

Synthesis of new 2,3-disubstituted pyridines containing a 1,2,3-triazole in the side-chain via one-pot copper-catalyzed azide-alkyne cycloaddition

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Abstract

A series of 1,2,3-triazole-containing pyridines has been synthesized using the Cu(II) catalyzed 'click approach' from sodium azide and corresponding halides. The synthesis involves the amidation of 2-amino-3-hydroxypyridine with benzoyl chloride or cinnamic acid followed by reaction with propargyl bromide to obtain *N*-(3-(prop-2-ynoxy)pyridin-2-yl)benzamide **5** and 3-phenyl-*N*-(3-(prop-2-ynoxy)-pyridin-2-yl)acrylamide **10** respectively. These compounds underwent one-pot tandem copper-catalyzed azidation and CuAAC reactions to provide compounds **6a-h** and **11a-g** in moderate to good yields.

Keywords: One-pot click chemistry, pyridine, 1,2,3-triazole, benzyl halides

Introduction

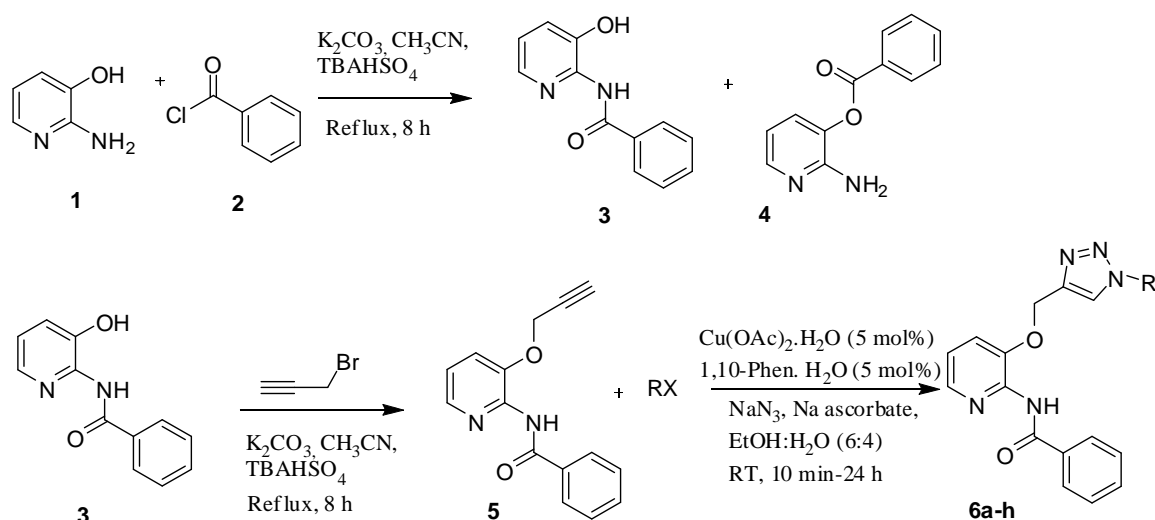
Due to their chemical and biological importance, heterocyclic moieties are attractive targets in medicinal and pharmaceutical chemistry.¹⁻² Among heterocyclic compounds, pyridine has proved to be the one of the most important moieties. Substituted pyridines have a major role in a wide variety of natural products, pharmaceutical drugs and various kinds of functional materials.³⁻⁴ For the synthesis of pyridines, various methods are known in the literature. John Spencer *et al.*⁵ synthesized libraries of pyridine derivatives, many of which contain a piperazine group at the 2-position. Sreekantha B. Jonnalagadda *et al.*⁶ synthesized highly substituted pyridines in good yields by the use of Au loaded MgO in one-pot, multicomponent system. Haider Behbehani *et al.*⁷ explored a series of 5-arylazo-2,3,6-trisubstituted pyridines from the reactions of 3-oxo-2-arylhydrazonopropanal with 3-oxo-3-phenylpropionitrile. Xie *et al.*⁸ synthesized 5,6-disubstituted pyridine-2,3-dione-3-thiosemicarbazone derivatives and 5,6-disubstituted pyridine-2,3-dione *S*-benzyl-3-thiosemicarbazones via oxidation-Michael additions, condensations and nucleophilic substitutions.

Cu-promoted coupling reactions have been extensively used for the synthesis of several molecules and biomolecules.⁹⁻¹¹ The azidation reaction has been used as a facile method for the transformation of an aryl halide into an aryl azide. Synthetic applications of these ar-

yl/alkyl azides have become highly attractive alternatives to establish nitrogen-linked aryl/alkyl scaffolds. This high yield and regioselective reaction has found numerous applications ranging from chemistry to biology. Copper-catalyzed azide-alkyne cycloaddition (CuAAC) reaction (click chemistry) has been widely utilized for the synthesis of biologically active 1,2,3-triazole compounds. Several therapeutically active compounds containing this moiety have been reported, viz., anti-HIV agents, antimicrobials, and kinase inhibitors.¹²⁻¹⁶ Moreover, Cu-promoted azidation and 1,3-dipolar [3 + 2] cycloaddition reactions between azides and terminal alkynes that can be carried out in one-pot synthesis are an attractive method. Herein, we demonstrate an efficient synthesis of novel 2,3-disubstituted pyridines by performing one-pot tandem copper-catalyzed azidation and CuAAC reaction.

