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PAPER

Palladium-catalyzed α-regioselective allylic amination of Morita–Baylis–Hillman acetates with simple aromatic amines†

Yan Wang,[a,b] Li Liu,*[a] Dong Wang[a] and Yong-Jun Chen[a]

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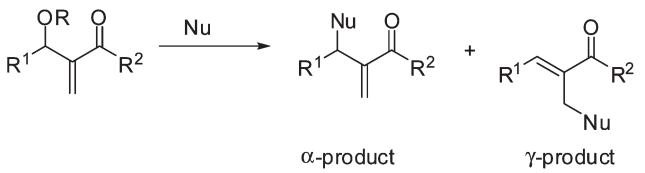
An efficient allylic amination of Morita–Baylis–Hillman acetates with simple aromatic amines provided good yields with excellent α-regioselectivity (up to exclusive α-product) under the catalysis of $Pd_2(dba)_3$/ferrocene-type diphosphine ligand.

Introduction

Recently, catalytic allylic substitution reactions have been developed very well.[1] Among them, the catalytic allylic amination, which provides an efficient synthetic approach to biologically active compounds with an allylamino moiety, has attracted considerable attention.[1,2] The allylic amination reaction would proceed in two regioselective ways to give α- and γ-products. Regioselective introduction of a nucleophile to either the α- or γ-position of the allylic moiety seems to be an urgent requirement and is becoming a powerful tool in synthetic organic chemistry.[3] For Morita–Baylis–Hillman (MBH) adducts, although Trost and coworkers[4] reported palladium catalyzed α-regioselective allylic substitution with *O*-nucleophile (Scheme 1), there were few applications of MBH adducts in allylic amination.[5] In 2002, Iqbal and co-workers[5a] first reported the palladium-catalyzed allylic amination of MBH acetates, but with moderate regioslectivity (α/γ = 3 : 1 to 6 : 1). Hamada and co-workers[5b] studied the asymmetric allylic amination reactions of MBH adducts, but avoided the problem of regioselectivity due to the molecular symmetry of the substrates used. How to extend the substrate-scope of the palladium-catalyzed allylic amination reactions into *N*-nucleophiles, especially simple aromatic amines and MBH adducts, and achieve the excellent α-regioselectivity for this conversion is still a challenge.

The products of allylic amination of MBH adducts with aromatic amines, α-methylene-β-amino carbonyl compounds, are widely applied in the synthesis of medicines and natural products.[6] They could be synthesized through aza-Morita–Baylis–Hillman reactions as well, but the limitation is obvious: the substrate, imine, derived from a simple aromatic amine, is not appropriate for the aza-MBH reactions.[7] Although a synthetic strategy of organocatalysis has been alternatively applied in the reactions between MBH acetates and aromatic amines,[8] the stoichiometric organocatalyst and ultrasound conditions are usually needed for these conversions. Herein, we describe a palladium-catalyzed α-regioselective allylic amination of MBH acetates with simple aromatic amines.[9]



Scheme 1 Allylic substitution of Morita–Baylis–Hillman adduct.

Results and discussion

Initially the model reaction between MBH acetate **1a** and a simple aromatic amine, aniline **2a** (Scheme 2) was carried out in dichloromethane (DCM). By employing $[Pd(C_3H_5)Cl]_2$ as a catalyst, triphenylphosphine as a ligand and K_2CO_3 as a base, the reaction proceeded smoothly to give the corresponding allylic amination products as a mixture of α-product (**3a**) and γ-product (**4a**) (α/γ = 2.8 : 1) in 90% conversion. The α-regioselectivity of the allylic amination reaction encouraged us to further optimize the reaction conditions including ligands (**L1–6**), metallic catalyst, bases and solvents for improving the α-regioselectivity. The experimental results are listed in Table 1. For the ferrocene-type diphosphine ligands,[10] the substituents at the phosphorus atom (**L3–5**) influenced the regioselectivity strongly (entries 3–5). Introduction of α-phenylamine group in the *ortho*-position of the ferrocene ring (**L6**) would increase the α-regioselectivity to α/γ = 3 : 1 (entry 6). The ligand bearing *t*-butyl group in the

[a]*Beijing National Laboratory for Molecular Sciences (BNLMS), CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China. E-mail: lliu@iccas.ac.cn; Fax: +86 010 6255 4449; Tel: +86 010 6255 4614*
[b]*Graduate School of Chinese Academy of Sciences, Beijing 100049, China*

