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Stereoselective and regioselective synthesis of N-substituted methyl 2-((azolyl)methyl)-3-arylacrylates from Baylis–Hillman acetates

Ayşen KÖSECELİ ÖZENÇ, İlhami ÇELİK*, Şule KÖKTEN
Department of Chemistry, Faculty of Science, Anadolu University, Eskişehir, Turkey

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Abstract: N-Substituted methyl 2-((azolyl)methyl)-3-arylacrylates were synthesized stereo- and regioselectively with one-pot reaction between Baylis–Hillman acetates and a suitable acylazole in the presence of K_2CO_3 as a base catalyst. The targeted N-substituted azole acrylates were efficiently obtained in good yields (39%–89%).

Key words: Imidazole, benzimidazole, benzotriazole, Baylis–Hillman acetates, N-substituted azole acrylates

1. Introduction

Heterocyclic compounds containing imidazole, benzimidazole, and benzotriazole skeletons are usually found as important core structures in a wide number of natural products and biologically active pharmaceuticals[1,2]. Some examples of clinically employed drugs such as ketoconazole,[3] omeprazole,[4] and alizapride[5] respectively have imidazole, benzimidazole, and benzotriazole rings (Figure 1). It is also known that many N-substituted derivatives of these azole rings play an important role in the medical field with many pharmacological activities including antimicrobial, antiviral, antidiabetic, and anticancer.[6–8] Heterocyclics bearing these ring systems are not only used to design medicinally important drugs. They are also used as corrosion inhibitors to protect metal and alloy surfaces[9] and as catalysts[10].

Baylis–Hillman reaction involving the coupling of an activated alkene with an electrophile in the presence of a tertiary amine base catalyst is one of the most powerful and useful carbon–carbon bond-forming processes and often yields a variety of multifunctional products, so-called Baylis–Hillman adducts. Because of the simplicity of this reaction in the easy construction of the C-C bond and its ability to accommodate a wide range of electrophiles, activated alkenes, and catalysts, many acyclic and cyclic compounds can be synthesized using these adducts.[11] N-Substituted azole acrylates derived from Baylis–Hillman adducts are also useful compounds containing azole units. They were used as an intermediate to prepare poly-fused heterocycles[12] and as a substrate to synthesize ionic liquids.[13] A few methods have been developed for their preparation. In these literature methods, N-substituted azole acrylates were either prepared from an intermediate that was obtained through bromination or acetylation of Baylis–Hillman adducts in two steps[14,15] or they were directly prepared from Baylis–Hillman adducts in a single step using carbonyldiimidazole (CDI)[13] (Figure 2). Although it is possible to access a wide range of azole derivatives using these methods, they still have some drawbacks, such as the use of highly reactive and toxic reagents to prepare starting compounds[17] or the need for previous activation of the OH group in Baylis–Hillman adducts.[14,15]

*Correspondence: ilcelik@anadolu.edu.tr

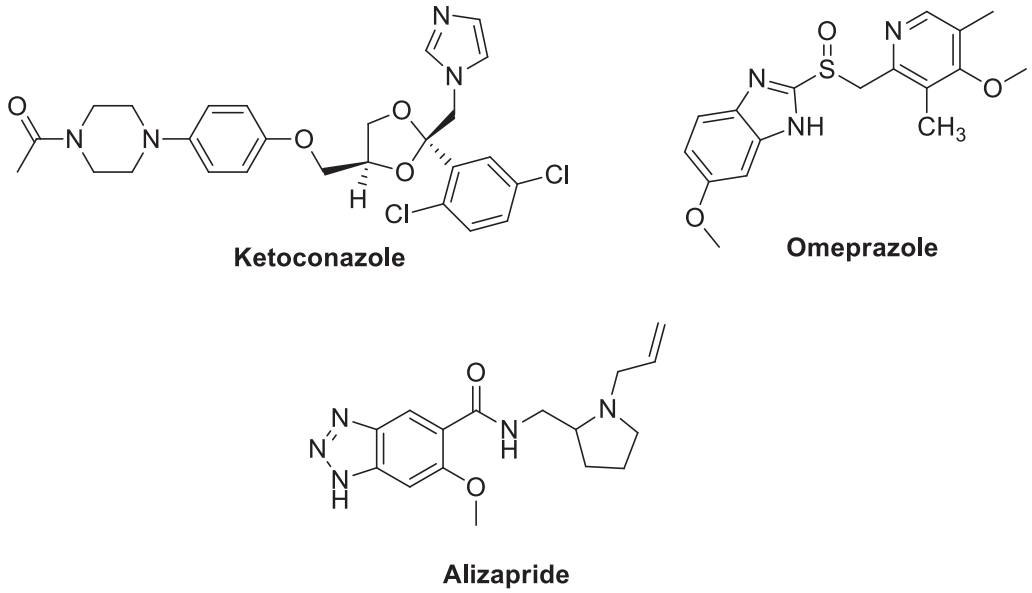


Figure 1. Some medicines bearing azole moiety.

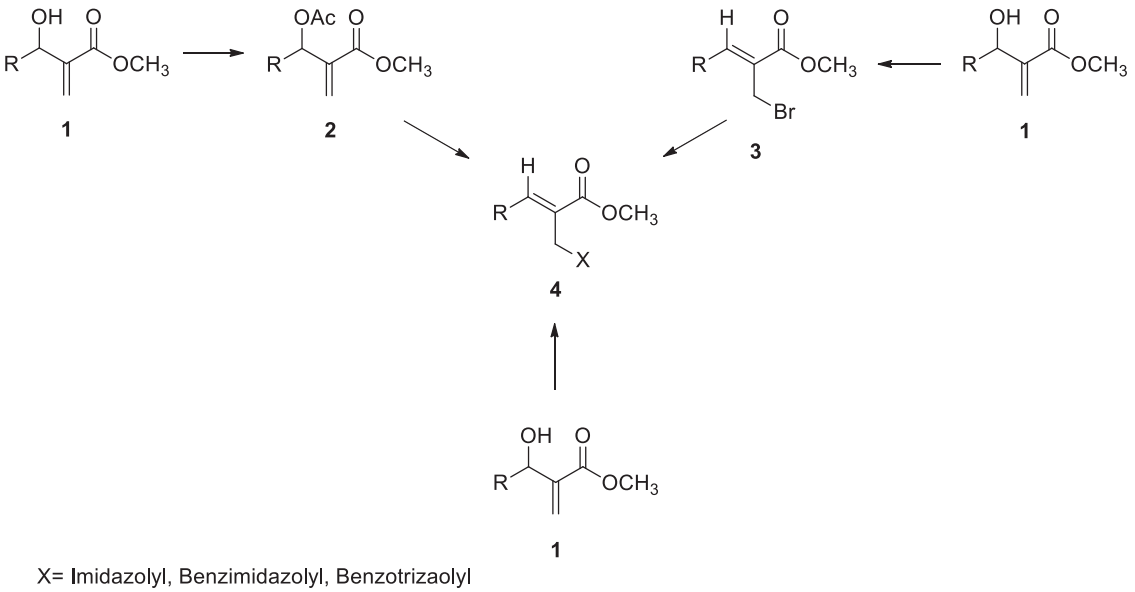
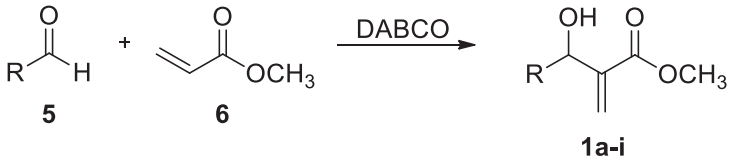


