Three-Component Synthesis of Homoallylic Amines Promoted by Carboxylic Acids

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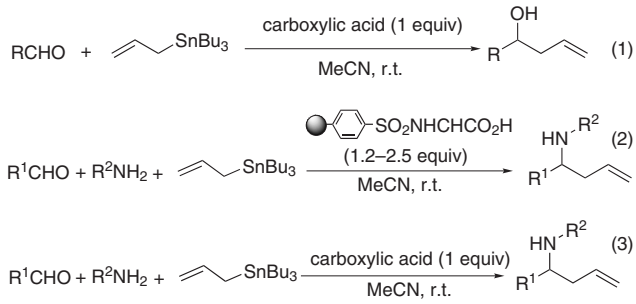
Abstract: A highly selective, three-component reaction promoted by carboxylic acids for the synthesis of homoallylic amines has been developed. By using maleic acid or trifluoroacetic acid as a promoter, the reaction between a variety of aldehydes, aromatic amines, and allyltin reagents proceeds smoothly to afford the corresponding homoallylic amines in moderate to quantitative yields under mild conditions.

Key words: allylations, carboxylic acids, imines, multicomponent reactions, tin



Scheme 1

The allylation of imines is an important method for the synthesis of synthetically useful homoallylic amines. Among several allylic metal reagents containing group 14 elements (e.g., Si, Ge, Sn), allyltin reagents have been the subject of extensive studies due to their good stability and reactivity.[1] In general, the allylation of imines with allyltributyltin is carried out in the presence of Lewis acids;[2] palladium [$PdCl_2(PPh_3)_2$] and platinum [$PtCl_2(PPh_3)_2$] complexes have also been utilized to catalyze this reaction.[3] The three-component reaction (aldehydes, amines, and allyltributyltin), which does not require the initial preparation of the imine, is a convenient method for the synthesis of homoallylic amines. However, as we know, traditional Lewis acids are ineffective in the three-component reaction because they decompose or lose their activity in the presence of water and amines.[4] Additionally, the selective allylation of imines is not so easy in the presence of an aldehyde.[2e] In recent years, a number of methods for the three-component reaction have been reported,[5] especially those using metal triflate salts as catalysts that are water tolerant, which provide good results.[5a,5b,5e,5f]

Recently, we found that carboxylic acids are efficient promoters of the allylation of aldehydes under mild conditions (Scheme 1, equation 1).[6] In this reaction, we proposed that the aldehydes might be activated by a hydrogen bond formed with the carboxylic acid. In addition, we reported that the polymer-supported sulfonamide of glycine is a highly efficient promoter for the allylation of aldehydes and it is also an efficient promoter for the three-component reaction of aldehydes, amines, and allyltributyltin (Scheme 1, equation 2).[7] Herein, we describe a detailed study of the three-component reaction promoted by commercially available carboxylic acids (Scheme 1, equation 3).

In an initial experiment to investigate the carboxylic acid mediated three-component reaction, we used 4-nitrobenzoic acid (1.0 equiv) as a promoter with benzaldehyde (1.0 equiv), aniline (1.0 equiv), and allyltributyltin (1.2 equiv) as the model substrates; 4-nitrobenzoic acid was selected as the promoter because it was found to be the best promoter for the allylation of aldehydes in acetonitrile.[6] The reaction proceeded rapidly and afforded homoallylic amine **5a** as the major product (81% yield) in five hours, however, the corresponding homoallylic alcohol **4a** was also observed (19% yield, Table 1, entry 5).