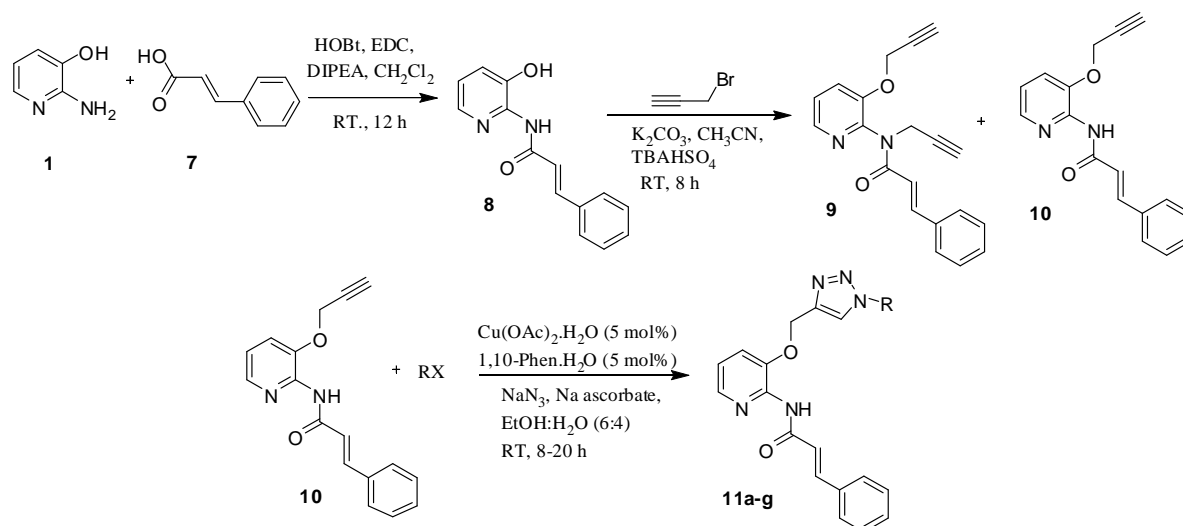
Results and Discussion

In our present work, the precursor of *N*-(3-(prop-2-ynoxy)-pyridin-2-yl)benzamide **5** was synthesized from an easily available starting material 2-amino-3-hydroxypyridine **1** (Scheme 1). Compound **1** was reacted with benzoyl chloride **2** in the presence of potassium carbonate and acetonitrile using tetrabutylammonium hydrogen sulfate (TBAHSO₄) as catalyst at reflux temperature for eight hours to give of *N*-(3-hydroxy-pyridin-2-yl)benzamide **3** and benzoic acid 2-amino-pyridin-3-yl ester **4** as white solids in 65% and 10% yields respectively. The crude **3** was > 95% pure according to ¹H NMR and was used in the next stage without further purification. The reaction of **3** with propargyl bromide and potassium carbonate in acetonitrile with TBAHSO₄ proceeded at reflux temperature for eight hours to give **5** as a brown coloured liquid in 70% yield. The final step was the synthesis of pyridine analogues containing a 1,2,3-triazole unit **6a-h** from **5** and various benzyl halides. A Cu-catalyzed click reaction was performed with **5** and benzyl chloride using sodium azide, copper(II) acetate as catalyst, sodium ascorbate as reducing agent and 1,10-phenanthroline.H₂O as ligand in EtOH:H₂O (6:4) at room temperature for 24 h to afford the crude product. Addition of cold water to the reaction mixture resulted in formation of a white precipitate. The crude product was then subjected to column chromatography to afford *N*-(3-((1-benzyl-1*H*-1,2,3-triazol-4-yl)methoxy)pyridin-2-yl)benzamide **6a** in 55% yield (Table 1, entry 1). Similarly, other 1,2,3-triazoles (**6b-h**, Table 1, entry 2-8) were synthesized by the reaction of compound **5** with other substituted benzyl halides and allyl bromide in moderate to good yields (55-82%). The structure of **6a** was confirmed by ¹H and ¹³C NMR analysis as well as mass spectrometry. In the ¹H NMR spectrum, the C5-proton of the triazole ring resonated at δ 7.57, the protons of the OCH₂ group appeared as a singlet at δ 5.50 and the protons of the NCH₂ group as a singlet at δ 5.29, along with aromatic proton signals. In the ¹³C NMR spectra, the OCH₂ carbon appeared at δ 62.7, the NCH₂ carbon appeared at δ 54.2, the C5-carbon of the triazole was at δ 123.1, and carbonyl group of the amide at δ 164.8, along with other carbons. In EI-MS, peak appeared at *m/z* = 386.3 for (M⁺+1) ion of **6a**. Higher yields of 1,2,3-triazoles were obtained when a fluorine atom was present in the benzyl moiety.



Scheme 1. Synthesis of *N*-(3-(1-substituted benzyl/allyl-1*H*-[1,2,3]-triazol-4-yl)methoxy)pyridine-2-yl)-3-phenyl-acrylamide

We also reacted **1** with cinnamic acid **7** in the presence of hydroxybenzotriazole (HOBT), *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDC) and diisopropylethylamine (DIPEA) in dichloromethane at room temperature for 12 hours to yield *N*-(3-hydroxy-pyridin-2-yl)-3-phenyl-acrylamide **8** in 80% yield (Scheme 2). Compound **8** was then further treated with propargyl bromide in potassium carbonate and acetonitrile using TBAHSO₄ as catalyst at room temperature for eight hours to give 3-phenyl-*N*-prop-2-ynyl-*N*-(3-prop-2-ynyloxy-pyridin-2-yl)acrylamide **9** and 3-phenyl-*N*-(3-(prop-2-ynyloxy)-pyridin-2-yl)acrylamide **10** in 10% and 55% yields respectively. The same reaction conducted at reflux temperature gave compound **9** in 60% yield along with traces of compound **10**.



Scheme 2. Synthesis of *N*-(3-(1-substituted benzyl/allyl-1*H*-[1,2,3]-triazol-4-yl)methoxy)pyridine-2-yl)-3-phenyl-acrylamide

Compound **10** underwent a copper-catalyzed click reaction with benzyl chloride using sodium azide in the presence of copper(II) acetate, sodium ascorbate and 1,10-phenanthroline.H₂O in EtOH:H₂O at room temperature for 20 hours. Addition of cold water to the reaction mixture resulted in a white precipitates of crude product which was then purified by column chromatography to give *N*-[3-(1-benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)pyridin-2-yl]-3-phenyl-acrylamide **11a** in 50% yield (Table 1, entry 9). In the ¹H NMR spectrum of this compound there was a singlet at δ 7.59 for the C5-proton of the triazole ring, proton signals for the OCH₂ at δ 5.64, for the NCH₂ at δ 5.30 and signals for other protons. In the ¹³C NMR of **11a**, the C5 carbon of the triazole ring resonated at δ 123.2, the OCH₂ carbon resonated at δ 62.4, the NCH₂ carbon at δ 54.3 and amide carbonyl group carbon resonated at δ 164.8, along with signals for the other carbons. In EI-MS, a peak appeared at *m/z* = 412.2 for (M⁺+1) ion of **11a**. An array of novel triazole derivatives **11a-g** was synthesized by varying the substitution on the benzyl group as well as allyl groups (Table 1, entry 9-15). The overall yields of compounds **6** and **11** were very good and the method is high yielding, simple, convenient and general. Structures of all newly synthesized compounds were characterized by ¹H and ¹³C NMR as well as mass spectrometry (Supporting Information).

Table 1. Physical data of compounds **6a-h** and **11a-g**

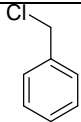
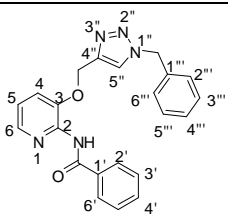
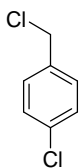
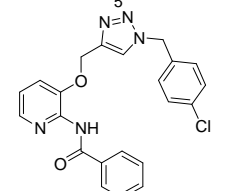
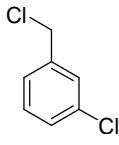
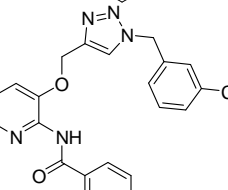
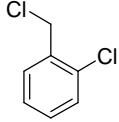
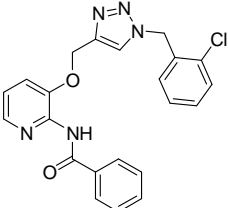
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2	6b			20 h	65	163 -164
3	6c			20 h	66	154 -157
4	6d			20 h	64	125-126

Table 1 (continued)

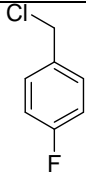
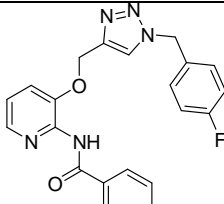
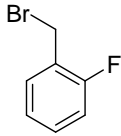
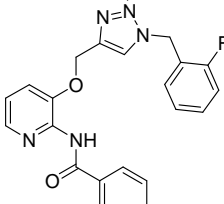
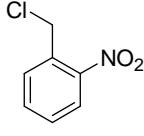
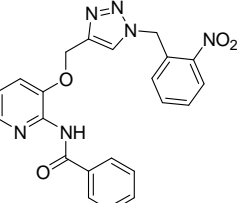
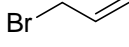
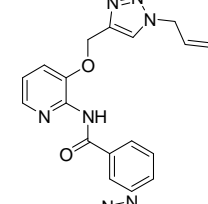
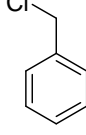
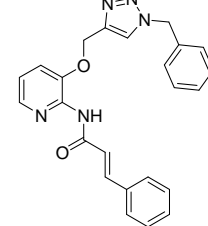
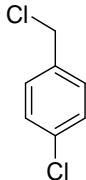
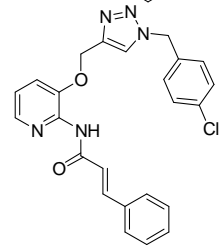
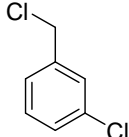
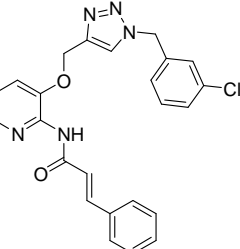
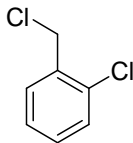
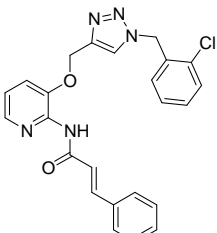
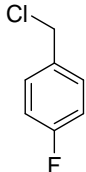
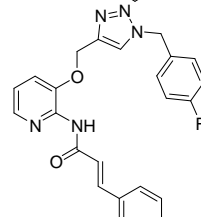
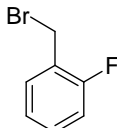
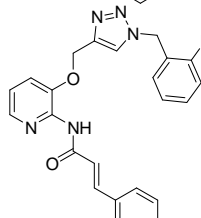
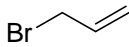
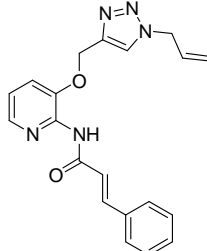
Entry	Compds.	RX	Product	Time	Yield (%)	mp (°C)
5	6e			10 min	82	165-168
6	6f			15 min	78	132-134
7	6g			24 h	60	119-123
8	6h			18 h	55	117-120
9	11a			20 h	50	125-126
10	11b			18 h	58	160-162
11	11c			20 h	57	161-163