Figure 2. Literature methods for the synthesis of N-substituted azole acrylates.

N-Acylazoles, which are effective acylating agents, are among the useful synthetic auxiliaries derived from these ring systems. They show great potential in organic synthesis as activated carboxylic acid derivatives to prepare amides,[18,19] esters,[18,20,21] thioesters,[18,21] ketones,[22,23] and some useful heterocycles.[24,25] Because there are few methods for the synthesis of N-substituted azole acrylates and the present methods have some drawbacks, herein we aimed to develop a more general method to synthesize N-substituted derivatives of imidazole, benzimidazole, and benzotriazole from the reaction between N-acylazoles and Baylis–Hillman adducts.

2. Results and discussion

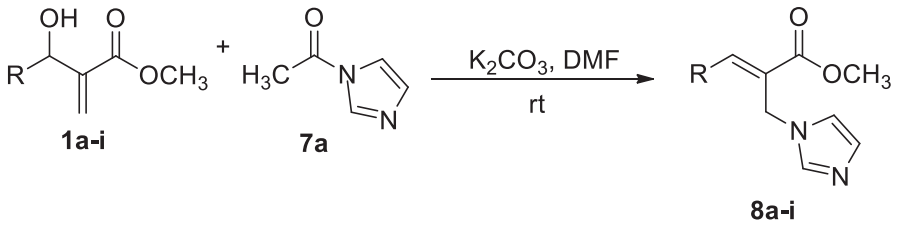
We first prepared Baylis–Hillman adducts **1a**–**1i** by treating a suitable aldehyde with methyl acrylate in the presence of DABCO according to the literature procedures[26,27] (Scheme 1). Next, *N*-acetylazoles **7a**–**7c** were prepared by modifying the method developed in the literature.[18]



Scheme 1. Synthesis of Baylis–Hillman adducts.

N-substituted azole acrylates were then obtained by the reaction of Baylis–Hillman adducts with *N*-acylazoles. Treatment of *N*-acetylimidazole with Baylis–Hillman acetates in DMF in the presence of K_2CO_3 at room temperature afforded the corresponding *N*-substituted-2-((imidazolyl)methyl)-3-acrylates in 39%–84% yields (Table 1).

Table 1. Synthesis of *N*-substituted-2-((imidazolyl)methyl)-3-acrylates.



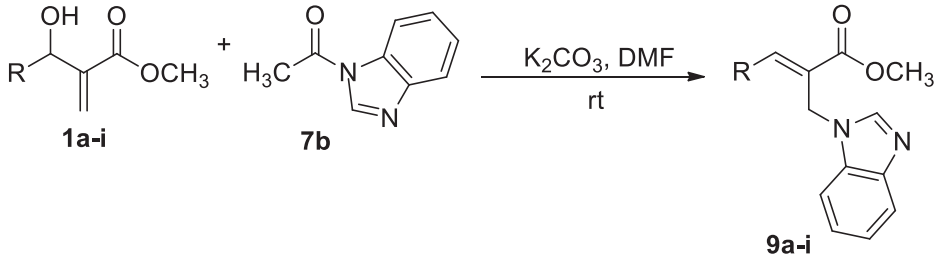
Entry	R	Yield (%)
1	Ph	**8a**, 58
2	4-Me-Ph	**8b**, 73
3	4-MeO-Ph	**8c**, 39
4	2-NO_2-Ph	**8d**, 84
5	4-F-Ph	**8e**, 50
6	3-Cl-Ph	**8f**, 42
7	2-py	**8g**, 57
8	2-furanyl	**8h**, 40
9	2-(3-Me-thiophenyl)	**8i**, 42

As an extension of this reaction, *N*-substituted-2-((benzimidazolyl)methyl)-3-acrylates were prepared using *N*-acetylbenzimidazole with 33%–65% yields under the same conditions (Table 2). In the literature method, necessary reaction conditions were more vigorous to synthesize benzimidazole acrylate derivatives and in some cases the obtained products had both E and Z isomers.[16] With the method used here only products having the E configuration were obtained.

We also examined the same reaction conditions while treating *N*-acetylbenzotriazole with Baylis–Hillman acetates to give *N*-substituted-2-((benzotriazolyl)methyl)-3-acrylates in 45%–89% yields (Table 3). At the end of the reaction, it was observed that two different products had formed. It was concluded that these two products were N-1 (Bt^1) and N-2 (Bt^2) isomers of benzotriazole according to their ^{13}C NMR spectra. In the ^{13}C NMR spectra, six C signals were observed for Bt^1 compounds. On the other hand, three C signals were

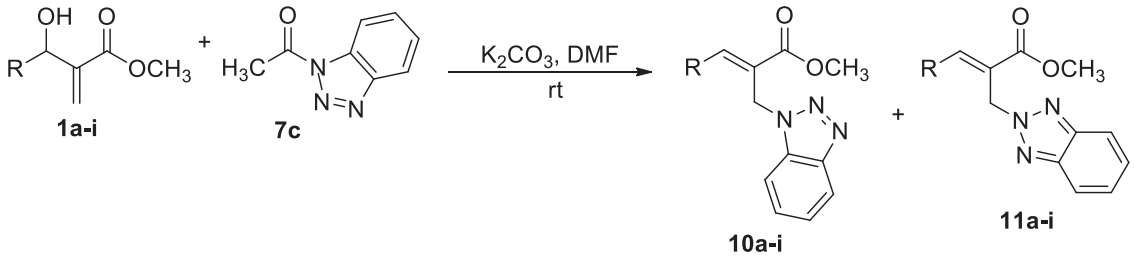
observed for Bt^2 compounds because of the symmetry in the molecules. Comparing the formation of the Bt^1 isomer to the Bt^2 isomer, the yields of Bt^1 are much higher than that of Bt^2 compounds. This shows that the reaction is regioselective.

