Cu (I) Catalyzed One Pot S_N-Click Reactions of Halogenated Coumarins and 1-*aza*-coumarins

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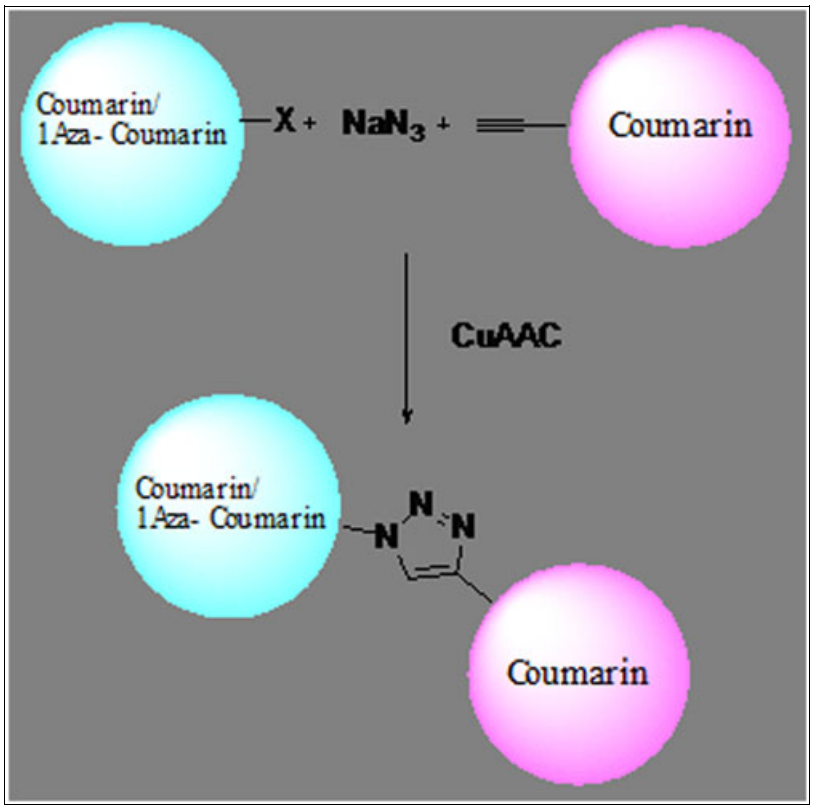

A one pot three component, copper catalyzed azide-alkyne cycloaddition reaction has been employed for the synthesis of *bis*-coumarinyl triazoles (**A**–**D**) using 4-chloro, 4-bromomethyl, 3-bromoacetyl and 4-bromomethyl-1-*aza*-coumarins (**I**–**IV**), sodium azide, and coumarin propargyl ethers (**V**–**IX**) in moderate yields.

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INTRODUCTION

The azide alkyne cycloaddition was initially investigated as a two component 1,3-dipolar cycloaddition and the use of Cu(I) salts has resulted in the regioselective formation of 1,4-substituted triazoles under the so-called click chemistry conditions. In situ generation of azides using suitable halides and sodium azide and their subsequent reaction with acetylenic dipolarophiles in a single pot makes this a three component reaction that was first realized in practice by Appukutam et al. under microwave conditions [1]. Since then, several different variants such as in copper nanoparticles [2] ($CuBr(PPh_3)_3$) [3], over copper(II) sulfate supported on alumina (Cu/Al_2O_3) under ball-milling conditions [4], and montmorillonite KSF clay supported CuO nanoparticles [5] have been developed. Direct arylation that is, S_NAr reactions have also been reported [6]. A one-pot, three-step Sonogashira cross-coupling-desilylation-cycloaddition sequence was developed for the convenient preparation of 1,4-disubstituted 1,2,3-triazoles [7]. A one pot multicomponent tandem copper-catalyzed azidation and copper catalyzed azide-alkyne cycloaddition reactions were developed to afford a library of 1-2′-thiazolyl-1,2,3-triazoles that were tested for their anticancer activity [8]. One-pot synthesis of novel 1,2,3-triazoles containing nitrogen, oxygen, and sulfur functionalized arms has also been reported [9].

Halohydrin dehalogenase has been used to bring about enantioselective azidolysis of aromatic epoxides to

1,2-azido alcohols that were subsequently ligated to alkynes producing chiral hydroxyl triazoles in a one-pot procedure with excellent enantiomeric excess [10]. The three-step, one-pot protocol based on decarboxylative coupling of alkynoic acids and 1,3-dipolar cycloaddition of azides enables a highly efficient synthesis of a variety of functionalized 1,2,3-triazoles [11]. A one-pot reaction for Cu(II)-catalyzed diazo transfer and Cu(I)-catalyzed azide-alkyne 1,3-dipolar cycloaddition have been reported to yield 1,4-disubstituted 1,2,3-triazoles in excellent yields from a variety of readily available amines without the need for isolation of the azide intermediates [12]. Triazolyl azido alcohols have been synthesized from terminal alkyne via oxirane ring-opening of epichlorohydrin [13].

The present work is aimed at adding a new dimension to the three component version of the azide alkyne cycloaddition. The in situ generated azides have been derived from heteroaryl halides, allyl halides, α-halo ketones, and isosteric systems represented by 4-chloro coumarins, 4-bromomethyl coumarins, 3-bromoacetyl coumarins, and 4-bromomethyl-1-*aza*-coumarins (carbostyrils), respectively. Regioisomeric dipolarophiles in the form of coumarinyl propargyl ethers have been used in this reaction. The resulting molecular matrices with rotatable bonds would provide the required conformational flexibility for biological activity.

CHEMISTRY

Heteroaryl halides employed in this work differ significantly in their reactivity towards nucleophiles. 4-Chloro coumarins [14], 4-bromomethyl coumarins [15], 3-bromoacetyl coumarins [16], and 4-bromomethyl-1-*aza*-coumarins(carbostyrils) [17] were synthesized in a two/three step sequence according to literature methods. Acetylenic dipolarophiles linked to hydroxy coumarins via an ether linkage have been prepared by the reaction of various hydroxy coumarins and propargyl bromides [18–21] (Fig 1).

