ISBN: 978-93-90847-90-7

4. Design, Synthesis and Characterization of 6-((1-(3-Substitutedbenzyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*]isoquinoline-1, 3(2*H*)-dione Derivatives.

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4.1 Introduction:

Substituted 1, 2, 3-triazoles are conveniently synthesized by a reaction between terminal alkynes and alkyl azides under Cu (I) catalysed click reaction. Some important aspects of the click reactions are summarized here.

4.1.1 Some 1, 2, 3-triazole based drugs:

1, 2, 3-Triazoles reveal a wide kind of pharmacological properties for example antituberculosis, [1] anti-HIV, [2] antimalarial, [3] antiepileptic, [4] antiallergic, [5] antileishmanial, [6] antifungal, [7, 8] anticancer [9, 10] and antibacterial [11, 12] activities. Moreover, they act as proton transport facilitators [13] in glycoside cluster arrays, [14, 15] spacers or linkers to dendrimers, [16, 17] DNA cleaving proxies, [18] structural gears in hyper branched polymers [19] and most vitally in liquid crystals. [20]

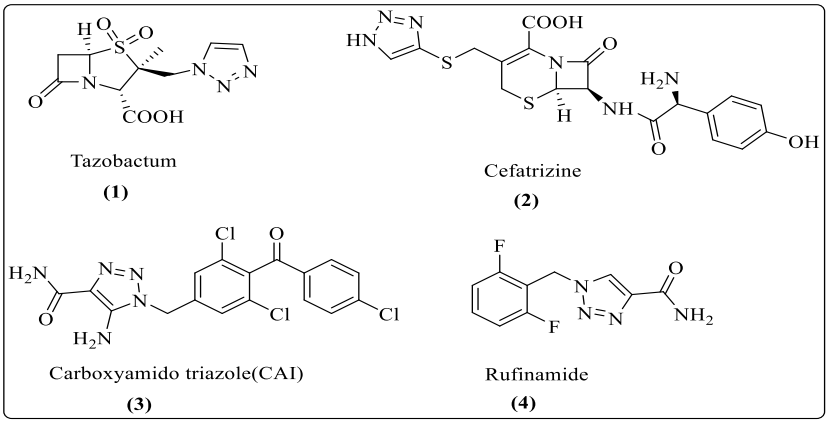
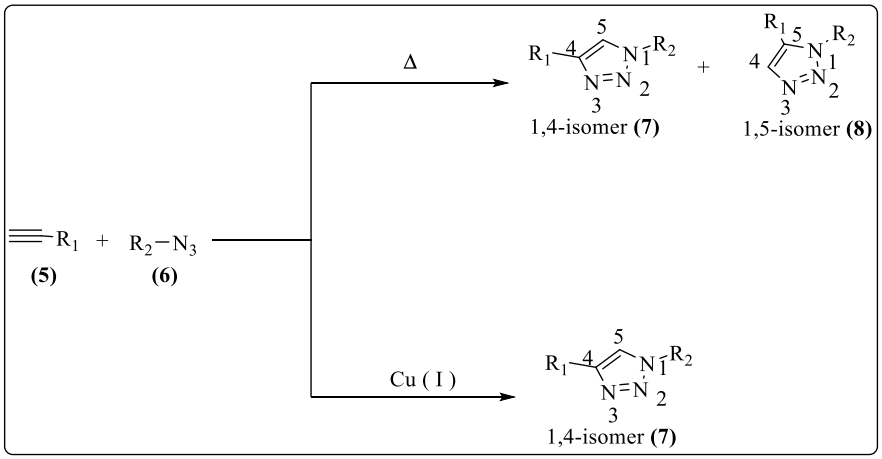


Figure 4.1: Previous Triazole drugs.

Overhead 1, 2, 3-triazoles are combined in around drugs. Tazobactam **(1)** [21] prevents the action of bacterial-β-lactamases. Cefatrizine **(2)** [22] stays a broad spectrum cephalosporin antibiotic. Carboxy amido triazole (CAI) **(3)** [23] is a calcium ion channel blocker. Rufinamide **(4)** [24] is an anticonvulsant and it is used in treatment of seizures allied with Lennox-Gastaut disorder in children, aged and adults.

4.1.2 1, 2, 3-Triazoles: Huisgen reaction:

Thermally attracted 1, 3-dipolar cycloaddition among a terminal alkyne **(1)** and azide **(2)** give regioisomeric 1, 2, 3-triazole moieties **(3&4) (Scheme-4.1)**. This cycloaddition, similarly so-called as Huisgen cycloadditions, was revealed at the foundation of the 20th century and its mechanisms were only exposed in the 1960s by Huisgen et. al., [25] the reaction is poorly regioselective, yielding both 1, 4 & 1, 5 regioisomers **(7&8)** [26] under warm conditions and necessary chromatographic separation into individuals.



Scheme-4.1: **The 1, 3-dipolar cycloadditions between azide and alkyne**

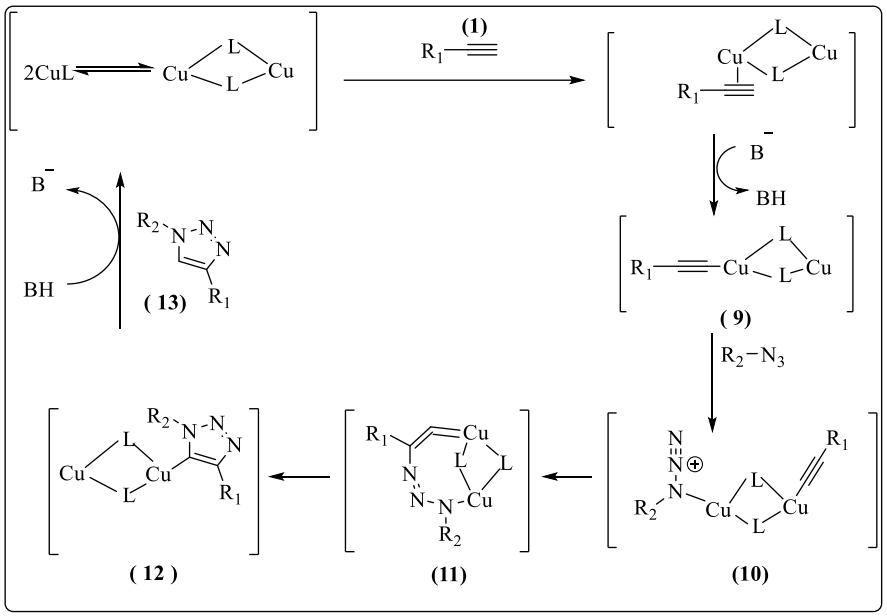
4.1.3 Click reaction:

The 1, 3-dipolar cycloaddition through azides and terminal alkynes catalysed via Cu (I) salts leads fully 1,4-disubstituted 1,2,3-triazoles **(7) (*Scheme-4.1*)** is produced click reaction, learned by Sharpless *et al.* [27] it is too referred by way of CuAAC (Cu Azide-Alkyne Cycloadditions) click reaction behaviours the usual catalytic system of copper (II) salts (e.g. $CuSO_4.5H_2O$ or $Cu(OAc)_2$) [28] in the incidence of a reducing agent, such equally sodium ascorbate or hydrazine [29] then TCEP (tris (2-carboxyethyl) phosphine) [30] by reasonable success, *tert*-butanol and aquatic mixture is used as solvent. Reducing agent converts Cu (II) to Cu (I), but occasionally it spirits down to Cu (0).

This is disallowed by using a proper ratio of sinking agent and catalyst or adding a copper stabilizing agent, such as THPTA (tris-(hydroxypropyltriazolylmethyl) amine). [31]Some of the key gains of the click reaction stand; 1) the reaction is highly regioselective leading to 1,4-disubstituted 1,2,3-triazoles. It naturally does not want hotness promotion but should be performed over a wide array of temperatures (0-160°C) in diversity of solvents (counting water) and over a wide range of pH values (5 through 12).