Table 2. Synthesis of *N*-substituted-2-((benzimidazolyl)methyl)-3-acrylates.



Entry	R	Yield (%)
1	Ph	**9a**, 44
2	4-Me-Ph	**9b**, 43
3	4-MeO-Ph	**9c**, 44
4	2-NO_2-Ph	**9d**, 65
5	4-F-Ph	**9e**, 42
6	3-Cl-Ph	**9f**, 42
7	2-py	**9g**, 41
8	2-furanyl	**9h**, 46
9	2-(3-Me-thiophenyl)	**9i**, 33

Table 3. Synthesis of *N*-substituted-2-((benzotriazolyl)methyl)-3-acrylates.

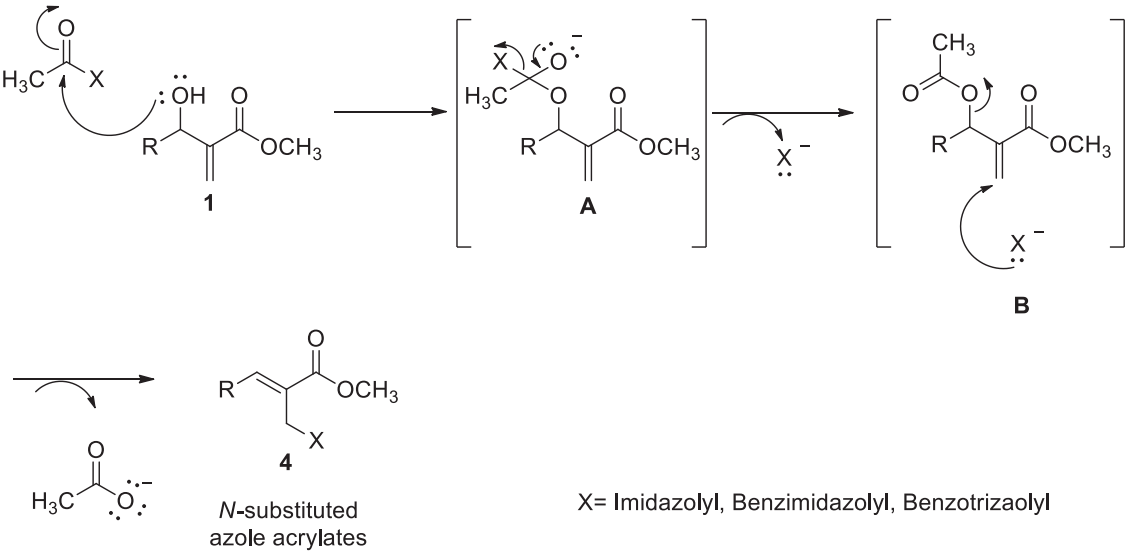


Entry	R	% Overall yield	% Yield of Bt^1	% Yield of Bt^2
1	Ph	85	**10a**, 67	**11a**, 18
2	4-Me-Ph	54	**10b**, 54	**11b**, 0
3	4-MeO-Ph	80	**10c**, 63	**11c**, 17
4	2-NO_2-Ph	89	**10d**, 70	**11d**, 19
5	4-F-Ph	77	**10e**, 60	**11e**, 17
6	3-Cl-Ph	80	**10f**, 68	**11f**, 12
7	2-py	64	**10g**, 53	**11g**, 11
8	2-furanyl	45	**10h**, 35	**11h**, 10
9	3-Me-2-thiophenyl	69	**10i**, 48	**11i**, 21

All the synthesized products were purified by column chromatography and their structures were identified by ^{1}H and ^{13}C NMR spectra. The obtained results were supported by elemental analysis and high-resolution mass spectrum (HRMS) data. The overall yields seemed to be satisfactory and the double bond configurations of these compounds were assigned on the basis of ^{1}H NMR spectra and by comparing data available in the

literature.[13,14,28] According to the literature, while the chemical shift value of the olefinic proton in the E-isomer is observed obviously downfield of the aromatic ring proton, the corresponding olefinic proton of the Z-isomer appears upfield.[28,29] When we went through the ^{1}H NMR spectra, we observed a chemical shift of a proton as a singlet appeared obviously downfield of the aromatic ring protons around 7.97–8.77 ppm for almost all compounds synthesized. In addition, the ^{1}H NMR spectra showed that there was no formation of the Z-isomer. As the chemical shift values of olefinic protons in ^{1}H NMR spectra and the data obtained from the literature are in accordance with each other, it was thought that all synthesized compounds had E configuration.

The proposed mechanism shown in Scheme 2 is a one-pot reaction that is first initiated by acylation of the hydroxyl group in Baylis–Hillman adducts. This follows Michael addition of the azole anion to alkene, which leads to the elimination of the acetyl group to afford the desired *N*-substituted azole acrylates.



Scheme 2. Proposed mechanism for the synthesis of *N*-substituted azole acrylates.

In conclusion, we have developed an efficient protocol for the stereo- and regioselective synthesis of *N*-substituted azole acrylates. With the use of readily available acylazoles, the methodology described here offers an alternative way to get *N*-substituted azole acrylates in a single step directly from Baylis–Hillman adducts.

3. Experimental

3.1. General procedure

All chemicals were purchased from commercial suppliers and used without further purification. Reactions were monitored by thin-layer chromatography and visualized under UV light. Melting points were recorded on a Mettler Toledo MP90 apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Advance 500 DPX spectrometer and an Agilent DD2 NMR (400 MHz) spectrometer in $CDCl_3$. HRMS data were recorded on a Shimadzu hybrid LC-MS-IT-TOF spectrometer. Elemental analyses were carried out on a VarioEL III instrument.

3.2. Synthesis of *N*-substituted-2-((imidazolyl)methyl)-3-acrylates (8a–8i)

To a solution of *N*-acetylimidazole **7a** (1 mmol) and a suitable Baylis–Hillman acetate **1** (1 mmol) in DMF (1 mL), K_2CO_3 (1 mmol) was added and the resulting mixture was stirred at room temperature until complete

consumption of *N*-acetylimidazole **7a**. The reaction mixture was then diluted with water (20 mL) and extracted with ethylacetate (3 × 20 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography over silica gel with EtOAc and hexane (1:1).