In a previous report, we demonstrated clearly that the acidity of the promoter is a crucial factor in the carboxylic acid mediated allylation of aldehydes.[6] Weak carboxylic acids ($pK_a \geq 4.2$) are almost inactive in the allylation of aldehydes. Therefore, we selected various weak carboxylic acids to improve the chemoselectivity. The results are summarized in Table 1. It is apparent that the selectivity of the reaction improves with increasing pK_a values from 4-nitrobenzoic acid (entry 5), 4-fluorobenzoic acid (entry 3), to 4-hydroxybenzoic acid (entry 1). As expected, the homoallylic amine was the sole product when using benzoic acid as a promoter ($pK_a \geq 4.2$), but the yield decreased and the reaction time was prolonged (entries 1 and 2). On the other hand, some strong carboxylic acids ($pK_a \leq 3.42$) were also screened in the three-component reaction. Very high chemoselectivity was obtained when stronger acids ($pK_a \leq 2.98$, entries 6–8) were used as promoters. The maleic acid mediated three-component reaction provided homoallylic amine **5a** in quantitative yield, and no homoallylic alcohol **4a** was observed (by ^1H NMR).

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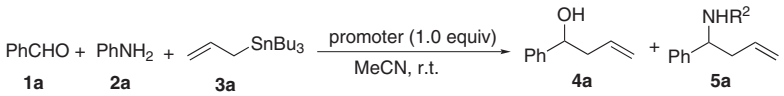
Table 1 The Effect of Various Carboxylic Acids on the Three-Component Reaction[a]



1a 2a 3a 4a 5a

Entry	Promoter	pK_a	Time	Yield[b] (%)	
				4a	**5a**
1	4-$HOC_6H_4CO_2H$	4.57	19 h	<1	>79
2	$PhCO_2H$	4.20	23 h	–[c]	74
3	4-$FC_6H_4CO_2H$	4.14	19 h	12	69
4	4-$ClC_6H_4CO_2H$	4.0	19 h	18	53
5	4-$O_2NC_6H_4CO_2H$	3.42	5 h	19	81
6	2-$HOC_6H_4CO_2H$	2.98	30 min	–[c]	84
7	1,2-$C_6H_4(CO_2H)_2$	2.89	30 min	–[c]	98
8	maleic acid	1.92	30 min	–[c]	quant.

[a] Ratio **1a/2a/3a** = 1.0:1.0:1.2 (equiv).
[b] Isolated yield or determined by ^{1}H NMR.
[c] No **4a** was observed.

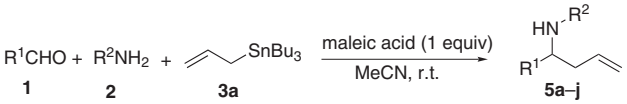
The scope of the carboxylic acid mediated three-component reaction was evaluated after optimum reaction conditions had been established; using maleic acid as a promoter, a set of aldehydes was investigated. As shown in Table 2, the electronic nature of the substituents on aromatic aldehydes has little influence on the reaction. High to quantitative yields were obtained in various cases (90–100%, entries 1–3, 6). The reaction of 2-furaldehyde also provided the corresponding homoallylic amine **5d** in good yield (entry 4). The three-component reaction of the cyclic aliphatic aldehyde cyclohexanecarbaldehyde gave **5e** in good yield (entry 5); however, the linear aliphatic aldehyde nonanal gave only a trace amount of the desired product and an enolization byproduct was observed by ^{1}H NMR (entry 13).[5i,8] A variety of amines were also tested. Obviously, the reaction of aromatic amines bearing an electron-donating group is highly efficient and excellent yields resulted (93–100%, entries 7, 8, 9). When 4-nitroaniline was used as the substrate, we isolated two allylation products, homoallylic amine **5j** and alcohol **4j** (ratio **5j/4j** 1.4:1.0, entry 10); however, by using the strong acid trifluoroacetic acid as a promoter, **5j** was obtained from 4-nitroaniline with high chemoselectivity (with no **4j**) and in 81% yield (entry 11). Finally, when aliphatic amines such as 2-phenylethanamine were used, none of the desired product was produced (entry 13).

The three-component reaction of substituted allyltin reagents was further investigated. As shown in Table 3, all the reactions of substituted allyltin reagents proceeded smoothly and afforded the γ-adduct exclusively in moderate to high yields (entries 1–4). The reaction favored the formation of the *syn*-isomer (ratio *syn*/*anti* ~ 3:1, entries 1–3) except allyltin **3e** (*syn*/*anti* = 49:51, entry 4).

