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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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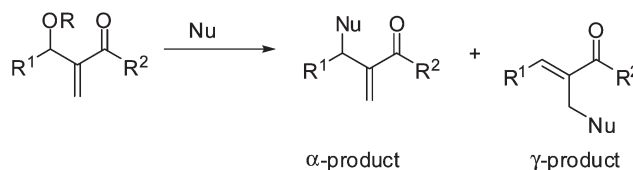
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An efficient allylic amination of Morita–Baylis–Hillman acetates with simple aromatic amines provided good yields with excellent α -regioselectivity (up to exclusive α -product) under the catalysis of $\text{Pd}_2(\text{dba})_3$ /ferrocene-type diphosphine 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 coworkers⁴ 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 regioselectivity ($\alpha/\gamma = 3 : 1$ 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



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

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

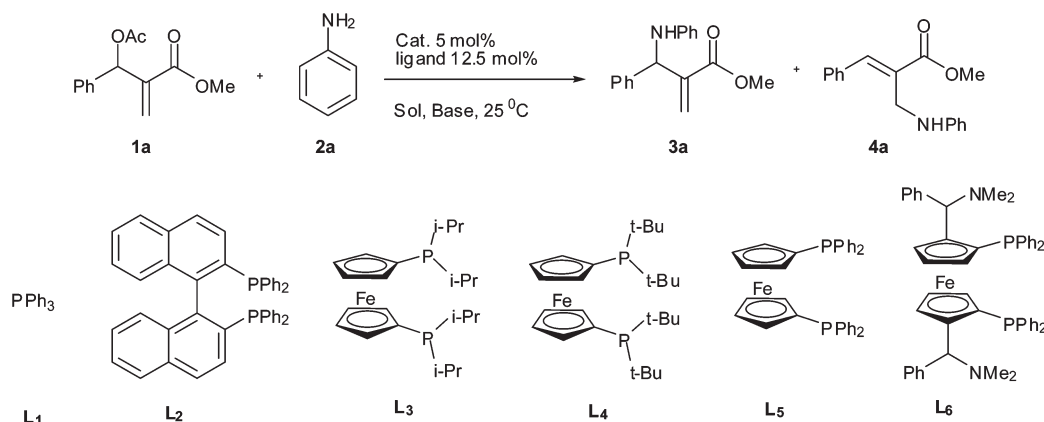
Results and discussion

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 $[\text{Pd}(\text{C}_3\text{H}_5\text{Cl})_2]$ 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**) ($\alpha/\gamma = 2.8 : 1$) 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 $\alpha/\gamma = 3 : 1$ (entry 6). The ligand bearing *t*-butyl group in the

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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	<i>t</i> (h)	Conv. ^b (%)	3a:4a ^b
1	[Pd(C ₃ H ₅)Cl] ₂	L1 ^c	DCM	K ₂ CO ₃	40	90	2.8 : 1
2	[Pd(C ₃ H ₅)Cl] ₂	L2	DCM	K ₂ CO ₃	24	98	1.4 : 1
3	[Pd(C ₃ H ₅)Cl] ₂	L3	DCM	K ₂ CO ₃	24	100	1 : 1
4	[Pd(C ₃ H ₅)Cl] ₂	L4	DCM	K ₂ CO ₃	24	97	11 : 1
5	[Pd(C ₃ H ₅)Cl] ₂	L5	DCM	K ₂ CO ₃	24	100	1 : 1
6	[Pd(C ₃ H ₅)Cl] ₂	L6	DCM	K ₂ CO ₃	24	100	3 : 1
7	Pd ₂ (dba) ₃	L4	DCM	K ₂ CO ₃	2	100	20 : 1
8	Pd(OAc) ₂	L4	DCM	K ₂ CO ₃	2	97	16 : 1
9	Pd(acac) ₂	L4	DCM	K ₂ CO ₃	2	98	1 : 1
10	PdCl ₂	L4	DCM	K ₂ CO 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 ₂ CO ₃	2	99	23 : 1
17	Pd ₂ (dba) ₃	L4	MeOH	K ₂ CO ₃	2	60	6 : 1
18	Pd ₂ (dba) ₃	L4	Toluene	K ₂ CO ₃	2	99	5 : 1
19	Pd ₂ (dba) ₃	L4	EA	K ₂ CO ₃	2	98	13 : 1
20	—	—	THF	K ₂ CO ₃	24	0	—
21	—	L4	THF	K ₂ CO ₃	24	0	—
22	Pd ₂ (dba) ₃	—	THF	K ₂ CO 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 ¹H 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 Pd₂(dba)₃ could give the better α -regioselectivity (α/γ = 20 : 1) in 100% conversion (entry 7). Pd(acac)₂ and PdCl₂ 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), K₂CO₃ 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 R² would influence the α -regioselectivity. Compare **1c** (R² = *n*-Bu) with **1d** (R² = *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 naphthyl-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

$ \begin{array}{c} \text{OAc} \\ \\ \text{R}^1\text{C}=\text{C}-\text{C}-\text{OR}^2 \\ \\ \text{NHPh} \end{array} + \text{2a} \xrightarrow[\text{THF, K}_2\text{CO}_3, 25^\circ\text{C}]{\text{Pd}_2(\text{dba})_3 \text{ 5 mol\%}, \text{L4 12.5 mol\%}} \begin{array}{c} \text{NHPh} \\ \\ \text{R}^1\text{C}=\text{C}-\text{C}-\text{OR}^2 \\ \\ \text{NHPh} \end{array} + \text{4} $			
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, <i>n</i> -Bu)	3c (40 : 1)	88
4	1d (phenyl, <i>t</i> -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 (<i>n</i> -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. Pd₂(dba)₃ (5 mol%) and **L4** (12.5 mol%) were used. ^b Determined by ¹H NMR of the mixture of crude products. ^c Isolated yield. ^d No γ-product was detected.