The in situ generation of azides was achieved by the reaction of halides (**I**–**IV**) with sodium azide in aqueous acetone at room temperature. After the completion of reaction (15–20 min), the acetylenic dipolarophile was added and the reaction was continued under click chemistry conditions [18]. Completion of the reaction is monitored by thin-layer chromatography (TLC) and usual workup, purification, and crystallization resulted in a series of pure triazoles (**A**–**D**).

RESULT AND DISCUSSION

The *ipso*-chloro displacement in the case of 4-chloro-coumarins (**I**) was found to occur at room temperature in aqueous acetone and the *bis*-coumarinyl triazole A (Scheme 1) were obtained by its reaction with dipolarophile (**VI**).

Formation of product **A1** (R = 6–CH_3) (Scheme 1) was confirmed by spectral analysis. IR spectrum exhibited an intense band at 1720 cm^{-1}, due to lactone carbonyl. It was further confirmed by ^{1}H–NMR, wherein the characteristic peak for coumarin that is, C_3─H proton for triazole linked coumarin was observed as a singlet at 6.9 ppm. The C_6─CH_3 resonated at 2.3 ppm as singlet. The C_3─H from ether linked coumarin resonated referred to here as $C_{3'}$─H proton resonated at 6.4 ppm as doublet with a coupling constant of 1.2 Hz, due to allylic coupling with $C_{4'}$─CH_3 that resonated at 2.4 ppm as doublet with coupling constant of 1.2 Hz. The O─CH_2 protons linking triazole to coumarin were observed at 5.4 ppm as singlet, the C_5─H of triazole that resonates downfield at 8.9 ppm confirms the formation of 1,4-substituted triazoles. In ^{13}C–NMR, the two lactone carbons resonated at 160.8 and 160.0 ppm, respectively, O─CH_2 resonated at 61 ppm, $C_{4'}$─CH_3 groups resonated at 18 ppm while as C_6─CH_3 resonated at 20 ppm, and remaining carbons resonated in the expected region between 101 and 159 ppm. Molecular ion peak at *m/z* 415 in the EI-MS confirmed the proposed structure.

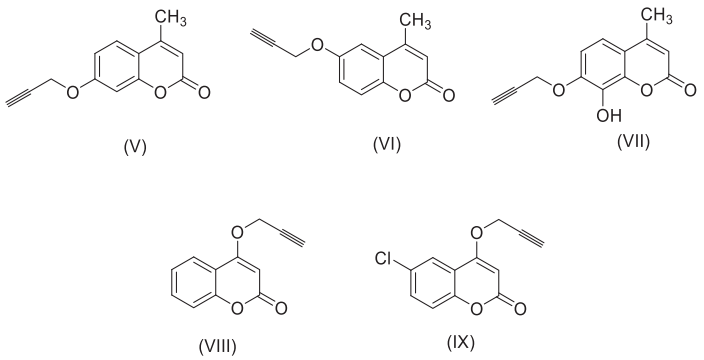
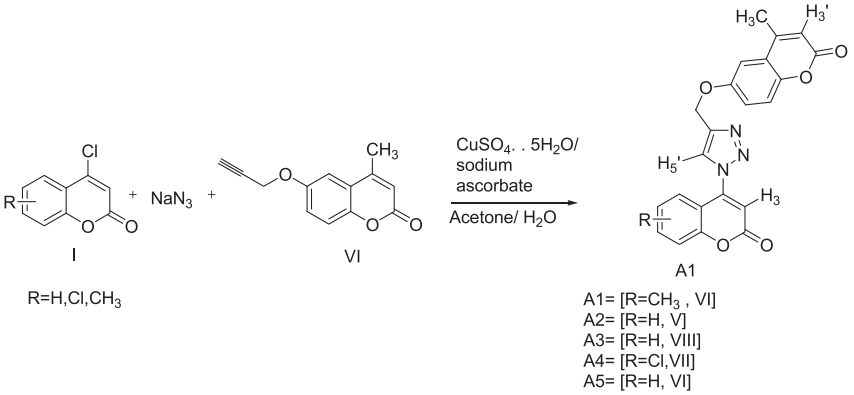


Figure 1. Coumarin linked acetylenic dipolarophiles employed in the three component one-pot reaction.

Scheme 1. Three component reaction of 4-chloro coumarins under click chemistry conditions.



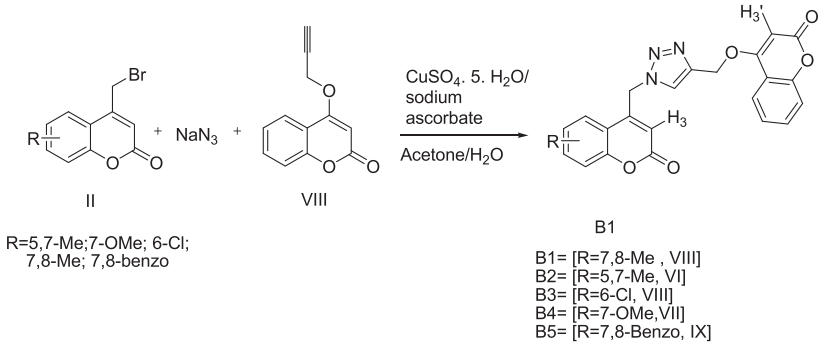
The in situ allylic substitution was observed during the reaction of 4-bromomethyl coumarins (**II**) with sodium azide at room temperature that is similar to their reactivity with substituted phenols [15]. *Bis*-coumarinyl triazoles **B** (Scheme 2) with more number of rotatable C─C bonds were generated by their reaction with dipolarophile **VIII**.