In the carboxylic acid mediated three-component reaction, both aldehyde and imine could be activated by the hydrogen bonding formed with the carboxylic acid (**I** and **II**, Path A, Scheme 2). As a result, homoallylic alcohol **4** and homoallylic amine **5** were produced simultaneously in the cases of in which 4-fluorobenzoic acid, 4-chlorobenzoic acid, and 4-nitrobenzoic acid were used as promoters ($3.42 \le pK_a \le 4.14$; Table 1, entries 3–5). On the other hand, the carboxylic acids (especially strong acids; $pK_a \le 2.98$; Table 1, entries 6–8) could form the iminium ion with imines selectively, and then the thus-produced iminium ion underwent nucleophilic attack by allyltin reagents and to provide the homoallylic amine adduct **5** exclusively.[9] This result could be explained by the fact that the activation of an iminium ion to form an imine by strong carboxylic acid is much stronger than that by forming a hydrogen bond with an aldehyde (**III**, Path B, Scheme 2).

The γ-adduct and *syn*-isomer selective results could be understood through an acyclic antiperiplanar transition state.[2c,2g,2h] In the carboxylic acid mediated allylation of imines, firstly, the imine was activated by the formation of the iminium salt with a carboxylic acid. Then, of the possible geometries, the antiperiplanar (**a**, Figure 1) will be the most favorable transition state, which has less steric crowding compared with the other five possible geometries (steric crowding order: **a** < **d** <**b**, **c**, **e**, **f**.), as a result, the *syn*-isomer was produced as the major adduct. The *anti*-adduct as the minor product could be explained by the fact that compared with strong Lewis acids, such as boron trifluoride–diethyl ether complex, the proton of the carboxylic acid is a small Lewis acid. The very low stereoselectivity provided by allyltin **3e** may be due to the

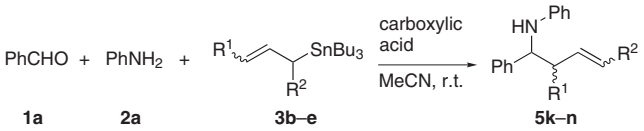
Table 2 The Scope of the Three-Component Reaction Promoted by Carboxylic Acids[a]



Entry	R^1	R^2	Time (min)	Product **5**	Yield[b] (%)
1	Ph	Ph	30	**5a**	100
2	4-$O_2NC_6H_4$	Ph	50	**5b**	90
3	3-$MeOC_6H_4$	Ph	50	**5c**	97
4	2-furyl	Ph	50	**5d**	71
5	Cy	Ph	50	**5e**	73
6	2,4-$Cl_2C_6H_3$	Ph	40	**5f**	97
7	Ph	3,4,5-$(MeO)_3C_6H_2$	50	**5g**	95
8	Ph	4-FC_6H_4	50	**5h**	100
9	Ph	4-$MeOC_6H_4$	50	**5i**	93
10	Ph	4-$O_2NC_6H_4$	50	**5j**	63[c]
11	Ph	4-$O_2NC_6H_4$	50	**5j**	81[d]
12	*n*-C_8H_{17}	Ph	50	–	trace
13	Ph	CH_2CH_2Ph	3 d	–	–[e]