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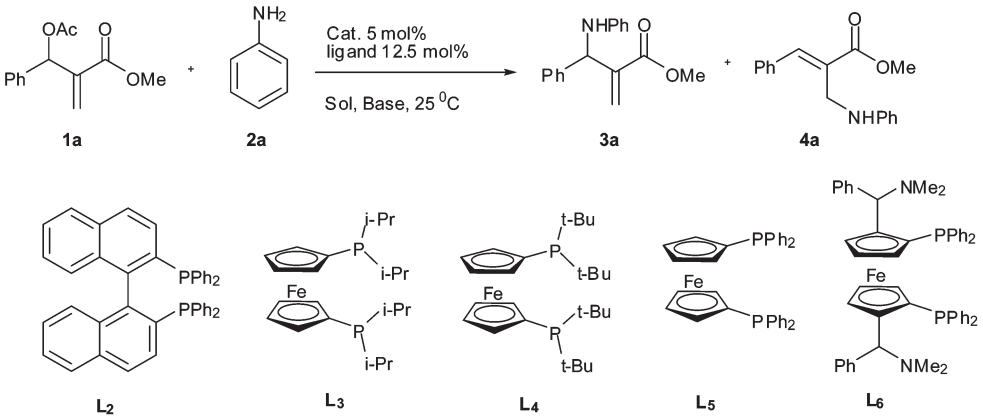


Scheme 2 Allylic amination of MBH adduct **1a** with aniline.

Table 1 Optimization of the reaction conditions for the allylic amination of MBH adduct **1a** with aniline **2a**[a]

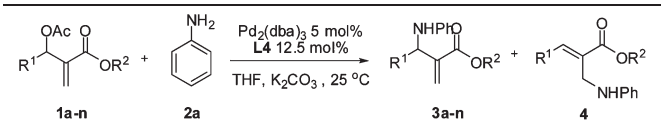
Entry	Catalyst	Ligand	Solvent	Base	*t*(h)	Conv.[b] (%)	**3a**:**4a**[b]
1	$[Pd(C_3H_5)Cl]_2$	**L1**[c]	DCM	K_2CO_3	40	90	2.8 : 1
2	$[Pd(C_3H_5)Cl]_2$	**L2**	DCM	K_2CO_3	24	98	1.4 : 1
3	$[Pd(C_3H_5)Cl]_2$	**L3**	DCM	K_2CO_3	24	100	1 : 1
4	$[Pd(C_3H_5)Cl]_2$	**L4**	DCM	K_2CO_3	24	97	11 : 1
5	$[Pd(C_3H_5)Cl]_2$	**L5**	DCM	K_2CO_3	24	100	1 : 1
6	$[Pd(C_3H_5)Cl]_2$	**L6**	DCM	K_2CO_3	24	100	3 : 1
7	$Pd_2(dba)_3$	**L4**	DCM	K_2CO_3	2	100	20 : 1
8	$Pd(OAc)_2$	**L4**	DCM	K_2CO_3	2	97	16 : 1
9	$Pd(acac)_2$	**L4**	DCM	K_2CO_3	2	98	1 : 1
10	$PdCl_2$	**L4**	DCM	K_2CO_3	2	71	3.5 : 1
11	$Pd_2(dba)_3$	**L4**	DCM	$KHCO_3$	2	98	15.5 : 1
12	$Pd_2(dba)_3$	**L4**	DCM	KOAc	2	100	12.2 : 1
13	$Pd_2(dba)_3$	**L4**	DCM	KOH	2	97	18.3 : 1
14	$Pd_2(dba)_3$	**L4**	DCM	NEt_3	2	99	8.5 : 1
15	$Pd_2(dba)_3$	**L4**	DCM	TMEDA	2	99	3.8 : 1
16	$Pd_2(dba)_3$	**L4**	THF	K_2CO_3	2	99	23 : 1
17	$Pd_2(dba)_3$	**L4**	MeOH	K_2CO_3	2	60	6 : 1
18	$Pd_2(dba)_3$	**L4**	Toluene	K_2CO_3	2	99	5 : 1
19	$Pd_2(dba)_3$	**L4**	EA	K_2CO_3	2	98	13 : 1
20	—	—	THF	K_2CO_3	24	0	—
21	—	**L4**	THF	K_2CO_3	24	0	—
22	$Pd_2(dba)_3$	—	THF	K_2CO_3	24	0	—

[a] All reactions were performed with **1a** (0.1 mmol), **2a** (0.3 mmol), base (0.3 mmol), in solvents (2 mL) at 25 °C in nitrogen atmosphere. Pd catalyst (10 mol%) and ligand (12.5 mol%) were used. [b] Determined by ^{1}H NMR of the mixture of crude products. [c] Loading of ligand **L1**: 25 mol%.

phosphorus atoms (**L4**) showed to be the best for the α-regioselectivity of the reaction of **1a** with **2a** (α/γ up to 11 : 1) (entry 4). Subsequently, the several metallic catalysts were examined (entries 7–10). It was noted that $Pd_2(dba)_3$ could give the better α-regioselectivity (α/γ = 20 : 1) in 100% conversion (entry 7). $Pd(acac)_2$ and $PdCl_2$ could catalyze the reaction of **1a** with **2a** in good conversions too, but with low α-regioselectivities (entries 9 and 10). Based on the experimental results of inorganic and organic bases, and the solvents (entries 11–19), K_2CO_3 and THF were the best choices. The experimental results showed that both the metallic catalyst and the ligand were necessary for the reaction of **1a** with **2a** (entries 20–22). It was awarded that the reaction was not catalyzed by the diphosphine reagent and the Pd-catalyst employed alone, respectively.