Table 1 (continued)

Entry	Compds.	RX	Product	Time	Yield (%)	mp (°C)
12	11d			18 h	56	128 -129
13	11e			8 h	58	169 -172
14	11f			8 h	55	138 -140
15	11g			20 h	45	120-122

Conclusions

An efficient and straightforward one pot copper catalyzed azidation and CuAAC reaction for constructing novel 1,2,3-triazole-containing pyridines has been developed. Utilizing easily available reaction materials, a small library of pyridine derivatives carrying side-chain 1,2,3-triazoles was rapidly and efficiently synthesized. Overall, we believe that the developed reaction method and novel series of pyridine substituted triazine should be considered as an important advance in medicinal and pharmaceutical chemistry.

Experimental Section

General. All chemicals and solvents were of commercial grade and used without further purification, supplied by spectrochemicals and Sigma-Aldrich. Melting points were determined in open capillaries and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on Jeol ECS-

400 MHz spectrometer at 400 MHz and 100 MHz respectively, using CDCl_3 as solvent. The chemical shifts are expressed in parts per million with TMS as internal reference and J values are given in Hz. Mass spectra were recorded on a Waters Micromass Q-ToF Micro (Milford, MA). Reactions were monitored by thin layer chromatography (TLC) with plates coated with silica gel HF-254. Column chromatography was performed with silica gel mesh size 60-120. Hexane: ethylacetate and ethyl acetate: methanol were used as solvent systems.

Synthesis of *N*-(3-hydroxypyridin-2-yl)benzamide (3) and benzoic acid 2-aminopyridin-3-yl ester (4). 2-Amino-3-hydroxy pyridine **1** (2 g, 18.17 mmol) was dissolved in acetonitrile (50 mL), K_2CO_3 (3 g, 21.75 mmol) and TBAHSO₄ (0.05 mmol). Benzoyl chloride **2** (3 g, 21.75 mmol) was added and the reaction mixture was heated to reflux for 8 h. The reaction mixture was neutralized with NaHCO_3 and extracted with chloroform, the extract dried over Na_2SO_4 , filtered and concentrated to get the crude product. The crude residue was then purified by column chromatography to get pure *N*-(3-hydroxy-pyridin-2-yl)benzamide (**3**) and benzoic acid 2-amino-pyridin-3-yl ester (**4**).

***N*-(3-hydroxypyridin-2-yl)benzamide (3).** Yield: 65%; mp 130-133 °C; ^1H NMR (400 MHz, CDCl_3): δ_{H} 8.62 (bs, 1H, NH), 8.34 (dd, $^2J_{\text{HH}}$ 4.80 Hz, $^3J_{\text{HH}}$ 1.48 Hz, 1H, H-6), 8.16 (dd, $^2J_{\text{HH}}$ 8.16 Hz, $^3J_{\text{HH}}$ 0.96 Hz, 2H, H-2',6'), 7.83 (d, $^3J_{\text{HH}}$ 7.04 Hz, 2H, H-3',5'), 7.77 (dd, $^2J_{\text{HH}}$ 4.8 Hz, $^3J_{\text{HH}}$ 8.08 Hz, 1H, H-4'), 7.60 (t, $^3J_{\text{HH}}$ 1.16 Hz, 1H, H-4), 7.40 (dd, $^2J_{\text{HH}}$ 7.32 Hz, $^3J_{\text{HH}}$ 5.67 Hz, 1H, H-5); MS (EI) : m/z 215.1 ($\text{M}^+ + 1$).

Benzoic acid 2-aminopyridin-3-yl ester (4). Yield: 10%; mp 160-162 °C; ^1H NMR (400 MHz, CDCl_3): δ_{H} 9.87 (bs, 2H, NH_2), 8.02 (dd, $^2J_{\text{HH}}$ 4.56 Hz, $^3J_{\text{HH}}$ 1.48 Hz, 2H, H-6,2'), 7.62 (t, $^3J_{\text{HH}}$ 1.20 Hz, 1H, H-6'), 7.58 (t, $^3J_{\text{HH}}$ 7.88 Hz, 1H, H-4), 7.51 (t, $^3J_{\text{HH}}$ 7.88 Hz, 2H, H-3',5'), 7.41 (dd, $^2J_{\text{HH}}$ 8.08 Hz, $^3J_{\text{HH}}$ 1.48 Hz, 1H, H-5), 7.11 (dd, $^2J_{\text{HH}}$ 8.08 Hz, $^3J_{\text{HH}}$ 4.64 Hz, 1H, H-4'); MS (EI) : m/z 215.1 ($\text{M}^+ + 1$).

Synthesis of *N*-(3-(prop-2-ynyloxy)pyridin-2-yl)benzamide (5). *N*-(3-Hydroxy-pyridin-2-yl)benzamide **3** (2 g, 10 mmol) was refluxed with propargyl bromide (1.17 g, 10 mmol) in the presence of K_2CO_3 (2 g, 15 mmol) and TBAHSO₄ (0.05 mmol) using acetonitrile as solvent for 8 h. Acetonitrile was removed under vacuum, CHCl_3 was added to it and the solution washed with water. The organic layer was dried over Na_2SO_4 , filtered and concentrated to give the crude product. The crude product was purified by column chromatography to produce a sticky brown liquid of compound **5**.

***N*-(3-(prop-2-ynyloxy)pyridin-2-yl)benzamide (5).** Yield: 70%; ^1H NMR (400 MHz, CDCl_3): δ_{H} 8.72 (bs, 1H, NH), 8.16 (dd, $^2J_{\text{HH}}$ 4.60 Hz, $^3J_{\text{HH}}$ 1.36 Hz, 1H, H-6), 7.94 (d, $^3J_{\text{HH}}$ 7.32 Hz, 2H, H-2',6'), 7.57-7.52 (m, 1H, H-4'), 7.50-7.46 (m, 2H, H-3',5'), 7.39 (dd, $^2J_{\text{HH}}$ 8.24 Hz, $^3J_{\text{HH}}$ 1.36 Hz, 1H, H-4), 7.11 (dd, $^2J_{\text{HH}}$ 8.28 Hz, $^3J_{\text{HH}}$ 4.36 Hz, 1H, H-5), 4.80 (d, $^3J_{\text{HH}}$ 2.28 Hz, 2H, O- CH_2), 2.60 (t, $^3J_{\text{HH}}$ 2.72 Hz, 1H, CH); ^{13}C NMR (100 MHz, CDCl_3): δ_{C} 164.6 (C=O), 143.3 (C-2), 140.7 (C-3), 134.8 (C-1'), 131.9 (C-6), 128.6 (C-2',6'), 127.3 (C-4,5), 119.8 (C-3',5'), 119.6 (C-4'), 59.0 (CH), 58.9 (O- CH_2), 56.5 (C); MS (EI) : m/z 253.2 ($\text{M}^+ + 1$); Anal. Calc. for $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.75; H, 4.96; N, 11.33.