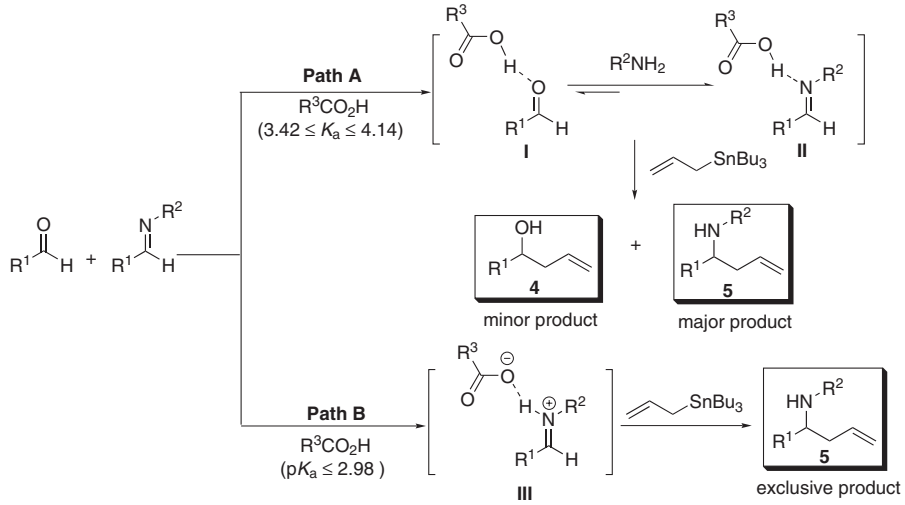
[a] Ratio **1/2/3** = 1.0:1.0:1.2 (equiv).
[b] Isolated yield.
[c] Two products were isolated, with the ratio of **5j/4j** = 1.4:1.0.
[d] Maleic acid and TFA were used as promoters.
[e] No desired product was observed.

Table 3 The Three-Component Reaction of Benzaldehyde, Aniline, and Substituted Allyltin Promoted by Carboxylic Acids



Entry	Allyltin	R^1	R^2	Carboxylic acid	Time (h)	Product	Ratio[a] *syn*/*anti*	Yield[b] (%)
1	**3b**[c]	Me	H	TFA	0.5	**5k**	73:27	quant.
2	**3c**[d]	Ph	H	maleic acid	1.0	**5l**	74:26	97
3	**3d**[e]	4-$MeOC_6H_4O$	H	maleic acid	2.0	**5m**	82:18	67
4	**3e**[d]	Me	OMOM	maleic acid	2.0	**5n**	49:51	52

[a] Determined by ^1H NMR.
[b] Total isolated yield.
[c] *E*/*Z* 85:15.
[d] *E*-Isomer.
[e] *Z*-Isomer.



Scheme 2

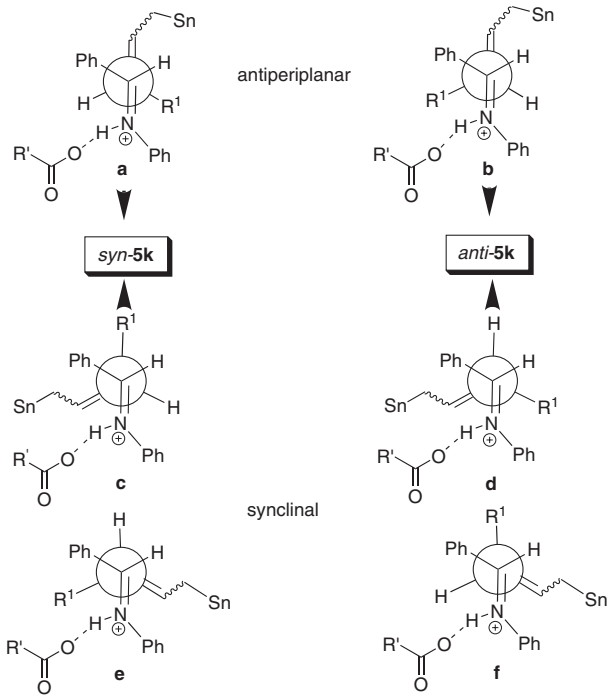


Figure 1 Acyclic transition states geometries proposed for the carboxylic acid mediated allylation of imines.

possible hydrogen bonding between the oxygen of the α-substituted group (adjoining tin atom) and the iminium ion.