In a typical example **B1** (R = 7,8–CH_3), IR spectrum exhibited an intense band at 1717 cm^{-1}, due to lactone carbonyl. It was further confirmed by ^{1}H–NMR, wherein the characteristic peak for coumarin that is, C_3─H proton for triazole linked coumarin was observed as a singlet at 5.8 ppm. The –CH_2 linking coumarin to triazoles resonated at 6.0 ppm. The C_3─H proton from ether linked coumarin resonated referred to here as $C_{3'}$─H proton resonated at 6.1 ppm. The O─CH_2 protons linking triazole to coumarin were observed at 5.4 ppm as singlet, the C_5─H of triazole that resonates downfield at 8.5 ppm confirms the formation of 1,4-substituted triazoles. The two methyl groups on coumarin resonated at 2.2 and 2.3 ppm, respectively. In ^{13}C–NMR, the two lactone carbons resonated at 164 and 161 ppm, respectively, O─CH_2 resonated at 62 ppm, N─CH_2 resonated at 49 ppm, the two methyl carbon on coumarin resonated at 11 and 19 ppm, respectively, and remaining carbons resonated in the expected region between 91 and 164 ppm. Molecular ion peak at *m/z* 429 in the EI-MS confirmed the proposed structure.

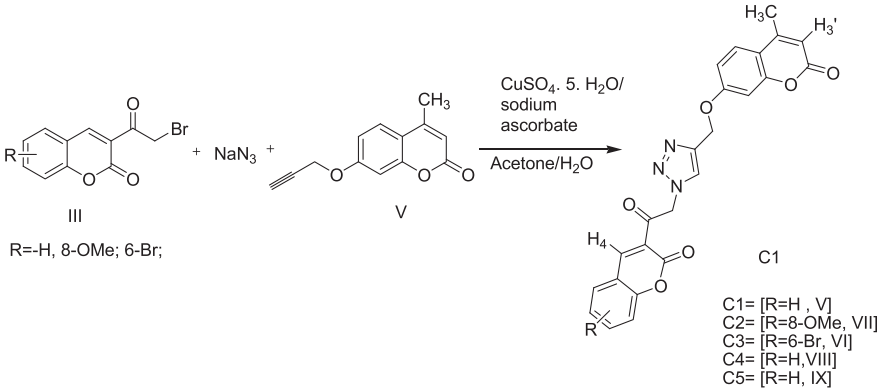
3-Bromoacetyl coumarins **III** were employed as model substrates for α-haloketones and the in situ generated α-azido ketones were reacted with acetylenic dipolarophile (**V**) to obtain regioisomeric *bis*-coumarinyl triazoles '**C**' (Scheme 3).

In a typical example **C1** (R ═ H), IR spectrum exhibited an intense band at 1716 cm^{-1}, due to lactone carbonyl. It was further confirmed by ^{1}H–NMR, the ─$COCH_2$ linking coumarin to triazoles resonated at 6.0 ppm. The C_3─H proton from ether linked coumarin resonated referred to here as $C_{3'}$─H proton resonated at 6.2 ppm as doublet with a coupling constant of 1.2 Hz, due to allylic coupling with C_4─CH_3 that resonated at 2.4 ppm as doublet with coupling constant of 1.2 Hz. The O─CH_2 protons linking triazole to coumarin were observed at 5.3 ppm as singlet, the C_5─H of triazole that resonates downfield at 8.8 ppm confirms the formation of 1,4-substituted triazoles. The C_4─H shows a characteristic peak at 8.2 ppm. In ^{13}C–NMR, the two lactone carbons resonated at 161and 160 ppm, respectively. The ketonic carbonyl group resonated at 189 ppm, O─CH_2 resonated at 61 ppm, N─CH_2 resonated at 58 ppm, the methyl carbon on coumarin resonated at 18 ppm, and remaining

Scheme 2. One-pot synthesis of *bis*-coumarinyl triazoles by click chemistry.



Scheme 3. One-pot click reaction of 3-bromoacetyl coumarins.



carbons resonated in the expected region between 101 and 158 ppm. A peak at *m/z* 442 in the EI-MS corresponded to the molecular ion.

The isosteric 4-bromomethyl-1-*aza* coumarin (carbostyril) **IV** similarly yielded triazoles '**D**', the structure of which was supported by spectral analysis.

Formation of product **D1** (Scheme 4) was confirmed by spectral analysis; IR spectrum exhibited an intense band at 1712 cm^{-1}, due to lactone carbonyl and at 1659 cm^{-1}, due lactam carbonyl. It was further confirmed by ^{1}H–NMR, wherein the characteristic peak for coumarin that is, C_3─H proton for triazole linked coumarin was observed as a singlet at 5.97 ppm. The ─CH_2 linking coumarin to triazoles resonated at 5.95 ppm. The C_3─H proton from ether linked coumarin resonated referred to here as $C_{3'}$─H proton resonated at 6.3 ppm as doublet with a coupling constant of 0.8 Hz, due to allylic coupling with C_4─CH_3 that resonated at 2.40 ppm as doublet with coupling constant of 0.8 Hz. The O─CH_2 protons linking triazole to coumarin were observed at 5.2 ppm as singlet, the C_5─H of triazole that resonates downfield at 8.3 ppm confirms the formation of 1,4-substituted triazoles and ring NH resonated at 10.9 ppm. In ^{13}C–NMR, the lactone carbons resonated at 160 ppm, O─CH_2 resonated at 61 ppm, N─CH_2 resonated at 49 ppm, the two methyl carbon on coumarin resonated at 17 and 18 ppm, and remaining carbons resonated in the expected region between 109 and 161 ppm. Molecular ion peak at *m/z* 428 in the EI-MS confirmed the proposed structure.

Structural diversity of the halides, however, did not affect the overall yield of the reactions significantly under click chemistry conditions (Table 1). Yields of the products **A**–**D** depended on the in situ generated azide.

However, the refluxing time for all the reactions was around 8 h. It is pertinent to mention that the yields of *bis*-coumarinyl triazoles in our earlier work by the reaction of 4-azidomethyl coumarins were in the range of 85–90% [22].

