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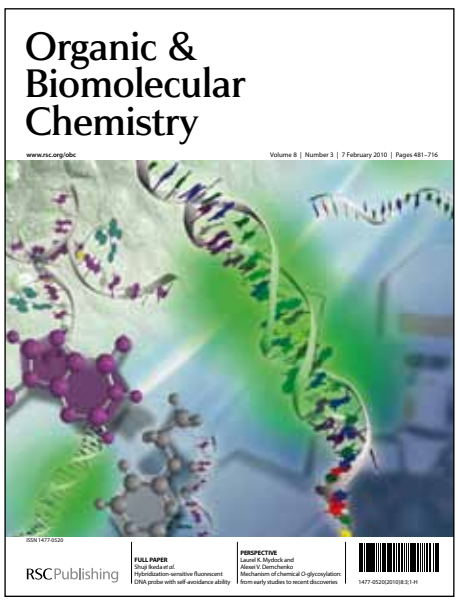

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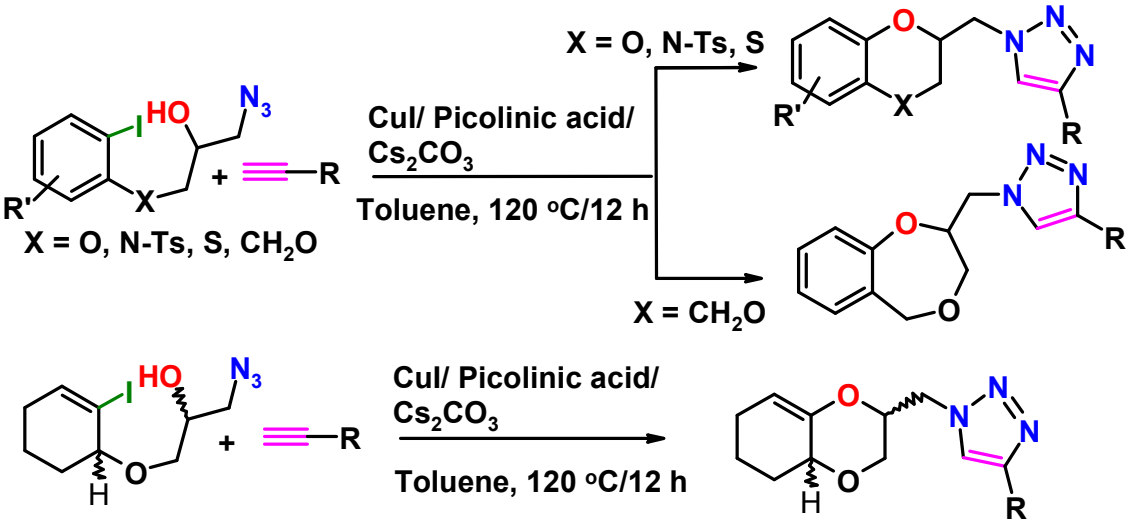

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ARTICLE TYPE

Dual catalysis by Cu(I): Facile single step click and intramolecular C-O bond formation leading to triazole tethered dihydrobenzodioxines/ benzoxazines/ benzoxathiines/ benzodioxepines

M. Nagarjuna Reddy[a] and K. C. Kumara Swamy*[a]

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

Dual copper catalysis, involving two different reactions, click (alkyne-azide) and carbon-oxygen bond formation (aryl iodide-secondary alcohol) in a single step, is reported. Synthesis of novel benzodioxines (benzodioxanes), benzoxazines, benzoxathiines and which feature benzo-condensed six or seven membered rings containing two hetero-atoms attached to a 1,2,3-triazole, is described. As an extension, such compounds were also synthesised by the ring opening of epoxide and cyclisation using Cu(I). All the key products have been characterized by single crystal X-ray crystallography.

Introduction

Among the copper catalysed reactions, the most promising atom economy reaction in the current scenario is the click reaction between alkynes and organic azides leading to triazoles because of the potential use of the products, ranging from medicinal chemistry to materials science.[1-2] In the last few years, copper catalysts are also extensively utilized in the construction of C-X (X = N, S, O, P) bond[3] with aryl halides as coupling partners. Hartwig and Buchwald reported the palladium catalyzed reactions with alcohols and aryl halide.[4] The main drawback in the palladium catalyzed reactions is the limited number of ligands and possibility of β-hydrogen elimination in secondary alcohols. As a result, copper catalysis is utilized in constructing carbon-oxygen[5] bond with secondary alcohol and arylhalides.[6] Research is focusing towards one-pot reactions to reduce wastage of chemicals, time and for its economical value.[7] Literature survey revealed that such one pot synthesis of dihydro-benzodioxine, benzoxazine and benzoxathiine having 1,2,3-triazole analogues is not reported till date. Benzo-condensed six membered heterocyclic compounds containing two heteroatoms have wide applications in medicinal chemistry.[8] Among these, benzo-dioxine (e.g., domoxin, piperoxan, eltoprazine, fluparoxan, idazoxan, prosympal) and benzoxathiine core structure are found in a variety of pharmaceutically useful (e.g., α-adrenergic blockers,[8g] estrogenic agent[8h]) compounds. We believe that derivatisation on these heterocycles will have substantial benefits in medicinal chemistry and hence are interested in constructing both these apparently-simple looking heterocyclic rings, with a variety of substituents.

As a part of our ongoing research into the transition-metal-catalyzed C-C, C-N and C-O bond forming reactions,[9] we planned to synthesise heterocyclic moieties tethered with triazole moiety. Recently, we showed a simple method for the one pot sequential, copper-catalyzed click reaction and intramolecular direct arylation of triazoles thus formed.[10] In continuation of this work, we intended to construct benzo-dioxine, -oxazine,-oxathiine and -dioxepine heterocyclic ring utilizing atom economical copper-catalysed click reaction and C-O bond formation in one-pot. The results in which Cu(I) species plays the role of a 'dual catalyst' are reported herein.

Results and Discussion

Generation of the required starting materials **2a-l** was accomplished as shown in Scheme **1**; details of experimental data for these substrates are given in the supplementary material.

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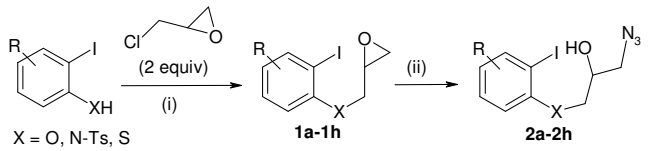
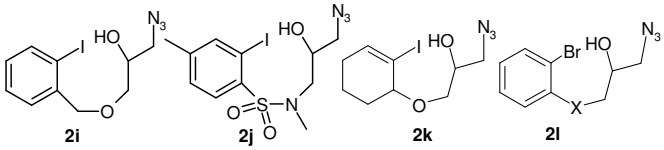


X = O, R = H (**1a**) X = O, R = H (**2a**)
X = O, R = 4-*t*Bu (**1b**) X = O, R = 4-*t*Bu (**2b**)
X = O, R = 4-Cl (**1c**) X = O, R = 4-Cl (**2c**)
X = O, R = 4,6-diMe (**1d**) X = O, R = 4,6-diMe (**2d**)
X = O, R = 3,4-(-C_4H_4-)(**1e**) X = O, R = 3,4-(-C_4H_4-) (**2e**)
X = NTs, R = H (**1f**) X = NTs, R = H (**2f**)
X = NTs, R = 4-Me (**1g**) X = NTs, R = 4-Me (**2g**)
X = S, R = H (**1h**) X = S, R = H (**2h**)

Conditions: (i) K_2CO_3 (1.5 equiv), CH_3CN, reflux, 12 h
(ii) NH_4Cl (2.0 equiv), NaN_3 (4.0 equiv), MeOH, 50 °C, 10 h



Scheme 1

Initial experiments were performed on 1-azido-3-(2-iodophenoxy)propan-2-ol **2a** and phenylacetylene in the presence of copper(I) iodide (10 mol %) and caesium carbonate (3 equiv) in toluene at 120 °C/ 12 h to effect click reaction and intramolecular C-O bond formation. This procedure afforded the triazole linked dihydrobenzodioxine **3** in 55% yield (Scheme **2**).

Conditions: CuI (10 mol %)/ Cs_2CO_3 (3.0 equiv)/ Toluene/ 120 °C/ 12 h

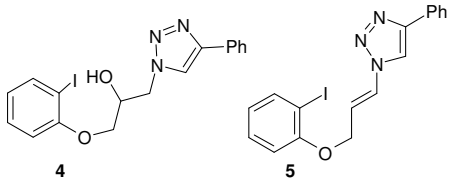
Scheme 2

Our next step was directed toward searching the best condition to maximize the yield of compound **3** by screening various reaction parameters as depicted in Table 1. Among the ligands employed for screening, bipyridine and picolinic acid proved to be promising in obtaining the compound **3** in good yield (Table 1, entries 5, 6), however, we selected to use picolinic acid as it is economically attractive and biocompatible. Other ligands employed were ineffective in increasing the yield. Then the effect of copper salts and base were examined (entries 7-10), they afforded lower yields. As a solvent, toluene was the best when compared to DMF, PEG-400 or water. In the case of diethyl carbonate as solvent, elimination product **5** was isolated along with 1,3-dipolar cyclised product **4** and the expected benzodioxine was not observed.

Table 1: Optimization of the reaction conditions for the synthesis of **3**[a]

Entry	CuX	Ligand	Base	Solvent	Yield (%)[b]
1	CuI	-----	Cs_2CO_3	Toluene	55[c]
2	CuI	DMEDA	Cs_2CO_3	Toluene	62
3	CuI	L-Proline	Cs_2CO_3	Toluene	49
4	CuI	8-Hydroxy-quinoline	Cs_2CO_3	Toluene	55
5	CuI	Bipyridine	Cs_2CO_3	Toluene	75
6	**CuI**	**Picolinic acid**	**Cs_2CO_3**	**Toluene**	**89**
7	CuBr	Picolinic acid	Cs_2CO_3	Toluene	71
8	CuCl	Picolinic acid	Cs_2CO_3	Toluene	66
9	Cu_2O	Picolinic acid	Cs_2CO_3	Toluene	48
10	CuI	Picolinic acid	K_2CO_3	Toluene	51
11	CuI	Picolinic acid	Cs_2CO_3	Water	25[c]
12	CuI	Picolinic acid	Cs_2CO_3	PEG-400	37[c]
13	CuI	Picolinic acid	Cs_2CO_3	Et_2CO_3	41[d]
14	CuI	Picolinic acid	Cs_2CO_3	DMF	55

[a]Quantities used: **2a** (0.5 mmol), phenylacetylene (0.55 mmol), CuX (10 mol%), ligand (20 mol%), base (3.0 equiv), Toluene (1 mL) at 120 °C (oil bath temperature). [b]isolated yields. [c]triazole **4** was remained (entry **1** - 30%; entry **11** - 50%; entry **12** - 37%). [d]ene-triazole **5** formed in 35%.