It gates as much as 10^7 times earlier than the uncatalyzed version. 2) This reaction was achieved in an aqueous media spending willingly reachable reagents and without elimination of atmospheric oxygen. 3) The reaction amid alkyne and azides is orthogonal to any functional group and performed without the protection of further functional groups inside the reactants. 4) The reaction yields are clean and do not need chromatographic separations. 5) The 1,4-disubstituted 1,2,3-triazoles are constant in reductive and oxidative situations, acid and basic hydrolysis indicating high aromatic stabilization. The high dipole moment (about 5D) [32] permits them to participate in hydrogen bonding, dipole-dipole and π-stacking interactions. [33]

4.1.4 Mechanism of click reaction:



Scheme 4.2: Proposed mechanism of click reaction

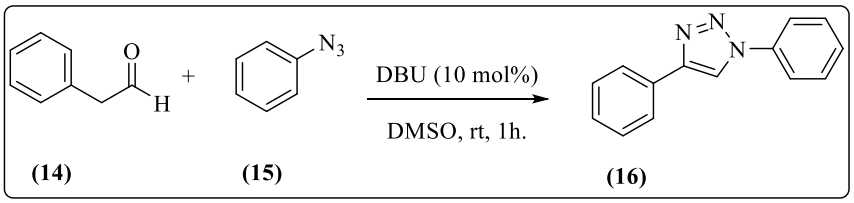
Mostly, cycloadditions proceed over a concerted mechanism. Though, experimentally dignified kinematic data and molecular forming performed on the CuAAC (Copper Azide-Alkyne Cycloadditions) reaction agree the preference for a stepwise reaction path (a stepwise catalysed CuAAC reaction has an activation fence 11 k.cal. mol^{-1} lower than a concerted catalysed reaction). [34] On the root of experimental evidence and the information that Cu (I) can eagerly addition itself into terminal alkynes [35] it stayed hypothesised that π complexation of a Cu (I) dimer to the alkyne is the first step. Then elimination of the terminal hydrogen from the alkyne arises to form Cu-acetylide. There are some different ways in which the Cu (I)-acetylide centres can be made, the π complexation of Cu (I) drop the pKa of the terminal alkyne by 9.8 pH units accepting the deprotonation and formation of Cu-acetylide **(9)** absence of a base. If an aprotic solvents acetonitrile, dichloromethane or toluene is used, in the attendance of stoichiometric amount of Cu (I) salts [e.g., CuI, Cu $(CH_3CN)_4$ PF_6, CuBr $(PPh_3)_4$ before a base frequently a tertiary amine (e.g., TEA, DIEA) added to induce the deprotonation step critical for the complexation. [36]

In the following step, azide nitrogen organises with a second Cu in the Cu (I) acetylide complex to form **(10)**. This method initiates the azide to nucleophilic attack from the acetylene carbon, due to proximity and electronic factors, permitting easy attack of the other end nitrogen on the second carbon of the alkyne, leading to a metallocycle **(11)**. The metallocycle then contracts forming the corresponding triazole **(12)**. Final protonation releases the Cu (I) catalyst from the 1, 2, 3-triazole to give product **(13)** and to restart another catalytic cycle (**Scheme 4.2**).

4.2 Some literature methods for synthesis of 1, 2, 3-triazoles:

4.2.1 Enolate mediated organic-click reaction:

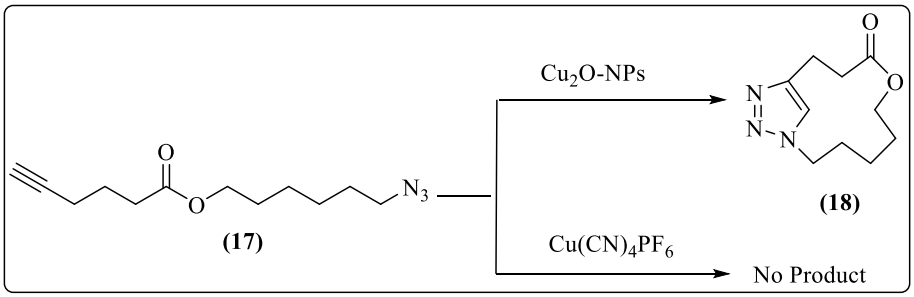
Ramachary *et al.* described [37] regioselective combination of 1,4-disubstituted 1,2,3-triazoles **(16)** built on enolate-mediated organo catalytic azide–aldehyde [3+2] cycloadditions (organo-click) reaction since commercially available enolisable aldehydes **(14)**, arylazides **(15)** and catalytic quantity of a tertiary amine.



Scheme 4.3: Synthesis of 1, 4-diphenyl-1*H*-1, 2, 3-triazole

4.2.2 Cu_2O-nanoparticles catalysed synthesis of 1, 2, 3-triazoles:

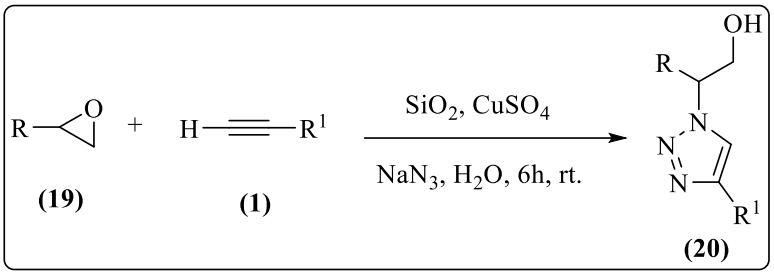
Duan *et al.* described [38] the production of cyclic 1, 2, 3-triazoles **(18)** catalysed by Cu_2O-nanoparticles (Cu_2O-NPs) in ethane nitrile by intramolecular 1, 3-dipolar cycloadditions.



Scheme 4.4: Synthesis of cyclic 1, 2, 3-triazoles.

4.2.3 Silica-coppersulphate catalysed synthesis of β-hydroxy triazoles:

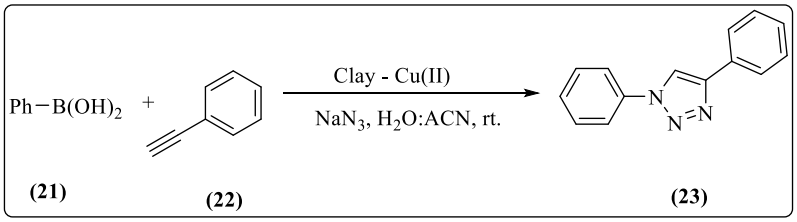
Hashjin *et al.* described [39] the synthesis of *β*-hydroxy triazoles **(20)** by a three-element one-pot abridgment of alkynes **(1)**, epoxides **(19)** and NaN_3 in the existence of catalytic amount of $SiO_2/CuSO_4$ in addition to ascorbic acid at ambient hotness in better yields with tiny reaction time sin aqua medium.



Scheme 4.5: Synthesis of *β*-hydroxy triazoles

4.2.4 Clay-copper catalysed synthesis of 1, 4-disubstituted 1, 2, 3-triazoles:

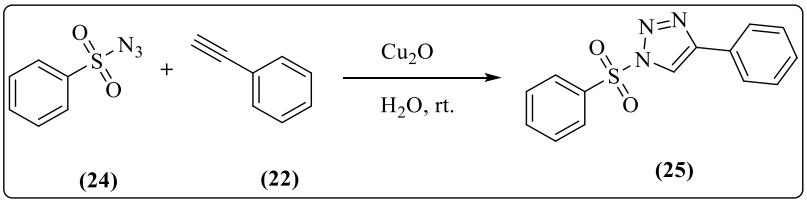
Shaber *et al.* conveyed [40] the fusion of the 1, 4-disubstituted 1, 2, 3-triazole **(23)** by a three-component one-pot compression of alkyne **(22)**, boronic acid **(21)** and NaN_3 in the incidence of a catalytic quantities of clay-Cu (II) catalyst, reflux condition with water: acetonitrile (1:1) mixture.



Scheme 4.6: Synthesis of 1, 4-disubstituted 1, 2, 3-triazole

4.2.5 Di copper oxide (Cu_2O) catalysed synthesis of triazoles:

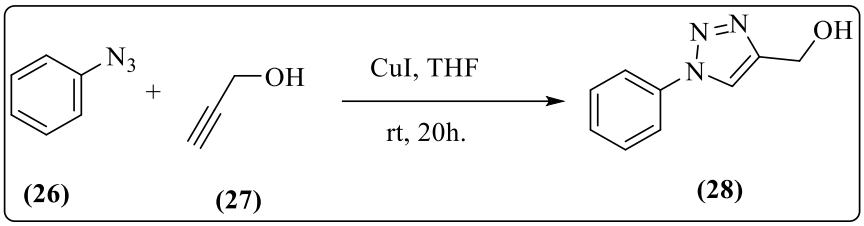
Ki Wang *et al.* learnt [41] blend of triazole **(25)** from a combination of alkyne **(22)** and tosylazide **(24)** in the existence of 8 mol% Cu_2O under well-ordered environments in 6hr.



Scheme 4.7: Synthesis of tosylated triazole

4.2.6 Copper iodide (I) catalysed synthesis of 1, 2, 3-triazole-4-yl-methanol:

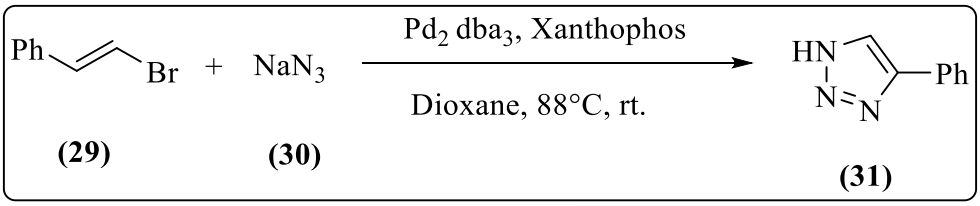
Nubia Boechat *et al.* conveyed [42] the production of 1, 2, 3-triazole-4-yl-methanol **(28)** via the 1, 3-dipolar cycloaddition reaction among propargylic alcohol **(27)** and aromatic azides **(26)** catalysed with Cu (I).