EXPERIMENTAL

The melting points were determined by open capillary method and are uncorrected. IR spectra (KBr disc) were recorded on Nicolet −5700 FT-IR spectrometer. ^{1}H NMR spectra were recorded on Bruker 400 MHz Spectrometer using DMSO-d_6 as solvent and tetramethylsilane as internal standard. The Chemical shifts are expressed in δ ppm. Mass spectra were recorded using Shimadzu GCMS-QP2010S. The elemental analysis was carried out using Hereaus CHN rapid analyzer. The purity of the compound was checked by TLC. All the chemicals purchased were of analytical grade and were used without further purification unless otherwise stated.

Scheme 4. One-pot S_N-allylic 1,3-dipolar click reaction of 4-bromomethyl-1-*aza*-coumarin.

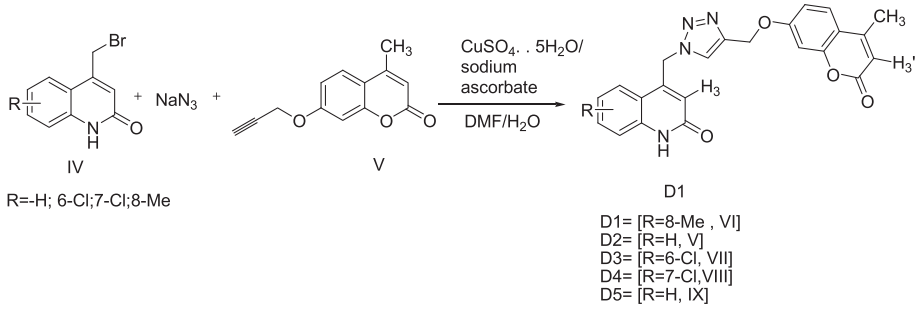


Table 1

Yields (isolated) for the triazoles **A**–**D**.

Compound	Yield (%)	Compound	Yield (%)
A1	75	**C1**	65
A2	70	**C2**	66
A3	71	**C3**	66
A4	68	**C4**	69
A5	71	**C5**	63
B1	68	**D1**	63
B2	69	**D2**	63
B3	66	**D3**	61
B4	62	**D4**	63
B5	66	**D5**	61

Synthesis of substituted 4-chloro coumarins (I). The required 4-chlorocoumarin were synthesized by chlorination of 4-hydroxy coumarin using $POCl_3$ [14].

Synthesis of substituted 4-bromomethyl-coumarins (II). All the required substituted 4-bromomethylcoumarin [15] have been synthesized by the Pechmann cyclization of various substituted phenols with 4-bromoethylacetoacetate.

Synthesis of substituted 3-bromoacetyl coumarins (General method) (III). The required 3-bromoacetylcoumarin is synthesized by bromination of 3-acetyl coumarin in chloroform [16].

Synthesis of substituted 4-bromomethyl-1-azacoumarins (carbostyrils) (IV). The required substituted 4-bromomethylcarbostyril have been synthesized by bromination of acetoacetanilides and cyclizing the intermediate (**2**) in sulphuric acid to give 4-bromomethyl-carbostyrils [17].

Synthesis of hydroxy-4-methyl coumarins. 7-Hydroxy-4-methyl coumarin, 6-hydroxy-4-methyl coumarin, and 7,8-dihydroxy-4-methyl coumarin were prepared by the Pechmann cyclization of the corresponding phenols with ethyl acetoacetate according to the literature reports [18–21].

Synthesis of substituted 4-hydroxy coumarins. Substituted 2-hydroxy acetophenone (**2**) (0.25 M) was dissolved in excess of diethyl carbonate (50 mL), followed by addition of excess of sodium metal (10 g), upon which vigorous reaction occurs, this is then refluxed on water bath for about 1 h and ethyl alcohol was added to reaction mixture to remove remaining sodium. The reaction mixture was quenched in water, if there is any separation of non-aqueous layer, it is discarded. The aqueous layer is separated out and acidified with 1:1 HCl to obtain substituted 4-hydroxy coumarin, which was then crystallized from ethanol in 60% yield [22].

Synthesis of coumarin propargyl ethers (V,**VI**,**VII**,**VII**, **IX**). Propargyl bromide (0.01 M) and anhydrous K_2CO_3 (0.015 M) were taken in dry acetone and was allowed to stir for 30 min. To this, hydroxyl coumarins (0.01 M) were added and the reaction was either stirred for 24 h or refluxed for 8 h on water bath. Reaction was quenched in ice-water and neutralized with 1:1 HCl, the precipitate obtained was then filtered and crystallized from ethanol in 75% yield [18–21].

General method for synthesis of (A1–A5, B1–B5, and C1–C5). Substituted halocoumarin (**I**,**II**,**III**) (0.001 M) and sodium azide (0.0012 M) (dissolved in water) and substituted coumarin propargyl ethers (0.001 M) were dissolved in 5 mL of acetone and the mixture was allowed to stir for 15 min. To this, Na_2CO_3 (0.003 M) and ascorbic acid (0.003 M) dissolved in 2.5 mL of water were added, followed by $CuSO_4.5H_2O$ (0.0015 M) dissolved in 2.5 mL of water was added. It was allowed to stir for 15 min and thereafter refluxed on water bath for 8 h. The reaction was monitored by TLC. After completion, the reaction mixture was cooled and the solid separated was filtered and recrystallized from DMF to obtain pure compound.