In conclusion, a highly selective three-component reaction promoted by carboxylic acids has been developed for the synthesis of homoallylic amines. By using commercially available maleic acid or trifluoroacetic acid as a promoter, the three-component reactions between a variety of aldehydes, aromatic amines, and allyltin reagents proceed smoothly to afford the corresponding homoallylic amines in moderate to quantitative yields under mild reaction conditions.

Allyltin reagents **3a**,[10] **3b**,[11] **3c**,[12] **3d**,[13] and **3e**[14] were prepared according to the reported literature. Commercially available carboxylic acids and MeCN were used without purification. Other solvents and reagents were purified under standard methods. Petroleum ether refers to the fraction boiling in the range 60–90 °C. Flash column chromatography was performed on silica gel (300–400 mesh, Qingdao, China). Melting points were measured on a Mettler FP62 or WRS-1A apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on EM-360A or Bruker-AM-300 300 MHz spectrometers with TMS as an internal standard. LRMS were obtained on a HP-5989A mass spectrometer. HRMS were performed on Fingian MAT8403 mass spectrometer.

N-(1-Phenylbut-3-enyl)aniline (5a); Typical Procedure

Benzaldehyde (53 mg, 0.5 mmol), aniline (47 mg, 0.5 mmol), maleic acid (58 mg, 0.5 mmol), and allyltributyltin (198 mg, 0.6 mmol) were added to MeCN (1.0 mL). The mixture was stirred at r.t. The reaction was monitored by TLC and when complete it was quenched with 2.0 M NaOH (2.0 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to furnish the crude product, which was purified by chromatography (silica gel, typical eluent: petroleum ether–EtOAc, 100:1) to afford homoallylic amine **5a**[5h] as a yellow oil; yield: 112 mg (100%).

IR (KBr, film): 3412, 3054, 2914, 1639, 1602, 1504, 1316, 920, 749 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.20 (m, 5 H), 7.10–7.04 (m, 2 H), 6.66–6.61 (m, 1 H), 6.50–6.47 (m, 2 H), 5.77–5.71 (m, 1 H), 5.21–5.12 (m, 2 H), 4.35 (s, 1 H), 4.15 (s, 1 H), 2.45–2.61 (m, 2 H).

N-[1-(4-Nitrophenyl)but-3-enyl]aniline (5b)[5h]

Yellow oil.

IR (KBr, film): 3410, 3077, 3021, 2979, 2914, 2853, 1640, 1603, 1518, 1344, 1289, 1108, 993, 854, 750 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.19–8.15 (m, 2 H), 7.55–7.51 (m, 2 H), 7.10–7.05 (m, 3 H), 6.70–6.65 (m, 1 H), 6.44–6.41 (dd, *J* = 7.5, 1.5 Hz, 2 H), 5.80–5.66 (m, 1 H), 5.24–5.17 (m, 2 H), 4.47 (s, 1 H), 4.24 (s, 1 H), 2.65–2.57 (m, 2 H).

N-[1-(3-Methoxyphenyl)but-3-enyl]aniline (5c)[7]

Yellow oil.

IR (KBr, film): 3048, 3015, 2935, 1639, 1602, 1501, 1266, 750 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26–7.24 (m, 2 H), 7.11–7.05 (m, 2 H), 6.97–6.92 (m, 2 H), 6.78–6.75 (m, 1 H), 6.66–6.61 (m, 1 H), 6.51–6.47 (m, 1 H), 5.81–5.71 (m, 1 H), 5.22–5.12 (m, 2 H), 4.31 (q, *J* = 5.1, 2.7, 5.3 Hz, 1 H), 4.13 (m, 1 H), 3.80 (s, 3 H), 2.63–2.56 (m, 1 H), 2.52–2.45 (m, 1 H).

N-[1-(2-Furyl)but-3-enyl]aniline (5d)[5h]
Pale yellow oil.