General procedure for synthesis of 6a-h. In a round bottom flask, $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ (5 mol%), 1,10-phenanthroline monohydrate (5 mol%) and sodium L-ascorbate (107 mg, 0.54 mmol) were added in EtOH:H₂O (6:4, 10 mL) and the mixture stirred for 5 mins at room

temperature. *N*-(3-(prop-2-ynoxy)-pyridin-2-yl)benzamide **5** (100 mg, 0.40 mmol), sodium azide (76 mg, 1.17 mmol) and the benzyl halide (0.40 mmol) were added to the reaction mixture with stirring at room temperature. Reaction time varied from 10 min to 24 h for various benzyl halides. After completion of the reaction (monitored by TLC), ice cold water was added to the reaction mixture till the product precipitated, it was filtered off and washed with cold water. The crude product was then dried under vacuum. The crude product was purified by column chromatography using AcOEt:MeOH (98:2) as eluent to give compounds **6a-h**.

***N*-(3-((1-benzyl-1*H*-1,2,3-triazol-4-yl)methoxy)pyridin-2-yl)benzamide (6a)**. Yield: 55%; mp 120-122 °C; ¹H NMR (400 MHz, CDCl₃): δ_H 8.50 (bs, 1H, NH), 8.13 (dd, ²J_(HH) 5.04 Hz, ³J_(HH) 1.36 Hz, 1H, H-6), 7.89-7.87 (m, 2H, H-C2',6'), 7.57-7.53 (m, 2H, H-4',5'), 7.48-7.44 (m, 2H, H-3',5'), 7.42 (dd, ²J_(HH) 8.24 Hz, ³J_(HH) 1.36 Hz, 1H, H-5), 7.35 (t, ³J_(HH) 2.76 Hz, 3H, H-2''',4''',6'''), 7.23-7.21 (m, 2H, H-3''',5'''), 7.09 (dd, ²J_(HH) 8.24 Hz, ³J_(HH) 5.04 Hz, 1H, H-4'), 5.50 (s, 2H, O-CH₂), 5.29 (s, 2H, N-CH₂); ¹³C NMR (100 MHz, CDCl₃): δ_C 164.8 (C=O), 144.6 (C-2), 143.2 (C-3), 142.1 (C-1',C-4''), 140.4 (C-1'''), 134.6 (C-5''), 131.9 (C-6), 129.1 (C-2',6'), 128.8 (C-4'), 128.6 (C-3',5'), 128.0 (C-2''',6'''), 127.4 (C-4), 123.1 (C-5), 120.4 (C4'''), 120.2 (3''',5'''), 62.7 (O-CH₂), 54.2 (N-CH₂); MS (EI) : *m/z* 386.3 (M⁺+1); Anal. Calc. for C₂₂H₁₉N₅O₂: C, 68.56; H, 4.97; N, 18.17. Found: C, 68.73; H, 5.23; N, 18.34.

***N*-(3-((1-(4-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)pyridin-2-yl)benzamide (6b)**. Yield: 65%; mp 163-164 °C; ¹H NMR (400 MHz, CDCl₃): δ_H 8.49 (bs, 1H, NH), 8.12 (d, ³J_(HH) 3.20 Hz, 1H, H-6), 7.88 (d, ³J_(HH) 7.32 Hz, 2H, H-2',6'), 7.58 (s, 1H, H-5''), 7.56 (d, ³J_(HH) 7.32 Hz, 1H, H-4), 7.48 (t, ³J_(HH) 7.32 Hz, 2H, H-3',5'), 7.41 (d, ³J_(HH) 7.76 Hz, 1H, H-5), 7.30 (d, ³J_(HH) 8.28 Hz, 2H, H-2''',6'''), 7.16 (d, ³J_(HH) 8.72 Hz, 2H, H-3''',5'''), 7.09-7.06 (m, 1H, H-4'''), 5.46 (s, 2H, O-CH₂), 5.29 (s, 2H, N-CH₂); ¹³C NMR (100 MHz, CDCl₃): δ_C 164.9 (C=O), 144.8 (C-2), 143.5 (C-3), 142.0 (C-1',4''), 140.3 (C-1'''), 134.8 (C-4'''), 134.5 (C-5''), 132.6 (C2''',6'''), 131.8 (C-6), 129.9 (C-2',6'), 129.0 (C-4'), 128.7 (C-3',5'), 127.4 (C-4), 123.2 (C-5), 122.9 (C-3'''), 120.7 (C-5'''), 62.7 (O-CH₂), 53.5 (N-CH₂); MS (EI) : *m/z* 420.1 (M⁺+1); Anal. Calc. for C₂₂H₁₈ClN₅O₂: C, 62.93; H, 4.32; N, 16.68. Found: C, 62.79; H, 4.48; N, 16.59.

***N*-(3-((1-(3-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)pyridin-2-yl)benzamide (6c)**. Yield: 66%; mp 154-157 °C; ¹H NMR (400 MHz, CDCl₃): δ_H 8.52 (bs, 1H, NH), 8.13 (dd, ²J_(HH) 5.04 Hz, ³J_(HH) 1.36 Hz, 1H, H-6), 7.90 (d, ³J_(HH) 6.88 Hz, 2H, H-2',6'), 7.61 (s, 1H, H-5''), 7.57-7.54 (m, 1H, H-4), 7.48 (t, ³J_(HH) 7.36 Hz, 2H, H-3',5'), 7.41 (dd, ²J_(HH) 8.24 Hz, ³J_(HH) 1.40 Hz, 1H, H-5), 7.33-7.28 (m, 2H, H-2''',6'''), 7.22 (t, ³J_(HH) 1.84 Hz, 1H, H-4'), 7.10 (dd, ²J_(HH) 8.24 Hz, ³J_(HH) 5.04 Hz, 2H, H-4''',5'''), 5.47 (s, 2H, O-CH₂), 5.31 (s, 2H, N-CH₂); ¹³C NMR (100 MHz, CDCl₃): δ_C 164.9 (C=O), 144.8 (C-2), 143.5 (C-3), 142.1 (C-1',4''), 140.7 (C-1'''), 140.3 (C-2'''), 136.1 (C-3'''), 134.9 (C-6'''), 134.6 (C-5''), 131.8 (C-6), 131.0 (C-2',6'), 129.0 (C-4'), 128.4 (C-3',5'), 127.4 (C-4), 123.0 (C-5), 121.2 (C-4'''), 120.0 (C-5'''), 62.7 (O-CH₂), 53.5 (N-CH₂); MS (EI) : *m/z* 420.1 (M⁺+1); Anal. Calc. for C₂₂H₁₈ClN₅O₂: C, 62.93; H, 4.32; N, 16.68. Found: C, 62.71; H, 4.53; N, 16.47.

***N*-(3-((1-(2-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)pyridin-2-yl)benzamide (6d)**. Yield: 64%; mp 125-126 °C; ¹H NMR (400 MHz, CDCl₃): δ_H 8.53 (bs, 1H, NH), 8.13 (dd, ²J_(HH) 5.04 Hz, ³J_(HH) 1.40 Hz, 1H, H-6), 7.90 (d, ³J_(HH) 7.32 Hz, 2H, H-2',6'), 7.66 (s, 1H, H-5''), 7.57-7.54 (m, 1H, H-5), 7.48 (t, ³J_(HH) 2.76 Hz, 2H, H-3',5'), 7.43-7.39 (m, 2H, H-

4''',6'''), 7.32-7.28 (m, 1H, H-3'''), 7.25-7.21 (m, 1H, H-5'''), 7.19 (dd, $^2J_{\text{HH}}$ 7.76 Hz, $^3J_{\text{HH}}$ 1.84 Hz, 1H, H-4), 7.09 (dd, $^2J_{\text{HH}}$ 8.24 Hz, $^3J_{\text{HH}}$ 5.04 Hz, 1H, H-4'), 5.64 (s, 2H, O-CH₂), 5.30 (s, 2H, N-CH₂); ¹³C NMR (100 MHz, CDCl₃): δ_c 164.9 (C=O), 144.6 (C-2), 143.1 (C-3), 142.1 (C-1',4''), 140.5 (C-1'''), 134.6 (C-5''), 133.5 (C-2'''), 131.9 (C-6), 130.5 (C-2',6'), 130.4 (C-3'''), 129.9 (C-4'), 128.6 (C-3',5'), 127.6 (C-6'''), 127.4 (C-4), 123.4 (C-5), 120.4 (C-4'''), 120.3 (C-5'''), 62.7 (O-CH₂), 51.5 (N-CH₂); MS (EI) : m/z 420.1 (M⁺+1); Anal. Calc. for C₂₂H₁₈ClN₅O₂: C, 62.93; H, 4.32; N, 16.68. Found: C, 62.59; H, 4.57; N, 16.85.