4-Methyl-6-((1-(6-methyl-2-oxo-2H-chromen-4-yl)-1H-1,2,3-triazol-4-yl)methoxy)-2H-chromen-2-one (A1). DMF, mp–218–200°C; yield–75%; IR (KBr, cm^{-1}) ν = 1730 (lactone C=O); ^{1}H NMR (300 MHz, DMSO-d_6), δ(ppm) = 2.3 (s, 3H, ─CH_3), 2.4 (d, 3H, $C_{4'}$─CH_3, J = 1.2 Hz), 5.4(s, 2H, O─CH_2), 6.4 (d, 1H, $C_{3'}$─H, J = 1.2 Hz), 6.9 (s, 1H, C_3─H), 7.3–7.6 (m, 6H, Ar─H), 8.9 (s,1H, tri–H); ^{13}C–NMR (100 MHz, DMSO-d_6, δppm) 18.1, 20.4, 61.2, 101.6, 110.8, 111.4, 112.6, 113.5, 114.0, 116.9, 124.7, 126.5, 126.7, 134.3, 134.4, 142.8, 145.8, 151.8, 153.3, 154.6, 159.5, 160.0, 160.8. EI-MS: *m/z*–415 (M^+., 3%); *Anal*. Calcd for $C_{23}H_{17}N_3O_5$ (%), Calcd: C, 66.50; H, 4.12; N, 10.12; Found: C, 66.40; H, 4.10; N, 10.11.

4-Methyl-7-((1-(2-oxo-2H-chromen-4-yl)-1H-1,2,3-triazol-4-yl)methoxy)-2H–chromen-2-one (A2). DMF, mp: 218–220°C; yield–70%; IR (KBr, cm^1), ν = 1716 (lactone C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 2.4(d, 3H, ─CH_3, J = 1.2 Hz), 5.4(s, 2H, O─CH_2), 6.2(d, 1H, $C_{3'}$─H, J = 1.2 Hz), 6.9 (s, 1H, C_3─H), 7.0–7.8 (m, 7H, Ar─H), 8.9(s, 1H, tri-H); ^{13}C–NMR (100 MHz, DMSO-d_6, δppm) 18.1, 61.2, 101.6, 110.7, 111.3, 112.5, 113.5, 114.3, 117.1, 124.9, 125.3, 126.5, 126.6, 133.4, 142.8, 145.8, 153.3, 153.6, 154.6 159.3, 160.0, 160.8; EI-MS: *m/z*–401 (M^+., 5%); *Anal*. Calcd for $C_{22}H_{15}N_3O_5$ (%), Calcd: C, 65.83; H, 3.77; N, 10.47; Found: C, 65.73; H, 3.71; N, 10.40.

4-(4-((2-Oxo-2H-chromen-4-yloxy)methyl)-1H-1,2,3-triazol-1-yl)-2H-chromen-2-one (A3). DMF, mp–210–212°C; yield–71%; IR (KBr, cm^{-1}), ν = 1720 (lactone C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 5.6 (s, 2H, O─CH_2), 6.2 (s, 1H, $C_{3'}$─H), 7.0 (s, 1H, C_3─H), 7.3–7.8 (m, 8H, Ar─H), 9.0 (s, 1H, tri-H); ^{13}C–NMR (100 MHz, DMSO-d_6, δppm) 62.4, 91.5, 110.8, 114.3, 115.0, 116.4, 117.1, 123.0, 124.2, 125.0, 125.4, 126.8, 132.8, 133.4, 142.0, 145.8, 152.7, 153.6, 159.4, 161.4, 164.2; EI-MS:

m/z−387 (M^+., 3%); *Anal*. Calcd for $C_{21}H_{13}N_3O_5$ (%), Calcd: C, 65.12; H, 3.38; N, 10.85; Found: C, 65.11; H, 3.38; N, 10.81.

7-((1-(6-Chloro-2-oxo-2H-chromen-4-yl)-1H-1,2,3-triazol-4-yl)methoxy)-8-hydroxy-4-methyl-2H-chromen-2-one (A4). DMF, mp–248–250°C; yield–68%; IR (KBr, cm^{-1}), *v* = 1732 (lactone C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 2.4 (d, 3H, ─CH_3, *J* = 1.2 Hz), 5.4 (s, 2H, O─CH_2), 6.4 (d, 1H, $C_{3'}$─H, *J* = 1.2 Hz), 6.9 (s, 1H, C_3─H), 7.0–7.6 (m, 5H, Ar─H), 8.9 (s, 1H, tri-H); ^{13}C–NMR (100 MHz, DMSO-d_6, δppm) 18.2, 61.4, 109.6, 111.4, 114.7, 115.6,117.6, 119.2, 119.8, 120.2,124.7, 126.4, 128.7, 133.0, 143.4, 144.5, 147.5, 152.3, 153.0, 154.1, 159.0, 159.8; EI-MS: *m/z*–451 (M^+., 9%), 453 (M + 2^+., 3%); *Anal*. Calcd for $C_{22}H_{14}ClN_3O_6$ (%), Calcd: C, 58.48; H, 3.12; N, 9.30; Found: C, 58.41; H, 3.10; N, 9.25.

4-Methyl-6-((1-(2-oxo-2H-chromen-4-yl)-1H-1,2,3-triazol-4-yl)methoxy)-2H-chromen-2-one (A5). DMF, mp–222–224°C; yield–71%; IR (KBr, cm^{-1}), *v* = 1720 (lactone C=O); ^{1}H NMR (300 MHz, DMSO-d_6), δ(ppm) = 2.4 (d, 3H, ─CH_3, *J* = 1.2 Hz), 5.4 (s, 2H, O─CH_2), 6.3 (d, 1H, $C_{3'}$─H, *J* = 1.2 Hz), 6.5 (s, 1H, C_3─H), 7.2–7.8 (m, 7H, Ar─H), 8.8 (s, 1H, tri-H); EI-MS: *m/z*−401 (M^+., 2%); *Anal*. Calcd for $C_{22}H_{15}N_3O_5$; (%), Calcd: C, 65.83; H, 3.77; N, 10.47; Found: C, 65.81; H, 3.67; N, 10.41.

