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# *N*-Acylazole mediated stereoselective and regioselective synthesis of *N*-substituted azole acrylonitriles

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**Abstract:** Regio- and stereoselective synthesis of *N*-substituted azole acrylonitriles has been achieved smoothly in *N*,*N*-dimethylformamide (DMF) in the presence of potassium carbonate ($K_2CO_3$) as a base catalyst. *N*-Substituted azole acrylonitriles were obtained in moderate to good yields (39%–87%) with a one-pot reaction between readily available *N*-acetylazoles and Baylis-Hillman nitriles. The structural determinations were accomplished by NOESY $^1$H NMR and X-ray crystallography.

**Key words:** Baylis–Hillman nitriles, benzimidazole, benzotriazole, *N*-substituted azole acrylonitriles

## 1. Introduction

Benzotriazole and benzimidazole are very useful subunits for the development of the potential chemotherapeutic agents. They act as precursors in many synthesis reactions and have proven to be versatile and valuable sources of medicinal agents as their derivatives show various pharmaceutical activities such as antimicrobial, antifungal, antitumor, and anthelmintic [1–5]. The literature studies based on the incorporation of benzotriazole and benzimidazole units in order to obtain their derivatives resulted in many drugs which have been on the market or are in clinical trials to cure many illnesses [6–8]. Among them are Vorozole [9], Alizapride [10], Albendazole [11], and Benomyl [12] (Figure 1).

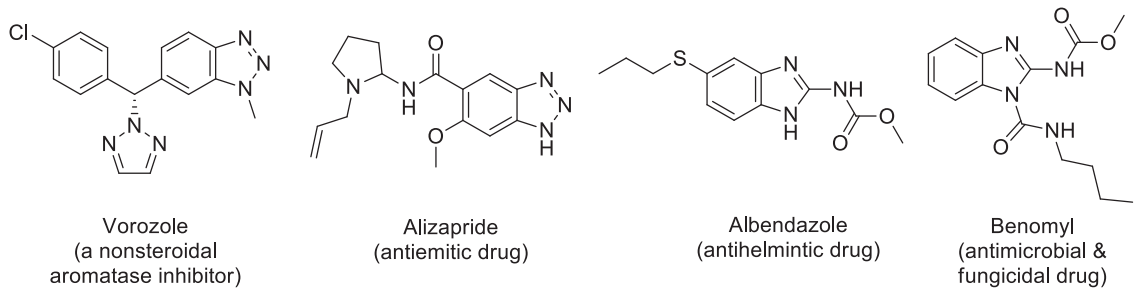


**Figure 1**. Some clinically important benzotriazole- and benzimidazole-based drugs.

There have been several reported works that showed some substituted acrylonitriles addressed to the bactericidal and cytotoxic activities in human cancer cell lines. Their benzotriazolyl and benzimidazolyl derivatives were also found to be active against both hematological and solid human tumors. Detailed structure-activity relationship studies have been carried out and from the analysis of data, it was deduced that the presence

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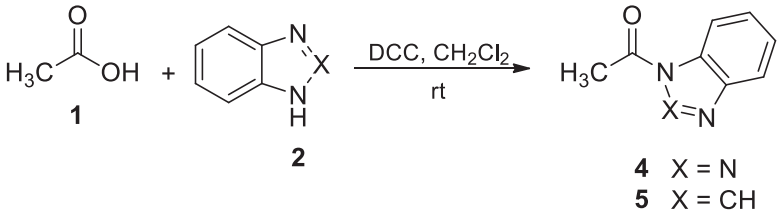
of acrylonitrile unit is required for good activity but the presence of azole unit is also necessary for killing cells [13,14]. On the other hand, the position of the azole ring attached to the acrylonitrile is not essential for the activity. Another study also revealed that the loss of activity was seen after the conversion of the cyano group into a carboxamido or carboxylic acid group [15].

Baylis–Hillman adducts offer an excellent platform for several chemical transformations because of the presence of three functional groups including a hydroxyl group, a double bond, and an electron withdrawing group in close proximity. They were illustrated as valuable precursors for the synthesis of heterocycles and many biologically active molecules [16,17]. We recently reported the synthesis of several $N$-substituted azole acrylates from the reaction between Baylis–Hillman adducts and $N$-acylazoles with quantitative yields in one-pot reaction [18]. $N$-Acylazoles are very important synthetic auxiliaries in organic synthesis as they are stable crystalline compounds and offer mild reaction conditions to prepare amides [19,20], esters, thioesters [21], ketones [22,23], and heterocycles [24–26].

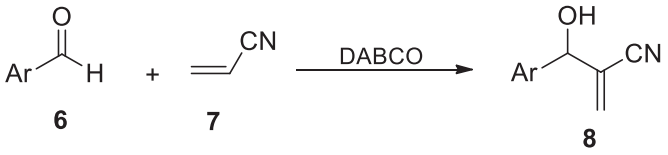
Based on their pharmacological importance and in line with our studies concerning the synthesis of azole derivatives from Baylis–Hillman adducts, we aimed to synthesize $N$-substituted benzotriazolyl and benzimidazolyl acrylonitriles with a versatile method.

## 2. Results and discussion

We first prepared the starting compounds in laboratory conditions by modifying the literature methods. $N$-Acetylbenzotriazoles and $N$-acetylbenzimidazoles were prepared by treating acetic acid with benzotriazole or benzimidazole in the presence of $N,N'$-dicyclohexylcarbodiimide at room temperature (Scheme 1). Baylis–Hillman nitriles were prepared from the reaction between suitable aldehydes and acrylonitrile catalyzed by 1,4-Diazabicyclo[2.2.2]octane (Scheme 2) [27,28]. Then, we started to synthesize the target compounds according to the method we previously described to prepare $N$-substituted azole acrylates. $N$-substituted benzotriazolyl acrylonitriles were afforded by the reaction of Baylis-Hillman nitriles with $N$-acetylbenzotriazole in DMF in the presence of $K_2CO_3$ at room temperature (Scheme 3).

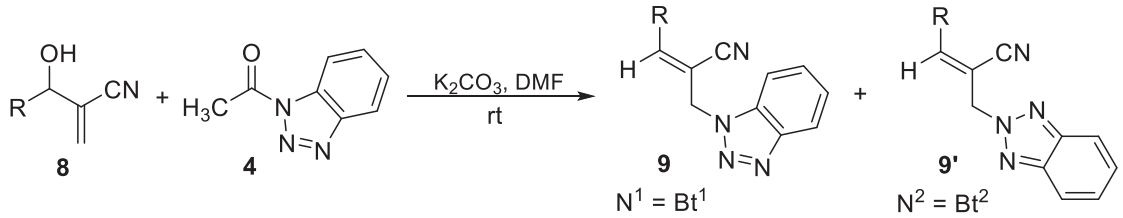



**Scheme 1**. Synthesis of $N$-acetylazoles.




**Scheme 2**. Synthesis of Baylis–Hillman nitriles.

All the synthesized products were purified by column chromatography and their structures were identified by NMR and FTIR spectral data. The obtained results were supported by high resolution mass spectra (HRMS).