With the optimized conditions (entry 6, Table 1) in hand, we conducted the reactions of various terminal acetylenes with **2a** for the synthesis of triazole based benzodioxine derivatives (Scheme 3). Both electron releasing and withdrawing groups on acetylene afforded triazole benzodioxane (**6-14**) in good yields, the method worked well for naphthyl, vinyl and aliphatic alkynes also. Activated alkynes also afforded good yield when reacted with substrate **2a**. To further explore the efficacy and generality of the method, reactions using different substituted 1-azido-3-(2-iodobenzyloxy)-propan-2-ol (**2b-e**) were investigated for this one-pot reaction to synthesise products **15-18** in good yields. Though two different kinds of reaction were performed in a single step, the yields (isolated) obtained were good in most cases. All the compounds were characterised by IR, NMR and HRMS and the structure of compound **16** was confirmed by X-ray crystallography (Figure **1**).

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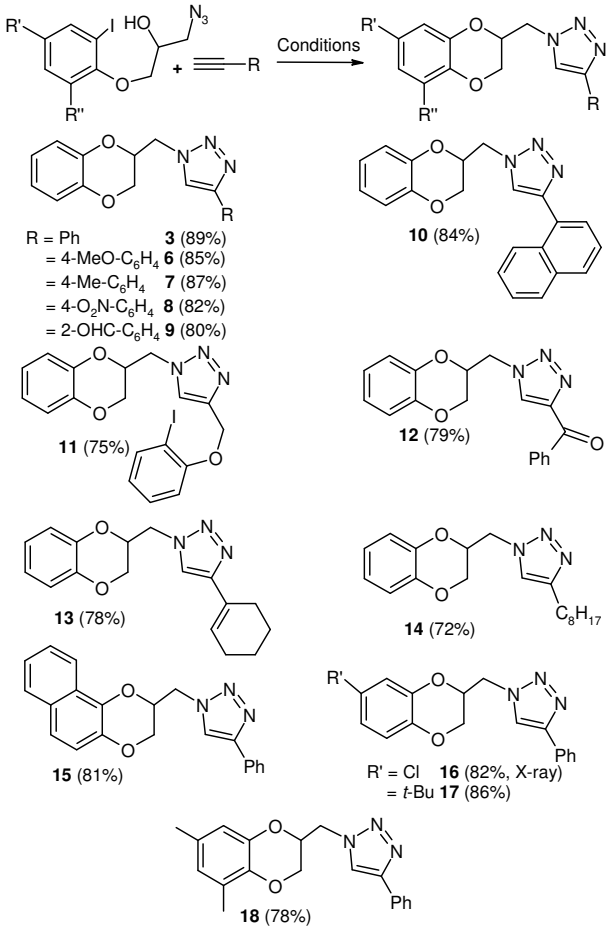


Conditions: CuI (10 mol %)/ Picolinic acid (20 mol %)/ Cs_2CO_3 (3.0 equiv)/ Toluene/ 120 °C/ 12 h

Scheme 3

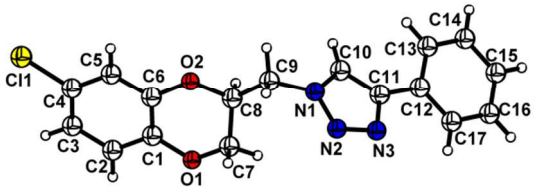
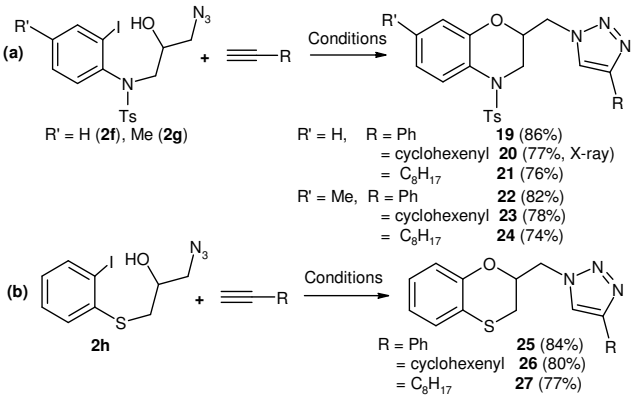


Figure 1. ORTEP diagram of compound **16**. Selected bond lengths [Å] with esd's in parentheses: C6-O2 1.376 (4) C8-O2 1.438 (4) N1-N2 1.338(4) N3-N2 1.314(4).

After synthesizing various substituted triazole based benzodioxine derivatives successfully, we planned to extend this methodology to benzoxazines and benzoxathiine based triazoles, as these moieties also have the same importance as that of benzodioxine derivatives. To achieve this, we prepared substrates **2f**, **2g** and **2h** from 2-iodoaniline and 2-iodothiophenol respectively as shown in Scheme **1** above. These substrates were reacted with phenyl, vinyl and aliphatic alkynes under the optimized conditions to furnish the expected triazole based benzoxazines (**19-24**) and benzoxathiines (**25-27**) in good yields (Scheme 4). Precursors **2f** and **2g** showed multiple peaks in NMR data due to the possibility of rotamers,[11] after cyclisation, the observed NMR data was as expected. The structure of compound **20** was further confirmed by X-ray crystallography (Figure **2**).



Conditions: CuI (10 mol %)/ Picolinic acid (20 mol %)/ Cs_2CO_3 (3.0 equiv)/ Toluene/ 120 °C/ 12 h

Scheme 4

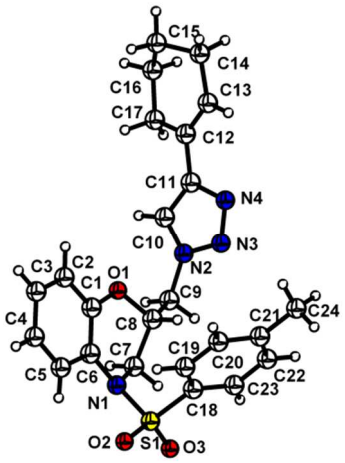


Figure 2. ORTEP diagram of compound **20**. Selected bond lengths [Å] with esd's in parentheses: C1-O1 1.366 (4) C8-O1 1.423 (3) N2-N3 1.335(4) N3-N4 1.303(4).

Till this point, we were successful in synthesising benzodioxines, benzoxazines and benzoxathiine derivatives. To expand this methodology, we made an effort to synthesise seven membered ring containing compounds also. To achieve this, substrate **2i** was prepared in two steps from 2-iodobenzyl alcohol and epichlorohydrin. Following the optimized condition, we conducted reaction between **2i** and terminal acetylenes which afforded triazole based benzodioxepine derivatives **28-31** in good yields. In this case also, gratifyingly, we were able to construct three new bonds in a single step involving click reaction and intramolecular C-O bond between secondary alcohol and aryl iodide. The structure of compound **30** was confirmed by X-ray crystallography (Figure **3**).

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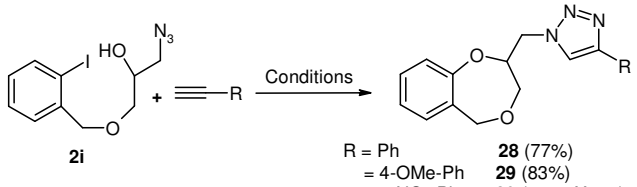


Conditions: CuI (10 mol %)/ Picolinic acid (20 mol %)/ Cs_2CO_3 (3.0 equiv)/ Toluene/ 120 °C/ 12 h

Scheme 5

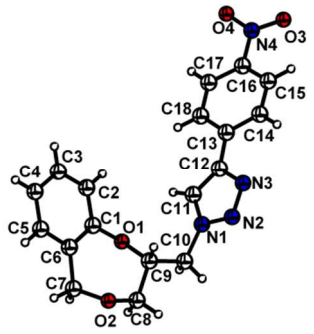
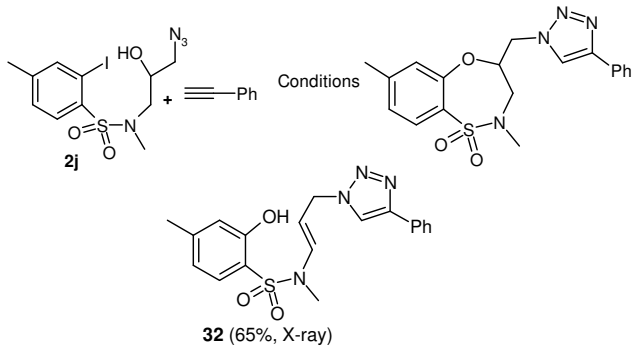


Figure 3. ORTEP diagram of compound **30**. Selected bond lengths [Å] with esd's in parentheses: C1-O1 1.381 (3) C9-O1 1.442 (2) N1-N2 1.341(3) N3-N2 1.310(3).

In a manner similar to above, we attempted to synthesise seven membered sultam moieties from **2j**. Precursor **2j** was synthesised from 4-methyl-2-iodo-sulfonamide and epichlorohydrin. Later, we performed reaction between **2j** and phenylacetylene in an effort to obtain seven membered sultam derivatives. To our surprise, this reaction led to the ring opened product **32** as shown in Scheme **6**. This product arises due to the abstraction of proton from CH_2 moiety adjacent to *N* and subsequent migration giving the ***phenolic*** derivative **32**. In our previous paper, under base mediated condition, we reported this kind of elimination and another group also reported this kind of phenol derivative from thiaflavans recently.[10,12] The structure of compound **32** was confirmed by X-ray crystallography (Figure **4**).



Conditions: CuI (10 mol %)/ Picolinic acid (20 mol %)/ Cs_2CO_3 (3.0 equiv)/ Toluene/ 120 °C/ 12 h

Scheme 6

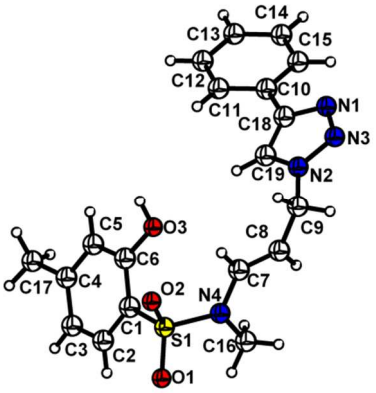
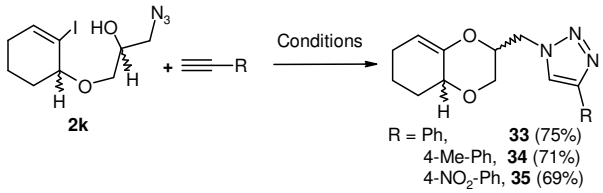


Figure 4. ORTEP diagram of compound **32**. Selected bond lengths [Å] with esd's in parentheses: C6-O3 1.353 (2) C7-C8 1.320 (2) N1-N3 1.313(2) N3-N2 1.326(2).