7,8-Dimethyl-4-((4-(((2-oxo-2H-chromen-4-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-2H-chromen-2-one (B1). DMF, mp–195–197°C; yield–68%; IR (KBr, cm^{-1}), *v* = 1717 (lactone C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 2.2 (s, 3H, ─CH_3), 2.3 (s, 3H, ─CH_3), 5.4 (s, 2H, O─CH_2), 5.8 (s, 1H, C_3─H), 6.0 (s, 2H, N─CH_2), 6.1 (s, 1H, $C_{3'}$─H), 7.2–7.7 (m, 6H, Ar─H), 8.5 (s, 1H, tri-H); ^{13}C–NMR (100 MHz, DMSO-d_6, δppm): 11.1, 19.8, 49.3, 62.6, 91.3, 112.6, 114.7, 115.0, 116.4, 121.4, 122.7, 124.0, 124.1, 125.7, 126.3, 132.7, 141.5, 142.0, 150.1, 151.2, 152.7, 159.5, 161.4, 164.2; EI-MS: *m/z*−429 (M^+., 5%); *Anal*. Calcd for $C_{24}H_{19}N_3O_5$ (%), Calcd: C, 67.13; H, 4.46; N, 9.79; Found: C, 67.10; H, 4.41; N, 9.72.

5,7-Dimethyl-4-((4-(((4-methyl-2-oxo-2H-chromen-6-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-2H-chromen-2-one (B2). DMF, mp–201–203°C; yield–69%; IR (KBr, cm^{-1}), *v* = 1716 (lactone C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 2.3 (s, 3H, ─CH_3), 2.4 (d, 3H, ─CH_3, *J* = 1.2 Hz), 2.6 (s, 3H, ─CH_3), 5.3 (s, 2H, O─CH_2), 5.1 (s, 1H, C_3─H), 6.1 (s, 2H, N─CH_2), 6.4 (d, 1H, $C_{3'}$─H, *J* = 1.2 Hz), 7.0–7.3 (m, 6H, Ar─H), 8.3 (s, 1H, tri-H); ^{13}C–NMR (100 MHz, DMSO d_6, δppm) 18.1, 20.6, 23.3, 52.2, 62.6, 109.6, 112.6, 114.7, 115.0, 116.4, 121.4, 122.7, 124.1, 124.7, 125.7, 126.3, 132.7, 141.5, 142.0, 150.1, 151.2, 152.7, 159.5, 159.7, 161.2; EI-MS: *m/z*−443 (M^+., 7%); *Anal*. Calcd for $C_{25}H_{21}N_3O_5$ (%), Calcd: C, 67.71; H, 4.77; N, 9.48; Found: C, 67.69; H, 4.72; N, 9.41.

6-Chloro-4-((4-(((2-oxo-2H-chromen-4-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-2H-chromen-2-one (B3). DMF, mp–293–295°C; yield–66%; IR (KBr, cm^{-1}), *v* = 1728 (lactone C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 5.4 (s, 2H, O─CH_2), 5.9 (s, 1H, C_3─H), 6.0 (s, 2H, N─CH_2), 6.1 (s, 1H, $C_{3'}$─H), 7.3–7.9 (m, 6H, Ar─H), 8.5 (s, 1H, tri-H) ^{13}C–NMR (100 MHz, DMSO-d_6, δppm) 49.0, 62.6, 91.3, 115.0, 115.2, 116.4, 118.5, 118.8, 122.7, 124.1, 124.3, 126.3, 128.6, 132.2, 132.8, 141.7, 148.9, 151.7, 152.7, 158.8, 161.4, 164.2; EI-MS: *m/z*–435(M^+., 12%), 437 (M + 2^+., 4%); *Anal*. Calcd for $C_{22}H_{14}ClN_3O_5$ (%), Calcd: C, 60.63; H, 3.24; N, 9.64; Found: C, 60.61; H, 3.24; N, 9.60.

8-Hydroxy-7-((1-((7-methoxy-2-oxo-2H-chromen-4-yl)methyl)-1H-1,2,3-triazol-4-yl)methoxy)-4-methyl-2H-chromen-2-one (B4). DMF, mp–242–244°C; yield–62%; IR (KBr, cm^{-1}), *v* = 1707 (lactone C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 2.3 (d, 3H, ─CH_3, *J* = 1.2 Hz), 3.8 (s, 3H, 7─OCH_3), 5.3 (s, 2H, O─CH_2), 5.1 (s, 1H, C_3─H), 5.9 (s, 2H, N─CH_2), 6.2 (d, 1H, $C_{3'}$─H, *J* = 1.2 Hz), 7.1–7.5 (m, 5H, Ar─H), 8.4 (s, 1H, tri-H); EI-MS: *m/z*–461(M^+.); *Anal*. Calcd for $C_{24}H_{19}N_3O_7$ (%), Calcd: C, 62.47; H, 4.15; N, 9.11; Found: C, 62.41; H, 4.10; N, 9.10.

4-((4-(((6-Chloro-2-oxo-2H-chromen-4-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)-2H-benzo[h]chromen-2-one (B5). DMF, mp–235–237°C; yield–66%; IR (KBr, cm^{-1}), *v* = 1716 (lactone C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 5.3 (s, 2H, O─CH_2), 5.8 (s, 1H, C_3─H), 6.0 (s, 2H, N─CH_2), 6.3 (s, 1H, $C_{3'}$─H), 7.1–7.9 (m, 9H, Ar─H), 8.4 (s, 1H, tri-H); EI-MS: *m/z*–485(M^+., 9%), 487 (M + 2^+., 3%); *Anal*. Calcd for $C_{26}H_{16}ClN_3O_5$ (%), Calcd: C, 64.27; H, 3.32; N, 8.65; Found: C, 64.23; H, 3.31; N, 8.65.