**Scheme 3**. Synthesis of $N$-substituted benzotriazolyl acrylonitriles.

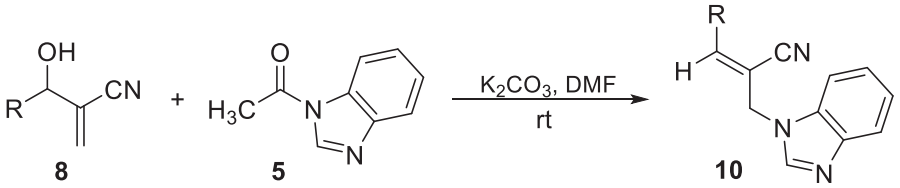
$N$-Substituted benzotriazolyl acrylonitriles were synthesized in 39%–87% yields (Table 1). While it was seen that the yields increased in the presence of electron donating groups on benzene ring in $N$-substituted benzotriazolyl acrylonitriles, they decreased in the presence of electron withdrawing groups on benzene ring. In some cases, we observed that there was another product, other than the target compound. We thought that these two products are N-1 ($Bt^1$) and N-2 ($Bt^2$) isomers of benzotriazole according to their $^{13}$C-NMR spectra. In $^{13}$C-NMR spectra, while six C signals for benzotriazolyl ring in $Bt^1$ isomers were observed, three C signals for benzotriazolyl ring in $Bt^2$ isomers were observed because of the symmetry in $Bt^2$ rings. Comparing the formation of $Bt^1$ isomer to that of $Bt^2$ isomer, in some cases, the yields of $Bt^1$ compounds are much higher than the yields of $Bt^2$ compounds. For the rest, $Bt^1$ was obtained as the sole product (Table 1). These results show that the developed reactions are regioselective. On the other hand, the $^1$H-NMR spectra of **9** and **9'** consist of singlet signals in the ranges of 6.97–7.49 ppm and 5.54–5.66 ppm, which are attributable to the vinylic-H and the protons of $-CH_2$, respectively. The IR spectra of compounds also contain a strong absorption at around 2204–2263 $cm^{-1}$, confirming the presence of CN group.

**Table 1**. Yields of $N$-substituted benzotriazolyl acrylonitriles.

| Entry | R | $Bt^1$ Yield (%) | $Bt^2$ Yield (%) | Overall Yield (%) |
|---|---|---|---|---|
| **1** | Ph | **9a**, 76 | **9'a**, 11 | 87 |
| **2** | 4-Me-Ph | **9b**, 71 | **9'b**, – | 71 |
| **3** | 4-MeO-Ph | **9c**, 67 | **9'c**, 17 | 84 |
| **4** | 4-F-Ph | **9d**, 67 | **9'd**, – | 67 |
| **5** | 3-Cl-Ph | **9e**, 63 | **9'e**, – | 63 |
| **6** | 2,4-$Cl_2$-Ph | **9f**, 52 | **9'f**, – | 52 |
| **7** | 4-Br-Ph | **9g**, 63 | **9'g**, – | 63 |
| **8** | 2-Furanyl | **9h**, 57 | **9'h**, – | 57 |
| **9** | 2-Thiophenyl | **9i**, 28 | **9'i**, 11 | 39 |

We repeated the same reaction conditions for the synthesis of $N$-substituted benzimidazolyl acrylonitriles employing the Baylis–Hillman nitriles with $N$-acetylbenzimidazole. Reactions took place in DMF in the presence of $K_2CO_3$ at room temperature (Scheme 4).

All the synthesized products were purified by column chromatography and the overall yields (39%–73%) seemed to be satisfactory (Table 2). While the yields of the obtained products increased in the presence of electron donating groups on benzene ring in $N$-substituted benzimidazolyl acrylonitriles, they decreased in the presence of electron withdrawing groups on benzene ring. The structures of isolated products were confirmed on




**Scheme 4**. Synthesis of $N$-substituted benzimidazolyl acrylonitriles.

the basis of $^1$H- and $^{13}$C-NMR spectra. The obtained results were also supported by FTIR spectroscopy and HRMS. In $^1$H-NMR spectra, a singlet signal assigned to the proton of CH in benzimidazole ring was observed at around 8.02–8.05 ppm for all compounds. Moreover, vinylic proton signals resonated as singlet between 6.75 and 7.01 ppm. A singlet signal for $CH_2$ protons was observed at around 5.06–5.58 ppm. The CN stretches in the IR spectra of **10** are similar to those observed for **9** and **9'**.

**Table 2**. Yields of $N$-substituted benzimidazolyl acrylonitriles.

| Entry | R | Yield (%) | Entry | R | Yield (%) |
|---|---|---|---|---|---|
| **1** | Ph | **10a**, 73 | **6** | 2,4-$Cl_2$-Ph | **10f**, 39 |
| **2** | 4-Me-Ph | **10b**, 56 | **7** | 4-Br-Ph | **10g**, 44 |
| **3** | 4-MeO-Ph | **10c**, 48 | **8** | 2-Furanyl | **10h**, 40 |
| **4** | 4-F-Ph | **10d**, 48 | **9** | 2-Thiophenyl | **10i**, 48 |
| **5** | 3-Cl-Ph | **10e**, 48 | | | |

After all the compounds were synthesized and characterized, it was thought that only one isomer was formed among the possible geometric isomers $E/Z$ that are said to have occurred for similar compounds in the literature [29–32]. According to the spectral data reported in the literature, while chemical shift values of the vinylic protons in the $E$-isomers appear obviously downfield of the aromatic protons, the corresponding values for the vinylic protons of the $Z$-isomers are generally observed upfield or overlapped with aromatic ring protons. In our spectral work, we observed vinylic proton signals at around 7.11–7.36 ppm for compounds **9**, 7.30–7.49 ppm for compounds **9′**, and 6.75–7.09 ppm for compounds **10**. Because of the upfield shift of vinylic proton signals, we ran 2D NOESY experiments and also used X-ray method for products **9a**, **9′a**, and **10a** to decide which double bond configuration is favorable.

In the 2D NOESY experiment carried out for compound **9a** (Figure 2), cross sectional peaks between the $H_{7,8}$ protons resonated at 5.59 ppm and $H_9$ and $H_6$ protons resonated at 7.67 and 7.23 ppm, respectively, were observed. The presence of these cross sectional peaks proved that these protons interacted spatially. Based on the results obtained from the 2D NOESY experiment, it was thought that **9a** compound has $Z$-configuration. We ran the same experiment for compound **9′a** (Figure 3). Because the presence of cross sectional peaks between $H_{5,6}$ protons resonated at 5.54 ppm and $H_7$ proton resonated at 7.35 ppm showing that these protons interacted spatially, we concluded that **9′a** also has $Z$-configuration. According to the 2D NOESY experiment run for compound **10a**, cross sectional peaks between $H_{7,8}$ protons resonated at 5.08 ppm and $H_6$, $H_9$, and $H_{13}$ protons resonated at 7.01, 7.43, and 7.88 ppm, respectively, were observed (Figure 4). This showed that $H_{7,8}$ protons interacted with $H_6$, $H_9$, and $H_{13}$ protons spatially. Therefore, compound **10a** was also thought as $Z$ isomer.