Thus copper catalyzed one-pot click reaction and intramolecular C-O bond formation was successfully employed on aryl halide precursors. We then wondered whether our methodology is applicable to make a carbon-oxygen bond between vinyl iodide and alcohol or not. To achieve this, substrate **2k** was prepared from 2-iodo-cyclohexenol and 3-chloro-2-epoxy propane (Scheme **1**). Later, substrate **2k** was subjected to optimized condition with terminal acetylenes to obtain 1,4-dioxine ring products. Substrate **2k** has two chiral centres, which shows a possibility of four stereoisomers. The presence of two sets of equal intensity peaks in the ^1H and ^{13}C NMR of these compounds suggests the presence of diastereomers in 1:1 ratio. Satisfyingly, though, the reaction does work efficiently in this case also.



Conditions: CuI (10 mol %)/ Picolinic acid (20 mol %)/ Cs_2CO_3 (3.0 equiv)/ Toluene/ 120 °C/ 12 h

Scheme 7

In general, it is expected that the aryl bromides are less reactive than aryl iodides in reactions such as those described above. In line with this, the reaction between bromo precursor **2l** and phenylacetylene utilizing the optimized condition described above afforded the expected benzodioxine **3** along with the uncyclised product **36** (Scheme 8). Thus, under these conditions, coupling of aryl/vinyl iodides are more successful than of aryl bromides towards a secondary alcohol.

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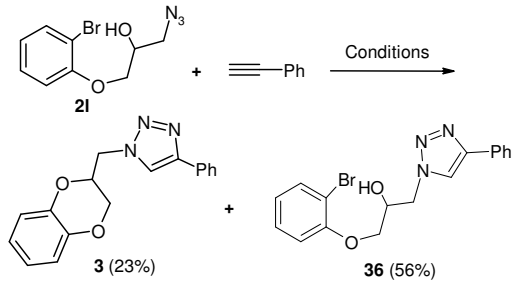
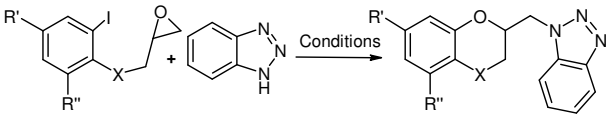


Conditions: CuI (10 mol %)/ Picolinic acid (20 mol %)/ Cs_2CO_3 (3.0 equiv)/Toluene/ 120 °C/ 24 h

Scheme 8

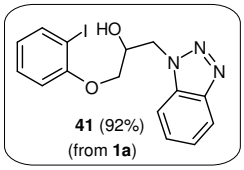
After utilising [Cu]-catalysis successfully in two mechanistically different reactions to construct triazole appended benzodioxines/benzoxazines, we envisioned to synthesise such derivatives starting from the epoxide **1**. There are only a handful of reports available related to ring opening of epoxides/aziridines and further cyclisation by copper-catalysis to obtain the benzodioxines/benzoxazine/benzothiines.[6] Thus, in a one-pot procedure starting from the epoxides (**1a, 1b, 1d, 1f**) the triazole fused benzodioxines (**37-39**) and benzoxazine (**40**) were obtained in good yield. This reaction involves the ring opening of epoxide by benzotriazole and intramolecular cyclisation forming a new C-O bond (Scheme 9). The intermediate **41** could be readily isolated by the reaction of benzotriazole with the epoxide **1a** under neat conditions at 100 °C.



1a, 1b, 1d, 1f

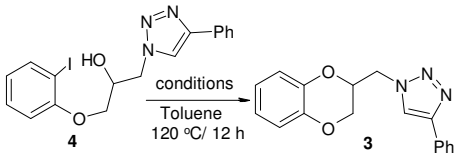
X = O, R' = R'' = H **37** (74%)
X = O, R' = tBu, R'' = H **38** (77%)
X = O, R' = R'' = Me **39** (73%)
X = N-Ts, R' = R'' = H **40** (81%)

Conditions: (i) 100 °C· 1h then CuI (10 mol %)/ Picolinic acid (20 mol %)/ Cs_2CO_3 (3.0 equiv)/Toluene/ 120 °C/ 12 h



Scheme 9

A possible pathway for the above sequential click reaction and intramolecular cyclisation involves two steps. First step involves the formation of 1,2,3-triazole from alkyne and azide *via* a dinuclear copper intermediate.[1d] This pathway is supported by a very recent paper of Worrell[13] *et al*. The second step involves the formation of C-O bond; here, we performed a series of reactions starting from **4** (Scheme 10) to check the effect of different conditions. There was no reaction when base (condition **a**) or copper catalyst (condition **b**) was absent. Notably, product **3** was observed in 62% of yield without addition of ligand (condition **c**) and in one-pot strategy we obtained 55% yield (cf. Scheme 1 above). In this case, the triazole and OH moieties act as bidentate ligand (similar to hydroxymethyl benzotriazole which is used in copper-catalysis[14] as a ligand). To achieve good yields in this methodology copper/ligand/base are required.

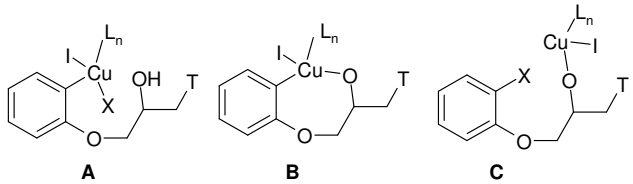


conditions

(a) CuI (10 mol %)/picolinic acid (20 mol %) **noreaction**
(b) Cs_2CO_3 (3.0 equiv) **noreaction**
(c) CuI (10 mol %)/Cs_2CO_3 (3.0 equiv) **62%**

Scheme 10

There are two plausible pathways[15-16] to explain the etherification step: (i) involves the oxidative addition of copper(I) source across C-X bond generating Cu(III) intermediate **A**, followed by replacement of X with the nucleophile in the presence of base forming complex **B**, or (ii) nucleophile reacts with Cu(I) source to form complex **C**[16] and further oxidative addition onto C-X bond leading to complex **B**. In both these pathways, reductive elimination[16c] is the final step affording the desired product **3**. Cs_2CO_3 acts as a base and picolinic acid (or picolinate) acts as the ligand (L). Recent reports favour the second mechanism.[16]



T = triazole; L = picolinic acid (picolinate)

Chart 1

Conclusion

We have successfully demonstrated a simple ***one-pot*** synthesis of 1,2,3-triazole appended benzodioxines (benzodioxanes), benzoxazines and benzoxathiine. The involvement of two different kinds of reaction, ***a click and an intramolecular carbon-oxygen bond formation using Cu(I) dual catalytic system***, should make this method appealing to synthetic chemists. These compounds were also synthesised by the ring opening of epoxide and cyclisaiton using Cu(I)**.** The wide applicability is also amply proven by the diverse range of substrates used. Finally, we have shown that this method is applicable to both aryl and vinyl iodide reactants and reaction with aryl bromides is sluggish.

Experimental Section

The general experimental conditions and synthesis of the precursors are described in the supplementary material.

General Procedure

An oven-dried Schlenk tube with a magnetic stirring bar was charged with CuI (10 mol%), picolinic acid (20 mol%), cesium carbonate (3.0 equiv), and toluene (1 mL) under nitrogen

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atmosphere. Later, 1-azido-3-(2-iodophenoxy)propan-2-ol (**2a**, 0.5 mmol) and phenyl acetylene (0.55 mmol) were added *via* syringe, and the contents heated at 120 °C (oil bath temperature) for 12 h. The mixture was then cooled to ambient temperature, diluted with 2-3 mL of ethyl acetate, passed through a plug of celite, and then washed with 20-30 mL of ethyl acetate. The organic layer was evaporated and the residue purified by column chromatography on silica gel by using hexane/ethyl acetate (75/25) as eluent to afford the desired product **3**. Compounds **6-32** were obtained using the same molar quantities in all the cases.

Compound 3: Yield 0.130 g (89%); mp 118-120 °C; IR (KBr, cm^{-1}) 3084, 1595, 1499, 1277, 1204, 1046, 766; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H, triazole-*H*), 7.85 (dd, *J* ~ 8.0 and 1.2 Hz, 2H, Ar-*H*), 7.44 (t, *J* ~ 8.0 Hz, 2H, Ar-*H*), 7.34-7.37 (m, 1H, Ar-*H*), 6.88-6.94 (m, 4H, Ar-*H*), 4.72-4.75 (m, 2H, CH_2), 4.66-4.69 (m, 1H, OC*H*), 4.37 (dd, *J* = 11.6 and 2.0 Hz, 1H, CH$_a$*H*$_b$), 3.94 (dd, *J* = 11.6 and 6.0 Hz, 1H, C*H*$_a$H$_b$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 142.8, 142.0, 130.4, 128.9, 128.3, 125.8, 122.2, 121.1, 117.5, 71.3 (O*C*H), 64.9 (O*C*H$_2$), 50.2 (N*C*H$_2$); HRMS (ESI) Calc. for $C_{17}H_{16}N_3O_2$ $[M+H]^+$ 294.1243, Found: 294.1245.

Compound 4: Yield 0.196 g (93%); mp 139-141 °C; IR (KBr, cm^{-1}) 3385, 1582, 1474, 1441, 1281, 1231, 1123, 1047, 760, 739; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H, triazole-*H*), 7.77-7.80 (m, 3H, Ar-*H*), 7.35-7.43 (m, 2H, Ar-*H*), 7.29-7.33 (m, 2H, Ar-*H*), 6.76-6.82 (m, 2H, Ar-*H*), 4.82 (dd, *J* = 14.0 and 4.0 Hz, 1H, CH$_a$*H*$_b$), 4.71 (dd, *J* = 14.0 and 6.4 Hz, 1H, C*H*$_a$H$_b$), 4.56-4.58 (m, 1H, C*H*OH), 4.01-4.08 (m, 2H, CH_2), 3.54 (br s, 1H, O*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 147.6, 139.4, 130.2, 129.8, 128.9, 128.3, 125.7, 123.5, 121.5, 112.6, 86.6 (*C*I), 69.9 (O*C*H), 68.7 (O*C*H$_2$), 53.1 (N*C*H$_2$); HRMS (ESI) Calc. for $C_{17}H_{17}IN_3O_2$ $[M+H]^+$ 422.0366, Found: 422.0368.

Compound 5: Yield 0.045 g (35%); mp 138-140 °C; IR (KBr, cm^{-1}) 3134, 1682, 1573, 1474, 1441, 1277, 1041, 997, 751, 690; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 1H, triazole-*H*), 7.79-7.88 (m, 3H, Ar-*H*), 7.62-7.65 (m, 1H, Ar-*H*), 7.32-7.47 (m, 4H, Ar-*H*), 6.88 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 6.77-6.80 (m, 1H, =C-*H*), 6.54-6.59 (m, 1H, =C-*H*), 4.81 (m, 2H, OCH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.6, 148.1, 139.8, 131.7, 130.1, 129.7, 129.0, 126.5, 125.9, 123.5, 117.3, 116.7, 112.6, 86.8 (*C*I), 66.5 (O*C*H$_2$); HRMS (ESI) Calc. for $C_{17}H_{15}IN_3O$ $[M+H]^+$ 404.0261, Found: 404.0263.