(*E*)-Methyl 2-((1-imidazolyl)methyl)-3-phenylacrylate (8a)

Yellow oil; yield (141 mg, 58%); ^{1}H NMR (500 MHz, $CDCl_3$): 8.03 (s, 1H), 7.48 (s, 1H), 7.42 (d, J = 7.4 Hz, 3H), 7.31 (d, J = 6.8 Hz, 2H), 7.01 (s, 1H), 6.85 (s, 1H), 4.96 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 166.9, 144.9, 137.0, 133.9, 129.7, 129.1, 129.0, 128.8, 127.0, 118.8, 52.5, 43.0; HRMS (IT-TOF); Anal. Calcd. for $C_{14}H_{14}N_2O_2$: m/z 243.1128; Found $[M+H]^+$: m/z 243.1126.

(*E*)-Methyl 2-((1-imidazolyl)methyl)-3-(*p*-tolyl)acrylate (8b)

Yellow oil; yield (188 mg, 73%); ^{1}H NMR (500 MHz, $CDCl_3$): 8.03 (s, 1H), 7.51 (s, 2H), 7.25 (s, 3H), 7.03 (s, 1H), 6.90 (s, 1H), 5.01 (s, 2H), 3.82 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 167.1, 145.0, 140.2, 137.0, 131.1, 129.8, 129.3, 129.0, 126.0, 118.8, 52.5, 43.1, 21.4; HRMS (IT-TOF); Anal. Calcd. for $C_{15}H_{16}N_2O_2$: m/z 257.1285; Found $[M+H]^+$: m/z 257.1284.

(*E*)-Methyl 2-((1-imidazolyl)methyl)-3-(4-methoxyphenyl)acrylate (8c)

Yellow solid; yield (106 mg, 39%); mp 88.0–89.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.02 (s, 1H), 7.54 (s, 1H), 7.32 (d, J = 10.0 Hz, 2H), 7.06 (s, 1H), 6.96 (d, J = 10.0 Hz, 2H), 6.93 (s, 1H), 5.03 (s, 2H), 3.86 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 167.4, 161.0, 144.9, 136.9, 131.1, 129.3, 126.2, 124.3, 118.7, 114.6, 55.4, 52.5, 43.2; Anal. Calcd for $C_{15}H_{16}N_2O_3$ (272.30): C, 66.16; H, 5.92; N, 10.29; Found: C, 66.08; H, 6.05; N, 10.21.

(*E*)-Methyl 2-((1-imidazolyl)methyl)-3-(2-nitrophenyl)acrylate (8d)

Light yellow solid; yield (242 mg, 84%); mp 85.0–87.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.29 (s, 1H), 8.26 (d, J = 10.0 Hz, 1H), 7.74 (t, J = 5.0 Hz, 1H), 7.65 (t, J = 7.5 Hz, 1H), 7.36 (s, 1H), 7.25 (d, J = 10.0 Hz, 1H), 7.00 (s, 1H), 6.80 (s, 1H), 4.79 (s, 2H), 3.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 166.1, 147.2, 141.8, 137.1, 134.1, 130.5, 130.3, 130.1, 129.5, 128.3, 125.5, 118.7, 52.8, 43.1; HRMS (IT-TOF); Anal. Calcd. for $C_{14}H_{13}N_3O_4$: m/z 288.0979; Found $[M+H]^+$: m/z 288.0970.

(*E*)-Methyl 2-((1-imidazolyl)methyl)-3-(4-fluorophenyl)acrylate (8e)

White solid; yield (131 mg, 50%); mp 101.0–102.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.03 (s, 1H), 7.50 (s, 1H), 7.35–7.32 (m, 2H), 7.16 (t, J = 7.5 Hz, 2H), 7.07 (s, 1H), 6.89 (s, 1H), 4.99 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 166.9, 143.8, 137.0, 131.0, 130.9, 129.6, 126.9, 118.7, 116.4, 116.2, 52.6, 42.9; HRMS (IT-TOF); Anal. Calcd. for $C_{14}H_{13}FN_2O_2$: m/z 261.1034; Found $[M+H]^+$: m/z 261.1030.

(*E*)-Methyl 2-((1-imidazolyl)methyl)-3-(3-chlorophenyl)acrylate (8f)

Light yellow solid; yield (116 mg, 42%); mp 80.0–81.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 7.97 (s, 1H), 7.47 (s, 1H), 7.43–7.39 (m, 2H), 7.32 (s, 1H), 7.20 (d, J = 10.0 Hz, 1H), 7.04 (s, 1H), 6.86 (s, 1H), 4.96 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 166.6, 143.0, 137.1, 135.7, 135.1, 130.4, 129.7, 129.5, 128.8, 128.6, 126.7, 118.7, 52.7, 42.8; HRMS (IT-TOF); Anal. Calcd. for $C_{14}H_{13}ClN_2O_2$: m/z 277.0738; Found $[M+H]^+$: m/z 277.0732.

(*E*)-Methyl 2-((1-imidazolyl)methyl)-3-(2-pyridinyl)acrylate (8g)

Brown solid; yield (138 mg, 57%); mp 96.0–97.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.77 (s, 1H), 7.82–7.76

(m, 3H), 7.43 (d, J = 10.0 Hz, 1H), 7.35 (t, J = 5.0 Hz, 1H), 7.18 (s, 1H), 6.99 (s, 1H), 5.70 (s, 2H), 3.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 167.4, 153.1, 149.8, 139.9, 138.1, 137.0, 130.5, 128.5, 127.7, 124.2, 119.7, 52.6, 41.8; HRMS (IT-TOF); Anal. Calcd. for $C_{13}H_{13}N_3O_2$: m/z 244.1081; Found $[M+H]^+$: m/z 244.1081.

(*E*)-Methyl 2-((1-imidazolyl)methyl)-3-(2-furanyl)acrylate (8h)

Light brown solid; yield (93 mg, 40%); mp 92.0–93.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): 7.62 (d, J = 9.6 Hz, 2H), 7.54 (s, 1H), 6.98 (d, J = 10.4 Hz, 2H), 6.75 (d, J = 3.2 Hz, 1H), 6.56 (t, J = 1.4 Hz, 1H), 5.27 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 167.4, 150.1, 145.9, 137.5, 128.9, 128.8, 122.1, 119.3, 119.2, 112.7, 52.5, 42.8; Anal. Calcd for $C_{12}H_{12}N_2O_3$ (232.24): C, 62.06; H, 5.21; N, 12.06; Found: C, 61.91; H, 5.17; N, 12.03.