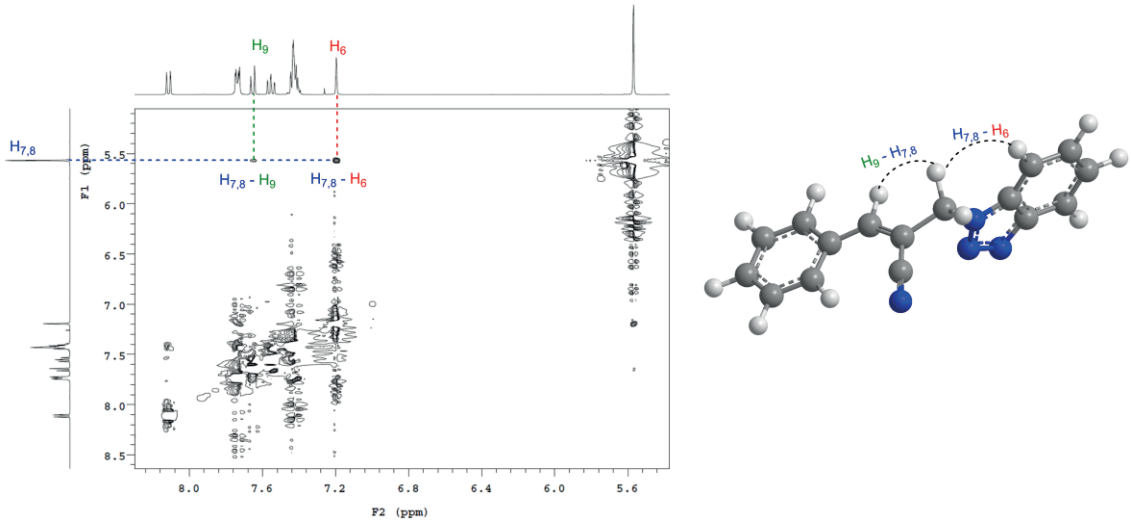



**Figure 2**. The 2D NOESY spectrum (**a**) and 3D structure (**b**) of **9a**.

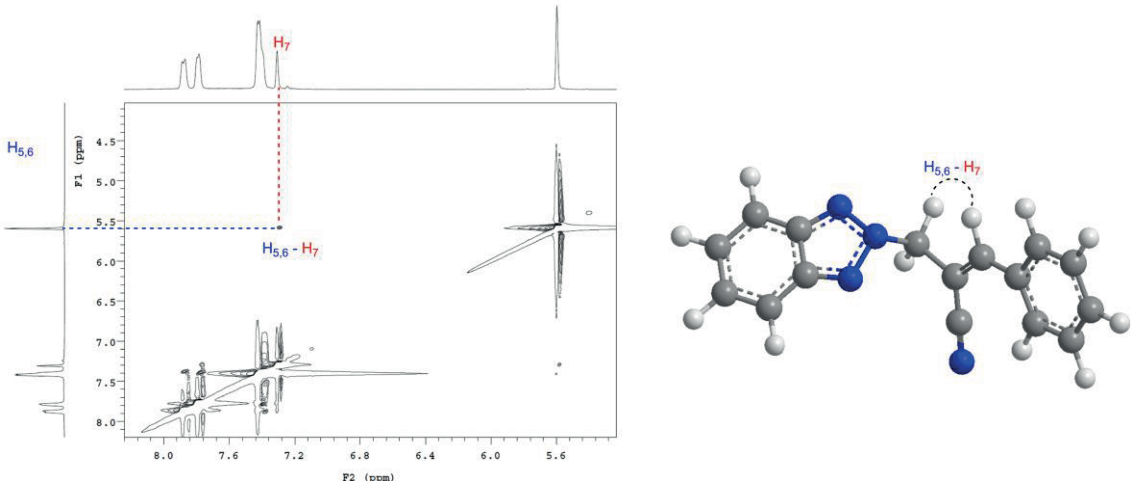



**Figure 3**. The 2D NOESY spectrum (**a**) and 3D structure (**b**) of **9′a**.

To support the results obtained from the NOESY experiments, X-ray diffraction analysis was performed for the same compounds (**9a, 9a′**, and **10a**). X-ray suitable crystals were obtained via layer diffusion using ethyl acetate/n-hexane as solvents. The compounds thermal ellipsoid plots are given in Figure 5 with 40% probability level and crystallographic data, refinement parameters, and selected bond lengths are shown in Tables 3 and 4. All the hydrogen atoms were added at the detected positions. The measured bond distances are in agreement with standard values. The measured N-N bond distances for all three compounds are close to each other between 1.297–1.345 Å. In addition, double bond distances between nitrogen atoms were found to be shorter than single bonds for compounds **9a** (N(1)–N(2)) and **9′a** (N(2)–N(3)) as 1.297 Å and 1.313, respectively. Due to the $sp^2$ hybridization, bond distances between $sp^2$ hybridized carbons were shorter than those involving $sp^3$ carbons in the range of 1.323–1.329 Å. From the single-crystal figures of compounds **9a**, **9a′**, and **10a**, it was seen that the vinylic protons and $CH_2$ protons are close spatially (Figure 5).