IR (KBr, film): 3411, 3035, 2921, 1640, 1603, 1504, 922, 749 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34 (s, 1 H), 7.16–7.11 (m, 2 H), 6.67 (t, *J* = 7.5 Hz, 1 H), 6.59 (d, *J* = 7.3 Hz, 2 H), 6.27 (d, *J* = 1.8 Hz, 1 H), 6.15 (s, 1 H), 5.79–5.70 (m, 1 H), 5.11 (t, *J* = 8.9, 15.9 Hz, 2 H), 4.53 (t, *J* = 6.0 Hz, 1 H), 3.98 (s, 1 H), 2.63 (t, *J* = 4.1, 7.1 Hz, 2 H).

N-(1-Cyclohexylbut-3-enyl)aniline (5e)[5i]
Pale yellow oil.

IR (KBr, film): 3412, 3053, 2961, 2926, 2853, 1640, 1601, 1505, 1259, 1005, 789, 691 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.16 (td, *J* = 2.1, 5.2, 1.1 Hz, 2 H), 6.65–6.54 (m, 3 H), 5.85–5.73 (m, 1 H), 5.08–5.02 (m, 2 H), 3.52 (s, 1 H), 3.28 (q, *J* = 5.4, 6.9, 5.3 Hz, 1 H), 2.37–2.32 (m, 1 H), 2.22–2.12 (m, 1 H), 1.85–1.04 (m, 11 H).

N-[1-(2,4-Dichlorophenyl)but-3-enyl]aniline (5f)
Pale yellow oil; R_f = 0.79 (petroleum ether–EtOAc, 50:1).

IR (KBr, film): 3414, 3079, 3053, 3020, 2979, 2918, 1639, 1603, 1588, 1500, 1468, 1315, 1266, 1046, 819, 749, 692 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.32–2.42 (m, 1 H), 2.62–2.71 (m, 1 H), 4.16 (d, *J* = 3.7 Hz, 1 H), 4.74–4.80 (m, 1 H), 5.17–5.25 (m, 2 H), 5.69–5.81 (m, 1 H), 6.39 (d, *J* = 8.6 Hz, 2 H), 6.64 (t, *J* = 7.7, 7.1 Hz, 1 H), 7.05–7.17 (m, 3 H), 7.35–7.40 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 40.7, 53.4, 113.4, 118.0, 119.0, 127.6, 128.7, 129.3, 129.6, 133.2, 133.3, 134.0, 139.1, 146.6.

LRMS (ESI): *m/z* = 292.0 (M^+).

HRMS (EI): *m/z* calcd for $C_{16}H_{15}Cl_2N$: 291.0582; found: 291.0581.

3,4,5-Trimethoxy-N-(1-phenylbut-3-enyl)aniline (5g)[7]
Pale yellow solid; mp 63–65 °C.

IR (KBr): 3384, 3062, 2998, 2934, 2840, 1639, 1611, 1510, 1453, 1237, 1127, 1010, 911, 732 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39–7.21 (m, 5 H), 5.84–5.73 (m, 1 H), 5.72 (s, 2 H), 5.23–5.15 (m, 2 H), 4.30 (q, *J* = 4.8, 3.2, 5.1 Hz, 1 H), 4.09 (s, 1 H), 3.70 (s, 3 H), 3.66 (s, 6 H), 2.63–2.56 (m, 1 H), 2.52–2.45 (m, 1 H).

4-Fluoro-N-(1-phenylbut-3-enyl)aniline (5h)[5h]
Pale yellow oil.

IR (KBr, film): 3415, 3062, 3030, 2977, 2912, 2855, 1639, 1613, 1509, 1221, 1315, 819, 702 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.37–2.56 (m, 2 H), 3.98 (br s, 1 H), 4.21–4.25 (m, 1 H), 5.06–5.14 (m, 2 H), 5.62–5.75 (m, 1 H), 6.31–6.36 (m, 2 H), 6.67–6.74 (m, 2 H), 7.15–7.31 (m, 5 H).

4-Methoxy-N-(1-phenylbut-3-enyl)aniline (5i)[5c]
Pale yellow oil.