4-Methyl-7-((1-(2-oxo-2-(2-oxo-2H-chromen-3-yl)ethyl)-1H-1,2,3-triazol-4-yl)methoxy)-2H-chromen-2-one (C1). DMF, mp–220–222°C; yield–65%; IR (KBr, cm^{-1}), *v* = 1716 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 2.4 (d, 3H, ─CH_3), 5.3 (s, 2H, O─CH_2), 6.0 (s, 2H, N─CH_2), 6.2 (d, 1H, $C_{3'}$─H), 7.0–8.0 (m, 7H, Ar─H), 8.2 (s, 1H, C_4─H) 8.8 (s, 1H, tri-H); ^{13}C–NMR (100 MHz, DMSO *d6*, δppm) 18.0, 58.2, 61.5, 101.5, 111.2, 112.6, 113.3, 116.6, 116.8, 117.9, 122.0, 125.1, 126.4, 131.1, 135.2, 148.5, 153.3, 154.6, 154.6, 158.5, 160.0, 161.0, 189.3; EI-MS: *m/z*−443 (1%, M^+.); *Anal*. Calcd for $C_{24}H_{17}N_3O_6$ (%), Calcd: C, 65.01; H, 3.86; N, 9.48; Found: C, 65.01; H, 3.80; N, 9.41.

8-Hydroxy-7-((1-(2-(8-methoxy-2-oxo-2H-chromen-3-yl)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methoxy)-4-methyl-2H-chromen-2-one (C2). DMF, mp–223–225°C; yield–66%; IR (KBr, cm^{-1}), *v* = 1724 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 2.4 (d, 3H, ─CH_3), 3.6 (s, 3H, ─OCH_3), 5.2 (s, 2H, O─CH_2), 5.9 (s, 2H, N─CH_2), 6.2 (d, 1H, $C_{3'}$─H), 7.3–7.8 (m, 5H, Ar─H), 8.3 (s, 1H, C4─H) 8.8 (s, 1H, tri-H); EI-MS: *m/z*−489(M^+.); *Anal*.

Calcd for $C_{25}H_{19}N_3O_8$ (%), Calcd: C, 61.35; H, 3.91; N, 8.59; Found: C, 61.31; H, 3.90; N, 8.53.

6-Bromo-3-(2-(4-(((4-methyl-2-oxo-2H-chromen-6-yl)oxy) methyl)-1H-1,2,3-triazol-1-yl)acetyl)-2H–chromen-2-one (C3). DMF, mp–190–192°C; yield–66%; IR (KBr, cm^{-1}), ν = 1714 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 2.4 (d, 3H, ─CH_3), 5.2 (s, 2H, O─CH_2), 5.9 (s, 2H, N─CH_2), 6.2 (d, 1H, $C_{3'}$─H), 7.3–8.0 (m, 6H, Ar─H), 8.2 (s, 1H, C_4─H) 8.8 (s, 1H, tri-H); EI-MS: *m/z*–521(M^+., 2%), 523 (M + 2^+., 2%); *Anal*. Calcd for $C_{24}H_{16}BrN_3O_6$ (%), Calcd: C, 55.19; H, 3.09; N, 8.05; Found: C, 55.12; H, 3.00; N, 8.05.

4-((1-(2-Oxo-2-(2-oxo-2H-chromen-3-yl)ethyl)-1H-1,2,3-triazol-4-yl)methoxy)-2H-chromen-2-one (C4). DMF, mp–198–200°C; yield–69%; IR (KBr, cm^{-1}), ν = 1714 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 5.5 (s, 2H, O─CH_2), 6.0 (s, 2H, N─CH_2), 6.2 (d, 1H, $C_{3'}$─H), 7.4–8.0 (m, 8H, Ar─H), 8.2 (s, 1H, C_4─H) 8.8 (s, 1H, tri-H); EI-MS: *m/z*–429(M^+.); *Anal*. Calcd for $C_{23}H_{15}N_3O_6$ (%), Calcd: C, 64.34; H, 3.52; N, 9.79; Found: C, 64.30; H, 3.51; N, 9.75.

6-Chloro-4-((1-(2-oxo-2-(2-oxo-2H-chromen-3-yl)ethyl)-1H-1,2,3-triazol-4-yl)methoxy)-2H-chromen-2-one (C5). DMF, mp–220–222°C; yield–63%; IR (KBr, cm^{-1}), ν = 1724 (C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 5.4 (s, 2H, O─CH_2), 6.0 (s, 2H, N─CH_2), 6.2 (d, 1H, $C_{3'}$─H), 7.3–8.0 (m, 7H, Ar─H), 8.1 (s, 1H, C_4─H) 8.8 (s, 1H, tri-H); EI-MS: *m/z*–463 (M^+., 3%), 465 (M + 2^+., 1%); *Anal*. Calcd for $C_{23}H_{14}ClN_3O_6$ (%), Calcd: C, 59.56; H, 3.04; N, 9.06; Found: C, 59.52; H, 3.04; N, 9.06.

General method for synthesis of (D1–D5). Substituted 4-bromomethyl carbostyrils (**IV**) (0.001 M) and sodium azide (0.0012 M) (dissolved in water) and substituted coumarin propargyl ethers (0.001 M) were dissolved in 5 mL of DMF and the mixture was allowed to stir for 15 min. To this, Na_2CO_3 (0.003 M) and ascorbic acid (0.003 M) dissolved in 2.5 mL of water were added, followed by $CuSO_4.5H_2O$ (0.0015 M) dissolved in 2.5 mL of water was added, upon which the reaction mixture turned yellow. It was allowed to stir for another 15 min, thereafter, it was refluxed on water bath for 8 h. The reaction was monitored by TLC. The reaction mixture was cooled and the solid separated was filtered off and was crystallized from DMF to obtain pure compound.