Scheme 4.8: Synthesis of 1, 2, 3-triazole-4-yl-methanol

4.2.7 Palladium catalysed synthesis of 1, 2, 3-triazoles:

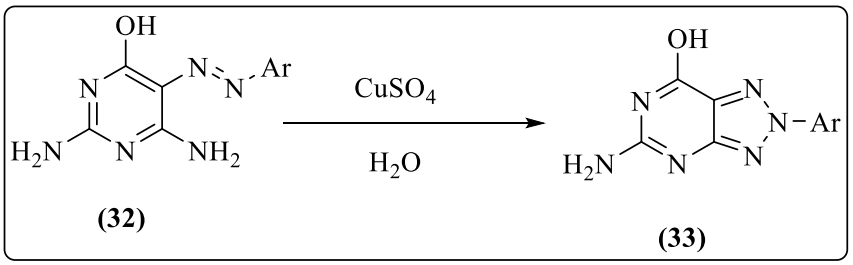
Barlnga *et al.* conveyed [43] palladium catalysed creation of 1, 2, 3-triazoles **(31)** from alkenyl bromides **(29)** and sodium azides **(30)** in the attendance of Pd_2dba_3, Xanthophos in dioxane.



Scheme 4.9: Synthesis of 4-phenyl-1*H*-1, 2, 3-triazole

4.2.8 Oxidative cyclisation of arylazo heterocycles to 1, 2, 3-triazoles:

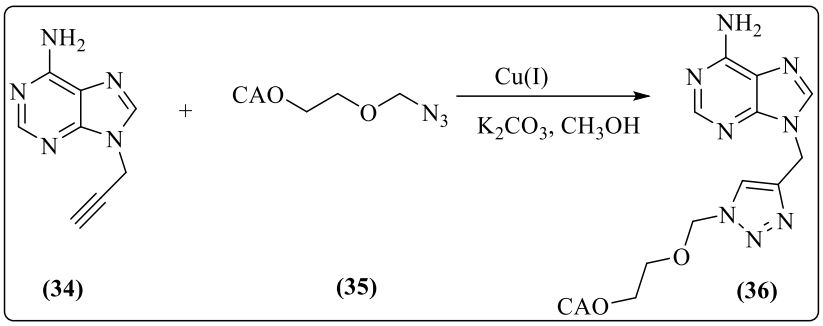
Boyr *et al.* conveyed [44] oxidative cyclisation of arylazo heterocycles **(32)** ensuring an amino cluster at *ortho* place in the occurrence of copper sulphate leads to 1, 2, 3-triazole **(33)**



Scheme 4.10: Synthesis of 1, 2, 3-triazole

4.2.9 Copper (I) catalysed 1, 3 dipolar cycloaddition reactions:

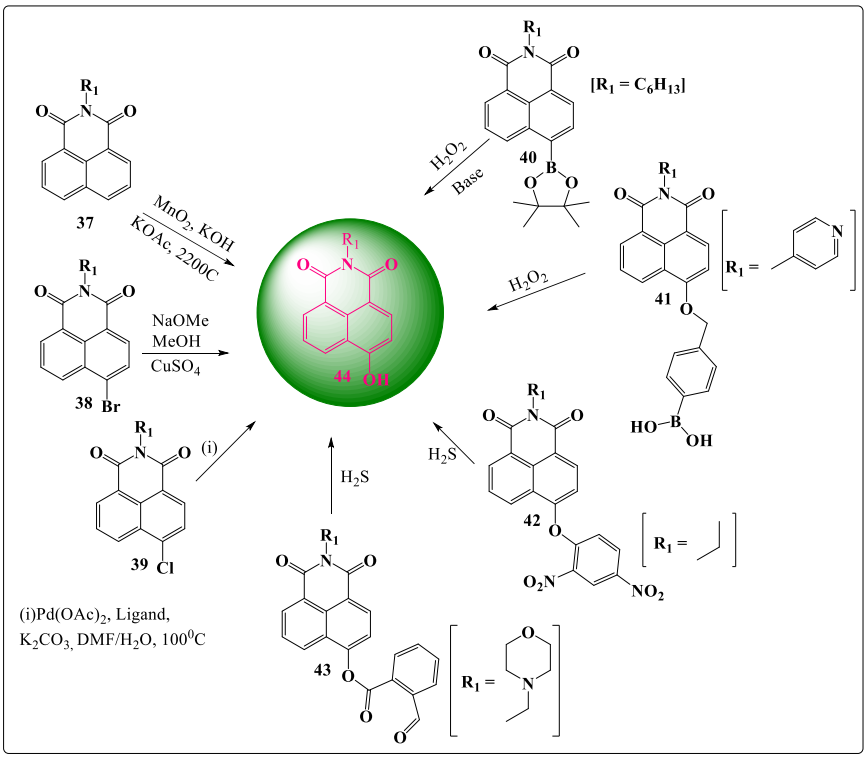
Shafran E.A reported [45]1,2,3- triazole review, a sequence of new 1,2,3-triazole acylo adenine nucleosides (**36**) allied to nucleobases were equipped *via* copper (I) catalyzed 1,3-dipolar cycloaddition of N-9 propargyl purine, N-1-propargyl pyrimidines (**34**) or N-1-propargyl indazoles per the azido-pseudo sugar (**35**) beneath microwave aided creation monitored by action with potassium carbonate and methanol.



Scheme 4.11: Synthesis of 1, 2, 3-triazole acylo adenine nucleosides

4.2.10 Various types Preparations of 4- hydroxy-N-Substituted 1, 8-Naphthalimide:

Synthesis of 4-hydroxy naphthalimides derivatives from 4-Chloro-*N*-substituted naphthalimide react with $Pd(OAc)_2$, Ligand,in Potassium carbonates and DMF Water at 100^0C. Then 4-Bromo1, 8-naphthalimide to give 4-HYdroxy-1, 8-naphthalimide in the presence of Sodium butoxide and Copper sulphate. Compound 18 and 19 to give 4-hydroxy 1, 8-naphthalimide in the presence of Hydrogen sulphide gas and compound 16 & 17 produce 4-hydroxy compound by the oxidation with hydrogen peroxide.



Scheme 4.12: Synthesis of 6-hydroxy-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2H)-dione

4.3 Present Work:

In this chapter defines the synthesis of novel 6-((1-(3-substitutedbenzyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo[*de*] isoquinoline-1, 3(2*H*)-dione derivatives (**56a-e**) and synthesis of 6-((1-(4-substitutedphenyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione derivatives **(55a-g)** regioselectively by humble click reaction conditions. involves the reaction of 2-phenyl-6-(prop-2-yn-1-yloxy)-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (**50**) with substituted aryl azides (**52a-g**) substituted benzylazides (**52a-e**).

Synthesis of 6-((1-(3-substitutedbenzyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo[*de*] isoquinoline-1, 3(2*H*)-dione derivatives (**56a-e**) and synthesis of 6-((1-(4-substitutedphenyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-
benzo [*de*] isoquinoline-1, 3(2*H*)-dione derivatives **(55a-g)** involves the following steps.

4.3.1 Synthesis of 6-hydroxy-2-phenyl-1H-benzo [de] isoquinoline-1, 3(2H)-dione (48).

4.3.2 Synthesis of 2-phenyl-6-(prop-2-yn-1-yloxy)-1H-benzo [de] isoquinoline-1, 3(2H)-dione (50).

4.3.3 Synthesis of phenyl azides (52a-e).

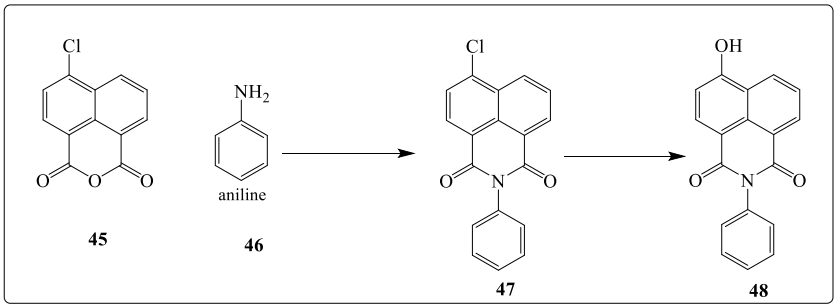
4.3.4 Synthesis of benzyl azides (54a-c).