With the optimal conditions determined, the scope of MBH acetates with different substituents (**1a–n**) was investigated (Table 2). For ester groups of MBH acetates, bulky ester group R^2 would influence the α-regioselectivity. Compare **1c** (R^2 = *n*-Bu) with **1d** (R^2 = *t*-Bu), the α-regioselectivity (the ratio of α to γ) decreased sharply down to 9 : 1 from 40 : 1 (entries 3 and 4). In most cases, the MBH acetates derived from the aromatic aldehyde either with electron-donating (**1f–g**) or electron-withdrawing group in 3- or 4-position of the phenyl group (**1h–j**) provided excellent α-regioselectivities (α/γ = 18 : 1 to exclusive α-product) (entries 6–10). However, when the substrate derived from the (2-bromophenyl)aldehyde (**1k**) was used, very poor regioselectivity (α/γ = 1 : 1) was obtained, probably due to the steric hindrance of the *ortho*-substituent (entry 11). The napthyl-substitutional MBH acetates (**1l**) could also afford the corresponding product in 95% yield with excellent α-regioselectivity (α/γ = 30 : 1) (entry 12). In addition to the MBH acetates derived from aromatic aldehydes, the reaction of MBH acetates derived

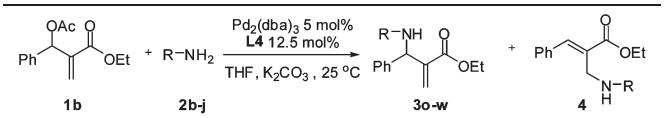
Table 2 Regioselective allylic amination of various MBH acetates[a]



Entry	MBH acetate (R^1, R^2)	Product[b] (**3**/**4** = α/γ)	Yield of **3**[c] (%)
1	**1a** (phenyl, Me)	**3a** (23 : 1)	95
2	**1b** (phenyl, Et)	**3b** (34 : 1)	87
3	**1c** (phenyl, *n*-Bu)	**3c** (40 : 1)	88
4	**1d** (phenyl, *t*-Bu)	**3d** (9 : 1)	89
5	**1e** (phenyl, Ph)	**3e** (5 : 1)	80
6	**1f** (4-OMe-phenyl, Et)	**3f** (1 : 0)	98
7	**1g** (4-Me-phenyl, Et)	**3g** (50 : 1)	98
8	**1h** (4-Cl-Phenyl, Et)	**3h** (18 : 1)	87
9	**1i** (4-Br-phenyl, Et)	**3i** (19 : 1)	88
10	**1j** (3-Br-phenyl, Et)	**3j** (27 : 1)	81
11	**1k** (2-Br-phenyl, Et)	**3k** (1 : 1)	48
12	**1l** (2-naphthyl, Et)	**3l** (30 : 1)	95
13	**1m** (ethyl, Et)	**3m** (1 : 0)[d]	98
14	**1n** (*n*-propyl, Me)	**3n** (1 : 0)[d]	95

[a] All reactions were performed with **1a–n** (0.2 mmol), **2a** (0.6 mmol), base (0.6 mmol), in THF (2 mL) at 25 °C in nitrogen atmosphere. $Pd_2(dba)_3$ (5 mol%) and **L4** (12.5 mol%) were used. [b] Determined by ^{1}H NMR of the mixture of crude products. [c] Isolated yield. [d] No γ-product was detected.

Table 3 α-Regioselective allylic amination of aniline derivatives with **1b**[a]



Entry	Amine (R)	Product[b] (**3**/**4** = α/γ)	Yield of **3**[c] (%)
1	**2a** (Phenyl)	**3b** (34 : 1)	87
2	**2b** (4-OMePhenyl)	**3o** (29 : 1)	90
3	**2c** (2-OMePhenyl)	**3p** (31 : 1)	94
4	**2d** (4-MePhenyl)	**3q** (28 : 1)	93
5	**2e** (2-MePhenyl)	**3r** (9 : 1)	84
6	**2f** 4-F-Phenyl	**3s** (20 : 1)	92
7	**2g** 4-Cl-Phenyl	**3t** (17 : 1)	92
8	**2h** 3-Cl-Phenyl	**3u** (16 : 1)	88
9	**2i** 3,5-Cl_2-Phenyl	**3v** (6 : 1)	75
10[d]	**2j** 1-napthyl	**3w** (20 : 1)	90

[a] All reactions were performed with **1b** (0.2 mmol), **2a–j** (0.6 mmol), base (0.6 mmol), in THF (2 mL) at 25 °C in nitrogen atmosphere. $Pd_2(dba)_3$ (5 mol%) and **L4** (12.5 mol%) were used. [b] Determined by ^{1}H NMR of the mixture of crude products. [c] Isolated yield. [d] The MBH acetate **1a** was used.

from alkylic aldehydes (**1m** and **1n**) proceeded smoothly and provided the α-products (**3m** and **3n**) exclusively (entries 13 and 14).

Various aromatic amines, aniline derivatives, were employed in the reaction with **1b** (Table 3). Excellent α-regioselectivities were observed in the reactions with aromatic amines bearing the electron-donating groups at the nitrogen atom (**2b–d**) and electron-withdrawing groups (**2f–h**) (entries 2–4 and 6–8). When (3,5-dichlorophenyl)amine (**2i**) was used, the yield and α-regioselectivity of the product (**3v**) decreased down to 75% yield and α/γ = 6 : 1 (entry 9).