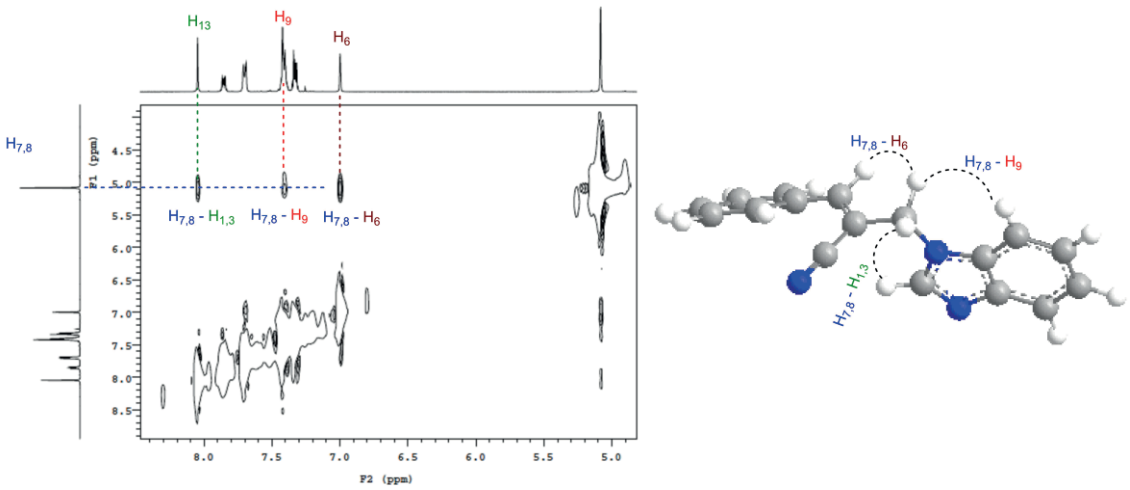



**Figure 4**. The 2D NOESY spectrum (**a**) and 3D structure (**b**) of **10a**.

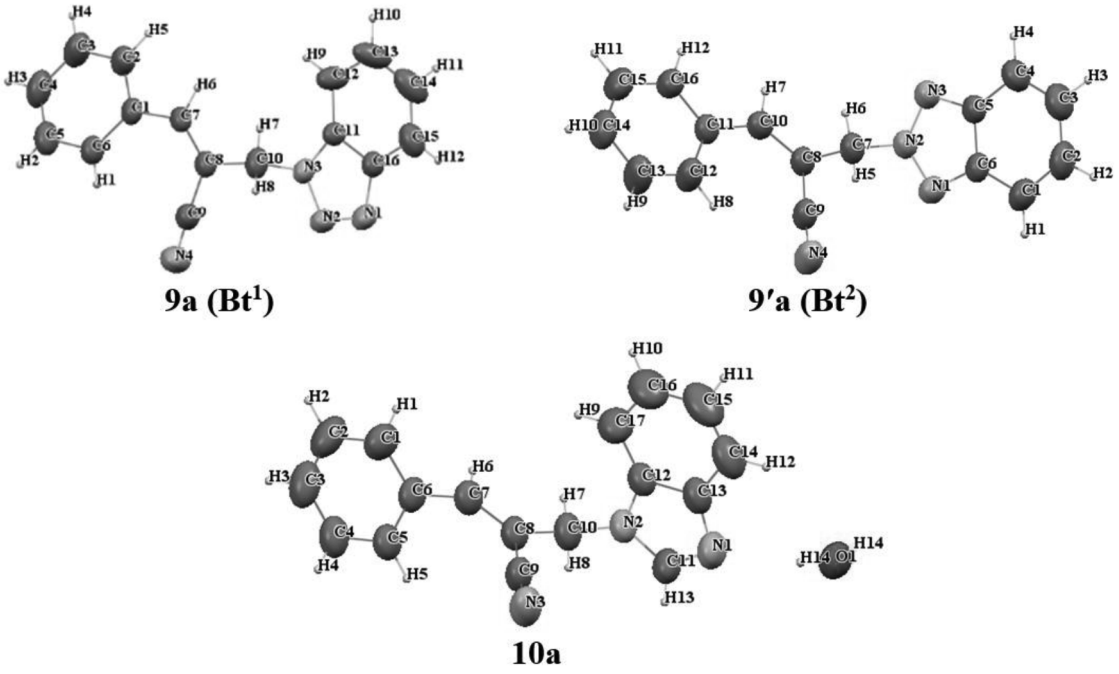



**Figure 5**. Thermal ellipsoid plots of the compounds **9a**, **9′a**, and **10a** at the 40% probability level.

Data obtained from the spectral work showed that all compounds have Z-configuration. Only one of the possible geometric isomers was obtained with the method used here, we concluded that the developed reactions are also found to be stereoselective. When the preparation of $N$-substituted azole acrylonitriles is compared with the preparation of $N$-substituted azole acrylates [18], different stereoisomers have been obtained. While $Z$-isomers of $N$-substituted azole acrylonitriles in this work are obtained, $E$-isomers of $N$-substituted azole acrylates in our previously published work have been obtained. In addition to these results, N-1 ($Bt^1$) isomer of benzotriazoleboth in this work and in our previous work has been obtained more than N-2 ($Bt^2$) isomer of benzotriazole.

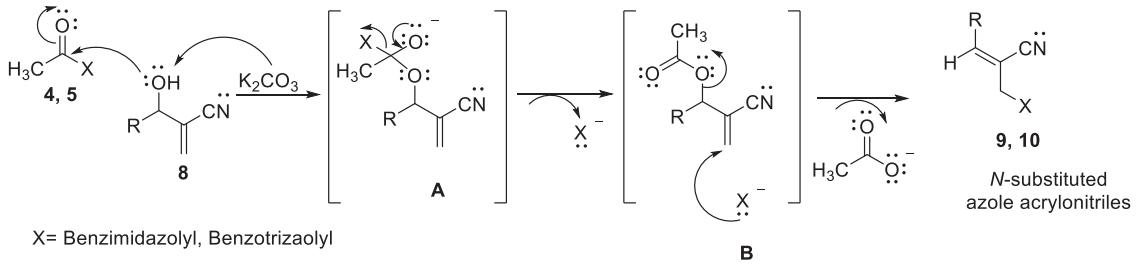
**Table 3**. Crystal data and structure refinement for **9a**, **9′a**, and **10a** compounds.

| | **9a** | **9′a** | **10a** |
|---|---|---|---|
| CCDC Number | 1850321 | 1850263 | 1850354 |
| Formula | $C_{16}H_{12}N_4$ | $C_{16}H_{12}N_4$ | $C_{17}H_{13}N_3$·0.5(HO) |
| Molecular weight | 260.30 | 260.30 | 267.81 |
| Temperature (K) | 296 | 296 (2) | 296 |
| Wavelength (Å) | 0.71073 | 0.71073 | 0.71073 |
| Crystal system | Monoclinic | monoclinic | Monoclinic, |
| Space group | P21/n | P21/n | C2/c |
| a (Å), $\alpha$ ($^o$) | 13.0856 (10), 90 | 13.564 (11), 90 | 23.909 (3), 90 |
| b (Å), $\beta$ ($^o$) | 7.1032 (6), 110.390(5) | 6.150 (5), 95.286 (17) | 9.6366 (12), 133.402(6) |
| c (Å), $\gamma$ ($^o$) | 15.6618 (12), 90 | 16.469 (13), 90 | 17.121 (2), 90 |
| Volume ($A^3$) | 1364.54 (19) | 1368.0 (19) | 2866.1(6) |
| Z | 4 | 4 | 8 |
| Calculated density ($Mg/m^3$) | 1.267 | 1.264 | 1.241 |
| Absorption coefficient ($mm^{-1}$) | 0.079 | 0.079 | 0.078 |
| F(000) | 544 | 544 | 1124 |
| Crystal size (mm) | 0.15 × 0.12 × 0.11 | 0.19 × 0.18 × 0.15 | 0.13 × 0.12 × 0.11 |
| Theta range for data collection | 2.51 to 24.98 deg. | 5.84 to 21.45 deg. | 2.38 to 22.06 deg. |
| Limiting indices | –17 ≤ h ≤ 17, –7 ≤ k ≤ 9, –20 ≤ l ≤ 20 | –9 ≤ h ≤ 16, –6 ≤ k ≤ 3, –19 ≤ l ≤ 3 | –31 ≤ h ≤ 31, –12 ≤ k ≤ 10, –22 ≤ l ≤ 22 |
| Reflections collected / unique | 3589/3375 [R(int) = 0.034] | 2031/1782 [R(int) = 0.023] | 11593/3595 [R(int) = 0.052] |
| Completeness to theta | 28.32° 99.4% | 25.00° 73.9% | 28.52° 98.7% |
| Absorption correction | Integration | Integration | Integration |
| Refinement method | Full-matrix least-squares on $F^2$ | Full-matrix least-squares on $F^2$ | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 3375 / 0 / 181 | 1782 / 0 / 181 | 3595 / 0 / 190 |
| Goodness-of-fit on $F^2$ | 1.043 | 1.024 | 1.326 |
| Final R indices [I>2sigma(I)] | R1 = 0.0448, wR2 = 0.1074 | R1 = 0.0544, wR2 = 0.1233 | R1 = 0.1087, wR2 = 0.3751 |
| R indices (all data) | R1 = 0.0722, wR2 = 0.1218 | R1 = 0.0868, wR2 = 0.1500 | R1 = 0.1574, wR2 = 0.4056 |
| Largest diff. peak and hole($e.A^{-3}$) | 0.12 and –0.20 | 0.11 and –0.11 | 0.30 and –0.24 |