4.3.5 Synthesis of 6-((1-(substutitedphenyl)-1H-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1H-benzo [de] isoquinoline-1, 3(2H)-dione drivatives (55a-i).

4.3.6 Synthesis of 6-((1-(substitutedbenzyl)-1H-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl
-1H-benzo [de] isoquinoline-1, 3(2H)-dione (56a-i).

4.3.7 Synthesis of 6-hydroxy-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (48):

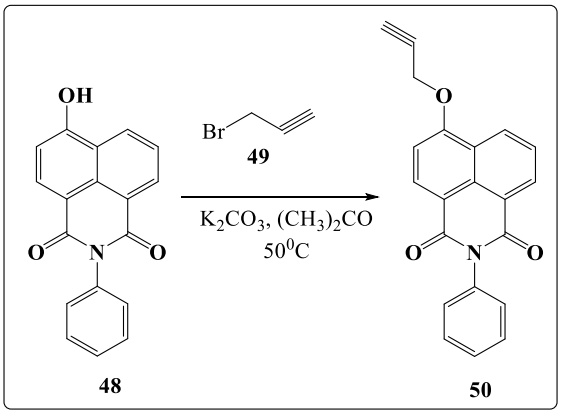
In the synthesis 6-hydroxy-2-phenyl-1*H*-benzo [*de*] isoquenoline-1, 3(2*H*)-dione (**48**) from NaOH react with 6-chloro-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (**47**)in which is turns to prepared from 6-chloronaphthalic anhydride(**45**) reacted with Aniline(**46**) in the presence of pyridine and methanol at 60°C temperature 4-5 hours reaction monitor by TLC. After the completion of the reaction as indicated by TLC the reaction mixture was allowed to cool at room temperature. The precipitate formed was filtered offand the products were recrystallized with ether to give the compound (**48**). Yield 85%, mp 111–113°C. ^{1}H **NMR** spectrum, δ, ppm: 8.53 (d, 1H), δ 8.48 (d, J = 2.4 Hz, 1H), δ 8.40 (s, 1H C-OH), δ 8.28d (J = 1.6, 7.7 Hz, 1H), δ 7.84 t (J =1.0, δ 7.7 Hz, 1H), δ 7.58-7.56 dd (3H), δ 7.46 dd (2H), δ 6.40 d (1H). **^{13}C NMR** spectrum, δC, ppm: 163.10 (C-OH), 1568.5(C=O), 138.0, 137.5, 132.8, 130.0, 129.0, 128.0, 125.4, 124.8, 123.2, 118.5, 114.4: Elemental Analysis: C, 74.69%; H, 3.88%; N, 4.88%; O, 6.63%. The **ESI MS** spectrum of **50** presented molecular ion peak at *m/z* 289.07 $[M+H]^{+}$.



Scheme 4.12: 6-hydroxy-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione.

Synthesis of 2-phenyl-6-(prop-2-yn-1-yloxy)-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (50):

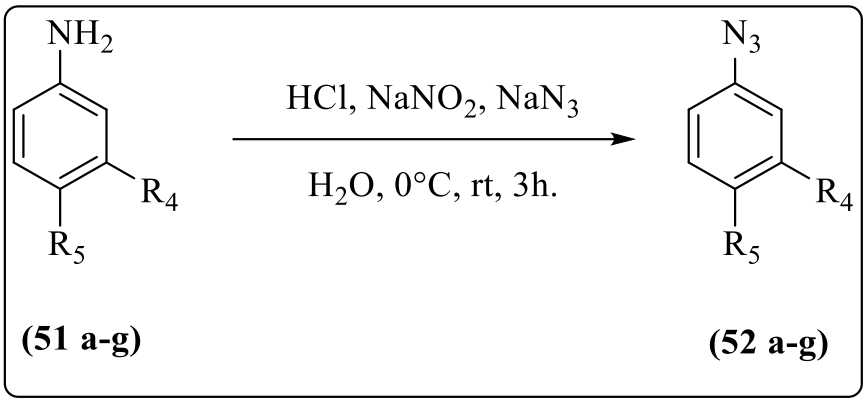
2-phenyl-6-(prop-2-yn-1-yloxy)-1*H*-benzo [*de*] isoquinoline-1, 3 (2*H*)-dione (**50**) were synthesized by the reaction of 6-hydroxy-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3 (2*H*)-dione. (**48**) by propargyl bromide (**49**) in the existence of potassium carbonate in dry acetone at 60°C. Products were purified by column chromatography and characterized by **IR, ^{1}H-NMR, ^{13}C-NMR** and **ESI MS**. The structure of 2-phenyl-6-(prop-2-yn-1-yloxy)-1*H*-benzo [*de*] isoquinoline-1, 3 (2*H*)-dione (**50**) were characterized from its spectral data. **IR** spectrum the alkyne (-C≡C-) group showed an absorption at 2125 cm^{-1} and ≡C-H absorption at 3100 cm^{-1}. The **^{1}H-NMR** (400MHz, $CDCl_3$) spectrum of **50** the acetylene (≡C-H) proton appeared at δ 2.52 (t, ≡CH, 1H) and the -OCH_2 protons observed at δ 4.86 (d, *J* = 2.4 Hz, OCH_2, 2H), δ 4.66, δ 5.13 (s, 2H), δ 6.36 (d, 1H), δ 7.41 (dd, 2H), δ 7.58-7.50 (s, 23H)δ 7. 76 (t, 1H), δ 8.40 (d, 1H), δ 8.22(d, 1H), δ 8. 60(d, 1H)In the **^{13}C-NMR** (100.6MHz, $CDCl_3$) of **50** the signals of propargyl carbons seemed at δ 79.15 (-C≡), 74.83 (≡CH), 62.85 (OCH_2) propargylic methylene, and the CH_2 of chromene ring attached shows at δ 61.66, and the characteristic chromanone (C-2) carbon observed at δ 64.29. The **ESI MS** spectrum of **50** presented molecular ion peak at m/z 328.10 $[M+H]^+$. Elemental Analysis: C, 77. 10; H, 4. 04; N, 4. 32; O, 14. 62.



Scheme 4.19: Synthesis of 2-phenyl-6-(prop-2-yn-1-yloxy)-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione

4.3.8 Synthesis of phenyl azides (52a-g):

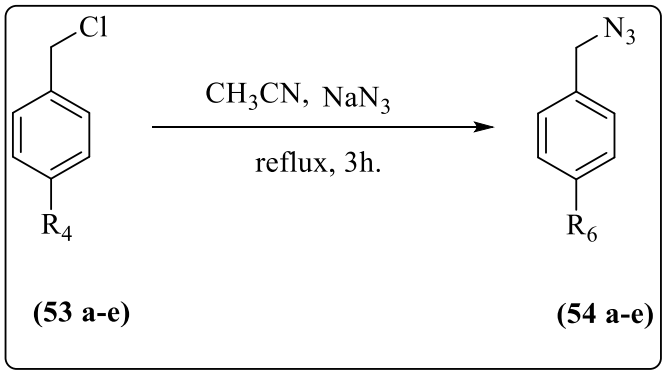
Substituted anilines on reaction by sodium nitrite, hydrochloric acid and sodium azide in DMF as a solvent beneath cool conditions offered phenyl azides (**52a-g**).



Scheme-19: Synthesis of substited Phenyl azide derivatives.

4.3.9 Synthesis of benzyl azides (54 a-e):

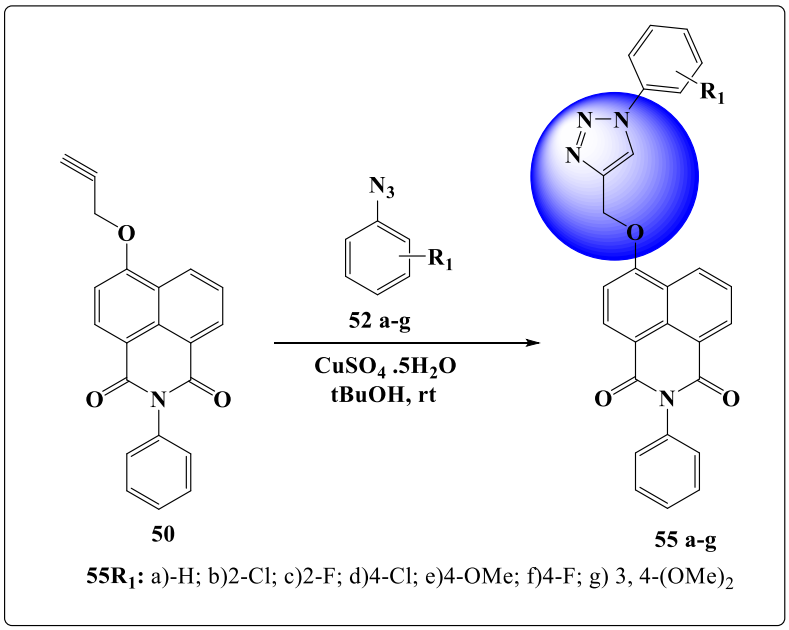
Substituted benzyl chlorides on reaction through sodium azide in acetonitrile beneath reflux condition provided benzyl azides (**54 a-e**).