Compound 6: Yield 0.138 g (85%); mp 116-118 °C; IR (KBr, cm^{-1}) 3115, 2936, 1615, 1561, 1497, 1456, 1362, 1248, 1177, 1103, 1024, 910, 837, 752; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H, triazole-*H*), 7.77 (dd, *J* = 6.8 and 2.0 Hz, 2H, Ar-*H*), 6.88-6.99 (m, 6H, Ar-*H*), 4.70-4.76 (m, 2H, CH_2), 4.63-4.67 (m, 1H, OC*H*), 4.36 (dd, *J* = 11.6 and 2.0 Hz, 1H, CH$_a$*H*$_b$), 3.93 (dd, *J* = 11.6 and 6.0 Hz, 1H, C*H*$_a$H$_b$), 3.85 (s, 3H, Ar-OCH_3);^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 148.0, 142.9, 142.0, 127.2, 123.1, 122.2, 120.2, 117.6, 117.5, 114.3, 71.4 (O*C*H), 65.0 (O*C*H$_2$), 55.4 (O*C*H$_3$), 50.2 (N*C*H$_2$); HRMS (ESI) Calc. for $C_{18}H_{18}N_3O_3$ $[M+H]^+$ 324.1349, Found: 324.1347.

Compound 7: Yield 0.134 g (87%); mp 138-140 °C; IR (KBr, cm^{-1}) 3088, 1595, 1499, 1454, 1277, 1204, 1046, 820, 747; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H, triazole-*H*), 7.73 (d, *J* = 8.4 Hz, 2H, Ar-*H*), 7.25 (d, *J* = 8.4 Hz, 2H, Ar-*H*), 6.89-6.94 (m, 4H, Ar-*H*), 4.71-4.74 (m, 2H, CH_2), 4.67-4.68 (m, 1H, O-C*H*), 4.37 (dd, *J* = 11.6 and 2.0 Hz, 1H, CH$_a$*H*$_b$), 3.94 (dd, *J* = 11.6 and 6.0 Hz, 1H, C*H*$_a$H$_b$), 2.93 (s, 3H, Ar-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 142.9, 142.0, 138.3, 129.6, 127.6, 125.8, 122.2, 120.7, 117.6, 71.4 (O*C*H), 65.0 (O*C*H$_2$), 50.2 (N*C*H$_2$), 21.4 (*C*H$_3$); HRMS (ESI) Calc. for $C_{18}H_{17}N_3O_2Na$ $[M+Na]^+$ 330.1219, Found: 330.1218.

Compound 8: Yield 0.139 g (82%); mp 154-156 °C; IR (KBr, cm^{-1}) 3086, 1597, 1518, 1501, 1462, 1350, 1279, 1049, 853, 750; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.8 Hz, 2H, Ar-*H*), 8.01-8.03 (m, 3H, triazole-*H*+Ar-*H*), 6.89-6.95 (m, 4H, Ar-*H*), 4.68-4.83 (m, 3H, OC*H*+CH_2), 4.39 (dd, *J* ~ 11.6 and 2.0 Hz, 1H, CH$_a$*H*$_b$), 3.96 (dd, *J* ~11.6 and 6.0 Hz, 1H, C*H*$_a$H$_b$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.4, 146.0, 142.7, 141.8, 136.6, 126.3, 124.4, 122.5, 122.3$_3$, 122.2$_7$, 117.6, 117.4, 71.2 (O*C*H), 64.8 (O*C*H$_2$), 50.4 (N*C*H$_2$); HRMS (ESI) Calc. for $C_{17}H_{15}N_4O_4$ $[M+H]^+$ 339.1094, Found: 339.1092.

Compound 9: Yield 0.128 g (80%); mp 108-110 °C; IR (KBr, cm^{-1}) 3138, 2916, 1688, 1595, 1497, 1466, 1271, 1198, 1109, 1038, 828, 777, 745; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.4 (s, 1H, C*H*O), 8.04 (d, *J* = 7.2 Hz, 1H, Ar-*H*), 7.98 (s, 1H, triazole-*H*), 7.74 (d, *J* ~ 7.2 Hz, 1H, Ar-*H*), 7.66-7.70 (m, 1H, Ar-*H*), 7.54 (t, *J* ~ 7.6 Hz, 1H, Ar-*H*), 6.89-6.94 (m, 4H, Ar-*H*), 4.69-4.85 (m, 3H, OC*H*+CH_2), 4.40 (dd, *J* = 11.6 and 2.4 Hz, 1H, CH$_a$*H*$_b$), 3.99 (dd, *J* ~ 11.6 and 6.0 Hz, 1H, C*H*$_a$H$_b$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.4, 145.0, 142.8, 141.8, 133.8, 132.7, 130.1, 129.1, 128.8, 124.8, 122.3, 117.6, 117.5, 71.3 (O*C*H), 64.9 (O*C*H$_2$), 50.4 (N*C*H$_2$); HRMS (ESI) Calc. for $C_{18}H_{16}N_3O_3$ $[M+H]^+$ 322.1192, Found: 322.1194.

Compound 10: Yield 0.144 g (84%); mp 129-131 °C; IR (KBr, cm^{-1}) 3052, 2912, 1591, 1497, 1466, 1265, 1204, 1119, 1053, 1038, 903, 799, 754; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36-8.38 (m, 1H, Ar-*H*), 7.95 (s, 1H, triazole-*H*), 7.90-7.93 (m, 2H, Ar-*H*), 7.75 (d, *J* = 7.2 Hz, 1H, Ar-*H*), 7.51-7.56 (m, 3H, Ar-*H*), 6.89-6.95 (m, 4H, Ar-*H*), 4.77-4.85 (m, 2H, CH_2), 4.71-4.74 (m, 1H, OC-*H*), 4.41 (dd, *J* = 11.6 and 2.0 Hz, 1H, CH$_a$*H*$_b$), 4.01 (dd, *J* = 11.6 and 6.0 Hz, 1H, C*H*$_a$H$_b$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2, 142.9, 142.0, 134.0, 131.2, 129.1, 128.6, 127.9, 127.4, 126.8, 126.1, 125.4$_2$, 125.3$_7$, 124.1, 122.2, 117.6, 117.5, 71.5 (O*C*H), 65.0 (O*C*H$_2$), 50.3 (N*C*H$_2$); HRMS (ESI) Calc. for $C_{21}H_{18}N_3O_2$ $[M+H]^+$ 344.1400, Found: 344.1398.

Compound 11: Yield 0.168 g (75%); mp 102-104 °C; IR (KBr, cm^{-1}) 3167, 2922, 1593, 1495, 1458, 1437, 1260, 1217, 1123, 1051, 1019, 928, 828, 747; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H, triazole-*H*), 7.77 (dd, *J* = 8.0 and 1.6 Hz, 1H, Ar-*H*), 7.29-7.33 (m, 1H, Ar-*H*), 6.98 (d, *J* = 8.0 Hz, 1H, Ar-*H*), 6.89 (br, 4H, Ar-*H*), 6.72-6.76 (m, 1H, Ar-*H*), 5.32 (s, 2H, OCH_2), 4.60-4.72 (m, 3H, OC*H* + CH_2), 4.34 (dd, *J* ~ 11.6 and 2.0 Hz, 1H, CH$_a$*H*$_b$), 3.89 (dd, *J* = 11.6 and 6.0 Hz, 1H, C*H*$_a$H$_b$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 144.5, 142.8, 141.8, 139.6, 129.7, 124.4, 123.3, 122.2, 122.1, 117.6, 117.5, 112.9, 86.8 (*C*I), 71.3 (O*C*H), 64.9 (O*C*H$_2$), 63.6 (O*C*H$_2$), 50.2 (N*C*H$_2$); HRMS (ESI) Calc. for $C_{18}H_{17}IN_3O_3$ $[M+H]^+$ 450.0315, Found: 450.0317.

Compound 12: Yield 0.127 g (79%); mp 149-151 °C; IR (KBr, cm^{-1}) 3129, 2924, 1645, 1595, 1526, 1493, 1254, 1080, 905, 829, 752; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41-8.44 (m, 2H, Ar-*H*), 8.39 (s, 1H, triazole-*H*), 7.61-7.65 (m, 1H, Ar-*H*), 7.52-7.56 (m, 2H, Ar-*H*), 6.89-6.95 (m, 4H, Ar-*H*), 4.67-4.85 (m, 3H, OC*H* + CH_2), 4.39 (dd, *J* ~ 11.6 and 2.0 Hz, 1H, CH$_a$*H*$_b$), 3.98 (dd, *J* = 11.6 and 6.0 Hz, 1H, C*H*$_a$H$_b$); ^{13}C NMR (100 MHz, $CDCl_3$) δ

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185.7, 148.4, 142.7, 141.7, 136.5, 133.5, 130.7, 129.9, 128.5, 122.4, 117.7, 117.6, 71.1 (O*C*H), 64.8 (O*C*H_2), 50.5 (N*C*H_2); HRMS (ESI) Calc. for $C_{18}H_{16}N_3O_3$ $[M+H]^+$ 322.1192, Found: 322.1189.

Compound 13: Yield 0.116 g (78%); mp 106-108 °C; IR (KBr, cm^{-1}) 3156, 3044, 2924, 1593, 1497, 1462, 1298, 1269, 1051, 1036, 905, 839, 750; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (s, 1H, triazole-*H*), 6.88-6.92 (m, 4H, Ar-*H*), 6.83-6.54 (m, 1H, alkene-*H*), 4.59-4.67 (m, 3H, OC*H* + CH_2), 4.32 (dd, J ~ 11.6 and 2.0 Hz, 1H, CH_aH_b), 3.87 (dd, J = 11.6 and 6.0 Hz, 1H, CH_aH_b), 2.28-2.41 (m, 2H, CH_2), 2.20-2.23 (m, 2H, CH_2), 1.66-1.79 (m, 4H, 2 CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 142.8, 142.0, 127.1, 125.4, 122.0, 119.7, 117.4, 71.4 (O*C*H), 64.9 (O*C*H_2), 50.0 (N*C*H_2), 26.4, 25.3, 22.4, 22.2; HRMS (ESI) Calc. for $C_{17}H_{20}N_3O_2$ $[M+H]^+$ 298.1556, Found: 298.1554.