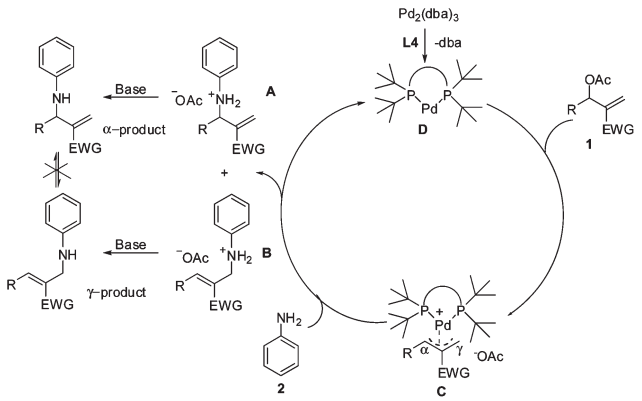


Fig. 1 The proposed mechanism.

As proposed by Mensah and co-workers[11] a plausible mechanism of Pd-catalyzed allylic amination reaction should be as in Fig. 1. The reactive intermediate **D** was formed by the exchange between $Pd_2(dba)_3$ and the diphosphine ligand. Thus, the intermediate **D** activated the MBH acetate **1** affording the cation complex **C**. The aromatic amine reacted with **C** to give a mixture of α-regioisomer **A** and γ-regioisomer **B**. In general, the steric hindrance of the α-position was bigger than in the γ-position resulting in the γ-isomer being the major product. However, in the case of transition state **C** of **L4**, the bulky *t*-butyl group approached the γ-position easier than the α-position due to the relatively less steric hindrance in the γ-position. Thus, the steric hindrance in α-position appeared to be less, leading to the attack in the α-position by the aromatic amine becoming major. The final products were formed after the leaving of acetic acid by the assistance of a base. Obviously, α-product was formed from intermediate **A**, while γ-product from **B**, respectively. As reported by us,[12] there was an equilibrium between α- and γ-product during the course of Brønsted acid-catalyzed allylic substitution reactions. It was implicated that the high α-regioselectivity of the reaction was probably from the conversion of γ-product formed in the beginning of the reaction to the α-product. However, the equilibrium between the two regioisomers was not observed in the course of Pd-catalyzed allylic amination reaction. The excellent α-regioselectivity was controlled by the Pd-catalyst/ligand and depended on the substrates used.

Conclusions

We developed an efficient allylic amination of Morita–Bayllis–Hillman acetates with simple aromatic amines catalyzed by $Pd_2(dba)_3$/ferrocene-type diphosphine ligand (**L4**) with excellent α-regioselectivity (up to exclusive α-product). The α-regioselectivity was controlled by the Pd-catalyst/ligand, especially the substituent at the phosphorus atom of the ligand, and depended on the substituents in the MBH acetate and aromatic amine used.

Experimental

General methods

^{1}H and ^{13}C NMR spectra were recorded on Bruker-AV 300 spectrometer and chemical shift reported in $CDCl_3$ with

tetramethylsilane as an internal standard. IR spectra were recorded on a Bruker tensor 27 infrared spectrometer. HRMS spectra were recorded on GCT-Mass Micromass spectrometer. All reactions were carried out in oven dried flasks. Common reagents were purchased from commercial sources and were used without further purification. The Morita–Baylis–Hillman acetates were prepared according to literature methods.[13] All reactions were performed under nitrogen atmosphere.

Typical experimental procedures for allylic amination reaction

A solution of 5 mol% $Pd_2(dba)_3$ catalyst and 12.5 mol% ligand **L4** in 1 mL THF was stirred at 25 °C for 0.5 h, a solution of MBH acetates **1a** (0.2 mmol) and aniline **2a** (0.6 mmol) in 1 mL THF, and 0.6 mmol K_2CO_3 (1 M) were added. The reaction mixture was stirred at 25 °C and monitored by TLC until the starting material disappeared. Then the reaction mixture was extracted by ethyl acetate. The organic phase was dried by Na_2SO_4, filtered and evaporated to afford a mixture of the crude products. The ratio of α- to γ-isomer was determined by ^{1}HNMR of the mixture at 5.41 and 7.91 ppm. The crude product was purified by flash column chromatography over silica gel (eluent: PE–EA = 20 : 1) to give **3a** as a yellow oil (51 mg, 95%).

Methyl 2-[(phenylamino)(phenyl)methyl]acrylate (3a).[8b] Compound **3a** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3401, 3052, 1717, 1513; ^{1}HNMR ($CDCl_3$, 300 MHz): 3.69 (s, 3H), 4.15 (s, 1H), 5.41 (s, 1H), 5.96 (s, 1H), 6.38 (s, 1H), 6.55–6.58 (m, 2H), 6.69–6.74 (m, 1H), 7.13–7.18 (m, 1H), 7.27–7.38 (m, 5H); ^{13}C NMR ($CDCl_3$, 75MHz): 52.0, 59.0, 113.5, 117.9, 126.2, 127.6, 127.9, 128.8, 129.2, 140.0, 140.6, 146.7, 166.7. ESI-HRMS *m/z* calcd for $C_{17}H_{17}NO_2$ 267.3224 (M^+), found 267.3221.