***N*-(3-((1-(4-Fluorobenzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)pyridin-2-yl)benzamide (6e).** Yield: 82%; mp 165-168 °C; ¹H NMR (400 MHz, CDCl₃): δ_H 8.52 (bs, 1H, NH), 8.12 (d, $^3J_{\text{HH}}$ 4.56 Hz, 1H, H-6), 7.88 (d, $^3J_{\text{HH}}$ 6.88 Hz, 2H, H-2',6'), 7.57 (s, 1H, H-5''), 7.56-7.54 (m, 1H, H-4), 7.47 (t, $^3J_{\text{HH}}$ 7.32 Hz, 2H, H-3',5'), 7.41 (dd, $^2J_{\text{HH}}$ 7.80 Hz, $^3J_{\text{HH}}$ 1.36 Hz, 1H, H-5), 7.22-7.19 (m, 2H, H-2''',6'''), 7.09 (dd, $^2J_{\text{HH}}$ 8.28 Hz, $^3J_{\text{HH}}$ 5.04 Hz, 1H, H-4'), 7.03-6.98 (m, 2H, H-3''',5'''), 5.46 (s, 2H, O-CH₂), 5.29 (s, 2H, N-CH₂); ¹³C NMR (100 MHz, CDCl₃): δ_c 164.9 (C=O), 144.8 (C-2), 143.4 (C-3), 142.0 (C-4''), 140.6 (C-1'), 140.3 (C-1'''), 134.5 (C-5''), 131.8 (C-6), 130.5 (C-2',6'), 130.0 (C-2'''), 129.3 (C-4'), 128.9 (C-3',5'), 128.3 (C-6'''), 127.4 (C-4), 123.2 (C-5), 120.0, 119.9 (C-3'''), 115.5, 115.3 (C-5'''), 62.7 (O-CH₂), 53.4 (N-CH₂); MS (EI) : m/z 404.2 (M⁺+1); Anal. Calc. for C₂₂H₁₈FN₅O₂: C, 65.50; H, 4.50; N, 17.36. Found: C, 65.38; H, 4.33; N, 17.51.

***N*-(3-((1-(2-Fluorobenzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)pyridin-2-yl)benzamide (6f).** Yield: 78%; mp 132-134 °C; ¹H NMR (400 MHz, CDCl₃): δ_H 8.53 (bs, 1H, NH), 8.13 (d, $^3J_{\text{HH}}$ 4.56 Hz, 1H, H-4), 7.90 (d, $^3J_{\text{HH}}$ 6.84 Hz, 2H, H-2',6'), 7.66 (s, 1H, H-5''), 7.57-7.53 (m, 1H, H-4), 7.48 (t, $^3J_{\text{HH}}$ 7.32 Hz, 2H, H-3',5'), 7.42 (dd, $^2J_{\text{HH}}$ 8.24 Hz, $^3J_{\text{HH}}$ 1.36 Hz, 1H, H-5), 7.37-7.32 (m, 1H, H-6'''), 7.24 (dd, $^2J_{\text{HH}}$ 7.80 Hz, $^3J_{\text{HH}}$ 1.84 Hz, 1H, H-4'), 7.13-7.05 (m, 3H, H-3''',4''',5'''), 5.56 (s, 2H, O-CH₂), 5.29 (s, 2H, N-CH₂); ¹³C NMR (100 MHz, CDCl₃): δ_c 164.8 (C=O), 144.6 (C-2), 143.2 (C-3), 142.1 (C-4''), 140.7 (C-1'), 140.4 (C-1'''), 134.7 (C-5''), 131.7 (C-6), 129.9 (C-2',6'), 128.9, 128.8 (C-2'''), 128.4 (C-4'), 127.4 (C-3',5'), 124.2 (C-6'''), 123.2 (C-4), 121.0 (C-4'''), 120.5 (C-3'''), 119.8, 119.7 (C-5'''), 62.7 (O-CH₂), 47.8 (N-CH₂); MS (EI) : m/z 404.2 (M⁺+1); Anal. Calc. for C₂₂H₁₈FN₅O₂: C, 65.50; H, 4.50; N, 17.36. Found: C, 65.33; H, 4.68; N, 17.18.

***N*-(3-((1-(2-Nitrobenzyl)-1*H*-1,2,3-triazol-4-yl)methoxy)pyridin-2-yl)benzamide (6g).** Yield: 60%; mp 119-123 °C; ¹H NMR (400 MHz, CDCl₃): δ_H 8.56 (bs, 1H, NH), 8.14 (dd, $^2J_{\text{HH}}$ 7.76 Hz, $^3J_{\text{HH}}$ 1.32 Hz, 2H, H-6,4'''), 7.90 (d, $^3J_{\text{HH}}$ 7.36 Hz, 2H, H-2',6'), 7.84 (s, 1H, H-5''), 7.58-7.50 (m, 3H, H-4,3',5'), 7.48 (m, 3H, H-5,4',6'''), 7.10-7.05 (m, 2H, H-3''',5'''), 5.90 (s, 2H, O-CH₂), 5.34 (s, 2H, N-CH₂); ¹³C NMR (100 MHz, CDCl₃): δ_c 164.8 (C=O), 147.3 (C-2'''), 144.6 (C-2), 142.1 (C-3,4''), 140.2 (C-1'), 140.0 (C-1'''), 134.5 (C-5''), 134.2 (C-3'''), 131.8 (C-6), 131.1 (C-2',6'), 130.0 (C-2'''), 129.8 (C-6'''), 129.0 (C-4'), 128.3 (C-3'), 127.4 (C-5'), 125.5 (C-4), 125.2 (C-4'''), 124.3 (C-4'''), 120.1 (C-3'''), 62.7 (O-CH₂), 51.0 (N-CH₂); MS (EI) : m/z 431.4 (M⁺+1); Anal. Calc. for C₂₂H₁₈N₆O₄: C, 61.39; H, 4.22; N, 19.53. Found: C, 61.47; H, 4.39; N, 19.76.

***N*-(3-((1-Allyl)-1*H*-1,2,3-triazol-4-yl)methoxy)pyridin-2-yl)benzamide (6h).** Yield: 55%; mp 117-120 °C; ¹H NMR (400 MHz, CDCl₃): δ_H 8.58 (bs, 1H, NH), 8.13 (d, $^3J_{\text{HH}}$ 4.12 Hz, 1H, H-6), 7.92-7.90 (m, 2H, H-2',6'), 7.65 (s, 1H, H-5''), 7.57-7.53 (m, 1H, H-5), 7.49-7.46 (m, 2H, H-3',5'), 7.43 (dd, $^2J_{\text{HH}}$ 7.80 Hz, $^3J_{\text{HH}}$ 1.36 Hz, 1H, H-4), 7.09 (dd, $^2J_{\text{HH}}$ 8.28 Hz,

$^3J_{\text{HH}}$ 4.56 Hz, 1H, H-4'), 6.00-5.93 (m, 1H, allyl-CH), 5.33-5.24 (m, 4H, allyl-CH₂, O-CH₂), 4.96-4.94 (m, 2H, N-CH₂); ^{13}C NMR (100 MHz, CDCl₃): δ_{c} 164.9 (C=O), 144.8 (C-2), 143.1 (C-3), 142.1 (C-4''), 134.6 (C-5''), 131.9 (C-6), 130.7 (C-2',6'), 128.6 (C-4'), 127.4 (C-3',5'), 123.0 (C-4), 120.2 (C-5), 62.7 (O-CH₂), 52.8 (N-CH₂); MS (EI) : m/z 336.3 (M⁺+1); Anal. Calc. for C₁₈H₁₇N₅O₂: C, 64.47; H, 5.11; N, 20.88. Found: C, 64.39; H, 5.39; N, 20.65.