Compound 14: Yield 0.118 g (72%); mp 75-77 °C; IR (KBr, cm^{-1}) 3063, 2924, 2851, 1597, 1501, 1464, 1279, 1053, 862, 743; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (s, 1H, triazole-*H*), 6.89-6.92 (m, 4H, Ar-*H*), 4.63-4.66 (m, 2H, CH_2), 4.58-4.61 (m, 1H, OC*H*), 4.32 (dd, J = 11.6 and 2.0 Hz, 1H, CH_aH_b), 3.87 (dd, J = 11.6 and 6.0 Hz, 1H, CH_aH_b), 2.72 (t, J = 6.8 Hz, 2H, CH_2), 1.66-1.69 (m, 2H, CH_2), 1.27-1.33 (m, 10H, 5 CH_2), 0.88 (t, J = 6.6 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.9, 142.9, 142.1, 122.1, 122.0, 117.5, 117.4, 71.5 (O*C*H), 65.0 (O*C*H_2), 50.0 (N*C*H_2), 31.9, 29.5, 29.4, 29.3, 25.7, 22.7, 14.2 (*C*H_3); HRMS (ESI) Calc. for $C_{19}H_{28}N_3O_2$ $[M+H]^+$ 330.2182 Found: 330.2178.

Compound 15: Yield 0.139 g (81%); mp 148-150 °C; IR (KBr, cm^{-1}) 3083, 1634, 1603, 1474, 1395, 1358, 1260, 1105, 1051, 978, 808, 768, 693; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.4 Hz, 1H, Ar-*H*), 7.84 (s, 1H, triazole-*H*), 7.78-7.83 (m, 3H, Ar-*H*), 7.45-7.52 (m, 1H, Ar-*H*), 7.40-7.45 (m, 4H, Ar-*H*), 7.33-7.37 (m, 1H, Ar-*H*), 7.13 (dd, J ~ 8.4 and 2.8 Hz, 1H, Ar-*H*), 4.78-4.88 (m, 3H, OC*H* + CH_2), 4.48 (dd, J ~ 11.6 and 2.0 Hz, 1H, CH_aH_b), 4.12 (dd, J = 11.6 and 4.8 Hz, 1H, CH_aH_b); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 138.4, 134.6, 130.4, 129.9, 129.0, 128.4, 127.9, 126.3, 125.8, 125.5, 124.7, 121.9, 121.1, 119.8, 118.3, 71.6 (O*C*H), 65.0 (O*C*H_2), 50.1 (N*C*H_2); HRMS (ESI) Calc. for $C_{21}H_{17}N_3O_2Na$ $[M+Na]^+$ 366.1219, Found: 366.1217.

Compound 16: Yield 0.134 g (82%); mp 137-140 °C; IR (KBr, cm^{-1}) 3094, 2924, 1588, 1493, 1462, 1275, 1200, 1084, 1038, 936, 856, 766, 693; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H, triazole-*H*), 7.84 (d, J = 8.0 Hz, 2H, Ar-*H*), 7.45 (t, J ~ 7.4 Hz, 2H, Ar-*H*), 7.36 (t, J ~ 7.4 Hz, 1H, Ar-*H*), 6.93-6.94 (m, 1H, Ar-*H*), 6.82-6.88 (m, 2H, Ar-*H*), 4.64-4.73 (m, 3H, OC*H* + CH_2), 4.36 (dd, J ~ 11.6 and 2.0 Hz, 1H, CH_aH_b), 3.91 (dd, J ~ 11.6 and 6.0 Hz, 1H, CH_aH_b); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 142.5, 141.6, 130.3, 129.0, 128.5, 126.7, 125.9, 122.2, 121.0, 118.4, 117.6, 71.6 (O*C*H), 64.9 (O*C*H_2), 50.1 (N*C*H_2); HRMS (ESI) Calc. for $C_{17}H_{15}ClN_3O_2$ $[M+H]^+$ 328.0854 and 330.0824, Found: 328.0853 and 330.0817. This compound was crystallized from dichloromethane/hexane (1:1) mixture at 25 °C. X-ray structure was determined for this compound.

Compound 17: Yield 0.150 g (86%); mp 166-169 °C; IR (KBr, cm^{-1}) 3092, 2963, 1582, 1503, 1466, 1310, 1269, 1231, 1088, 1073, 918, 764; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H, triazole-*H*), 7.85 (dd, J = 8.4 and 1.2 Hz, 2H, Ar-*H*), 7.45 (t, J ~ 7.4 Hz, 2H, Ar-*H*), 7.36 (t, J ~ 7.4 Hz, 1H, Ar-*H*), 6.91-6.95 (m, 2H, Ar-*H*), 6.84 (d, J = 8.4 Hz, 1H, Ar-*H*), 4.63-4.74 (m, 3H, OC*H* + CH_2), 4.34 (dd, J = 11.6 and 2.0 Hz, 1H, CH_aH_b), 3.90 (dd, J = 11.6 and 6.4 Hz, 1H, CH_aH_b), 1.29 (s, 9H, C(CH_3)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 145.7, 141.4, 140.4, 130.5, 129.0, 128.4, 125.9, 121.1, 119.2, 116.9, 114.4, 71.5 (O*C*H), 65.0 (O*C*H_2), 50.4 (N*C*H_2), 34.4, 31.5; HRMS (ESI) Calc. for $C_{21}H_{24}N_3O_2$ $[M+H]^+$ 350.1869, Found: 350.1867.

Compound 18: Yield 0.134 g (78%); mp 126-128 °C; IR (KBr, cm^{-1}) 3127, 2922, 1603, 1499, 1439, 1318, 1217, 1074, 1028, 859, 766, 693; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H, triazole-*H*), 7.84-7.86 (m, 2H, Ar-*H*), 7.35-7.46 (m, 3H, Ar-*H*), 6.58-6.59 (m, 2H, Ar-*H*), 4.61-4.74 (m, 3H, OC*H* + CH_2), 4.35 (dd, J = 11.6 and 2.0 Hz, 1H, CH_aH_b), 3.93 (dd, J = 11.6 and 6.0 Hz, 1H, CH_aH_b), 2.17 and 2.24 (2 s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 141.3, 138.7, 130.9, 130.4, 128.9, 128.3, 126.7, 125.8, 124.2, 121.1, 115.2, 71.3 (O*C*H), 64.9 (O*C*H_2), 50.3 (N*C*H_2), 20.7 and 15.4 (2 *C*H_3); HRMS (ESI) Calc. for $C_{19}H_{19}N_3O_2Na$ $[M+Na]^+$ 344.1375, Found: 344.1377.

Compound 19: Yield 0.192 g (86%); mp 163-165 °C; IR (KBr, cm^{-1}) 3136, 2918, 1588, 1480, 1449, 1340, 1242, 1159, 1066, 910, 848, 760; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82-7.84 (m, 2H, Ar-*H*), 7.81 (s, 1H, triazole-*H*), 7.78 (dd, J = 8.4 and 1.6 Hz, 1H, Ar-*H*), 7.52 (d, J = 8.0 Hz, 2H, Ar-*H*), 7.44 (t, J ~ 7.6 Hz, 2H, Ar-*H*), 7.35 (t, J ~ 7.6 Hz, 1H, Ar-*H*), 7.22 (d, J = 8.4 Hz, 2H, Ar-*H*), 7.08 (t, J = 7.2 Hz, 1H, Ar-*H*), 6.96 (t, J = 7.2 Hz, 1H, Ar-*H*), 6.87 (dd, J ~ 8.4 and 1.2 Hz, 1H, Ar-*H*), 4.60 (d, J = 4.8 Hz, 2H, NCH_2), 4.33 (dd, J = 14.4 and 2.4 Hz, 1H, NCH_aH_b), 3.83-3.89 (m, 1H, OC*H*), 3.14 (dd, J = 14.4 and 9.6 Hz, 1H, NCH_aH_b), 2.37 (s, 3H, ArCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 145.9, 144.7, 135.3, 130.3, 130.2, 129.0, 128.5, 127.2, 126.4, 125.8, 124.4, 123.5, 121.7, 120.9, 117.4, 70.3 (O*C*H), 51.4 (N*C*H_2), 45.8 (N*C*H_2), 21.7 (Ar*C*H_3); HRMS (ESI) Calc. for $C_{24}H_{23}N_4O_3S$ $[M+H]^+$ 447.1492, Found: 447.1489.

Compound 20: Yield 0.173 g (77%); mp 168-170 °C; IR (KBr, cm^{-1}) 3134, 2920, 1655, 1584, 1479, 1447, 1342, 1238, 1167, 1068, 942, 856, 762, 657, 564; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J ~ 8.0 Hz, 1H, Ar-*H*), 7.48 (d, J = 8.0 Hz, 2H, Ar-*H*), 7.43 (s, 1H, triazole-*H*), 7.22 (d, J ~ 8.0 Hz, 2H, Ar-*H*), 7.07 (t, J ~ 7.6 Hz, 1H, Ar-*H*), 6.95 (t, J = 7.6 Hz, 1H, Ar-*H*), 6.84 (d, J = 8.0 Hz, 1H, Ar-*H*), 6.52 (s, 1H, cyclohexenyl-*H*), 4.51 (d, J = 4.8 Hz, 2H, NCH_2), 4.29 (dd, J ~ 14.4 and 2.4 Hz, 1H, NCH_aH_b), 3.75-3.77 (m, 1H, OC*H*), 3.05 (dd, J = 14.4 and 9.6 Hz, 1H, NCH_aH_b), 2.38 (br s, 5H, CH_2+ArCH_3), 2.19-2.20 (m, 2H, CH_2), 1.65-1.78 (m, 4H, 2 CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 145.9, 144.6, 135.2, 130.1, 127.2, 127.0, 126.3, 125.5, 124.4, 123.4, 121.6, 119.6, 117.4, 70.2 (O*C*H), 51.2 (N*C*H_2), 45.7 (N*C*H_2), 26.4, 25.3, 22.4, 22.2, 21.6 (Ar*C*H_3); HRMS (ESI) Calc. for $C_{24}H_{27}N_4O_3S$ $[M+H]^+$ 451.1805, Found: 451.1806. This compound was crystallized from dichloromethane/hexane (2:1) mixture at 25 °C. X-ray structure was determined for this compound.