IR (KBr, film): 3403, 3061, 2999, 2831, 1639, 1512, 1452, 1239, 1037, 819, 702 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.44–2.62 (m, 2 H), 3.67 (s, 3 H), 3.92 (br s, 1 H), 4.28–4.33 (m, 1 H), 5.12–5.21 (m, 2 H), 5.72–5.78 (m, 1 H), 6.44–6.48 (m, 2 H), 6.66–6.69 (m, 2 H), 7.20–7.38 (m, 5 H).

4-Nitro-N-(1-phenylbut-3-enyl)aniline (5j)[5i]
Pale yellow solid; mp 102–104 °C.

IR (KBr, film): 3351, 3080, 3001, 2874, 1641, 1601, 1533, 1483, 1304, 1282, 1111, 991, 831 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.53–2.66 (m, 2 H), 4.49 (t, *J* = 7.2, 5.4 Hz, 1 H), 4.95 (br s, 1 H), 5.18–5.25 (m, 2 H), 5.67–5.80 (m, 1 H), 6.42 (d, *J* = 6.9 Hz, 2 H), 7.25–7.37 (m, 5 H), 7.96 (d, *J* = 8.8 Hz, 2 H).

N-(2-Methyl-1-phenylbut-3-enyl)aniline (5k)[2c]
Pale yellow oil.

IR (KBr, film): 3414, 3054, 2967, 1930, 2872, 1638, 1602, 1504, 1452, 1317, 1282, 919, 748, 701 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) (mixture of *syn*- and *anti*-isomers): δ = 0.97 (d, *J* = 7.1 Hz, 3 H), 2.48–2.55 (m, 0.27 H) (*anti*), 2.64–2.71 (m, 0.73 H) (*syn*), 4.06 (d, *J* = 6.9 Hz, 0.27 H) (*anti*), 4.20 (br s, 1 H), 4.33 (d, *J* = 4.4 Hz, 0.73 H) (*syn*), 5.10–5.21 (m, 2 H), 5.675.79 (m, 1 H), 6.45 (d, *J* = 8.2 Hz, 2 H), 6.58 (t, *J* = 7.3 Hz, 1 H), 7.02–7.07 (m, 2 H), 7.19–7.36 (m, 5 H).

N-(1,2-Diphenylbut-3-enyl)aniline (5l)
White solid; mp 81–83 °C; R_f = 0.70 (petroleum ether–EtOAc, 8:1).

IR (KBr, film): 3404, 3083, 3053, 3022, 2869, 1636, 1601, 1501, 1452, 1311, 1265, 1076, 934, 747, 696 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) (mixture of *syn*- and *anti*-isomers): δ = 3.51 (t, *J* = 8.5 Hz, 0.26 H) (*anti*), 3.66 (t, *J* = 7.3, 8.1 Hz, 0.74 H) (*syn*), 4.13 (br s, 0.74 H) (*syn*), 4.47 (d, *J* = 7.8 Hz, 0.26 H) (*anti*), 4.58 (d, *J* = 6.9 Hz, 0.74 H) (*syn*), 4.92–5.26 (m, 2 H), 5.91–6.03 (m, 0.74 H) (*syn*), 6.11–6.23 (m, 0.24 H) (*anti*), 6.39–6.64 (m, 3 H), 6.98–7.29 (m, 12 H).

^{13}C NMR (75 MHz, $CDCl_3$) (mixture of *syn*- and *anti*-isomers): δ = 57.2 (*syn*), 58.4 (*anti*), 62.0 (*syn*), 62.4 (*anti*), 113.8, 117.6, 117.7, 118.2, 127.2, 127.3, 127.4, 127.9, 128.2, 128.2, 128.5, 128.6, 128.7, 128.7, 129.1, 129.2, 137.8 (*syn*), 138.7 (*anti*), 140.3 (*syn*), 140.8 (*anti*), 141.4 (*syn*), 142.0 (*anti*), 147.2 (*syn*), 147.4 (*anti*).

