-(4-Chlorophenylamino)-6-methyl-8-phenyloct-6-en-1-ol (4c). IR (neat) 3402 (m), 2931 (s), 1596 (s), 1496 (s), 1450 (w), 1056 (w), 740 (s), 702 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.50–1.68 (m, 4H), 1.71 (s, 3H), 2.21 (d, J=6.8 Hz, 2H), 3.36 (dd, J=6.8, 15.6 Hz, 2H), 3.46 (dd, J=6.8, 10.0 Hz, 1H), 3.62 (t, J=6.0 Hz, 2H), 5.40 (t, J=6.8 Hz, 1H), 6.44–7.23 (m, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.3, 29.0, 31.4, 34.4, 45.4, 51.4, 62.9, 114.1, 121.5, 125.8, 126.8, 128.2, 129.0, 133.0, 141.2, 146.4; HRMS calcd for $C_{21}H_{26}ClNO$: 343.1703; Found *m/z* (relative intensity): 343.1696 (M^+, 83), 267 (100).

4.4.1.5. (*E*)-5-(2-Methoxyphenylamino)-7-methyl-9-phenylnon-7-en-1-ol (5a). IR (neat) 3418 (m), 2932 (s), 1597 (m), 1512 (s), 1458 (m), 1227 (m), 1034 (m), 733 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.24–1.59 (m, 7H), 1.72 (s, 3H), 2.23 (dd, J=13.6, 6.8 Hz, 1H), 2.30 (dd, J=13.6, 6.8 Hz, 1H), 3.34 (d, J=7.3 Hz, 2H), 3.50 (t, J=6.8 Hz, 1H), 3.59 (t, J=6.1 Hz, 2H), 3.77 (s, 3H), 5.41 (t, J=7.3 Hz, 1H), 6.59 (dd, J=7.7, 1.3 Hz, 1H), 6.61 (dd, J=7.7, 1.3 Hz, 1H), 6.74 (dd, J=7.7, 1.3 Hz, 1H), 6.83 (dt, J=7.7, 1.3 Hz, 1H), 7.12–7.17 (m, 3H), 7.22–7.26 (t, J=7.5, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.5, 22.0, 32.9, 34.3, 34.6, 45.4, 50.9, 55.4, 62.9, 109.6, 109.7, 115.6, 121.2, 125.6, 126.0, 128.2, 128.3, 133.4, 137.8, 141.3, 146.7; HRMS calcd for $C_{23}H_{31}NO_2$: 353.2355; Found *m/z* (relative intensity): 353.2356 (M^+, 100).

4.4.1.6. (*E*)-7-Methyl-9-phenyl-5-(phenylamino)non-7-en-1-ol (5c). IR (neat) 3400 (m), 2934 (s), 1601 (s), 1504 (s), 1452 (w), 1431 (w), 1072 (w), 746 (s), 694 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.40–1.61 (m, 7H), 1.72 (s, 3H), 2.24 (d, J=6.1 Hz, 2H), 3.35 (d, J=7.3 Hz, 2H), 3.50 (t, J=6.1 Hz, 1H), 3.60 (t, J=6.2 Hz, 2H), 5.41 (t, J=7.3 Hz, 1H), 6.53 (d, J=8.1 Hz, 2H), 6.65 (t, J=7.3 Hz, 1H), 7.12–7.15 (m, 5H), 7.24–7.28 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.3, 21.9, 32.8, 34.3, 34.6, 45.3, 51.0, 62.8, 112.8, 116.7, 125.7, 126.3, 128.2, 128.3, 129.1, 133.3, 141.2, 147.8; HRMS calcd for $C_{22}H_{29}NO$: 323.2249; Found *m/z* (relative intensity): 324.2247 (M^+, 22), 323 (46).