Compound 21: Yield 0.183 g (76%); mp 68-70 °C; IR (KBr, cm^{-1}) 3162, 2915, 2849, 1594, 1479, 1449, 1348, 1233, 1162, 1068, 926, 800, 762, 663, 575; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, J ~ 8.0 and 1.6 Hz, 1H, Ar-*H*), 7.50 (d, J = 8.4 Hz, 2H, Ar-*H*), 7.32 (s, 1H, triazole-*H*), 7.24 (d, J = 8.4 Hz, 2H, Ar-*H*), 7.05-7.09 (m, 1H, Ar-*H*), 6.93-6.97 (m, 1H, Ar-*H*), 6.84 (dd, J = 8.0 and 1.2 Hz, 1H, Ar-*H*), 4.50 (d, J = 4.8 Hz, 2H, NCH_2), 4.28 (dd, J =

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14.4 and 2.4 Hz, 1H, NCH_aH_b), 3.81-3.85 (m, 1H, OC*H*), 3.05 (dd, *J* ~ 14.4 and 9.6 Hz, 1H, NCH_aH_b), 2.70 (t, *J* ~ 7.4 Hz, 2H, CH_2), 2.39 (s, 3H, $ArCH_3$), 1.62-1.69 (m, 2H, CH_2), 1.26-1.31 (m, 10H, 5 CH_2), 0.87 (t, *J* ~ 6.4 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 145.9, 144.7, 135.3, 130.2, 127.2, 126.3, 124.4, 123.5, 122.0, 121.6, 117.4, 70.2 (O*C*H), 51.2 (N*C*H_2), 45.8 (N*C*H_2), 31.9, 29.4$_4$, 29.3$_9$, 29.3, 25.7, 22.7, 21.7 (Ar*C*H_3), 14.2; HRMS (ESI) Calc. for $C_{26}H_{35}N_4O_3S$ $[M+H]^+$ 483.2431, Found: 483.2428.

Compound 22: Yield 0.189 g (82%); mp 176-178 °C; IR (KBr, cm^{-1}) 3053, 2915, 1578, 1495, 1430, 1358, 1260, 1161, 1062, 931, 810, 762, 668; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.4 Hz, 2H, Ar-*H*), 7.78 (s, 1H, triazole-*H*), 7.65 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 7.50 (d, *J* = 8.0 Hz, 2H, Ar-*H*), 7.45 (t, *J* ~ 7.6 Hz, 2H, Ar-*H*), 7.36 (t, *J* ~ 7.6 Hz, 1H, Ar-*H*), 7.22 (d, *J* = 8.0 Hz, 2H, Ar-*H*), 6.78 (dd, *J* = 8.4 and 1.6 Hz, 1H, Ar-*H*), 6.68 (br, 1H, Ar-*H*), 4.56-4.58 (m, 2H, N*C*H_2), 4.30 (dd, *J* = 14.4 and 2.4 Hz, 1H, NCH_aH_b), 3.77-3.82 (m, 1H, O-C*H*), 3.11 (dd, *J* ~14.4 and 9.6 Hz, 1H, NCH_aH_b), 2.28 and 2.37 (2 s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 145.7, 144.6, 136.7, 135.2, 130.3, 130.2, 129.0, 128.5, 127.3, 125.8, 124.3, 122.7, 120.9, 120.8, 117.7, 70.1 (O*C*H), 51.5 (N*C*H_2), 45.9 (N*C*H_2), 20.9 and 21.7 (2 *C*H_3); HRMS (ESI) Calc. for $C_{25}H_{24}N_4O_3SNa$ $[M+Na]^+$ 483.1467, Found: 483.1465.

Compound 23: Yield 0.181 g (78%); mp 170-173 °C; IR (KBr, cm^{-1}) 3139, 2920, 1583, 1501, 1435, 1353, 1260, 1161, 1057, 932, 816, 673, 531; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 7.48 (d, *J* = 8.4 Hz, 2H, Ar-*H*), 7.42 (s, 1H, triazole-*H*), 7.22 (d, *J* = 8.4 Hz, 2H, Ar-*H*), 6.77 (dd, *J* = 8.4 and 1.6 Hz, 1H, Ar-*H*), 6.65-6.66 (m, 1H, Ar-*H*), 6.52-6.54 (m, 1H, =C*H*), 4.49 (d, *J* = 4.8 Hz, 2H, N*C*H_2), 4.26 (dd, *J* = 14.4 and 2.4 Hz, 1H, NCH_aH_b), 3.68-3.73 (m, 1H, OC*H*), 3.03 (dd, *J* ~ 14.4 and 9.6 Hz, 1H, NCH_aH_b), 2.38-2.39 (m, 5H, CH_2+ArCH_3), 2.28 (s, 3H, CH_3), 2.20-2.22 (m, 2H, CH_2), 1.67-1.81 (m, 4H, 2 CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.7, 145.7, 144.5, 136.6, 135.2, 130.1, 127.2, 127.0, 125.5, 124.3, 122.5, 120.7, 119.6, 117.6, 70.0 (O*C*H), 51.2 (N*C*H_2), 45.8 (N*C*H_2), 26.3, 25.3, 22.4, 22.2, 21.6, 20.9; HRMS (ESI) Calc. for $C_{25}H_{29}N_4O_3S$ $[M+H]^+$ 465.1961, Found: 465.1960.

Compound 24: Yield 0.184 g (74%); mp 78-80 °C; IR (KBr, cm^{-1}) 3117, 2920, 2854, 1588, 1501, 1451, 1358, 1260, 1161, 1057, 931, 816, 668, 536; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 7.49 (d, *J* = 8.4 Hz, 2H, Ar-*H*), 7.31 (s, 1H, triazole-*H*), 7.23-7.27 (m, 2H, Ar-*H*), 6.77 (dd, *J* = 8.4 and 1.2 Hz, 1H, Ar-*H*), 6.66 (s, 1H, Ar-*H*), 4.48 (d, *J* = 4.8 Hz, 2H, N*C*H_2), 4.25 (dd, *J* = 14.4 and 2.4 Hz, 1H, NCH_aH_b), 3.74-3.76 (m, 1H, OC*H*), 3.01 (dd, *J* ~ 14.4 and 9.6 Hz, 1H, NCH_aH_b), 2.70 (t, *J* ~ 7.8 Hz, 2H, CH_2), 2.28 and 2.39 (2 s, 6H, 2 ArCH_3), 1.62-1.68 (m, 2H, CH_2), 1.26-1.31 (m, 10H, 5 CH_2), 0.87 (t, *J* = 6.8 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 145.7, 144.5, 136.6, 135.2, 130.1, 127.2, 124.3, 122.5, 122.0, 120.7, 117.6, 70.0 (O*C*H), 51.2 (N*C*H_2), 45.9 (N*C*H_2), 31.9, 29.4$_3$, 29.3$_9$, 29.3, 25.7, 22.7, 21.7, 20.9, 14.2; HRMS (ESI) Calc. for $C_{27}H_{37}N_4O_3S$ $[M+H]^+$ 497.2587, Found: 497.2588.

Compound 25: Yield 0.130 g (84%); mp 84-86 °C; IR (KBr, cm^{-1}) 3140, 2948, 2915, 1611, 1573, 1468, 1436, 1260, 1222, 1079, 1047, 915, 756, 690; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H, triazole-*H*), 7.83-7.86 (m, 2H, Ar-*H*), 7.45 (t, *J* ~ 7.6 Hz, 2H, Ar-*H*), 7.36 (t, *J* ~ 7.6 Hz, 1H, Ar-*H*), 7.02-7.09 (m, 2H, Ar-*H*), 6.86-6.92 (m, 2H, Ar-*H*), 4.73-4.82 (m, 3H, CH_2+OC*H*), 3.14 (dd, *J* ~ 13.2 and 1.6 Hz, 1H, CH_aH_b), 2.92 (dd, *J* ~ 13.2 and 7.6 Hz, 1H, CH_aH_b); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 148.0, 130.4, 128.9, 128.3, 127.5, 126.1, 125.8, 122.2, 121.0, 118.6, 116.9, 72.5 (O*C*H), 53.1 (N*C*H_2), 26.9 (S*C*H_2); HRMS (ESI) Calc. for $C_{17}H_{16}N_3OS$ $[M+H]^+$ 310.1015, Found: 310.1012.

Compound 26: Yield 0.125 g (80 %); mp 98-100 °C; IR (KBr, cm^{-1}) 3140, 2931, 2855, 1737, 1567, 1479, 1447, 1271, 1222, 1074, 1019, 904, 800, 751; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (s, 1H, triazole-*H*), 7.00-7.06 (m, 2H, Ar-*H*), 6.83-6.89 (m, 2H, Ar-*H*), 6.52-6.57 (m, 1H, cyclohexenyl-*H*), 4.64-4.69 (m, 3H, CH_2+OC*H*), 2.85 (dd, *J* = 13.2 and 7.2 Hz, 1H, CH_aH_b), 3.06 (dd, *J* = 13.2 and 1.6 Hz, 1H, CH_aH_b), 2.19-2.39 (m, 4H, 2 CH_2), 1.65-1.78 (m, 4H, 2 CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 149.7, 127.5, 127.1, 126.0, 125.3, 122.1, 119.7, 118.5, 116.9, 72.5 (O*C*H), 52.9 (N*C*H_2), 26.9 (S*C*H_2), 26.4, 25.3, 22.4, 22.2; HRMS (ESI) Calc. for $C_{17}H_{20}N_3OS$ $[M+H]^+$ 314.1328, Found: 314.1327.

Compound 27: Yield 0.133 g (77%); mp 70-72 °C; IR (KBr, cm^{-1}) 3112, 3057, 2920, 2844, 1573, 1474, 1436, 1293, 1233, 1052, 997, 866, 734; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (s, 1H, triazole-*H*), 7.01-7.07 (m, 2H, Ar-*H*), 6.83-6.91 (m, 2H, Ar-*H*), 4.65-4.72 (m, 3H, CH_2+OC*H*), 3.10 (dd, *J* ~ 13.2 and 1.6 Hz, 1H, CH_aH_b), 2.86 (dd, *J* ~ 13.2 and 6.4 Hz, 1H, CH_aH_b), 2.72 (t, *J* ~ 7.6 Hz, 2H, CH_2), 1.66-1.68 (m, 2H, CH_2), 1.27-1.32 (m, 10H, 5 CH_2), 0.86-0.89 (m, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.4, 148.8, 127.5, 126.1, 122.2, 122.0, 118.6, 117.0, 72.6 (O*C*H), 52.9 (N*C*H_2), 31.9, 29.5, 29.4, 29.3, 27.0 (S*C*H_2), 25.7, 22.7, 14.2; HRMS (ESI) Calc. for $C_{19}H_{28}N_3OS$ $[M+H]^+$ 346.1954, Found: 346.1955.

Compound 28: Yield 0.118 g (77%); mp 125-127 °C; IR (KBr, cm^{-1}) 3127, 2940, 2845, 1602, 1582, 1487, 1454, 1248, 1194, 1105, 1082, 905, 766, 694; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 1H, triazole-*H*), 7.90 (dd, *J* = 8.4 and 1.2 Hz, 2H, Ar-*H*), 7.46 (t, *J* ~ 7.6 Hz, 2H, Ar-*H*), 7.37-7.38 (m, 1H, Ar-*H*), 7.05-7.19 (m, 3H, Ar-*H*), 6.84 (d, *J* = 8.0 Hz, 1H, Ar-*H*), 4.68 (s, 2H, OCH_2), 4.57-4.62 (m, 2H, CH_2), 4.34-4.35 (m, 1H, OC*H*), 4.21 (dd, *J* = 12.8 and 1.2 Hz, 1H, CH_aH_b), 3.74 (dd, *J* = 12.8 and 8.4 Hz, 1H, CH_aH_b); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 147.9, 132.3, 130.6, 129.6, 129.3, 129.0, 128.3, 125.8, 124.2, 121.1, 121.0, 80.7 (OCH_2), 74.3 (O*C*H), 73.5 (OCH_2), 51.2 (N*C*H_2); HRMS (ESI) Calc. for $C_{18}H_{17}N_3O_2Na$ $[M+Na]^+$ 330.1219, Found: 330.1218.