Scheme 4.20: Synthesis of 4-subtituted *p*-benzyl azide derivatives

4.3.10 Synthesis of 6-((1-(substutitedphenyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione drivatives (55a-g):

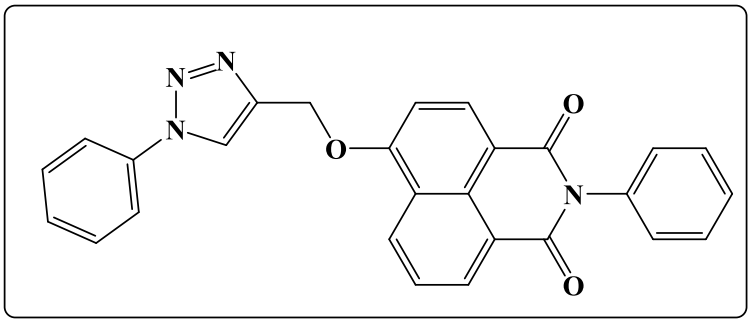
6-((1-(substutitedphenyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (**55a-g**), were synthesized by the reaction of 2-phenyl-6-(prop-2-yn-1-yloxy)-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (**50**) and dissimilar substituted phenyl azides (**52a-g**) in presence of $CuSO_4.5H_2O$ and sodium ascorbate in tertiary butanol and water as solvent at room temperature. These were purified by column chromatography and characterized by **IR, ^{1}H-NMR, ^{13}C-NMR** and **ESI MS**.



Scheme 4.21: Synthesis of 6-((1-(substutitedphenyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione derivatives.

The structure of 6-((1-(substutitedphenyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (55a) was characterized from its spectral data. In the **IR** spectrum the disappearance of -C≡C- peak at 2125 cm-1 and N=N adsorption was observed at 1505 cm-1. The **^{1}H-NMR** (400MHz, $CDCl_3$) spectrum of 55a the triazole ring proton appeared as a singlet at δ 8. 10 (s, N-CH=**)**, the naphthalimide H-2 protons appeared as singlet at δ 8. 22 (d), the $–OCH_2$ protons attached triazole ring appeared singlet at δ 5. 20. In the **^{13}C-NMR** (100.6MHz, $CDCl_3$) of 55a the signals due to triazole ring carbon appeared at δ 144.6, (C-OCH_2-) carbon at δ 119.1, the near to $–OCH_2$ carbon triazole ring attached appear at δ 72. 7. The **ESI MS** spectrum of 55a presented the quasi molecular ion peak at m/z 446.50 $[M+H]^+$. The analytical and spectral data of 55a-i is assumed in the experimental section.

Synthesis of 2-phenyl-6-((1-phenyl-1*H*-1, 2, 3-triazol-4-yl) methoxy)-1*H* benzo [*de*] isoquinoli ne-1, 3(2*H*)-dione (55a):



Light brown solid. **Yield:** 94%, **m.p:** 159-161°C.

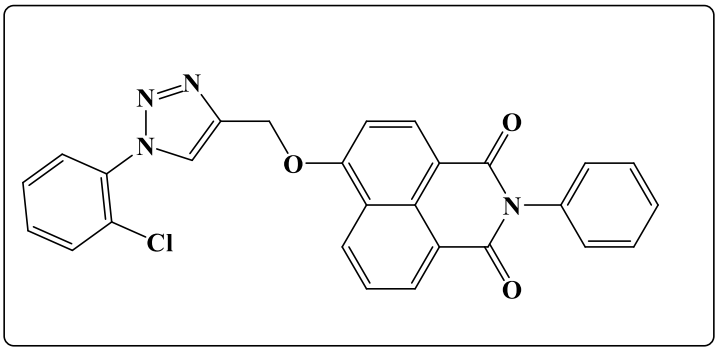
IR (KBr): 1505 (N=N), 3100 (C-H str) cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$)**:** δ 8. 68 (dd, *J* = 15.3, 7.8 Hz, H-5, Ar), 8. 40 (d, H-7 Ar), 8. 22 (d, H-2, 1H), 8. 10 (s, CH, 5membered 1H), 7.44 – 7.70 (m, Aromatic ring protons 11H), 6.32 (d, H-4, 1H), 5.23 (s, OCH_2, 2H), **^{13}C-NMR** (101 MHz, $CDCl_3$)**:** δ 166.81 (C-4), 158.58 (C-1, C-8 Amide C), 144.22, 138. 6, 137.31, 137.01, 133. 00, 132.50, 129.10, 128.51, 128.31, 128.00, 125.01, 124.61, 124.52, 120. 57 , 120.00, 119.00, 117.51, 106. 00, 72. 81(OCH_2).

ESI MS (m/z): Molecular ion peak at m/z 446. 51 $[M+H]^+$;

Elemental Analysis: C, 72.60; H, 4.10; N, 12.55; O, 10.75.

Synthesis of 6-((1-(2-chlorophenyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (55b):



White sol id. **Yield:** 83%, **m.p:** 120-122°C.

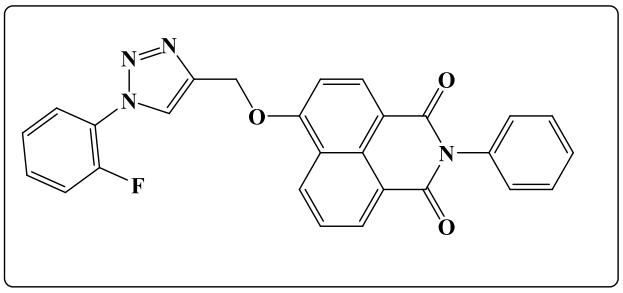
IR (KBr): 1502 (N=N), 3075 (C-H str) cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$)**:** δ 8. 61 (d, H-5, 1H), 8. 40 (d, H-7, H), 8. 30 (d, *J* = 2.2 Hz, H-2, 1H), 8. 10 (s, CH, 5membered 1H), 7. 81 (t, H-6 1H), 7.65 (d, 1H), 7. 61 – 7. 56 (m, 5H), 7. 45-7.42 (m, *J* = 8.1, 0.9 Hz, 4H), 6.35 (d, *J* = 7.7, 1.6 Hz, 1H), 5.20 (s, -OCH_2-2H). **^{13}C-NMR** (101 MHz, $CDCl_3$)**:** δ 166.54 (4C-OCH_2-), 158.62 (C=O), 144. 45 (-OCH_2-5triazole ring), 138.21, 137.51, 133.21, 132.11, 132. 10, 132.09, 132.05, 130.14, 129.84, 128.92, 128.81, 128.64, 128.10, 128.00, 125.04, 124.45, 119.11, 117. 14, 106.81, 72.79 (OCH_2).

ESI MS (m/z): Molecular ion peak at m/z 480.95 $[M+H]^+$.

Elemental Analysis: C, 67.46; H, 3.60; Cl, 7.41; N, 11.70; O, 9.94.

Synthesis of 6-((1-(2-fluorophenyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (55c):



White solid. **Yield:** 82%, **m.p:** 178-180°C.

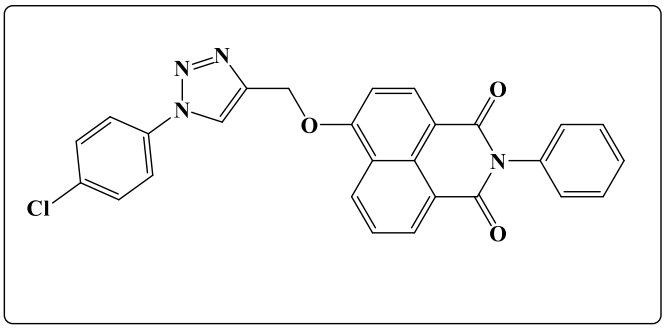
IR (KBr): 1506 (N=N), 3078 (C-H str) cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$)**:** δ 8. 61 (d, H-5, 1H), 8. 40 (d, H-7, H), 8. 30 (d, *J* = 2.2 Hz, H-2, 1H), 8. 10 (s, CH, 5membered 1H), 7. 81 (t, H-6 1H), 7. 64 – 7. 57 (m, 5H), 7. 45 (d, *J* = 8.1, 0.9 Hz, 2H), 7. 28 (d, *J* = 7.6, 1.1 Hz, 1H), 7.36 (t. 1H), 7. 20 (d, 2-F, 1H), 6.35 (d, *J* = 7.7, 1.6 Hz, 1H), 5.20 (s, -OCH_2-2H). **^{13}C-NMR** (101 MHz, $CDCl_3$)**:** δ 166.54 (4C-OCH_2-), 166. 12 (Ar-2-F, C), 158.62 (C=O), 144. 45 (-OCH_2-5triazole ring), 137.92, 137.35, 133.14, 132.75, 131.24, 130.26, 129.11, 128.65, 128.10, 128.00, 125.11, 124.44, 124.36, 119.11, 117.25, 117.04, 115.56, 106.44, 72.79 (OCH_2).