Ethyl 2-(phenyl(phenylamino)methyl)acrylate (3b).[8e] Compound **3b** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3402, 3050, 1712, 1507; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.20 (t, 3H, J = 7.2 Hz), 4.08–4.19 (m, 3H), 5.41 (s, 1H), 5.93 (s, 1H), 6.38 (s, 1H), 6.57 (d, 2H, J = 7.8 Hz), 6.71 (t, 1H, J = 7.2 Hz), 7.15 (t, 2H, J = 7.8 Hz), 7.27–7.33 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.1, 59.0, 60.8, 113.5, 117.9, 126.0, 127.6, 127.8, 128.8, 129.2, 140.3, 140.8, 146.8, 166.2. ESI-HRMS *m/z* calcd for $C_{18}H_{19}NO_2$ 281.1416 (M^+), found 286.1411.

Butyl 2-[(phenylamino)(phenyl)methyl]acrylate (3c). Compound **3c** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3410, 2958, 1714, 1503; ^{1}HNMR ($CDCl_3$, 300 MHz): 0.79 (t, 3H, J = 7.5 Hz), 1.13–1.25 (m, 2H), 1.43–1.52 (m, 2H), 3.95–4.08 (m, 3H), 5.33 (s, 1H), 5.86 (s, 1H), 6.32 (s, 1H), 6.50 (d, 2H, J = 7.8 Hz), 6.64 (t, 1H, J = 7.8 Hz), 7.08 (t, 2H, J = 7.8 Hz), 7.16–7.28 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): 12.6, 18.0, 29.5, 58.0, 63.6, 112.4, 116.8, 125.0, 126.5, 126.7, 127.7, 128.1, 139.2, 139.7, 145.7, 165.3; ESI-HRMS *m/z* calcd for $C_{20}H_{24}NO_2$ 310.1801 (M^+), found 310.1796.

***tert*-Butyl 2-[(phenylamino)(phenyl)methyl]acrylate (3d).** Compound **3d** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3478, 2974, 1700, 1514; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.35 (s, 9H), 4.13 (d, 1H, J = 4.8 Hz), 5.34 (d, 1H, J = 4.8 Hz), 5.81 (s, 1H), 6.30 (s, 1H), 6.58 (d, 2H, J = 7.8 Hz), 6.72 (t, 1H, J = 7.8 Hz), 7.16 (t, 2H, J = 7.8 Hz), 7.19–7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): 27.9, 59.1, 81.2, 113.4, 117.8, 125.2, 127.5, 127.6, 128.6, 129.2, 141.0, 141.7, 146.9, 165.5; ESI-HRMS *m/z* calcd for $C_{20}H_{24}NO_2$ 310.1801 (M^+), found 310.1799.

Phenyl 2-[(phenylamino)(phenyl)methyl]acrylate (3e). Compound **3e** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3408, 2972, 1727, 1500; ^{1}HNMR ($CDCl_3$, 300 MHz): 4.20 (d, 1H, J = 1.5 Hz), 5.50 (d, 1H, J = 1.8 Hz), 6.13 (s, 1H), 6.61–6.63 (m, 3H), 6.74 (t, 1H, J = 7.2 Hz), 6.94–6.97 (m, 2H), 7.16–7.20 (m, 3H), 7.28–7.44 (m, 7H); ^{13}C NMR ($CDCl_3$, 75 MHz): 59.2, 113.5, 118.1, 121.5, 125.9, 127.7, 127.7, 128.0, 128.9, 129.3, 129.4, 139.9, 140.5, 146.7, 150.5, 165.8; ESI-HRMS *m/z* calcd for $C_{22}H_{20}NO_2$ 330.1488 (M^+), found 330.1485.

Ethyl 2-((4-methoxyphenyl)(phenylamino)methyl)acrylate (3f). Compound **3f** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3412, 2982, 1712, 1507; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.20 (t, 3H, J = 7.2 Hz), 3.76 (s, 3H), 4.09–4.18 (m, 3H), 5.35 (s, 1H), 5.92 (s, 1H), 6.35 (s, 1H), 6.55 (d, 2H, J = 8.1 Hz), 6.70 (t, 1H, J = 7.2 Hz), 6.85 (d, 2H, J = 8.7 Hz), 7.14 (t, 2H, J = 8.1 Hz), 7.27 (d, 2H, J = 8.7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.1, 55.3, 58.4, 60.8, 113.4, 114.1, 117.8, 125.5, 128.8, 129.2, 132.9, 140.5, 146.8, 159.2, 166.4; ESI-HRMS *m/z* calcd for $C_{19}H_{22}NO_3$ 312.1601 (M^+), found 312.1600.