8-Methyl-4-((4-(((4-methyl-2-oxo-2H-chromen-6-yl)oxy) methyl)-1H-1,2,3-triazol-1-yl)methyl)quinolin-2(1H)-one (D1). DMF, mp–262–264°C; yield–63%; IR (KBr, cm^{-1}), ν = 1712 (lactone C=O); ν =1659 (amide C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 2.40 (d, 3H, ─CH_3, J = 0.8 Hz), 2.42 (s, 3H, ─CH_3), 5.2 (s, 2H, O─CH_2), 5.95 (s, 2H, N─CH_2), 5.97 (s, 1H, C_3─H), 6.3 (s, 1H, $C_{3'}$─H, J = 0.8 Hz), 7.0–7.6 (m, 6H, Ar─H), 8.3 (s, 1H, tri-H), 10.9 (s, 1H, NH); ^{13}C–NMR (100 MHz, DMSO-d_6, δppm); 17.1, 18.1, 49.9, 61.6, 109.6, 114.6, 117.0, 117.4, 119.7, 120.1, 121.6, 121.8, 124.0, 125.5, 132.1, 137.2, 142.8, 145.7, 147.4, 152.9, 154.1, 159.8, 161.4; EI-MS: *m/z*–428 (M^+., 2%); *Anal*. Calcd for $C_{24}H_{20}N_4O_4$ (%), Calcd: C, 67.28; H, 4.71; N, 13.08; Found: C, 67.21; H, 4.70; N, 13.02.

4-((4-(((4-Methyl-2-oxo-2H-chromen-7-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)quinolin-2(1H)-one (D2). DMF, mp–242–244°C; yield–63%; IR (KBr, cm^{-1}), ν = 1722 (lactone C=O); ν = 1665 (amide C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 2.3 (d, 3H, ─CH_3, J = 1.2 Hz), 5.2 (s, 2H, O─CH_2), 5.95 (s, 2H, N─CH_2), 5.98 (s, 1H, C_3─H), 6.2 (s, 1H, $C_{3'}$─H, J = 1.2 Hz), 7.0–7.8 (m, 7H, Ar─H), 8.3 (s, 1H, tri-H), 11.8 (s, 1H, NH); ^{13}C–NMR (100 MHz, DMSO-d_6, δppm); 18.0, 49.6, 61.5, 101.6, 111.2, 112.5, 113.3, 115.7, 118.2, 120.4, 121.9, 122.5, 123.9, 16.4, 17.5, 129.0, 130.0, 138.9, 142.4, 145.2, 154.5, 160.9, 161.1; EI-MS: *m/z*–414 (M^+., 4%); *Anal*. Calcd for $C_{23}H_{18}N_4O_4$ (%), Calcd: C, 66.66; H, 4.38; N, 13.52; Found: C, 66.60; H, 4.31; N, 13.51.

6-Chloro-4-((4-(((8-hydroxy-4-methyl-2-oxo-2H-chromen-7-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)quinolin-2(1H)-one (D3). DMF, mp–228–230°C; yield–61%; IR (KBr, cm^{-1}), ν = 1727 (lactone C=O); ν = 1666 (amide C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 2.3 (d, 3H, ─CH_3, J = 1.2 Hz), 5.3 (s, 2H, O─CH_2), 6.0 (s, 2H, N─CH_2), 6.2 (s, 1H, C_3─H), 6.4 (s, 1H, $C_{3'}$─H, J = 1.2 Hz), 7.2–7.6 (m, 5H, Ar─H), 8.5 (s, 1H, tri-H), 11.5 (s, 1H, NH); EI-MS: *m/z*–464(M^+., 3%), 466 (M + 2^+., 1%); *Anal*. Calcd for $C_{23}H_{17}ClN_4O_5$ (%), Calcd: C, 59.43; H, 3.69; N, 12.05; Found: C, 59.40; H, 3.60; N, 12.00.

7-Chloro-4-((4-(((2-oxo-2H-chromen-4-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)quinolin-2(1H)-one (D4). DMF, mp–268–270°C; yield–63%; IR (KBr, cm^{-1}), ν = 1715 (lactone C=O); ν = 1662 (amide C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 5.4 (s, 2H, O─CH_2), 5.9 (s, 2H, N─CH_2), 6.0 (s, 1H, C_3─H), 6.1 (s, 1H, $C_{3'}$─H), 7.2–7.8 (m, 7H, Ar─H), 8.5 (s, 1H, tri-H), 11.9 (s, 1H, NH); ^{13}C–NMR (100 MHz, DMSO-d_6, δppm); 49.6, 62.6, 91.3, 114.9, 115.9, 116.4, 120.9, 122.0, 122.8, 124.2, 126.0, 126.1, 132.8, 135.3, 139.9, 141.5, 144.9, 152.7, 161.0, 161.4, 161.2; EI-MS: *m/z*–434 (M^+., 15%), 436 (M + 2^+., 5%); *Anal*. Calcd for $C_{22}H_{15}ClN_4O_4$ (%), Calcd: C, 60.77; H, 3.48; N, 12.88; found: C, 60.71; H, 3.42; N, 12.83.

4-((4-(((6-Chloro-2-oxo-2H-chromen-4-yl)oxy)methyl)-1H-1,2,3-triazol-1-yl)methyl)quinolin-2(1H)-one (D5). DMF, mp–293–295°C; yield–61%; IR (KBr, cm^{-1}), ν = 1718 (lactone C=O); ν = 1660 (amide C=O); ^{1}H NMR (400 MHz, DMSO-d_6), δ(ppm) = 5.3 (s, 2H, O─CH_2), 5.9 (s, 2H, N─CH_2), 6.0 (s, 1H, C_3─H), 6.4 (s, 1H, $C_{3'}$─H), 7.2–7.8 (m, 7H, Ar─H), 8.3 (s, 1H, tri-H), 11.9 (s, 1H, NH); EI-MS: *m/z*–434 (M^+., 3%), 436 (M + 2^+., 1%); *Anal*. Calcd for $C_{22}H_{15}ClN_4O_4$ (%), Calcd: C, 60.77; H, 3.48; N, 12.88; Found: C, 60.71; H, 3.44; N, 12.88.

CONCLUSION

The one-pot click chemistry retains the regioselectivity expected for Cu(I) catalysis. Heterocyclic azides generated in situ provide a simpler method for construction of triazoles in moderate yields which is lesser than that observed in the reaction of azides and alkynes.

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