ESI MS (m/z): Molecular ion peak at m/z 464.48 $[M+H]^+$.

Elemental Analysis: C, 69.86; H, 3.65; F, 4.11; N, 12.10; O, 10.30.

Synthesis of 6-((1-(4-chlorophenyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (55d):



White solid. **Yield:** 82%, **m.p:** 157-159°C.

IR (KBr): 1506 (N=N), 3078 (C-H str) cm^{-1}.

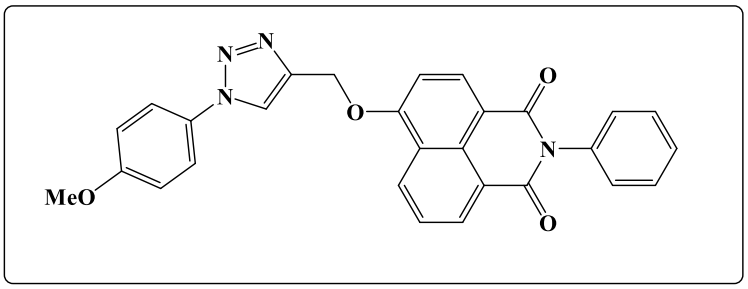
^{1}H-NMR (500 MHz, $CDCl_3$)**:** δ 8. 61 (d, H-5, 1H), 8. 40 (d, H-7, H), 8. 30 (d, *J* = 2.2 Hz, H-2, 1H), 8. 10 (s, CH, 5membered 1H), 7. 81 (t, H-6 1H), 7. 61 – 7. 56 (m, 5H), 7. 45-7.42 (m, *J* = 8.1, 0.9 Hz, 4H), 6.35 (d, *J* = 7.7, 1.6 Hz, 1H), 5.20 (s, -OCH_2-2H). **^{13}C-NMR** (101 MHz, $CDCl_3$)**:** δ 166.54 (4C-OCH_2-), 158.62 (C=O), 144. 45 (-OCH_2-5triazole ring),

138.21, 137.51, 133.51, 132.11, 129.39, 128.92, 128.81, 128.14, 125.04, 124.45, 122.12, 119.18, 117. 81, 106.51, 72.79 (OCH_2).

ESI MS (m/z): Molecular ion peak at m/z 480.01$[M+H]^+$.

Elemental Analysis: C, 67.46; H, 3.62; Cl, 7.41; N, 11.71; O, 9.94.

Synthesis of 6-((1-(4-methoxyphenyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (55e):



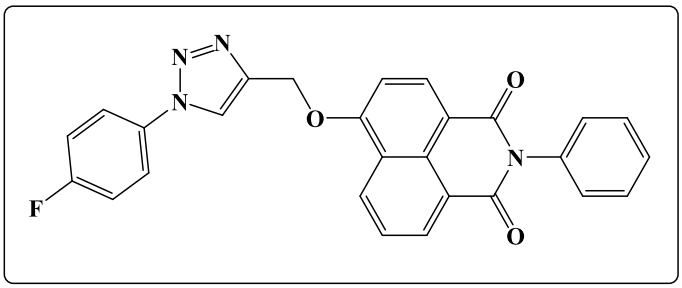
Brown solid. **Yield:** 84%, **m.p:** 188-190°C.

IR (KBr): 1502 (N=N), 3075 (C-H str) cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$)**:** δ 8. 61 (d, H-5, 1H), 8. 40 (d, H-7, H), 8. 30 (d, *J* = 2.2 Hz, H-2, 1H), 8. 10 (s, CH, 5membered 1H), 7. 81 (t, H-6 1H), 7. 58 – 7. 50 (d, 3H), 7. 45 (d, *J* = 8.1, 0.9 Hz, 2H), 7. 28 (d, *J* = 7.6, 1.1 Hz, 1H), 6.70 (t, *J* = 7.7, 1.6 Hz, 2H), 6.30 (d, 1H), 5.20 (s, 2H), 3.87 (s, OCH_3, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$)**:** δ 166.54 (4C-OCH_2-), 158.62 (C=O), 153.15 (ArC-OMe), 150. 00 (ArC-OMe), 144. 45 (-OCH_2-5triazole ring), 137.92, 137.51, 133.10, 132.79, 129.00, 128.62, 125.22, 124.99, 122.12, 119.11, 118.92, 117. 75, 114.76, 109.42, 106.51, 72.91 (OCH_2), 56.68 (OCH_3).

ESI MS (m/z): Molecular ion peak at m/z 476.19 $[M+H]^+$. **Elemental Analysis:** C, 70.58; H, 4.23; N, 11.76; O, 13.43.

Synthesis of 6-((1-(4-fluorophenyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (55f):



White solid. **Yield:** 82%, **m.p:** 167-169°C.

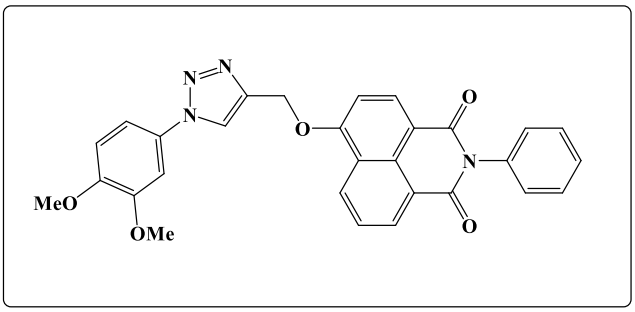
IR (KBr): 1506 (N=N), 3078 (C-H str) cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$)**:** δ 8. 61 (d, H-5, 1H), 8. 40 (d, H-7, H), 8. 30 (d, *J* = 2.2 Hz, H-2, 1H), 8. 10 (s, CH, 5membered 1H), 7. 81 (t, H-6 1H), 7. 61 – 7. 41 (m, 5H), 7. 45 (d, *J* = 8.1, 0.9 Hz, 2H), 7. 28 (d, *J* = 7.6, 1.1 Hz, Ar-F, 1H), 6.35 (d, *J* = 7.7, 1.6 Hz, 1H), 5.20 (s, -OCH_2-2H). **^{13}C-NMR** (101 MHz, $CDCl_3$)**:** δ 166.54 (4C-OCH_{2-}), 162.92, 158.62 (C=O), 144. 45 (-OCH_2-5triazole ring), 137.92, 137.51, 133.10, 133.00, 132.79, 129.11, 128.14, 128.09, 125.11, 124.55, 122.12, 119.11, 117. 72, 115.56, 106.51, 72.89 (OCH_2).

ESI MS (m/z): Molecular ion peak at m/z 464.42 $[M+H]^+$.

Elemental Analysis: C, 69.81; H, 3.67; F, 4.11; N, 12.06; O, 10.33.

Synthesis of 6-((1-(*m, p*-dimethoxyphenyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3 (2*H*)-dione (55g):



Brownish yellow solid. **Yield:** 84%, **m.p:** 197-199°C.

IR (KBr): 1502 (N=N), 3075 (C-H str) cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$)**:** δ 8. 61 (d, H-5, 1H), 8. 40 (d, H-7, H), 8. 30 (d, *J* = 2.2 Hz, H-2, 1H), 8. 10 (s, CH, 5membered 1H), 7. 81 (t, H-6 1H), 7. 58 – 7. 50 (d, 3H), 7. 45 (d, *J* = 8.1, 0.9 Hz, 2H), 7. 28 (d, *J* = 7.6, 1.1 Hz, 1H), 6.70 (t, *J* = 7.7, 1.6 Hz, 2H), 6.30 (d, 1H), 5.20 (s, 2H), 3.87 (s, OCH_3, 6H). **^{13}C-NMR** (101 MHz, $CDCl_3$)**:** δ 166.54 (4C-OCH_{2-}), 158.62 (C=O), 153.15 (ArC-OMe), 150. 00 (ArC-OMe), 144. 45 (-OCH_2-5triazole ring), 137.92, 137.51, 133.10, 132.79, 129.00, 128.62, 125.22, 124.99, 122.12, 119.11, 118.92, 117. 75, 114.76, 109.42, 106.51, 72.91 (OCH_2), 56.68 (OCH_3).

ESI MS (m/z): Molecular ion peak at m/z 507.52 $[M+H]^+$.

Elemental Analysis: C, 68.78; H, 4.42; N, 11.09; O, 15.81.