Synthesis of *N*-(3-hydroxypyridin-2-yl)-3-phenylacrylamide **8.** In a 100 ml round bottom flask, cinnamic acid (2.6 g, 18 mmol) was stirred in CH₂Cl₂ (50 mL) at 0 °C in the presence of HOBt (5.4 g, 40 mmol), EDC (6.2 g, 40 mmol) and DIPEA (2.5 g, 20 mmol). 2-Amino-3-hydroxy pyridine **1** (2 g, 18 mmol) was added to the above suspension and the mixture stirred at room temperature for 12 h. After completion of the reaction, the reaction mixture was extracted with water. The organic layer was separated, dried over Na₂SO₄, filtered and concentrated to get crude product. Purification with column chromatography resulted in compound **8** as a yellow solid.

***N*-(3-hydroxypyridin-2-yl)-3-phenylacrylamide (**8**).** Yield: 80%; mp 145-147 °C; ^1H NMR (400 MHz, CDCl₃): δ_{H} 10.90 (bs, 1H, OH), 10.20 (bs, 1H, NH), 7.94 (d, $^3J_{\text{HH}}$ 4.12 Hz, 1H, H-6), 7.88 (d, J_{HH} 15.12 Hz, 1H, H-5), 7.52-7.50 (m, 2H, H-2',6'), 7.44-7.38 (m, 4H, CH, H-4,3',5'), 7.19 (dd, $^2J_{\text{HH}}$ 7.80 Hz, $^3J_{\text{HH}}$ 4.56 Hz, 1H, H-4'), 6.75 (d, $^3J_{\text{HH}}$ 15.60 Hz, 1H, CH); ^{13}C NMR (100 MHz, CDCl₃): δ_{c} 166.3 (C=O), 145.4 (C-2), 145.1 (C-3), 140.5 (C-1'), 138.2 (CH), 133.9 (CH), 131.0 (C-6), 130.3 (C-2'), 129.3 (C-6'), 128.6 (C-4'), 128.4 (C-3'), 128.0 (C-5'), 118.5 (C-4), 117.4 (C-5). MS (EI) : m/z 241.1 (M⁺+1).

Synthesis of 3-phenyl-*N*-prop-2-ynyl-*N*-(3-(prop-2-ynyloxy)pyridin-2-yl)acrylamide (9**) and 3-phenyl-*N*-(3-(prop-2-ynyloxy)pyridin-2-yl)acrylamide (**10**).** *N*-(3-Hydroxy-pyridin-2-yl)-3-phenyl-acrylamide **8** (2 g, 10 mmol) was treated with propargyl bromide (1.17 g, 10 mmol) in the presence of K₂CO₃ (2 g, 15 mmol) and TBAHSO₄ (0.05 mmol) using acetonitrile as solvent. When the reaction was carried out at room temperature for 8 h, the resulting compounds were obtained as yellow solids of 3-phenyl-*N*-(3-(prop-2-ynyloxy)-pyridin-2-yl)acrylamide (**10**) and 3-phenyl-*N*-prop-2-ynyl-*N*-(3-(prop-2-ynyloxy)-pyridin-2-yl)acrylamide (**9**) in 55% and 10% yields respectively. Acetonitrile was removed under vacuum, extracted with CHCl₃ and water, the organic layer separated and dried over Na₂SO₄ to get the crude product. Column chromatography was required in order to get the corresponding compounds **9** and **10**. When this reaction was carried out at reflux temperature for 8 h, it resulted in formation of yellowish liquid of 3-phenyl-*N*-prop-2-ynyl-*N*-(3-(prop-2-ynyloxy)-pyridin-2-yl)acrylamide (**9**) in 60% yield with traces of compound **10**.

3-Phenyl-*N*-prop-2-ynyl-*N*-(3-(prop-2-ynyloxy)-pyridin-2-yl)acrylamide (9**).** Yield: 60%; ^1H NMR (400 MHz, CDCl₃): δ_{H} 8.72 (dd, $^2J_{\text{HH}}$ 4.60 Hz, $^3J_{\text{HH}}$ 1.40 Hz, 1H, H-6), 7.74 (d, $^3J_{\text{HH}}$ 15.12 Hz, 1H, H-5), 7.53 (dd, $^2J_{\text{HH}}$ 8.24 Hz, $^3J_{\text{HH}}$ 1.36 Hz, 1H, H-2'), 7.38 (dd, $^2J_{\text{HH}}$ 8.24 Hz, $^3J_{\text{HH}}$ 4.56 Hz, 1H, H-6'), 7.34 (dd, $^2J_{\text{HH}}$ 5.96 Hz, $^3J_{\text{HH}}$ 2.20 Hz, 2H, H-4,4'), 7.28 (d, $^3J_{\text{HH}}$ 2.28 Hz, 3H, CH, H-3',5'), 6.23 (d, $^3J_{\text{HH}}$ 15.12 Hz, 1H, CH), 4.74 (d, $^3J_{\text{HH}}$ 2.15 Hz, 2H, O-CH₂), 4.71 (d, $^3J_{\text{HH}}$ 2.28 Hz, 2H, N-CH₂), 2.40 (t, $^3J_{\text{HH}}$ 2.30 Hz, 1H, CH), 2.14 (d, $^3J_{\text{HH}}$ 2.72 Hz, 1H, CH). MS (EI) : m/z 317.1 (M⁺+1); Anal. Calc. for C₂₀H₁₆N₂O₂: C, 75.93; H, 5.10; N, 8.86. Found: C, 75.67; H, 4.99; N, 8.93.

3-Phenyl-*N*-(3-(prop-2-ynyloxy)pyridin-2-yl)acrylamide (10**).** Yield: 55%; mp 129-131 °C; ^1H NMR (400 MHz, CDCl₃): δ_{H} 8.10 (d, $^3J_{\text{HH}}$ 4.56 Hz, 2H, NH, H-6), 7.85 (d, $^3J_{\text{HH}}$

16.04 Hz, 1H, H-5), 7.60-7.57 (m, 2H, H-2',6'), 7.41-7.34 (m, 4H, CH,H-4,3',5'), 7.32 (dd, $^2J_{\text{HH}}$ 8.24 Hz, $^3J_{\text{HH}}$ 1.36 Hz, 1H, H-4'), 7.05 (dd, $^2J_{\text{HH}}$ 8.24 Hz, $^3J_{\text{HH}}$ 5.04 Hz, 1H, CH), 4.79 (d, $^3J_{\text{HH}}$ 2.28 Hz, 2H, O-CH₂), 2.60 (t, $^3J_{\text{HH}}$ 2.30 Hz, 1H, CH); ¹³C NMR (100 MHz, CDCl₃): δ_c 164.8 (C=O), 143.3 (C-2), 142.3 (C-3), 142.2 (C-1'), 140.1 (CH), 134.8 (CH), 129.8 (C-6), 128.7 (C-2',6'), 128.1 (C-4'), 120.6 (C-3',5'), 119.2 (C-4), 119.1 (C-5), 56.3 (O-CH₂); MS (EI) : *m/z* 279.3 (M⁺+1); Anal. Calc. for C₁₇H₁₄N₂O₂: C, 73.37; H, 5.07; N, 10.07. Found: C, 73.60; H, 5.32; N, 10.29.