**Table 4**. Selected bond lengths (Å) of the compounds.

| Bond distances (Å) | | |
|---|---|---|
| **9a** | **9′a** | **10a** |
| N(3)-C(10) 1.448(2) | N(2)-C(7) 1.448(4) | N(2)-C(10) 1.448(5) |
| C(8)-C(10) 1.508(2) | C(8)-C(7) 1.512(4) | C(8)-C(10) 1.510(5) |
| N(4)-C(9) 1.139(2) | N(4)-C(9) 1.139(4) | N(3)-C(9) 1.131(5) |
| C(7)-C(8) 1.329(2) | C(8)-C(10) 1.325(3) | C(7)-C(8) 1.323(5) |
| N(2)-N(3) 1.345(2) | N(1)-N(2) 1.318(3) | N(2)-C(11) 1.331(5) |
| N(1)-N(2) 1.297(2) | N(2)-N(3) 1.313(3) | N(1)-C(11) 1.293(6) |
| C(8)-C(9) 1.426(2) | C(8)-C(9) 1.408(5) | C(8)-C(9) 1.416(5) |

The proposed mechanism shown in Scheme 5 is a one-pot reaction which is first initiated by acylation of hydroxyl group in Baylis-Hillman adducts. This is followed by Michael addition of azole anion to alkene which leads to the elimination of acetyl group to afford the desired *N*-substituted azole acrylonitriles.




**Scheme 5**. Possible mechanism for *N*-substituted azole acrylonitriles.

### 2.1. Conclusion

In conclusion, a very efficient protocol was introduced here as the sole method to access *N*-substituted-2-((azolyl) methyl)-3-arylacrylonitriles. Considering readily available reagents, mild reaction conditions and good stereo- and regioselectivity, this method is valuable for the preparation of compounds coupled with a heterocyclic skeleton of great biological value.

## 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 (TLC) and visualized under UV light. Melting points were recorded on Mettler Toledo MP90 apparatus and are uncorrected. The $^{1}$H (500 MHz) and $^{13}$C (400 MHz) NMR spectra were recorded on a Bruker Advance 500 DPX spectrometer in $CDCl_3$. The 2D NOESY spectra were recorded on an Agilent DD2 400 MHz spectrometer in $CDCl_3$. The IR spectra were recorded on Perkin Elmer 100 FTIR. The HRMS spectra were recorded on a Shimadzu hybrid LC-MS-IT-TOF spectrometer. Single crystal data collection was performed on a Bruker AXS APEX CCD diffractometer equipped with a Mo K$\alpha$ radiation ($\lambda$ = 0.71073) source at 296 K. The data process was done with the Bruker SMART program package [33]. Using Olex2 [34], the structures were solved with the SHELXT [35] structure solution program using direct methods and refined with the same refinement package using the direct methods and refined with full-matrix least squares methods on $F^2$.

### 3.2. Synthesis of *N*-substituted-2-((1- and 2-benzotriazolyl)methyl)-3-acrylonitriles (9a–i) (9'a, 9'c, 9'i)

To a solution of a convenient Baylis-Hillman nitrile **1** (1 mmol) and *N*-acetylbenzotriazole (1 mmol, 161 mg) in DMF (5 mL), $K_2CO_3$ (1 mmol, 138 mg) was added and the resulting mixture was stirred at room temperature until the starting materials disappeared on TLC. Then, water (20 mL) was poured into the reaction mixture and extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with brine and dried over anhydrous $Na_2SO_4$. After the removal of solvent under reduced pressure, the residue was purified by flash chromatography over silica gel with Ethyl acetate: Hexane (1:3) and crystallized in diethyl ether.

#### 3.2.1. (*Z*)-2-((1-benzotriazolyl)methyl)-3-phenylacrylonitrile (9a)

White solid; Yield (197 mg, 76%); mp. 104.2 °C; IR $\upsilon_{max}$ (KBr): 2209 cm$^{-1}$ (CN), 3050, 3086 cm$^{-1}$ (aromatic C-H), 1452, 1496, 1615 cm$^{-1}$ (aromatic C=C); $^{1}$H NMR (500 MHz, $CDCl_3$): 8.13 (d, $J$= 8.3 Hz, 1H), 7.77

(d, $J$= 6.8 Hz, 2H), 7.67 (d, $J$= 8.0 Hz, 1H), 7.58 (t, $J$= 7.8 Hz, 1H), 7.44 (m, 4H), 7.23 (s, 1H), 5.59 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): 147.4, 146.3, 132.8, 132.1, 131.5, 129.3, 129.1, 128.3, 124.5, 120.4, 117.2, 109,3, 104.7, 51.4; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{16}H_{12}N_4$: 261.1135; found: 261.1137.

#### 3.2.2. (*Z*)-2-((2-benzotriazolyl)methyl)-3-phenylacrylonitrile (9'a)

White solid; Yield (29 mg, 11%); mp. 101.4 °C; IR $\upsilon_{max}$ (KBr): 2215 cm$^{-1}$ (CN), 3019, 3062, 3091 cm$^{-1}$ (aromatic C-H), 1449, 1495, 1620 cm$^{-1}$ (aromatic C=C); $^1$H NMR (500 MHz, $CDCl_3$): 7.92 (m, 2H), 7.83 (d, $J$= 6.8 Hz, 2H), 7.45 (m, 5H), 7.35 (s, 1H), 5.64 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): 148.3, 144.9, 132.3, 131.5, 129.4, 129.0, 127.0, 118.3, 116.9, 104.6, 59.6; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{16}H_{12}N_4$: 261.1124; found: 261.1137.

#### 3.2.3. (*Z*)-2-((1-benzotriazolyl)methyl)-3-(*p*-tolyl)acrylonitrile (9b)

Yellow solid; Yield (194 mg, 71%); mp. 120.9 °C; IR $\upsilon_{max}$ (KBr): 2236 cm$^{-1}$ (CN), 3033, 3065, 3089 cm$^{-1}$ (aromatic C-H), 1455, 1493, 1608 cm$^{-1}$ (aromatic C=C); $^1$H NMR (500 MHz, $CDCl_3$): 8.13 (d, $J$= 8.2 Hz, 1H), 7.68 (m, 3H), 7.57 (t, $J$= 7.9 Hz, 1H), 7.44 (t, $J$= 7.6 Hz, 1H), 7.24 (d, $J$= 8.2 Hz, 2H), 7.20 (s, 1H), 5.57 (s, 2H) 2.40 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): 147.5, 146.3, 142.3, 132.8, 129.8, 129.5, 129.3, 128.2, 124.4, 120.4, 117.5, 109.3, 103.3, 51.2, 21.6; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{17}H_{14}N_4$: 275.1291; found: 275.1296.