4.4.1.7. (*E*)-4-(*p*-Tolylamino)-6-methyl-8-phenyloct-6-en-1-ol (5d). IR (neat) 3394 (m), 2931 (s), 1620 (m), 1519 (s), 1450 (m), 1319 (w), 732 (s), 702 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.57–1.63 (m, 6H), 1.81 (s, 3H), 2.32 (d, J=7.8 Hz, 2H), 2.32 (s, 3H), 3.44 (dd, J=2.8, 7.3 Hz, 2H), 3.55 (dd, J=7.8, 11.7 Hz, 1H), 3.65 (t, J=6.3 Hz, 2H), 5.49 (t, J=7.3 Hz, 1H), 6.54–7.25 (m, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.9, 20.0, 21.6, 32.4, 34.0, 45.0, 50.1, 62.3, 112.7, 125.3, 125.5, 125.9, 127.8, 127.9, 129.3, 133.0, 140.9, 145.2; HRMS calcd for $C_{23}H_{31}NO$: 337.2406; Found *m/z* (relative intensity); 337.2391 (M^+, 9), 64.17 (1), 192.14 (100).

4.4.1.8. (*E*)-5-(2-Fluorophenylamino)-7-methyl-9-phenylnon-7-en-1-ol (5e). IR (neat) 3418 (m), 2932 (s), 1620 (m), 1520 (s), 1450 (m), 1335 (m), 740 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.26–1.64 (m, 7H), 1.71 (s, 3H), 2.26 (d, J=6.3 Hz, 2H), 3.34 (d, J=7.3 Hz, 2H), 3.52 (t, J=6.3 Hz, 1H), 5.41 (t, J=7.3 Hz, 2H), 6.56 (q, J=7.6 Hz, 1H), 6.67 (t, J=8.5 Hz, 1H), 6.92 (d, J=8.5 Hz, 1H), 6.95 (t, J=7.3 Hz, 1H), 7.12 (d, J=7.3 Hz, 2H), 7.16 (t, J=7.3 Hz, 1H), 7.25 (t, J=7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.3, 22.0, 32.7, 34.2, 34.7, 45.4, 51.0, 62.7, 111.9, 111.94, 114.3, 114.5, 115.7, 115.8, 124.36, 124.39, 125.6, 126.4, 128.1, 128.2, 132.9, 136.2, 136.4, 141.1, 150.2, 152.6; HRMS calcd for $C_{22}H_{28}FNO$: 341.2155; Found *m/z* (relative intensity): 341.2141 (M^+, 100).

4.4.1.9. (*E*)-5-(4-Fluorophenylamino)-7-methyl-9-phenylnon-7-en-1-ol (5f). IR (neat) 3395 (s), 2932 (s), 1647 (w), 1512 (s), 1450 (w), 1219 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.26–1.57 (m, 6H), 1.70 (s, 3H), 2.21 (t, J=6.2 Hz, 2H), 3.34 (d, J=7.1 Hz, 2H), 3.39 (t, J=6.2 Hz, 1H), 3.57 (t, J=6.3 Hz, 2H), 5.39 (t, J=7.1 Hz, 1H), 6.43 (dd, J=8.8, 4.4 Hz, 2H), 6.83 (t, J=8.8 Hz, 2H), 7.12 (d, J=7.3 Hz, 2H), 7.16 (t, J=7.3 Hz, 1H), 7.24 (t, J=7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.3, 22.0, 32.7, 34.3, 34.7, 45.3, 51.9, 62.6, 113.6, 113.7, 115.4, 115.6, 125.7, 126.4, 128.1, 128.3, 133.2, 141.2, 144.24, 144.26, 154.1, 156.5; HRMS calcd for $C_{22}H_{28}FNO$: 341.2155; Found *m/z* (relative intensity): 341.2146 (M^+, 100).

4.4.1.10. (*E*)-5-(2-Chlorophenylamino)-7-methyl-9-phenylnon-7-en-1-ol (5g). IR (neat) 3410 (s), 2932 (s), 1597 (s), 1512 (s), 1458 (m), 1327 (m), 1034 (m), 741 (s), 694 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.22–1.67 (m, 7H), 1.72 (s, 3H), 2.29 (d, J=6.3 Hz), 3.34 (d, J=7.3 Hz, 2H), 3.55 (q, J=6.3 Hz, 1H), 3.61 (t, J=5.7 Hz, 2H), 4.15 (d, J=7.3 Hz, 1H), 5.43 (t, J=7.3 Hz, 1H), 6.57 (t, J=7.6 Hz, 1H), 6.63 (d, J=7.6 Hz, 1H) 7.07–7.18 (m, 3H), 7.21–7.26 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.4, 22.0, 32.8, 34.4, 34.6, 45.3, 51.2, 62.8, 111.1, 116.5, 119.1, 125.7, 126.6, 128.2, 128.3, 129.2, 132.9, 141.2, 143.6; HRMS calcd for $C_{22}H_{28}ClNO$: 357.1859; Found *m/z* (relative intensity): 357.1848 (M^+, 100).