General procedure for synthesis of 11a-g. In a round bottom flask, Cu(OAc)₂.H₂O (5 mol%), 1,10-phenanthroline monohydrate (5 mol%) and sodium L-ascorbate (107 mg, 0.47 mmol) were added in EtOH:H₂O (6:4, 10 mL) and the mixture stirred for 5 mins at room temperature. Compound **10** (100 mg, 0.35 mmol), sodium azide (76 mg, 1.02 mmol) and the corresponding benzyl halide (0.40 mmol) were added to the reaction mixture and it was stirred at room temperature. Reaction time varied from 8 to 20 h for various benzyl halides. After completion of reaction (monitored by TLC), ice cold water was added to reaction mixture till the product precipitated out. It was filtered off and washed with cold water. The crude product was purified by column chromatography using AcOEt:MeOH (98:2) as eluent to get compound **11a-g**.

***N*-[3-(1-Benzyl-1*H*-[1,2,3]triazol-4-ylmethoxy)pyridin-2-yl]-3-phenyl-acrylamide (11a).** Yield: 50%; mp 125-126 °C; ¹H NMR (400 MHz, CDCl₃): δ_H 8.11 (bs, 1H, NH), 8.06 (dd, $^2J_{\text{HH}}$ 4.56 Hz, $^3J_{\text{HH}}$ 0.92 Hz, 1H, H-6), 7.82 (d, $^3J_{\text{HH}}$ 15.6 Hz, 1H, H-5), 7.59-7.57 (m, 3H, H-5'',2',6'), 7.41-7.37 (m, 4H, CH,H-3',4',5'), 7.36-7.32 (m, 4H, H-2''',3''',5''',6'''), 7.31-7.27 (m, 2H, H-4,4'''), 7.03 (dd, $^2J_{\text{HH}}$ 8.28 Hz, $^3J_{\text{HH}}$ 5.04 Hz, 1H, CH), 5.54 (s, 2H, N-CH₂), 5.26 (s, 2H, N-CH₂); ¹³C NMR (100 MHz, CDCl₃): δ_c 164.8 (C=O), 143.2 (C-2), 143.0 (C-3), 142.1 (C-1,4''), 139.9 (C-1'''), 134.9 (C-5''), 134.0 (CH), 129.9 (CH), 129.2 (C-6), 128.9 (C-2',6'), 128.7 (C-4'), 128.1 (C-3',5'), 127.9 (C-2''',6'''), 127.1 (C-4), 123.2 (C-5), 120.6 (C-4'''), 119.5 (C-3''',5'''), 62.4 (O-CH₂), 54.3 (N-CH₂); MS (EI) : *m/z* 412.2 (M⁺+1); Anal. Calc. for C₂₄H₂₁N₅O₂: C, 70.06; H, 5.14; N, 17.02. Found: C, 70.27; H, 4.82; N, 17.37.

***N*-{3-[1-(4-Chloro-benzyl)-1*H*-[1,2,3]triazol-4-ylmethoxy]-pyridin-2-yl}-3-phenyl-acrylamide (11b).** Yield: 58%; mp 160-162 °C; ¹H NMR (400 MHz, CDCl₃): δ_H 8.07 (bs, 1H, NH), 8.06 (dd, $^2J_{\text{HH}}$ 4.80 Hz, $^3J_{\text{HH}}$ 1.60 Hz, 1H, H-6), 7.82 (d, $^3J_{\text{HH}}$ 15.56 Hz, 1H, H-5), 7.60-7.59 (m, 2H, H-2',6'), 7.57 (s, 1H, H-5''), 7.41-7.39 (m, 2H, CH, H-4'), 7.38 (d, $^3J_{\text{HH}}$ 1.36 Hz, 2H, H-5',6'), 7.37-7.34 (m, 2H, H-2''',6'''), 7.33 (t, $^3J_{\text{HH}}$ 2.28 Hz, 1H, H-4), 7.23-7.21 (m, 2H, H-3''',5'''), 7.04 (dd, $^2J_{\text{HH}}$ 8.24 Hz, $^3J_{\text{HH}}$ 5.04 Hz, 1H, CH), 5.51 (s, 2H, O-CH₂), 5.26 (s, 2H, N-CH₂); ¹³C NMR (100 MHz, CDCl₃): δ_c 164.8 (C=O), 143.3 (C-2), 143.2 (C-3), 142.1 (C-1',4''), 140.0 (C-1'''), 135.0 (C-4'''), 134.9 (C-5''), 134.1 (CH), 132.5 (C-2''',6'''), 130.0 (CH), 129.9 (C-2',6'), 129.5 (C-4'), 129.4 (C-3'), 128.8 (C-5'), 128.1 (C-4), 123.1 (C-5), 120.5 (C-3'''), 119.5 (C-5'''), 62.4 (O-CH₂), 53.6 (N-CH₂); MS (EI) : *m/z* 446.3 (M⁺+1); Anal. Calc. for C₂₄H₂₀ClN₅O₂: C, 64.65; H, 4.52; N, 15.71. Found: C, 64.37; H, 4.73; N, 15.82.

***N*-{3-[1-(3-Chloro-benzyl)-1*H*-[1,2,3]triazol-4-ylmethoxy]pyridin-2-yl}-3-phenyl-acrylamide (11c).** Yield: 57%; mp 161-163 °C; ¹H NMR (400 MHz, CDCl₃): δ_H 8.30 (bs, 1H, NH), 8.06 (dd, $^2J_{\text{HH}}$ 5.04 Hz, $^3J_{\text{HH}}$ 0.92 Hz, 1H, H-6), 7.82 (d, $^3J_{\text{HH}}$ 16.04 Hz, 1H, H-5), 7.66 (s, 1H, H-5''), 7.59-7.56 (m, 2H, H-2',6'), 7.40-7.39 (m, 2H, CH, H-4'), 7.38 (d, $^3J_{\text{HH}}$

1.84 Hz, 3H, H-4,5',6'), 7.32-7.30 (m, 2H, H-2''',6'''), 7.28 (s, 1H, H-2'''), 7.15 (d, $^3J_{\text{HH}}$ 6.88 Hz, 1H, H-4'''), 7.06 (dd, $^2J_{\text{HH}}$ 7.80 Hz, $^3J_{\text{HH}}$ 5.04 Hz, 1H, CH), 5.51 (s, 2H, O-CH₂), 5.29 (s, 2H, N-CH₂); ^{13}C NMR (100 MHz, CDCl₃): δ_{c} 164.8 (C=O), 145.9 (C-2), 143.6 (C-3), 143.4 (C-1',4''), 143.3 (C-1'''), 142.2 (C-2'''), 139.8 (C-3'''), 136.0 (C-6'''), 135.0 (CH), 134.8 (C-5'''), 130.4 (CH), 129.9 (C-6), 129.1 (C-2',6'), 128.8 (C-4'), 128.7 (C-3'), 128.2 (C-5'), 128.1 (C-4), 123.3 (C-5), 120.5 (C-4'''), 119.8 (C-5'''), 62.5 (O-CH₂), 53.6 (N-CH₂); MS (EI) : m/z 446.3 (M⁺+1); Anal. Calc. for C₂₄H₂₀ClN₅O₂: C, 64.65; H, 4.52; N, 15.71. Found: C, 64.23; H, 4.29; N, 15.90.