Ethyl 2-((phenylamino)(*p*-tolyl)methyl)acrylate (3g). Compound **3g** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3437, 2982, 1713, 1504; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.13 (t, 3H, J = 7.2 Hz), 2.25 (s, 3H), 4.00–4.11 (m, 3H), 5.29 (s, 1H), 5.85 (s, 1H), 6.28 (s, 1H), 6.48 (d, 2H, J = 8.1 Hz), 6.62 (t, 1H, J = 7.5 Hz), 7.04–7.09 (m, 4H), 7.17 (d, 2H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.1, 21.2, 58.7, 60.8, 113.4, 117.8, 125.7, 127.5, 129.2, 129.4, 137.5, 137.8, 140.4, 146.8, 166.3; ESI-HRMS *m/z* calcd for $C_{19}H_{22}NO_2$ 296.1645 (M^+), found 296.1642.

Ethyl 2-((4-chlorophenyl)(phenylamino)methyl)acrylate (3h). Compound **3h** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3402, 2961, 1711, 1501; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.22 (t, 3H, J = 7.2 Hz), 4.11–4.19 (m, 3H), 5.38 (s, 1H), 5.92 (s, 1H), 6.39 (s, 1H), 6.57 (d, 2H, J = 7.8 Hz), 6.73 (t, 1H, J = 7.2 Hz), 7.16 (t, 2H, J = 7.5 Hz), 7.31 (s, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.1, 58.5, 61.0, 113.5, 118.1, 126.4, 128.9, 129.2, 133.5, 139.3, 140.1, 146.5, 166.0; ESI-HRMS *m/z* calcd for $C_{18}H_{19}ClNO_2$ 316.1098 (M^+), found 316.1094.

Ethyl 2-((4-bromophenyl)(phenylamino)methyl)acrylate (3i). Compound **3i** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3391, 2981, 1711, 1502; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.22 (t, 3H, J = 7.2 Hz), 4.11–4.19 (m, 3H), 5.35–5.37 (d, 1H, J = 5.4 Hz), 5.91 (s, 1H), 6.39 (s, 1H), 6.56 (d, 2H, J = 8.1 Hz), 6.73 (t, 1H, J = 7.2 Hz), 7.16 (t, 2H, J = 7.8 Hz), 7.25 (d, 2H, J = 7.2 Hz), 7.46 (d, 2H, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.1, 58.6, 61.0, 113.6, 118.2, 121.7, 126.5, 129.3, 131.9, 139.9, 140.0, 146.5, 166.0; ESI-HRMS *m/z* calcd for $C_{18}H_{19}BrNO_2$ 360.0594 (M^+), found 360.0588.

Ethyl 2-((3-bromophenyl)(phenylamino)methyl)acrylate (3j). Compound **3j** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3475, 2981, 1699, 1509; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.23 (t, 3H, J = 7.2 Hz), 4.14–4.19 (m, 3H), 5.37 (d, 1H, J = 5.4 Hz), 5.92 (s, 1H), 6.41 (s, 1H), 6.57 (d, 2H, J = 7.8 Hz), 6.73 (t, 1H, J = 7.5 Hz), 7.13–7.17 (m, 3H), 7.19 (d, 1H, J = 3.3 Hz), 7.23 (d, 1H, J = 5.4 Hz), 7.30 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.1, 58.6, 61.0, 113.5, 118.2, 122.8, 126.2, 126.7, 129.3, 130.3, 130.5, 130.9, 139.9, 143.1, 146.5, 165.9; ESI-HRMS m/z calcd for $C_{18}H_{19}BrNO_2$ 360.0594 (M^+), found 360.0588.

Ethyl 2-((2-bromophenyl)(phenylamino)methyl)acrylate (3k). Compound **3k** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3522, 2981, 1711, 1503; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.21 (t, 3H, J = 7.2 Hz), 4.07 (d, 1H, J = 5.7 Hz), 4.13–4.23 (m, 2H), 5.77 (s, 1H), 5.81 (d, 1H, J = 5.7 Hz), 6.44 (s, 1H), 6.56 (d, 2H, J = 7.5 Hz), 6.72 (t, 1H, J = 7.2 Hz), 7.12–7.18 (m, 3H), 7.25–7.39 (m, 1H), 7.39–7.40 (m, 1H), 7.59–7.61 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.1, 57.9, 61.0, 113.3, 118.0, 124.7, 127.4, 127.7, 128.5, 129.2, 129.2, 133.3, 139.6, 139.9, 146.6, 166.1; ESI-HRMS m/z calcd for $C_{18}H_{19}BrNO_2$ 360.0594 (M^+), found 360.0591.

Ethyl 2-[(naphthalen-2-yl)(phenylamino)methyl]acrylate (3l). Compound **3l** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3407, 2980, 1711, 1502; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.19 (t, 3H, J = 7.2 Hz), 4.09–4.17 (m, 2H), 4.24 (br, 1H), 5.58 (s, 1H), 5.99 (s, 1H), 6.44 (s, 1H), 6.61 (d, 2H, J = 7.8 Hz), 6.73 (t, 1H, J = 7.5 Hz), 7.14–7.19 (m, 2H), 7.46–7.48 (m, 3H), 7.79–7.84 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.1, 59.1, 60.9, 113.5, 118.0, 125.8, 126.1, 126.2, 127.7, 128.1, 128.6, 129.2, 133.0, 133.4, 138.1, 140.4, 146.8, 166.3; ESI-HRMS m/z calcd for $C_{22}H_{22}NO_2$ 332.1645 (M^+), found 332.1641.