#### 3.2.4. (*Z*)-2-((1-benzotriazolyl)methyl)-3-(4-methoxyphenyl)acrylonitrile (9c)

White solid; Yield (195 mg, 67%); mp. 105.1 °C; IR $\upsilon_{max}$ (KBr): 2204 cm$^{-1}$ (CN), 3049, 3066, 3078 cm$^{-1}$ (aromatic C-H), 1442, 1548, 1600 cm$^{-1}$ (aromatic C=C); $^1$H NMR (500 MHz, $CDCl_3$): 8.13 (d, $J$= 8.2 Hz, 1H), 7.77 (d, $J$= 8.8 Hz, 2H), 7.69 (d, $J$= 8.5 Hz, 1H), 7.57 (t, $J$= 7.4 Hz, 1H), 7.44 (t, $J$= 7.5 Hz, 1H), 7.18 (s, 1H), 6.95 (d, $J$= 8.8 Hz, 2H), 5.66 (s, 2H), 3.86 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): 162.2, 147.1, 131.7, 131.3, 128.2, 124.9, 124.4, 120.4, 117.9, 114.8, 114.5, 109.4, 101.2, 55.5, 51.6, 21.6; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{17}H_{14}N_4O$: 291.1240; found: 291.1251.

#### 3.2.5. (*Z*)-2-((2-benzotriazolyl)methyl)-3-(4-methoxyphenyl)acrylonitrile (9'c)

Yellow solid; Yield (50 mg, 17%); mp. 98.3 °C; IR $\upsilon_{max}$ (KBr): 2254 cm$^{-1}$ (CN), 3014, 3025, 3043 cm$^{-1}$ (aromatic C-H), 1450, 1514, 1600 cm$^{-1}$ (aromatic C = C); $^1$H NMR (500 MHz, $CDCl_3$): 7.91 (dd, $J$= 3.1, 6.6 Hz, 2H), 7.83 (d, $J$= 8.9 Hz, 2H), 7.43 (dd, $J$= 3.3, 6.7 Hz, 2H), 7.30 (s, 1H), 6.96 (d, $J$= 8.8 Hz, 2H), 5.60 (s, 2H), 3,87(s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): 162.1, 148.1, 144.9, 131.5, 126.9, 125.1, 118.3, 117.5, 114.4, 101.2, 59.9, 55.5; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{17}H_{14}N_4O$: 291.1240; found: 291.1250.

#### 3.2.6. (*Z*)-2-((1-benzotriazolyl)methyl)-3-(4-fluorophenyl)acrylonitrile (9d)

Yellow solid; Yield (185 mg, 67%); mp. 109.1–114.3 °C; IR $\upsilon_{max}$ (KBr): 2214 cm$^{-1}$ (CN), 3041, 3065 cm$^{-1}$ (aromatic C-H), 1421, 1509, 1600 cm$^{-1}$ (aromatic C=C); $^1$H NMR (500 MHz, $CDCl_3$): 8.14 (d, $J$= 8.2 Hz, 1H), 7.78 (dd, $J$= 5.3, 8.7 Hz, 1H), 7.68 (d, $J$= 8.2 Hz, 2H), 7.58 (t, $J$= 7.4 Hz, 1H), 7.45 (t, $J$= 7.3 Hz, 1H), 7.18 (s, 1H), 7.13 (t, $J$= 8.7 Hz, 2H), 5.58 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): 165.3, 146.3, 146.0,

132.8, 131.5, 128.5, 128.3, 124.5, 120.4, 117.1, 116.4, 109.2, 104.4, 51.3; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{16}H_{11}N_4F$: 279.1046; found: 279.1041.

### 3.2.7. (*Z*)-2-((1-benzotriazolyl)methyl)-3-(3-chlorophenyl)acrylonitrile (9e)

White solid; Yield (186 mg, 63%); mp. 130.5–131.9 °C; IR $\upsilon_{max}$ (KBr): 2263 $cm^{-1}$ (CN), 3027, 3063 $cm^{-1}$ (aromatic C-H), 1452, 1568, 1614 $cm^{-1}$ (aromatic C=C); $^1H$ NMR (500 MHz, $CDCl_3$): 8.15 (d, $J$= 8.5 Hz, 1H), 7.67 (m, 3H), 7.60 (t, $J$= 7.6 Hz, 1H), 7.46 (m, 2H), 7.39 (t, $J$= 7.8 Hz, 1H), 7.11 (s, 1H), 5.59 (s, 2H); $^{13}C$ NMR (125 MHz, $CDCl_3$): 146.3, 145.5, 135.1, 133.8, 132.8, 131.4, 130.3, 129.3, 128.4, 127.0, 124.6, 120.6, 116.6, 109.1, 106.9, 51.1; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{16}H_{11}N_4Cl$: 295.0750; found: 295.0745.

### 3.2.8. (*Z*)-2-((1-benzotriazolyl)methyl)-3-(2,4-dichlorophenyl)acrylonitrile (9f)

Orange solid; Yield (171 mg, 52%); mp. 130.8–136.3 °C; IR $\upsilon_{max}$ (KBr): 2222 $cm^{-1}$ (CN), 3034, 3075 $cm^{-1}$ (aromatic C-H), 1453, 1470, 1586 $cm^{-1}$ (aromatic C=C); $^1H$ NMR (500 MHz, $CDCl_3$): 8.15 (d, $J$= 8.5 Hz, 1H), 7.92 (d, $J$= 8,5 1H), 7.66 (d, $J$= 8.2 Hz, 1H), 7.60 (t, $J$ = 8.1 Hz, 1H), 7.46 (m, 3H), 7.35 (d, $J$= 6.9 Hz, 1H), 5.63 (s, 2H); $^{13}C$ NMR (125 MHz, $CDCl_3$): 146.3, 142.5, 137.7, 135.3, 132.8, 130.0, 129.9, 129.1, 128.4, 127.9, 124.6, 120.6, 116.1, 109.1, 108.8, 51.0; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{16}H_{11}N_4Cl_2$: 329.0355; found: 329.0356.

### 3.2.9. (*Z*)-2-((1-benzotriazolyl)methyl)-3-(4-bromophenyl)acrylonitrile (9g)

White solid; Yield (214 mg, 63%); mp. 107.7–110.3 °C; IR $\upsilon_{max}$ (KBr): 2232 $cm^{-1}$ (CN), 3032, 3040, 3068 $cm^{-1}$ (aromatic C-H), 1458, 1507, 1610 $cm^{-1}$ (aromatic C=C); $^1H$ NMR (500 MHz, $CDCl_3$): 8.14 (d, $J$= 8.5 Hz, 1H), 7.66 (d, $J$= 8.2 Hz, 1H), 7.58 (m, 5H), 7.46 (t, $J$= 7,8 Hz, 1H), 7.14 (s, 1H), 5.58 (s, 2H); $^{13}C$ NMR (125 MHz, $CDCl_3$): 146.2, 146.0, 132.8, 132.4, 130.9, 130.6, 128.4, 126.1, 124.6, 120.5, 117.0, 109.2, 105.5, 51.2; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{16}H_{11}N_4Br$: 339.0255; found: 339.0240.