(*E*)-Methyl 2-((1-imidazolyl)methyl)-3-(2-(3-methyl)thiophenyl)acrylate (8i)

Yellow solid; yield (109 mg, 42%); mp 99.0–100.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.17 (s, 1H), 7.62 (s, 1H), 7.48 (d, J= 5.0 Hz, 1H), 7.03 (s, 2H), 7.02 (d, J= 5.0 Hz, 1H), 5.23 (s, 2H), 3.83 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 167.5, 144.5, 137.3, 134.5, 130.9, 130.0, 129.2, 129.1, 121.2, 118.9, 52.5, 43.2, 14.8; Anal. Calcd for $C_{13}H_{14}N_2O_2S$ (262.33): C, 59.52; H, 5.38; N, 10.68; Found: C, 59.42; H, 5.39; N, 10.58.

3.3. Synthesis of *N*-substituted-2-((benzimidazolyl)methyl)-3-acrylates (9a–9i)

To a solution of N-acetylbenzimidazole **7b** (1 mmol) and a suitable Baylis–Hillman acetate **1** (1 mmol) in DMF (1 mL), K_2CO_3 (1 mmol) was added and the resulting mixture was stirred at room temperature until complete consumption of N-acetylbenzimidazole. The reaction mixture was then diluted with water (20 mL) and extracted with ethylacetate (3 × 20 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography over silica gel with EtOAc and hexane (1:1).

(*E*)-Methyl 2-((1-benzimidazolyl)methyl)-3-phenylacrylate (9a)

Colorless oil; yield (128 mg, 44%); ^{1}H NMR (400 MHz, $CDCl_3$): 8.08 (s, 1H), 7.90 (s, 1H), 7.74 (d, J= 8.4 Hz, 1H), 7.45–7.42 (m, 3H), 7.35–7.33 (m, 2H), 7.21 (t, J= 7.8 Hz, 1H), 7.14 (t, J= 7.6 Hz, 1H), 6.94 (d, J= 8.0 Hz, 1H), 5.20 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 166.8, 144.8, 143.6, 143.0, 140.3, 134.0, 133.6, 129.8, 129.1, 126.5, 122.8, 122.1, 120.2, 109.8, 52.5, 41.0; Anal. Calcd for $C_{18}H_{16}N_2O_2$ (292.33): C, 73.95; H, 5.52; N, 9.58; Found: C, 74.25; H, 5.60; N, 9.69.

(*E*)-Methyl 2-((1-benzimidazolyl)methyl)-3-(p-tolyl)acrylate (9b)

Yellow oil; yield (132 mg, 43%); ^{1}H NMR (500 MHz, $CDCl_3$): 8.11 (s, 1H), 7.95 (s, 1H), 7.80 (d, J = 10.0 Hz, 1H), 7.33–7.27 (m, 3H), 7.25–7.20 (m, 3H), 7.07 (d, J = 5.0 Hz, 1H), 5.25 (s, 2H), 3.79 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 167.0, 145.1, 143.8, 143.0, 140.3, 133.8, 131.1, 129.9, 129.3, 125.5, 122.8, 122.1, 120.3, 109.8, 52.5, 41.2, 21.5; HRMS (IT-TOF); Anal. Calcd. for $C_{19}H_{18}N_2O_2$: m/z 307.1441; Found $[M+H]^+$: m/z 307.1444.

(*E*)-Methyl 2-((1-benzimidazolyl)methyl)-3-(4-methoxyphenyl)acrylate (9c)

Light yellow oil; yield (142 mg, 44%); ^{1}H NMR (500 MHz, $CDCl_3$): 8.10 (s, 1H), 7.95 (s, 1H), 7.81 (d, J = 10.0 Hz, 1H), 7.35 (d, J = 10.0 Hz, 3H), 7.29–7.24 (m, 1H), 7.14 (d, J = 5.0 Hz, 1H), 6.97 (d, J = 10.0 Hz, 2H), 5.26 (s, 2H), 3.87 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 167.2, 161.1, 144.9, 143.8, 142.8, 133.8, 131.3, 126.3, 123.7, 122.9, 122.2, 120.3, 114.6, 109.8, 55.5, 52.4, 41.4; HRMS (IT-TOF); Anal. Calcd. for $C_{19}H_{18}N_2O_3$: m/z 323.1390; Found $[M+H]^+$: m/z 323.1390.

(*E*)-Methyl 2-((1-benzoimidazolyl)methyl)-3-(2-nitrophenyl)acrylate (9d)

Light yellow solid; yield (218 mg, 65%); mp 126.0–128.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): 8.26 (s, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.77 (s, 1H), 7.68 (d, J = 7.6 Hz, 1H), 7.61–7.53 (m, 2H), 7.21–7.12 (m, 3H), 6.93 (d, J = 8.0 Hz, 1H), 5.03 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 166.2, 147.0, 143.3, 142.9, 141.6, 133.9, 133.3, 130.3, 130.2, 129.9, 127.7, 125.4, 122.9, 122.2, 120.3, 109.4, 52.8, 41.3; Anal. Calcd for $C_{18}H_{15}N_3O_4$ (337.33): C, 64.09; H, 4.48; N, 12.46; Found: C, 64.14; H, 4.54; N, 12.54.

(*E*)-Methyl 2-((1-benzimidazolyl)methyl)-3-(4-fluorophenyl)acrylate (9e)

White solid; yield (130 mg, 42%); mp 83.0–85.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): 8.04 (s, 1H), 7.90 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.34–7.31 (m, 2H), 7.25–7.23 (m, 1H), 7.21–7.16 (m, 1H), 7.14–7.10 (m, 2H), 6.97 (d, J = 8.0 Hz, 1H), 5.17 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 166.7, 163.4, 143.7, 142.8, 133.6, 131.2, 130.0, 126.2, 122.9, 122.2, 120.4, 116.5, 116.3, 109.6, 52.6, 41.0; Anal. Calcd for $C_{18}H_{15}FN_2O_2$ (310.32): C, 69.67; H, 4.87; N, 9.03; Found: C, 69.64; H, 4.95; N, 9.05.