Ethyl 2-methylene-3-(phenylamino)pentanoate (3m). Compound **3m** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3477, 2970, 1709, 1505; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.00 (t, 3H, J = 7.2 Hz), 1.31 (t, 3H, J = 7.2 Hz), 1.58–1.87 (m, 2H), 4.03 (br, 1H), 4.18–4.27 (m, 3H), 5.71 (s, 1H), 6.20 (s, 1H), 6.54 (d, 2H, J = 7.8 Hz), 6.67 (t, 1H, J = 7.5 Hz), 7.14 (t, 1H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): 10.9, 14.2, 28.5, 56.4, 60.7, 113.4, 117.4, 125.1, 129.2, 141.0, 147.1, 166.6; ESI-HRMS m/z calcd for $C_{14}H_{20}NO_2$ 234.1489 (M^+), found 234.1488.

Ethyl 2-methylene-3-(phenylamino)hexanoate (3n). Compound **3n** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3407, 2957, 1714, 1505; ^{1}HNMR ($CDCl_3$, 300 MHz): 0.94 (t, 3H, J = 7.2 Hz), 1.40–1.76 (m, 4H), 3.77 (s, 3H), 4.01 (br, 1H), 4.23–4.28 (m, 1H), 5.73 (s, 1H), 6.18 (s, 1H), 6.53 (d, 2H, J = 7.8 Hz), 6.67 (t, 1H, J = 7.5 Hz), 7.13 (t, 1H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): 13.9, 19.7, 37.8, 51.8, 54.7, 113.4, 117.4, 125.3, 129.2, 141.1, 147.0, 167.0; ESI-HRMS m/z calcd for $C_{14}H_{20}NO_2$ 234.1489 (M^+), found 234.1486.

Ethyl 2-[((4-methoxyphenyl)amino)(phenyl)methyl]acrylate (3o). Compound **3o** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3438, 2930, 1712, 1512; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.18–1.26 (m, 3H), 3.72 (s, 3H), 4.00 (br, 1H), 4.12–4.15 (m, 2H), 5.33 (s, 1H), 5.92 (s, 1H), 6.37 (s, 1H), 6.53 (d, 2H, J = 8.7 Hz), 6.75 (d, 2H, J = 8.7 Hz), 7.24–7.38 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.1, 55.7, 59.8, 60.8, 114.7, 114.8, 125.9, 127.5, 127.7, 128.7, 140.6, 141.0, 141.0, 152.3, 166.3; ESI-HRMS m/z calcd for $C_{19}H_{22}NO_3$ 312.1594 (M^+), found 312.1592.

Ethyl 2-[((2-methoxyphenyl)amino)(phenyl)methyl]acrylate (3p). Compound **3p** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3417, 2960, 1715, 1509; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.13 (t, 3H, J = 7.2 Hz), 3.74 (s, 3H), 3.97–4.15 (m, 2H), 4.61 (d, 1H, J = 5.1 Hz), 5.34 (d, 1H, J = 4.8 Hz), 5.83 (s, 1H), 6.31 (s, 1H), 6.43 (d, 1H, J = 7.8 Hz), 6.57–6.58 (m, 1H), 6.61 (d, 1H, J = 7.5 Hz), 6.69–6.77 (m, 2H), 7.20–7.32 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.4, 55.7, 59.0, 61.1, 109.7, 111.3, 117.3, 121.4, 126.0, 128.0, 128.0, 129.0, 137.0, 140.8, 141.2, 147.1, 166.6; ESI-HRMS m/z calcd for $C_{19}H_{22}NO_3$ 312.1594 (M^+), found 312.1591.

Ethyl 2-((*p*-tolylamino)(phenyl)methyl)acrylate (3q). Compound **3q** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3396, 2982, 1713, 1518; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.20 (t, 3H, J = 7.2 Hz), 2.22 (s, 3H), 4.04 (br, 1H), 4.08–4.19 (m, 2H), 5.34 (s, 1H), 5.93 (s, 1H), 6.38 (s, 1H), 6.50 (d, 1H, J = 8.4 Hz), 6.97 (d, 1H, J = 8.4 Hz), 7.26–7.38 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.1, 20.4, 59.3, 60.8, 113.6, 125.9, 127.1, 127.6, 127.7, 128.7, 129.7, 140.5, 140.9, 144.5, 166.3; ESI-HRMS m/z calcd for $C_{19}H_{22}NO_2$ 296.1645 (M^+), found 296.1640.