### 3.2.10. (*Z*)-2-((1-benzotriazolyl)methyl)-3-(2-furanyl)acrylonitrile (9h)

Green solid; Yield (143 mg, 57%); mp. 114.6 °C; IR $\upsilon_{max}$ (KBr): 2215 $cm^{-1}$ (CN), 3043 $cm^{-1}$ (aromatic C-H), 1445, 1546, 1610 $cm^{-1}$ (aromatic C=C); $^1H$ NMR (500 MHz, $CDCl_3$): 8.13 (d, $J$= 7.5 Hz, 1H), 7.66 (d, $J$ = 8.0 Hz, 1H), 7.58 (t, $J$ = 7.5 Hz, 2H), 7.45 (t, $J$ = 7.8 Hz, 1H), 7.01 (d, $J$ = 3.5 Hz, 1H), 6.97 (s, 1H) 6.54 (m, 1H), 5.54 (s, 2H); $^{13}C$ NMR (125 MHz, $CDCl_3$): 148.5, 146.3, 145.8, 133.4, 132.7, 128.3, 124.5, 120.4, 117.2, 116.3, 112.8, 109,3, 100.5, 50.5; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{14}H_{10}N_4O$: 251.0934; found: 251.0927.

### 3.2.11. (*Z*)-2-((1-benzotriazolyl)methyl)-3-(2-thiophenyl)acrylonitrile (9i)

White solid; Yield (75 mg, 28%); mp. 135.0–138.5 °C; IR $\upsilon_{max}$ (KBr): 2242 $cm^{-1}$ (CN), 3035, 3078, 3091 $cm^{-1}$ (aromatic C-H), 1453, 1493, 1613 $cm^{-1}$ (aromatic C=C); $^1H$ NMR (500 MHz, $CDCl_3$): 8.13 (d, $J$= 8.2 Hz, 1H), 7.67 (d, $J$= 8,2 Hz, 1H), 7.57 (m, 3H), 7.45 (t, $J$= 7,8 Hz, 1H), 7.36 (s, 1H), 7.13 (t, $J$= 4.9 Hz, 1H), 5.56 (s, 2H); $^{13}C$ NMR (125 MHz, $CDCl_3$): 146.3, 139.9, 136.1, 133.5, 132.8, 131.3, 128.3, 127.9, 124.5, 120.4, 117.5, 109.3, 101.0, 50.7; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{14}H_{10}N_4S$: 267.0699; found: 267.0705.

#### 3.2.12. (*Z*)-2-((2-benzotriazolyl)methyl)-3-(2-thiophenyl)acrylonitrile (9'i)

Yellow solid; Yield (30 mg, 11%); mp. 131.4–133.2 °C; IR $\upsilon_{max}$ (KBr): 2205 $cm^{-1}$ (CN), 3043 $cm^{-1}$ (aromatic C-H), 1448, 1458, 1614 $cm^{-1}$ (aromatic C=C); $^1$H NMR (500 MHz, $CDCl_3$): 7.91 (dd, $J$= 3.2, 6.6 Hz, 2H), 7.60 (m, 2H), 7.49 (s, 1H), 7.43 (dd, $J$= 3.2, 6.7 Hz, 2H), 7.14 (t, $J$= 8.9 Hz, 1H), 5.61 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): 144.9, 140.8, 136.3, 133.5, 131.3, 127.8, 127.0, 118.3, 117.1, 101.3, 59.1; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{14}H_{10}N_4S$: 267.0699; found: 267.0703.

### 3.3. Synthesis of *N*-substituted-2-((benzimidazolyl)methyl)-3-acrylonitriles (10a-i)

To a solution of a convenient Baylis-Hillman acetate **1** (1 mmol) and *N*-acetylbenzimidazole (1 mmol, 160 mg) in DMF (5 mL), $K_2CO_3$ (1 mmol, 138 mg) was added and the resulting mixture was stirred at room temperature until the starting materials disappeared on TLC. Then, water (20 mL) was poured into the reaction mixture and extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with brine and dried over anhydrous $Na_2SO_4$. After the removal of solvent under reduced pressure, the residue was purified by flash chromatography over silica gel with Ethyl acetate: Hexane (1:3) and then crystallized in diethyl ether.

#### 3.3.1. (*Z*)-2-((1-benzoimidazolyl)methyl)-3-phenylacrylonitrile (10a)

White solid; Yield (189 mg, 73%); mp. 92.2 °C; IR $\upsilon_{max}$ (KBr): 2213 $cm^{-1}$ (CN), 3026, 3044, 3068 $cm^{-1}$ (aromatic C-H), 1458, 1500, 1614 $cm^{-1}$ (aromatic C=C); $^1$H NMR (500 MHz, $CDCl_3$): 8.03 (s, 1H), 7.88 (m, 1H), 7.72 (s, 2H), 7.43 (m, 4H), 7.34 (s, 2H), 7.01 (s, 1H), 5.08 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): 145.6, 144.0, 142.9, 133.4, 132.1, 131.4, 129.1, 129.0, 123.7, 122.9, 120.9, 117.0, 109.6, 105.7, 48.5; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{17}H_{13}N_3$: 260.1182; found: 260.1184.

#### 3.3.2. (*Z*)-2-((1-benzoimidazolyl)methyl)-3-(p-tolyl)acrylonitrile (10b)

White solid; Yield (154 mg, 56%); mp. 85.8 °C; IR $\upsilon_{max}$ (KBr): 2267 $cm^{-1}$ (CN), 3035, 3076 $cm^{-1}$ (aromatic C-H), 1460, 1489, 1613 $cm^{-1}$ (aromatic C=C); $^1$H NMR (500 MHz, $CDCl_3$): 8.13 (d, $J$= 8.5 Hz, 1H), 7.69 (d, $J$= 8.5 Hz, 2H), 7.56 (m, 5H), 7.45 (m, 2H), 5.58 (s, 2H), 1.28 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): 147.8, 146.1, 133.0, 132.6, 132.1, 131.1, 130.9, 128.3, 125.4, 124.5, 120.5, 118.1, 109.8, 109.1, 46.0, 29.7; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{18}H_{15}N_3$: 274.1339; found: 274.1348.

#### 3.3.3. (*Z*)-2-((1-benzoimidazolyl)methyl)-3-(4-methoxyphenyl)acrylonitrile (10c)

White solid; Yield (139 mg, 48%); mp. 109.3 °C; IR $\upsilon_{max}$ (KBr): 2234 $cm^{-1}$ (CN), 3035, 3058, 3087 $cm^{-1}$ (aromatic C-H), 1494, 1513, 1601$cm^{-1}$ (aromatic C=C); $^1$H NMR (500 MHz, $CDCl_3$): 8.04 (s, 1H), 7.87 (m, 1H), 7.73 (d, $J$= 8.8 Hz, 2H), 7.44 (m, 1H), 7.36 (m, 2H), 6.95 (t, $J$= 8.8 Hz, 3H), 5.07 (s, 2H), 3.86 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): 162.0, 145.3, 144.0, 142.9, 133.4, 131.4, 131.2, 124.9, 123.7, 122.8, 120.9, 114.5, 109.7, 102.3, 55.5, 48.7; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{18}H_{15}N_3O$: 290.1288; found: 290.1295.