***N*-{3-[1-(2-Chloro-benzyl)-1*H*-[1,2,3]triazol-4-ylmethoxy]pyridin-2-yl}-3-phenyl-acrylamide (11d).** Yield: 56%; mp 128-129 °C; ^1H NMR (400 MHz, CDCl₃): δ_{H} 8.09 (bs, 1H, NH), 8.07 (dd, $^2J_{\text{HH}}$ 5.04 Hz, $^3J_{\text{HH}}$ 0.92 Hz, 1H, H-6), 7.59 (dd, $^2J_{\text{HH}}$ 7.80 Hz, $^3J_{\text{HH}}$ 1.36 Hz, 1H, H-5), 7.43 (s, 1H, H-5''), 7.41-7.39 (m, 2H, H-2',6'), 7.38 (d, $^3J_{\text{HH}}$ 1.36 Hz, 2H, H-3',5'), 7.33 (dd, $^2J_{\text{HH}}$ 6.88 Hz, $^3J_{\text{HH}}$ 2.28 Hz, 1H, CH), 7.29-7.27 (m, 2H, H-4,4'), 7.26 (d, $^3J_{\text{HH}}$ 1.36 Hz, 1H, H-3'''), 7.25-7.23 (m, 2H, H-5''',6'''), 7.16-7.11 (m, 1H, H-4'''), 7.04 (dd, $^2J_{\text{HH}}$ 7.80 Hz, $^3J_{\text{HH}}$ 5.04 Hz, 1H, CH), 5.68 (s, 2H, O-CH₂), 5.27 (s, 2H, N-CH₂); ^{13}C NMR (100 MHz, CDCl₃): δ_{c} 164.8 (C=O), 144.5 (C-2), 143.2 (C-3), 142.9 (C-1',4''), 140.0 (C-1'''), 135.1 (CH), 134.9 (C-5'''), 133.2 (C-2'''), 131.9 (CH), 130.5 (C-6), 130.4 (C-2',6'), 130.0 (C-3'''), 129.8 (C-4'), 129.2 (C-3'), 128.7 (C-5'), 128.1 (C-6'''), 127.6 (C-4), 123.5 (C-5), 120.6 (C-4'''), 119.5 (C-5'''), 62.4 (O-CH₂), 51.6 (N-CH₂); MS (EI) : m/z 446.3 (M⁺+1); Anal. Calc. for C₂₄H₂₀ClN₅O₂: C, 64.65; H, 4.52; N, 15.71. Found: C, 64.73; H, 4.17; N, 15.33.

***N*-{3-[1-(4-Fluoro-benzyl)-1*H*-[1,2,3]triazol-4-ylmethoxy]-pyridin-2-yl}-3-phenyl-crylamide (11e).** Yield: 58%; mp 169-172 °C; ^1H NMR (400 MHz, CDCl₃): δ_{H} 8.20 (bs, 1H, NH), 8.05 (d, $^3J_{\text{HH}}$ 4.56 Hz, 1H, H-6), 7.81 (d, $^3J_{\text{HH}}$ 15.56 Hz, 1H, H-5), 7.62 (s, 1H, H-5''), 7.58-7.56 (m, 2H, H-2',6'), 7.39 (d, $^3J_{\text{HH}}$ 1.84 Hz, 2H, H-3',5'), 7.38-7.36 (m, 2H, CH, H-4), 7.29-7.27 (m, 3H, H-2''',6'''), 7.07 (d, $^3J_{\text{HH}}$ 8.68 Hz, 2H, H-3''',5'''), 7.06 (d, $^3J_{\text{HH}}$ 2.28 Hz, 1H, CH), 5.50 (s, 2H, O-CH₂), 5.26 (s, 2H, N-CH₂); ^{13}C NMR (100 MHz, CDCl₃): δ_{c} 164.1 (C=O), 143.4 (C-2), 143.2 (C-3), 142.1 (C-4''), 139.8 (C-1'), 135.3 (CH), 134.8 (C-5''), 130.1 (CH), 130.0 (C-6), 129.9 (C-2'), 129.8 (C-6'), 128.7 (C-2'''), 128.1 (C-4'), 126.5 (C-3',5'), 123.1 (C-6'''), 120.6 (C-4), 119.6 (C-5), 116.3 (C-3'''), 114.0 (C-5'''), 62.5 (O-CH₂), 53.5 (N-CH₂); MS (EI) : m/z 430.2 (M⁺+1); Anal. Calc. for C₂₄H₂₀FN₅O₂: C, 67.12; H, 4.69; N, 16.31. Found: C, 66.83; H, 4.53; N, 16.43.

***N*-{3-[1-(2-Fluoro-benzyl)-1*H*-[1,2,3]triazol-4-ylmethoxy]pyridin-2-yl}-3-phenyl-acrylamide (11f).** Yield: 55%; mp 138-140 °C; ^1H NMR (400 MHz, CDCl₃): δ_{H} 8.16 (bs, 1H, NH), 8.05 (s, 1H, H-6), 7.81 (d, $^3J_{\text{HH}}$ 15.60 Hz, 1H, H-5), 7.70 (s, 1H, H-5''), 7.58 (d, $^3J_{\text{HH}}$ 2.40 Hz, 1H, H-2'), 7.37-7.28 (m, 7H, CH, H-4,3',4',5',6',3'''), 7.16-7.07 (m, 4H, CH, H-4''',5''',6'''), 5.60 (s, 2H, O-CH₂), 5.26 (s, 2H, N-CH₂); ^{13}C NMR (100 MHz, CDCl₃): δ_{c} 161.7 (C=O), 144.5 (C-2), 143.1 (C-3), 143.0 (C-4''), 140.3 (C-1',1'''), 135.6 (CH), 134.9 (C-5''), 131.1 (CH), 131.0 (C-6), 130.6 (C-2',6'), 129.9 (C-2'''), 128.7 (C-4'), 128.1 (C-3'), 124.9 (C-5'), 123.4 (C-6'''), 121.5 (C-4), 121.3 (C-4'''), 119.5 (C-3'''), 115.7 (C-5'''), 62.4 (O-CH₂), 47.9 (N-CH₂); MS (EI) : m/z 430.2 (M⁺+1); Anal. Calc. for C₂₄H₂₀FN₅O₂: C, 67.12; H, 4.69; N, 16.31. Found: C, 67.43; H, 4.53; N, 16.56.

***N*-[3-(1-Allyl-1*H*-[1,2,3]triazol-4-ylmethoxy)pyridin-2-yl]-3-phenyl-acrylamide (11g).** Yield: 45%; mp 120-122 °C; ¹H NMR (400 MHz, CDCl₃): δ_H 8.45 (bs, 1H, NH), 8.29 (dd, ²J_(HH) 7.76 Hz, ³J_(HH) 1.80 Hz, 1H, H-6), 8.12 (s, 1H, H-5), 8.07-8.03 (m, 1H, H-2'), 7.82 (s, 1H, H-5''), 7.81-7.77 (m, 3H, H-3',5',6'), 7.68 (dd, ²J_(HH) 8.28 Hz, ³J_(HH) 4.60 Hz, 1H, H-4'), 7.60-7.57 (m, 1H, CH), 7.42-7.37 (m, 2H, CH, H-4), 6.10-5.87 (m, 1H, allyl-CH), 5.57-5.42 (m, 1H, allyl-CH), 5.37-5.31 (m, 3H, allyl-CH, O-CH₂), 5.01-4.91 (m, 2H, N-CH₂); ¹³C NMR (100 MHz, CDCl₃): δ_C 161.9 (C=O), 144.6 (C-2), 143.3 (C-3), 143.1 (C-4''), 140.0 (CH), 135.0 (C-5''), 131.2 (CH), 130.8 (C-6), 130.0 (C-2',6'), 128.8 (C-4'), 128.3 (C-3',5'), 123.6 (C-4), 120.8 (C-5), 62.6 (O-CH₂), 48.0 (N-CH₂); MS (EI) : *m/z* 362.2 (M⁺+1); Anal. Calc. for C₂₀H₁₉N₅O₂: C, 66.47; H, 5.30; N, 19.38. Found: C, 66.14; H, 5.11; N, 19.52.

Supporting Information

Supporting information (Experimental details, ¹H and ¹³C NMR spectra for the compounds **3-5**, **6a-h**, **8-10** and **11a-g**), associated with this article can be found, in the online version.

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