LRMS (ESI): *m/z* = 300.2 $(M + 1)^+$.

HRMS (MALDI): *m/z* calcd for $C_{22}H_{22}N^+$: 300.1740; found 300.1746.

N-[2-(4-Methoxyphenoxy)-1-phenylbut-3-enyl]aniline (5m)
Pale yellow oil; R_f = 0.57 (petroleum ether–EtOAc, 8:1).

IR (KBr, film): 3412, 3052, 3024, 2951, 2906, 2833, 1602, 1504, 1453, 1314, 1224, 1180, 1105, 1036, 993, 826, 750, 700 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) (mixture of *syn*- and *anti*-isomers): δ = 3.73 (s, 3 H), 4.58 (br 1 H), 4.65 (s, 1 H), 4.83 (t, *J* = 5.2, 3.8 Hz, 1 H), 5.27–5.36 (m, 2 H), 5.65–5.81 (m, 0.82 H) (*syn*), 5.86–5.92 (m, 0.18 H) (*anti*), 6.50–6.85 (m, 7 H), 7.04 (t, *J* = 8.2, 7.3 Hz, 2 H), 7.23–7.41 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$) (mixture of *syn* and *anti* isomers): δ = 55.7, 55.7, 61.1, 62.1, 83.4, 84.4, 113.9, 114.0, 114.6, 114.7, 117.7, 118.0, 118.1, 118.9, 119.1, 127.6, 127.6, 127.9, 128.5, 128.5, 129.2, 133.7, 135.5, 139.5, 140.5, 147.2, 147.5, 151.9, 152.2, 154.5, 154.6.

LRMS (ESI): *m/z* 346.2 $(M + 1)^+$.

HRMS (MALDI): *m/z* calcd for $C_{23}H_{23}NO_2^+$: 346.1811; found 346.1801.

N-[4-(Methoxymethoxy)-2-methyl-1-phenylbut-3-enyl]aniline (5n)
Pale yellow oil; R_f = 0.60 (petroleum ether–EtOAc, 8:1).

IR (KBr, film): 3412, 3025, 2960, 2929, 2828, 1663, 1602, 1504, 1452, 1314, 1159, 1036, 922, 749, 693 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) (mixture of *syn*- and *anti*-isomers): δ = 0.82 (d, *J* = 6.8 Hz, 0.51 H) (*anti*), 0.97 (d, *J* = 6.9 Hz, 0.49 H) (*syn*), 2.91–3.02 (m, 0.51 H), 3.25–3.32 (m, 0.49 H) (*syn*), 3.42 (d, *J* = 5.9 Hz, 3 H) (*anti*), 3.86 (d, *J* = 8.7 Hz, 0.51 H) (*anti*), 4.21–4.27 (m, 0.49 H) (*syn*), 4.32 (d, *J* = 3.9 Hz, 0.49 H) (*syn*), 4.42–4.48 (m, 0.51 H) (*anti*), 4.58 (br s, 1 H), 4.83 (s, 2 H), 6.20 (q, *J* = 6.2, 1 H), 6.41 (t, *J* = 8.8 Hz, 2 H), 6.55–6.60 (m, 1 H), 6.99 (t, *J* = 7.2, 8.6 Hz, 2 H), 7.19–7.40 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$) (mixture of *syn*- and *anti*-isomers): δ = 17.9, 18.2, 34.9, 36.8, 56.0, 56.0, 62.5, 64.2, 96.6, 110.1, 112.1, 113.1, 113.2, 116.7, 116.9, 126.9, 127.0, 127.6, 127.9, 127.9, 128.3, 129.0, 129.0, 140.7, 143.2, 143.3, 143.7, 147.5, 148.1.

LRMS (ESI): *m*/*z* 298.2 $(M + 1)^+$.

HRMS (MALDI): *m*/*z* calcd for $C_{19}H_{23}NO_2Na^+$: 320.1628; found 320.1621.

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