### 3.3.4. (*Z*)-2-((1-benzoimidazolyl)methyl)-3-(4-fluorophenyl)acrylonitrile (10d)

White solid; Yield (132 mg, 48%); mp. 110.8 °C; IR $\upsilon_{max}$ (KBr): 2212 $cm^{-1}$ (CN), 3037, 3079 $cm^{-1}$ (aromatic C-H), 1464, 1511, 1599 $cm^{-1}$ (aromatic C=C); $^{1}$H NMR (500 MHz, $CDCl_3$): 8.04 (s, 1H), 7.88 (dd, $J$ = 3.1, 6.0 Hz, 1H), 7.44 (dd, $J$= 3.2, 8.5 Hz, 2H), 7.42 (m, 1H), 7.36 (m, 2H), 7.13 (t, $J$= 8.7 Hz, 2H), 6.95 (s, 1H), 5.10 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): 165.2, 146.8, 144.1, 142.9, 133.4, 131.4, 128.4, 123.8, 122.9, 121.0, 116.9, 116.4, 109.5, 105.3, 48.4; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{17}H_{12}N_3F$: 278.1088; found: 278.1094.

### 3.3.5. (*Z*)-2-((1-benzoimidazolyl)methyl)-3-(3-chlorophenyl)acrylonitrile (10e)

Yellow solid; Yield (141 mg, 48%); mp. 126.5 °C; IR $\upsilon_{max}$ (KBr): 2260 $cm^{-1}$ (CN), 3029, 3078 $cm^{-1}$ (aromatic C-H), 1460, 1497, 1616 $cm^{-1}$ (aromatic C=C); $^{1}$H NMR (500 MHz, $CDCl_3$): 8.04 (s, 1H), 7.89 (m, 1H), 7.64 (t, $J$= 8.4 Hz, 2H), 7.38 (m, 5H), 6.90 (s, 1H), 5.11 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): 144.0, 143.6, 142.9, 135.1, 133.7, 133.3, 131.3, 130.4, 129.2, 126.9, 123.9, 123.0, 121.0, 116.4, 109.5, 107.6, 48.3; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{17}H_{12}N_3Cl$: 294.0793; found: 294.0806.

### 3.3.6. (*Z*)-2-((1-benzoimidazolyl)methyl)-3-(2,4-dichlorophenyl)acrylonitrile (10f)

Light brown solid; Yield (128 mg, 39%); mp. 144.7 °C; IR $\upsilon_{max}$ (KBr): 2218 $cm^{-1}$ (CN), 3078, 3098 $cm^{-1}$ (aromatic C-H), 1457, 1496, 1584 $cm^{-1}$ (aromatic C=C); $^{1}$H NMR (500 MHz, $CDCl_3$): 8.05 (s, 1H), 7.89 (d, $J$ = 6.1 Hz, 2H), 7.47 (s, 1H), 7.44 (d, $J$= 9.2 Hz, 1H), 7.35 (m, 4H), 5.15 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): 144.0, 142.8, 141.2, 137.6, 135.2, 133.2, 130.0, 129.8, 129.1, 127.8, 123.9, 123.0, 121.0, 115.9, 109.8, 109.5, 48.3; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{17}H_{12}N_3Cl_2$: 328.0403; found: 328.0407.

### 3.3.7. (*Z*)-2-((1-benzoimidazolyl)methyl)-3-(4-bromophenyl)acrylonitrile (10g)

Yellow solid; Yield (149 mg, 44%); mp. 129.2 °C; IR $\upsilon_{max}$ (KBr): 2215 $cm^{-1}$ (CN), 3043, 3076 $cm^{-1}$ (aromatic C-H), 1460, 1510, 1613 $cm^{-1}$ (aromatic C=C); $^{1}$H NMR (500 MHz, $CDCl_3$): 8.02 (s, 1H), 7.87 (t, $J$= 4.6 Hz, 1H), 7.56 (m, 4H), 7.40 (m, 1H), 7.35 (m, 2H), 6.91 (s, 1H), 5.07 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): 144.1, 143.9, 142.9, 133.3, 132.4, 130.9, 130.5, 125.9, 123.9, 123.0, 120.9, 116.7, 109.5, 106.6, 48.4; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{17}H_{12}N_3Br$: 338.0287; found: 338.0283.

### 3.3.8. (*Z*)-2-((1-benzoimidazolyl)methyl)-3-(2-furanyl)acrylonitrile (10h)

Yellow solid; Yield (100 mg, 40%); mp. 98.1 °C; IR $\upsilon_{max}$ (KBr): 2214 $cm^{-1}$ (CN), 3043, 3067, 3097 $cm^{-1}$ (aromatic C-H), 1460, 1497, 1614 $cm^{-1}$ (aromatic C=C); $^{1}$H NMR (500 MHz, $CDCl_3$): 8.02 (s, 1H), 7.88 (m, 1H), 7.58 (s, 1H), 7.37 (m, 3H), 6.97 (d, $J$ = 3.8 Hz, 1H), 6.75 (s, 1H), 6.54 (t, $J$= 1.6 Hz, 1H), 5.06 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): 148.4, 145.6, 144.0, 142.8, 133.3, 131.6, 123.8, 122.9, 120.9, 116.9, 116.5, 112.7, 109.6, 101.7, 47.6; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{15}H_{11}N_3O$: 250.0975; found: 250.0982.

### 3.3.9. (*Z*)-2-((1-benzoimidazolyl)methyl)-3-(2-thiophenyl)acrylonitrile (10i)

White solid; Yield (127 mg, 48%); mp. 128.4 °C; IR $\upsilon_{max}$ (KBr): 2231 $cm^{-1}$ (CN), 3026, 3058, 3080 $cm^{-1}$ (aromatic C-H), 1462, 1496, 1618 $cm^{-1}$ (aromatic C=C); $^{1}$H NMR (500 MHz, $CDCl_3$): 8.03 (s, 1H), 7.88 (m, 1H), 7.57 (d, $J$= 5.0 Hz, 1H), 7.51 (d, $J$= 3.4 Hz, 1H), 7.44 (m, 1H), 7.36 (m, 2H), 7.12 (m, 2H), 5.08 (s, 2H);

$^{13}$C NMR (125 MHz, $CDCl_3$): 144.0, 142.8, 137.9, 136.1, 133.4, 133.2, 131.0, 127.9, 123.8, 122.9, 120.9, 117.2, 109.6, 102.2, 47.8; HRMS (ESI): $m/z$ $[M+H]^+$ calcd for $C_{15}H_{11}N_3S$: 266.0746; found: 266.0750.

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