(*E*)-Methyl 2-((1-benzimidazolyl)methyl)-3-(3-chlorophenyl)acrylate (9f)

White solid; yield (136 mg, 42%); mp 83.5–84.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.03 (s, 1H), 7.94 (s, 1H), 7.80 (d, J = 5.0 Hz, 1H), 7.47–7.40 (m, 2H), 7.38 (s, 1H), 7.27–7.22 (m, 3H), 6.98 (d, J = 5.0 Hz, 1H), 5.22 (s, 2H), 3.80 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 166.5, 143.7, 143.1, 142.9, 135.8, 135.2, 133.6, 130.4, 129.8, 129.0, 128.1, 126.9, 123.0, 122.2, 120.4, 109.6, 52.7, 40.9; Anal. Calcd for $C_{18}H_{15}ClN_2O_2$ (326.78): C, 66.16; H, 4.63; N, 8.57; Found: C, 66.45; H, 4.59; N, 8.68.

(*E*)-Methyl 2-((1-benzimidazolyl)methyl)-3-(2-pyridinyl)acrylate (9g)

Brown solid; yield (120 mg, 41%); mp 97.5–100.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): 8.74 (d, J = 4.2 Hz, 1H), 8.16 (s, 1H), 7.82 (d, J = 1.6 Hz, 1H), 7.79 (dd, J = 7.6, 2.0 Hz, 1H), 7.73 (dd, J = 6.6, 1.8 Hz, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.40–7.38 (m, 1H), 7.35–7.32 (m, 1H), 7.22–7.14 (m, 2H), 5.95 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 167.3, 153.2, 149.8, 144.2, 143.4, 140.0, 137.1, 134.2, 130.1, 127.8, 124.3, 122.5, 121.7, 120.0, 110.5, 52.5, 40.2; HRMS (IT-TOF); Anal. Calcd. for $C_{17}H_{15}N_3O_2$: m/z 294.1237; Found $[M+H]^+$: m/z 294.1243.

(*E*)-Methyl 2-((1-benzimidazolyl)methyl)-3-(2-furanyl)acrylate (9h)

Brown solid; yield (130 mg, 46%); mp 115.5–116.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.04 (s, 1H), 7.79 (s, 1H), 7.67 (s, 2H), 7.41 (s, 1H), 7.26 (t, J = 5.0 Hz, 2H), 6.84 (d, J = 5.0 Hz, 1H), 6.62 (d, J = 5.0 Hz, 1H), 5.57 (s, 2H), 3.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 167.3, 150.1, 146.0, 143.6, 143.5, 134.1, 129.2, 122.8, 121.9, 121.4, 120.2, 119.5, 112.8, 110.2, 52.5, 41.5; Anal. Calcd for $C_{16}H_{14}N_2O_3$ (282.29): C, 68.07; H, 5.00; N, 9.92; Found: C, 67.73; H, 5.05; N, 9.61.

(*E*)-Methyl 2-((1-benzoimidazolyl)methyl)-3-(2-(3-methyl)thiophenyl)acrylate (9i)

White solid; yield (102 mg, 33%); mp 131.5–132.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$): 8.23 (s, 1H), 7.88 (s, 1H), 7.78–7.75 (m, 1H), 7.40 (d, J = 5.2 Hz, 1H), 7.37–7.34 (m, 1H), 7.27–7.22 (m, 2H), 6.97 (d, J = 5.2 Hz, 1H), 5.37 (s, 2H), 3.74 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 167.3, 144.5, 143.8, 142.6, 135.1, 133.9, 130.9, 129.9, 129.5, 122.8, 122.1, 122.0, 120.3, 110.0, 52.5, 41.7, 14.8; Anal. Calcd for $C_{17}H_{16}N_2O_2S$ (312.39): C, 65.36; H, 5.16; N, 8.97; Found: C, 65.25; H, 5.18; N, 8.85.

3.4. Synthesis of *N*-substituted-2-((1- and 2-benzotriazolyl)methyl)-3-acrylates (10a–10i and 11a–11i)

To a solution of *N*-acetylbenzotriazole **7c** (1 mmol) and a suitable Baylis–Hillman acetate **1** (1 mmol) in DMF (1 mL), K_2CO_3 (1 mmol) was added and the resulting mixture was stirred at room temperature until complete consumption of *N*-acetylbenzotriazole. The reaction mixture was then diluted with water (20 mL) and extracted with ethylacetate (3 × 20 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography over silica gel with EtOAc and hexane (1:4).

(*E*)-Methyl 2-((1-benzotriazolyl)methyl)-3-phenylacrylate (10a)

White solid; yield (196 mg, 67%); mp 89.0–90.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.18 (s, 1H), 8.08 (dd, J = 8.4, 0.8 Hz, 1H), 7.75–7.74 (m, 2H), 7.64 (dd, J = 8.4, 0.8 Hz, 1H), 7.53–7.39 (m, 5H), 5.62 (s, 2H), 3.74 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 167.0, 145.8, 145.4, 134.0, 133.5, 129.7, 129.4, 128.9, 127.3, 125.7, 123.8, 119.9, 110.1, 52.4, 44.7; Anal. Calcd for $C_{17}H_{15}N_3O_2$ (293.32): C, 69.61; H, 5.15; N, 14.33; Found: C, 69.81; H, 5.15; N, 14.36.

(*E*)-Methyl 2-((2-benzotriazolyl)methyl)-3-phenylacrylate (11a)

White solid; yield (53 mg, 18%); mp 102.5–103.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$): 8.18 (s, 1H), 7.88 (dd, J = 6.8, 3.2 Hz, 2H), 7.55–7.53 (m, 2H), 7.40–7.36 (m, 5H), 5.74 (s, 2H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 167.0, 145.5, 144.4, 134.0, 129.7, 129.3, 128.9, 126.2, 125.0, 118.2, 53.0, 52.5; Anal. Calcd for $C_{17}H_{15}N_3O_2$ (293.32): C, 69.61; H, 5.15; N, 14.33; Found: C, 69.71; H, 5.19; N, 14.32.

(*E*)-Methyl 2-((1-benzotriazolyl)methyl)-3-(p-tolyl)acrylate (10b)

White solid; yield (167 mg, 54%); mp 83.0–85.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): 8.10 (s, 1H), 8.04 (dd, J = 7.2, 0.8 Hz, 1H), 7.61–7.58 (m, 3H), 7.46 (td, J = 7.6, 1.2 Hz, 1H), 7.34 (td, J = 7.6, 1.2 Hz, 1H), 7.22 (s, 1H), 5.60 (s, 2H), 3.69 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 167.1, 145.7, 145.5, 140.1, 133.5, 131.1, 129.6, 129.5, 127.2, 124.7, 123.8, 119.9, 110.1, 52.3, 44.8, 21.4; Anal. Calcd for $C_{18}H_{17}N_3O_2$ (307.35): C, 70.34; H, 5.58; N, 13.67; Found: C, 70.48; H, 5.60; N, 13.68.