The structure of 6-((1-(4-substutitedphenyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (**55a**) was characterized from its spectral data. In the **IR** spectrum the disappearance of -C≡C- peak at 2125 cm^{-1} and N=N adsorption was observed at 1505 cm^{-1}. The **^{1}H-NMR** (400MHz, $CDCl_3$) spectrum of **55a** the triazole ring proton appeared as a singlet at δ 7.61 (s, H-5", 1H), the chromene H-2 protons appeared as

singlet at δ 5.07 (s), the –OCH_2 protons attached triazole ring appeared singlet at δ 4.86, and -CH_2 attach with chromene ring protons appeared at δ 4.66.

In the **^{13}C-NMR** (100.6MHz, $CDCl_3$) of **55a** the signals due to triazole ring carbon (C-4") appeared at δ 139.63, (C-5") carbon at δ 122.00, the –OCH_2 carbon triazole ring attached appear at δ 67.61 and the OCH_2 carbon attached with chromene ring appeared at 66.68, and the (C-2) of chromene carbon appear at δ 64.33. The **ESI MS** spectrum of **55a** presented the quasi molecular ion peak at m/z 396.20 $[M+H]^+$. The analytical and spectral data of **55a-g** is assumed in the experimental section.

4.3.11 Synthesis of 6-((1-(substitutedbenzyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl:

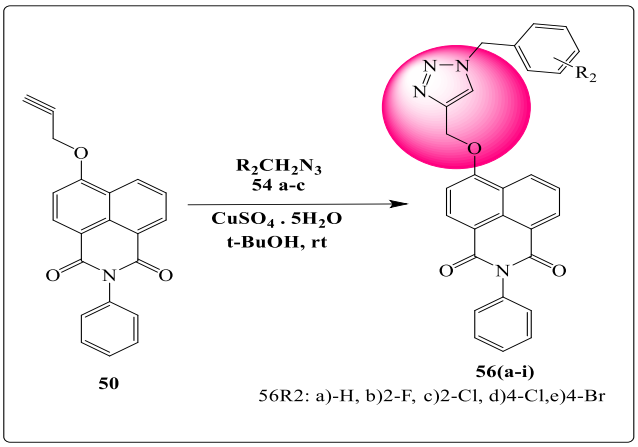
-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (56a-e).

2-phenyl-6-(prop-2-yn-1-yloxy)-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (**50**) (0.1g, 0.36 mmol) and dissimilar substituted benzyl azides (0.04g, 0.43 mmol) (**54a-e**) were melted in DMF (5 mL).

To this sodium ascorbate (0.3 mmol, 300 µL of freshly prepared 1M solution in water) was added, charted by copper (II) sulphate pentahydrate (7.5mg, 0.03 mmol, in 100µL of water) and tertiary butanol as solvent. The homogeneous blend was stirred forcefully overnight, until mixture was dilute with water (50 ml), cooled in ice, and the precipitous was together by filtration.

After washing the precipitate with cold water (2×30 mL), the crude produce was filtered by column chromatography to develop pure solution and TLC analysis indicated finish consumption of the reactants.

The purification was done by using pet ether-ethyl acetate (7:3) to obtain the pure products **56a-e.**



Scheme 4.22: Synthesis of 6-((1-(substitutedbenzyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl
-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione derivatives.

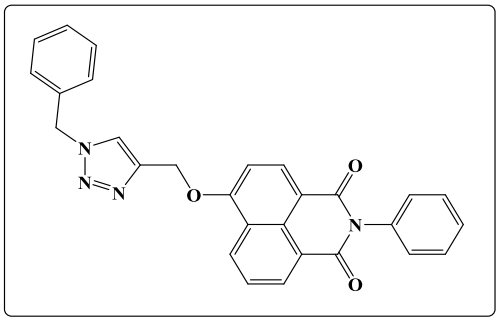
The structure of 6-((1-(substitutedbenzyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl -1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (**56a**) was characterized from its spectral data. In the **IR** spectrum the disappearance of -C≡C- peak at 2125 cm^{-1} and N=N adsorption was observed at 1509 cm^{-1}. The **^{1}H-NMR** (400MHz, $CDCl_3$) spectrum of **56a** the triazole ring proton appeared as a singlet at δ 7.65 (s, H-5", 1H), the Naphthalene H-2 protons appeared as singlet at δ 8. 24 and the $–OCH_2$ protons attached triazole ring appeared at δ 5.22 (s, 2H), the CH_2 protons attached with naphthalene ring appeared at δ 5. 20 and benzyl -CH_2 at δ 5.51. In the **^{13}C-NMR** (100.6MHz, $CDCl_3$) of **55a** the signals due to triazole ring carbons appeared at δ 142. 51 and 122.50, OCH_2 carbon attaching with triazole carbon appeared at δ 72. 73, and the $–CH_2$- (benzyl) appear at δ 57.20. The **ESI MS** spectrum of **56a** presented the quasi molecular ion peak at m/z 460.52 $[M+H]^+$. The analytical and spectral data of **56a-i** is assumed in the experimental section.

4.4 Conclusion:

1-phenyl-4-(((4-phenyl-2H-chromen-3-yl)methoxy)methyl)-1H-1,2,3-triazole **(52a-i)** and 6-((1-(substitutedbenzyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl -1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (**56a-e)** were synthesized regioselectively under click reaction conditions with high yields and those were confirmed from **^{1}H-NMR, ^{13}C-NMR, IR** and **ESI-MS** spectral data.

4.5 Experimental Section:

Synthesis of 6-((1-benzyl-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3 (2*H*)-dione (56a):



Light brown solid. **Yield:** 94%, **m.p:** 160-162°C.

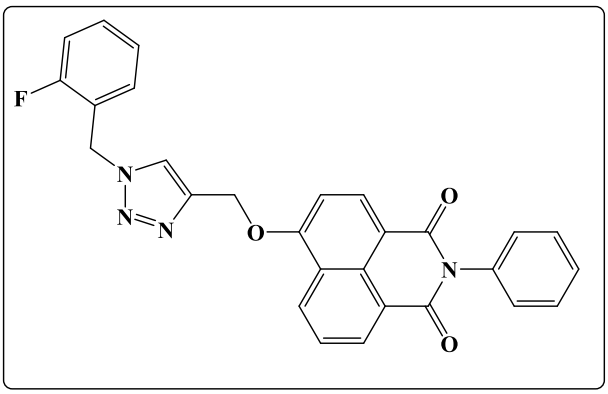
IR (KBr): 1502 (N=N), 3075 (C-H str) cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$)**:** δ 8. 62 (d, *J* = 15.3, 7.8 Hz, H-5, Ar), 8. 40 (d, H-7 Ar), 8. 22 (d, H-2, 1H), 7. 80 (t, 1H, Ar), 7. 65-7. 56(m, 4H), 7. 45-7. 39 (m, 7H), 6.25(d, 1H), 5. 46 (s, Benzyl protons, 2H), 5. 20 (s, OCH_2-, 2H), **^{13}C-NMR** (101 MHz, $CDCl_3$)**:** δ 166.50 (C-4), 158.58 (C-1, C-8 Amide C), 142.31 (-OCH_2-triazole ring attached C), 137.83, 137.30, 133. 79, 133.12, 132.71, 129.10, 128.61, 128.12, 128.02, 127.62, 125.71, 124.93, 124. 41, 123.01, 117.73, 106. 40, 72. 71(OCH_2), 57.32 (Ar-CH_2-).

ESI MS (m/z): Molecular ion peak at m/z 460. 51 $[M+H]^+$;

Elemental Analysis: C, 73.06; H, 4.38; N, 12.18; O, 10.43.

Synthesis of 6-((1-(2-fluorobenzyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3 (2*H*)-dione (56b):



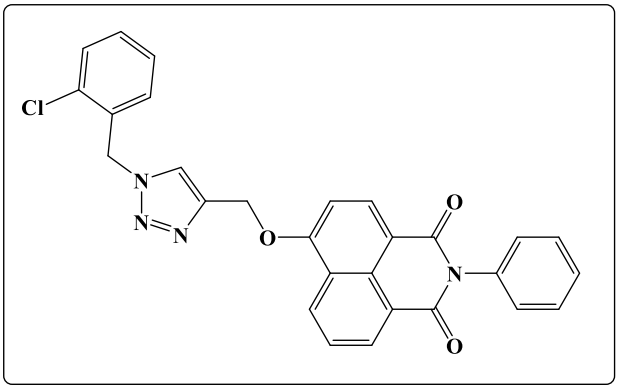
Light yellow solid. **Yield:** 94%, **m.p:** 160-162°C.