Compound 29: Yield 0.140 g (83%); mp 140-142 °C; IR (KBr, cm^{-1}) 3106, 2845, 1605, 1582, 1503, 1487, 1454, 1250, 1107, 1032, 907, 822; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H, triazole-*H*), 7.81 (d, *J* ~ 8.4 Hz, 2H, Ar-*H*), 7.16-7.21 (m, 2H, Ar-*H*), 7.05 (t, *J* ~ 7.6 Hz, 1H, Ar-*H*), 6.99 (d, *J* = 8.4 Hz, 2H, Ar-*H*), 6.85 (d, *J* = 8.0 Hz, 1H, Ar-*H*), 4.68 (s, 2H, OCH_2), 4.56-4.61 (m, 2H, CH_2), 4.34-4.35 (m, 1H, OC*H*), 4.20 (d, *J* = 12.8 Hz, 1H, CH_aH_b), 3.86 (s, 3H, OCH_3), 3.74 (dd, *J* = 12.8 and 8.4 Hz, 1H, CH_aH_b); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 157.4, 147.8, 132.4, 129.6, 129.3, 127.1, 124.2, 123.3, 121.0, 120.3, 114.4, 80.8 (OCH_2), 74.3 (O*C*H), 73.5 (OCH_2), 55.4 (OCH_3), 51.2 (N*C*H_2); HRMS (ESI) Calc. for $C_{19}H_{19}N_3O_3Na$ $[M+Na]^+$ 360.1324, Found: 360.1326.

Compound 30: Yield 0.127 g (72%); mp 169-171 °C; IR (KBr,

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cm^{-1}) 3148, 2853, 1605, 1516, 1464, 1337, 1244, 1109, 1071, 853, 754; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, J = 8.8 Hz, 2H, Ar-*H*), 8.16 (s, 1H, triazole-*H*), 8.06 (d, J = 8.8 Hz, 2H, Ar-*H*), 7.18-7.22 (m, 2H, Ar-*H*), 7.06 (t, J ~ 7.2 Hz, 1H, Ar-*H*), 6.82 (d, J = 8.0 Hz, 1H, Ar-*H*), 4.59-4.72 (m, 4H, 2 CH_2), 4.36-4.37 (m, 1H, OC*H*), 4.23 (dd, J ~ 12.8 and 1.6 Hz, 1H, CH$_a$*H*$_b$), 3.74 (dd, J = 12.8 and 8.4 Hz, 1H, C*H*$_a$H$_b$); ^{13}C NMR (400 MHz, $CDCl_3$) δ 157.2, 147.5, 145.7, 136.8, 132.3, 129.6, 129.4, 126.3, 124.5, 124.4, 122.6, 120.9, 80.5 (O*C*H$_2$), 74.3 (O*C*H), 73.5 (O*C*H$_2$), 51.5 (N*C*H$_2$); HRMS (ESI) Calc. for $C_{18}H_{16}N_4O_4Na$ [M+Na]$^+$ 375.1070, Found: 375.1068. This compound was crystallized from ethyl acetate/hexane (1:1) mixture at 25 ^{o}C. X-ray structure was determined for this compound.

Compound 31: Yield 0.107 g (69%); mp 122-124 ^{o}C; IR (KBr, cm^{-1}) 3148, 2936, 2834, 1580, 1487, 1454, 1267, 1248, 1227, 1121, 1071, 993, 907, 770; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (s, 1H, triazole-*H*), 7.15-7,23 (m, 2H, Ar-*H*), 7.04-7.06 (m, 1H, Ar-*H*), 6.85 (d, J = 8.0 Hz, 1H, Ar-*H*), 6.56-6.57 (m, 1H, cyclohexenyl-*H*), 4.66 (s, 2H, OCH_2), 4.50-4.55 (m, 2H, CH_2), 4.28-4.30 (m, 1H, OC*H*), 4.13 (dd, J = 12.8 and 1.6 Hz, 1H, CH$_a$*H*$_b$), 3.70 (dd, J = 12.8 and 8.4 Hz, 1H, C*H*$_a$H$_b$), 2.21-2.43 (m, 4H, 2 CH_2), 1.68-1.82 (m, 4H, 2 CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 149.6, 132.3, 129.5, 129.3, 127.2, 125.2, 124.2, 121.0, 119.7, 80.7 (O*C*H$_2$), 74.3 (O*C*H), 73.5 (O*C*H$_2$), 51.1 (N*C*H$_2$), 22.3, 22.5, 25.3 and 26.5 (4 *C*H$_2$); HRMS (ESI) Calc. for $C_{18}H_{22}N_3O_2$ [M+H]$^+$ 312.1713, Found: 312.1711.

Compound 32: Yield 0.125 g (65%); mp 166-169 ^{o}C; IR (KBr, cm^{-1}) 3332, 3125, 2918, 2856, 1676, 1614, 1563, 1454, 1324, 1242, 1117, 952, 910, 750; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H, O*H*), 7.93 (s, 1H, triazole-*H*), 7.85 (d, J = 8.0 Hz, 2H, Ar-*H*), 7.44-7.48 (m, 3H, Ar-*H*), 7.31-7.40 (m, 2H, Ar-*H*), 6.86 (s, 1H, Ar-*H*), 6.84 (d, J = 8.4 Hz, 1H, =C*H*), 6.16-6.23 (m, 1H, =C*H*), 3.93 (d, J = 6.0 Hz, 2H, CH_2), 2.37 and 2.84 (2 s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.5, 148.2, 147.2, 129.8, 129.1, 128.8, 128.2, 127.6, 126.0, 121.9, 119.2, 117.3, 116.7, 115.5, 49.5 (N*C*H$_2$), 34.8, 21.7; HRMS (ESI) Calc. for $C_{19}H_{20}N_4O_3SNa$ [M+Na]$^+$ 407.1154, Found: 407.1153. This compound was crystallized from dichloromethane/hexane (2:1) mixture at 25 ^{o}C. X-ray structure was determined for this compound.

Compound 33: (approx. 1:1 diastereomeric ratio),Yield 0.111 g (75%); gummy solid; IR (neat, cm^{-1}) 3134, 2942, 2860, 1734, 1677, 1468, 1441, 1353, 1260, 1162, 1112, 767, 701; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H, triazole-*H*), 7.83-7.86 (m, 5H, Ar-*H*), 7.32-7.45 (m, 6H, Ar-*H*), 5.20 (m, 2H, =C*H*), 3.80-4.84 (m, 11H), 3.42-3.47 (m, 1H), 1.43-2.08 (m, 12H), due to the presence of isomers, number of protons is doubled in the assignment; ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.7, 147.0, 130.6, 128.9, 128.2, 125.8, 121.1, 120.9, 108.8, 107.6, 75.0, 73.3, 72.3, 71.3, 67.6, 66.5, 51.1, 50.2, 29.4, 29.2, 23.8, 23.6, 20.5, due to the presence of isomers, number of carbons is more in the spectrum; HRMS (ESI) Calc. for $C_{17}H_{20}N_3O_2$ [M+H]$^+$ 298.1556, Found: 298.1552.

Compound 34: (approx. 1:1 diastereomeric ratio),Yield 0.11 g (71%); gummysolid; IR (neat, cm^{-1}) 3134, 2942, 2860, 1742, 1682, 1496, 1447, 1353, 1260, 1167, 1112, 822, 729; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 and 7.90 (2 s, 2H, triazole-*H*), 7.71-7.75 (m, 4H, Ar-*H*), 7. 23-7.27 (m, 4H, Ar-*H*), 5.18-5.19 (m, 2H, =C*H*), 3.79-4.82 (m, 11H), 3.41-3.46 (m, 1H), 2.38 (s, 6H), 1.53-2.11 (m, 12H), due to the presence of isomers, number of protons is doubled in the assignment; ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 148.0, 147.8, 147.1, 138.1, 129.6, 127.8, 127.7, 125.7, 120.8, 120.5, 108.9, 107.6, 75.0, 73.3, 72.3, 71.3, 69.6, 67.7, 66.6, 51.1, 50.2, 29.5, 29.3, 23.8, 23.6, 21.4, 20.5, due to the presence of isomers, number of carbons is more in the spectrum; HRMS (ESI) Calc. for $C_{18}H_{22}N_3O_2$ [M+H]$^+$ 312.1713, Found: 312.1712.

Compound 35: (approx. 1:1 diastereomeric ratio),Yield 0.118 g (69%); mp 142-145 ^{o}C; IR (KBr, cm^{-1}) 3151, 2948, 2860, 1731, 1682, 1605, 1507, 1458, 1337, 1156, 1112, 855, 756; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29-8.31 (m, 4H, Ar-*H*), 8.10 (s, 1H, triazole-*H*), 8.01-8.04 (m, 5H, Ar-*H*), 5.20-5.21 (m, 2H, =C*H*), 3.83-4.90 (m, 11H), 3.45-3.48 (m, 1H), 1.53-2.12 (m, 12H), due to the presence of isomers, number of protons is doubled in the assignment; ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 147.3, 147.0, 145.8, 145.6, 136.9, 126.2, 124.3, 122.6, 122.3, 109.0, 107.9, 74.9, 73.2, 72.4, 71.3, 67.6, 66.6, 51.3, 50.5, 29.4, 29.2, 23.8, 23.5, 20.5, due to the presence of isomers, number of carbons is more in the spectrum; HRMS (ESI) Calc. for $C_{17}H_{19}N_3O_4$ [M+H]$^+$ 343.1407, Found: 343.1404.