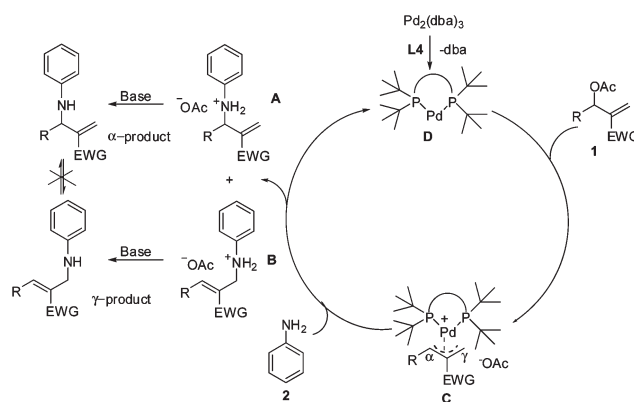
Table 3 α-Regioselective allylic amination of aniline derivatives with **1b**^a

$ \begin{array}{c} \text{OAc} \\ \\ \text{Ph}-\text{C}=\text{C}-\text{C}-\text{OEt} \\ \\ \text{NHPh} \end{array} + \text{R-NH}_2 \xrightarrow[\text{THF, K}_2\text{CO}_3, 25^\circ\text{C}]{\text{Pd}_2(\text{dba})_3 \text{ 5 mol\%}, \text{L4 12.5 mol\%}} \begin{array}{c} \text{R-NH} \\ \\ \text{Ph}-\text{C}=\text{C}-\text{C}-\text{OEt} \\ \\ \text{NHPh} \end{array} + \text{4} $			
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-naphthyl	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. Pd₂(dba)₃ (5 mol%) and **L4** (12.5 mol%) were used. ^b Determined by ¹H NMR of the mixture of crude products. ^c Isolated yield. ^d The MBH acetate **1a** was used.

from allylic 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-workers¹¹ 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 Pd₂(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–Baylis–Hillman acetates with simple aromatic amines catalyzed by Pd₂(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

¹H and ¹³C NMR spectra were recorded on Bruker-AV 300 spectrometer and chemical shift reported in CDCl₃ 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% Pd₂(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 K₂CO₃ (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 Na₂SO₄, filtered and evaporated to afford a mixture of the crude products. The ratio of α- to γ-isomer was determined by ¹HNMR 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; ¹HNMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 75 MHz): 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 C₁₇H₁₇NO₂ 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; ¹HNMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 C₁₈H₁₉NO₂ 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; ¹HNMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 C₂₀H₂₄NO₂ 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; ¹HNMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 C₂₀H₂₄NO₂ 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; ¹HNMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 C₂₂H₂₀NO₂ 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; ¹HNMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 C₁₉H₂₂NO₃ 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; ¹HNMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 C₁₉H₂₂NO₂ 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; ¹HNMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 C₁₈H₁₉ClNO₂ 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; ¹HNMR (CDCl₃, 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); ¹³C NMR (CDCl₃, 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 C₁₈H₁₉BrNO₂ 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; ^1H NMR (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 $\text{C}_{18}\text{H}_{19}\text{BrNO}_2$ 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; ^1H NMR (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 $\text{C}_{18}\text{H}_{19}\text{BrNO}_2$ 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; ^1H NMR (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 $\text{C}_{22}\text{H}_{22}\text{NO}_2$ 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; ^1H NMR (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 $\text{C}_{14}\text{H}_{20}\text{NO}_2$ 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; ^1H NMR (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 $\text{C}_{14}\text{H}_{20}\text{NO}_2$ 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; ^1H NMR (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 $\text{C}_{19}\text{H}_{22}\text{NO}_3$ 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; ^1H NMR (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 $\text{C}_{19}\text{H}_{22}\text{NO}_3$ 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; ^1H NMR (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 $\text{C}_{19}\text{H}_{22}\text{NO}_2$ 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; ^1H NMR (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 $\text{C}_{19}\text{H}_{22}\text{NO}_2$ 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; ^1H NMR (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 $\text{C}_{18}\text{H}_{19}\text{FNO}_2$ 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; ^1H NMR (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 $\text{C}_{18}\text{H}_{19}\text{ClNO}_2$ 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; ^1H NMR (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 $\text{C}_{18}\text{H}_{19}\text{ClNO}_2$ 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; ^1H NMR (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 $\text{C}_{18}\text{H}_{18}\text{Cl}_2\text{NO}_2$ 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; ^1H NMR (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 $\text{C}_{21}\text{H}_{20}\text{NO}_2$ 318.1408 (M^+), found 318.1405.

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