(*E*)-Methyl 2-((1-benzotriazolyl)methyl)-3-(4-methoyphenyl)acrylate (10c)

White solid; yield (205 mg, 63%); mp 90.0–91.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.12 (s, 1H), 8.08 (d, J = 8.5 Hz, 1H), 7.76 (d, J = 8.5 Hz, 2H), 7.68 (d, J = 8.5 Hz, 1H), 7.51 (t, J = 7.5 Hz, 1H), 7.39 (t, J = 7.5 Hz, 1H), 6.99 (d, J = 8.5 Hz, 2H), 5.66 (s, 2H), 3.87 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 167.4, 161.0, 145.8, 145.3, 133.5, 131.7, 127.3, 126.4, 123.8, 123.2, 119.9, 114.4, 110.3, 55.4, 52.3, 45.0; Anal. Calcd for $C_{18}H_{17}N_3O_3$ (323.35): C, 66.86; H, 5.30; N, 13.00; Found: C, 66.67; H, 5.28; N, 12.93.

(*E*)-Methyl 2-((2-benzotriazolyl)methyl)-3-(4-methoxyphenyl)acrylate (11c)

White solid; yield (55 mg, 17%); mp 89.0–90.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.17 (s, 1H), 7.93 (dd, J = 6.5, 3.0 Hz, 2H), 7.56 (d, J = 9.0 Hz, 2H), 7.41 (dd, J = 6.5, 3.0 Hz, 2H), 6.95 (d, J = 9.0 Hz, 2H), 5.81 (s, 2H), 3.84 (s, 3H), 3.81 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 167.4, 161.0, 145.4, 144.4, 131.5, 126.6, 126.2, 122.7, 118.2, 114.4, 55.4, 53.2, 52.4; Anal. Calcd for $C_{18}H_{17}N_3O_3$ (323.35): C, 66.86; H, 5.30; N, 13.00; Found: C, 66.79; H, 5.24; N, 12.98.

(*E*)-Methyl 2-((1-benzotriazolyl)methyl)-3-(2-nitrophenyl)acrylate (10d)

Yellow solid; yield (236 mg, 70%); mp 107.0–108.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.37 (s, 1H), 8.22

(d, J = 10.0 Hz, 1H), 8.08 (d, J = 10.0 Hz, 1H), 8.03 (d, J = 10.0 Hz, 1H), 7.75 (t, J = 7.5 Hz, 1H), 7.66 (d, J = 5.0 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.52 (t, J = 7.5 Hz, 1H), 7.38, (t, J = 7.5 Hz, 1H), 5.42 (s, 2H), 3.78 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 166.1, 147.1, 145.6, 142.1, 134.3, 133.4, 131.3, 130.0, 130.0, 127.5, 126.8, 125.0, 124.0, 119.8, 110.0, 52.7, 44.7; Anal. Calcd for $C_{17}H_{14}N_4O_4$ (338.32): C, 60.35; H, 4.17; N, 16.56; Found: C, 60.49; H, 4.13; N, 16.69.

(*E*)-Methyl 2-((2-benzotriazolyl)methyl)-3-(2-nitrophenyl)acrylate (11d)

Yellow solid; yield (65 mg, 19%); mp 110.5–111.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$): 8.40 (s, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.83 (dd, J = 6.6, 3.0 Hz, 2H), 7.77 (d, J = 7.2 Hz, 1H), 7.60 (t, J = 7.4 Hz, 1H), 7.52 (t, J = 8.2 Hz, 1H), 7.35 (dd, J = 6.8, 3.2 Hz, 2H), 5.51 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 165.9, 144.3, 142.4, 134.1, 130.6, 130.2, 130.0, 126.4, 126.3, 125.1, 118.1, 109.4, 52.8, 52.7; Anal. Calcd for $C_{17}H_{14}N_4O_4$ (338.32): C, 60.35; H, 4.17; N, 16.56; Found: C, 60.40; H, 4.22; N, 16.25.

(*E*)-Methyl 2-((1-benzotriazol-1-yl)methyl)-3-(4-fluorophenyl)acrylate (10e)

White solid; yield (188 mg, 60%); mp 112.0–113.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.12 (s, 1H), 8.09 (d, J = 10.0 Hz, 1H), 7.82–7.79 (m, 2H), 7.69 (d, J = 5.0 Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H), 7.40 (t, J = 10.0 Hz, 1H), 7.17 (t, J = 10.0 Hz, 2H), 5.59 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 166.9, 163.5, 145.7, 144.2, 133.6, 131.6, 130.0, 127.4, 125.6, 123.9, 119.9, 116.1, 110.1, 52.5, 44.6; Anal. Calcd for $C_{17}H_{14}FN_3O_2$ (311.31): C, 65.59; H, 4.53; N, 13.50; Found: C, 65.34; H, 4.71; N, 13.48.

(*E*)-Methyl 2-((2-benzotriazolyl)methyl)-3-(4-fluorophenyl)acrylate (11e)

White solid; yield (53 mg, 17%); mp 114.0–115.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.17 (s, 1H), 7.93–7.91 (m, 2H), 7.63–7.60 (m, 2H), 7.43–7.41 (m, 2H), 7.13 (t, J = 7.5 Hz, 2H), 5.76 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 166.9, 163.5, 144.5, 144.4, 131.5, 130.2, 126.4, 124.9, 118.2, 116.1, 52.9, 52.6; Anal. Calcd for $C_{17}H_{14}FN_3O_2$ (311.31): C, 65.59; H, 4.53; N, 13.50; Found: C, 65.87; H, 4.62; N, 13.49.

(*E*)-Methyl 2-((1-benzotriazolyl)methyl)-3-(3-chlorophenyl)acrylate (10f)

White solid; yield (223 mg, 68%); mp 87.0–88.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.09 (d, J = 8.4 Hz, 1H), 7.64 (d, J = 8.4 Hz, 1H), 7.53 (td, J = 7.7, 0.9 Hz, 1H), 7.40 (td, J = 7.6, 0.9 Hz, 1H), 7.29–7.23 (m, 3H), 7.14–7.12 (m, 1H), 6.85 (s, 1H), 5.62 (s, 2H), 3.61 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 166.7, 146.1, 138.3, 136.3, 134.1, 133.0, 129.4, 128.8, 128.6, 128.5, 127.8, 126.8, 124.2, 120.1, 109.7, 52.1, 50.9; Anal. Calcd for $C_{17}H_{14}ClN_3O_2$ (327.76): C, 62.30; H, 4.31; N, 12.82; Found: C, 62.51; H, 4.35; N, 12.87.