4.4.1.11. (*E*)-5-(4-Chlorophenylamino)-7-methyl-9-phenylnon-7-en-1-ol (5h). IR (neat) 3404 (m), 2936 (s), 1599 (s), 1497 (s) 1319 (m), 814 (m), 743 (m), 698 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.39–1.58 (m, 6H), 1.71 (s, 3H), 2.19 (d, J=13.7, 7.6 Hz, 1H), 2.26 (dd, J=13.7, 6.0 Hz, 1H), 3.34 (dd, J=7.3 Hz, 2H), 3.43 (dd, J=7.6, 6.0 Hz, 1H), 3.60 (t, J=6.3 Hz, 2H), 5.40 (t, J=7.3 Hz, 1H), 6.43 (d, J=8.8 Hz, 2H), 7.06 (d, J=8.8 Hz, 2H), 7.12 (d, J=7.3 Hz, 2H), 7.17 (t, J=7.3 Hz, 1H), 7.25 (t, J=7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.3, 22.0, 32.8, 34.4, 34.7, 45.3, 51.4, 62.8, 113.9, 121.2, 125.8, 126.6, 128.2, 128.4, 129.0, 133.1, 141.2, 146.5; HRMS calcd for $C_{22}H_{28}ClNO$: 357.1859; Found *m/z* (relative intensity): 357.1844 (M^+, 100).

4.4.1.12. (*E*)-5-(2-Bromophenylamino)-7-methyl-9-phenylnon-7-en-1-ol (5i). IR (neat) 3402 (s), 2932 (m), 1597 (s), 1504 (s), 1458 (m), 1319 (m), 1281 (w), 1018 (w), 741 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.43–1.69 (m, 6H), 1.72 (s, 3H), 2.29 (dd, J=6.5, 3.4 Hz, 2H),

3.35 (d, J=7.3 Hz, 2H), 3.56 (quintet, J=6.5 Hz, 1H), 3.61 (t, J=6.5 Hz, 2H), 4.17 (d, J=7.4 Hz, 2H), 5.44 (t, J=7.4 Hz, 1H), 6.50 (t, J=7.6 Hz, 1H), 6.61 (d, J=8.0 Hz, 1H), 7.11–7.18 (m, 4H), 7.24 (t, J=7.3 Hz, 2H), 7.39 (d, J=8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.5, 22.0, 32.8, 34.4, 34.6, 45.3, 51.4, 62.8, 109.9, 111.3, 117.0, 125.7, 126.7, 128.25, 128.30, 128.32, 132.5, 132.9, 141.1, 144.5; HRMS calcd for $C_{22}H_{28}BrNO$: 401.1354; Found *m/z* (relative intensity): 401.1342 (M^+, 100).

4.4.1.13. (*E*)-5-(4-Bromophenylamino)-7-methyl-9-phenylnon-7-en-1-ol (5j). IR (neat) 3402 (m), 2932 (s), 1597 (m), 1497 (s), 1450 (w), 1319 (w), 1072 (w), 741 (w), 694 (w) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.26–1.49 (m, 6H), 1.63 (s, 3H), 2.11 (dd, J=13.1, 7.6 Hz, 1H), 2.19 (dd, J=13.1, 5.9 Hz, 1H), 3.27 (dd, J=6.9 Hz, 4.3 Hz, 2H), 3.37 (br s, 1H), 3.53 (t, J=6.3 Hz, 2H), 5.32 (t, J=6.9 Hz, 1H), 6.31 (d, J=8.8 Hz, 2H), 7.04 (d, J=7.3 Hz, 2H), 7.10 (t, J=7.3 Hz, 1H), 7.12 (d, J=8.8 Hz, 2H), 7.19 (t, J=7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.3, 22.0, 32.8, 34.4, 34.7, 45.3, 51.3, 62.8, 108.2, 114.3, 125.8, 126.7, 128.2, 128.4, 131.9, 141.2, 146.9; HRMS calcd for $C_{22}H_{28}BrNO$: 401.1354; Found *m/z* (relative intensity): 401.1338 (M^+, 100).

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