Ethyl 2-((*o*-tolylamino)(phenyl)methyl)acrylate (3r). Compound **3r** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3412, 2981, 1712, 1510; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.24 (t, 3H, J = 7.2 Hz), 2.18 (s, 3H), 4.08 (br, 1H), 4.11–4.24 (m, 2H), 5.50 (s, 1H), 5.93 (s, 1H), 6.41 (s, 1H), 6.54 (d, 1H, J = 7.8 Hz), 6.71 (d, 1H, J = 7.2 Hz), 7.08–7.13 (m, 2H), 7.28–7.33 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.4, 17.9, 59.2, 61.1, 111.3, 117.8, 122.5, 126.2, 127.3, 127.8, 129.1, 130.4, 140.7, 141.2, 145.0, 166.6; ESI-HRMS m/z calcd for $C_{19}H_{22}NO_2$ 296.1645 (M^+), found 296.1641.

Ethyl 2-[((4-fluorophenyl)amino)(phenyl)methyl]acrylate (3s). Compound **3s** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3413, 2983, 1712, 1511; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.20 (t, 3H, J = 7.2 Hz), 4.08–4.18 (m, 3H), 5.34 (s, 1H), 5.89 (s, 1H), 6.38 (s, 1H), 6.47–6.52 (m, 2H), 6.85 (t, 2H, J = 8.7 Hz), 7.27–7.32 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.1, 59.6, 60.9, 114.3, 114.4, 115.5, 115.8, 126.0, 127.5, 127.8, 128.5, 128.8, 129.3, 140.3, 140.6, 143.1, 143.1, 154.4, 157.6, 166.2; ESI-HRMS m/z calcd for $C_{18}H_{19}FNO_2$ 300.1394 (M^+), found 300.1391.

Ethyl 2-[((4-chlorophenyl)amino)(phenyl)methyl]acrylate (3t). Compound **3t** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3413, 2982, 1712, 1497; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.21 (t, 3H, J = 7.2 Hz), 4.10–4.20 (m, 3H), 5.34 (s, 1H), 5.88 (s, 1H), 6.38 (s, 1H), 6.49 (d, 2H, J = 8.7 Hz), 7.09 (d, 2H, J = 9.0 Hz), 7.28–7.34 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.1, 59.1, 60.9, 114.6, 122.5, 126.0, 127.5, 127.9, 128.5, 128.8, 129.0, 140.1, 140.3, 145.3, 166.1; ESI-HRMS m/z calcd for $C_{18}H_{19}ClNO_2$ 316.1099 (M^+), found 316.1093.

Ethyl 2-[((3-chlorophenyl)amino)(phenyl)methyl]acrylate (3u). Compound **3u** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}):

3415, 2990, 1703, 1595; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.21 (t, 3H, J = 7.2 Hz), 4.10–4.27 (m, 3H), 5.38 (d, 1H, J = 5.4 Hz), 5.89 (s, 1H), 6.40 (s, 1H), 6.42–6.46 (m, 1H), 6.54–6.56 (m, 1H), 6.66–6.69 (m, 1H), 7.05 (t, 1H, J = 8.1 Hz), 7.29–7.30 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.4, 59.3, 61.2, 112.0, 113.5, 118.1, 126.4, 127.8, 128.3, 129.2, 130.5, 135.3, 140.3, 140.5, 148.2, 166.4; ESI-HRMS m/z calcd for $C_{18}H_{19}ClNO_2$ 316.1099 (M^+), found 316.1093.

Ethyl 2-[((3,5-dichlorophenyl)amino)(phenyl)methyl]acrylate (3v). Compound **3v** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3414, 2981, 1710, 1591; ^{1}HNMR ($CDCl_3$, 300 MHz): 1.21 (t, 3H, J = 7.2 Hz), 4.10–4.21 (m, 2H), 4.37 (d, 1H, J = 6.0 Hz), 5.35 (d, 1H, J = 6.0 Hz), 5.86 (s, 1H), 6.41 (s, 1H), 6.43 (s, 2H), 6.69 (s, 1H), 7.32–7.36 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.0, 58.9, 61.0, 111.6, 117.7, 126.3, 127.3, 128.1, 128.9, 135.4, 139.6, 139.7, 148.3, 165.9; ESI-HRMS m/z calcd for $C_{18}H_{18}Cl_2NO_2$ 350.0709 (M^+), found 350.0705.

Ethyl 2-[((naphthalen-1-yl)amino)(phenyl)methyl]acrylate (3w). Compound **3w** was isolated as a yellow oil, IR ν_{max} (KBr, cm^{-1}): 3419, 2980, 1711, 1580; ^{1}HNMR ($CDCl_3$, 300 MHz): 3.73 (s, 3H), 4.92 (d, 1H, J = 3.9 Hz), 5.62 (d, 1H, J = 4.2 Hz), 6.00 (s, 1H), 6.40 (s, 1H), 6.51 (d, 1H, J = 7.2 Hz), 7.23–7.47 (m, 9H), 7.78–7.80 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 52.0, 59.1, 106.0, 118.0, 119.9, 123.4, 124.9, 125.8, 126.2, 126.5, 127.7, 128.0, 128.8, 128.9, 134.3, 139.6, 140.6, 141.6, 166.8; ESI-HRMS m/z calcd for $C_{21}H_{20}NO_2$ 318.1408 (M^+), found 318.1405.

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