Compound 36: Yield 0.104 g (56 %); Mp 139-141 ^{o}C; IR (KBr, cm^{-1}) 3364, 3134, 1567, 1479, 1447, 1288, 1233, 1118, 1052, 958, 745, 690; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H, triazole-*H*), 7.73 (d, J ~ 7.6 Hz, 2H, Ar-*H*), 7.55 (d, J = 8.0 Hz, 1H, Ar-*H*), 7.39 (t, J ~ 7.6 Hz, 2H, Ar-*H*), 7.32 (t, J ~ 7.6 Hz, 1H, Ar-*H*), 7.24-7.28 (m, 1H, Ar-*H*), 6.87-6.91 (m, 2H, Ar-*H*), 4.79 (dd, J = 14.0 and 3.6 Hz, 1H, CH$_a$*H*$_b$), 4.65 (dd, J = 14.0 and 6.4 Hz, 1H, C*H*$_a$H$_b$), 4.58-4.59 (m, 1H, OC*H*), 4.02-4.07 (m, 2H, CH_2),3.77 (br, 1H, O*H*); ^{13}C NMR(400 MHz, $CDCl_3$) δ 154.4, 147.7, 133.5, 130.3, 128.9, 128.8, 128.3, 125.7, 123.0, 121.6, 113.9, 112.4, 70.0, 68.8, 53.0; HRMS (ESI) Calc. for $C_{17}H_{17}BrN_3O_2$ [M+H]$^+$ 375.0505 and 376.0663, Found: 375.0508 and 376.0491.

General procedure for the synthesis compounds 37-41:

An oven-dried Schlenk tube with a magnetic stirring bar was charged with benzotriazole (0.5 mmol) and epoxide (0.5 mmol) and then heated at 100 ^{o}C for 2 h. Later, CuI (10 mol%), picolinic acid (20 mol%), cesium carbonate (3.0 equiv.), and toluene (1 mL) were added under nitrogen atmosphere and the contents heated at 120 ^{o}C (oil bath temperature) for 12 h. The mixture was then cooled to ambient temperature, diluted with 2-3 mL of ethyl acetate, passed through a plug of celite, and then washed with 20-30 mL of ethyl acetate. The organic layer was evaporated and the residue purified by column chromatography on silica gel by using hexane/ethyl acetate (75/25) as eluent to afford the desired product. Compounds **37**-**40** were synthesised following the molar quantities mentioned above in each case. Compound **41** was isolated without addition of copper-catalyst.

Compound 37: Yield 0.99 g (74 %); Mp 128-130 ^{o}C; IR (KBr, cm^{-1}) 1594, 1506, 1451, 1342, 1265, 1194, 1040, 914, 832, 750; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.4Hz, 1H, Ar-*H*), 7.50-7.59 (m, 2H, Ar-*H*), 7.38-7.42 (m, 1H, Ar-*H*), 6.83-6.93 (m, 4H, Ar-*H*), 4.96 (d, J = 5.6 Hz, 2H, CH_2), 4.74-4.78 (m, 1H, OC*H*), 4.36 (dd, J ~ 12.0 and 2.4 Hz, 1H, CH$_a$*H*$_b$), 3.96 (dd, J = 12.0 and 6.0 Hz, 1H, C*H*$_a$H$_b$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9, 142.8, 142.0, 133.8, 127.8, 124.2, 122.1, 120.0, 117.5,

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117.4, 109.9, 71.9, 65.0, 48.1; HRMS (ESI) Calc. for $C_{15}H_{14}N_3O_2$ $[M+H]^+$ 268.1087, Found: 268.1088.

Compound 38: Yield 0.124 g (77 %); Mp 115-116 ^oC; IR (KBr, cm^{-1}) 2953, 2871, 1595, 1452, 1321, 1266, 1058, 915, 822, 745; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.4 Hz, 1H, Ar-*H*), 7.48-7.54 (m, 2H, Ar-*H*), 7.38-7.42 (m, 1H, Ar-*H*), 6.91 (dd, J ~ 8.4 and 2.4 Hz, 1H, Ar-*H*), 6.84-6.86 (m, 2H, Ar-*H*), 4.95 (d, J = 6.0 Hz, 2H, CH_2), 4.73-4.78 (m, 1H, OC*H*), 4.33 (dd, J ~ 11.6 and 2.4 Hz, 1H, CH_aH_b), 3.98 (dd, J = 11.6 and 5.6 Hz, 1H, CH_aH_b), 1.28 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 145.6, 141.3, 142.4, 133.9, 127.8, 124.2, 120.1, 119.0, 116.8, 114.7, 109.9, 72.0, 65.1, 48.0, 34.3, 31.5; HRMS (ESI) Calc. for $C_{19}H_{22}N_3O_2$ $[M+H]^+$ 324.1713, Found: 324.1711.

Compound 39: Yield 0.108 g (73 %); Mp 119-121 ^oC; IR (KBr, cm^{-1}) 2921, 1605, 1496, 1447, 1321, 1211, 1151, 1118, 1063, 904, 833, 751; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.4 Hz, 1H, Ar-*H*), 7.59 (d, J = 8.4 Hz, 1H, Ar-*H*), 7.52 (t, J = 7.6 Hz, 1H, Ar-*H*), 7.40 (t, J = 7.6 Hz, 1H, Ar-*H*), 6.56 (s, 1H, Ar-*H*), 6.50 (s, 1H, Ar-*H*), 4.94 (d, J = 5.6 Hz, 2H, CH_2), 4.70-4.72 (m, 1H, OC*H*), 4.34 (dd, J = 11.6 and 2.0 Hz, 1H, CH_aH_b), 3.94 (dd, J = 11.6 and 6.0 Hz, 1H, CH_aH_b), 2.17 and 2.21 (2 s, 6H, 2 CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 141.5, 138.8, 133.9, 130.9, 127.8, 126.7, 124.2, 124.1, 120.0, 115.4, 110.0, 71.9, 65.1, 48.2, 20.7, 15.4, HRMS (ESI) Calc. for $C_{17}H_{18}N_3O_2$ $[M+H]^+$ 296.1400, Found: 296.1404.

Compound 40: Yield 0.170 g (81 %); Mp 142-144 ^oC; IR (KBr, cm^{-1}) 3047, 2915, 1595, 1490, 1447, 1348, 1255, 1162, 1068, 915, 849, 750; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.0 Hz, 1H, Ar-*H*), 7.78 (d, J = 8.0 Hz, 1H, Ar-*H*), 7.51-7.53 (m, 2H, Ar-*H*), 7.38-7.43 (m, 3H, Ar-*H*), 7.03-7.10 (m, 3H, Ar-*H*), 6.94 (t, J = 7.6 Hz, 1H, Ar-*H*), 6.77 (d, J = 8.4 Hz, 1H, Ar-*H*), 4.80 (d, J = 4.8 Hz, 2H, CH_2), 4.36 (dd, J ~ 14.4 and 2.0 Hz, 1H, CH_aH_b), 3.76-3.78 (m, 1H, OC*H*), 3.17 (dd, J = 14.4 and 10.0 Hz, 1H, CH_aH_b), 2.32 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 144.6, 135.2, 133.7, 130.1, 127.8, 127.1, 126.4, 124.8, 124.3, 123.4, 121.6, 120.2, 117.4, 109.8, 70.5, 49.5, 46.2, 21.6; HRMS (ESI) Calc. for $C_{22}H_{21}N_3O_2S$ $[M+H]^+$ 421.1335, Found: 421.1334.

Compound 41: Yield 0.182 g (92 %); Mp 138-140 ^oC; IR (KBr, cm^{-1}) 3238, 1584, 1474, 1463, 1441, 1278, 1249, 1118, 1058, 751; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.4 Hz, 1H, Ar-*H*), 7.78 (d, J = 7.6 Hz, 1H, Ar-*H*), 7.69 (d, J = 8.4 Hz, 1H, Ar-*H*), 7.46 (t, J ~ 7.6 Hz, 1H, Ar-*H*), 7.29-7.33 (m, 2H, Ar-*H*), 6.74-6.80 (m, 2H, Ar-*H*), 5.03 (dd, J ~ 12.0 and 4.0 Hz, 1H, CH_aH_b), 4.92 (dd, J ~ 14.4 and 6.8 Hz, 1H, CH_aH_b), 4.67-4.68 (m, 1H, OC*H*), 4.06-4.09 (m, 2H, CH_2), 3.75 (d, J = 5.6 Hz, 1H, O*H*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 145.5, 139.4, 133.9, 129.8, 127.7, 124.2, 123.5, 119.7, 112.5, 110.1, 86.6 (*C*I), 69.9, 69.2, 50.8; HRMS (ESI) Calc. for $C_{15}H_{15}IN_3O_2$ $[M+H]^+$ 396.0210, Found: 396.0205.

Single crystal X-ray data were collected on a Bruker AXS-SMART or OXFORD diffractometer using Mo-K_α (λ = 0.71073 Å) radiation. The structures were solved by direct methods and refined by full-matrix least squares method using standard procedures.[13] Absorption corrections were done using SADABS program, where applicable. In general, all non-hydrogen atoms were refined anisotropically; hydrogen atoms were fixed by geometry or located by a Difference Fourier map and refined isotropically.

Crystal data

16: $C_{17}H_{14}ClN_3O_2$, M = 327.76, Monoclinic, Space group *P2(1)/c*, a = 11.1770(11), b = 5.4737(4), c = 25.780(3) Å, β = 100.299(9)^o, V = 1551.8(3) Å^3, Z = 4, μ = 0.259 mm^{-1}, data/restraints/parameters: 2742 / 0 / 208, R indices ($I > 2\sigma(I)$): R1 = 0.0599, *wR*2 (all data) = 0.1575. CCDC No. 929370.

20: $C_{24}H_{26}N_4O_3S$, M = 450.55, Monoclinic, Space group *P2(1)/n*, a = 8.5356(5), b = 10.9149(6), c = 24.3049(16) Å, β = 95.720(6)^o, V = 2253.1(2) Å^3, Z = 4, μ = 0.178 mm^{-1}, data/restraints/parameters: 3948 / 0 / 290, R indices ($I > 2\sigma(I)$): R1 = 0.0699, *wR*2 (all data) = 0.1956. CCDC No. 929371.

30: $C_{18}H_{16}N_4O_4$, M = 352.35, Triclinic, Space group *P-1*, a = 6.0255(6), b = 10.3665(11), c = 12.6263(14) Å, α = 92.903(9)^o, β = 97.168(8)^o, γ = 94.666(8)^o, V = 840.11(15) Å^3, Z = 2, μ = 0.101 mm^{-1}, data/restraints/parameters: 2948/ 0/235, R indices ($I > 2\sigma(I)$): R1 = 0.0549, *wR*2 (all data) = 0.1525. CCDC No. 929372.

32: $C_{19}H_{20}N_4O_3S$, M = 384.45, Monoclinic, Space group *P2(1)/c*, a = 8.4958(6), b = 11.6503(8), c = 18.9628(14) Å, β = 94.116(1)^o, V = 1872.1(2) Å^3, Z = 4, μ = 0.201 mm^{-1}, data/restraints/parameters: 3694 / 0 / 247, R indices ($I > 2\sigma(I)$): R1 = 0.0419, *wR*2 (all data) = 0.1269. CCDC No. 929373.

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Notes and references

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† Electronic Supplementary Information (ESI) available [details on the synthesis of precursors **1a-1k** and **2a-2k**, ^1H and ^{13}C NMR spectra, and CIF files. See DOI: 10.1039/b000000x/

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