IR (KBr): 1502 (N=N), 3075 (C-H str) cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$)**:** δ 8. 62 (d, *J* = 15.3, 7.8 Hz, H-5, Ar), 8. 40 (d, H-7 Ar), 8. 22 (d, H-2, 1H), 7. 80 (t, 1H, Ar), 7. 65-7. 55(m, 6H), 7. 45 (d, 2H), 7.16(d, 1H), 7. 06(t, 1H), 6. 36(d, 1H), 5. 50 (s, Benzyl-CH_2-protons, 2H), 5. 20 (s, OCH_2-, 2H), **^{13}C-NMR** (101 MHz, $CDCl_3$)**:** δ 166.52 (C-4), 161.51(F-2C-Ar), 158.58 (C-1, C-8 Amide C), 137.81, 137. 31, 133.11, 132. 72, 130. 64, 128. 93, 128. 64, 128. 10, 128. 00, 127. 3, 124. 62, 124. 42, 124. 21, 122. 01(-OCH_2- triazole ring attached C), 117.73, 115. 41, 106. 40, 72. 71(OCH_2), 57.32 (Ar-CH_2-).; **ESI MS (m/z):** Molecular ion peak at m/z 478. 51 $[M+H]^+$;

Elemental Analysis: C, 70.32; H, 4.02; F, 3. 98, N, 11.72; O, 10.07.

Synthesis of 6-((1-(2-chlorobenzyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3 (2*H*)-dione (56c).

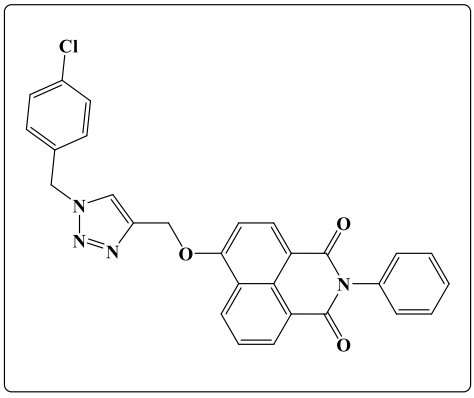


Light crimsons red solid. **Yield:** 94%, **m.p:** 160-162°C.

IR (KBr): 1502 (N=N), 3075 (C-H str) cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$)**:** δ 8. 62 (d, *J* = 15.3, 7.8 Hz, H-5, Ar), 8. 40 (d, H-7 Ar), 8. 22 (d, H-2, 1H), 7. 80 (t, 1H, Ar), 7. 65-7. 60 (m, 5H), 7. 45 (d, 2H), 7.20-7. 10(dd, 3H), 6. 36(d, 1H), 5. 50 (s, Benzyl-CH_2-protons, 2H), 5. 20 (s, OCH_2-, 2H), **^{13}C-NMR** (101 MHz, $CDCl_3$)**:** δ 166.53 (C-4), 158.58 (C-1, C-8 Amide C), 147.31, 138. 10, 137.82, 137.31, 134. 32(Cl-2C-Ar), 133.11, 132. 72, 130. 41, 128. 93, 128. 74, 128. 60, 128. 12, 128. 00, 126. 73, 124. 91, 124. 42, 122. 91(-OCH_2- triazole ring attached C), 117.73, 106. 40, 72. 71(OCH_2), 57.32 (Ar-CH_2-).; **ESI MS (m/z):** Molecular ion peak at m/z 494. 98 $[M+H]^+$.; **Elemental Analysis:** C, 67.98; H, 3.92; Cl, 7. 20, N, 11.34; O, 9.72.

Synthesis of 6-((1-(4-chlorobenzyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3 (2*H*)-dione (56d):



Light Yellow solid.**Yield:** 94%, **m.p:** 160-162°C.

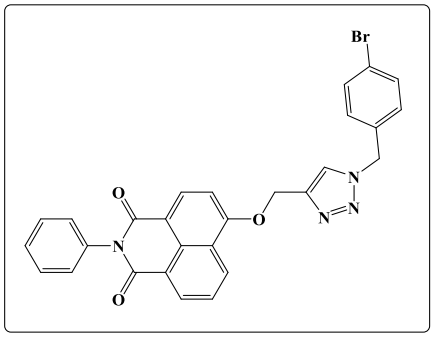
IR (KBr): 1502 (N=N), 3075 (C-H str) cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$)**:** δ 8. 62 (d, *J* = 15.3, 7.8 Hz, H-5, Ar), 8. 40 (d, H-7 Ar), 8. 22 (d, H-2, 1H), 7. 69 (d, 1H, Ar), 7. 65-7. 52 (m, 4H), 7. 45 (dd, 2H), 7.32 (dd, 2H), 7. 12(dd, 2H), 6. 36(d, 1H), 5. 50 (s, Benzyl-CH_2-protons, 2H), 5. 20 (s, OCH_2-, 2H), **^{13}C-NMR** (101 MHz, $CDCl_3$)**:** δ 166.53 (C-4), 158.58 (C-1, C-8 Amide C), 142.31, 137.82, 137.31, 134. 32(Cl-2C-Ar), 133.11, 131. 32, 128. 93, 128. 74, 128. 60, 128. 12, 128. 00, 124. 91, 117. 72, 106. 71, 72. 73(-OCH_2- triazole ring attached C), 57.32 (Ar-CH_2-).;

ESI MS (m/z): Molecular ion peak at m/z 494. 96 $[M+H]^+$;

Elemental Analysis: C, 67.98; H, 3.90; Cl, 7. 20, N, 11.34; O, 9.72.

Synthesis of 6-((1-(4-bromobenzyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3 (2*H*)-dione (56e):



Pale yellow solid. **Yield:** 94%, **m.p:** 160-162°C.

IR (KBr): 1502 (N=N), 3075 (C-H str) cm^{-1}.

^{1}H-NMR (400 MHz, $CDCl_3$)**:** δ 8. 62 (d, *J* = 15.3, 7.8 Hz, H-5, Ar), 8. 40 (d, H-7 Ar), 8. 22 (d, H-2, 1H), 7. 79-7. 71(dd, 3H, Ar), 7. 65-7. 52 (m, 4H), 7. 45 (dd, 2H), 7.09 (dd, 2H), 6. 36(d, 1H), 5. 46 (s, Benzyl-CH_2-protons, 2H), 5. 20 (s, OCH_2-, 2H), **^{13}C-NMR** (101 MHz, $CDCl_3$)**:** δ 166.58 (C-4), 158.58 (C-1, C-8 Amide C), 142.31, 137.82, 137.31, 135. 21, 133.11, 131. 32, 72, 131. 51, 131. 22, 128. 91, 128. 60, 128. 12, 128. 00, 124. 91, 124. 46, 122. 90, 120. 10(Br-4C, Ar), 117. 72, 106. 41, 72. 73(-OCH_2- triazole ring attached C), 57.32 (Ar-CH_2-);

ESI MS (m/z): Molecular ion peak at m/z 539. 35 $[M+H]^+$;

Elemental Analysis: C, 62.39; H, 3.56; Br, 14. 85, N, 10.35; O, 8.91.

The structure of 1-benzyl-4-(((4-phenyl-2*H*-chromen-3-yl) methoxy) methyl)-1*H*-1,2,3-triazole (**56a**) was characterized from its spectral data. In the **IR** spectrum the disappearance of -C≡C- peak at 2125 cm^{-1} and N=N adsorption was observed at 1509 cm^{-1}.

The **^{1}H-NMR** (400MHz, $CDCl_3$) spectrum of **53a** the triazole ring proton appeared as a singlet at δ 7.44 (s, H-5", 1H), the chromene H-2 protons appeared as singlet at δ 5.07 and the –OCH_2 protons attached triazole ring appeared at δ 5.18 (s, 2H), the CH_2 protons attached with chromene ring appered at δ 5.14 and benzyl -CH_2 at δ 5.51. In the **^{13}C-NMR** (100.6MHz, $CDCl_3$) of **56a** the signals due to triazole ring carbons (C-4"), (C-5") appeared at δ 139.44 and 121.40, OCH_2 carbon attaching with triazole carbon appeared at δ 67.67, the CH_2 protons of chromene ring attached shows at δ 66.46 and thechromene (C-2) appear at δ 64.30 and –CH_2- (benzyl) appear at δ 54.20. The **ESI MS** spectrum of **56a** presented the quasi molecular ion peak at m/z 410.26 $[M+H]^+$. The analytical and spectral data of **56a-e**is assumed in the experimental section.

4.6 Conclusion:

6-((1-(substutitedphenyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione **(55a-g)** and 6-((1-(substitutedbenzyl)-1*H*-1, 2, 3-triazol-4-yl) methoxy)-2-phenyl-1*H*-benzo [*de*] isoquinoline-1, 3(2*H*)-dione (**56a-e)** were synthesized regioselectively under click reaction conditions with high yields and those were confirmed from **^{1}H-NMR, ^{13}C-NMR, IR** and **ESI-MS** spectral data.

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