(*E*)-Methyl 2-((2-benzotriazolyl)methyl)-3-(3-chlorophenyl)acrylate (11f)

White solid; yield (40 mg, 12%); mp 104.0–105.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.13 (s, 1H), 7.92 (dd, J = 6.3, 3.0 Hz, 2H), 7.60 (s, 1H), 7.50 (s, 1H), 7.43–7.36 (m, 4H), 5.74 (s, 2H), 3.81 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 166.6, 144.4, 143.8, 135.8, 134.9, 130.2, 129.7, 129.3, 127.1, 126.5, 126.4, 118.2, 52.7, 52.6; HRMS (IT-TOF); Anal. Calcd. for $C_{17}H_{14}ClN_3O_2$: m/z 328.0847; Found $[M+H]^+$: m/z 328.0840.

(*E*)-Methyl 2-((1-benzotriazolyl)methyl)-3-(2-pyridinyl)acrylate (10g)

Light brown solid; yield (156 mg, 53%); mp 114.0–116.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.68 (d, J = 4.5 Hz, 1H), 8.04 (d, J = 8.5 Hz, 1H), 7.93 (s, 1H), 7.81 (td, J = 7.8, 1.8 Hz, 1H), 7.64 (d, J = 8.5 Hz, 1H), 7.59 (d, J = 7.5 Hz, 1H), 7.44 (td, J = 7.5, 1.0 Hz, 1H), 7.35–7.29 (m, 2H), 6.43 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 167.1, 153.3, 149.7, 145.7, 140.9, 137.0, 133.5, 129.0, 127.6, 126.9, 124.1, 123.6, 119.7, 110.5, 52.5, 44.0; HRMS (IT-TOF); Anal. Calcd. for $C_{16}H_{14}N_4O_2$: m/z 295.1190; Found [M+H]+: m/z 295.1192.

(*E*)-Methyl 2-((2-benzotriazolyl)methyl)-3-(2-pyridinyl)acrylate (11g)

Light brown solid; yield (32 mg, 11%); mp 138.0–140.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 7.38 (d, J = 4.5 Hz, 1H), 6.74 (s, 1H), 6.60 (dd, J = 6.5, 3.0 Hz, 2H), 6.47 (dd, J = 7.8, 1.8 Hz, 1H), 6.27 (d, J = 8.0 Hz, 1H), 6.08 (dd, J = 6.5, 3.0 Hz, 2H), 6.01–5.98 (m, 1H), 5.27 (s, 2H), 2.61 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 162.4, 148.5, 145.1, 139.5, 136.6, 132.0, 123.4, 122.6, 121.2, 119.2, 113.3, 47.8, 47.2; HRMS (IT-TOF); Anal. Calcd. for $C_{16}H_{14}N_4O_2$: m/z 295.1190; Found [M+H]+: m/z 295.1190.

(*E*)-Methyl 2-((1-benzotriazolyl)methyl)-3-(2-furanyl)acrylate (10h)

Light yellow solid; yield (100 mg, 35%); mp 128.0–130.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.03 (d, J = 8.3 Hz, 1H), 7.75 (s, 1H), 7.60 (d, J = 8.1 Hz, 2H), 7.44 (t, J = 7.6 Hz, 1H), 7.33 (t, J = 7.7 Hz, 1H), 6.95 (d, J = 3.2 Hz, 1H), 6.56–6.55 (m, 1H), 5.98 (s, 2H), 3.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 168.3, 151.0, 147.0, 146.7, 134.0, 131.1, 127.9, 124.4, 121.1, 120.5, 120.0, 113.3, 110.8, 52.7, 45.2; Anal. Calcd for $C_{15}H_{13}N_3O_3$ (283.28): C, 63.60; H, 4.63; N, 14.83; Found: C, 63.78; H, 4.70; N, 14.86.

(*E*)-Methyl 2-((2-benzotriazolyl)methyl)-3-(2-furanyl)acrylate (11h)

Yellow solid; yield (28 mg, 10%); mp 76–78 °C; ^{1}H NMR (400 MHz, $CDCl_3$): 7.82 (dd, J = 6.4, 3.2 Hz, 2H), 7.78 (s, 1H), 7.51 (d, J = 1.2 Hz, 1H), 7.31 (dd, J = 6.6, 3.2 Hz, 2H), 6.81 (d, J = 3.6 Hz, 1H), 6.47 (dd, J = 3.0, 1.6 Hz, 1H), 6.05 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 167.3, 150.1, 146.0, 144.2, 130.6, 126.0, 119.8, 118.8, 118.1, 112.5, 52.7, 52.5; Anal. Calcd for $C_{15}H_{13}N_3O_3$ (283.28): C, 63.60; H, 4.63; N, 14.83; Found: C, 63.40; H, 4.82; N, 14.72.

(*E*)-Methyl 2-((1-benzotriazolyl)methyl)-3-(2-(3-methyl)thiophenyl)acrylate (10i)

White solid; yield (151 mg, 48%); mp 134.0–135.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 8.14 (s, 1H), 8.05 (d, J = 8.3 Hz, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.49–7.44 (m, 2H), 7.35 (t, J = 7.5 Hz, 1H), 7.15 (s, 1H), 5.81 (s, 2H), 3.74 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 168.3, 146.8, 139.7, 138.4, 137.2, 137.1, 134.1, 128.0, 127.8, 124.5, 121.5, 120.6, 110.9, 52.7, 45.3, 15.6; Anal. Calcd for $C_{16}H_{15}N_3O_2S$ (313.37): C, 61.32; H, 4.82; N, 13.41; Found: C, 61.17; H, 4.83; N, 13.31.

(*E*)-Methyl 2-((2-benzotriazolyl)methyl)-3-(2-(3-methyl)thiophenyl)acrylate (11i)

White solid; yield (66 mg, 21%); mp 137.0–138.0 °C; ^{1}H NMR (500 MHz, DMSO-d_6): 8.40 (s, 1H), 7.89 (dd, J = 6.6, 3.1 Hz, 2H), 7.40–7.36 (m, 3H), 6.96 (d, J = 5.1 Hz, 1H), 6.03 (s, 2H), 3.83 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): 168.6, 145.3, 145.0, 136.7, 131.4, 131.3, 130.5, 126.9, 120.0, 118.9, 53.1, 52.8, 14.9; Anal. Calcd for $C_{16}H_{15}N_3O_2S$ (313.37): C, 61.32; H, 4.82; N, 13.41; Found: C, 61.53; H, 4.77; N, 13.32.

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